IMPLEMENTING A DRY EYE SERVICE IN PRIMARY OPTOMETRIC CARE

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Doctor of Philosophy

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Thesis Summary

The aim of this thesis was to understand the demand and uptake of private optometric community services outside the scope of traditional services having the outcome of supplying spectacles, and of locally commissioned shared care schemes. Dry eye is known to reduce quality of life, be highly prevalent, underdiagnosed and clinically significant. Dry eye is a condition with poor association and discordance between signs and symptoms, and so is poorly managed. Dry eye does not command priority in secondary care where patients sometimes present when self-help measures fail, considering it is generally not sight threatening.

The global consensus on dry eye have recommended a tiered management approach highlighting advanced pharmacological care options that could be applied by optometrists with an independent prescribing qualification. Emerging technologies also show promise in advanced dry eye diagnostics and management but the investments required means that practices need to develop a strong business plan to make them commercially viable.

This research was based on a single independent optometric practice and two hospitals with a relationship to the practice. Service blueprinting was applied to the dry eye service to demonstrate its usefulness in optometric service innovation. Decision tree analysis and principal component analysis were used to discriminate between people self-reporting dry eye, to predict severity, and to identify clinical tests to explain the variability between those with predominately evaporative dry eye from a sample of patients. Despite having signs of dry eye, there were no differences in visual outcomes post-lens surgery based on dry eye sign status, and there were no strong trends to link discontinuation of contact lens wear to dry eye. Dry eye is a condition that presents to the local eye casualty department that can be managed within the community along with other conditions that may have an acute or recurring presentation.

Keywords: Dry eye
Service blueprinting
Tear homeostasis
Contact lens dropout
Shared care

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List of Abbreviations

%PB: Percentage of Partial Blinks

ACES: Acute Community Eye-care Services

A&E: Accident and Emergency

AOP: Association of Optometrists

APCOS: Acute Primary Care Ophthalmology Service

A&SQ: Amblyopia and Strabismus Questionnaire

Asym: Asymptotic

AutoCM: Auto Contractive Map

BCLA: British Contact Lens Association

b.d.: twice daily

BDNF: brain-derived neurotrophic factor

BE: Both Eyes

CCGs: Clinical Commissioning Groups

CEBM: Centre for Evidence-Based Medicine

CET: Continuing Education and Training

CHAID: Chi-squared Automatic Interaction Detection

CL: Contact Lens

CLADE: Contact Lens Associated Dry Eye

CLIDE: Contact Lens Induced Dry Eye

CLD: Contact Lens Discomfort

CLDO: Contact Lens Dropout

CLE: Clear Lens Extraction

CMG: Clinical Management Guidelines

CN: Cranial Nerve

Cx: Customer

D: Dioptres

DEQ-5: Dry Eye Questionnaire Five

DEWS: Dry Eye Workshop

DHA: docosahexanoeic acids

DTA: Decision Tree Analysis

DVA: Logarithm of the Minimum Angle of Resolution equivalent distance visual acuity

EOS: Enhanced Optometric Services

EPA: eicosapentaenoic acid

Eye cas: eye casualty

FUSS: Fife Uveitis Shared-Care Scheme

GCA: General Cell Arteritis

GOC: General Optical Council

GOS: General Ophthalmic Services

GP: General Practitioner

GRADE: Grading of Recommendations Assessment, Development and Evaluation

GTCAT: Glaucoma Treatment Compliance Assessment Tool

gutt: drops

HES: Hospital Eye Service

HLO: Healthy Living Optician

HP: Hydroxypropyl

HSK: Herpes Simplex Keratitis

ICL: Implantable Contact Lens

IOL: Intraocular lens

IP: independent prescribing

IRPL: Intense Regulated Pulsed Light

KMO: Kaiser-Meyer-Olkin

KPI: Key Performance Indicator

KTP: Knowledge Transfer Partnership

LASEK: Laser Assisted Sub-Epithelial Keratectomy

LASIK: Laser Assisted In Situ Keratomileusis

LE: Left Eye

logMAR: Logarithm of the Minimum Angle of Resolution

LOCSU: Local Optical Committee Support Unit

Max.: Maximum

Mdn: Median

MECS: Minor Eye Conditions Services

MF: Multifocal Intraocular Implant

MG: Meibomian Gland

MGD: Meibomian Gland Dysfunction

MG DO: Meibomian Gland Dropout

MGE: Meibomian Gland Evaluator

Min.: Minimum

NAION: Non-Arteritis Anterior Ischemic Optic Neuropathy

NEHEM: National Eye Health Epidemiological Model

NDP: Non-Dispensing Pharmacist

NHS: National Health Service

NIBUT: Non-Invasive Tear Breakup Time

NICE: National Institute for Health and Care Excellence

No.: Number

No abnorm: No abnormality

nocte: at night

oc: eye ointment

OCT: Optical Coherence Tomography

o.d.: once daily

OHCPs: Oral Health Care Professionals

ONP: Ophthalmic Nurse Practitioners

ONS: Office of National Statistics

OSDI: Ocular Surface Disease Index

OT: Optometry Today

PCA: Principal Component Analysis

PEARS: Primary Eye-care Assessment and Referral Service

PF: Preservative Free

p.o.: oral medication

prn: when necessary

PVD: Posterior Vitreous Detachment

Pxs: Patients

qds: four times daily

RCOphth: Royal College of Ophthalmologists

RE: Right Eye

RESTORE: Restasis Review of Efficacy and Safety vs Tears in the Relief of Dry Eye

RGP: Rigid Gas Permeable lens

RVO: Retinal Vein Occlusion

SCH: Subconjunctival Haemorrhage

SCL: Soft Contact Lens

SER: Spherical Equivalent Refraction

SLT: Selective Laser Trabeculoplasty

S oc.: without ocular

SPARC: See/Plan/Act/Refine/Communicate

SPEED: Standard Patient Evaluation of Eye Dryness

Std Dev: Standard Deviation

Surg: Surgery

SWOT: Strengths, Weaknesses, Opportunities and Threats

TBUT: fluorescein Tear Breakup Time

tds: three times daily

TFOS: Tear Film and Ocular Surface Society

TRP: Temporal Reframing of Price

TTO: Tea Tree Oil

UK: United Kingdom

UP: Unit Pricing

US: United States of America

VA: Visual Acuity

WOPEC: Wales Optometry Postgraduate Education Centre

YAG: Yttrium-Aluminium-Garnet

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CHAPTER 1
Introduction

The National Health Service (NHS) that provides government-funded medical and health care services for UK residents at the point of use is often reported as overstretched due to insufficient financing and the growing health needs of an ageing population. There is a general trend towards an older patient base in line with the ageing population in the UK with around 20.7% of the UK population (estimated at 66 million in mid-2017) expected to be aged 65 years or over by the year 2027, compared with 15.9% reported in 2007 (ONS, 2018). In order to address the burden on the NHS, there has been a shift of services into the primary sector. Primary care providers including pharmacists, dentists and optometrists have seen changes to their traditional roles and scope of practice in order to address current needs. This thesis relates to the expanding role of optometrists, but the next few sections will briefly discuss the expanding role of pharmacists, dentists and optometrists. Some of the examples provided represent the expanding roles of primary care providers outside of the UK.

1.1: Expanding role of pharmacists

There has been a shift in the pharmacist's role from dispensing or preparation and supply of medicines to patient-centred clinical care in many countries with differences based on regulatory, economic and organisational contexts (Schindel et al., 2017). Murphy et al. (2018) evaluated an incentivized service in Canada referred to as the Bloom Programme, which used a capitation funding model to help improve patient outcomes including those related to treatment optimization, reducing polypharmacy, and facilitating withdrawal from medications for patients living with mental illness and addictions (Murphy et al., 2018). It was concluded that pharmacists are well placed in facilitating confidential medication management in mental illness and addiction care (Murphy et al., 2018). There has been noted effectiveness for UK pharmacist-led services including smoking cessation counselling, prescriber education, medication review and medication review in nursing homes (Silcock et al., 2004). Additionally, immunization privileges allow pharmacists to offer expanded prescriber services, such as the administration of influenza vaccines to the public (Gerges et al., 2018).

Clinical or non-dispensing (NDP) pharmacists have a collaborative role in general practice framed as quality management (Hazen et al., 2019). NDP pharmacists conduct clinical medication reviews especially for elderly patients with polypharmacy and multi-morbidities, mobilise pharmaceutical evidence as required such as active mechanism and possible side effects, and offer tailored solutions with the expertise to deviate from a prescription guideline or to suggest a non-pharmaceutical

alternative (Hazen et al., 2019). Tan et al. (2014) report that NDPs within Australian primary health care clinics were effective in identifying and resolving medication-related problems, such as polypharmacy and improving medication adherence.

1.2: Expanding role of dentists

There is renewed interest in expanding the role of oral health care professionals (OHCPs) that is dentists, dental therapists, oral health therapists, dental hygienists, dental assistants, and dental nurses in smoking cessation interventions, anthropometric assessments and obesity management (Brown et al., 2019; Arora et al., 2019). Childhood obesity is an increasingly prevalent worldwide public health concern with guidelines suggesting general practitioners (GPs) should routinely identify and address overweight and obesity among children (Villarosa et al., 2018). In reality, research suggests screening for overweight status through the use of Body Mass Index percentile charts is not prioritsed by GPs (Villarosa et al., 2018). OHCPs are well placed in the community having regular contact with children and their families to address risk factors, such as a high sugar diet to prevent dental caries, peridontal disease and obesity (Arora et al., 2019). The main perceived barriers for OHCPs in provision of nutrition and behaviour modification-related counselling services in routine clinical practice included lack of training in anthropometry and counselling skills, fear of offending or appearing judgmental towards patients, insufficient clinical time to deliver such services, patients' rejection of weight loss advice or feelings of embarassment, lack of reimbursement, and lack of framework for appropriate referrals (Arora et al., 2019).

The desire to enhance one's physical appearance and smile at any age perhaps influenced by popular media, has led to the continued growth and increased demand for elective aesthetic dental services, such as tooth whitening and veneers (Theobald et al., 2006). As part of their regular clincal practice, some dentists have engaged in the delivery of non-surgical facial aesthetics such as the use of dermal fillers, and botulinum toxin for cosmetic application and to treat temporomandibular joint disorders, migraines and teeth grinding (Walker et al., 2017). Similar to dentistry, there are examples of optometric practices that have incorporated aesthetic services, namely non-invasive procedures utilising radiofrequency to improve periorbital skin tautness, and the prescribing of drugs and serums to help thicken and lengthen eyelashes (https://www.visionoptique.com/anti-aging-eyecare/). Ocular cosmetic procedures including limbal-defining contact lenses (CL), tattooed permanent eye makeup, blepharoplasty, laser removal of iris pigment, and eyelash extensions are also becoming more popular. The global false eyelashes market alone is expected to garner 1,883 million US dollars by the end of 2024 (MRF, 2019).

1.3: Expanding role of optometrists

Adoption of advanced equipment to improve detection and monitoring of eye disease, and electronic records and communication to facilitate practice efficiency, clinical record keeping and co-management with secondary care, has widened the scope of optometric practice (Dabasia et al., 2014). Dabasia et al. (2014) noted the use of newer imaging modalities such as OCT imaging were more commonly found at independent practices, and that practitioners using newer imaging modalities were more likely to use other specialist equipment and participate in locally commissioned shared care schemes. Changes to UK statutory legislation in 1999 meant that community optometrists could manage patients with ocular conditions without referring to a medical practitioner, and further amendments in 2005 meant that optometrists could refer patients to the care of optometrist colleagues with a higher specialism or qualifications (Baker et al., 2016). Medicine legislation has also changed to enable community optometrists to manage ocular conditions using pharmacological interventions (Baker et al., 2016).

Community optometry and ophthalmology-optometry partnerships may help alleviate the demand on the hospital eye services, considering ophthalmology are one of the largest outpatient specialties in the NHS (NHS Digital, 2018). Ophthalmology saw the highest recorded number of attendances for an outpatient specialty with 7.6 million attendances in 2017-2018 (NHS Digital, 2018). Alternative models of care are being explored with the expanding role of community optometrists at the forefront of strategies to reduce the burden on overstretched ophthalmology services (Baker et al., 2016). In a virtual clinic for example, data from ophthalmic subspecialties are collected and triaged by trained staff who are not necessarily medically trained, and analysed and acted upon by an optometrist-ophthalmologist partnership or ophthalmologist team at a different point in time (Wright & Diamond, 2015; Trikha et al., 2012; Tsaousis et al., 2016). The increasing availability of wide field imaging devices enables the possibility of virtual clinics that have the potential to reduce waiting times for a clinic appointment, reduce unnecessary follow-ups, and offer a new strategy to cope with the challenge of the ageing population. Virtual clinic reviews as an alternative mode of health care delivery have been largely accepted by patients with diabetic retinopathy and maculopathy, and glaucoma (Ahnood et al., 2018; Court & Austin, 2015; Kotecha et al., 2017).

Findings by Gazzard et al. (2019) suggest selective laser trabeculoplasty (SLT) should be offered as first-line treatment for open angle glaucoma and ocular hypertension rather than use of ocular therapeutics, which could significantly impact current care pathways and the role of optometrists. A rise in the number of SLT procedures performed and possible demand for SLT would mean a requirement for optometrists to discuss and offer SLT as a management option for eligible patients. There are currently a small number of optometrists who perform SLT under medical supervision,

and an increase in demand for SLT could result in greater uptake of further training to enable more optometrists to deliver this service and to continue with participation in monitoring schemes.

The emergence of multi-disciplinary clinics to address patient needs and improve overall wellness and health include chiropractic and optometry services (http://specsandspines.com/), concussion rehabilitation co-management (https://www.gvtc.ca/), and integration of audiology services. The University Health Network's Multidisciplinary Sjögren's Syndrome Clinic in Toronto, Ontario, Canada sees a collaboration amongst specialists in rheumatology, ophthalmology/optometry, otolaryngology and dentistry to seek a diagnosis of Sjögren's Syndrome for patients (https://www.uhn.ca/Arthritis/PatientsFamilies/Clinics_Tests/Sjogren_Clinic). The Visual Perception Clinic in the Newcastle Eye Centre, UK, provide a multidisciplinary service that addresses complex visual problems in older people with management plans formulated through discussions amongst specialists in ophthalmology, neurology, and psychiatry with support from optometrists, orthoptists and radiologists (Han et al., 2012). Along with a higher prevalence of visual comorbidities with increasing age, there is also a higher prevalence of neurological and cognitive impairment (Jackson & Owsley, 2003; Clemons et al., 2006). A one-stop service for patients with atypical presentations of neurodegenerative disease in the presence or absence of eye pathology could help prevent frequent visits of patients to multiple practices, delays to diagnosis and disconnected referrals to different specialties (Han et al., 2012).

Hearing loss affects approximately 40% of people aged over 50 years in the UK (Age UK, 2019), and there is a growing trend of optometric practices introducing audiology services either through employing an in-house audiologist, or partnering with an audiology business or an independent provider. Following completion of the KTP project at BBR Optometry Ltd. (discussed in section 1.6), the practice began to offer audiology services with the help of the Hearing Care Partnership. The Hearing Care Partnership launched in July 2017 is the UK's sole "optician only" hearing care company that connects audiology with independent optometry by providing the audiologist, training to the optometric team and marketing (OT, 2019). The Hearing Care Partnership operates a non-compete business model meaning that it will not integrate its services into more than one practice in the same town, and through the relationship with Leightons Opticians & Hearing Care also shares business insight to support optical retail services (OT, 2019). Audiology services available at BBR Optometry Ltd. include complimentary hearing tests, ear wax removal, tinnitus consultations and hearing protection.

Community-enhanced services or enhanced optometric services (EOS) are any optometrist delivered service within primary care outside the scope of the GOS contract, which provides for routine sight testing (Baker et al., 2016). Scotland have a unique GOS contract different from elsewhere in the

UK that has been in operation since April 2006, and offers all Scotland residents, not just those belonging to specified groups, an NHS funded eye examination and a supplementary eye exam for further testing or monitoring if clinically required (Shickle et al., 2015). This thesis will focus on community optometric practice and EOS in England. EOS are negotiated and commissioned locally according to community needs and priorities, and differ by patient eligibility, training requirements for participating practitioners, and fee structures (Shickle et al., 2015). EOS aim to enhance referral quality and reduce false positive referrals to the hospital eye service (HES), to ease capacity on the HES by monitoring chronic ocular disease, and to make use of optometric expertise (Baker et al., 2016). An example of an EOS that has expanded the traditional role of an optometrist is the Healthy Living Optician (HLO) scheme rolled out in Dudley, UK, in 2015 (Dudley LOC, 2019). Following the success of a Health Living Pharmacy service in the area, the HLO allows optometrists to offer health and lifestyle-related advice including alcohol screening, weight management, smoking cessation, NHS health checks and referral into support services (Dudley LOC, 2019). EOS in Herefordshire where the current study is based includes cataract post-operative assessments, cataract referrals, children's vision, glaucoma referral refinement, glaucoma repeat readings, ocular hypertension monitoring, low vision, and minor eye conditions service described in more detail in chapter six.

Participation in EOS offer credibility to optometrists as eye health professionals rather than salespersons perhaps leading to better continuity of care and practice loyalty (Shickle et al., 2015). Although EOS are well received by stakeholders and patients perhaps due to a reduction in waiting times and loss to follow-up from HES, their long-term sustainability is not established (Baker et al., 2016). A challenge to private specialist optometric services in the UK is the patient's perception of value given free or subsidised eyecare in the UK is available through the NHS. Wolffsohn et al. (2011) determined that although there was high interest for a specialist service to manage ocular allergy amongst a large sample of patients attending practices in the West Midlands, UK, only about one quarter of patients were willing to pay for such services. There was poor distinction between ocular and systemic allergy, with almost all patients feeling their current self-management was effective (Wolffsohn et al., 2011).

Leamon et al. (2014) conducted focus groups consisting of population groups at increased risk of preventable sight loss including Pakistani, Black Caribbean and white socio-economically deprived communities across five UK locations, and found that the demand for optometric services was mainly in response to visual symptoms and was associated with the purchase of spectacles rather than eye health. Factors influencing people's attitudes and behaviours towards optometric services in the UK include (Bell & O'Brien, 1997; Cross et al., 2007; Patel et al., 2006; Awobem et al., 2009):

- There is limited knowledge regarding the function of regular eye examinations in preventative health care
- Expense or concern about the cost of spectacles
- Fatalism or acceptance that deteriorating eyesight is part of the ageing process

Leamon et al. (2014) suggest that uptake of optometric services may be improved through co-production of non-retail services that resonate with local communities.

Service blueprinting, described in chapter two, could be applied to the development of shared or EOS to enhance accountability between stakeholders and improve service quality by defining clinical pathways and administrative processes, training requirements, fees, and key performance indicators (KPIs). For example, there is currently no standardisation of cataract clinical pathways in the UK (Bowes et al., 2018). Bowes et al. (2018) describe successful outcomes against KPIs agreed under a service-level agreement between the HES and community optometrists with an accreditation scheme in the Cambridgeshire cataract shared care scheme. Notably, there was an improvement in the listing and feedback return rates, and reduction in unsuitable referrals (Bowes et al., 2018).

Dry eye is topical considering it is known to impact vision, quality of life, mental health and work productivity (Stapleton et al., 2017; Miljanovic et al., 2007; Han et al., 2017; Sun et al., 2017; Matthews et al., 2017; van Landingham et al., 2014). Dry eye is known to be highly prevalent, underdiagnosed and clinically significant. This thesis aims to evaluate the local need for a private speciality dry eye service and demonstrates the implementation of such a service at BBR Optometry Ltd. There is currently no clear guidance on how to set up a speciality dry eye clinic. There is also no standardisation of clinical care for dry eye patients although the non-profit organization, the Tear Film and Ocular Surface Society (TFOS), have created the Dry Eye Workshop II (DEWS II) report that represents a global consensus concerning multiple aspects of dry eye disease (Nelson et al., 2017).

1.4: Dry eye background

The global definition of dry eye is:

> *"a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles." (Craig et al., 2017)*

Dry eye has been reported as one of the most common ocular conditions affecting women more than men with increasing age, and has a global estimated prevalence of 5% to 50% (Stapleton et al., 2017). The prevalence, that is the proportion of dry eye within a population at a given time, varies depending on the definition of dry eye used with diagnosis based on symptoms with or without signs, and the features of the population analysed (Stapleton et al., 2017). A retrospective analysis using an algorithm to identify a dry eye population based on medical diagnostics code claims indicative of dry eye disease and prescriptions of cyclosporine ophthalmic emulsion from 9.7 million Military Health System beneficiaries in the American Department of Defense, found annual dry eye prevalence and incidence increased with age starting at ages 18 to 39 (Dana et al., 2019b). It would appear from the dry eye criteria or threshold questionnaire values outlined earlier that more women account for a higher proportion of self-reported symptomatic dry eye with 60% and 70% of respondents being women from the OSDI and SPEED respectively. However, it is also important to note that more women than men completed the questionnaires. Approximately 57% of OSDI respondents and 66% of SPEED respondents were women. In Herefordshire, females outnumber males at almost all ages over 40 with 98 men for every 100 women, and differences more evident once ages approach the late seventies (Herefordshire Council, 2018).

Understanding the natural history, prevalence and incidence of a condition is important when planning to develop a specialist service to address the needs of the target user of the service. There is currently limited study on the area relating to the natural history of treated and untreated dry eye disease, which requires further research (Stapleton et al., 2017; McDonnell et al., 2017). Bron et al. (2009) suggest dry eye is a progressive condition with stages of initiation, reflex compensation and loss of the compensatory response that may result in a hybrid state of combination aqueous deficient and evaporative dry eye. This theoretical model suggests that dry eye worsens without intervention over time and plateaus at a certain point in time, supporting the view of early prophylactic care. Conversely, findings in a retrospective study by Lienert et al. (2016) showed the most common perception of subjects with dry eye was that there was no change in their dryness or visual symptoms. The authors propose that dry eye progresses despite treatment in cases where severe symptoms are present at diagnosis (Lienert et al., 2016). The average duration of dry eye disease was 14.5 ± 7.7 years in women aged 61.2 to 89.9 years, and 10.5 ± 9.5 years in men aged 60.2 to 97.3 years (Lienert et al., 2016). At a statistically significant level ($P < 0.0001$), more women than men had experienced

severe symptoms (Lienert et al., 2016). Factors other than a history of severe symptoms associated with a worsening of dry eye symptoms and social impact were monthly spending on treatments valued at over twenty US dollars, a history of blepharitis or Meibomian gland dysfunction and use of systemic beta-blockers (Lienert et al., 2016).

There are a limited number of studies reporting on the incidence or rate of new cases of dry eye disease over a given time frame (Stapleton et al., 2017). Moss et al. (2008) determined using a population of mainly Caucasian residents between the ages of 48 and 91 from Beaver Dam, Wisconsin, USA that 21.6% (95% confidence interval 19.9-23.3%) of individuals developed symptomatic dry eye disease over 10 years. There were 2412 subjects identified as persons at risk for incidence of dry eye, and women composed 56% of the cohort (Moss et al., 2008). After adjusting for age, incidence of dry eye was greater in women (25.0%) compared to men (17.2%, $p < 0.001$) and incidence was also higher in subjects aged 80 years or older (Moss et al., 2008). The profile of these subjects is similar to those in the current analysis in terms of age, ethnicity and socioeconomic class, however, it is important to note that in the Moss et al. (2008) study, no objective testing was performed to determine the presence of dry eye and determination of dry eye status relied on self-reports alone. Dry eye was described as a foreign body sensation accompanied by itching and burning not related to allergy and experienced for a minimum of three months (Moss et al., 2008). It was of the authors' opinion that subjects with dry eye are best placed to judge the presence of the condition, considering tests commonly performed to diagnose dry eye lacked in sensitivity and specificity (Moss et al., 2008). The challenges practitioners face in diagnosing dry eye are discussed in chapter three. Moss et al. (2008) also noted use of diuretics, antidepressants, and oral steroids were associated with a greater risk of dry eye incidence. A British population-based cross-sectional association study (Vehof et al., 2014) of 3824 women from the Twins UK cohort aged 20 to 87 years used a questionnaire to evaluate dry eye disease and associated risk factors, and estimated the incidence of dry eye as defined by the Beaver Dam Eye study (Moss et al., 2008). Vehof et al. (2014) determined that the incidence of symptomatic dry eye was 10.4% (95% confidence interval 9.1-11.7%) over a two-year time period.

Stapleton et al. (2017) present the risk factors for dry eye disease categorized according to being modifiable or non-modifiable, and the level of evidence as consistent, probable or inconclusive. Table three from the TFOS DEWS II epidemiology report has been replicated and presented in table 2.8. Knowledge of these risk factor could help identify people from the general practice population who may benefit from a dry eye service. Dry eye by nature has a heterogeneous disease process with numerous extraneous variables that are challenging to grade or measure and can affect signs and symptoms of dry eye (Foulks, 2003; Skelly et al., 2012). Knowledge of these extraneous variables both modifiable and non-modifiable could help with identifying those that may benefit from a dry

eye service. For example, demographics such as age and sex (Stapleton et al., 2017; Eisner, 2015; Schaumberg et al., 2009), as well as geographical factors including seasonal pollen exposure, levels of humidity and air pollution, which may affect dry eye disease (Novack et al., 2017).

Visual display terminals have shown to suppress blinking and alter tear dynamics leading to increased tear evaporation and dry eye (Tsubota & Nakamori, 1995; Nakamori et al., 1997; Uchino et al., 2008; Kojima et al., 2011; Uchino et al., 2013). Lid abnormalities including entropion, ectropion, paralysis and thyroid eye disease can result in signs and symptoms of dry eye (McMonnies, 2007), and so objective testing for dry eye following screening with a questionnaire at the time of an eye examination may help segment those customers who may benefit from a more in-depth dry eye assessment and onwards ophthalmology referral. Corneal staining, which is a relatively late manifestation of dry eye and common outcome measure of dry eye studies, and neuropathic corneas can result when there is a history of viral keratitis or corneal refractive surgery (Kheirkhah et al., 2015; Gallar et al., 2004; Novack et al., 2017). Therefore, taking a comprehensive history could help in selecting potential customers of the service. Other external factors that can influence dry eye status include use of systemic medications such as steroids, immunosuppressants, parasympathomimetic agents, and antihistamines, and local therapies including hypotensive, antimicrobial, cyclosporine, and autologous serum tear drops (Urzua et al., 2012; Quinto et al., 2008; Gomes et al., 2017; Dana et al., 2019a). Contact lenses also have the potential to influence dry eye symptoms (Dumbleton et al., 2013), and this will be discussed in chapter five.

	Consistent[a]	Probable[b]	Inconclusive[c]
Non-modifiable	Aging Female sex Asian race Meibomian gland dysfunction Connective tissue diseases Sjögren's syndrome	Diabetes Rosacea Viral infection Thyroid eye disease Psychiatric conditions Pterygium	Hispanic ethnicity Menopause Acne Sarcoidosis
Modifiable	Androgen deficiency Computer use Contact lens wear Hormone replacement therapy Hematopoietic stem cell transplantation Environment: pollution, low humidity, sick building syndrome Medications: antihistamines, antidepressants, anxiolytics, isotretinoin	Low fatty acid intake Refractive surgery Allergic conjunctivitis Medications: anticholinergic, diuretics, betablockers	Smoking Alcohol Pregnancy Demodex infestation Botulinum toxin injection Medications: multivitamins, oral contraceptives

Table 2.8: Risks factors for dry eye diseases replicated from the TFOS DEWS II epidemiology report [a] Consistent evidence implies the existences of at least one adequately powered and otherwise well-conducted study published in a peer-reviewed journal, along with the existence of a plausible biological rationale and corroborating basic research or clinical data.; [b] Suggestive evidence implies the existence of either inconclusive information from peer-reviewed publications or inconclusive or limited information to support the association, but either not published or published somewhere other than in a peer-reviewed journal.; [c] Inconclusive evidence implies either directly conflicting information in peer-reviewed publications, or inconclusive information but with some basis for a biological rationale.

A mostly consistent non-modifiable risk factor for dry eye disease is Asian ethnicity (North and South East Asian) (Stapleton et al., 2017). In studies using the same diagnostic criteria, gender and age range, there appears to be a higher estimated abnormal tear function amongst Asians compared to Caucasians perhaps due to differences in susceptibility to dry eye or due to geographical differences (Stapleton et al., 2017). However, research in Singapore does not show that there is a significant difference in prevalence of symptomatic dry eye between Asians and Caucasians (Tong et al., 2009; Tan et al., 2015). All of the customers involved in completing the dry eye questionnaires in the current analysis were Caucasian, once again reflecting the characteristics of the population in the area. The ethnic composition of Herefordshire according to a 2011 consensus was 93.7% white English, Welsh, Scottish, Northern Irish, British compared to 80.5% in England (Herefordshire Council, 2018).

There is currently no consensus on a gold standard for assessment of dry eye severity although the primary determinant for management strategy chosen is based on the severity of disease (Behrens et al., 2006; B. Sullivan, 2014). It is well established that perceived symptom severity or self-reported symptoms may not equate to clinical signs of dry eye and vice versa, which may be due to diurnal variation or changes in symptoms over time and the influences of age, sex and ethnicity on

symptoms (B. D. Sullivan et al., 2014; Cardona et al., 2010; Tran et al., 2013; Schaumberg et al., 2003). The concept of a clinically important difference is likely to be more important than a numerical statistically significant difference when it comes to health or quality of life for people affected by a particular condition (Copay et al., 2007; Jaeschke et al., 1989). So, although there are statistical differences between different dry eye symptom classification groups, what may be most meaningful is the minimum clinically important difference threshold value or the smallest change that is important to patients (Stratford et al., 1998; Novack et al., 2017). Miller et al. (2010) used observational data from the Restasis Review of Efficacy and Safety vs Tears in the Relief of Dry Eye (RESTORE) registry to estimate the minimal clinically important difference for the OSDI questionnaire to range from 4.5 to 7.3 for mild or moderate dry eye, and from 7.3 to 13.4 for severe dry eye cases.

1.5: Dry eye diagnostics & management

The new definition for dry eye disease amended by the Tear Film and Ocular Surface Society (TFOS) Dry Eye Workshop (DEWS) II, and presented in section 1.4, does not indicate that specific signs of dry eye must be present for diagnosis. The definition characterizes dry eye as a multifactorial disease of the ocular surface with a loss of homeostasis or the body's ability to maintain equilibrium, and sequelae associated with tear film instability (Craig et al., 2017). Dry eye disease can be sub-categorized on a spectrum where the signs are predominately evaporative or aqueous-deficient in origin, as overlapping between components often occurs (Craig et al., 2017). An evaporative element to dry eye due to conditions affecting the eyelids or the ocular surface is thought to be more common than an aqueous deficient one due to conditions affecting the lacrimal gland, with Meibomian Gland Dysfunction (MGD) considered the main cause of evaporative dry eye in clinic and population-based studies (Lemp et al., 2012; Viso et al., 2011; Tong et al., 2010). The predominately evaporative dry eye sub-classification including cases of MGD, is thought to have a prevalence ranging from 38% to 68% in different populations (Schaumberg et al., 2011; Foulks et al., 2012; Lemp & Nichols, 2009; Lemp et al., 2012; Stapleton et al., 2017).

There is currently no one sign or symptom that correlates absolutely with dry eye disease, in part due to the dynamic nature of dry eye with signs and symptoms that can fluctuate over time, and vary in severity (Sullivan et al., 2012; Sullivan et al., 2010). The traditional approach to evaluating new diagnostic tests required dry eye and normal subjects to satisfy all criteria within a series of sensitive thresholds, despite evidence that signs and symptoms are uncorrelated across the wider population, and do not develop at the same time (Kallarackal et al., 2002; Moore et al., 2009; Begley et al., 2003; Nichols et al., 2004; Mizuno et al., 2010; Fuentes-Paez et al., 2011; Sullivan et al., 2014). As discussed previously, it is common to encounter a patient who is very symptomatic, but does not

exhibit any signs of dry eye and vice versa. Studies excluding a large number of dry eye patients because they do not satisfy certain criteria prevents randomization, and gaps in the inclusion criteria introduce sampling bias and spectrum bias respectively (Wolffsohn et al., 2017). The DEWS II Diagnostic Methodology Subcommittee outlined the recommended diagnostic homeostatic marker tests for dry eye disease, and additional metrics for the identification of dry eye disease subtypes (Wolffsohn et al., 2017). It is advised to perform tests from least to most invasive as the sequence of tests can affect results (Foulks, 2003).

The DEWS II Diagnostic Methodology Subcommittee advised the administration of a validated symptom questionnaire at the start of a patient interaction to establish whether additional dry eye evaluation is clinically necessary (Wolffsohn et al., 2017). Similar to clinical signs of dry eye disease, quantifying symptoms accurately rather than reporting during non-scripted verbal interviews is important to monitor the progression of dry eye and response to treatments. Dry eye questionnaires assessing symptoms have been used to screen for dry eye disease, to grade disease severity in practical settings, and for epidemiological studies (Chia et al., 2003; Lee et al., 2002; McCarty et al., 1998; Moss et al., 2000; Schaumberg et al., 2003; Schein et al., 1997; Doughty et al.,1997; Begley et al., 2002; McMonnies & Ho, 1987; Schiffman et al., 2000). A scale characteristic required for a questionnaire to be considered a measurement is called unidimensionality, where items measuring a single underlying trait should produce data that varies along a simple number line with large measurements representing a large quality of the trait and vice versa (Ngo et al., 2013). Dimensionality can be determined using principal component, factor, and Rasch analyses (Ngo et al., 2013). Two commonly used questionnaires for dry eye symptoms assessment, the OSDI and the Standardized Patient Evaluation of Eye Dryness (SPEED), are included in the consultation for dry eye assessment at BBR Optometry Ltd. All clinical tests conducted at BBR Optometry Ltd. and included in this chapter's analyses are outlined in table 3.1.

The OSDI questionnaire developed by the Outcomes Research Group at Allergan Inc (Irvine, CA) has been shown to be a valid and reliable tool for grading the severity of eye disease with good sensitivity and specificity in distinguishing between those with and without dry eye, and it can be used as an endpoint in clinical trials to test the efficacy of new dry eye treatments (Schiffman et al., 2000; Simpson et al., 2008). The OSDI is the most widely used questionnaire for dry eye disease clinical trials, and was chosen by the Diagnostic Methodology Subcommittee of the Tear Film and Ocular Surface Society (TFOS) as one of the recommended symptom questionnaires for practitioner use (Wolffsohn et al., 2017). The Report of the TFOS International Dry Eye Workshop (DEWS II) is a global consensus concerning multiple aspects of dry eye disease created by 12 sub-committees made up of 150 experts from 23 countries (Nelson et al., 2017). The other recommended symptom questionnaire in the consensus view of the committee was the Dry Eye Questionnaire (DEQ-5) for

its short length and discriminative ability (Chalmers et al., 2010). There are 12-items in the OSDI relating to frequency of dry eye symptoms, and issues with visual functioning and environmental triggers related to dry eye. The total OSDI score can range from 0 to 100 and is derived from the formula: (sum of scores) x 25/ (no. of questions answered), where each question item is scored 0, 1, 2, 3, 4 for none, some, half, most or all of the time respectively. For questions regarding visual functioning and environmental triggers there is the option of selecting not applicable. The total OSDI questionnaire score can be used to classify the severity of dry eye with scores of 0-12 representing normal or non-dry eye status, total scores ranging from 13-22 indicating mild dry eye, total scores ranging from 23-32 indicating moderate dry eye, and total scores ranging from 33-100 indicating severe dry eye (Miller et al., 2010).

The SPEED questionnaire is an eight-item validated dry eye questionnaire designed by TearScience (Morrisville, NC) that has been shown to have good internal consistency, good discriminant validity using the OSDI, and correlates well with clinical tests of Meibomian gland functionality, age, corneal staining, and lipid layer thickness (Ngo et al., 2013; Asiedu et al., 2016; Finis et al., 2014a). The total SPEED score can range from 0 to 28 and is derived from the summation of the frequency and severity parts of the questionnaire. The symptoms asked by SPEED are dryness or grittiness or scratchiness, soreness or irritation, burning or watering and eye fatigue reported and scored with a Likert scale as 0, 1, 2, 3 for never, sometimes, often and constant respectively. SPEED also asks whether these symptoms pose no problems, were tolerable, uncomfortable, bothersome and intolerable scored as 0, 1, 2, 3, 4 respectively. The SPEED questionnaire as defined by the OSDI questionnaire has been shown to differentiate between asymptomatic and dry eye symptomatic groups (Ngo et al., 2013). There are no agreed criteria for symptomatic dry eye for screening or classification of symptom severity for SPEED, although total SPEED scores $\geq$ six and three symptom categories including no symptoms (total SPEED 0), mild to moderate (total SPEED 1-9) and severe (total SPEED $\geq$ 10) have been suggested (Blackie et al., 2009; Asiedu et al., 2017).

Procedure	Equipment/Materials	Measurements
Symptom Assessment	Ocular Surface Disease Index (OSDI) questionnaire (Allergan Inc, Irvine, CA, USA)	12 items Ocular symptoms (0-4) Vision-related function (0-4 or not applicable) Environmental triggers (0-4 or not applicable) Total score (0-100) = (sum of scores) x 25/ (no. of questions answered)
	Standard Patient Evaluation of Eye Dryness (SPEED) questionnaire (TearScience, Morrisville, NC, USA)	8 items Severity score (0-12) Frequency score (0-16) Total score (0-28)
Tear Osmolarity	TearLab (TearLab Corporation, San Diego, CA, USA)	Tear osmolarity (mOsm/L)
Tear Film Interferometry and number of partial and complete blinks	LipiView II Ocular Surface Interferometer with Dynamic Meibomian Imaging (TearScience, Morrisville, NC, USA)	Average Lipid Layer Thickness (nm) Number of partial blinks Total number of blinks Percentage of partial blinks= (number of partial blinks/ total number of blinks) x 100
Meibography	LipiView II Ocular Surface Interferometer with Dynamic Meibomian Imaging (TearScience, Morrisville, NC, USA)	MeiboGrade Gland dropout (0-3) MeiboGrade Gland duct dilation (0-3)
Meibomian Gland Expressibility	Korb Meibomian Gland Evaluator (TearScience, Morrisville, NC, USA)	Total number of functional glands at the lower lid margin temporally, centrally and nasally (0-15)
Fluorescein tear breakup time	Fluorets and saline (Bausch & Lomb, Rochester, NY, USA)	Tear breakup time (seconds)

Table 3.1: Clinical dry eye diagnostics used at BBR Optometry Ltd. and included in the current analyses.

Tear osmolarity is a measure of tear film composition with variations affecting tear film stability. Tear osmolarity is an objective marker for dry eye disease frequently reported as the best measure to diagnose dry eye across the various severity levels and subtypes (Wojtowicz et al., 2011; Kanellopoulos & Asimellis, 2016; Lemp et al., 2011; Potvin et al., 2015). Hyperosmolarity arising as a result of water evaporation from the exposed ocular surface in situations of excessive evaporation or reduced aqueous tear flow, or a combination of these events causes a loss of goblet cells, disturbance of mucin expression, and initiates a release of inflammatory mediators into the tears resulting in damage to the ocular surface (Wolffsohn et al., 2017). Physiological stress on the cornea caused by hyperosmolarity can also lead to nerve damage (Hirata et al., 2015). Studies have shown that current measurement techniques can be highly variable with some commercially

available systems requiring at least three measures to achieve reliable results (Bunya et al., 2015; Szczesna-Iskander, 2016). The TearLab system (TearLab Corporation, San Diego, CA, USA) is used at BBR Optometry Ltd. and evaluates tear osmolarity from 50 nL samples collected from the lower lid tear meniscus of both eyes. The literature proposes threshold values ranging from 305 mOsm/L to 316 mOsm/L with reported sensitivities of 64% to 91%, specificities from 78% to 96%, and positive predictive values of 85% to 98.4% (Versura et al., 2010; Jacobi et al., 2011; Schargus et al., 2015a; Schargus et al., 2015b; Khanal et al., 2008; Tomlinson et al., 2010). The cut-off value of 308 mOsm/L has been widely accepted for use in clinical practice to help diagnose mild- moderate dry eye. Inter-eye variability in tear osmolarity has been shown to be greatest in people with dry eye disease, and larger inter-eye differences have been found in more severe cases (Jacobi et al., 2011; Gibard et al., 1978; Lemp et al., 2011). Transient increases in tear osmolarity have been observed under conditions of tear instability when tear evaporation increases leading to tear breakup, such as prolonged interblink periods or due to exposure to increased humidity and wind speed (Liu et al., 2009; Peng et al., 2014). An inter-eye difference in tear osmolarity greater than 8 mOsm/L is considered to be potentially indicative of a loss in tear film homeostasis suggestive of dry eye disease (Sullivan, 2014).

The LipiView II Ocular Surface Interferometer with Dynamic Meibomian Imaging used at BBR Optometry Ltd. (TearScience, Morrisville, NC, USA) employs interferometry to measure the thickness of the lipid layer in 20 seconds by analysing the tear film over the lower half of the cornea (Wolffsohn et al., 2017). The tear film is measured using an interferometry colour assessment by specular reflection with an estimation of the lipid layer thickness based on the observed mean interference colours (Eom et al., 2013). The patient is positioned on the forehead and chin rest, and instructed to maintain fixation on an internal target (three light-emitting diodes) whilst continuing to blink. The operator then adjusts the camera focus prior to capturing the image. The instrument has a sensitivity of 65.8% and a specificity of 63.4% using a threshold value of 75 nm to identify MGD (Finis et al., 2013). The LipiView II also captures blink dynamics with a high-resolution video, analysing blink patterns, and detecting partial blinks. Partial or incomplete blinking can lead to symptoms, and corneal staining signs of dry eye (Wolffsohn et al., 2017). The function of a complete blink is to distribute meibum for re-formation of the tear film lipid layer, clear debris and provide mechanical protection to the eye (Knop et al., 2009; Linton et al., 1961; Knop & Knop, 2009; Doane, 1981; Tutt et al., 2000; Bron et al., 2004; McMonnies, 2007; Cruz et al., 2011; Carney & Hill, 1982; Forst, 1987; Nakamori et al., 1997; Rambold et al., 2002). High-definition imaging of the Meibomian gland morphological structure is possible using the LipiView II. The MeiboGrade score from TearScience for the lower lids only was used in the current analyses to quantify the degree of Meibomian gland atrophy referred to as dropout, and Meibomian gland duct dilation with 0, 1, 2, 3 corresponding to none, mild, moderate and severe changes respectively, based on

previously described histopathologic changes in the Meibomian glands (Jester et al., 1981; Mathers et al., 1981; Robin et al., 1985; Gutgesell et al., 1982; Jester et al., 1989).

Meibomian gland expressibility is thought to be a measure of the function of the Meibomian glands embedded within the tarsal plate of the eyelids, which secrete a component of the lipid layer of the tear film called meibum required for ocular surface health (Wolffsohn et al., 2017). The eyelid is compressed against the globe using an instrument called the Korb Meibomian Gland Evaluator (TearScience, Morrisville, NC, USA) to simulate forced blinking, and the consistency and colour of the secretion as well as an absence of a secretion are documented qualitatively (Korb & Blackie, 2008; Blackie & Korb, 2009). The Korb Meibomian Gland Evaluator applies a standard force of 1.25 g/mm^2 to the external surfaces of the lower eyelid, and the exact area of contact surface is 8.76 x 4.45 mm = 38.95 mm^2 (Blackie & Korb, 2010). Using 16x magnification on the slit lamp, five consecutive Meibomian gland orifices in the temporal, central and nasal sections of the lower lids are expressed using the Korb Meibomian Gland Evaluator for no longer than 10 seconds. The total number of Meibomian glands yielding liquid secretion is then scored from 0 to 15.

Fluorescein tear breakup time remains one of the most commonly used tests for assessing tear film stability in clinical practice, despite it being a subjective metric with fluorescein itself possibility reducing tear film stability, and having uncertain diagnostic value for people with mild to moderate dry eye disease (Cardona et al., 2011; Downie et al., 2013; Turner et al., 2005; Graham et al., 2010; Smith et al., 2008; Lemp et al., 2011; Sullivan et al., 2012; Mengher et al., 1985a; Mooi et al., 2017). Sodium fluorescein is instilled in the eye using an impregnated strip to enhance the visibility of the tear film. The tear film is observed using a slit lamp biomicroscope through cobalt blue illumination and a Wratten-12 yellow barrier filter. The interval of time in seconds that elapses between a complete blink and the appearance of the first break or dark patch in the tear film is known as the fluorescein tear breakup time (Lemp et al., 1970; Norn, 1969). A value of less than 10 seconds indicates a dry eye diagnosis, but if small more controlled volumes of fluorescein are used, the reference value can be five seconds (Lemp & Hamill, 1973; Abelson et al., 2002; Abelson et al., 2012). Considering the effect of fluorescein on tear film stability as well as factors including temperature, humidity, and air circulation, non-invasive tear breakup time (NIBUT) is becoming a more popular, preferred dry eye metric in clinical practice and academia (Wolffsohn et al., 2017). Automated systems can detect and map locations of tear breakup over time, and specific software can measure NIBUT as indicated by surface irregularities and localised changes in corneal power (Best et al., 2012; Hong et al., 2013; Goto et al., 2004; Goto et al., 2003; Kojima et al., 2004; Gumus et al., 2011).

An evidence-based management algorithm was proposed by Jones et al. (2017) with the intention of assisting eye health care practitioners given the complex nature of dry eye that varies in severity and amongst those affected. The algorithm, seen in appendix 1.1, developed by TFOS was not meant to be rigid or formulaic, and it was anticipated that it would need to be adapted to suit individuals. The first level of treatment begins with conventional over-the-counter products, and when the customer no longer responds to treatment or exhibits a greater level of disease severity, the next level of management is recommended and sometimes the previous therapy may also continue (Jones et al., 2017). BBR Optometry Ltd. offer various step two level in-practice treatment options as outlined in the TFOS DEWS II staged management and treatment algorithm for dry eye (appendix 1.1), which are described in detail in appendix 1.2. Additionally, BBR Optometry Ltd. are unique in that the practice employs aspiring and current independent prescribing optometrists, who can provide private prescriptions for pharmacological management of dry eye where required. Careful review to ensure compliance with recommended management options and to establish improvements in symptoms, and signs of dry eye should take place from one to three months following initiation of management with the exception of cyclosporine given therapeutic action can take several months to occur (Jones et al., 2017).

1.6: BBR Optometry Ltd.

BBR Optometry Ltd. is located in the city of Hereford, which has an estimated population of 60,800 residents (Herefordshire Council, 2018). Hereford is the centre for most facilities in the predominately rural county of Herefordshire situated in the south-west of the West Midlands region bordering Wales (Herefordshire Council, 2018). Herefordshire has an older age profile compared to England and Wales as a whole with 24% versus 18% of the population aged 65 years and over, and a high proportion of residents in their early fifties and above thought due to the baby booms following World War II and in the 1960s (Herefordshire Council, 2018).

BBR Optometry Ltd. is a large independent optometric practice with five consulting rooms, two patient waiting areas, a pre-screening room, an imaging room and large shop floor area for spectacle dispensing. The practice is easily accessible via public transport, and nearby the County Hospital Victoria Eye Unit, local general practitioner and dental surgeries, pharmacies, and other small independent businesses. There are three pay and display car parks located in the vicinity of the practice, and limited pay and display parking on the street where the practice is situated.

Three national chain optometric practices are also located in the city of Hereford. BBR Optometry Ltd. distinguishes itself from local competitors by offering longer consultation durations than usual, professionally qualified dispensing staff, participation in all local community-enhanced services,

and private specialist services. Private specialist services include optical coherence tomography (OCT), ultra-wide field imaging, therapeutic management, specialist CL fitting, dry eye consultations and access to novel in-practice treatments for dry eye. The business model at BBR Optometry Ltd. is orientated around a lower volume of sales, but a higher average revenue per patient via professional fees and optical products.

In regards to explicit service promises, BBR Optometry Ltd. have a mission statement that summarises the aims and values of their firm, and reflects the desire of the practice directors to uphold a reputation for clinical excellence. The mission statement is "to deliver the best standard of eye care to all our patients in a friendly, professional environment," and tangibles listed on the practice website include:

- Optician Awards Winner 2015, the enhanced services award
- Rodenstock Centre of Excellence 2015 first place
- Rodenstock Solitaire 2 Category lenses first place
- Optician Awards Finalist 2018
- Registered with the General Optical Council
- Investors in People- Gold
- World Council of Optometry Supporter
- ISO 9001 Quality Management Certification via QSL ISO Quality Services Ltd.
- Member of Herefordshire & Worcestershire Chamber of Commerce

This research was part of a wider collaborative Knowledge Transfer Partnership (KTP) project between BBR Optometry Ltd. and Aston University's Business Partnership Unit. The KTP project was intended to grow BBR Optometry Ltd. as a business and optometric practice by applying knowledge and insights derived from the research presented in this thesis. The final achieved objective for the KTP project was to embed a service for the non-routine patient to establish BBR Optometry Ltd. as capable of diagnosing and managing complex, chronic eye conditions at the highest level, whilst introducing new revenue streams. The dry eye service required re-structuring in terms of fees, timings, standards of care, and possible outcomes, ultimately differentiating BBR Optometry Ltd. from local competition and future-proofing the business. The KTP project was part funded by BBR Optometry Ltd. and by Innovate UK. The certificate of KTP project completion, and assessment of the final KTP report can be seen in appendix 1.3 and 1.2.

1.7: Research aims and objectives

Presently, the literature on dry eye concerns specific clinical tests and management options, but does not focus on how a practitioner can set up a speciality service, and sustain a dry eye clinic in community optometric practice. Optometric practices offer varying levels of dry eye care from consultations using traditional or modern diagnostic tests, and different staged treatment options depending on practice investment in in-practice therapies, including those that are device-assisted, and in higher education to offer prescription medication. Dry eye services are not currently part of traditional EOS to the best of the author's knowledge, and tend to be privately funded by patients. Chapter two will use a single optometric practice site, BBR Optometry Ltd. described in section 1.6, to investigate the local demand for establishing a dry eye service, demonstrate the usefulness of service blueprinting, and evaluate the possible tangible benefits of implementing a dry eye service on other aspects of an optometric business. Chapter three will use a retrospective analysis and objective statistical methods to determine the most important clinical screening questions and tests that are predictive of dry eye from a sample of patients from BBR Optometry Ltd., where an advanced dry eye service in terms of offering the latest diagnostics and therapies was implemented.

Dry eye is thought to impact the success of other optometric services including the outcome of referrals for cataract surgery and the success of CL fittings. Chapter four explores retrospectively, the possible effect of dry eye on visual and clinical outcomes at a private hospital where optometrists from BBR Optometry Ltd. commonly refer patients for lens replacement surgery. Chapter five will determine retrospectively whether dryness and ocular discomfort are main reasons for CL dropout at BBR Optometry Ltd., and perhaps offer evidence for the utility of prophylactic dry eye care prior to surgery and CL fitting, which can impact the tear film and ocular surface, and impede ocular wellness. Dry eye is a condition that does not command priority in the HES with overstretched and limited resources for effective long-term management. Chapter six aims to provide a glimpse into the possible number of dry eye cases attending a local hospital for dry eye-related concerns, and other ocular concerns that could be managed in the community rather than a hospital setting.

CHAPTER 2 ABSTRACT
Application of service experience management concepts for the development of specialist community optometric services

PURPOSE: To determine the local need for establishing a private dry eye service at BBR Optometry Ltd., and to demonstrate the usefulness of service blueprinting in the context of an optometric practice. A third aim was to provide insight into the dry eye service user at BBR Optometry Ltd. by assessing whether utilisation of the dry eye service would lead to: conversion to Eyelife™ membership or Eyelife™ upgrades, more structured dry eye product purchasing behaviour, and fewer clinical attendances for dry eye related concerns.

METHODS: Customers aged 18 years and over attending for an eye examination were asked to randomly complete one of two validated dry eye questionnaires, the Ocular Surface Disease Index (OSDI) or the Standard Patient Evaluation of Eye Dryness (SPEED) survey. Kruskal- Wallis tests were conducted using a commercially available statistical software package (SPSS for Mac, version 24.0, IBM-SPSS, Chicago, IL, USA) to determine if there were differences in OSDI scores, SPEED scores, and ages between groups of respondents with different OSDI and SPEED symptom severity classifications.

Service blueprinting is an element of service quality management that relates to the design of standards for new services, and to reduce provider gaps outlined in the Gaps model of service quality (Parasuraman et al., 1985). The role of a service blueprint is to aid strategic implementation of new services with existing services, and to avoid process and delivery errors. BBR Optometry Ltd.'s Tear clinic was used as a case study to demonstrate how service blueprinting can be applied to optometric practice as a template for new optometric service provision and integration into existing systems.

Data including Eyelife™ status, dry eye product and spectacle transactions, and number of practice attendances, were analysed for customers who had a dry eye consultation and compared from a time period of one year prior to the consultation, and one year following the dry eye review appointment.

RESULTS: 25% (67/274) of customers identified as having symptomatic dry eye with the widely accepted criterion of OSDI ≥ 13, and 39% (198/506) of customers identified as having symptomatic dry eye with the criterion of SPEED ≥ six. Overall, the average age of respondents was 64.47 ± 14.57 and 65.60 ± 15.25 for the OSDI and SPEED questionnaires respectively. Focusing on the results of the pairwise comparisons, there were statistically significant differences in the distribution of total OSDI scores between the normal OSDI classification group and all other symptomatic OSDI groups. There were no statistically significant differences in the total OSDI score distributions between the mild and moderate, mild and severe, and moderate and severe groups. For the distribution of total SPEED scores, the pairwise comparisons across SPEED classification groups were statistically significant for all possible combinations. There were no statistically significant differences in the age distributions across symptom severity classifications for either of the questionnaires.

The average age of customers attending for a dry eye consultation was 65.71 ± 12.72, and 67 were females and 27 were males. Overall the majority of customers utilising the dry eye service were exisitng BBR Optometry Ltd. customers and of the new customers, only two of the 26 converted to Eyelife™. Customers utilising the dry eye service preferred to purchase products at point of sale versus subscribing to a monthly direct debit system, and were more likely if at all to purchase spectacles following their eye examination irrespective of when they had a dry eye consultation.

CONCLUSIONS: Understanding and applying concepts from the service experience management sector complements clinical work, and future studies could assess the effectiveness of a service blueprint in an optometric setting including analysis of service quality audits, assessment of customer lifetime value, and measures of service conversions and usage.

CHAPTER 2
Application of service experience management concepts for the development of specialist community optometric services

2.1: Introduction

Dry eye is a commonly occurring ocular condition that drives people to seek professional advice (Bradley et al., 2019; Stapleton et al., 2017). Anecdotally, optometrists at BBR Optometry Ltd. had noticed that numerous customers attending for annual eye examinations or perceived ocular emergency appointments had described symptoms of ocular discomfort as their main concern or requested advice regarding intermittent ocular discomfort. Developing an advanced dry eye service offering aimed to differentiate BBR Optometry Ltd. from competitors in the industry, and also allow enough time to fully and efficiently formally investigate customer concerns related to dry eye. It has been demonstrated that too little clinic time spent with customers to explain management threatens customer motivation for maintaining therapy and compliance (Lim & Ngah, 1991; Gascon et al., 2004; Moore et al., 2004; Lawson et al., 2005). A secondary aim was also to reduce walk-in emergency or multiple excessive appointments in general, and ensure Eyelife^{TM} monthly direct debit fees (described in section 2.2.3) were cost effective and not overstretched.

Customer participation is important in health care services with the desired outcome of met needs and benefits potentially possible if the customers perform their roles effectively (Bowen, 1986). The topics of adherence and compliance will be discussed in this chapter. The "service bottom line" is business profitability and sustainability, which is frequently a result of customer purchasing behaviour and attitudes towards a service provider. Service quality is one of the fundamental predictors of business performance (Wilson et al., 2016). Consistent quality service delivery performances and strategies to achieve these are important to ensure longevity in the market.

This chapter aims to:

- Identify whether there is a need or demand for establishing a dry eye service at BBR Optometry Ltd.
- Demonstrate the usefulness of service blueprinting in the context of an optometric practice
- Identify purchasing behaviour of dry eye customers at BBR Optometry Ltd., and determine whether customers utilising the dry eye service subscribe to other aspects of the practice

For the purposes of this chapter, users of BBR Optometry Ltd.'s dry eye service will be referred to as 'customers'. The term 'client' or the synonym 'customer' as opposed to 'patient' to denote a recipient of healthcare was introduced in the mid-twentieth century in order to avoid a connotation of disability, impairment or being ill (Shevell, 2009). The modern individual is informed and

participative in their healthcare and wellbeing, rather than a passive acceptor as the term 'patient' implies. Deber et al. (2005) surveyed Canadian outpatient clinical populations of people with breast cancer, prostate disease, fracture and HIV who found the term 'patient' much less objectionable than alternatives suggested by the authors including 'client', 'customer', 'consumer', 'partner' and 'survivor' because it did not incorporate an assumption of a market relationship. Other studies have shown that individuals preferred to be referred to as 'patients' albeit they did not permit participants to specify that they liked more than one term (Nair, 1998; Lloyd et al., 2001; Wing, 1997). Perhaps for people with suspect dry eye issues especially in mild forms, 'customer' is a more appropriate term than 'patient' considering the individual may not perceive themselves as sick or injured, and are able to compare costs and benefits of service providers.

2.1.1: Optometric market in the UK

Traditional services in optometric practice are a combination of professional and retail with elements of the eye examination including advice and referral, and the dispensing of spectacles and contact lenses. The acquiring of Tesco Opticians by Vision Express at the end of 2017 meant introduction of the brand to more than 200 supermarket sites, and Asda's own optometric services operation is likely to gain from the proposed merger of the supermarket with Sainsbury's (Mintel, 2019). Although online sales of spectacles remain underdeveloped compared with other retail sectors, growth is expected due to advances in technology that will help online customers visualise the appearance and fit of their chosen frames (Mintel, 2019). Additionally, many of the online selling pioneers have been bought by Essilor, and stores like Superdrug are entering the online market for prescription spectacles (Mintel, 2017).

The cornerstone of promotional strategy in the optometric industry has been conspicuous discounting (e.g. 2 for 1 glasses offer via Specsavers Opticians). However, the actual current trend observed has been brand building by large chains including opticians within John Lewis in conjunction with Luxottica, in order to reduce the focus on discounting (Mintel, 2017). The market share for independent practices therefore is continuing to be depleted. In order to differentiate themselves and compete with local competition and online retailers, practices can become involved in enhanced local community scheme services such as the Minor Eyecare Conditions Services (MECS) described in chapter six, add related services such as domiciliary and hearing care to their portfolio of services, and offer private specialist services.

Private optometric services currently exist for dry eye management, pre- and post-operative care for laser refractive and clear lens extraction surgeries, EyePrint prosthetics for bespoke scleral lenses to manage keratoconus (https://eyeprintpro.com/), myopia control, orthokeratology, orthoptics, sports

vision, and for dyslexia and reading difficulties. The key in the eye care industry market is to provide the appropriate product that creates value and addresses the customer's needs from therapeutics, eye glasses, contact lenses and services. The components of each private specialist service will vary between practices and ultimately excellent service quality will enable a practice to stand out against competition. Community optometry practices have the necessary task of establishing themselves as the practice of choice in the customer's mind in order to achieve key organisational goals such as long-term survival and profitability. Practices need to differentiate themselves from their competitors in their service element as having excellent products alone is not sufficient, and companies cannot compete on price alone (Boulding et al., 1993).

2.1.2: The concept of Service quality

Service quality is a measure of how well customer needs and requirements are met, and how well customer expectations and service level delivery align (Wilson et al., 2016). The basic characteristics of services make it challenging to deliver consistent quality including being heterogeneous across time, organizations and people with customers having unique demands, and no two services being performed precisely alike (Fisk et al., 1993; Lovelock & Gummesson, 2004; Wilson et al., 2016; Vargo et al., 2004). Fluctuations in demand can be difficult to manage as a service is intangible and cannot be inventoried or trialled before purchase (Bitner et al., 2008). The eye examination itself is an example of the intangible nature of a service in the optometric industry. Generally, the quality of the service and customer satisfaction depends on what happens during the transaction since services are simultaneously produced and consumed (Reimer & Kuehn, 2005). Clues to the likely quality of the service lie within tangible evidence, such as décor and ambience. Demand forecasting or capacity utilisation is critical for services which are perishable, meaning services cannot be saved, stored, resold or returned (Wilson et al., 2016). Prior to implementing a service for dry eye management, BBR Optometry Ltd. were interested in the prevalence of dry eye amongst their customer base and a demographic profile analysis was conducted.

Service quality reflects the customer's perception of the service dimensions namely, reliability, responsiveness, assurance, empathy and tangibles (Parauraman et al., 1988). Customers compare their perceptions of service experiences relating to their level of satisfaction, with their expectations of what the service performance should be when judging service quality (Parauraman et al., 1988). Desired service is often shaped by those personal needs essential to the physical or psychological wellbeing of the customer (Wilson et al., 2016). The Gaps model of service quality is a framework for understanding and improving service delivery (Parasuraman et al., 1985), seen in figure 2.1. The Gaps model suggests that the customer perception of service quality is driven by differences between

customers' expectations about the performance of a general class of service providers, and their evaluation of the actual performance of a specific firm within that class (Cronin & Taylor, 1992).

The service provider gaps involved in delivering and marketing a service are (Parasuraman et al., 1985):

- *Provider gap one/ Knowledge gap:* Not knowing what customers expect. This is the difference between customer expectations of a service and the company's understanding of those expectations.
- *Provider gap two/ Standards gap:* Not selecting the right service quality designs and standards
- *Provider gap three/ Delivery gap:* Not delivering to service designs and standards
- *Provider gap four/ Communication gap:* Not matching performances to promises
- *Gap five/ Customer or Service gap:* the difference between customer expectations and perceptions that is a function of the four provider gaps

Figure 2.1: The Gaps model of service quality (Parasuraman et al., 1985)

The SERVQUAL instrument or scale published by Parauraman et al. in 1988 is used to operationalise the Gaps model from the service user perspective. For more information on the SERVQUAL instrument and applications to optometric businesses refer to appendix 2.1. The Grönroos model published in 1984 is another model of service quality that is less widely known compared to the one developed later by Parasuraman et al. (1985), and identifies technical quality (i.e. what customers receive), functional quality (i.e. how customers receive the service) and

corporate image as principal components of service quality (Woodall, 2001). The SERVPERF is another approach to measure service quality other than the SERVQUAL that only uses the performance dimension of the Parasuraman et al. (1985) model (Cronin & Taylor, 1992).

Service blueprinting, which will be discussed in this chapter, is an effective tool used in service development and design to help avoid provider gap two. Provider gap two is reduced by having services that are designed well, clear customer-driven standards and appropriate physical evidence and surroundings in place (Bitner et al., 2008). One of the most important ways to avoid provider gap two is to clearly design services free of subjectivity, bias, oversimplification, and incompleteness (Wilson et al., 2016). The Mayo Clinic with health service centers in Minnesota, Florida and Arizona in the US is the largest multi-speciality group practice in the world. In 2002, the Mayo Clinic initiated a programme for service delivery innovation called the SPARC (see/plan/act/refine/communicate) Innovation Programme (Duncan & Breslin, 2009). Live prototyping through SPARC has provided more information on the patient journey than structured questionnaires and focus groups, highlighting the importance of service planning and experiential learning when it comes to health care delivery and meeting patient needs (Duncan & Breslin, 2009).

The extent to which customers recognise and are willing to accept variations in the desired service to adequate service is called the zone of tolerance (Johnston, 1995; Yap & Sweeney, 2007). When the service performance falls outside this zone, the customer views the service in either a positive or negative way (Johnston, 1995; Yap & Sweeney, 2007). The zone of tolerance can expand and contract between customers and for the same customer, influenced by multiple factors including company-controlled factors such as price (Johnston, 1995; Yap & Sweeney, 2007). For example, customers with time pressures in their professional and or personal lives on any given day, desire short wait times in general and a hold a restricted range for the length of acceptable wait times. If the customer's appointment does not commence when expected it can influence their judgment of adequate service. However, recognition of situational factors such as an ocular emergency requiring attention prior to the customer's appointment and requiring more time by the service provider may widen the zone of tolerance. The amount of time spent in the waiting room at the last optometric visit may also affect the zone of tolerance. Customers can estimate what will happen in the next service encounter, referred to as predicted service, from previous experiences. Therefore, some customers may expect an additional amount of time, separate from their eye examination, spent in the waiting area or undergoing preliminary tests before seeing the optometrist.

When customers perceive that alternative services exists, the level of service the customer finds acceptable rises, consequently narrowing the zone of tolerance (Johnston, 1995; Yap & Sweeney, 2007). Examples of alternative services include other dry eye specialist care providers or self-service

through trial and error of over-the-counter dry eye products. It is important to learn about service alternatives the customer views as comparable, rather than just those in the business' competitive set as it is likely to include more than just other optometric practices and is a factor in influencing the level of perceived adequate service. This activity is important in order to reduce provider gap one, also referred to the knowledge gap, to understand what customers expect and to improve service delivery (Parasuraman et al., 1985). Optometrists in their dry eye service marketing may wish to highlight the frustration of trial and error of ocular lubricants by customers in attempts to self-treat or suggested by their pharmacist or general practitioner (GP) due to their perception that they need tear replacement rather than solutions for evaporative dry eye, which is the most common form of dry eye described further in chapter one. Initially self-treating with over-the-counter products may be a viable option to address potential dry eye concerns that the customer finds easier, more convenient and less costly than identifying a dry eye service provider. Also, when fees are high and tangibles such as diagnostic technology are impressive, customers expect quality reliable service and tend to be less tolerant of poor service (Johnston, 1995; Yap & Sweeney, 2007).

2.1.3: The concept of customer satisfaction

Customer satisfaction can be defined as the overall attitude towards a service provider or an emotional reaction to a discrepancy in what the customer anticipates and what is experienced in regards to fulfilment of some need, goal or desire (Hansemark & Albinsson, 2004). Parasuraman et al. (1994) clarify that customer satisfaction is specific to each transaction, while service quality is the customer's general attitude towards the business.

A German study sought to determine the extent of agreement or congruence between optometric service provider's perceptions of customer satisfaction and customer-reported satisfaction using mail surveys (Yavas et al., 2008). The importance being that accurate knowledge about customers and assessment of customer perceptions can lead to customer retention as well as stronger business performance and success. A list of 28 attributes customers use in evaluating core optometric services relating to basic facilities, product and service offerings, core services such as diagnosis of the eyesight problem, and after-sales services including warranties and guarantees were generated from focus groups with the two target respondent group types (Yavas et al., 2008). Customer respondents were asked to indicate their level of satisfaction with these attributes on a five-point scale, and members of a professional association of German optometrists were asked to indicate how satisfied they thought their customers were using the same scale and set of attributes (Yavas et al., 2008). The survey used was not a validated instrument. Data collected was analysed separately for the groups using principal components analysis, which is a technique that was used and is explained in chapter three.

Results from the Yavas et al. (2008) study showed a discrepancy between optometrists and their customers with the medical service dimension emerging as the most important factor for optometrists but appearing second for customers. This is another example of provider gap one, whereby service providers have inaccurate perceptions of what customers actually expect (Parasuraman et al., 1985). The only other dimension or factor approaching congruence was customer commitment/store design, which appeared second for optometrists and third for customers as the most important element for evaluating optometric services (Yavas et al., 2008). Items pertaining to selection on lenses and frames, and offers by the store were the most important to customers suggesting customers put more emphasis on functional rather than technical quality of optometric services (Yavas et al., 2008). That is, the production and delivery of services were more important than what the customer received, which is the end result of the service. Health care service providers tend to judge core service quality by adherence to standards or generally accepted procedures. However, customers may not be aware of these nor use the same criteria in deciding how satisfied they are with the service provided (Harvey, 1998). McColl-Kennedy et al. (2017) suggest that in a health care setting, where customers can experience heightened emotions due to risks associated with health, service providers can enhance wellbeing and the overall service experience by creating a supportive culture from the design of the physical environment to the design of service processes.

2.2: Method

This study received approval from the Life and Health Sciences Ethics Committee at Aston University (Project #1276), and adhered to the tenets of the Declaration of Helsinki.

2.2.1: Identification of dry eye customers using two validated dry eye questionnaires

To determine the prevalence of dry eye symptoms presenting at BBR Optometry Ltd., customers aged 18 years and over attending for an eye examination were asked to randomly complete one of two validated dry eye questionnaires, the Ocular Surface Disease Index (OSDI) or the Standard Patient Evaluation of Eye Dryness (SPEED) survey, and consented to having their data itemised for research regarding service enhancement. The questionnaires used were discussed in chapter one and can be found in appendix 2.2. An initial explanation was given to the customer, and the questionnaire was self-completed voluntarily by the customer. The questionnaires were completed by consecutively presenting customers to avoid bias of subject selection.

The SPEED questionnaire was administered over a six-month period from April to September 2015, and the OSDI questionnaire was used for a further six-month timeframe from October 2015 to March

2016. The total OSDI and SPEED score, age and sex for each anonymised customer were recorded in Microsoft Excel (Microsoft Corporation, Redmond, Washington, USA). The age recorded was that of the customer when one of the questionnaires was completed. Kruskal- Wallis tests were conducted using a commercially available statistical software package (SPSS for Mac, version 24.0, IBM-SPSS, Chicago, IL, USA) to determine if there were differences in OSDI scores, SPEED scores, and ages between groups of participants with different OSDI and SPEED symptom severity classifications.

2.2.2: Developing a Service blueprint for new services

The new product development process and implementation stage for manufactured goods tends to be more structured compared to service firms due to the challenges of coordinating human resources, technology, internal processes and facilities within already existing systems (Griffin, 1997; Thomke, 2003). Incorporating BBR Optometry Ltd.'s dry eye service into existing systems rather than treating it as a standalone service was challenging due to the complexities of internal processes. Front end planning involves idea generation for the new service, which can include learning about competitor's offerings, collaborating with third parties, and developing licensing agreements and joint ventures (Rigby and Zook, 2002). BBR Optometry Ltd. utilised existing relationships with Scope Ophthalmics who were current providers of dry eye diagnostics, and management options namely, the TearLab osmolarity system, the Hycosan ocular lubricant range and BlephEx^{TM} to further develop the service concept. The next step was to estimate the economic feasibility of the new service and potential profit implications. The activity-based costing method introduced to the practice by Dr Patel and discussed in her PhD thesis (2015) was applied to produce more precise cost allocations in determination of fees for the dry eye service (Baird et al., 2004).

The second aspect of the service innovation and development process after front-end planning is implementation (Wilson et al., 2016). A detailed service blueprint represents the implementation plan for the new service that is refined and evolves with input from stakeholders such as contact employees. Unfortunately, there was no pilot run of the service to ensure that operational details were functioning smoothly in the development process. This was most likely due to overexcitement from the practice directors who were keen to implement the service, and had a false sense that staff with prior dry eye training but limited experience with the dry eye diagnostics were well equipped to deliver the intended service. Mistakes or service failures in the design are more difficult to correct when the actual market introduction is the first test of whether the service functions as planned. Some difficult encounters with customers could have been avoided if this step was not overlooked.

There is a greater risk for customer dissatisfaction when problems occur early in the service encounter. Situations that resulted in uncomfortable and challenging encounters for the practitioner delivering the service included customers being told to attend for further tests but not understanding they had been booked for a dry eye consultation with associated additional fees, and customers not being told what to expect at the consultation which in turn affected the accuracy of clinical test results. In particular, customers would attend wearing their contact lenses, and one customer's partner had organised annual leave to drive the customer to their consultation, believing that one of the clinical tests would involve dilation impeding the customer's own ability to drive. Prior to the formalisation of the service, in-practice diagnostics and treatments were initiated haphazardly, and at the early stages of service development senior practitioners continued to operate in this manner, which was a source of frustration for the practitioner delivering the service and confusion to customers.

The service blueprint outlines all steps involved in the service process so that all employees understand the process and are aware of their roles in its delivery (Shostack, 1984; Shostack, 1987). Service blueprinting is not a set of rigid rules for designing services, it is defined as "a tool for simultaneously depicting the service process, the points of customer contact and evidence of service from the customer's point of view" (Wilson et al., 2016). Service blueprinting overcomes the problems of relying on words alone to describe service processes because everyone can visualise the process exactly as it was intended. The key components of service blueprints are shown in figure 2.2 and explained below (Wilson et al., 2016; Bitner et al., 2008; Fließ & Kleinaltenkamp, 2004; Patrício et al., 2008).

Figure 2.2: Service blueprint components (Wilson et al., 2016)

Service blueprint components (Wilson et al., 2016):

- *Customer actions:* it includes steps, choices, activities and interactions that customers perform in the process of purchasing, consuming and evaluating the service depicted chronologically across the top of the blueprint.
- *Onstage employee actions:* steps and activities the contact employees perform that are visible to the customer. In technology delivered services like self-service websites and interactive kiosks, this area can be relabelled or divided into two distinct spaces including onstage/visible technology, and the backstage contact person action area would be irrelevant.
- *Backstage employee actions:* steps and activities that occur behind the scenes to support onstage activities
- *Support processes:* covers the internal services, steps and interactions that take place to support the contact employees in delivering the service. There is no customer contact in these steps.
- *Physical evidence:* tangible things that a customer can see, hear, smell or touch as they go through the service experience typically listed above each point of contact

The four key action areas are separated by three horizontal lines (Wilson et al., 2016):

- *Line of interaction:* direct interactions between the customer and organization. A service encounter has occurred whenever a vertical line crosses the horizontal line of interaction.
- *Line of visibility:* this line separates all service activities that are visible to the customers from those that are not visible
- *Line of internal interaction:* separates contact employees from those of other service support activities and people

The boxes shown in figure 2.2 represent the steps performed or experienced by the person at that level. The chronology of the actions conducted by the service customer and provider are represented along the horizontal axis, and the different areas of actions are distinguished along the y-axis (Fließ & Kleinaltenkamp, 2004). Creation of the service blueprint starts with the customer's view of the process and their experience, and involves collaboration with all employees to gain the benefit of different perspectives. The whole process needs to be easy, convenient and timely from the customer's point of view. The basic steps involved in building a service blueprint can be found in figure 2.3 (Bitner et al., 2008). Service blueprints are not meant to be inflexible, and Wilson et al. (2016) note that services are always changing whether or not it is deliberate or unplanned to enhance quality from the customer's point of view. The creation of a blueprint allows clarification of the service concept, development of a shared vision for those involved in delivery, highlighting of

complexities that were not initially obvious, and delineation of responsibilities (Wilson et al., 2016; Bitner et al., 2008).

Figure 2.3: Steps involved in building a service blueprint (Wilson et al., 2016)

Successful execution of a service is just as important as innovation to drive growth for a business (Noble and Mokwa, 1999; Walker et al., 2002; Cadwallader et al., 2010). Changes in service delivery may affect an employee's role, and the motivation of employees to participate in implementing a service will determine whether they serve as facilitators who embrace, execute and promote the service or serve as barriers in its success (Cadwallader et al., 2010). Collaboration when creating service blueprints from all departments including frontline staff can avoid internal problems caused by lack of employee commitment, and understanding of individual capabilities to best deliver the service (Averett, 2001). Lack of sufficient support for frontline staff can result in provider gap three, whereby guidelines for service delivery do not lead to high quality service delivery (Parasuraman et al., 1985). Lack of understanding about the service offering and the way it is delivered can also result in provider gap four, considering customer expectations are fashioned by external communications of an organisation (Parasuraman et al., 1985). Efforts to reduce provider gaps three and four associated with service design, delivery and marketing, in turn affect gap five (Parasuraman et al., 1985).

Studies have shown employees are more disposed towards a task and feel more positive towards an innovation if they are empowered to choose to act (task autonomy), and understand their role in the service process (Saavedra & Kwun, 2000; Dodd & Ganster, 1996; Whitaker et al., 2007; Cadwallader et al., 2010). Frontline employees who have greater role clarity about new services having received additional training and exposed to internal promotion, are more likely and motivated to recommend it to customers. Providing employees with resources such as training tools, and time to integrate new services to cope with internal process change refers to agent enablement, and is required to reduce aversion due to potential additional stress associated with changes to existing job routines and increase adoption of innovations (Umashankar et al., 2011). The speed of new service development and the amount of information collected about customer problems has been shown to increase in services where collaboration between employees in service innovation exists (Ordanini & Parasuraman, 2011).

Servicescape is a commonly used term to describe the physical surroundings of a service company, which includes exterior and interior design, ambient conditions such as temperature, noise, odour as well as other tangible aspects of the business such as leaflets and all communication material (Reimer & Kuehn, 2005). The servicescape is the designed places calculated to produce commercially significant actions (Arnould et al., 1998). The effects of servicescape can be conceptualised using the Stimulus-Organism-Response paradigm that suggests environmental stimuli from the servicescape has an effect on organic states like emotions, which then influences customer reactions (Dedeoglu et al., 2018). Customers only spend as much time in the service provider's environment as necessary for utilitarian services such as insurance, retail banking, dry cleaning, dental clinics and optometric practices (Reimer & Kuehn, 2005). It is thought tangibles in utilitarian services are of significantly less important than in hedonic services (i.e. services for fun and pleasure), however, the servicescape has been shown to have a direct and indirect effect on the perceived service quality (Reimer & Kuehn, 2005). The objective of the blueprint presented in section 2.3.2 was primarily to communicate the general nature of the dry eye service, and demonstrates use of blueprinting for private optometric service innovation.

2.2.3: Evaluation of customer activity following use of new services

BBR Optometry Ltd. introduced new practice management software, I-clarity (I-clarity, Radyr, Cardiff), and fee structure in 2012, including a premium fee for an eye examination with the senior optometrist. BBR Optometry Ltd. have a monthly direct debit payment plan for professional care available to customers called Eyelife^{TM}. There are three tiers of Eyelife^{TM} shown in table 2.1, which differ by monthly fees and levels of discounts on products. Eyelife^{TM} members are encouraged to have annual as opposed to two-yearly eye examinations. The professional care packages include:

- Priority appointments to see preferred optometrist or dispensing optician
- Exclusive access to premieres of new eyewear and services
- As many extended eye examinations as required irrespective of the length of each visit
- Extended eye examinations include supplementary tests such as fundus photography using Optomap ultra-wide field imaging, optical coherence tomography (OCT) and corneal topography
- Discount off spectacles and sunglasses on as many pairs as wanted
- 50% off repairs and replacement spectacles
- Contact lens trial
- Family Discount

Additional benefits for a Dry Eyelife™ member include annual dry eye review appointments and eligibility for home delivery of products with an additional fee depending on the products used. An additional fee is added to the Eyelife™ price if the customer is a contact lens wearer due to the likelihood of more frequent consultations at £2 extra per month for standard contact lens wearers and £4 per month for complex contact lenses (extended wear, keratoconus, multifocals). This additional amount does not include any contact lenses or cleaning solutions, although customers have the option to combine Eyelife™ with any contact lens product. The minimum Eyelife™ contract period is 18 months and discounts apply to products purchased throughout the time of being an Eyelife™ member.

Monthly Payment Plan	Monthly Direct Debit	Spectacle Discount
Eyelife™ Optimum	£11.50	20%
Eyelife™ Elite	£16.00	35%
Dry Eyelife™	£20.00	35%

Table 2.1: A summary of monthly payment plans offered to spectacle only wearers at BBR Optometry Ltd. (Fees as of April 18, 2019).

Dry eye diagnostics and treatments were introduced to the practice in January 2014, but implemented in an impromptu manner until 2015. Return on investment was recouped for dry eye diagnostics TearLab and LipiView II, and the LipiFlow treatment unit and consumables by incorporating it into the monthly direct debit fee. The fees for the dry eye service and in-practice treatments seen in tables 2.2 and 2.3 reflect the fees at the time of the analysis. BBR Optometry Ltd. partnered with Scope Ophthalmics to re-brand the service as Tear Clinic, and hosted a launch event in July 2017. The Tear Clinic was officially opened by the Mayor of Hereford in September 2017.

The Tear Clinic leaflet can be found in appendix 2.3. Information regarding the Tear Clinic consultation for customers at the time of the analysis read:

> "Your optometrist suspects you are experiencing symptoms of ocular surface disease and have recommended a Tear Clinic consultation. The 40-minute consultation will involve measuring the saltiness of your tears with a TearLab osmolarity test, the thickness of your tear film's oil layer, and the number of partial blinks over a 20-second interval. Your oil producing glands will be imaged using LipiView II Dynamic Meibomian Imaging technology and your lashes, lids and ocular surface will be carefully assessed using diagnostic stains that will not affect your ability to drive. The optometrist will recommend a management plan tailored to your needs, which may require a combination of in-practice and at-home therapies. A 20-minute review appointment is usually scheduled four weeks later. We will monitor your ocular surface health using appropriate tests and questionnaires to help track your symptoms."

	Fee	Consultation & Review	Products recommended included
Eyelife™	£80.00	✓	×
Non- Eyelife™	£190.00	✓	✓

Table 2.2: Customer information on dry eye consultation fees and what is included at BBR Optometry Ltd. at the time of the analysis.

Treatment	**Eyelife™**	**Non-Eyelife™**
LipiFlow Thermal Pulsation for two eyes	£499.00	
BlephEx™ microblepharoexfoliation	£24.00	£52.00
Dissolvable punctal plugs	£60.00	£109.00
Permanent punctal plugs	£200.00	£234.00
Demodex 40-day (includes two boxes of Cliradex)	£144.00	£228.00

Table 2.3: In-practice treatments available at BBR Optometry Ltd. at the time of the analysis.

All dry eye consultations at BBR Optometry Ltd. are followed by a review appointment recommended one month later. The mainstay of early treatment for dry eye remains to be over-the-counter lubrication although very few randomized controlled trials have compared inter-product superiority. Moreover, future studies on the impact of different formulations on tear film composition by sub-type of dry eye disease are required (Jones et al., 2017). It is important to be aware of the local clinical commissioning group prescribing guidelines, and the formulary for dry eye in order to predict what products customers may have trialled previously having visited their GP for dry eye concerns, and aware of products that can be requested on NHS prescription for customers if required. The formulary is designed on a tiered system according to prescription costs, and is not reflective of what is commercially available. Approximately £25.79 worth of products for step one level dry eye management (heat mask, lid cleanser, ocular lubricant) were factored into the fee charged to non-Eyelife™ customers for a dry consultation and review appointment.

Nutritional supplements available at BBR Optometry Ltd., namely Omega Eye capsules containing omega-3 oils and vitamin D3 from purified fish oil, were not included in the analysis of expected products spend. This is because the cost of Omega Eye is not covered in the dry eye consultation fee, and some customers may have already been using a form of omega-3 fatty acid (n-3 fatty acids) supplementation sourced elsewhere or preferred to modify their dietary habits versus using supplements. Education regarding potential dietary modifications including oral essential fatty acid supplementation is listed in step one of the recommended staged management and recommendation for dry eye developed by the TFOS DEWS II management and therapy subcommittee (Jones et al., 2017). Since the publication of DEWS II, a multicentre, double-blind clinical trial found that patients

with moderate to severe dry eye disease randomly assigned to receive a daily oral dose of 3000 mg of fish derived n-3 eicosapentaenoic (EPA) and docosahexaenoic acids (DHA) for 12 months did not have significantly better outcomes than those who were assigned to receive an olive oil placebo (Asbell et al., 2018).

Prior to July 2015, there was no way of easily tracking customers who were attending the practice outside their routine eye examination for dry eye concerns and dry eye treatments until analysis codes identifying customers with dry eye were utilised on the practice management software. Customers segmented as having had a dry eye consultation or in-practice treatment could then be easily identifiable. The intentions behind this feature were to empower practice staff to actively enquire about replenishing dry eye products when customers attended the practice, and to aid notifying these customers when the practice was altering recommendations in accordance with the latest literature or introducing a new element such as a diagnostic or treatment to enhance the service offering. Similarly, customer records include an analysis code identifying which tier of Eyelife^{TM} they subscribe to, if at all.

The aim of the retrospective analysis was to assess whether utilisation of the dry eye service would lead to:

- Conversion to Eyelife^{TM} or Eyelife^{TM} upgrades
- More structured dry eye product purchasing behaviour
- Fewer clinical attendances for dry eye related concerns

Data was analysed for customers who had a dry eye consultation from a time period of one year prior to the consultation and one year following the dry eye review appointment, which typically occurs one month post-consultation. Electronic records of dry eye customers were analysed at the practice site. The customer's age was derived from the date of birth to time of the dry eye consultation. All data collected was anonymised and tabulated in Microsoft Excel (Microsoft Corporation, Redmond, Washington, USA).

2.3: Results

2.3.1: Determining the demand for a dry eye clinic and patterns of presentation

A total of 506 SPEED questionnaires and 274 OSDI questionnaires were itemised for analysis. Approximately 3861 patients attend the practice for eye examinations every 6 months, representing a response rate of 13.1% for the SPEED and 7.1% for the OSDI questionnaire. There were 67 customers identified as having symptomatic dry eye (25%) with the widely accepted criterion of

OSDI ≥ 13 (discussed in chapter one). The mean OSDI score for symptomatic dry eye using this criterion was 23.72 ± 11.66. The mean, median, and mode ages of these customers were 62.30 ± 15.53, 64, and 76 respectively. Ages ranged from 26 to 89 years, and the age distribution can be seen in figure 2.4. There were more females than males (40:27).

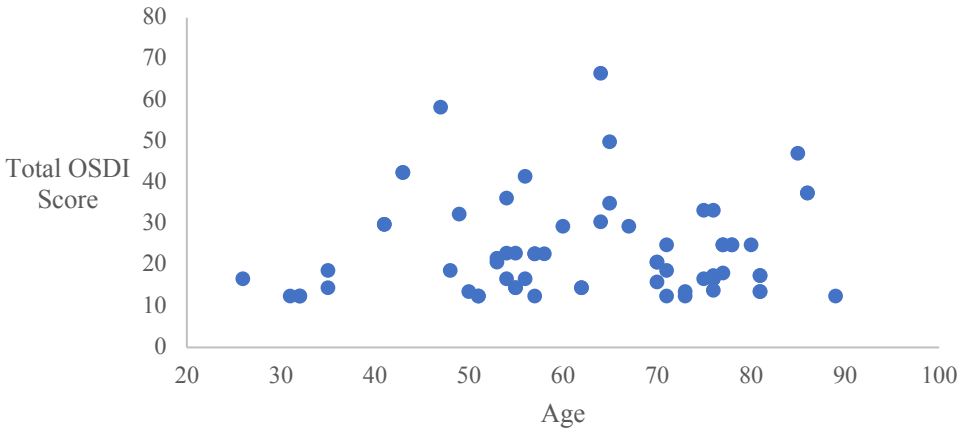


Figure 2.4: Prevalence of dry eye in the sample defined as total OSDI score ≥ 13

There were 198 customers identified as having symptomatic dry eye (39%) with the criterion of SPEED ≥ six. The mean SPEED score for symptomatic dry eye using this criterion was 10.40 ± 4.45. The mean, median, and mode ages of these customers were 65.13 ± 15.91, 67, and 63 respectively. Ages ranged from 19 to 111 years, and the age distribution can be seen in figure 2.5. There were more females than males (139:59).

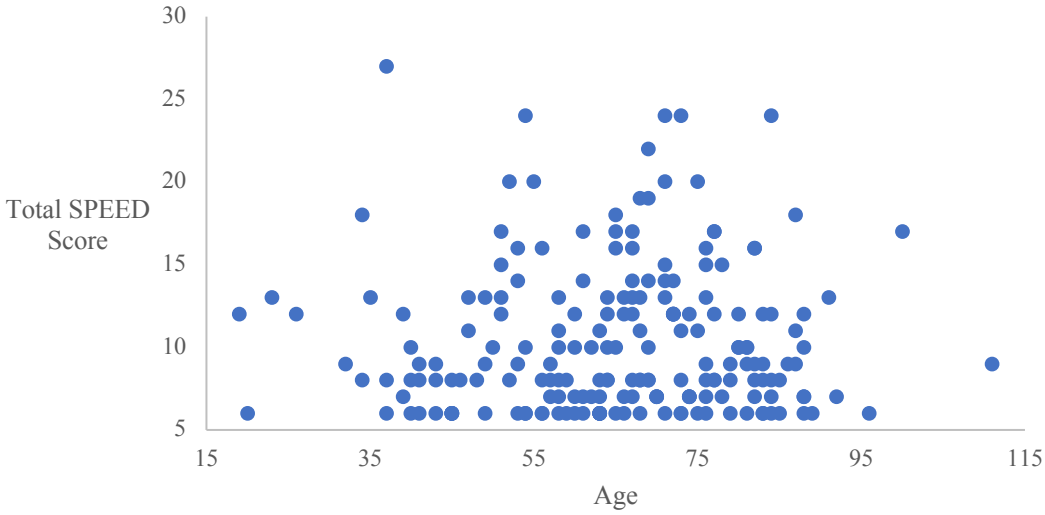


Figure 2.5: Prevalence of dry eye in the sample defined as total SPEED score ≥ six

The customer questionnaire data was segmented by previously described classification categories for both the OSDI and SPEED. The analyses can be seen in table 2.4 and 2.5.

	Normal	Mild	Moderate	Severe
Total OSDI score range	0 - 12	13 - 22	23 - 32	33 - 100
Sample size	207	37	16	14
Mean OSDI score	2.62 ± 3.33	15.70 ± 2.76	25.86 ± 2.90	42.46 ± 9.73
Mean age (years)	65.17 ± 14.17	61.22 ± 16.77	63.44 ± 12.32	63.86 ± 15.12
Age range (years)	20 - 89	26 - 89	41 - 81	43 - 86
Number of females	115	21	10	9
Number of males	92	16	6	5

Table 2.4: The breakdown of customer data in each OSDI symptom category

A Kruskal-Wallis test was run to determine if there were differences in OSDI scores between four groups of participants with different OSDI symptom severity classifications: "normal" (n = 207), "mild" (n = 37), "moderate" (n=16) and "severe" (n=14). Distributions of OSDI scores were not similar for all groups, as assessed by visual inspection of a boxplot (see appendix 2.4). The distributions of OSDI scores were statistically significantly different between groups, $\chi^2(3) = 163.371$, $p < 0.0005$.

Subsequently, pairwise comparisons were performed using Dunn's (1964) procedure with a Bonferroni correction for multiple comparisons in order to reduce the risk of a Type I error (Laerd Statistics, 2017). A Type I error is when a result is declared as statistically significant when it is not, and can increase with every pairwise comparison made thereafter (Laerd Statistics, 2017). The procedure described by Dunn (1964) uses the entire data set when making each pairwise comparison in a manner analogous to post hoc tests following a one-way ANOVA (Laerd Statistics, 2017). A one-way ANOVA was not conducted as all assumptions could not be met as outlined by Laerd Statistics (2017). There was a genuinely unusual outlier, and the dependent variables were not normally distributed for each group of the independent variable as indicated by the Shaprio-Wilk test (i.e. $p<0.50$ indicating the assumption of normality is violated). Another method for pairwise comparisons that was not used, is to run multiple separate Mann-Whitney U tests with a correction for multiple comparisons, which only use the data involved in each specific pairwise comparison. There is no agreement on which method should be used for pairwise comparisons and it is possible that results from the two methods could disagree substantially, indicating the need for replication studies using larger samples (Sheskin, 2011). Adjusted *p*-values are presented. This post hoc analysis revealed statistically significant differences in OSDI scores between the normal (mean rank = 104.00) and mild (mean rank = 226.00) ($p<0.0005$), normal and moderate (mean rank = 252.50) ($p<0.0005$), and normal and severe (mean rank = 267.50) ($p<0.0005$) OSDI classification groups, but not between any other group combinations.

A Kruskal-Wallis test was conducted to determine if there were differences in age between groups that differed in their OSDI classification. The distribution of age was not statistically significant across the categories of OSDI classification, $\chi^2(3) = 1.647$, $p = .649$.

	No symptoms	Mild to moderate	Severe
Total SPEED score range	0	1 - 9	10 - 28
Sample size	103	312	91
Mean SPEED score	0 ± 0	4.48 ± 2.25	14.22 ± 3.83
Mean age (years)	67.76 ± 15.47	64.96 ± 15.13	65.35 ± 15.20
Age range (years)	20 - 94	20 - 111	19 - 100
Number of females	61	203	70
Number of males	42	109	21

Table 2.5: The breakdown of customer data in each SPEED symptom category

A Kruskal-Wallis test was run to determine if there were differences in total SPEED scores between three groups of participants with different SPEED symptom severity classifications: "no symptoms" (n = 103), "mild to moderate" (n = 312), and "severe" (n = 91) symptoms. The dependent variables were not normally distributed for each group of the independent variable as indicated by the Shaprio-Wilk test. Distributions of SPEED scores were not similar for all groups, as assessed by visual inspection of a boxplot (see appendix 2.5). The distributions of SPEED scores were statistically significantly different between groups, $\chi^2(2) = 384.968$, $p < 0.0005$. Subsequently, pairwise comparisons were performed using Dunn's (1964) procedure with a Bonferroni correction for multiple comparisons. Adjusted *p*-values are presented. This post hoc analysis revealed statistically significant differences in SPEED scores between no symptoms (mean rank = 52) and the mild-moderate symptom group (mean rank = 259.50) ($p < 0.0005$), no symptoms and severe symptoms group (mean rank = 461) ($p < 0.0005$), and the mild-moderate and severe symptom group ($p < 0.0005$).

A Kruskal-Wallis test was conducted to determine if there were differences in age between groups that differed in their SPEED classification. The distribution of age was not statistically significant across the categories of SPEED classification, $\chi^2(2) = 4.290$, $p = .117$. The post hoc statistical power calculation of the presented sample size was 99% for OSDI and SPEED data (appendix 2.6 & 2.7; Faul et al., 2009).

2.3.2: Service blueprinting and implementation of a dry eye clinic at BBR Optometry Ltd.

Explicit service promises are statements made about the service by the organization to the customer either verbally or in written materials that can influence customer expectations (Wilson et al., 2016). Members of the organization may overpromise to obtain business or inadvertently by stating their

estimates of predicted service delivery that may be remedied by using a service blueprint (Wilson et al., 2016). The service blueprint created to communicate the general nature of the dry eye service, and that demonstrates use of blueprinting for private optometric service innovation can be seen in figure 2.6.

Under-promising may make customer expectations seem more realistic, but may also reduce the competitive appeal of the service and have the inadvertent effect of lowering customer perceptions of the service, particularly for new customers (Wilson et al., 2016; Boulding et al., 1993). Additionally, some members of an organization may not know the appropriate promises to make because services are customized in the context of a dry eye service and treatment outcomes are not easily defined and repeated due to the nature of dry eye. A specialist service is difficult to evaluate before purchase and direct experience of the service with customers often relying on online and offline word-of-mouth communication via recommendations, testimonials, reviews on social media or blogs to shape their expectations (Wilson et al., 2016). Businesses must consistently exceed the adequate service level and reach the desired service level to develop and intensify customer loyalty (Wilson et al., 2016).

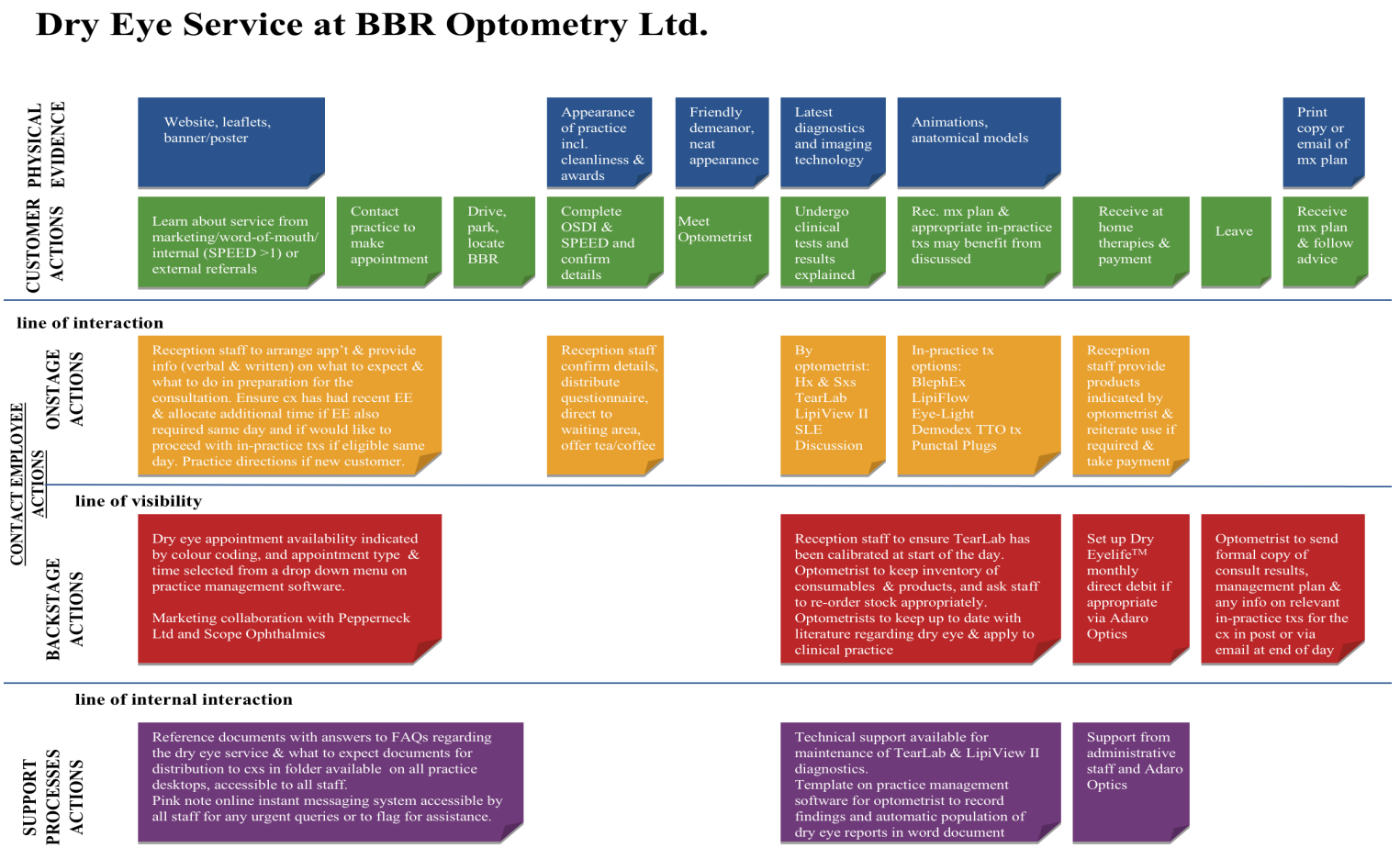


Figure 2.6: BBR Optometry Ltd. blueprint for the Dry eye service developed for the purpose of the study (app't= appointment; EE= eye exam; cx= customer; tx= treatments)

The rebranding of the dry eye service to Tear Clinic in July 2017 and launch event provided the opportunity to showcase BBR Optometry Ltd.'s dry eye diagnostics in the form of mini-consultations. Existing BBR Optometry Ltd. patients were encouraged to bring family members and friends to the event. A specialist service is difficult to evaluate before purchase and direct experience of the service, and so the launch event provided a glimpse into the new service, and led to a spike in Tear Clinic activity. A study by Hindi et al. (2019b) found that patients felt the most effective promotional strategies to enhance the credibility of extended pharmacy services were first-hand experience and word-of-mouth. The Tear Clinic launch event in July 2017 followed by a visit from the mayor in September 2017 led to an exponential increase in dry eye related activity net profit and LipiFlow treatments.

BBR Optometry Ltd. adopted a strategy that focused on existing customers due to new customer acquisition being costlier. Mittal and Lassar (1998) reported that acquiring new customers can cost five times more than the costs of retaining current customers, and so it is more profitable to concentrate efforts on retaining current customers. In cases where services are long-term, such as in optometric care, customers rely heavily on credence qualities, that is perceived value of health advice, for service evaluation and employees have the potential to develop more personal connections with customers from building rapport over the years leading to greater customer relational value and satisfaction (Yoon et al., 2004; Chan et al., 2010; Fleming et al., 2005). Customers may have a greater incentive to remain involved with the company providing professional services, that is, affective commitment, if friendly and enjoyable interpersonal relationships add value for the customer (Patterson & Smith, 2003). Distribution of dry eye questionnaires to existing customers utilising BBR Optometry Ltd.'s current services was an attempt to gauge the need for a dry eye service. Leaflets regarding the service were placed in the waiting area visible to customers, and clinicians proactively distributed the leaflet to customers they deemed would benefit from the service. Clinicians were encouraged to engage in a conversation regarding the service if screening SPEED questionnaires completed on arrival to the practice prior to the eye examination totalled a score greater than zero, and if symptoms and signs of dry eye were noted.

Initially, the focus of service development was on customer acquisition via external referrals from fellow primary care and ophthalmology colleagues. Ophthalmology colleagues and nurses working in the hospital eye department were made aware of the dry service and were given leaflets to signpost and provide to patients attending eye casualty for non-urgent matters including suspect dry eye. In chapter six, we see that a proportion of people self-refer to eye casualty for advice regarding dry eye concerns. Dry eye is chronic but not sight threatening, so does not command priority in hospital practice. At first, the target for marketing the dry eye service were ophthalmic consultants within an 80-mile radius from Birmingham. An event at the Aston conference centre was organised to pitch

the idea of a mobile dry eye service led by BBR Optometry Ltd. and to begin a discussion amongst ophthalmology colleagues regarding possible interest and need for a mobile LipiFlow treatment service. Secondly, an educational open house style evening session was organised for local pharmacists and GPs at the practice to spread awareness of the Tear Clinic. Unfortunately, there was lack of engagement by eye health professional stakeholders for both planned activities. Thus, the focus shifted from capturing people for entry into the service by external clinical recommendation to redirecting marketing strategies towards the customer. Other BBR Optometry Ltd. activities that attempted to acquire new customers included:

- Demonstrated components of a dry eye consultation including use of LipiView II and performed a LipiFlow procedure on a customer for an audience of optometrists at the Nuffield Bristol.
- Provided a LipiFlow mobile service for consultants at the Midland Eye hospital, Solihull
- Attempted to contact the local firefighter department for community outreach and media exposure
- Created dry eye service leaflets for distribution at The Courtyard Centre for the Arts, which is the leading arts provider in Herefordshire and a registered charity. BBR Optometry Ltd. are "Friends of the Courtyard", members of the Courtyard's business club and provided sponsorship for the Director's chair appeal initiative.
- Utilised marketing services from Scope Ophthalmics and Pepperneck Ltd. to generate leaflets (see appendix 2.3) and event invitations.
- Presented on experiences in delivering a dry eye clinic at the 2017 BCLA international conference, and at the 2018 Herefordshire Local Optical Committee Annual General Meeting to further BBR Optometry Ltd.'s reputation as a provider of advanced dry eye care.

In the service blueprint presented in figure 2.6, all clinical examinations were carried out by the same optometrist. However, increasingly automated technology allows diagnostic testing such as corneal topography and optical coherence tomography, to be carried out by practice support staff rather than by the optometrist. Using practice support staff to carry out some functions, such as Tearlab testing and Lipiview II analysis, would allow the optometrist more time to spend on the interpretation of the results, emphasizing the SERVQUAL dimensions of assurance and empathy by explaining to the customer the importance of the test, its relevance to them and long-term management options.

The dry eye service continues to be reviewed in terms of process and physical layout using the service blueprint presented as a guide. There was an early issue with the optometrist inadvertently conducting over the phone consultations, which may have provided customers with assurance and

empathy, and perhaps yielded intangible benefits for the practice but at the actual expense of the practice. The automatic redirection of dry eye clinic related queries and acceptance of these phone calls by the optometrist was time-consuming for the clinician and did not always lead to a consultation booking. At the outset, these over the phone consultations gave the optometrist insight into customer concerns, and allowed rehearsal and trial of dialogue for both dry eye as a chronic condition explanations and discussions regarding treatment options. Further ongoing staff training in group and one-to-one settings both internally and via dry eye product suppliers, and creation of electronic and print resource materials to support staff and for customer information put an end to lengthy conversations outside of clinical time.

As a backstage action, it is important to have administration time allocated for the practitioner delivering the service. This dedicated time allows the completion of personalised reports and allows the practitioner to educate themselves with current literature to ensure evidenced-based management recommendations are given to customers. In the area of dry eye, new products and novel treatments are being developed to manage customer symptoms. For example, newer lubricants attempt to replace specific aspects of the tear film that are believed to be deficient, with the aim of stabilising the tears, protecting the ocular surface and reducing the level of ocular surface inflammation. The practitioner may need to attend workshops and conferences to learn about the latest research, and then find ways to adapt these findings into practical solutions for their customers to deliver the highest level of service quality.

Optional inclusions for a service blueprint include time indicators to assess service efficiency and whether or not customer expectations are being met, quality key performance indicators (KPIs), customer's emotional state, and sketches where words are not enough (Interaction Design Foundation, 2019). Depth can also be added to the service blueprint by noting moments of truth, internal and external pain points, and opportunities for improvement (Bitner et al., 2008):

- *A moment of truth* is the interaction between the customer and organization that must go right in order for the customer to have a quality experience. Moments of truth are critical encounter points with an organization that can shape a customer's impression (Duncan & Breslin, 2009).
- *Internal pain points* refer to gaps felt inside the organization that the customer is unaware of but leads to internal friction and inefficiencies.
- *External pain points* are felt by the customer and lead to the perception of poor service quality.

For example, the automatic redirection of dry eye queries to one optometrist was an internal pain point, which was soon resolved. Another internal pain point was the location of the TearLab Osmolarity system (TearLab Corp., San Diego, CA, USA), which consists of 3 components: a pen powered by a rechargeable battery, a test card with microchip, and system reader (NICE, 2015b). The TearLab osmolairty system was CE marked as an In Vitro Diagnostics Device (Class IIa) in October 2008, and is used at point of care to measure tear osmolarity (discussed in chapter 1), help diagnose dry eye and aid monitoring treatment (NICE, 2015b). The pen holds the test card that collects and analyses 50 nanolitres of tear fluid from the inferior lateral meniscus (NICE, 2015b). The system reader is a countertop unit that calculates and displays the tear osmolarity measurement on a liquid crystal display screen (NICE, 2015b). When a tear sample has been successfully collected, the user has a finite time (40 seconds) to return the pen to the system reader dock before the test information is lost (TearLab Corp, 2017). The system reader is affected by temperature and must not be placed in an area that can be influenced by external heating or cooling sources, such as adjacent to a computer or other equipment that gives off heat, next to an air conditioning or heating duct, or next to a window (TearLab Corp, 2017).

The TearLab system reader was originally located in a central room with other optometric diagnostics for routine eye examinations on the second floor of the practice building as it was used haphazardly, and a central location was key for potential use by four optometrists with consultation rooms on the same floor level. BBR Optometry Ltd. had a practice refurbishment in April 2016 and a room on the ground level (first floor) was allocated for dry eye related appointments along with the LipiView II Ocular Surface Interferometer with Dynamic Meibomian Imaging diagnostic unit (TearScience, Morrisville, NC, USA), which is also a countertop unit, although the TearLab osmolarity system remained on the second floor. This was an internal pain point for the practitioner delivering the service as well as a potential external pain point given the order of clinical tests (discussed in chapter one) and the journey of the customer through the practice in order to deliver the dry eye service were disjointed. Customers would arrive at reception, climb the practice stairs, have a few clinical tests, and be guided back down the stairs to the designated dry eye room where the remainder of the consultation would take place. These issues were soon remedied by relocating all dry eye diagnostics in one temperature controlled windowless room, and using the only consulting room with a reclining chair for in-practice treatments to improve customer comfort. One of the backstage actions of frontline staff is to calibrate the TearLab Osmolarity system prior to the start of clinics each day. The two pens are tested with an electronic check card each day to verify that the system is working within manufactured calibration specifications (NICE, 2015b). The optometrist delivering the service, tests each new batch of test cards with the normal and high osmolarity control solutions to verify the quantitative functioning of the osmolarity test cards (NICE, 2015b), and regularly monitors the test card supply.

In the practice's aim to be completely paperless for physical evidence of technological prowess and professionalism, and to improve the practice aesthetic, Microsoft surface tablets in addition to desktop computers were introduced. The primary uses of the tablets were to create appointments and carry out spectacle orders, and there was an attempt at one stage to trial paperless dry eye questionnaires via Qualtrics Survey Software. Utilisation of the Qualtrics Survey Software would have been useful in gathering information from consenting customers to monitor service demand in a manner less labour intensive than analysing hard copies of questionnaires. However, from direct observation and staff feedback, it was determined that the print physical copies of the questionnaire often served as a reminder for front staff to prompt customers to complete it. Although there was a practice network desktop link for the questionnaire, it was not being completed and often the tablets were misplaced.

BBR Optometry Ltd. established contact with a third-party supplier via Scope Ophthalmics, Adaro Optics in 2016 to maintain existing direct debits for clinical care, enhance service for contact lens customers and allow scope for home delivery of dry eye products. Adaro Optics are mentioned in figure 2.6, behind the line of visibility. The set-up of monthly direct debits is an example of a moment of truth, whereby dissatisfaction can follow if customers are incorrectly charged a given fee. Other moments of truth include customer travel to the appointment, and can take place at registration, in the waiting area, and during the consultation.

It is possible customer satisfaction can be affected by travel costs as for most customers, specialist services are not local (Steinbach, 2018). At BBR Optometry Ltd. there are several pay and display parking areas on the street where the practice is situated, and car parks nearby a pedestrian passageway. Travelling to an unfamiliar area for specialist consultations and competitively priced novel treatments can be stressful enough for a customer who may already be stressed about their health condition. Practice staff are trained to offer directions and guide customers to the practice website, which highlights these parking areas nearest the practice.

At the point of inquiry or appointment booking, it is important for minimum call holding time and for staff to have a friendly, helpful, and polite tone. Practice staff should be able to answer questions about products and procedures or refer questions as needed for immediate answer, ask customers for time and date preferences, encourage customers to check the practice website, and verbalise how the practice looks forward to seeing the customer. At the point of reception and being seated in the waiting area, it is important for customers to experience a clean, attractive and comfortable area with educational materials displayed to stimulate queries. Reception staff should immediately welcome customers and have a professional appearance. At the point of consultation, the optometrist should arrive with minimal wait, greet customer warmly, wash hands in front of customer before performing

any clinical tests, explain the purpose of each test in layman's language as performed, emphasize concern for the customers' long-term ocular health, encourage questions, summarize findings, hypothesize as to the cause of expressed problems, and recommend the best solution to the customer's need. Most customers want their concerns to be addressed with practical solutions, and feel they are being listened to and treated as an individual.

The process of report generation is automated with templates on the practice software created to improve the ease of recording clinical test results and presenting outcomes to customers in the form of a report that can be printed or emailed. Customers who do not have internet access are given paper copy, tear away, management plans that can be individualised from templates created by Scope Ophthalmics including images of the products recommended and tick boxes identifying the recommended products whilst they are waiting for the full report to arrive in the post. At present, BBR Optometry Ltd. does not use any formal measurement techniques to ensure the level of service quality that management is striving to achieve and relies on customer complaints. The service design does not currently provide any opportunities to gather customer feedback.

2.3.3: Retrospective analysis of customer activity following use of the dry eye service at BBR Optometry Ltd.

In total, there were 94 customer records analysed retrospectively. Data was analysed for customers who had a dry eye consultation from a time period of one year prior to the consultation and one year following the dry eye review appointment, which typically occurs one-month post-consultation. There were 39 customers with available information for one year prior and one year following the review visit. There were 68 customers with available information for one year prior and less than one year following the review visit. The average post-dry eye review appointment time period for these customers was 5.22 ± 2.66 months. There were 13 records excluded from the analysis because these customers were also contact lens wearers, and contact lens wearers by nature may require multiple appointments depending on whether they are new or existing wearers.

The average age of customers attending for a dry eye consultation was 65.71 ± 12.72, and 67 were females and 27 were males. Approximately 37% (35/94) of customers were seen for a dry eye consultation less than one month following their eye examination, and 42% (39/94) were seen between one to six months later. There were three customers seen on the same day for a combined eye examination and dry eye consultation appointment, an unknown time frame for nine customers, and the remaining eight customers were seen for a dry eye consultation over eight months following their eye examination.

At the time of the dry eye consultation, 24% (23/94) of customers were Eyelife™ members. Overall, 28% (26/94) of customers were new to the practice and attending specifically to utilise the dry eye service. The distribution of customers' Eyelife™ status prior to and following their dry eye consultation can be seen in figure 2.7.

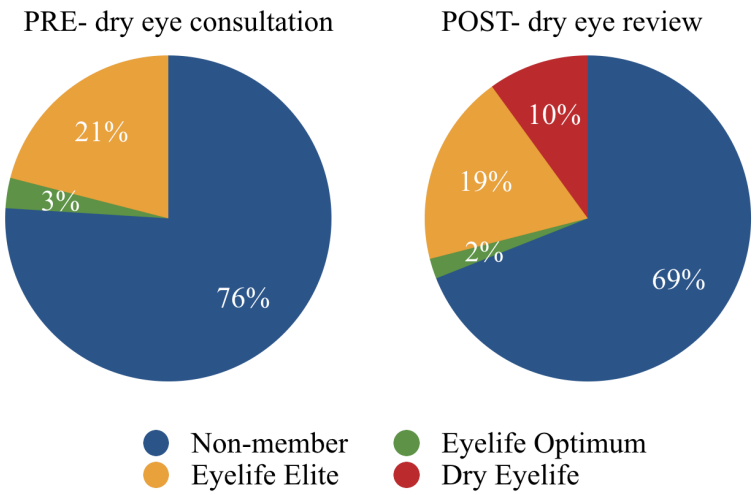


Figure 2.7: Distribution of customers' Eyelife™ status prior to and following their dry eye consultation.

Eyelife™ conversions and upgrades occurred for 11% (n=10) of customers following their dry eye review appointment, whilst others continued as Non-Eyelife™ members or on their current tier of Eyelife™ without upgrading. Half of these upgrading customers were non-Eyelife™ members at the time of consultation, and two of these were new customers to the practice and upgraded to Dry Eyelife™. The breakdown can be seen in table 2.6.

Eyelife™ Conversions & Upgrades	No. of customers
Non-member to Elite	1
Non-member to Dry	4
Optimum to Dry	1
Elite to Dry	4

Table 2.6: Summary breakdown of Eyelife™ conversions and upgrades following the dry eye review appointment at BBR Optometry Ltd.

Customers purchase their first supply of recommended dry eye products at the time of the dry eye consultation (included or additional fee based on Eyelife™ status), and often purchase additional products, including ocular lubricant at the time of their one-month review appointment. There is also the option of signing up to Dry Eyelife™ and having home delivery of products. For traditional at-home therapies supplied at BBR Optometry Ltd., most 7.5 ml bottles of ocular lubricant offer a one month's supply of product, and lid cleanser about two months' worth of product. Most microwaveable eye masks recommend replacement from six months to one year. The yearly cost of

at-home therapies to the customer were calculated for each customer based on their specific product recommendations and expected frequency of use.

In regards to dry eye product transactions, where full year post-consultation information was available (n=37):

- The actual annual total value of product transactions fell below what was expected consistently.
- 17 customers did not purchase any product outside what was included in their dry eye consultation fee
- All customers who did not purchase any dry eye product outside of their dry eye consultation, that is one year before or after, were all non-Eyelife^{TM} members. Only six of these 17 customers were new to the practice.
- 13 customers purchased more dry eye products post-dry eye consultation (eight Non-members, one Eyelife^{TM} Optimum, four Eyelife^{TM} Elite). Three of the non-member customers were new to the practice and two of these became Dry Eyelife^{TM} members
- Seven customers purchased less dry eye products post- dry eye consultation (four Non-members, one Eyelife^{TM} Optimum, two Eyelife^{TM} Elite)

Following a dry eye consultation and review appointment, an annual dry eye review appointment outside the routine eye examination is recommended. The recommendation is that most adults should have their eyes tested every two years, however, an optometrist may recommend an eye examination for adults more often than every two years if the person has been diagnosed with diabetes, are aged 40 years or over with a family history of glaucoma, are aged 70 years or over, or if it is deemed clinically necessary by the practitioner (NHS, 2016). Eyelife^{TM} members tend to have eye examinations yearly. In regards to the number of clinical appointments, where full year post-consultation information was available (n=37), the customers could be split into thirds based on changes in their attendance seen in table 2.7. For customers attending for more appointments post-review, there were on average 2 ± 1 more clinical appointments.

	Greater attendances	Fewer attendances	No change
Number of Customers	12	12	13
Eyelife™ pre-consult status ratio (Non-member: Optimum: Elite)	10: 2: 0	9:3:0	11:2:0
Reasons	BlephEx™ treatment LipiFlow treatment Dry eye review (n=4) Due for eye examination Pre- and post-operative cataract surgery appointment	Not due or overdue for eye examination Prior to dry eye consultation had post-operative cataract surgery or glaucoma referral refinement appointment Previously attended for 1-3 additional 20 minute clinical visits	Lost to follow-up after LipiFlow treatment Attended practice for dry eye consultation & review only

Table 2.7: Comparing number of clinical appointments one-year following a dry eye review appointment to visits in a one-year time period prior to the dry eye consultation.

In regards to spectacle purchase transactions, where full year post-consultation information was available (n=37):

- There were nine customers who had more spectacle purchase transactions following their dry eye review than prior to their dry eye consultation. All but two were non-Eyelife™ members prior to the dry consultation (one Eyelife™ Optimum the other, Elite). The average spectacle dispense value for this group was £459.14 ± £350.12. This seemed to be related to customers purchasing spectacles following their eye examination within the one year time frame following their dry eye review. One non-member customer who became a Eyelife™ Elite member following their dry eye consultation had purchased spectacles at a transaction value of £429.00 in the one-year period prior to the dry eye consultation and in the year following the dry eye review at a transaction value of £592.82. More than half of this group also converted or upgraded their Eyelife™ status (Non-member to Elite: one; Non-member to Dry: two; Optimum to Elite: one; Optimum to Dry: one).
- There were nine customers who had less spectacle purchase transactions following their dry eye review than prior to their dry eye consultation. Prior to their dry eye consultations, there were four Non-members, one Eyelife™ Optimum, and four Eyelife™ Elite members. There was only one customer from this group who upgraded from Eyelife™ Optimum to Elite, whilst all others did not change their Eyelife™ status. This seemed to be related to these customers having their eye examinations in the one year period prior to their dry eye consultation.
- There were no changes in spectacle purchasing behaviours noted for the remaining customers (n=19) who did not purchase spectacles and were all non-members with the exception of one customer who was an Eyelife™ Optimum member at the time prior to the dry eye consultation. There were no conversions or upgrades post- dry eye review.

2.4: Discussion

2.4.1: Identifying the local demand for a dry eye service and the dry eye customer

Completed questionnaires were analysed retrospectively and requirements for reception staff to provide clarification on any questionnaire items was not reported. There was a larger number of completed SPEED versus OSDI questionnaires collected over a similar timeframe, which may be due in part to greater customer engagement with a questionnaire having fewer items. Questionnaires can be tedious and time-consuming for some respondents, and chapter three will also explore methods to determine the most important items from the SPEED and OSDI in a sample of dry eye sufferers. Additionally, the number of completed questionnaires could have been limited by factors such as customers arriving late for their appointments with not enough time allocated to participate or by varying levels of staff co-operation in administering the questionnaire. The current contact lens wearing status of questionnaire respondents were not determined, which may reflect a limitation to the study. The potential relationship between ocular discomfort and contact lens wear will be discussed in chapter five.

Focusing on the results of the pairwise comparisons, there were statistically significant differences in the distribution of total OSDI scores between the normal OSDI classification group and all other symptomatic OSDI groups. Approximately half of the customers segmented in the normal OSDI classification scored a total of zero, meaning these participants self-reported no symptoms of dry eye whatsoever. There were no statistically significant differences in the total OSDI score distributions between the mild and moderate, mild and severe, and moderate and severe groups. For the distribution of total SPEED scores, the pairwise comparisons across SPEED classification groups were statistically significant for all possible combinations. There were no statistically significant differences in the age distributions across symptom severity classifications for either of the questionnaires.

There were a higher proportion of normal cases identified by the OSDI questionnaire, and a higher proportion of mild to moderate dry eye cases identified by the SPEED questionnaire. The time of year from which the questionnaires were collected may partially account for this observation, considering the location of BBR Optometry Ltd. in Hereford as a trading centre for a wider agricultural and rural area. Hay fever, an allergy caused by pollen or dust, can cause considerable ocular discomfort including watery eyes, which can mimic dry eye symptoms and is an item appearing only on the SPEED questionnaire (“burning or watering”). A greater number of pollen types have peak release periods that occur in the months when the SPEED questionnaire was administered (April-September) compared to when the OSDI was administered (October- March) (College of Optometrists, 2018). Ideally all customers would have completed both questionnaires or the questionnaires would have been administered over the same months. However, one of the main

objectives of this study was to determine the local demand for a dry eye clinic versus a detailed comparative analysis of the OSDI and SPEED questionnaires. Finis et al. (2014a) in a retrospective analysis determined that although both the OSDI and SPEED were found to be suitable for detecting symptoms of dry eye that the results of the questionnaires could not be used interchangeably.

The proportion of customers self-reporting absolutely no dry eye symptoms, scoring zero, from the completed questionnaires was 38% for the OSDI and 20% for the SPEED. Therefore, the majority of respondents reported some degree of ocular discomfort whether or not the symptoms transpired to be attributed to a dry eye problem, which is not known from the current analysis. Overall, the average age of respondents was 64.47 ± 14.57 and 65.60 ± 15.25 for the OSDI and SPEED questionnaires respectively, which may reflect the age demographic of the practice location. The number of people aged 85 or over has increased by 50% between 2001 and 2016 in Herefordshire compared to 38% nationally (Herefordshire Council, 2018). Some research shows an increase in dry eye prevalence with age (McCarty et al., 1998; Lee et al., 2002; Schaumberg et al., 2003; Schaumberg et al., 2009; Farrand et al., 2017; Caffery et al., 2019), whilst others do not (Schein et al., 1997; Chia et al., 2003; Lin et al., 2005) perhaps due to use of samples with a narrower age range. It has been postulated that the higher incidence and prevalence of dry eye in women may be due to sex-related differences attributed to the effects of hormones and also disparities in care-seeking behaviours related to gender (McCarty et al., 1998; Moss et al., 2000; Chia et al., 2003; Moss et al., 2008; Mather et al., 1998; Smith et al., 2004; Sullivan et al., 2017).

Grouping customers with needs or priorities in common and strategizing to target them is a marketing technique referred to as market segmentation (Toor, 2014). For example, adolescents or teenagers were identified as a segment of the contact lens market who were the most promising category to achieve growth by penetration (Toor, 2014). Therefore, tactics such as special discounts, digital promotion, and promotion of daily disposable contact lenses for convenience were employed to target this segment of the market (Toor, 2014). Perhaps based on the demographic profile, and differentiation of the severity types of dry eye from a sample of BBR Optometry Ltd. customers attending for a full eye examination, a different marketing mix in terms of product or service, price, promotion and place could be used to target potential benefactors of the dry eye service, i.e. more people with mild-moderate dry eye symptoms, and women over the age of 60.

2.4.2: Using a service blueprint to facilitate customer focused optometric services

In the service marketing literature, affective responses have been associated with behavioural intentions such as loyalty, recommendation and willingness to pay more in hedonic (e.g. tourism, leisure, entertainment and luxury), and utilitarian service contexts such as in banking and healthcare

services (Bigné et al., 2008; Chan et al., 2015; Jani & Han, 2015; Koenig-Lewis & Palmer, 2014; Ladhari, 2009; Ng & Russell-Bennett, 2015; Ladhari et al., 2017). It is thought that emotions act as the mediator in the service process with customers' emotional reactions influenced by perceived service quality and servicescape, and in turn customers' emotional reactions impact perceptions of product quality and behavioural intentions (Ladhari et al., 2017). In an optometric setting emotions can be elicited by customer interactions with optometrists and support staff, which will most likely be positive and favourable if the staff present as competent, credible, reliable, and empathetic whilst offering a personalized service (Ladhari et al., 2017). An understanding of the service blueprint can contribute to staff feeling confident in regards to service delivery. Customers are more motivated to recommend the service either by word-of-mouth or via social media if they had a positive service experience.

Ladhari et al. (2017) investigated the role of emotional satisfaction in a Canadian optometry clinic and found perceived service quality (service reliability, empathy, assurance and responsiveness) had a greater effect on customer emotions than did the service environment for traditional services. Reliability refers to the extent to which optometrists and practice staff offer the promised service correctly the first time, assurance reflects the aptitude of staff to inspire trust with their knowledge, responsiveness refers to the willingness to provide prompt service, and empathy refers to the level of individualised attention the practice staff offers customers (Ladhari et al., 2017). Ambiance in the form of light and odour, and layout also influenced emotional satisfaction and purchase intentions (Ladhari et al., 2017). In an increasingly competitive environment, optometric practices need to continue to create value for their customers by differentiating their product and service offerings, and by providing a satisfying experience, which can be achieved through the use of structured planning with a service blueprint. There are various online resources for the busy practitioner to learn about principles regarding services (appendix 2.8).

A qualitative study conducted by Hindi et al. (2019b) in Greater Manchester, England, used marketing theory to investigate factors which could influence the utilisation and integration of community pharmacy services for patients with common long-term conditions, namely type-II diabetes, asthma, or chronic obstructive pulmonary disease. Data collection and analysis from focus groups including patients with type-II diabetes and respiratory conditions, pharmacists and GPs were framed using the "7Ps" extended marketing mix that an organization should account for to successfully market their service to target customers which are "product, price, place, promotion, people, process, and physical evidence." (Hindi et al., 2019b) Appropriate distribution of services within primary care, improvements in communication and incentivising joint working between pharmacies and GP practices, enhancing consistency and quality of pharmacy services, and strategically promoting community pharmacy services were identified as influential factors in the

integration of community pharmacy services within the primary care pathway for long-term conditions (Hindi et al., 2019b).

Patients with long term conditions, such as dry eye, require regular monitoring of their health and management regimens in order to ensure appropriate use of medication or products and lifestyle education (Hindi et al., 2019b). The recommendations from stakeholders in the Hindi et al. (2019b) study could be extended to optometric services. For example, pharmacy services with clear specifications focusing on specific interventions to reduce variability in the service process were preferred by stakeholders, highlighting the importance of a service blueprint and communication of a condensed version for fellow health care providers and customers to understand the service workflow or customer journey intended to deliver quality care. Similar to the recognition of the capabilities of community optometrists by ophthalmologists to be discussed in chapter six, the added value of pharmacy services for patient convenience and freeing up GP time to focus on more complex cases was noted although inter-professional tensions arising from funding conflicts was thought to be a barrier for collaboration between GPs and pharmacists. The physical evidence in regards to limited space and poor-quality consultation rooms affected the lack of confidence view adopted by patients and GPs in community pharmacies' ability to expand services, which could apply to optometric services depending on whether practices are perceived as more commercial or retail than clinical.

Community optometry services have traditionally been separate from pharmacy and GP services, which is perhaps why primary care colleagues may not be aware of or necessarily supportive of private specialist services due to concerns about financial motives, competencies and encroachment on professional boundaries as seen with extended pharmacy services (Bradley et al., 2012). Considering many patients seek endorsement of specialist services by their GP, a lack of GP awareness or support could greatly impact the awareness, demand and use of that service as also seen with pharmacy services (Hall et al., 2018; Hindi et al., 2019a). For this reason, the primary focus for customer acquisition was through primary care colleagues, and BBR Optometry Ltd. hand delivered invitations to local GP surgeries and pharmacies for educational, 'service taster' events hosted at the practice. There was little uptake, however, existence of an appropriate system to share relevant information with GPs was noted in the creation of the service blueprint to improve integration of services (Hindi et al., 2019b).

There is an automated system and protocol of generating reports with clinical test results and planned management following each dry eye consultation. The customer often requests a copy of the report be sent to their GP for both information, and to request prescriptions for recommended products. It is hoped that positive outcomes and demonstration of monitoring with the latest diagnostics via dry

eye reports, and access to novel treatments will raise the profile of BBR Optometry Ltd. as a specialist dry eye service provider in the community. It is protocol for optometrists participating in their locally commissioned ocular emergency service (described in chapter six) to provide GPs with a letter outlining the nature of the service user's visit and exam outcome. When the service user is deemed to have a dry eye problem, a Tear Clinic leaflet for information on the dry eye service is given to the individual and also sent to the GP with the exam outcome report.

Attempts at service expansion by providing a mobile service for other optometric practices who could not afford dry eye diagnostics and novel treatments but wished to offer these services to their customers was met by conflicting views. The mobile service offered a viable alternative to customers with signs and symptoms of evaporative dry eye secondary to Meibomian Gland Dysfunction (MGD) without the need for large capital investment in a unit and the continued expense of stocking consumables by eye health care providers. There were fears from optometrists that customers would switch providers due to the perception that their practice was inferior to the mobile service provider's practice. The plan for a mobile service could potentially still be feasible and profitable for the practice in private hospital settings for pre- and post-operative refractive surgery care depending on the lead ophthalmologist's approach to ocular surface health.

TearScience, a privately held medical device manufacturer dedicated to evaluating Meibomian gland health and treating MGD and suppliers of BBR Optometry Ltd.'s LipiView II and LipiFlow were acquired by Johnson & Johnson Vision's surgical vision operating company, Abbott Medical Optics, in 2017. BBR Optometry Ltd. were early adopters of the TearScience technology and now with the backing of Johnson & Johnson Vision, a well-known global leader in eye health, there may be more UK representation for support and exposure to enhance and promote the dry eye service. Other future endeavours for the business would be to capitalize on digital media and offer online booking for all appointments to improve the ease and convenience of the service.

Retail aspects of an optometric service can be monitored with KPIs such as same day conversion, profit, and average spend per customer, whilst customer service aspects can be measured using questionnaires including the SERVQUAL, SERVPERF and SERVPEX (Parasuraman et al., 1988; Cronin & Taylor, 1992; Robledo, 2001). A common question used in patient questionnaires to measure patient satisfaction levels is "how likely are you to recommend our service to friends and family if they needed similar care or treatment?" (Steinbach, 2018) The possible answers include "extremely likely, likely, neither likely or unlikely, unlikely, extremely unlikely, and don't know", which give a good indication of a patient's experience in routine patient surveys (Steinbach, 2018). Further research could apply a measure of service quality such as SERVQUAL to yield a more

detailed picture of what customers think about the dry eye service at BBR Optometry Ltd. rather than a few items regarding customer service.

Perceived service quality can be measured in terms of ratings with respect to specific attributes relating to the customer's experience using a five-point Likert scale ranging from very dissatisfied to very satisfied, which can be used to improve overall satisfaction and increase loyalty (Lonial & Raju, 2015). Customer care attributes could be the optometrist's explanation of the customer's condition and treatment, explanation of expected outcomes from treatment, the optometrist's willingness to include the customer in decisions about care and treatment, the thoroughness of care, and willingness of the optometrist to answer questions. The current BBR Optometry Ltd. dry eye service design does not provide any opportunities to gather customer feedback other than from customer complaints or direct feedback to the optometrist carrying out the consultation in the form of praise or criticism.

Examples of feedback from customers:

- *"Why is the specialist performing all the tests?"*
  The practitioner originally envisaged the service to function as seen in other specialist clinics, where the specialist interprets the findings and communicates recommendations rather than collecting data or conducting the required tests. From this viewpoint, customers may judge the actual specialist nature of the practice if the specialist is taking part in all aspects of the customer journey similar to if a chef acts as the host, waiter and chef in a restaurant setting. The collection of data by another member of staff gives the practitioner time to digest findings, and to explain and communicate findings rather than seeming rushed to complete all tasks. Additionally, treatments such as BlephEx™ microblepharoexfoliation could be conducted by clinical support staff with sufficient training, likened to a dental hygienist. This treatment can be standalone or performed in conjunction as a priming procedure prior to LipiFlow by the practitioner.
- *"I was happy with the consultation and clinical review but not the booking process."*
  This point highlighted training needs for staff. In one particular case, the customer was wrongfully given the standard advice for those attending regular eye examinations which was the chance they could be dilated and not to drive prior to their appointment. This advice led to great disruption to the customer including having her partner take time off work to drive her to the practice being located outside the county.

Some large chain optometric practices (referred to as multiples), deliver electronic surveys to their customers following an eye examination with incentives such as entry into a draw to win £100 worth of vouchers or a gift card for completion of the survey. Other optometric practices simply list a contact on their website with whom to address complaints for customer feedback. Customer insight

programmes like sporadic mystery shopping or customer polling with satisfaction index ratings can be useful for service improvements but can also be labour intensive, costly, and may not produce information to help service providers make a practical difference to their business (Yavas et al., 2008). Jill Clark, Specsavers Director of Customer Services, comments in a case study for Maze Feedback Ltd. that use of the Maze System software enables collection of customer feedback at store level on a daily basis and connects this to company strategic imperatives to further reduce provider gap one (Maze Feedback Ltd., 2019; Parasuraman et al., 1985).

Training materials to target key strategic themes such as reducing waiting times have been developed from customer engagement with the Maze system, and there is specific focus on neutral responses from surveys to understand the customer's response in order to rectify matters arising and provide immediate remedies where appropriate. The Maze System allows stores to motivate their employees on a daily basis through short morning meetings offering praise, defining focus areas, and identifying challenges and solutions that can be actioned. The Maze System provides a process of continuous improvement and learning for store colleagues, and can be exploited across other areas of the business including internal surveys covering employee engagement. The "bottom line" business benefit from utilising a system like Maze is to retain customer loyalty for future needs and to convert customers to ambassadors of the brand.

Operational issues highlighted in the generation of the service blueprint included:

- Products issued to Non-Eyelife^{TM} customers at the time of their Tear Clinic consultation that are factored into the consultation fee were not being scanned through the practice management system in order to keep an accurate record of stock. Staff were trained and resource materials provided with step by step, screen by screen instructions on how to enter products onto the practice management system. A backstage action of staff is to keep stock of all diagnostic and treatment consumables as well as product inventory.
- Optometrists offering treatments prior to full dry eye work up in an ad hoc fashion, putting the clinician performing the treatment at risk and in an uncomfortable situation. There was a need to alter the practice culture and to close gaps within the service. On one occasion, a customer attended for an in-practice treatment (*Demodex* tea tree oil) with an optometrist who did not recommend the treatment and in the absence of any preliminary dry eye testing. The customer noted there was no prior discussion of fees, timings, what to expect and no written information given for the customer to make an informed choice regarding the treatment suggested. The fact that the customer attended as she was told despite understanding why, demonstrates the level of trust that some customers have within the practice. However, this incident resulted in 20 minutes of wasted clinical time as the customer was not a subscriber to Eyelife^{TM} and there was not enough time allocated to

complete a full consultation. The practitioner could not justify charging the patient for a discussion that should have occurred at the time of the recommendation.

- Additionally, there was an issue with optometrists citing special fees for certain customers, which in turn diminished the service structure and offering. These customers offered a consultation at a reduced fee did not return for dry eye follow-up or interact in any other capacity with the practice business. The practice management software now incorporates coloured coded labelled buttons that automatically generate the appropriate fees when selected on the onscreen till to avoid any confusion.

It is now standard procedure for all those 18 years old or over presenting for an eye examination to complete a SPEED questionnaire in order to identify those people who may benefit from a Tear Clinic consultation and to bring their attention to the Tear Clinic service. Reception staff actively engage with customers they notice purchasing dry eye related products who have not had Tear Clinic consultations by discussing the service and providing written material to promote awareness of the service. Often reception and clinical assistant staff are multi-tasking and it is not possible to discuss the service completely, which is why a leaflet and two-page document outlining what to expect if you book an appointment, fees, and the "do's and don'ts" prior to attending your appointment was created. The trifold leaflet does not contain any fees, however the document accessible on all practice desktops is printable and changeable when needed. Similarly, the practice website contains specific consultation and treatment fees in a PDF document, which can be altered as the market changes by management staff.

Reception staff include the SPEED questionnaire with the customer's record as one of the results of the pre-assessments presented to the optometrist. The presenting complaint may or may not be dry eye related but the results of the SPEED questionnaire can facilitate a conversation on the Tear Clinic service offering if self-reported symptoms of dry eye could not be addressed in full or these symptoms were secondary to a primary concern. Development of the blueprint also led to the realisation of a need for consent forms for in-practice treatment to ensure customers are making a voluntary informed decision about whether or not to proceed with treatment that was recommended by an eye health practitioner and accept the risks associated with the treatment including the possibility of no effect. The forms are signed by both the customer and performing optometrist, and scanned to the customer's record.

A service blueprint can be simple or intricate and complex with diagrams for each step and fully developed internal processes to isolate problems in the service process (Wilson et al., 2016). Various purposes for a service blueprint can be seen in table 2.9 (Fließ & Kleinaltenkamp, 2004). Service blueprints are useful as they draw attention to operational deficiencies, suggest critical points for

measurement and feedback in the service process, and facilitate a platform for innovation (Wilson et al., 2016; Bitner, 2008). Service blueprinting allows visualisation of the entire service system to enhance understanding of the process, and provides opportunities for discussions on service design which may involve agreements and compromises. Analysing a blueprint helps direct discussions regarding a service, and makes it is easier to suggest changes in the patient journey that may result in better service quality and gauge efficiency of work within an organization. For example, upskilling staff to carry out the dry eye diagnostics in order to save clinical chair time, and allow the optometrist to be the interpreter of clinical tests and explainer for management of a complex dry eye problem.

Customer participation refers to the degree of effort and involvement required to produce and deliver the service. The level of customer participation in a dry eye service involves following pre-appointment instructions, providing information to the service provider on ocular and relevant medical history and symptoms, and following agreed recommendations. Despite written instructions, some customers attended dry eye consultations wearing their contact lenses, which can affect the assessment of the tear film. In one case, the customer was happy to rebook their appointment but this resulted in wasted clinical chair time. Customers are now also reminded verbally when confirming their appointment of not to use any drops or wear contact lenses prior to their appointment. Future technological advancements may mean customers can book their own appointments and replenish their dry eye products via an online account with the practice. One of the aims of customer participation is to reduce the costs associated with delivering the service (Lovelock & Young, 1979).

Purpose of the service blueprint	Area of focus & Questions that may be asked
Understand the customer's view of the process or the customer experience	Read the blueprint from left to right in the customer action area • How is the service initiated by the customer? • What choices does the customer make? • Is the customer highly involved in creating the service or are few actions required of the customer? • What is the physical evidence of the service from the customer's point of view? • Is the evidence consistent with the organization's strategy and positioning?
Understand contact employee's roles	Read the blueprint from left to right directly above and below the line of visibility • How rational, efficient and effective is the process? • Who interacts with customers, when and how often? • Is one person responsible for the customer or is the customer passed off from one contact employee to another
Understand the integration of the various elements of the service process or to identify where particular employees fit into the bigger picture	Analyse the blueprint vertically • What actions are being performed backstage to support critical customer interaction points? • What are the associated support actions? • How are handoffs from one employee to another taking place?
Service redesign	Look at the blueprint as a whole • How might the complexity of the process be changed? • How will changes from the customer's point of view impact the contact employee and other internal processes and vice versa? • Could the service system be changed to improve overall efficiency and productivity? • Are there likely bottlenecks or failure points in the service process where improvement measures can be introduced and failures tracked to avoid recurrence?

Table 2.9: Excerpt adapted from Wilson et al. (2016) that demonstrates a service blueprint can be read in different ways depending on the purpose.

Once a service process has been successfully implemented, continual evaluation is required to ensure continued effectiveness and efficiency for the business. It is important that customer feedback or the customer perspective is considered in the future to understand customers' expectations and deliver high quality service. There is evidence in the literature demonstrating that frequently, researchers do not report outcomes valued by patients, referred to as customers in this discussion, who are the most important stakeholders directly affected by the findings (Saldanha et al., 2018; Saldana et al., 2017; Alkhaffaf et al., 2017; Le et al., 2016; Glasziou et al., 2014; Chalmers & Glasziou, 2009).

There are many examples of service innovation in optometric care and it is important that services remain customer focused or centred. Wright & Diamond (2015) introduced a new model of glaucoma service delivery whereby technicians and optometrists triage people with glaucoma into groups defined by risk of blindness, allowing virtual review via an internet-based virtual clinic of those at higher risk by a glaucoma specialist. This shared care glaucoma programme aims to reduce the risk that people are treated or followed-up unnecessarily (Wright & Diamond, 2015).

Although the responsibility for commissioning vision screening for children lies with local authorities and it is not mandated, the UK National Screening Committee recommends children aged four to five years old undergo vision screening in an orthoptist-led programme to detect amblyopia (PHE, 2017). Donaldson et al. (2018) distributed online surveys and questionnaires to parents of children in primary school reception and year one classes from 14 schools across five London boroughs to investigate the attitudes of parents towards eye care for their young children and possible barriers to accessing eye care for this age group. The study found that only 15% of families whose children attended a school with a screening programme in place knew of its existence, and there were parental misconceptions around eye care, which highlighted the need for marketing efforts to spread awareness of the service and to improve education around the importance of utilising existing vision screening programmes (Donaldson et al., 2018).

Subtle macular abnormalities are often the cause of an unhappy patient following an optimal surgical outcome for cataract surgery (Klein et al., 2016; Hirnschall et al., 2016). A prospective, interventional case series conducted by Sudhalkar et al. (2019) aimed to determine the utility of routine preoperative OCT examination to detect asymptomatic macular pathologies in those scheduled for cataract surgery. Subclinical macular changes detected with OCT were found in 9.21% of eyes scheduled for cataract surgery, which in turn influenced the choice of intraocular lens (IOL) or choice of concurrent therapy (Sudhalkar et al., 2019). Although the asymptomatic lesions did not seem to significantly influence postoperative visual acuity in the short term for the case series presented, it was recommended that OCT may be appropriate for those considering multifocal IOL implantation for preoperative counselling and to manage patient expectations (Sudhalkar et al., 2019).

Multiple performance measures may be considered in predicting the success of a new service including financial performance in regards to revenue growth, profitability and return on investment, and relationship enhancement referring to the impact of a new service on customer loyalty and image enhancement (Normann, 2000). Utilitarian services tend to focus on service quality and operational metrics such as waiting time to predict customer satisfaction and customer loyalty, and the role of emotions should also be considered (Rychalski & Hudson, 2017). The innovation and adoption of new services is a planned process with elements of improvisation and anarchy as development and delivery of the service often occur simultaneously (Edvardsson et al., 1995). A service blueprint can help facilitate the design of a new community optometric service as demonstrated in this case study of the dry eye service at BBR Optometry Ltd.

2.4.3: Service utilisation, customer switching, customer engagement and business recommendations for BBR Optometry Ltd.'s dry eye service

Overall the majority of customers (72%) utilising the dry eye service were exisitng BBR Optometry Ltd. customers and of the new customers to BBR Optometry Ltd., only two of the 26 converted to Eyelife™ members (both to Dry Eyelife™) demonstrating the difficulties associated with acquiring new customers. Dr Patel, in her doctoral thesis (2015), demonstrated that monthly payments offer an alternative business model to the traditional loss leading model for high street optometric practice, and enables optometric services to be self-sustainable without cross subsidy with optical product sales. The loss leading business strategy attempts to attract customers by offering low-priced private eye examination fees in the hope that customers will purchase high- margin spectacles and relies on a high volume of sales. This strategy works well for refraction based traditional eye examinations but may form a barrier to widening the scope of clinically oriented services within optometric practices.

Dr Patel (2015) determined from a sample of BBR Optometry Ltd. customers that Eyelife™ Elite members generated greater clinical service revenue and profits compared to customers paying fees at point of sale. Eyelife™ Elite members had a significantly greater mean spectacle dispense rate compared to the non-member group, with 63% of members as opposed to 30% non-members purchasing more than one pair over the course of the 18-month retrospective audit (Patel, 2015). The initial average spend on spectacles before discount was found to be statistically greater for Eyelife™ Elite members suggesting the discount incentive Eyelife™ offers, encourages customers to upgrade to higher priced products (Patel, 2015). In regards to the dry eye service, the majority of new customers had travelled from outside the county as far as London and Singapore to specifically utilise the service for consultaitons or novel treatments, and therefore did not plan to interact with any other aspects of the business. These customers did not see the benefit of subscribing to Eyelife™ due to geographical reasons, which would not allow convenient regular access to the practice for future services.

New customers attending as a result of their own online research or at the recommendation by primary or secondary care colleagues tended to be geographically based outside of Hereford (e.g. Gloucestershire, Daventry, Dudley, Coventry, Bristol, London, Solihull, Northampton, Cyprus, Powys), and so failed to return for follow-up. Customers failing to attend their review appointments were contacted via telephone by the optometrist who conducted the consultation to determine reasons for failing to attend. One customer from Wolverhampton opted out of returning for the review appointment because there was symptomatic improvement after following the recommended management plan. The customer thanked the optometrist for their care and stated she would return if any problems were experienced. Another customer failed to return for review following LipiFlow

treatment because although there was “slight” symptomatic improvement, it was not at a level of improvement the customer had hoped or expected.

In the current analysis, only 11% of customers (4/37) attended for a dry eye review one year following their initial dry eye consultation and review appointment. In a prospective telephone survey for people who were lost to follow-up (i.e. discontinued visits for > two years) in a dedicated hospital-based dry eye clinic, three broad categorization groups emerged to explain failure to attend: stabilized dry eye condition, personal/social factors and perceived insufficiency of healthcare delivery (Poon et al., 2014). Poon et al. (2014) determined from a cohort of dry eye patients that loss to follow-up was relatively common, with females and older patients less likely to fail to attend. The most common reason for loss to follow-up was stabilized dry eye condition where the condition could be self-managed, especially for patients younger than 50 years of age, and more likely due to personal/social reasons in patients older than 50 years of age (Poon et al., 2014). Personal and social reasons included perceived obstacles to attending further visits, such as direct and indirect costs, and the inconvenience of commuting as there is only one national center with a dedicated dry eye service in Singapore (Poon et al., 2014). Patients in the dry eye clinic with other pressing systemic diseases considered dry eye to have a lower priority in their hospital visits, and conditions such as anxiety and depression associated with dry eye were also found to affect a decision to return to the dry eye clinic for review (Poon et al., 2014). Dry eye as a condition may itself be explanatory for loss to follow-up, as it is known to fluctuate in severity with customers failing to attend for review if there is a substantial symptom-free period or symptoms are perceived to be tolerable (Poon et al., 2014). Poon et al. (2014) postulate that dry eye patients suffering from severe symptoms or anxiety may require more consultations for immediate relief or reassurance beyond what existing resources can provide, leading to frequent switching of providers and loss to follow-up.

Customer switching behaviour is a result of increased competition and the ability to shop comparatively whereby customers continue to use the service category but switch from one service provider to another (Keaveney & Parthasarathy, 2001; Nasir & Nasir, 2005). It is important to analyse customer satisfaction and service quality to predict potential defection causes, and develop strategies for customer retention and loyalty (Nasir & Nasir, 2005; Lonial & Raju, 2015). Russ (2008) suggests monthly payment plans may increase customer retention by introducing a switching barrier whereby customers are more likely to continue at the current practice because choosing to cancel the direct debit means contacting the practice or bank first. In a retrospective audit of BBR Optometry Ltd. customers wearing daily disposable soft contact lenses over a fixed period of 18 months, Patel et al. (2015) determined eye examination service uptake and volume of lens purchases were greater for customers that were members of Eyelife^{TM} compared to non-members. Members of Eyelife^{TM} purchased almost twice as many contact lens units compared to non-members, but there

was not a significant difference in the spectacle sale revenue or profits between the groups despite accompanying discounts with the monthly payment plan (Patel et al., 2015). One of the main implications from the audit was that charging appropriately for professional services provides an opportunity for high street optometrists to compete with online contact lens suppliers and supply products at competitive prices to encourage customer loyatly to the practice (Patel et al., 2015). The authors noted advantages of adopting this pricing structure with a higher professional fee and lower commodity cost are that monthly payment plans allow services to become self-sustainable without relying on cross-subsidy with products, and income generated from services are VAT exempt (Patel et al., 2015).

Customer satisfaction is a key element in any customer retention approach as are strategies of developing strong interpersonal relationships or introducing switching service provider costs to create barriers to customer defection (Jones et al., 2000). Switching barriers are factors which make it more challenging or costly for a customer to change providers (Jones et al., 2000). Jones et al. (2000) after surveying customers regarding their banking and hairstyling/barbering service providers found that switching barriers had no influence on repurchase intentions when satisfaction was high, and positively affected repurchase intention when satisfaction was low. Therefore, switching barriers may allow a business to rectify short term fluctuations in service quality or sub-optimal performances that might have otherwise have resulted in customer defection. Switching barriers may be appropriate for businesses who generally satisfy their customers but want a form of insurance against switching behaviours when their customers experience the occasional perhaps unavoidable service failure (Tax et al., 1998). However, services with switching barriers and ongoing customer dissatisfaction can lead to failure as customers may feel entrapped, and engage in negative word-of-mouth (Jones et al., 2000). Additionally, high turnover in service personnel could result in high turnover of customers when strong interpersonal relationships exist and the customer feels more loyal to the personnel rather than the service firm (Beatty et al., 1996).

Repurchase intention is a form of loyalty behaviour that can be related to high affective commitment and is defined as the customer's judgment about engaging in future activity with a service provider and what form the activity will take (Bayraktar et al., 2012). Customer satisfaction has a significant effect on customer retention and repurchase intention in a range of services (Liao et al., 2017; Larivière et al., 2016). However, rated satisfaction has also been shown to be completely unrelated to repurchase behaviour due to levels of response bias, and customer satisfaction is not always a sufficient condition for future intentions (Mittal & Kamakura, 2001; McDougall & Levesque, 2000; Blut et al., 2014). Chen & Chen (2017) in the context of professional financial insurance services found affective commitment was a stronger predictor of repurchase intention, and no relationship between customer satisfaction and repurchase intention was found. There is evidence that customers

who participate in services demonstrate higher repeat purchase behaviour and low sensitivity to price increases, in turn creating a competitive advantage for the service provider that is difficult for competitors to match (Hsieh & Yen, 2005; Prahalad & Ramaswamy, 2004).

Disappointment which arises from comparison between the obtained results and the outcome that could have been achieved if the service provider's actions had been different, is a predictor of word-of-mouth and switching behaviour (Zeelenberg et al. 1998; Zeelenberg & Pieters, 2004). It is thought co-production, that is customer participation in service specification and delivery, could lead to lower disappointment and dissatisfaction levels and less negative word-of-mouth and switching behaviours because customers take part of the responsibility for a service failure (Yen et al., 2004; Pacheco et al., 2017). Examples of co-production include requesting an off the menu meal at a restaurant, designing a workout programme with a personal trainer at the gym, and being involved in creating a dry eye management plan. Although the results were based on restaurant and gym service contexts, co-production was positively related to perceived control and decreased customer negative emotion reactions towards the service provider when there were service failures (Pacheco et al., 2017).

Purchasing decisions can become automatic when habits form, however, repurchasing decisions regarding relatively expensive goods such as jewellery, houses and bespoke spectacle frames are scrutinised intensely as they are high involvement products (Petty & Cacioppo, 1984). Customers can easily search online for information on all dry eye products, novel treatments and dry eye service providers to evaluate alternatives, and use other providers as external reference points to influence post-consumption assessment of the service purchased and repurchase decisions (Yim et al., 2007). Customer loyalty can be a major driver of success, and source of sustained growth and profit with loyal customers more likely to positively endorse the business, and display willingness to pay premium costs (Wien & Olsen, 2014; Zeelenberg & Pieters, 2004; Reichheld & Schefter, 2000).

There was absolutely no uptake of the home delivery of products option for Dry Eyelife^{TM} members. Customers expressed preferring to pay as and when products were needed. It would seem that customers utilising the dry eye service preferred to purchase products at point of sale versus subscribing to a monthly direct debit system. Perhaps an initial bulk supply is more useful and should be explored or trialled in the future to help with dry eye management compliance given the fluctuating nature of dry eye and potential disuse of products in times when no symptoms are experienced. Product bundling is when several items are promoted as a bundle rather than as sold separately, and price bundling is when separate products are sold in a package at a discount in order to the enhance the customers' perception of value and cost saving (Arora, 2008). One

drawback of such an option is if the customer wants the choice of buying the desired product and only a few of the optional items included in the bundle (Arora, 2008).

Arora (2008) found that a bundling pricing approach for whitening dental care and complementary products was effective for purchase intention, which perhaps could be applied to the selling of dry eye products and promotion of novel dry eye treatments at BBR Optometry Ltd. As indicated in the disparity between expected and actual annual product customer spending, customers are not using the products as recommended given the lack of replenishment in the time period expected. For example, the Mono Dose System (COMOD®) of Scope Ophthalmics' preservative and phosphate free ocular lubricant range stocked at the practice predicts monthly replacement if used four times daily, and control tip pumps of some lid cleansers supplied at the practice predict two-monthly replacement for daily use. These findings led to the introduction of automatically generated emails issued to Tear clinic customers one month after their reviews or at the expected review time reminding them of direct debit options for products or option of having products purchased in bulk due to the trend observed that patients do not return for products. This is to improve practitioner-customer communication when it comes to explaining the chronicity of dry eye and enforcing preventative practice. Reception staff have also been trained to ensure details are taken and a record created for "walk-in" customers who purchase products but do not attend the practice for clinical appointments in order to communicate the potential benefits of a dry eye consultation or to notify of new products or treatments.

It was hypothesized that there would be more structured purchasing behaviour post-dry eye consultaiton for dry eye products but this was not the case. Almost half of customers (46%), who also happened to be non-Eyelife^{TM} members did not purchase any dry eye product outside what was provided at the dry eye consultation, that is either one year prior or one year following their initial dry eye review appointment. It is unclear as to whether these customers did not value the recommendations given, felt their dry eye condition was under control, decided to purchase products online or elsewhere at more competitive prices, or whether those customers new to the practice returned to their local practitioner for ongoing care. Another factor to consider is whether customers were successful in having recommended ocular lubricants issued on prescription by their GP according to the local dry eye formulary. For example, Scope Ophthalmics offer two identical products in different sized bottles with the larger 10 ml bottle available on the NHS (Hycosan Extra= Hyloforte).

Attractiveness of alternatives is another factor in customer defection, which refers to customer perceptions regarding the availability of viable competing alternatives in the marketplace. It has been hypothesized that lower attractiveness of competing alternatives is associated with higher

levels of retention and repurchase intentions as the perceived benefits of defecting or switching would be relatively low (Jones et al., 2000). Perhaps the dry eye customers seen at BBR Optometry Ltd. were content with the consultation and were attracted by lower product prices including exam fees and spectacles elsewhere. Anecdotally, some customers express preferring to be seen by an independent practitioner for a "proper eye examination" at a practice that invests in the latest technology and diagnostics, and are willing to pay for care or a supplemental fee outside what is covered by the NHS eye examination but then purchase products elsewhere at a reduced cost. In the future, customer feedback measures should be used to enhance the service, and develop ways to retain customers.

Temporal reframing of price (TRP), unit pricing (UP) and usage-based UP are tactics that do not involve changes or reductions to retail prices but rather reframing to a different form to create favourable price perceptions and purchasing decisions from customers (Carlson et al., 2007; Hardesty et al., 2007; Kwortnik et al., 2006). TRP reframes the price as smaller amounts based on time units to aid price perception in the context of stand-alone decisions, whilst UP reframes the price based on units, volume or servings for value-conscious customers comparing similar items (Shirai, 2017). In a charitable donation scenario, Gourville et al. (1998) showed that the likelihood of donation was higher in the TRP form, which encouraged the retrieval of small daily expenses such as $1 per day for coffee, lunch, or taxi fare, compared to the aggregate annual amount. TRP can generate higher perceived price attractiveness but also has been shown to generate negative customer perceptions including higher perceived complexity of the price structure and greater feeling of being manipulated (Bambauer-Sachse & Mangold, 2009). TRP has been shown to be most effective in positively affecting purchase intention when even price endings were used, when it was applied to higher prices and shorter time periods and among customers with low calculation affinities (Bambauer-Sachse & Grewal, 2011).

Shirai (2017) found in a laboratory experiment involving students and a print advertisement for tea leaves packed in tin boxes that usage-based UP was evaluated as better than TRP and measure-based UP because it was the most understandable and preferential as the information relates to actual consumption. It may be more effective to use TRP to reframe the costs of dry eye treatments which may be similar to the cost of varifocals or bespoke spectacles, and usage based UP to reframe the costs of dry eye products. For example, Kwortnik et al. (2006) found that in addition to usage-based UP, information on the usage count or consumption speed gave more credibility to the UP information for favourable evaluations of laundry detergent brands such as the number of uses per washing load. If customers are aware of how many drops are in each bottle or are aware of how long a bottle should last them in terms of supply, they can assess and gauge their usage of the product and its value.

The manner in which a price is communicated to the market, referred to as framing, can mediate purchase intentions (Arora, 2008). Positively framed messages emphasize product or service benefits such as efficacy and in comparison, with competitor offerings or gains to the customer. Negatively framed messages concentrate on the benefits foregone or the adverse consequences of not using a product or service (Arora, 2008). Marketers use both positively or gain-based, and negatively or loss framed messages as a communication strategy to persuade customers to purchase in promotional appeals, and the literature is mixed on which is more effective at gaining compliance (Arora, 2008). The study referenced previously by Arora (2008) suggested that using positively framed messages for teeth whitening products were more effective in gaining compliance. In health care decisions regarding prevention of a risky consequence, positively framed messages are thought to be preferred (likelihood of surviving surgery), whilst negatively framed messages are thought to be more effective in detection of a risky consequence (Rothman & Salovey, 1997). Utilisation of video capture on the LipiView II unit allows practitioners and customers to review blinking habits during the consultation, and the dynamic Meibomian gland imaging function of the unit captures high-definition images of the oil-producing glands. Perhaps in addition to presenting physical evidence of structural changes to the Meibomian glands due to the progression of evaporative dry eye to customers utilising the service, marketing materials with these images and negatively framed messages ("people with suspect dry eye related concerns who do not have a consultation have a decreased chance of treating a more manageable stage of dry eye") could be generated, and their effect on purchase intention analysed.

In terms of clinical attendance, it was hypothesized that customers attending multiples appointments per year prior to their Tear Clinic consultation would have fewer attendances following their consultation after a targeted approach was taken to manage their ocular surface health issues. However, this could not be determined accurately in the current analysis given previous history of new customers was unknown. It was not known how many practitioners or health care providers the customer had actually seen prior to attending BBR Optometry Ltd. for a dry eye consultation. Reasons for customers attending the practice for multiple clinical appointments following the dry eye consultation within the one-year window include uptake of novel treatments and dry eye review appointments or because they were due an eye examination or required pre- and post-operative care following cataract surgery.

Reasons for customers attending the practice for less clinical appointments following the dry eye consultation within the one-year window include they were not quite due for their yearly or two-yearly eye examination, perhaps multiple appointments were no longer necessary because customers' needs were met, customers relocated from the area, or were dissatisfied with the service.

There were six customers who had fewer practice attendances for clinical appointments one year after their dry eye review appointment, with previous multiple visits due to emergency appointments in addition to routine eye examinations. One customer in particular attended the practice on three occasions with issues related to dry eye prior to their dry eye consultation. For reasons unknown, the customer had not returned for any further appointments at the time of the analysis. Reasons for no changes in attendance were potentially due to the regularity of eye examinations as Eyelife^{TM} Optimum members were in this category, or because customers were attending the practice for the purpose of utilising the dry eye service only. It seems customers are more likely if at all to purchase spectacles following their eye examination irrespective of when they have a dry eye consultation.
Dry eye is a chronic condition requiring at present regular and long-term use of recommended regimens to achieve sustained symptomatic relief. However, the therapeutic potential of self-applied, at-home therapy will be limited by compliance that is often influenced by financial costs, preference, perceived efficacy, convenience and adverse effects (Jin et al., 2008). In regards to ocular conditions, treatment adherence may be limited by the ability to instil eye drops (Stone et al., 2009). Therapeutic compliance considers compliance with other advice including following suggested environmental and dietary changes such as avoiding exposure to tobacco smoke and improving general hydration, and factors such as uptake of cosmetic procedures outside the practitioner's control can also impact on dry eye status (Jones et al., 2017; Gomes et al., 2017).

It has been estimated that the rate of compliance for short-term therapy is much higher than both long-term medication therapies and lifestyle changes (Jin et al., 2008). Reported types of non-compliance (Vermiere et al., 2001; Cummings et al., 1982; Cramer et al., 1990; Feinstein, 1990; Burnier et al., 2003; Blaschke et al., 2011) applicable to dry eye management are:

- Missed doses
- Stopping treatment too soon or lack of persistence
- Delaying in seeking healthcare
- Non-participation in clinic visits
- Failure to follow the practitioner's instructions
- "Drug holidays" where customers stop the therapy for a while and then restart, and
- "White-coat compliance" which means customers are compliant to the regimen around the time of clinic appointments

Patient-centred factors such as age and gender have been identified in therapeutic compliance with studies showing those over the age of 55 years and women to have both increased and decreased compliance or no effect at all (Jin et al., 2008). It has been hypothesized that cognitive and physical difficulties such as applying eye drops may be reasons for non-compliance in older people, which is

often non-intentional (Jin et al., 2008). There are dropper aids available commercially, and supply and open display or access to these within an optometric practice may make customers more compliant with therapies. A negative contributing factor to poor compliance in those with long-term illnesses is the fear of dependence on long-term medication, the worry of diminishing effectiveness of medication over time, low motivation to change behaviours, and negative attitude towards therapy (Apter et al., 2003; Bender & Bender, 2005; Lim & Ngah, 1991; Hernandez-Ronquillo et al., 2003; Spikman et al., 2003; Jin et al., 2008). In regards to dry eye, anecdotally customers seem to have a negative attitude towards therapy especially if it is something they have trialled or been recommended previously. People with conditions similar to dry eye that fluctuate in their severity or do not have severe symptoms in the initial phase, such as asthma and hypertension, have been shown to demonstrate poor compliance (Hungin et al., 1999; Kyngas & Lahdenpera, 1999; Vlasnik et al., 2005). Perceived health status has also been shown to effect compliance with customers conducting their own cost-benefit analysis of therapy such as whether benefits outweigh constraints seen on their daily life like using a warm compress or applying ocular lubricant (Jin et al., 2008). It is important for customers to understand their condition and the role they play in their treatment to aid compliance.

Not all dry eye products are available on prescription, and so the cost of long-term management constitutes a large portion of a customer's disposable income. There are currently reimbursements from the National Health Service for two heating masks only: Eyebag and Meibopatch. It is estimated that the annual cost associated with the management of dry eye sufferers by ophthalmologists in the UK is about $11,000.00 US per person (Clegg et al., 2006). Typically, dry eye sufferers will self-treat with over-the-counter products or are managed in primary care but cases can present to hospital eye casualty departments as demonstrated in chapter six, and a proportion of severe cases may require management by an ophthalmologist. Compliance to therapy is threatened if the customer feels the cost of management is a financial burden (Jin et al., 2008), and customers may choose to stretch their drops past their discard date although most remain sterile six months from opening, or may be tempted to purchase cheaper inferior products that could lead to drop toxicity or other problems.

In the current analysis, there were instances of customers wanting quick fixes where at present one cannot be offered for dry eye. Intuitively, it would seem likely that compliance would be enhanced with commercially available solutions such as impregnated sterile pads for eyelid hygiene and blepharitis management, however, cost seems to be a factor where products are not available on NHS prescription and customers incur a fee. For example, an average customer price for Johnson's Baby Shampoo is £2.50 for 500ml, and so if 5ml is used per day in a 1:10 dilution then the annual cost would be less than £10 per year. Use of diluted baby shampoo has traditionally been the

mainstay of blepharitis management advice, which may be a familiar recommendation to dry eye customers. Commercially available wipes used at BBR Optometry Ltd. cost the customer about 50p each, which amounts to around £180 per year assuming one treatment every day and using a different area of the same wipe for the fellow eye (Jones et al., 2017). For customers, the benefits of the product may need to justify the price or the perceived convenience of a product may offset the difference in financial costs between two treatment options. Improvements could be made in regards to communication of outcomes from novel treatments and information on efficacy given the nature of these options as not being widely available, and perhaps lack of knowledge or scepticism on the part of fellow health care colleagues affecting uptake.

The following points outline the "bottom line" for BBR Optometry Ltd.'s dry eye service:

- A net profit of over £40,000.00 was generated from the dry eye clinic in under three years.
- Over 150 dry eye consultations performed since implementation in July 2015.
- BBR Optometry Ltd. now offer the equivalent of a half day dry eye clinic per week with numbers increasing due to greater exposure and awareness of the service.
- Appointment types, times, and fees are embedded into the practice management software giving staff the confidence to book and suggest dry eye consultations.
- Templates for testing, reports, consent forms, setting up product direct debits, booking information and fees are embedded into the practice management software. Marketing materials and Tear Clinic performance tracking (i.e. Number of patients seen monthly, Tear clinic turnover, costs etc.) are readily accessible as are all dry eye resources on the practice desktop under the "Dry eye specialty service" folder.
- BBR Optometry Ltd. has established itself as a provider of advanced dry eye care with more than one independent-prescribing optometrist able to provide more advanced recommendations for complex cases.
- Changes to costs of LipiFlow consumables and remaining stock meant offering treatments at a lower fee to generate higher volume of sales and awareness for the treatment given the initial equipment costs were amortised. Johnson and Johnson acquired Tear Science in 2017 and representation in the UK may result in improved support for marketing and clinical affairs. The introduction of a reusable cable with disposable activator for LipiFlow treatment will reduce waste and costs per treatment to the practice.

2.5: Management recommendations

The Gaps model is a useful framework for understanding service quality (Parasuraman et al., 1985). The most critical service quality gap to close is the customer gap (gap five), which is the difference between customer expectations and perceptions. The four provider gaps that occur in organizations are responsible for the customer gap, and organizations must decide where to start or in what order to proceed, to reduce the customer gap and make it as narrow as possible. The work presented in this thesis highlighted the use of service blueprinting in private optometric service innovation, which pertains to the Gaps model as a means to reduce provider gap two. A summary of the activities undertaken, and that could be undertaken to close the provider gaps are presented in table 2.10.

Provider gap	Activities to reduce the Provider gap
1) Knowledge gap: Not knowing what customers expect	• Learn about service alternatives the customer views as comparable, such as other dry eye service providers, and over-the-counter products or self-treatments • Determine whether there is a local need for a given service via surveys or questionnaires • Facilitate communication between reception and clinical support staff with optometrists and managers to understand what customers expect • Collect structured customer feedback regarding certain aspects of a private service
2) Standards gap: Not selecting the right service quality designs and standards	• Develop a service blueprint designed to correspond to customer expectations, for e.g. having dry eye concerns addressed with a structured exam using the latest diagnostics, and a discussion on findings and management options • Create a service standard using evidence-based clinical practice and/or global consensus • Provide clear fees and timings, and outline precisely what will need to take place prior to the consultation, as well as what to expect during and after the consultation • The dry eye customer journey at BBR Optometry Ltd. was enhanced by relocating all appropriate diagnostics to one room • Provide physical evidence of the service offering with appropriate signage, leaflets and TV loop in the customer waiting areas that do not contain jargon, and use a dry eye questionnaire for screening purposes as part of the pre-assessment protocol for eye examinations. • Consider multiple measures of success to track service quality goals: financial performance (profitability), relationship enhancement (customer loyalty & effect on other services or products), and market development (potential to apply to new customer segments, such as dry eye evaluation for contact lens wearers and those referrable for lens replacement)
3) Delivery gap: Not delivering to service designs and standards	• Provide sufficient support for frontline staff including one-to-one training, access to concise reference documents, and role play. It is important for employees to understand how dry eye impacts the lives of customers, the tests conducted to determine type of dry eye, and the tiers of management delivered by the practice. • Utilisation of service intermediaries to enhance employees' dry eye product knowledge, and confidence in calibration and performing dry eye diagnostics • More than one optometrist was trained to deliver the dry eye service, in order to account for appointment availability and demand fluctuations. Optometrists are provided with reference documents, grading scales, and templates for ease in record keeping and the generation of customer management plans.

4) Communication gap: Not matching performances to promises	• Provide external messages for customers to return and create more structural bonds e.g. Eyelife™ • Provide reminders to customers to replenish products or consider in-practice treatments one-month following their review appointment, given dry eye is a chronic condition • Schedule regular meetings with all staff to communicate any changes to the current dry eye service offering, and to identify any training needs

Table 2.10: Summary of the activities undertaken, and that could be undertaken to close provider gaps one to four from the Gaps model of service quality (Parasuraman et al., 1985).

Management of any service requires a way to audit the service performance and capabilities of an organization, which can be done using the Service quality Gaps model audit shown in appendix 2.9. Future work could examine all factors that affect the size of each provider gap for private optometric services, such as the Tear Clinic, using the Service quality Gaps model audit (appendix 2.9). Organizations could also perform a SERVQUAL audit (see appendix 2.1), to assess service quality management from an internal point of view in order to highlight points which need to be addressed with input from members of staff representing all service roles including managers, clinical assistants and optometrists. An additional SERVQUAL audit could include customers, in order to yield a more detailed picture of what customers think about private optometric services, namely the dry eye service. These activities are worthwhile for those businesses who seriously wish to improve service quality in a crowded optometric market.

2.6: Conclusion

There is currently no cure for dry eye disease with the mainstay of management focusing on palliative relief. However, BBR Optometry Ltd. aim to use a targeted approach to determine the sub-classification of dry eye, and use the DEWS II staged management algorithm as the basis for recommendations. Approximately 26% of BBR Optometry Ltd. adult customers attending for an eye examination and voluntary completed a dry eye questionnaire, self-reported some degree of dry eye. After identifying a local service need, considering the customer's point of view in developing a service blueprint and implementing the service, the service is continually reviewed. Chapter three looks at determining the most efficient clinical tests for the dry eye service.

Service blueprinting can be used for the development and implementation of other possible optometric care pathways in the community, for example myopia control and specialist contact lenses, sports vision, and concussion rehabilitation. Service blueprinting lays the framework for the intended service that can be used as a reference when changes may cloud direction for practices that are attempting to differentiate themselves from competition in the market. A service blueprint is not rigid and can be altered with the goal of avoiding provider gap two, and improving service quality. Input from employees at all levels and roles is critical, with the role and actions of the customer

being the centre of focus, and including customers in the process. By analysing purchase behaviour patterns, practices can learn more about their customers at an operational level in order to plan changes to their current service, re-direct focus, brainstorm strategies to retain or acquire new customers, and determine where to direct energy in terms of time, development and further resources. There is a business case for a dry eye service at BBR Optometry Ltd. in terms of primary profitability, secondary profitability (conversion to Eyelife^{TM}), and reputation for clinical excellence. Another challenge in the implementation of new services is to identify or segment customers who would benefit from the new services, and this will be explored further in chapters four, five and six.

CHAPTER 3 ABSTRACT
Application of decision tree analysis and principal component analysis to dry eye questionnaires and clinical tests

PURPOSE: The current analysis aimed to identify objectively, which combination of commercially available clinical tests invested in by BBR Optometry Ltd. should be included in dry eye consultations for predicting evaporative dry eye, and to create a more efficient dry eye consultation.

METHODS: Multivariate analysis was performed using SPSS version 24.0 (IBM SPSS Statistics, Chicago, IL), and involved decision tree analysis (DTA) using the Chi-squared Automatic Interaction Detection (CHAID) tree growing method (Kass, 1980). DTA was used in the current analysis to explore whether clinical tests (lipid layer thickness, percentage of partial blinks, Meibomian gland evaluator score, fluorescein tear breakup time, Meibomian gland dropout and Meibomian gland duct dilation), or the variables age and sex were predictive of dry eye symptom status i.e. having some degree of dry eye symptoms or none at all in a clinical population of patients from an independent optometric practice attending for an eye examination or a dry eye consultation. A second DTA was applied to explore whether there were clinical tests predictive of dry eye symptom severity according to the OSDI score amongst dry eye patients with a predominantly evaporative component.

Principal Component Analysis (PCA) was performed. The aim of PCA is to arrive at a simple structure, meaning each variable loads strongly onto only one principal component (>0.40), and each principal component includes a number of strongly loading variables (Pallant, 2016). According to Pallant (2016), there should be three or more items loading onto each component. An exploratory factor analysis approach was taken to determine which items from the SPEED and OSDI dry eye questionnaires were the most important questions to explain variation in evaporative dry eye cases seen at BBR Optometry Ltd. In a second PCA, all clinical tests (as analysed with DTA) including total SPEED and total OSDI dry eye scores were listed as variables to determine which were key to explaining variation amongst the evaporative dry eye cases seen**.** The later analysis was re-run with the total SPEED and OSDI scores replaced by the "Jessica score," which was derived from the first PCA, consisting of the most important items from the two dry eye questionnaires.

RESULTS: Important predictive questions for dry eye included those relating to frequency of soreness or irritation, and the impact on visual functioning for daily tasks. Based on the right eye DTA model, the selection of clinical tests available at BBR Optometry Ltd. that are potentially predictive of predominately evaporative dry eye in order of importance include: fluorescein tear breakup time especially if it is ≤ to 9 seconds, there is some degree of Meibomian gland dropout, and a total Meibomian gland evaluator score that is between 1 and 9. Sex may also be a predictive factor for dry eye status if the fluorescein tear breakup time is between 9 and 12 seconds, with women more likely to be affected with dry eye.

According to a two-factor solution (simple structure), the most important dry eye questions were SPEED item 2, and OSDI item 6. In the second PCA, the most important clinical tests identified were Meibomian gland duct dilation, OSDI total score, fluorescein TBUT and percentage of partial blinks. In the third PCA, the tests identified as the most responsible for the variability observed amongst predominantly evaporative dry eye cases were: Meibomian gland duct dilation, percentage of partial blinks, fluorescein tear breakup time, and the "Jessica score".

CONCLUSIONS: These results derived objectively using statistical means suggest that asking certain questions regarding dry eye symptoms, performing an accessible, quick test of fluorescein tear breakup time, and utilising technology invested in by the practice could deliver a sufficient level of clinical testing to identify evaporative dry eye.

CHAPTER 3
Application of decision tree analysis and principal component analysis to dry eye questionnaires and clinical tests

3.1: Introduction

Optometrists are at the forefront of providing long-term management of dry eye and so accurate diagnosis is fundamental. Practitioners are tasked with choosing from a battery of clinical tests, where one test may affect the results of a subsequent test, to provide high quality care to dry eye patients when it has been demonstrated there is relatively poor association and often discordance between signs and symptoms (Johnson, 2009; Downie & Keller, 2015; Sullivan et al., 2014; Baudouin et al., 2014; Nichols et al., 2004a; Schein et al., 1997; Hay et al., 1998). Self-reporting of dry eye symptoms has shown to be more reliable and accurate than results of dry eye clinical tests (Schiffman et al., 2000; Nichols et al., 1999; McMonnies, 1986; Lee & Hyun, 1988; Nichols et al., 2004a). It is thought neural mechanisms may underlie the complexity of dry eye symptoms with desensitization of the cornea to stimuli in severe or longstanding dry eye corresponding to a reduction in symptoms of ocular discomfort (Baudouin et al., 2014; Savini et al., 2008). Hyperalgesia or heightened sensitivity to pain may have the opposite effect, causing an individual to be considerably symptomatic in the absence of clinical signs in early or mild cases of dry eye (Rosenthal & Borsook, 2012; Belmonte et al., 2004a).

Dry eye disease affects up to 50% of adults and is one of the most common reasons that people seek care from an optometrist or ophthalmologist (Stapleton et al., 2017; Barabino et al., 2016). There is currently no gold standard test for diagnosing dry eye disease, and so various clinical tests are conducted and there is considerable variation in self-reported clinical care approaches among optometrists and ophthalmologists. The dry diagnostics used at BBR Optometry Ltd. are described in chapter one. A study using an online survey regarding current practice patterns for the evaluation of dry eye patients sent to ophthalmologists affiliated with the Scheie Eye Institute or Wills Eye Hospital in Philadelphia, USA, found the most common clinical test conducted was corneal fluorescein staining, the most frequently used newer diagnostic test was tear osmolarity, and that the majority of respondents felt there was a need for an evidence-based standardized screening tool to decide which patients should be referred for a Sjögren's syndrome workup (Bunya et al., 2018). Sjögren's syndrome is a chronic autoimmune disease characterized by irreversible damage to the lacrimal and salivary glands leading to aqueous deficient dry eye associated with a significant reduction in tear production and ocular surface inflammation, and loss of saliva production (Ramos-Casals et al., 2012; Vitali et al., 2002; Segal et al., 2009; Kassan & Moutsopoulos, 2004). Unfortunately for those affected, there is an average delay in diagnosis of up to seven years from the onset of symptoms due to the nonspecific nature of early manifestations (Kassan & Moutsopoulos, 2004; Kruszka & O'Brian, 2009; Manthorpe et al., 1997). Interestingly, the majority

of respondents to the online survey reported that they do not routinely use a standard severity grading scale in their everyday practice to assess dry eye because they felt it was too time consuming or that is was not clinically useful (Bunya et al., 2018). A retrospective review of records from North American optometric practices to assess customary methods in the monitoring of dry eye disease in Sjögren's syndrome found practitioners based in private practice were more likely to use symptom questionnaires and grading scales, and to describe anterior blepharitis, whilst those based in academic settings were more likely to record tear breakup time and tear meniscus height (Acs et al., 2018).

An online survey distributed to optometrists with a special interest in anterior eye disease and/or contact lenses in Australia and the United Kingdom (UK) aimed to compare the self-reported clinical practice behaviours, and found practitioners in both regions deemed symptom assessment as the most important diagnostic (Downie et al., 2016). UK practitioners used conjunctival signs and tear meniscus height evaluations more than Australian optometrists to diagnose dry eye, whilst Australian optometrists placed more emphasis on fluorescein tear breakup time (Downie et al., 2016). A similar cross-sectional survey was used to evaluate self-reported clinical practices of New Zealand optometrists and ophthalmologists (Xue et al., 2017). Patient symptoms were also ranked as one of the most valuable diagnostic approaches in dry eye, in addition to the evaluation of the Meibomian glands by 90% of respondents (Xue et al., 2017). Most practitioners selected six or more techniques within any single dry eye assessment, and the use of validated dry eye questionnaires and standardised grading scales were infrequent (Xue et al., 2017).

The purpose of the current study was to objectively determine the most valuable clinical tests conducted at BBR Optometry Ltd. to:

1) Discriminate between people self-reporting dry eye from those that do not report dry eye symptoms, and

2) Predict the Ocular Surface Disease Index (OSDI) dry eye severity amongst patients with predominately evaporative dry eye using decision tree analysis.

Principal component analysis was applied to a dataset of patients with predominantly evaporative dry eye at BBR Optometry Ltd. to:

1) Determine which questions regarding dry eye symptoms were the most important from two validated questionnaires, and

2) Determine which clinical tests including total questionnaire scores are key to explaining the variability between these patients.

The findings of these analyses could help inform changes in the design of the current dry eye service at BBR Optometry Ltd. to improve efficiency from the layout of the practice to utility of certain tests for objective screening of dry eye at eye examinations and preliminary assessments for contact lens trial appointments.

3.2: Method

This study received approval from the Life and Health Sciences Ethics Committee at Aston University (Project #1276) and adhered to the tenets of the Declaration of Helsinki. This was a retrospective analysis of anonymised patient records with all data collected in an independent practice with a dedicated dry eye service (BBR Optometry Ltd., Hereford, England). The objective was to determine the clinical tests that were predictive of dry eye at BBR Optometry Ltd. All data were collected by the author, and the same examination room and equipment were used throughout. The dry eye group consisted of all patients scoring greater than zero on the SPEED questionnaire and presenting for privately funded dry eye consultations. There were 149 patients seen in the dry eye clinic. This was a retrospective analysis of pre-collected data, so the number of eyes available was fixed and limited in the dry eye group by the demand and awareness of the dry eye service at the practice.

3.2.1: Decision Tree Analysis

Decision Tree Analysis (DTA) was considered in favour of previously used statistical methods, as it considers all factors at the same time. DTA is a form of multivariate analysis widely used since 1959, which automatically identifies a hierarchy of independent discrete and continuous variables regardless of the frequency distribution of the continuous variables in order to predict an outcome (IBM, 2016). DTA can be used to identify cases likely to be members of a particular group, to assign cases into one of several categories, to create rules that predict future events, to select predictors from a large set of variables, to identify relationships between subgroups, and determine the most useful classification of independent variables (IBM, 2016). DTA has been applied to medical diagnostic classification problems including breast cancer detection, thyroid nodular lesion detection and otoneurological diseases (Kuo et al., 2001; Nagy et al., 1999; Viikki et al., 1999).

Multivariate analysis was performed using SPSS version 24.0 (IBM SPSS Statistics, Chicago, IL), and involved DTA using the Chi-squared Automatic Interaction Detection (CHAID) tree growing method (Kass, 1980). DTA is presented graphically as a branching diagram that eases interpretation. At each step, the CHAID algorithm chooses the independent variable that has the strongest interaction with the dependent variable. The most important independent variable is used to create

the first branches of the tree followed by the next most important independent variable with each subsection within the lower branch referred to as a child node. CHAID uses p-values of the Chi-square as the splitting criteria, and so detects the factors that are statistically best at segmenting the population as per the intended classes (Guillon & Maissa, 2005b). Findings in this analysis were tested for statistical significance at the 95% level ($P<0.05$). The CHAID algorithm allows binary and multi-way splits, and branching ceases once there are no other independent variables that can influence the dependent variable. The CHAID algorithm does not produce a fixed model and allows a combination of factors to identify differences in subgroups (Guillon & Maissa, 2005b).

DTA has been applied previously in ophthalmic research (Yu et al., 2011; Frick et al., 2009; Guillon & Maissa, 2005a; Guillon & Maissa, 2005b; Twa et al., 2005; Chiang et al., 2011; Rushton et al., 2016; Dunstone et al., 2013; Pancholi et al., 2018). In a study estimating the annual direct and indirect costs of treating dry eye in the United States, a decision tree analytical model was used to differentiate between patients obtaining medical care, and those who self-managed (Yu et al., 2011). The subgroups were further split into the severity classification of dry eye, the various treatments used, and their associated costs (Yu et al., 2011). The authors preferred this method of analysis for the ease of updating data, and reanalysing data over time to estimate future health care budget requirements (Yu et al., 2011). Frick et al. (2009) used DTA to compare cost-effectiveness of two methods of screening for refractive error in urban and rural India.

A study by Guillon and Maissa (2005b) used DTA and CHAID with Answer Tree Software to determine the diagnostic value of individual questions of the McMonnies questionnaire to detect dry eye in daily soft contact lens wearers and non-wearers. The most predictive question for the detection of dry eye in both lens wearers and non-wearers was the frequency of ocular dryness with scratchiness, symptoms of burning and sensitivity to cigarette smoke identified as additional indicators of dry eye problems (Guillon & Maissa, 2005b). The authors comment that using CHAID statistical analysis in the study made it possible to reduce the number of questions, and identify the questions that best predicted dry eye symptoms in routine clinical practice without needing to administer a full dry eye questionnaire, which can be time-consuming (Guillon & Maissa, 2005b). The same authors used CHAID in a different study examining bulbar conjunctival staining with sodium fluorescein and lissamine green dyes in contact lens wearers and non-wearers to identify discriminant factors and associated cut-off values for dryness symptoms amongst the clinical findings (Guillon & Maissa, 2005a). Subjects were identified as asymptomatic or symptomatic based on their McMonnies questionnaire score. Staining with both dyes were discriminating factors for symptomatic subjects who did not wear contact lenses, and amongst daily soft contact lens wearers only Lissamine green staining was a discriminating factor (Guillon & Maissa, 2005a). The authors concluded with a recommendation for practitioners to include assessment of the conjunctiva with

lissamine green staining for contact lens wearers, and non-wearers complaining of dry eyes in a work-up for ocular surface disease (Guillon & Maissa, 2005a).

Using the WEKA C4.5 Java based program to generate a decision tree, a study by Twa et al. (2005) discriminate between normal and keratoconic corneal shapes in an objective way. The authors note the advantages of this approach to quantify videokeratography data to support clinical decision making, which include quick computational speed, scalability for analysis of large volumes of data and interpretability (Twa et al., 2005). Chiang et al. (2011) used DTA to overcome limitations associated with missing data using logistic regression, that is often a common issue with postal surveys in survey-related research. Chiang et al. (2011) applied DTA to the area of eye care service delivery, and identified the most important predictors related to better low vision coverage. Rushton et al. (2016) used DTA to determine influencers on the relationship between unaided vision and refractive error in order to develop new equations useful in simulators for teaching purposes. DTA ruled out variables including sex, contact lens wear, iris colour and axis of astigmatism as having a significant effect on unaided vision, and so were not included in further regression analysis (Rushton et al., 2016). Dunstone et al. (2013) used DTA in their investigation into the habits and attitudes of UK optometrists to retinoscopy. The authors found DTA to be the most appropriate statistical analysis due to its hierarchical element compared to multiple regression and multiple discriminant analysis, which have no explicit hierarchy in determining the potential influencing factors, such as date of qualification and practice type on the habits and attitudes to retinoscopy (Dunstone et al., 2013). Pancholi et al. (2018) used DTA to identify the most and least influential variables on self-assessment accuracy in relation to clinical decision-making learning objectives for two cohorts of second-year optometry students, where one group utilized virtual patient software.

DTA was used in the current analysis to explore whether clinical tests or the variables age and sex were predictive of dry eye symptom status i.e. having some degree of dry eye symptoms or none at all in a clinical population of patients from an independent optometric practice attending for an eye examination or a dry eye consultation. A second DTA was applied to explore whether there were clinical tests predictive of dry eye symptom severity according to the OSDI score amongst dry eye patients with a predominantly evaporative component.

3.2.2: Principal Component Analysis

Principal Component Analysis (PCA) is a data reduction technique that makes no distinction between independent and dependent variables unlike DTA, which can be used for data reduction and reduces the number of independent variables needed to predict a dependent variable. PCA differs from multiple regression in examining relationships between variables by treating both

independent and dependent variables the same. PCA summarises a large set of variables using a smaller set of factors or components by identifying groups among the intercorrelations of the original sample. That is, PCA is used to determine whether the relationships between variables can be explained by a smaller number of components, also referred to as factors (Armstrong & Eperjesi, 2008). The first principal component accounts for the maximum variance, whilst the remaining successive principal components explain decreasing proportions of the residual variance (Armstrong & Eperjesi, 2008). PCA can be performed on a set of intercorrelated continuous or polychotomous ordinal variables.

PCA is one of the simplest and most commonly used methods for extracting a few important questions from several questionnaires or a few important clinical tests from a large battery of tests. Researchers use factor analytic techniques to develop and evaluate tests and scales, refining and reducing a large number of questions and scale items to develop a smaller number of subscales. Additionally, factor analysis techniques are useful prior to multiple regression or multivariate analysis of variance analyses in order to isolate a manageable number of related variables from a large set of data (Pallant, 2016).

Application of PCA in ophthalmic research may include describing and summarising differences or variations in quantitative measures of relevant clinical and pathological features of patients with a specific disease, such as age-related macular degeneration (Armstrong & Eperjesi, 2008). An objective might be to determine whether clusters of features might represent distinct subtypes of a disease or to establish which of the features best explain the pattern of heterogeneity (Armstrong & Eperjesi, 2008). An investigator might have a hypothesis for the underlying factors that might explain variation in clinical features among people with a particular condition, and can use PCA to test this hypothesis. The variables under study in PCA could also be questions that form part of a questionnaire to verify whether the items included are actually assessing the aspect under investigation or in other words, to validate questionnaires attempting to relate subjective aspects of a patient's experience with more objective measures (Armstrong & Eperjesi, 2008). The following are examples of factor analytic techniques used in ophthalmic research and further examples are provided in appendix 3.1.

Relating to Dry Eye:

- Borchman et al. (2012) used PCA to detect subtle differences in nuclear magnetic resonance spectroscopic data that quantified the composition of human meibum including hydrocarbon chain moieties and products of lipid oxidation, and to assess whether or not spectra of meibum from those with MGD according to the criteria of Foulks and Bron (2003), differed from those of age-matched donors who did not have MGD.

- Asiedu (2017) conducted a hospital based cross –sectional study of 127 glaucoma patients with dry eye identified by having a clinical diagnosis of dry eye (no subtype specified) or OSDI score ≥13 to investigate if the SPEED questionnaire acts as a measure of dry eye severity, and whether it is unidimensional as previously reported (Ngo et al.., 2013) using Rasch analysis. Previous analyses used fit statistics alone on a smaller sample to claim unidimensionality, which has been criticised with the recommendation to perform PCA on the standardised model residuals. PCA of the standardized model residuals was a useful alternative to detect multidimensionality in the study as well as unidimensionality in a proposed six-item SPEED questionnaire, that removed eye fatigue items to include items pertaining to only the symptoms reported the most (Williamson et al., 2014; Asiedu, 2017).

Relating to Assessment of Questionnaires:

- Barker & Mansberger (2019) used PCA to determine construct validity of a reduced version of the Glaucoma Treatment Compliance Assessment Tool (GTCAT), which was translated to Brazilian Portuguese. A sample of 76 glaucoma patients was used, and it was determined that 14 questions loaded onto seven principal components accounting for 73.5% of the variance in responses. The results were consistent with the Health Belief Model that characterizes health behaviour including adherence with glaucoma therapy (Barker & Mansberger, 2019). The results suggested that the sample size was adequate because orthogonal rotation determined that the GTCAT converged into the same number of components as the original questionnaire after excluding statements if they did not have a factor loading >0.50 on any component, if there was only a single statement on any component or if they cross-loaded >0.30 onto multiple components (Barker & Mansberger, 2019).
- The Amblyopia and Strabismus 26 item questionnaire (A&SQ) was developed to assess quality of life in amblyopia and/or strabismus. van de Graaf et al. (2009) used PCA with orthogonal Varimax rotation, and data from 296 respondents to determine the pattern of correlations between responses, and confirmed the a priori hypothesized dimensions including social contact and cosmetic problems, near distance estimation, diplopia, visual disorientation, fear of losing the better eye and far distance estimation.

There are three steps involved in PCA:

1. *Assessment of the suitability of the data for PCA*.

   PCA assumptions include:

   - *Adequate sample size:* Armstrong & Hilton (2011) suggest a minimum of five cases per variable if there are at least 100 cases. The correlation coefficients among the variables

tends to be less reliable with small samples (Pallant, 2016). Tabachnick and Fidell (2007) recommend a minimum sample size of 150, and a ratio of at least five cases for each of the variables.

- *Factorability:* that the variables can usefully be reduced to a smaller number of principal components. That is, the strength of the relationship between the variables needs to be considered (Pallant, 2016). The sample will be deemed suitable for PCA if the following three criteria are met:
  a. Variable intercorrelations of greater than ± 0.3 should be frequent.
  b. The Kaiser-Meyer-Olkin (KMO) test of sampling adequacy is a measure of the shared variance in the items and should exceed 0.6.
  c. Bartlett's test of sphericity, which uses the chi-square distribution, should be statistically significant ($p<0.05$). This test is overly sensitive and so $p<0.05$ indicates checking of the other indicators prior to deciding on suitability.
- *Linearity:* that the intercorrelations between variables are linear and not curvilinear. Tabachnick and Fidell (2007) suggest a spot check of some combination of variables rather than checking multiple scatterplots.
- *Minimal outliers:* PCA can be sensitive to outliers so measures should be taken to ensure that extreme values are removed (Pallant, 2016).

2. *Extraction of principal components that contribute the most to the explanation of the variance in the data set.* Kaiser's criterion is a commonly used technique whereby only components with eigenvalues of one or more are selected. Each principal component is associated with an eigenvalue, which is a measure of how much variance in the data is explained by each principal component. Kaiser's criterion has been criticised for retaining too many components (Pallant, 2016). The Catell's scree test is another technique to assist in the decision concerning the number of components to select. It is a graphical representation of the components that make up the x-axis, and their corresponding eigenvalues which make up the y-axis. SPSS can be used to plot each of the eigenvalues of the components in descending order, and the components that fall above a break in the plot where the shape of the curve changes direction, and becomes horizontal are retained. The Catell's scree test also tends to overestimate the number of components, considering the precise cut-off point is quite subjective leading to over-extraction of components (Pallant, 2016; Henson & Roberts, 2006). Armstrong & Eperjesi (2008) note that the first principal component will often contain a disproportionate amount of the variance and that is it not worthwhile to examine more than the first three principal components.

3. *Rotation and interpretation of principal components.* PCA determines the correlations between each variable and the extracted principal components, and these are referred to as factor loadings (Armstrong & Eperjesi, 2008). In an ideal situation, each of the variables should load onto a single principal component, but variables are often complex and load onto multiple principal components (Armstrong & Eperjesi, 2008). Rotation is the name of a process designed to ease the detection of patterns, and includes orthogonal and oblique methods. The investigator must choose which method- orthogonal (uncorrelated) or oblique (correlated)- is used. Orthogonal methods fail if there are correlations between principal components. Varimax is the most frequently used orthogonal method offered in SPSS. Oblique methods still work if there are correlations between principal components. Direct Oblimin is the most frequently used oblique method offered in SPSS (Pallant, 2016). When the pattern of correlations between the items is clear, the two methods often result in similar solutions (Tabachnick & Fidell, 2007). Results from orthogonal rotations tend to be easier to interpret and report, but assume that the underlying constructs are not correlated and independent (Tabachnick & Fidell, 2007). Many researchers conduct both types of rotations, and choose the clearest output to interpret. It is suggested to use the oblique rotational technique initially, as it provides information about the degree of correlation between the components (Pallant, 2016).

The aim of PCA is to arrive at a simple structure, meaning each variable loads strongly onto only one principal component (>0.4), and each principal component includes a number of strongly loading variables (Pallant, 2016). According to Pallant (2016), there should be three or more items loading onto each component. The procedure of choosing a variable whose loading was larger than a certain value as significant does not take into account sample size, and is arbitrary. Guidelines vary within the literature on this point, with three to five components with strong loadings considered at >0.50 to >0.70, and no cross loading onto another factor with a loading of >0.32 or >0.40 (Beavers et al., 2013). A communality loading of ≥0.70, where communality is a measure of how much a variable's variance is explained from PCA ranging from 0 to 1 prior to rotation, is considered ideal because it suggests that about half of the variance of that item is accounted for by the factor (Beavers et al., 2013). The number of components that are retained influence the communality values and so interpretation should take place once the components to be retained have been decided (Pallant, 2016). Stevens method is a more rigorous way to test the factor loadings statistically, and is given for a sample size of 'N' by the equation: Critical value = $5.152/\sqrt{(N-2)}$ (Armstrong & Eperjesi, 2008). Therefore, any variable whose factor loading exceeds this critical value, may be deemed significantly correlated with a principal component. Pett et al. (2003) recommend removing weak items, which include those with <0.30 correlation with other factors and does not provide a conceptually vital dimension to the measure, or complex variables that cross-load >0.40 onto more

than one factor. Pett et al. (2003) suggest factoring the data after removing the weak items for a stronger structure or PCA output.

The adequacy of a sample size can be determined after the analysis has been conducted, with principal components having three or more factor loadings of 0.60 or higher reducing the influence of the sample size (Guadagnoli & Velicer, 1988; Fabrigar et al., 1999; MacCallum et al., 2001). However, Hogarty et al. (2005) suggest a large sample to decrease sampling error, and Beavers et al. (2013) recommend planning to collect a sample of at least 150 cases for initial structure exploration. There is no definitive method for determining the minimum sample size for studies using PCA. A method to generate a rough estimate of the sample suggested by Dunne in DTA would not be useful in the current analysis, as it does not alter the findings of the PCA (M.C.M. Dunne, personal communication, August 2, 2018). The rule of thumb suggested by Armstrong and Hilton (2011) of using a minimum of five cases per variable if there are at least 100 cases was used.

An exploratory factor analysis approach was taken to determine which items from the SPEED and OSDI dry eye questionnaires were the most important questions to explain variation in evaporative dry eye subjects seen at BBR Optometry Ltd. In a second PCA, all clinical tests including total SPEED and total OSDI dry eye scores were listed as variables to determine which were key to explaining variation amongst the evaporative dry eye subjects seen. The later analysis was re-run with the total SPEED and OSDI scores replaced by the "Jessica score," which was derived from the first structure, consisting of the most important items from the two dry eye questionnaires.

3.3: Results

3.3.1: Decision Tree Analysis to predict symptomatic dry eye status

There were 149 patients seen in the dry eye clinic. Data from patients who were contact lens wearers, (n=21), not classified as having predominantly evaporative dry eye (n=12), and had missing values (n=14) were excluded from the analysis. For CHAID, missing scale and ordinal independent variables are included in the analysis as a single combined category (IBM, 2016). The algorithm decides whether to merge the missing category with its most similar category or to keep it as a separate category (IBM, 2016), and so to avoid confusion, the cases with missing data were excluded. The normal group consisted of 63 patients who were presenting for a routine eye examination, did not self-report any symptoms of dry eye via the SPEED questionnaire used as a screening tool for dry eye at BBR Optometry Ltd. i.e. scored zero, and volunteered to take part in the analysis. Data from normal patients who were contact lens wearers were excluded from the analysis (n=3). Table 3.2 shows the population demographics for both groups.

	Dry Eye	Normal
Number	102	60
Male: Female	23: 79	28: 32
Mean age (years)	66.21 ± 10.82	67.25 ± 12.31
Median age (years)	67.5	69.5
Mode age (years)	74	75
Age range (years)	28-93	21-87

Table 3.2: Population demographics

Decision tree analysis was carried out, using the chi-squared automatic interaction detection tree growing method, to determine the influence of age, sex, lipid layer thickness, percentage of partial blinks, Meibomian gland evaluator score, fluorescein tear breakup time, Meibomian gland dropout and Meibomian gland duct dilation on symptomatic dry eye status. Tree growth was limited to a minimum of 16 cases in each parent node, eight cases in each child node and a maximum tree depth of eight. The tree growth levels for CHAID control the maximum number of levels of growth beneath the root node or in other words, the amount of tree branching levels that are allowed. By default, SPSS automatically sets this to a depth of three for CHAID, although it is possible for the eight independent variables to exert their effects at eight branching levels. In order to allow for this, and to avoid artificially restricting tree growth, a custom value of eight was entered. The CHAID default settings for minimum parent and child nodes specify a sample size of 100 for parent nodes and 50 for child nodes. There were only 162 cases, meaning only one level of branching would be possible with these settings. A rule of thumb is that the smallest node should be no smaller than 5% of the total sample (0.05 x 162), so the parent node was set to 16, and the child node to eight (Morrison-Fokken, PhD thesis 2017).

For nominal dependent variables, the likelihood ratio chi-square statistic is more robust than the Pearson method, and is the preferred method for smaller samples (IBM, 2016). The Bonferroni correction to adjust significance values was not used in the detailed analysis of right eye and left data to avoid a type II error, and for the purposes of exploratory testing. Armstrong (2014) suggests that the use of the Bonferroni correction in this type of DTA, reduces the power of the statistical test. The Bonferroni correction was initially applied given all the independent variables were being tested for any significant comparisons, and the results were not going to be used as hypotheses for further study (Armstrong, 2014). Armstrong (2014) notes how authors comparing the results of correcting and not correcting significance values can potentially complicate interpretation of their data. Table 3.3 outlines the results of the current analysis with and without the Bonferroni correction applied for the right eye and left eye data. Adjusting significance values using the Bonferroni method led to reduced tree growth for both eyes, however, the accuracy of the model for the right eye data did not change at 75%, with the same order of influence for three independent variables. An additional two factors were identified without the Bonferroni correction for the right eye data that

took precedence over the independent variable sex. The two models generated for the left eye with and without the correction were similar in strength, having two independent variables in common.

The child nodes were adjusted for results without application of the Bonferroni correction for right and left eye data to determine whether doing so would result in similar findings between the eyes (see Table 3.4). Fluorescein tear breakup time was the first and most important independent variable listed in all decision tree analyses, albeit with different branch splitting criteria between the eyes. Up until the minimum number of cases in the child node was increased in number by 15, fluorescein tear breakup time and Meibomian gland dropout both were independent variables included in right and left eye DTA. DTA (CHAID) automatically determined that Meibomian duct dilation and lipid layer thickness were not important predictors of symptomatic dry eye status for both right and left eye data. Age appeared in left eye DTA only.

Data was analysed from each eye separately to avoid the problem of rejecting useful data (Armstrong, 2013). In some ophthalmic research where either eye could have been chosen for study, the eye is often self-selected on clinical grounds as the eye in which the signs and symptoms of disease were most evident (Armstrong, 2013). This was not possible for the dry eye subgroup due to the complex nature of dry eye with most patients unable to identify the most or least symptomatic eye. In the normal subgroup, where no dry eye was self-reported, one eye could not be selected over the other for analysis. It is also possible that there may be systematic differences between right and left eyes with a condition being more prevalent in one versus the other (Armstrong, 2013). A study by Yenice et al. (2006) showed a correlation between site of glaucomatous visual field defect, and headache involvement supporting the hypothesis that a migraine attack could impact the ipsilateral optic nerve supply. Therefore, if early visual field defects favour the right eye in right-sided migraine attacks, selecting the right eye only for analysis may provide a random sample of right eyes but could result in a biased sample of all eyes.

	RE with Bonferroni correction	RE without Bonferroni correction	LE with Bonferroni correction	LE without Bonferroni correction
Number of nodes	8	14	7	11
Number of Terminal nodes	5	9	4	7
Depth	2	4	3	4
Risk estimate	0.253	0.253	0.259	0.272
Accuracy of model	74.7%	74.7%	74.1%	72.8%
Independent variables included	TBUT MG DO Sex	TBUT MG DO MGE % PB Sex	TBUT Sex MG DO	TBUT Age MGE MG DO

Table 3.3: DTA results for both eyes separately, with and without the Bonferroni correction applied. All DTA branches were statistically significant ($p<0.05$). RE= right eye; LE= left eye; TBUT= Fluorescein tear breakup time; MG DO= Meibomian Gland Dropout; MGE= Meibomian gland evaluator score; %PB= Percentage of partial blinks.

	RE Initial analysis	LE Initial analysis	RE Child node increased by 5	LE Child node increased by 5	RE Child node increased by 10	LE Child node increased by 10	RE Child node increased by 15	LE Child node increased by 15
Number of nodes	14	11	12	7	10	7	5	3
Number of Terminal nodes	9	7	7	4	6	4	3	2
Depth	4	4	5	3	3	3	2	1
Risk estimate	0.253	0.272	0.272	0.259	0.272	0.259	0.272	0.340
Accuracy of model	74.7%	72.8%	72.8%	74.1%	72.8%	74.1%	72.8%	66%
Independent variables included	TBUT MG DO MGE % PB Sex	TBUT Age MGE MG DO	TBUT (2 levels of branching) MG DO MGE (2 levels of branching)	TBUT Sex MG DO	TBUT MG DO %PB Sex	TBUT Sex MG DO	TBUT MG DO	Sex

Table 3.4: Results of right eye (RE) and left eye (LE) data without Bonferroni correction applied. For exploratory purposes, the child nodes were adjusted by increments of 5 to determine whether doing so would results in similar decision trees between the eyes. All DTA branches were statistically significant ($p<0.05$). TBUT= Fluorescein tear breakup time; MG DO= Meibomian Gland Dropout; MGE= Meibomian gland evaluator score; %PB= Percentage of partial blinks.

The Bonferroni correction to adjust significance values was not used in the following detailed analysis of right eye and left eye decision trees for reasons explained previously. The right eye DTA will be reported on first, as this was the strongest model and had the greatest number of nodes and terminal nodes. The Model summary table seen in figure 3.1 confirms the specifications selected, and summarises the results of the DTA by the CHAID method. It was noted that five of the eight independent variables were included, and this is what is meant by data reduction in DTA. DTA (CHAID) automatically determined that age, lipid layer thickness and Meibomian gland duct

dilation were not important predictors of dry eye status. The depth of the resulting tree (four) was less than what was allowed for (eight), so decision tree growth was not artificially restricted.

Model Summary

Specifications	Growing Method	CHAID
	Dependent Variable	Dry_Eye_Status
	Independent Variables	Age, Sex, RE_Lipid_layer_thickness, RE_Percentage_of_partial_blinks, RE_Meibomian_gland_evaluator_score, RE_Fluorescein_tear_breakup_time, RE_Meibomian_gland_dropout, RE_Meibomian_gland_duct_dilation
	Validation	None
	Maximum Tree Depth	8
	Minimum Cases in Parent Node	16
	Minimum Cases in Child Node	8
Results	Independent Variables Included	RE_Fluorescein_tear_breakup_time, RE_Meibomian_gland_dropout, RE_Meibomian_gland_evaluator_score, RE_Percentage_of_partial_blinks, Sex
	Number of Nodes	14
	Number of Terminal Nodes	9
	Depth	4

Figure 3.1: Model summary for right eye DTA by the CHAID method

Figure 3.2 shows the DTA for right eye data. Fluorescein tear breakup time was the most important predictor of dry eye status: Chi-square (2, n = 162) = 28.65, $p < 0.001$. The other predictors of dry eye status in order of importance included:

- Meibomian gland dropout: Chi-square (1, n = 118) = 12.02, $p < 0.05$
- Meibomian gland evaluator score: Chi-square (2, n = 85) = 12.19, $p < 0.05$
- Percentage of partial blinks: Chi-square (2, n = 59) = 10.18, $p < 0.05$
- Sex: Chi-square (1, n = 29) = 5.49, $p < 0.05$

The independent variables age, lipid layer thickness and Meibomian gland duct dilation did not show a statistically significant influence. The decision tree classified 75% of the subjects correctly, and had 9 terminal nodes:

- The first (9.3% of the sample) included those with a fluorescein tear breakup time greater than 12 seconds and showed 87% of subjects were from the normal subgroup.
- The second (20.4% of the sample) included those with a fluorescein tear breakup time less than or equal to 9 seconds, no Meibomian gland dropout, and showed a similar proportion of dry eye and normal subjects (51.5% and 48.5% respectively).
- The third (10.5% of the sample) included those with a fluorescein tear breakup time between 9 and 12 seconds who were women, and showed a slightly greater proportion of dry eye subjects (58.8%).
- The fourth (7.4% of the sample) included those with a fluorescein tear breakup time between 9 and 12 seconds who were men, and showed a greater proportion of normal subjects (83%).
- The fifth (6.8% of the sample) included those with a fluorescein tear breakup time less than or equal to 9 seconds, had some degree of Meibomian gland dropout, and a total Meibomian gland evaluator score less than or equal to one, and showed a greater proportion of dry eye subjects (64%).
- The sixth (9.3% of the sample), included those with a fluorescein tear breakup time less than or equal to 9 seconds, had some degree of Meibomian gland dropout, and a total Meibomian gland evaluator score greater than 9, and showed a greater proportion of dry eye subjects (60%).
- The seventh (8% of the sample), included those with a fluorescein tear breakup time less than or equal to 9 seconds, had some degree of Meibomian gland dropout, a total Meibomian gland evaluator score between 1 and 9, and less than or equal to 12.5% partial blinking rate, and comprised 100% of dry eye subjects.
- The eighth (11.1% of the sample), included those with a fluorescein tear breakup time less than or equal to 9 seconds, had some degree of Meibomian gland dropout, a total Meibomian gland evaluator score between 1 and 9, and a partial blinking rate of between 12.5% and 45.5%, and showed predominately dry eye subjects (78%).
- The ninth (17.3% of the sample), included those with a fluorescein tear breakup time less than or equal to 9 seconds, had some degree of Meibomian gland dropout, a total Meibomian gland evaluator score between 1 and 9, and a partial blinking rate greater than 45.5%, and comprised 100% of dry eye subjects.

It would appear that five of the nine terminal nodes are based on less than or equal to 15 observations, which may render the model prone to spurious observations. The Risk table provides an estimate of the proportion of incorrectly classified cases, and its standard error (IBM, 2016). A risk estimate close to zero indicates an optimum decision tree model, and can be used to compare decision tree models. The Classification table shows the number of cases classified correctly and incorrectly for each category of the dependent variable, and also provides the overall percentage accuracy of the decision tree (IBM, 2016). The risk and classification table for the right eye DTA can be seen in figure 3.3, showing the model is highly sensitive (96% of dry eye subjects identified as having dry eye), and overall 75% accurate.

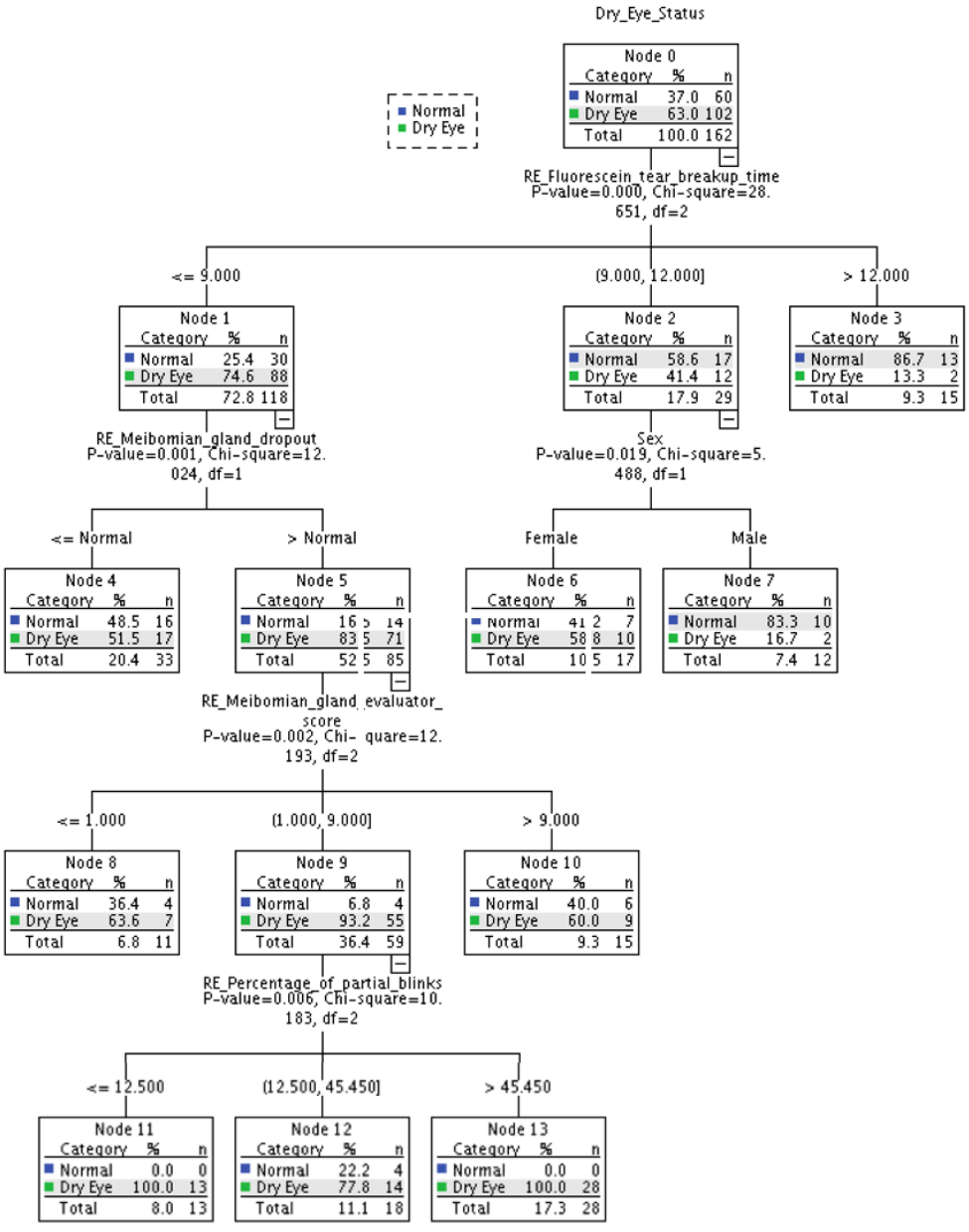


Figure 3.2: Decision tree for right eye showing which clinical tests can predict dry eye status.

Risk

Estimate	Std. Error
.253	.034

Growing Method: CHAID
Dependent Variable: Dry_Eye_Status

Classification

Observed	Predicted: Normal	Predicted: Dry Eye	Percent Correct
Normal	23	37	38.3%
Dry Eye	4	98	96.1%
Overall Percentage	16.7%	83.3%	74.7%

Growing Method: CHAID
Dependent Variable: Dry_Eye_Status

Figure 3.3: Risk and Classification table for right eye data.

The Model summary table and DTA for left eye data can be found in appendix 3.2. The left eye DTA considered separately is less sensitive and more specific than the right eye DTA, although these values do not reach above 90%.

G*Power is a tool used to compute statistical power analyses. G*Power does not include sample size calculations for DTA, however, a rule of thumb that applies to analyses such as DTA has been suggested by Armstrong & Hilton (2011). It is suggested to use a minimum of five cases per independent variable, if there at least 100 cases. This rule indicates that the sample of 162 cases used in the current analyses are sufficient, as there are over 100 cases, and five cases multiplied by 8 independent variables only requires 40 cases.

Another method suggested by Dunne for sample size calculations, involves simulating duplication of the original sample size and re-running the DTA, maintaining all original data variations including the minimum number of cases in child and parent nodes, and keeping the custom maximum tree depth to reflect the number of independent variables to be tested (M.C.M. Dunne, personal communication, August 2, 2018). The process is repeated until all independent variables are included in the decision tree, to produce a rough estimate of the required minimum sample size for future studies. The pitfalls of this estimation include the risk of creating an over-fitted decision tree with branches having strict rules and sparse data, and it does not guarantee that a larger study on different cases will necessarily include all independent variables. Nevertheless, when I tried this method for dry eye status as a nominal dependent variable, all independent variables were included with a sample size of 324 for right eye data (Table 3.5). The risk estimates did improve, as indicated by a reduced risk value in the DTA with a larger sample size. The increased number of terminal

nodes reflects how the tree becomes more complicated as the sample grows. The order in which independent variables are included in the decision tree roughly indicates those variables most likely to emerge in larger sample studies.

Sample	Terminal	Depth	Risk	Independent variables included in order of influence
162	9	4	0.253	TBUT, MG DO, MGE, %PB, Sex
324	24	4	0.148	TBUT, %PB, MG DO, Sex, MG DDil, MGE, Age, LLT

Table 3.5: Determining the minimum sample size for future studies using right eye DTA. Terminal= number of decision tree terminal nodes from Model Summary table; Depth= depth of decision tree from Model Summary table; Risk= risk estimate from Risk tables; TBUT= Fluorescein tear breakup time; MG DO= Meibomian Gland Dropout; MGE= Meibomian gland evaluator score; %PB= Percentage of partial blinks; MG Dil= Meibomian gland duct dilation; LLT= Lipid layer thickness

3.3.2: Decision Tree Analysis to predict total OSDI score for dry eye patients

The second objective was to apply DTA to investigate which clinical tests, if any, were predictive of the total OSDI questionnaire score i.e. OSDI dry eye severity amongst predominantly evaporative dry eye patients at BBR Optometry Ltd. DTA was carried out, using the chi-squared automatic interaction detection tree growing method, to determine the influence of age, sex, TearLab osmolarity, lipid layer thickness, percentage of partial blinks, Meibomian gland evaluator score, fluorescein tear breakup time, Meibomian gland dropout and Meibomian gland duct dilation on OSDI dry eye severity.

The data from the dry eye group in the first DTA was used, and a further 19 cases excluded because the total OSDI questionnaire score or the additional independent variable, TearLab osmolarity, were not recorded. TearLab osmolarity was not a clinical test included in the collection of normative data in section 3.3.1, given the cost of TearLab consumables. The total OSDI questionnaire score can be used to classify the severity of dry eye with scores of 0-12 representing normal or non-dry eye status, total scores ranging from 13-22 indicating mild dry eye, total scores ranging from 23-32 indicating moderate dry eye, and total scores ranging from 33-100 indicating severe dry eye (Miller et al., 2010). The distribution and population demographics of the sample are presented in table 3.6. Tree growth was limited to a minimum of eight cases in each parent node, four cases in each child node (0.05 x 83), and a maximum tree depth of nine (number of independent variables). For reasons explained previously, the likelihood ratio chi-square statistic was used, and the Bonferroni correction to adjust significance values was not used in right eye DTA.

OSDI Classification	Normal	Mild	Moderate	Severe
Average score	8.05 ± 2.93	16.84 ± 2.42	27.48 ± 2.51	50.52 ± 15.22
Number	13 (15.7%)	22 (26.8%)	13 (15.7%)	35 (42.2%)
Male: Female	3:10	6:16	5:8	4:31
Mean age (years)	68.85 ± 10.13	63.32 ± 10.85	68.54 ± 11.40	65.31 ± 10.29
Median age (years)	70	67	71	67
Mode age (years)	66	71	66	74
Age range (years)	46-86	39-81	46-93	28-84

Table 3.6: Population demographics for BBR Optometry Ltd. dry eye patients grouped based on OSDI classification where total scores ranging from 0-12 indicate normal/ non-dry eye status, total scores ranging from 13-22 indicate mild dry eye, total scores ranging from 23-32 indicate moderate dry eye, and total scores ranging from 33-100 indicate severe dry eye.

The Model summary table seen in figure 3.7, confirms the specifications selected, and summarises the results of the DTA by the CHAID method for right eye findings. It was noted that two of the nine independent variables were included. DTA (CHAID) automatically determined that age, sex, lipid layer thickness, percentage of partial blinks, fluorescein tear breakup time, Meibomian gland dropout and Meibomian gland duct dilation were not important predictors of OSDI dry eye severity. The depth of the resulting tree (two) was less than what was allowed for (nine), so decision tree growth was not artificially restricted.

Model Summary

Specifications	Growing Method	CHAID
	Dependent Variable	OSDI_Classification
	Independent Variables	Age, Sex, RE_TearLab_osmolarity, RE_Lipid_layer_thickness, RE_Percentage_of_partial_blinks, RE_Meibomian_gland_evaluator_score, RE_Fluorescein_tear_breakup_time, RE_Meibomian_gland_dropout, RE_Meibomian_gland_duct_dilation
	Validation	None
	Maximum Tree Depth	9
	Minimum Cases in Parent Node	8
	Minimum Cases in Child Node	4
Results	Independent Variables Included	RE_Meibomian_gland_evaluator_score, RE_TearLab_osmolarity
	Number of Nodes	6
	Number of Terminal Nodes	4
	Depth	2

Figure 3.7: Model summary for right eye DTA

Figure 3.8 shows the DTA for right eye data. Meibomian gland evaluator score was the most important predictor of OSDI classification i.e. OSDI dry eye severity amongst BBR Optometry Ltd. evaporative dry eye patients: Chi-square (6, n = 83) = 12.79, $p < 0.05$. The other predictor of OSDI

dry eye severity amongst evaporative dry eye patients was TearLab osmolarity: Chi-square (2, n = 16) = 10.85, $p < 0.05$. None of the other independent variables listed in figure 3.7 showed a statistically significant influence. The decision tree classified 46% of the subjects correctly, and had four terminal nodes:

- The first (70% of the sample) included those with a total Meibomian gland evaluator score less than or equal to eight, and showed 40% of subjects were from the severe OSDI classification.
- The second (10.8% of the sample) included those with a total Meibomian gland evaluator score greater than 11, and showed 33% of subjects were from the mild OSDI classification.
- The third (7.2% of the sample) included those with a total Meibomian gland evaluator score between eight and 11, TearLab osmolarity less than or equal to 298 mOsm/L, and showed 50% of subjects were from the moderate OSDI classification.
- The fourth (12% of the sample) included those with a total Meibomian gland evaluator score between eight and 11, TearLab osmolarity greater than 298 mOsm/L, and showed 90% of subjects were from the severe OSDI classification.

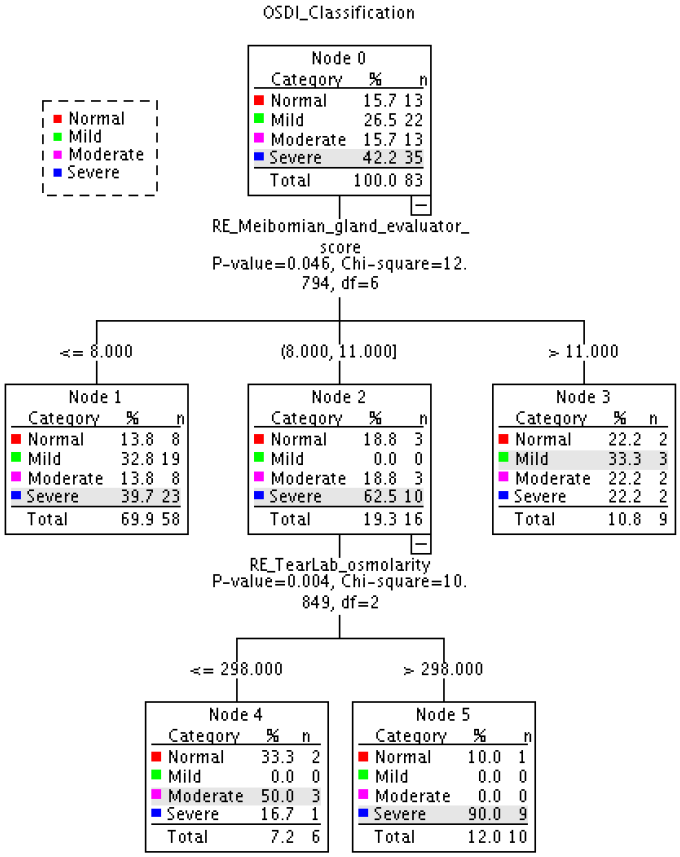


Figure 3.8: Decision tree for right eye showing which clinical tests can predict OSDI dry eye severity amongst evaporative dry eye patients

Three of the four terminal nodes are based on less than or equal to 10 observations, which may render the model prone to spurious observations. The risk and classification table for the right eye DTA can be seen in figure 3.9, showing the model is overall 46% accurate, and highly sensitive in predicting subjects with severe OSDI classification only.

Risk

Estimate	Std. Error
.542	.055

Growing Method: CHAID
Dependent Variable: OSDI_Classification

Classification

	Predicted				
Observed	Normal	Mild	Moderate	Severe	Percent Correct
Normal	0	2	2	9	0.0%
Mild	0	3	0	19	13.6%
Moderate	0	2	3	8	23.1%
Severe	0	2	1	32	91.4%
Overall Percentage	0.0%	10.8%	7.2%	81.9%	45.8%

Growing Method: CHAID
Dependent Variable: OSDI_Classification

Figure 3.9: Risk and Classification table for right eye data.

In regards to sample size calculations, and the rule of thumb applied to DTA suggested by Armstrong & Hilton (2011), the sample of 83 subjects used in the current analysis was not sufficient as there were not over 100 subjects. Using Dunne's method to produce a rough estimate of the required minimum sample size for future studies, it was found that increasing the original sample size for right eye decision trees did not include all independent variables. The majority of independent variables (eight out of nine) were included when the sample size was 249 for right decision trees with models, showing the estimated risk of 0.169. The model had the following independent variables included: Meibomian gland evaluator score, age, lipid layer thickness, Meibomian gland dropout and duct dilation, TearLab osmolarity, fluorescein tear breakup time, and percentage of partial blinks.

3.3.3: Principal Component Analysis: Questionnaire items

Twenty dry eye questionnaire item variables were subjected to PCA using SPSS version 24. There were 149 patients seen in the dry eye clinic at BBR Optometry Ltd., and 84 of these had complete composite scores recorded for both the SPEED (eight items) and OSDI (12 items) dry eye questionnaires. Nine of these subjects were excluded as they were not diagnosed as having predominantly dry eye, and a further 10 subjects were excluded because they were contact lens wearers. The population demographics for this analysis can be seen in table 3.7. Prior to performing

PCA, the adequacy of the sample size was assessed using the rule of thumb suggested by Armstrong and Hilton (2011), which is to use a minimum of five subjects per variable if there are at least 100 cases. This rule indicated that the sample of 65 subjects used above was insufficient. However, PCA was carried out regardless for exploratory purposes, considering the view that the influence of the sample size reduced when principal components were found to have three or more factor loadings of 0.60 or higher after the PCA was conducted (Guadagnoli & Velicer, 1988; Fabrigar et al., 1999; MacCallum et al., 2001). The factorability of the data was also assessed prior to performing PCA (Pallant, 2016). Inspection of the correlation matrix showed that correlation coefficients between the questionnaire items did not often exceed ± 0.30 with about 33% (62/190) exceeding ± 0.30. Bartlett's test of sphericity was statistically significant: chi-square (190, n = 65) = 809.30, $p<0.001$. The Kaiser-Meyer-Olkin value was above 0.60 (0.668). The PCA was carried out as two of the three indicators supported the factorability of the data.

	Predominately Evaporative Dry Eye Subjects with composite SPEED & OSDI dry eye scores
Number	65
Male: Female	17: 48
Mean age (years)	66.78 ± 11.65
Median age (years)	69
Mode age (years)	71
Age range (years)	28-93

Table 3.7: Population demographics

Principal component analysis revealed the presence of six principal components with eigenvalues exceeding one, using the Kaiser's criterion. These explained 31%, 14%, 9%, 8%, 7 %, and 5% of the variance respectively, a cumulative total of 74%. Inspection of the Catell's scree test plot (figure 3.10) did not reveal a clear break, which could be taken as after the second component, after the third component or after the sixth component. Nevertheless, the six principal components were retained.

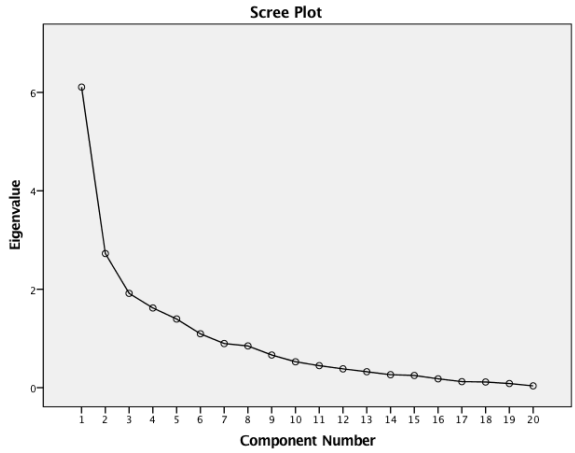


Figure 3.10: Catell's scree test plot generated from SPSS for a six-factor solution

Direct Oblimin rotation was performed to aid in the interpretation of these six components. The Pattern Matrix, which arises from Direct Oblimin rotation, shows the rotated factor loadings of each of the questionnaire items on the six extracted principal components. The Structure Matrix tables, which is unique to Direct Oblimin rotation, provides information about the correlation between questionnaire items and the principal components. The Communalities output table gives information about how much of the variance in each item is explained by the principal components with values of <0.30 indicating that an item might not fit well with the other items in its component, and that the analysis should be repeated without the item, especially if the purpose of the PCA was to improve or refine a scale. None of the items showed values <0.30, and 70% (14/20) had communalities >0.70, suggesting half of the variance of those items are accounted for by the principal component (Beavers et al., 2013). The results can be seen in table 3.8.

Item	Pattern Matrix						Structure Matrix						Communalities
	Component						Component						
	1	2	3	4	5	6	1	2	3	4	5	6	
SPEED_2	**0.829**	-0.030	0.089	0.212	0.069	-0.130	**0.893**	0.131	0.285	**0.354**	**0.397**	-0.073	0.874
SPEED_6	**0.808**	-0.151	0.074	0.053	0.102	-0.243	**0.836**	-0.021	0.250	0.163	**0.358**	-0.189	0.788
SPEED_8	**0.803**	0.183	-0.147	-0.038	0.034	0.258	**0.812**	0.253	0.018	0.134	**0.311**	0.291	0.777
SPEED_4	**0.758**	0.196	-0.056	-0.024	0.071	0.185	**0.797**	0.276	0.107	0.160	**0.352**	0.218	0.714
OSDI_3	**0.601**	0.100	0.153	0.114	0.222	-0.228	**0.721**	0.249	**0.313**	0.291	**0.487**	-0.190	0.691
OSDI_4	0.085	**0.898**	0.026	-0.189	-0.078	0.089	0.147	**0.887**	0.073	0.243	0.254	0.032	0.799
OSDI_6	0.023	**0.875**	0.051	0.001	0.055	0.066	0.133	**0.839**	0.021	0.036	0.099	0.048	0.755
OSDI_5	0.234	**0.682**	0.131	-0.014	0.040	-0.275	**0.327**	**0.724**	0.184	0.205	0.272	-0.289	0.682
OSDI_9	-0.064	**0.602**	0.088	**0.317**	-0.049	0.100	0.055	**0.661**	0.111	**0.459**	0.141	0.084	0.552
OSDI_7	-0.281	**0.463**	-0.288	**0.439**	0.234	-0.137	-0.152	**0.595**	-0.260	**0.527**	0.297	-0.157	0.715
SPEED_3	-0.040	0.118	**0.909**	-0.039	0.058	0.008	0.167	0.125	**0.906**	0.098	0.187	0.011	0.838
SPEED_7	-0.047	0.081	**0.901**	-0.006	0.045	-0.091	0.149	0.097	**0.897**	0.113	0.169	-0.086	0.824
OSDI_12	0.034	-0.041	0.062	**0.822**	0.052	0.042	0.267	0.054	**0.618**	**0.609**	0.233	0.275	0.750
OSDI_11	**0.334**	-0.049	0.004	**0.742**	-0.148	0.165	0.189	0.177	0.167	**0.837**	0.249	0.078	0.714
OSDI_8	-0.092	**0.301**	-0.121	**0.592**	0.151	**-0.328**	**0.405**	0.133	0.134	**0.755**	0.121	0.213	0.707
OSDI_10	0.060	-0.091	**0.539**	**0.546**	0.032	0.239	0.039	**0.483**	-0.054	**0.661**	0.298	**-0.323**	0.691
SPEED_5	0.032	-0.007	0.016	-0.074	**0.920**	0.099	**0.333**	0.166	0.143	0.142	**0.915**	0.106	0.854
SPEED_1	0.011	-0.061	0.096	-0.040	**0.895**	0.079	**0.318**	0.115	0.218	0.162	**0.890**	0.090	0.815
OSDI_2	**0.405**	-0.034	-0.019	0.055	**0.569**	-0.017	**0.593**	0.142	0.146	0.235	**0.706**	0.013	0.647
OSDI_1	-0.032	0.073	-0.025	0.124	0.208	**0.770**	0.101	0.112	0.022	0.211	0.243	**0.772**	0.675

Table 3.8: Pattern and Structure Matrix for PCA with Direct Oblimin Rotation of Six Factor Solution of SPEED & OSDI dry eye questionnaire items. Loadings with coefficients greater than ± 0.30 for each item are bolded.

The Stevens method was used to determine the critical value for which factor loadings exceeding this value would be deemed significantly correlated with a principal component, i.e. Critical value = 5.152/√(N-2 where N = 65. Therefore, if the factor loading was >0.60, it was deemed significantly correlated with a principal component, and referred to as having a strong loading. Additionally, weak items which included those with <0.30 correlation with other factors, and variables that cross-loaded >0.40 onto more than one factor were not considered. Dry eye questions SPEED 2, SPEED 6, SPEED 8, SPEED 4 and OSDI 3 had strong loadings on principal component one, that could be interpreted as the frequency and severity of soreness or irritation, and fatigue symptoms. Variables OSDI 4, OSDI 6, OSDI 5 and OSDI 9 had strong loadings on principal component 2, that could be interpreted as effect of dry eye on quality of vision at distance and near. There were less than 3 items

loading on principal components 3-6, so this solution was not optimal, and a simple structure did not arise.

- Variables SPEED 3 and SPEED 7 regarding frequency and severity of burning or watering had strong loadings on principal component 3.
- Variables OSDI 12 and OSDI 11 regarding exacerbation of ocular discomfort in areas that are air conditioned or in areas with low humidity had strong loadings on principal component 4.
- Variables SPEED 5 and SPEED 1 regarding severity and frequency of dryness, grittiness or scratchiness had strong loadings on principal component 5.
- Variable OSDI 1 regarding experiencing symptoms of eyes that are sensitive to light had a strong loading on principal component 6.

The Component Correlation Matrix in table 3.9 shows the strength of the relationship between principal components (Pallant, 2016). Absolute values of less than ± 0.30 indicate that it is reasonable to assume both principal components are not related, which is the assumption underlying the use of the Varimax i.e. orthogonal rotational method. Only principal components one and five showed a correlation slightly above the threshold at 0.331, and it is likely the findings of the Direct Oblimin rotation would be similar to those of the Varimax rotation.

Component Correlation Matrix

Component	1	2	3	4	5	6
1	1.000	.105	.199	.155	.331	.055
2	.105	1.000	.010	.249	.210	-.042
3	.199	.010	1.000	.110	.138	.013
4	.155	.249	.110	1.000	.225	.038
5	.331	.210	.138	.225	1.000	.008
6	.055	-.042	.013	.038	.008	1.000

Extraction Method: Principal Component Analysis.
Rotation Method: Oblimin with Kaiser Normalization.

Table 3.9: Component Correlation Matrix

If one considers principal components 1-6, despite knowing that principal components 3-6 each had less than three loadings, then the most important dry eye questions from the OSDI and SPEED questionnaires would be:

1. SPEED 2: How frequently do you experience soreness or irritation in your eyes?
2. OSDI 4: Have you experienced blurred vision during the last week?
3. SPEED 3: How frequently do you experience burning or watering?
4. OSDI 12: Have your eyes felt uncomfortable in areas that are air conditioned during the last week?
5. SPEED 5: How severe are your symptoms of ocular dryness, grittiness or scratchiness?
6. OSDI 1: Have you experienced eyes that are sensitive to light during the last week?

The Likert scale options used for SPEED frequency of symptoms responses include never, sometimes, often and constant, and the options used for SPEED severity of symptoms responses are no problems, tolerable, uncomfortable, bothersome and intolerable. OSDI Likert scale options for experiencing symptoms of dry eye include none, some, half, most or all of the time, and questions regarding environmental-specific exacerbations of dry symptoms include the item "not applicable."

Otherwise, if one considers those principal components having more than three items with factor loadings that are >0.60, then the most important questions come from principal components 1 and 2, which are questions SPEED 2 and OSDI 4. Re-consideration of the SPSS output for the Component Matrix showed the unrotated loadings of each of the items on the six components, with most of the items loaded at a level >0.40 on the first two components. As the default, SPSS uses the Kaiser criterion to retain all components with eigenvalues above one (Pallant, 2016). Very few items loaded on components 3-6, suggesting that a two-factor solution might be more appropriate. The Pattern Matrix showed three or more items with loadings greater than the critical value of 0.60 on principal components 1 and 2, further supporting the decision to re-run the analysis after retaining only two components.

For the two-factor solution, only 56.6% of the variance was explained, compared with 74% explained by the six-factor solution. Principal component 1 contributed to 37% of the variance and principal component 2 contributed to 19% of the variance. After rotating the two-factor solution (Direct Oblimin), new matrices were generated and can be seen in figure 3.11, table 3.10 and table 3.11. In order to arrive at the final two-factor solution, items were removed that had values less than 0.30 in the Communalities table, and the analysis was repeated. The six question items removed included: SPEED 3, SPEED 7, OSDI 1, OSDI 10, OSDI 11 and OSDI 12. Most of these items appeared in principal components 3-6 in the six-factor solution. The final rotated two-factor solution revealed the presence of a simple structure with both components showing a number of strong loadings (three or more > ±0.60), and all variables loading substantially on only one component (no cross-loading).

Component Matrix[a]

	Component	
	1	2
SPEED_2	.798	-.362
OSDI_3	.775	
SPEED_4	.730	
OSDI_2	.708	
SPEED_8	.704	
SPEED_6	.668	-.483
SPEED_5	.624	
SPEED_1	.602	
OSDI_5	.601	.430
OSDI_7	.308	.666
OSDI_6	.548	.660
OSDI_4	.419	.606
OSDI_9	.406	.578
OSDI_8	.426	.500

Extraction Method: Principal Component Analysis.

a. 2 components extracted.

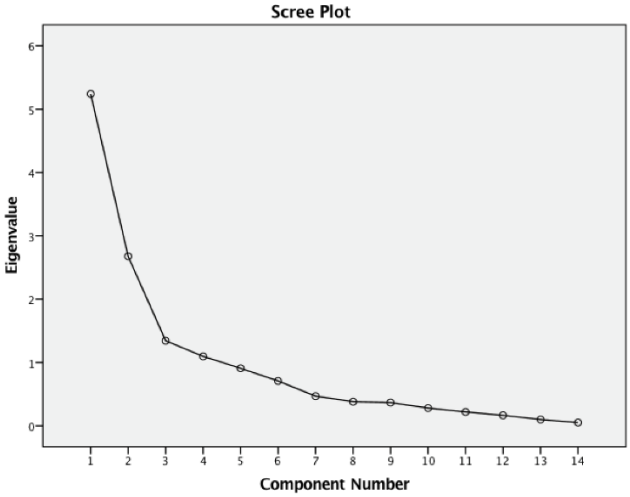


Figure 3.11: Output generated from SPSS including table of unrotated loadings from the Component Matrix and the Catell's scree test plot for a two-factor solution

Item	Pattern Matrix		Structure Matrix		Communalities
	Component		Component		
	1	2	1	2	
SPEED_2	**0.887**	-0.047	**0.875**	0.178	0.768
SPEED_6	**0.852**	-0.212	**0.799**	0.004	0.680
OSDI_3	**0.763**	0.109	**0.791**	0.302	0.637
OSDI_2	**0.755**	0.009	**0.763**	0.244	0.573
SPEED_4	**0.750**	0.054	**0.757**	0.200	0.585
SPEED_8	**0.744**	0.019	**0.749**	0.208	0.561
SPEED_1	**0.625**	0.035	**0.642**	0.231	0.403
SPEED_5	**0.624**	0.073	**0.634**	0.193	0.417
OSDI_6	0.055	**0.842**	0.268	**0.856**	0.735
OSDI_7	-0.149	**0.757**	0.168	**0.737**	0.538
OSDI_4	-0.020	**0.742**	0.043	**0.719**	0.543
OSDI_9	-0.013	**0.709**	0.166	**0.706**	0.498
OSDI_8	0.051	**0.642**	0.402	**0.702**	0.431
OSDI_5	0.240	**0.641**	0.213	**0.654**	0.546

Table 3.10: Pattern and Structure Matrix for PCA with Direct Oblimin Rotation of Two Factor Solution of SPEED & OSDI dry eye questionnaire items. Loadings with coefficients greater than ± 0.30 for each item are bolded.

Component Correlation Matrix

Component	1	2
1	1.000	.253
2	.253	1.000

Extraction Method: Principal Component Analysis.
Rotation Method: Oblimin with Kaiser Normalization.

Table 3.11: Component Correlation Matrix for the two-factor solution

Dry eye questions SPEED 2, SPEED 6, OSDI 3, OSDI 2, SPEED 4, SPEED 8, SPEED 1, and SPEED 5 had strong loadings on principal component 1 that could be interpreted as the frequency

and severity for symptoms of soreness or irritation, grittiness, fatigue, dryness or scratchiness. The most important question in principal component 1 was the same for both the two- and six-factor solution, as well as the SPEED items, but in a different order of importance. An additional SPEED and OSDI item appeared in the two-factor solution. The only SPEED items that were not included were symptoms regarding the frequency and severity of burning or watering. It was interesting that the order of importance followed the format of the questionnaire with questions on frequency first, followed by questions on the severity of the symptom experienced.

Variables OSDI 6, OSDI 7, OSDI 4, OSDI 9, OSDI 8 and OSDI 5 had strong loadings on principal component 2 that could be interpreted as the effect of dry eye on limiting visual performance or the effect of dry eye on visual functioning for everyday tasks including reading, driving at night, watching TV, and using a computer or bank machine. The most important question in principal component 2 differed between the solutions with OSDI 4 in the six-factor solution, and OSDI 6 in the two-factor solution although both loaded strongly on component 2, and dealt with the effect of dry eye on quality of vision. Once again, the two-factor solution had the same items listed in different order of importance, and included two additional variables. Therefore, the most important dry eye questions from the OSDI and SPEED questionnaires considered together were:

1. SPEED 2: How frequently do you experience soreness or irritation in your eyes?
2. OSDI 6: Have problems with your eyes limited you in reading during the last week?

There was a weak positive correlation between the two components ($r = 0.253$) in the two-factor solution, and it is reasonable to assume that both principal components were not related. Therefore, rotating a smaller number of components led to a more optimal solution.

In a separate PCA to follow looking at all clinical tests in section 3.3.5, the "Jessica score" will be introduced which is the sum of questions SPEED 2 and OSDI 6 that has a minimum score of 0 and a maximum score of seven, with higher scores indicating subjects who experience symptoms of soreness or irritation more often that limits their ability to read most of the time. The distribution of the "Jessica score" can be seen in figure 3.12, where the average score was 3.00 ± 1.78 with a mode of 2 and median of 3.

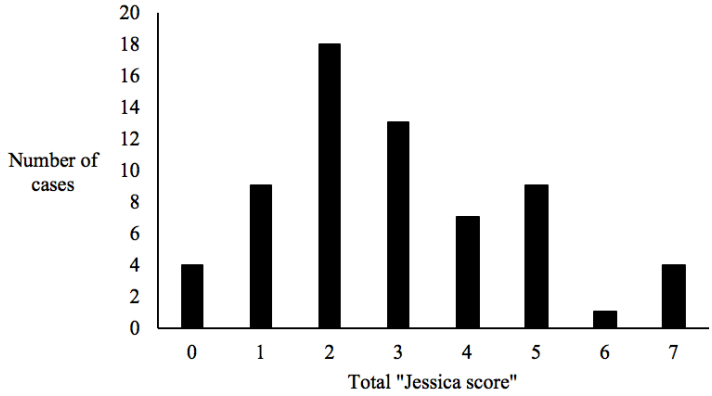


Figure 3.12: Distribution of the "Jessica Score" in a sample of predominately evaporative dry eye subjects presenting to BBR Optometry Ltd.

3.3.4: Principal Component Analysis: Total questionnaire scores and clinical test items

Principal component is based on the eigendecomposition of a cross-product matrix, and thus requires complete data sets without missing values (Dray & Josse, 2015). When there is incomplete data, a popular approach is to delete individuals, and/or variables containing missing vales prior to applying PCA, which can lead to an important loss of information including the detection of patterns (Dray & Josse, 2015). The standard PCA algorithm can be adapted so that missing vales are not considered in the computations. One strategy is the mean imputation method, which replaces missing values for each variable by the mean of the observed values. A complete data set is obtained, and can then be analysed by a standard PCA. The issue with this method is that the variance of the imputed variables, and the correlations between variables are reduced as the distribution of the data is distorted (Little & Rubin, 2002). The listwise exclusion method omits an entire case with missing values on any of the variables, and is the default setting in SPSS. In the pairwise exclusion method, the statistical procedure cannot include a particular variable when it has a missing value but can still use the case when analysing other variables with non-missing values. The pairwise exclusion method allows one to use more of their data, however, this strategy can cause problems with the computation of correlation matrices with outputs of negative eignenvalues due to statistical analyses based on a different subset of subjects (IBM Support, 2019). Of the 149 patients attending for a dry eye consultation at BBR Optometry Ltd., 21 subjects were excluded due to contact lens wear and a further 12 as they did not represent predominantly evaporative dry eye subjects. Therefore, a total of 116 subjects were used in the current PCA, although there were missing entries for some of the nine variables. The pairwise exclusion method was utilized, and the right and left eyes were considered separately.

Nine clinical test variables were subjected to PCA using SPSS version 24. The population demographics for this analysis can be seen in table 3.12. Prior to performing PCA for right eye data,

the adequacy of the sample size was assessed utilising the rule of thumb suggested by Armstrong and Hilton (2011), which is to use a minimum of five subjects per variable if there are at least 100 subjects. This rule indicated that the sample of 116 subjects was sufficient. The factorability of the data was also assessed. Inspection of the correlation matrices showed that correlation coefficients between the clinical test items for right eye data did not often exceed ± 0.30 with about 11% (4/36) exceeding ± 0.30. Bartlett's test of sphericity was statistically significant: chi-square (36, n = 116) = 89.17, $p<0.001$ for right eye data. The Kaiser-Meyer-Olkin value was less than 0.60 for right eye at 0.586. Only one of the three indicators supported the factorability of the data indicating that the sample is probably not suitable for data factor analysis. For exploratory purposes, although the suitability of the sample remains questionable for two criterions, factor analysis proceeded.

	Predominately Evaporative Dry Eye Subjects
Number	116
Male: Female	28: 88
Mean age (years)	66.69 ± 12.10
Median age (years)	68
Mode age (years)	74
Age range (years)	26-97

Table 3.12: Population demographics

PCA revealed the presence of four principal components with eigenvalues exceeding one. These explained a proportion of the variance with a cumulative total of about 66%. The percentage of variance for each component can be seen in table 3.13.

Principal Component	Extraction Sums of squared loadings percent of variance
1	23.273
2	17.573
3	14.027
4	11.139

Table 3.13: Percentage of variance for principal components for right eye data.

Inspection of the Catell's scree test plots did not reveal clear breaks, which could be taken at the fifth component for each PCA. Nevertheless, the four principal components were retained and oblimin rotation was performed to aid in the interpretation of these components.

Table 3.14 shows the pattern coefficients, structure coefficients and communalities for each clinical test variable for right eye data, in relation to the four principal components. The meibography clinical test variables assessing Meibomian gland duct dilation and Meibomian gland dropout had strong

loadings (> ±0.60) on principal component 1 that could be interpreted as measures of Meibomian gland structure. The variables total OSDI and total SPEED questionnaire scores had strong loadings on principal 2 that could be interpreted as measures of dry eye symptoms. The variables fluorescein tear breakup time and TearLab tear osmolarity had strong loadings on principal component 3 that could be interpreted as measures of tear film stability. The variable percentage of partial blinks had a strong loading on principal component 4 that could be interpreted as measure of dynamic eyelid aspects.

In the PCA for right eye data, the variable average lipid layer thickness loaded strongly on component 4, which would make sense as it is also a dynamic measure of posterior eyelid aspects. The variable of total Meibomian gland evaluator score loaded on principal component 1 and 4 (1>4) for right eye data although both at levels less than ±0.60 indicating it as a weak item. Unfortunately, a simple structure did not arise.

Item	Pattern Matrix				Structure Matrix				Communalities
	Component				Component				
	1	2	3	4	1	2	3	4	
RE_Meibomian_Gland_Duct_Dilation	**-0.773**	0.011	-0.127	0.164	**-0.793**	-0.065	0.222	-0.249	0.579
RE_Meibomian_Gland_Dropout	**-0.762**	-0.094	0.147	-0.108	**-0.732**	0.026	-0.061	0.031	0.67
RE_Meibomian_Gland_Evaluator_score	**0.509**	0.056	-0.286	**0.381**	**0.603**	0.023	**-0.352**	**0.485**	0.594
Total_OSDI_Score	0.020	**0.863**	0.048	0.113	0.010	**0.861**	0.070	0.096	0.758
Total_SPEED_Score	0.072	**0.859**	-0.010	-0.173	0.016	**0.860**	0.020	-0.178	0.771
RE_Fluorescein_tear_breakup_time	-0.135	0.096	**-0.805**	0.057	-0.050	0.071	**-0.792**	0.070	0.655
RE_TearLab_Osmolarity	-0.216	0.214	**0.705**	0.137	-0.265	0.242	**0.726**	0.059	0.629
RE_Percentage_of_partial_blinks	-0.165	0.000	-0.045	**0.838**	-0.011	-0.014	-0.070	**0.811**	0.684
RE_Lipid_layer_thickness	**0.345**	-0.112	0.220	**0.607**	**0.436**	-0.128	0.154	**0.661**	0.6

Table 3.14: Pattern and Structure Matrix for PCA with Direct Oblimin Rotation of Four Factor Solution of BBR Optometry Ltd. clinical test items for right eye data. Loadings with coefficients greater than ± 0.30 for each item are bolded.

If only the first items from each of the components are considered, the most important clinical tests in order of importantce are Meibomian gland duct dilation, OSDI total score, fluorescein tear breakup time, and percentage of partial blinks respectively. There was a weak correlation between the four factors ($r < \pm 0.30$), and hence the assumption that each principal component are not related holds true so the findings of Oblimin rotation would be similar to those of the Varimax rotation.

3.3.5: Principal Component Analysis: Total "Jessica score" and clinical test items

Recall the "Jessica score" derived from the two-factor solution in 3.3.3, which is the sum of questions SPEED 2 and OSDI 6 that has a minimum score of zero, and a maximum score of seven with higher scores indicating subjects who experience symptoms of soreness or irritation more often that limits their ability to read most of the time. The later analysis in 3.3.4 was re-run for right eye data, with the total SPEED and OSDI scores replaced by the "Jessica score" for the sample presented in 3.3.3 that is, those predominately evaporative dry eye subjects who had full composite OSDI and

SPEED scores reported. The rule of thumb suggested by Armstrong and Hilton (2011) indicated that the sample of 65 subjects was insufficient. The factorability of the data was also assessed. Inspection of the correlation matrices showed that correlation coefficients between the clinical test items for right eye data did not often exceed ± 0.30 with about 18% (5/28) exceeding ± 0.30. Bartlett's test of sphericity was statistically significant: chi-square (28, n = 65) = 75.20, $p<0.001$ for right eye data. The Kaiser-Meyer-Olkin value was greater than 0.60 for right eye data at 0.614. Only two of the three indicators supported the factorability of the data, indicating that the sample may not be suitable for factor analysis. For exploratory purposes, although the size and suitability of the sample remains questionable for one criterion, factor analysis proceeded.

PCA revealed the presence of four principal components with eigenvalues exceeding one. These explained a similar proportion of the variance with a cumulative total of about 72%. The percentage (%) of variance for each component can be seen in table 3.15.

Principal Component	Extraction Sums of squared loadings percent of variance
1	29.477
2	15.483
3	14.599
4	12.842

Table 3.15: Percentage (%) of variance for principal components for right eye data.

Inspection of the Catell's scree test plots did not reveal clear breaks, with the possibility of a first break at component 2 for each PCA. Nevertheless, the four principal components were retained, and oblimin rotation was performed to aid in the interpretation of these components.

Table 3.16 shows the pattern coefficients, structure coefficients and communalities for each clinical test variable for right eye data, in relation to the four principal components. The meibography clinical test variables assessing Meibomian gland duct dilation and Meibomian gland dropout had strong loadings (> ±0.60) that could be interpreted as measures of Meibomian gland structure. The variable total "Jessica score" had a strong loading on principal 4 that could be interpreted as measure of dry eye symptoms. The variables fluorescein tear breakup time, and TearLab tear osmolarity had strong loadings on principal component 2 with right eye data that could be interpreted as measures of tear film stability. The variable percentage of partial blinks had a strong loading on principal component 3 with right eye data that could be interpreted as measure of dynamic eyelid aspects. The variable average lipid layer thickness cross-loaded onto 2 principal components interpreted as relating to Meibomian gland structure and dynamic eyelid aspects, albeit weakly (component 1 loading <

±0.40). The variable TearLab tear osmolarity loaded onto three principal components relating to tear film stability, and weakly (<±0.60) to dry eye symptoms, and Meibomian gland structure. Unfortunately, a simple structure did not arise.

Item	Pattern Matrix				Structure Matrix				Communalities
	Component				Component				
	1	2	3	4	1	2	3	4	
RE_Meibomian_Gland_Dropout	**-0.885**	0.060	0.079	-0.153	**-0.873**	-0.069	-0.014	-0.171	0.794
RE_Meibomian_Gland_Evaluator_score	**0.799**	0.119	-0.007	-0.086	**0.812**	0.219	0.072	-0.058	0.679
RE_Meibomian_Gland_Duct_Dilation	**-0.628**	-0.010	-0.095	-0.089	**-0.641**	-0.096	-0.160	-0.106	0.428
RE_Percentage_of_partial_blinks	-0.093	**0.887**	0.209	0.007	0.046	**0.870**	0.180	0.060	0.805
RE_Lipid_layer_thickness	**0.390**	**0.672**	-0.209	-0.098	**0.455**	**0.722**	-0.185	-0.049	0.706
RE_Fluorescein_tear_breakup_time	-0.082	0.181	**0.849**	0.202	0.034	0.163	**0.838**	0.217	0.782
RE_TearLab_Osmolarity	**-0.322**	0.210	**-0.629**	**0.427**	**-0.348**	0.207	**-0.664**	**0.426**	0.755
Total_Jessica_Score	0.213	-0.077	0.102	**0.882**	0.236	0.002	0.133	**0.884**	0.843

Table 3.16: Pattern and Structure Matrix for PCA with Direct Oblimin Rotation of Four Factor Solution of BBR Optometry Ltd. clinical test items including the "Jessica score" for right eye data. Loadings with coefficients greater than ± 0.30 for each item are bolded.

If only the first items from each of the components are considered, the most important clinical tests or dry eye diagnostics at BBR Optometry Ltd. include Meibomian gland duct dropout, percentage of partial blinks, fluorescein tear breakup time, and the "Jessica score". There was a weak correlation between the four factors ($r < \pm 0.30$), and hence the assumption that each principal component are not related holds true so the findings of Oblimin rotation would be similar to those of the Varimax rotation. All component matrices, Catell's scree test plots and component correlation matrices can be found in appendix 3.3.

3.4: Discussion

3.4.1: Decision Tree Analysis to predict symptomatic dry eye status

Subjects were allocated to the dry eye group on the basis that they scored greater than zero on the SPEED questionnaire, attended for a dry eye consultation, and were attending of their own free will due to concerns regarding a possible dry eye condition. Subjects allocated to the normal group were those BBR Optometry Ltd. patients attending for an eye examination, who did not identify as having a dry eye problem based on their SPEED dry eye questionnaire scores. It is possible that these subjects had pre-symptomatic dry eye or had come to accept symptoms related to dry eye as normal age-related changes or associated with environmental conditions or use of cosmetics, and so did not identify as having a dry eye problem.

The current analysis applies to predominantly evaporative dry eye subjects, and so cannot comment on other forms of dry eye i.e. predominantly aqueous deficient dry eye subjects. The sample is biased towards inclusion of evaporative dry eye subjects, and perhaps more severe cases of dry eye since these patients have presented to BBR Optometry Ltd. for a full dry eye work-up. The majority of

predominantly evaporative dry eye subjects were confirmed as self-reporting more severe symptoms, i.e. scoring over 33 on the OSDI questionnaire, in section 3.3.3. Previous studies have shown that a common form of evaporative dry eye, MGD, may play a role in severe dry eye conditions such as Sjögren's syndrome with these patients presenting with impaired Meibomian gland function when compared to non-dry eye controls although the mechanism is unclear (Kang et al., 2018).

There were no specific criteria used for the diagnosis of predominately evaporative dry eye, and subjects were classified as such retrospectively based on notes of plugging of the Meibomian gland orifices, turbid Meibomian gland secretions, the presence of telangiectasia on the posterior eyelid margin, and recommendations for lid hygiene, warm compresses and lid hygiene according to the DEWS II staged management and treatment recommendations for dry eye (Jones et al., 2017). Previous studies have used cut-off values for questionnaire results such as OSDI ≥13 or 20 to define a dry eye sample or simply stated that a subjective evaluation of dry eye symptoms or a clinical diagnosis of dry eye was made without specifying a sub-classification or inclusion criteria (Ngo et al., 2013; Asiedu, 2017; Simpson et al., 2008; Stapleton et al., 2017). The current analysis involved a clinical sample, and no active recruitment of subjects meeting set inclusion criteria. The same practitioner (the author) carried out the dry eye consultations, and collected data for the normal group. Therefore, knowledge of the patient symptoms assessed prior to clinical testing may have biased the practitioner when performing dry eye tests to expect either more or less severe test outcomes. However, given the nature of the current analyses where patients are privately funding dry eye consultations, a masked examiner would not be feasible as a practitioner requires all information on signs and symptoms in order to make decisions on clinical management. No subjects with Steven-Johnson syndrome, vitamin A deficiency, rheumatoid arthritis, Wegener granulomatosis, sarcoidosis, leukaemia, Riley-Day syndrome, systemic lupus erythematosus or Sjögren's syndrome were included in any of the analyses in order to report on predominately evaporative dry eye as other studies have done (Ngo et al., 2013).

Previous studies have established that ocular symptoms are much more frequent in soft contact lens wearers than in noncontact lens wearers, and a different aetiology for dry eye amongst these groups has been suggested (Guillon & Maissa, 2005b; McMonnies & Ho, 1986; Vajdic et al., 1999). The two terms for dryness related to contact lens wear are contact lens induced dry eye (CLIDE) whereby signs and symptoms of dry eye did not exist before contact lens wear, and contact lens associated dry eye (CLADE) where pre-exisitng dry eye cannot be discounted (Gomes et al., 2017). There are reported discrepancies with the association between contact lens wear and MGD, perhaps due to limitations in methodology, small sample sizes, and lack of information on contact lens replacement and removal intervals (Korb & Henriquez, 1980; Henriquez & Korb, 1981; Schaumberg et al., 2011;

Machalinska et al., 2015; Arita et al., 2009). However, structural changes including meibomian gland duct shortening has been detected in contact lens wearers with symptoms related to dry eye (Arita et al., 2009). Therefore, contact lens wearers were excluded from the analysis. The potential relationship between dry eye and discontinuation of contact lens wear is discussed in chapter five.

Fluorescein tear breakup time was the consistent, most important discriminator for dry eye status (RE DTA: ≤ 9, 9-12 and >12). Tear breakup results when evaporation due to external factors, such as a dry or windy environment leads to a lowering of the ocular surface temperature, and an increase in cation and protein concentration (Mori et al., 1997). These changes are detected by temperature-sensitive and chemical receptors on the cornea, which stimulate a blink to reform the tear film (Belmonte et al., 2004b; Caterina, 2007; Lee & Caterina, 2005; Schepers & Ringkamp, 2009; Lawrenson et al., 2005). As expected, there were a larger number of normal subjects when fluorescein tear breakup time was at its greatest level, and a small number of subjects with dry eye in these nodes. Ngo et al. (2013) noted that fluorescein tear breakup time was not statistically different between symptomatic (OSDI ≥13) and asymptomatic groups. However, in the asymptomatic group, there was large variation observed in measured fluorescein tear break up time, as well as in conjunctival staining with fluorescein and lissamine green, and in measures of tear volume with Schirmer's strips (Ngo et al., 2013). The DEWS II methodology subcommittee have identified tear breakup time as a critical diagnostic test for dry eye diagnosis, although non-invasive methods versus use of fluorescein if available are recommended with a value of <10 seconds taken to be a positive marker for loss of homeostasis (Wolffsohn et al., 2017). Fluorescein tear breakup time measurements followed tear osmolarity testing for dry eye patients considering the invasive nature of applying fluorescein to the tear film. Ideally, three objective measurements of tear breakup would be taken non-invasively with the median value recorded using an automated algorithm. Positive tests for dry have found to be as low as 2.7 seconds, though cut off values of up to 10 seconds have been found subjectively (Hong et al., 2013; Mengher et al., 1985b).

Meibomian gland dropout was the second most important discriminator for right eye DTA (RE DTA: ≤ normal, > normal). Anatomically, the Meibomian glands are modified sebaceous glands embedded in the tarsal plate of the eyelids that are regulated neurally, and hormonally to secrete a mixture of various polar and nonpolar lipids, phospholipids, sterol esters, wax esters, and cholesterol (Blackie et al., 2010). Histopathological evidence from animals and humans suggest that MGD is characterized by hyperkeratinisation of the Meibomian gland duct epithelium, resulting in narrowing of ducts and obstruction of individual glands due to the sloughing of keratinized cells into the ducts (Blackie et al., 2010). Other changes that can result from stagnation of the Meibomian glands include a compensatory thickening of the glands or duct dilation, and tortuosity followed by gland atrophy

(Tomlinson et al., 2011; Baudouin et al., 2016; Knop et al., 2011; Korb & Henriquez, 1980; Blackie et al., 2010). Meibography allows imaging of the silhouette of the Meibomian gland structure. It has been suggested that meibography should be interpreted in the context of other clinical parameters, rather than a standalone indicator for the diagnosis of MGD (Pult & Riede-Pult, 2012; Arita et al., 2009; Finis et al., 2015; Lemp et al., 2012). A positive correlation between tear fluid secretion and area of severe Meibomian gland atrophy has been shown, and thought to be part of a compensatory mechanism in patients with MGD (Arita et al., 2015). Structural changes to the Meibomian glands are less marked in those with aqueous deficient dry eye than evaporative dry eye, according to studies utilising meibography (Arita et al., 2015; Arita et al., 2010).

Total Meibomian gland evaluator score was the third most important predictor for dry eye status for right eye DTA (RE DTA: ≤ 1, 1-9, > 9). The three discriminators in the DTA reflect how both structural and functional changes to the Meibomian glands can predict evaporative dry eye status, and how the model is good at identifying more advanced cases of dry eye. A cross-sectional study of 538 meibomian gland dysfunction patients and 21 healthy controls in a Norwegian cohort conducted by Adil et al. (2018) found the mean dropout meibogrades, similar to the scale used in the current analysis, were significantly higher in the patients with meibomian gland dysfunction, and the sensitivity and specificity of the meibograde as a diagnostic metric using a cut-off value of 0.50 was 96.7% and 85% respectively. Interestingly, symptoms qualified using the OSDI score did not correlate with the measure of Meibomian gland morphology (Adil et al., 2018). Other studies have also shown inconsistent results when exploring the relationship between Meibomian gland structural changes, and clinical tests for dry eye (Pult & Riede-Pult, 2012; Feng et al., 2014; Arita et al., 2009; Cuevas et al., 2012; Jie et al., 2009; Srinivasan et al., 2012).

Interestingly, there was a similar proportion of normal and dry eye subjects in right eye DTA when there was a reduced fluorescein tear breakup time, and no Meibomian gland dropout (node 4). Similarly, there was an even number of dry eye and normal subjects for those with a reduced fluorescein tear breakup time, less than or equal to 74 years old, had a reduced number of functional Meibomian glands, and no or mild Meibomian gland dropout (node 9). Perhaps where there is tear film instability, and mild or no structural changes to the Meibomian glands, there is an individual threshold for dry eye status or dry eye symptoms. Nonobvious Meibomian gland dysfunction describes the precursor to obstructive Meibomian gland dysfunction that may be present with minimal or absent signs of inflammation and pathology, and can be detected with physical expression of the Meibomian glands and reports of excess blinking to maintain clear vision (Blackie et al., 2010). Symptoms are not usually present in milder forms of evaporative dry eye or Meibomian gland dysfunction until the integrity of the tear film is challenged by changes in the humidity or

temperature of the environment, prolonged use of computers or contact lens use (Foulks & Bron, 2003; Borchman et al., 2009; Fenga et al., 2008; Henriquez & Korb, 1981).

DTA (CHAID) automatically determined that Meibomian duct dilation and lipid layer thickness were not important predictors of symptomatic dry eye status, which was unexpected. The lipid layer formed by the secretion of the Meibomian glands has many known functions including:

- Reducing the loss of tears from evaporation (Mishima & Maurice, 1961)
- Stabilising the aqueous component of the tear film (Holly, 1985)
- Reducing the surface tension of tears by drawing water into the tear film (Lemp et al., 1970)
- Thickening the aqueous component of the tears, providing a smooth optical surface (Bron & Tiffany, 2004)
- Preventing the overflow of tears, maceration of the skin at the eyelid margin, and contamination by sebaceous gland secretions from facial skin (Blackie et al., 2010)

A reduction in the tear film lipid layer thickness measured with LipiView interferometer has been associated with upper and lower eyelid Meibomian gland atrophy leading to a shorter tear breakup time, and with increased friction during the action of a blink (Eom et al., 2013; Tung et al., 2014). Infrared spectroscopic studies suggest that stiffer, more ordered viscous meibum lipid arrangements in meibomian gland dysfunction are unlikely to spread on the tear film, and impede meibum flow with less lipid on the lid margin leading to increased tear evaporation (Borchman et al., 2011). A small study using lipid absorbent Sebutape to collect meibum has suggested that the amount of lipid on the lid margin may not affect tear stability because there is 17 times more pooled lipid than is required to cover the ocular surface even with MGD (Ashraf et al., 2011). A cross-sectional study of 139 patients with evaporative dry eye classified as having obstructive or non-obstructive Meibomian gland dysfunction, determined that lipid layer thickness measurements and tear meniscus height measurements could be useful in the differential diagnosis of these subtypes (Sang et al., 2018). A classification of obstructive Meibomian gland dysfunction was made in the presence of altered gland secretion, and changes in lid morphology including plugging of the orifices and poor meibum expression by digital pressure application as per the universally accepted diagnostic criteria proposed by the International Workshop on Meibomian gland dysfunction (Sang et al., 2018; Tomlinson et al., 2011). Although there was no assessment of healthy controls, the authors proposed the hypothesis that non-obstructive or nonobvious Meibomian gland dysfunction may be due to a hyposecretory mechanism that does not involve inflammation, given that fewer expressing glands was associated with a thinner lipid layer thickness (Sang et al., 2018). Higher median lipid layer thickness values were found in patients with obstructive Meibomian gland dysfunction as reported elsewhere (Jung et al., 2016) even though the tear film assessed by tear breakup time was unstable,

suggesting tear film evaporation may not necessarily be correlated with lipid layer thickness (Sang et al., 2018). It has been postulated that bacterial lipolytic exoenzymes produced by commensal bacteria in patients with Meibomian gland dysfunction can alter the composition of normal lipid components, and induce eyelid and ocular surface inflammation, ultimately affecting the lipid layer thickness (Sang et al., 2018).

The interpretation of epidemiological study results is complicated by the absence of a validated combination of clinical tests to confirm a diagnosis of dry eye and its subtypes, and previously a lack of standardized or agreed definitions (Stapleton et al., 2017). A meta-analysis by Stapleton et al. (2017) found that the prevalence of dry eye disease including MGD increases with age from aged 50, and more markedly beyond the age of 80 with signs showing a greater increase per decade than symptoms. There are also studies that do not show a significant association between age and dry eye disease, which is not the major reported finding (Tong et al., 2009; Han et al., 2011; Tan et al., 2015; Schein et al., 1997; Lin et al., 2003). The authors of the DEWS II Epidemiology report also acknowledge the limited number of prevalence studies in younger populations (Stapleton et al., 2017). There may be overlap between normal and dry eye subjects with studies showing an association between older age, and an increase in positive signs of dry eye, such as low tear production or tear instability indicated by a tear break up time ≤10 seconds in a normal population (Lu et al., 2008; Guo et al., 2010; Uchino et al., 2006; Ozdemir & Temizdemir, 2010; Cho & Brown, 1993). Studies have shown age-related differences with a decline in the number of Meibomian glands after the age of 30 (Artia et al., 2008), as well as Meibomian gland expressibility by about half at 80 years old (Mathers & Lane, 1998; Norn, 1987). Other age-related changes to Meibomian gland and lid anatomy that tend to increase in those over 50 years old include lid margin vascularity, keratinization, and telangiectasia (Den et al., 2006; Hykin & Bron, 1992). Tear osmolarity and meibum opacity are other variables that have been shown to increase with age (Mather et al., 1996; Mathers & Lane, 1998). The pathological threshold for changes in tear instability and production with age is not established, although the DEWS II diagnostic subcommittee consider ± two standard deviations from the mean value as the cut-off value for accepted tests (Stapleton et al., 2017). Prevalence rates by sex seem to become significant only with age, with women more likely to be impacted by dry eye than men (Stapleton et al., 2017).

There was higher proportion of women than men seen for dry eye consultations at BBR Optometry Ltd. Although some studies have shown otherwise (Tong et al., 2009; Guo et al., 2010; Tan et al., 2015; Onwubiko et al., 2014; Pouyeh et al., 2012), female sex has been consistently associated with dry eye disease (Uchino et al., 2011; Ahn et al., 2014; Um et al., 2014; Moss et al., 2008; Jie et al., 2009; Han et al., 2011; Viso et al., 2009; Hashemi et al., 2014; Malet et al., 2014; Paulsen et al., 2014; Sahai & Malik, 2005; Nichols et al., 2005; Galor et al., 2011; Kim et al., 2011; Galor et al.,

2012; Basak et al., 2012; Li et al., 2015). Numerous sex-related differences in the anatomy, physiology, and pathophysiology of structures in the eye have been identified with the variation attributed to the effects of sex steroids, hypothalamic-pituitary hormones, glucocorticoids, insulin, insulin-like growth factor 1, thyroid hormones, sex chromosome complement, sex-specific autosomal factors and epigenetics (Sullivan et al., 2017). In a cross-sectional study involving 3824 British female twins from the TwinsUK cohort, there was a peak increase in dry eye prevalence in the 40 to 50-year-old group (Vehof et al., 2014). Important risk factors for dry eye disease in this group were identified as immune-mediated disease, ocular surgery history and chronic pain syndromes, such as irritable bowel syndrome and fibromyalgia (Vehof et al., 2014). It is hypothesized that chronic pain in dry eye disease may be due to neuropathic pain, and sex-differences may be due to different underlying biological mechanisms (Sullivan et al., 2017). The impact of sex on dry eye status is uncertain for Meibomian gland dysfunction (Stapleton et al., 2017). In the current analysis, 77% of patients within the dry eye group were female, and 53% of subjects within the normal group were female. The right eye decision tree branches from having a fluorescein tear breakup time between 9 and 12 seconds based on sex to two terminal nodes, with subjects more likely to have dry eye if they were female (node 6, n=17), and less likely if they were male (node 7, n=12).

In addition to sex, defined as distinguishing a person based on their biological characteristics, gender which is rooted in biology but shaped by socially constructed characteristics can also affect dry eye disease risk and presentation of the disease (Sullivan et al., 2017). A cross-sectional study of 755 patients from a tertiary dry eye clinic found significantly higher symptom scores in women compared to men with similar severity levels in clinical signs, similar to results of a previous study (Vehof et al., 2018; Schaumberg et al., 2013). Vehof et al. (2018) also found lower correlation between symptoms and signs in women. Some studies have shown increased ocular surface sensitivity in women compared to men (Golebiowski et al., 2008; Golbiowski et al., 2012; du Toit et al., 2001; Acosta et al., 2006; Teson et al., 2012), which may explain the findings of Vehof et al. (2018) and others that do not find any sex differences (De Paiva & Pflugfelder, 2004; Bourcier et al., 2005). Future work is required to determine the role of corneal and conjunctival sensitivity in the symptoms of dry eye disease, and possible sex-differences. Sex-related differences have been found in reported impact of dry eye disease on visual quality indicators, and visual activities with women reporting greater levels of impact and women also more likely to report greater feelings of depression than men (Schaumberg et al., 2003). Depression is a risk factor for dry eye, and a comorbidity of which women are more at risk, with non-ocular studies suggesting depression can lead to increased pain (Fillingim et al., 2009). Another explanation for observed increased symptoms in women might be that as part of the feminine gender role, women are more likely to report pain (Sullivan et al., 2017).

Branching in the right eye decision tree following findings of TBUT ≤ 9 seconds, some degree of Meibomian gland dropout, and a total Meibomian gland evaluator score ranging from one to nine was based on percentage of partial blinks in a way that was not expected (three-ways). Node 11 (n=13) representing subjects where there was ≤12.5% of partial blinking, and node 13 (n=28) representing subjects where there was >45.45% of partial blinking, show 100% of subjects were identified as dry eye. However, both nodes represent opposite sides of the spectrum with a partial blinking rate of 40% or greater indicating blinking exercises may be encouraged, and related to evaporative dry eye. Node 12 (n=18) representing subjects where there was between 12.5% and 45.45% of partial blinking showed the subjects were predominately dry eye (78%). Therefore, the percentage of partial blinks does not seem to be a great discriminator for dry eye status, but perhaps represents an artefact from the CHAID algorithm. Of note, were the 22% or four subjects identified as normal in node 12, perhaps due to the small sample numbers or showing how although dry eye symptoms may not be present, there is a possibility that signs of dry eye disease could be present.

Based on the stronger model (RE DTA), the selection of clinical tests available at BBR Optometry Ltd. that are potentially predictive of predominately evaporative dry eye in order of importance include: fluorescein tear breakup time especially if it is ≤ to 9 seconds, there is some degree of Meibomian gland dropout, and a total Meibomian gland evaluator score that is between 1 and 9. Sex may also be a predictive factor for dry eye status if the fluorescein tear breakup time is between 9 and 12 seconds, with women more likely to be affected with dry eye.

3.4.2: Decision Tree Analysis to predict total OSDI score for dry eye patients

Therapy for dry eye is based upon disease severity according to the staged management algorithm proposed by members of the DEWS II Management and Therapy Subcommittee (Jones et al., 2017). DTA was applied to determine which clinical tests were predictive of OSDI dry eye severity amongst patients with predominately evaporative dry eye. It would appear that three of the four terminal nodes in the right eye DTA were based on less than or equal to 10 observations, which may render the entire model prone to spurious observations. The model is also under 50% accurate, and highly sensitive for severe OSDI classifications. Overall, the weak model would suggest that the total Meibomian gland evaluator score (value ≤ eight) or functionality of the Meibomian glands is a predictive factor for predominately evaporative dry eye sufferers identifying as having severe symptoms based on the OSDI questionnaire classification. However, the sample size was not sufficient to draw conclusions. The full set of data collected could not be used in DTA due to missing values, which can be a problem with data collection in a busy clinical setting, especially when data is analysed retrospectively. Some questionnaires were not completed in full, and there were few rare occurrences of technical malfunctions, which meant certain tests could not be performed at the time

of the dry eye consultation. Considering the same data set was used, albeit with slightly more subjects, the model generated in 3.3.2 may only apply when considering severe dry eye subjects.

There are several external factors that can impact the tear film and risks for dry eye, hence prior to attending for a dry eye consultation at BBR Optometry Ltd., patients are advised to:

- Cease use of any drops or ointment for at least 24 hours or at least four hours prior to the appointment if there is use of hypotensive drops.
- Avoid use of oil-based facial cosmetics around the eye on the day of assessment.
- Not swim in a chlorinated pool for at least 12 hours prior to the appointment.
- Bring a list of current medication.
- Bring in a list of products used to manage dry eye or the actual products used at present.

It is interesting to find that 16% of patients using BBR Optometry Ltd.'s services for dry eye concerns, and who were offered management options for evaporative dry eye, scored normal in the OSDI classification. Overall there were more severe OSDI classifications (42%) than mild classifications (27%), followed by a similar proportion of normal and moderate subjects reflecting the patient's perception of their dry eye status or symptom severity. The average age was 65.84 ± 10.80 with a similar age distribution across all OSDI classifications, and there more females than males (65:18).

Meibomian gland evaluator score was the most important variable for right eye DTA in predicting dry eye severity amongst predominately evaporative dry eye patients. The Meibomian gland evaluator score was also consistently listed as the most important independent variable for right eye DTA when using Dunne's suggested method to produce a rough estimate of the required minimum sample size for future studies. Previously for right eye DTA, Meibomian gland evaluator score was also an important independent variable (third most important) in predicting dry eye symptom status with different discriminating values of ≤1, 1-9 or >9. The first terminal node (node 1) in the current analysis comprised of predominately severe OSDI classifications (40%) when the Meibomian gland evaluator score was ≤8, followed by mild subjects, and then moderate and normal subjects equally, which is not what one would expect. The discriminating values for this DTA were ≤ 8, 8-11 or > 11. Perhaps these odd findings are due to the small sample size.

The Meibomian gland evaluator score otherwise known as the Meibomian gland yielding liquid secretion is a measure of Meibomian gland expressibility, which is thought to reveal information on the status of Meibomian gland activity and/or function (Wolffsohn, 2017). The number of expressible glands has been correlated to dry eye symptoms with lower expressibility in the nasal

and central regions of the lower eyelid found in subjects with a SPEED score ≥10 (Korb & Blackie, 2008). According to the DEWS II Diagnostic Methodology Subcommittee, the diagnostic value of Meibomian gland expressibility, and duct appearance has not yet been established in dry eye disease although it is recommended to be performed alongside meibography for subtype classification of dry eye disease (Wolffsohn et al., 2017; Tomlinson et al., 2011). In patients with severe Meibomian gland dysfunction, the meibum can be opaque and have a tooth-paste like consistency rather than being clear and easily expressed in people without Meibomian gland dysfunction (Wolffsohn, 2017). Variation in the expressibility of Meibomian glands has also been noted in a small group of normal young subjects, and it is thought that only a proportion of the glands are actively secreting at any point in time with the nasal glands being the most active followed by the central, and then the temporal glands (Tomlinson et al., 2011; Blackie & Korb, 2010). It has been reported that on average six to 10 of the Meibomian glands of the lower lid secrete liquid at any given time (Norn, 1987; Korb & Blackie, 2008). Previous research has shown that individual Meibomian glands require about two hours of recovery time to express liquid secretion after being drained of its contents, which can be done in eight to 20 seconds upon application of a constant force of 1 g/mm^2 (Blackie & Korb, 2009). Therefore, the replenish rate of a Meibomian gland could be a confounding variable when using the Meibomian gland evaluator score as a dry eye diagnostic, and the effects of touching, rubbing or squeezing the eyelids on total scores should be considered.

It has been postulated that only the function of a proportion of the total number of glands are required to maintain the marginal lipid reservoirs (Blackie et al., 2010), and that a reduction in Meibomian gland expressivity is an indicator of dry eye disease (Pflugfelder et al., 1998). The difficulty for the practitioner is deciding whether a gland is not expressible for physiological reasons or for pathological reason, such as the presence of Meibomian gland dysfunction. A major contributor of Meibomian gland dysfunction pathogenesis is the hyperkeratinisation of the meibomian gland orifice and gland obstruction that could lead to an increase in intra-ductal pressure and duct dilation although a lack of meibum secretion is also an explanation for observed increase in gland thickness (Adil et al., 2018; Baudouin et al., 2016; Knop et al., 2011; Bron & Tiffany, 2004). The Meibomian gland evaluator score is not a standalone diagnostic with current techniques, although having a standardized measure of controlled force and specifying the location of functional glands from the temporal-central-nasal sections of the lower lid introduces consistency.

Additionally, the second predictor accounting for only 16 subjects with evaporative dry eye was TearLab tear osmolarity, which branched into two nodes from subjects having Meibomian gland evaluator scores between 8 and 11 with ≤298 or >298 mOsms/L as the splitting factor. A value >308 mOsms/L in either eye or an inter-eye difference ≥8 mOsms/L are widely accepted as good signs of

loss in tear film homeostasis and representing ocular surface disease (Bron et al., 2014). The current DTA did not generate the diagnostic cut-off value of 308 although a measure of 298 mOsms/L falls within the range of tear osmolarity normal classification (Wilcox et al., 2017). In the third terminal node (node 4) with TearLab tear osmolarity ≤298 mOsms/L there were three, two and one case of moderate, normal and severe OSDI classifications respectively. In the fourth terminal node (node 5) with TearLab tear osmolarity >298 mOsms/L there were predominately severe OSDI classifications (90%, n=9), and one single normal OSDI classification. Tear osmolarity has been shown previously to be the clinical test with the highest correlation to disease severity with values of 302.2 ± 8.3 mOsm/L, 315.0 ± 11.4 mOsm/L, and 336.4 ± 22.3 mOsm/L corresponding to a classification of normal, mild to moderate, and severe respectively (Sullivan et al., 2010; Willcox et al., 2017).

Considering the higher tear osmolarity value of the two eyes may be more indicative of the dry eye disease process (Wolffsohn et al., 2017). This approach has been approved by the Food and Drug Administration for commercially available tests to assess treatment efficacy due to larger observable changes, instead of using the average or single eye values (Sullivan et al., 2012; Keech et al., 2013; Downie & Keller, 2015). The inter-ocular difference in tear osmolarity as an independent variable considering an 8 mOsms/L inter-eye difference is also thought to provide insight about the stability of the tear film (Lemp et al., 2011).

When re-running the right eye DTA with the same CHAID settings to include tear osmolarity interocular difference and removing TearLab tear osmolarity as an independent variable, the same results for the first branching level were generated, and Meibomian gland dropout was identified as the second most important variable but not at a significant level (p=0.05). Severe OSDI classifications dominated both terminal nodes branching from subjects with Meibomian gland evaluator scores between 8 and 11, but with an odd discriminant value and two-way split (≤ 0.5 and > 0.5). The new model was less accurate with a risk estimate of 0.566, compared to the model in figure 3.8, and more highly sensitive for the severe OSDI classification (94.3%). In a large cross-sectional study, TearLab tear osmolarity was found to be significantly increased in subjects with Meibomian gland dysfunction compared to controls (Adil et al., 2018), which has been noted previously (Mather et al., 1991; Mathers et al., 1996; Gilbard et al., 1989; Baudouin et al., 2013). It is thought that lower tear osmolarity values in the early phase of Meibomian gland dysfunction or where Meibomian gland atrophy exists, might be due to a compensatory increase in tear film production that eventually leads to exhausted Meibomian and lacrimal glands in advanced disease, when an overlap between evaporative and aqueous-deficient dry eye results (Adil et al., 2018; Arita et al., 2015).

Considering OSDI scores and correlation with clinical tests for dry eye patients, McAlinden et al. (2017) found that there were weak correlations between OSDI scores and best corrected logMAR visual acuity, fluorescein tear breakup time, Schirmer I testing, and corneal fluorescein staining using Spearman's rank correlation coefficient in a sample of 238 participants with a confirmed diagnosis of dry eye disease. Participants were recruited from the Eye Hospital of Wenzhou Medical University, and there was no differentiation in terms of the subtype of dry eye disease.

3.4.3: Principal Component Analysis: Questionnaire items

Questionnaires are often validated for their discriminative ability using patient groups with Sjögren's Syndrome versus non- Sjögren's Syndrome aqueous-deficient dry eye, and/or healthy controls, with little focus on evaporative dry eye, which is considered the most common form of dry eye (Wolffsohn et al., 2017). The OSDI is identified as a vision- related quality of life questionnaire, whilst the SPEED is a dry eye symptom questionnaire (Guillemin et al., 2012). Previous factor analysis to determine dimensionality of the questionnaires discussed in this chapter revealed three subscales interpreted as vision-related function, ocular symptoms, and environmental triggers for the OSDI (Schiffman et al., 2000), and three factors interpreted as dryness, burning, and fatigue/soreness accounting for 70.8% of variance in the data for the SPEED that was based on a small sample (n=50) of symptomatic dry eye and asymptomatic subjects (Ngo, 2013). There may be criticism for applying PCA to both SPEED and OSDI items in a single analysis, however, a high correlation between the two questionnaires has been shown, as well as measurement invariance suggesting people with a high OSDI score will also have a high SPEED score, and vice versa (Ngo, 2013).

PCA can be used to characterize the dataset, and potentially offer diagnostic direction in the context of evaporative dry eye. The first principal component in PCA explains the variation seen in the sample the most. From the initial PCA it would appear that SPEED and OSDI questions concerning the frequency and severity of ocular discomfort described as soreness, irritation, grittiness, fatigue, dryness, and scratchiness account for or explain most of the variation seen in the sample of predominately evaporative dry eye patients at BBR Optometry Ltd. The first component might explain the differences in severity classification of evaporative dry eye or more generally, the first component might explain the variation seen in the current sample. From the results presented in section 3.3.3 it is known that the majority of predominately evaporative dry eye subjects had severe OSDI classifications so perhaps the questions identified in principal component 1 explain the variation most, amongst severe dry eye subjects or those who experience severe symptoms of dry eye.

According to the two-factor solution, dry eye questions SPEED 2, SPEED 6, OSDI 3, OSDI 2, SPEED 4, SPEED 8, SPEED 1 and SPEED 5 had strong loadings on principal component 1 that could be interpreted as the frequency and severity for symptoms of soreness or irritation, grittiness, fatigue, dryness or scratchiness. Variables OSDI 6, OSDI 7, OSDI 4, OSDI 9, OSDI 8 and OSDI 5 had strong loadings on principal component 2 that could be interpreted as the effect of dry eye on limiting visual performance or the effect of dry eye on visual functioning for everyday tasks including reading, driving at night, watching TV and using a computer or bank machine. The most important dry eye questions from the OSDI and SPEED questionnaires considered together were:

1. SPEED 2: How frequently do you experience soreness or irritation in your eyes?
2. OSDI 6: Have problems with your eyes limited you in reading during the last week?

Nichols et al. (2004b) found that the most commonly reported symptom of dryness amongst dry eye patients was dryness followed by ocular fatigue, grittiness, redness and soreness, which is in agreement with other studies (Nichols et al., 1999; Shimmura et al., 1999; Toda et al., 1993; Begley et al., 2001). Prior to generating this optimal two-factor solution, six items were removed from the analysis because the communalities table showed these items had values <0.30 indicating that they might not fit well with the other items in its component. The six questions removed included: SPEED 3, SPEED 7, OSDI 1, OSDI 10, OSDI 11 and OSDI 12. The SPEED question items are regarding the frequency and severity of symptoms of burning or watering. The OSDI question items relate to whether one experiences eyes that are sensitive to light or to possible environmental triggers for uncomfortable eyes such as windy conditions, areas with low humidity that are very dry, and areas that are air conditioned. An online survey sent to 400 eye health care professionals including ophthalmologists, corneal specialists, and optometrists in North Carolina was used to assess the perceptions of dry eye management in clinical practice and with a 25% response rate, reported burning was the most frequent symptom described by patients followed by foreign body sensation, and tearing (Williamson et al., 2014). The SPEED questionnaire asks about burning whilst this frequently reported symptom is not asked about in the OSDI, and was not deemed an important questionnaire item in the current analysis. Respondents to the survey (Williamson et al., 2014) were found to be more likely to use patient history to guide their clinical decisions rather than objective signs, which has also been reported elsewhere (Korb, 2000; Nichols et al., 2000).

The sample size of 65 was insufficient according to the rule of thumb suggested by Armstrong and Hilton (2011) previously, however, it has been noted that the influence of the sample size reduces when principal components are found to have three of more factor loadings of 0.60 or higher after the PCA is conducted, which was reported in the current analysis. According to the two-factor simple and optimal solution, there were more SPEED questions in the first principal than OSDI items, and the second principal component only included OSDI items.

Frequently reported symptoms of dry eye such as grittiness and burning are nonspecific to dry eye, and share commonalities with a range of other ocular conditions. The DEWS II Diagnostic methodology subcommittee recommends the use of eight triaging questions seen in table 3.17 to aid in the differential diagnosis of dry eye, considering signs and symptoms of other conditions can mimic dry eye disease (Wolffsohn et al., 2017).

How severe is the eye discomfort?	Unless severe, dry eye patients with signs of irritation such as dryness and grittiness rather than 'pain.' If pain is present, investigate for signs of trauma/ infection/ ulceration.
Do you have any mouth dryness or enlarged glands?	Trigger for Sjögren's syndrome investigation
How long have your symptoms lasted and was there any triggering event?	Dry eye is a chronic condition, present from morning to evening but generally worse at the end of the day, so if sudden onset or linked with an event, examine for trauma/ ulceration/ infection.
Is your vision affected and does it clear on blinking?	Vision is generally impaired prolonged staring, but should largely recover after a blink; a reduction in vision which does not improve with blinking, particularly with sudden onset, requires an urgent ophthalmic examination.
Are the symptoms or any redness much worse in one eye than the other?	Dry eye is generally a bilateral condition, so if symptoms or redness are much greater in one eye than the other, detailed eye examination is required to exclude trauma and infection.
Do the eyes itch, are they swollen, crusty or have they given off any discharge?	Itching is usually associated with allergies while a mucopurulent discharge is associated with ocular infection.
Do you wear contact lenses?	Contact lenses can induce dry eye signs and symptoms and appropriate management strategies should be employed by the contact lens prescriber.
Have you been diagnosed with any general health conditions (including recent respiratory infections) or are you taking any medications?	Patients should be advised to mention their symptoms to the health professionals managing their condition, as modified treatment may minimise or alleviate their dry eye.

Table 3.17: Initial triaging questions for the differential diagnosis of dry eye disease recommended by the DEWS II Diagnostic methodology subcommittee (Wolffsohn et al., 2017).

3.4.4: Principal Component Analysis: Total questionnaire scores and clinical test items

Only one of the three indicators supported the factorability of the data, indicating that the sample is probably not suitable for data factor analysis. For exploratory purposes, although the suitability of the sample remains questionable for two criterions, factor analysis proceeded. The meibography

clinical test variables assessing Meibomian gland duct dilation and Meibomian gland dropout had strong loadings (>0.60) on principal component 1 that could be interpreted as measures of Meibomian gland structure. The variables total OSDI and total SPEED questionnaire scores had strong loadings on principal 2 that could be interpreted as measures of dry eye symptoms. The variables fluorescein tear breakup time and TearLab tear osmolarity had strong loadings on principal component 3 that could be interpreted as measures of tear film stability. The variable percentage of partial blinks had a strong loading on principal component 4 that could be interpreted as measure of dynamic eyelid aspects.

The variables fluorescein tear breakup time and tear osmolarity had strong loadings on principal component 3 for right eye data that could be interpreted as measures of tear film stability. A cross-sectional study of non- contact lens wearers and soft contact lens wearers recruited from an American university campus with a mean age of 28, found there were no clinically significant relationships between TearLab tear osmolarity and fluorescein tear breakup time, non-invasive tear breakup time or dry eye symptoms (Yeh et al., 2015). Perhaps these tests are assessing different aspects of tear film stability. Yeh et al. (2015) comment that the osmolarity of tears collected at the tear meniscus may not be the same as localized areas of evaporation on the exposed regions of the cornea. It is also important to consider that measurements in the current analyses were collected at only one point in time at the dry eye consultation, and may not reflect fluctuations.

Percentage of partial blinks was an important test in right eye DTA with three cut-off categories of ≤12.5%, 12.5%-45.5%, and >45.5% although it was not a good discriminator for dry eye status with only four normal subjects found in the second category. Percentage of partial blinks was found in the fourth principal component for right eye data PCA on clinical tests, interpreted as measures of dynamic eyelid aspects, and responsible for a proportion of observed variability amongst evaporative dry eye patients at BBR Optometry Ltd. According to the DEWS II Diagnostic Methodology Subcommittee, the appropriate diagnostic cut-off values or threshold as well as sensitivity and specificity figures for incomplete blinking still require investigation (Wolffsohn et al., 2017). The variable average lipid layer thickness also loaded onto the fourth principal component perhaps justifying the use of the LipiView II diagnostic for dry eye consultations at BBR Optometry Ltd., which measures both lipid layer thickness and partial blinking. Incomplete blinking has been suggested as a predisposing factor towards the development of evaporative dry eye, given it has been shown to relate to Meibomian gland morphology and lipid layer thickness (Craig et al., 2016; Wang et al., 2018).

An age, gender and ethnicity-matched cross-sectional study by Wang et al. (2018), found incomplete blinking was associated with a two-fold increased risk of dry eye disease. Higher OSDI scores,

greater levels of Meibomian gland dropout, and poorer tear film lipid layer thickness were found in participants exhibiting incomplete blinking (Wang et al., 2018). The 154 participants in the study conducted at the University of Auckland clinic were not informed about the blink assessment during the initial consenting process, and the presence of incomplete blinking was determined by slow motion playback of a 2-minute infra-red video recording using the Keratograph 5 M (Oculus, Germany) or by clinical observation during history-taking (Wang et al., 2018). The percentage of partial blinks has also been correlated to symptoms, and lid parallel conjunctival folds (Berry et al., 2008; Pult et al., 2013).

In the literature, there is a wide range for the percentage of incomplete blinks in a population of healthy, non- dry eye individuals varying from 10% to 80%, which may be explained by differences in methodology (Doane, 1981; Carney & Hill, 1982; Abelson & Holly, 1977; Doane 1980; Collins et al., 2006). The interblink interval is variable between subjects, and can be altered by systemic conditions associated with Meibomian gland dysfunction such as Parkinson disease, cranial nerve VII palsy, and Grave's orbitopathy (Karson et al., 1984; Shah et al., 2012; Takahashi & Kakizaki, 2015; Wan et al., 2016; Kim et al., 2015), and tasks involving visual concentration like computer work (Tsubota & Nakamori, 1993; Cardona et al., 2011; Hirota et al., 2013; Portello et al., 2013; Himebaugh et al., 2009; Patel et al., 1991). The time lapse between blinks can be decreased in dry eye disease, and can be increased with the use of artificial tears (Pult et al., 2013; McMonnies, 2007; Tsubota et al., 1996). Incomplete blinking is a potentially modifiable behaviour with repeated forceful blinking reported to increase the thickness of the tear film lipid layer (Korb et al., 1994), and use of blinking training such as an animation to encourage blinking in computer users has shown to improve dry eye symptoms (McMonnies, 2011; McMonnies, 2007; Jones et al., 2017; Nosch et al., 2015).

For all of the factor solutions, symptoms only loaded onto one component at a level of >0.30 and so perhaps should be considered independently. Ngo et al. (2013) characterized the psychometric properties of SPEED showing it to be repeatable and valid for the measurement of dry eye symptoms, and found clinical measures of fluorescein and lissamine green staining of the cornea, and measures of Meibomian gland function including Meibomian gland score and Meibomian gland yielding liquid secretion score correlated significantly ($p < 0.05$) with SPEED scores.

3.4.5: Principal Component Analysis: Total "Jessica score" and clinical test items

Considering right eye datasets for the most important principal component items, the tests identified as the most important and responsible for the variability observed amongst predominantly evaporative dry eye subjects were: Meibomian gland duct dilation, fluorescein tear breakup time,

percentage of partial blinks and assessment of dry eye symptomology with either the total OSDI score or total "Jessica score". The variable total Meibomian gland evaluator score did not appear in the PCA including the "Jessica score" as the most important item of any principal component. Interestingly, all the tests to account for dry eye variability included lid and tear parameters, and symptoms.

According to the DEWS II Diagnostic Methodology Subcommittee, after symptom screening with the dry eye questionnaire five (DEQ-5) or OSDI, the three recommended tests are tear breakup time (ideally non-invasive), tear osmolarity and ocular surface staining with fluorescein and lissamine green staining observing the cornea, conjunctival and eyelid margin (Wolffsohn et al., 2017). The next most important recommended tests are tear volume assessment with tear meniscus height evaluation, and assessments of lipid thickness and dynamics for Meibomian gland dysfunction to help distinguish between predominately evaporative and aqueous deficient dry eye, which informs management of the condition (Wolffsohn et al., 2017). Prior to DEWS II, the multinational ODISSEY European Consensus group comprising of ophthalmologists, used a consensus-based approach to assess 14 commonly used dry eye severity criteria, and agreed symptom-based assessment and corneal fluorescein staining were sufficient to diagnose severe dry eye disease (Baudouin et al., 2014). The group designed an algorithm to assist practitioners when there is discordance between the two criteria, and the presence of one out of eight criteria in addition to having an OSDI ≥33 and a corneal fluorescein score ≥3 on the Oxford scheme, such as tear osmolarity >328 mOsm/L indicates a diagnosis of severe dry eye disease (Baudouin et al., 2014). An example of a commercially available tool to aid practitioners with dry eye diagnosis is the electronic tablet app created for professionals called the "Dry Eye Tool Box" that incorporates a screening algorithm for dry eye, and assesses dry eye likelihood and classification, but is yet to be validated (Pult, 2014).

Use of novel tools may be better suited to extract information in complex diseases where understanding the disease phenotype will help in identifying specific biomarkers, and thus new treatment targets. Baldini et al. (2018) compared results in discriminating different subsets of Primary Sjögren's syndrome using a data mining tool based on a novel fourth generation artificial neural network called Auto Contractive Map (AutoCM) versus conventional PCA. Primary Sjögren's syndrome is a complex chronic disorder, and there is a need to develop clear disease phenotypes for more effective, specific, and targeted treatments (Baldini et al., 2018). There were no subjects with Sjögren's syndrome in the current analyses. In the Baldini et al. (2018) study, the analysis was restricted to 37 demographic, clinical and laboratory variables for a cohort of 542 subjects. Although both analyses confirmed associations between autoantibody positivity, and several clinical manifestations, AutoCM overcomes limitations of PCA including analysing non-

linear relationships between variables, and not immediately evident graphical representations (Baldini et al., 2018). AutoCM allowed discrimination between patients with predominant glandular manifestations, and no or mild extra-glandular features from those with a more severe clinical profile, and highlighted rheumatoid factor as a risk factor associated with the development of mucosa-associated lymphoid tissue lymphoma of the salivary glands, besides other traditional lymphoproliferative risk factors (Baldini et al., 2018).

Deep machine learning or a special type referred to as, deep convolutional neural networks optimized for images, can objectively uncover previous unknown associations between an array of parameters from vast datasets without the need for a clear hypothesis at the outset (Poplin et al. (2018). Poplin et al. (2018) showed how trained deep learning models could be applied to retinal fundus images to predict cardiovascular risk factors such as age, gender, smoking status, and cardiac health from anatomical features not previously thought to be present or quantifiable in retinal images. Similar application of deep learning has been able to diagnose melanoma and diabetic retinopathy from medical images at a level comparable to human experts (Esteva et al., 2017; Gulshan et al., 2016). Computer-based deep machine learning and artificial intelligence will impact teaching and clinical optometric practice both supporting and complimenting the optometrists with possible implications for dry eye management in the shift towards precision medicine, whereby healthcare is customised for the individual. Computer led intelligence advancements could aid in the screening and diagnosis of eye conditions, leaving optometrist- patient interactions focused on explaining conditions, prognosis and treatment options.

3.5: Conclusion

The reality of confirming a dry eye diagnosis, let alone management, is complex. The current analysis explored the possibility of identifying objectively, which combination of commercially available clinical tests invested in by BBR Optometry Ltd. should be included in dry eye consultations conducted at the private optometric practice for predicting dry eye, namely of evaporative aetiology. Based on the stronger model (RE DTA), the selection of clinical tests that are potentially predictive of predominately evaporative dry eye in order of importance include:

- Fluorescein tear breakup time, especially if it is ≤ nine seconds and/or between nine and 12 seconds in women.
- Meibography to determine if there is some degree of Meibomian gland dropout.
- Meibomian gland expressibility with a total Meibomian gland evaluator score cut-off that is between one and nine.

Fluorescein tear breakup time is a simple test that can be incorporated into most eye examinations, and is a standard test for contact lens trials and assessments at BBR Optometry Ltd. This metric appeared in all the DTA and PCA results as an important test, and contributor of variability amongst evaporative dry eye patients. The use of LipiView II to screen for dry eye, and to communicate management recommendations could improve efficiency within the practice from avoiding spectacle remakes related to unstable tear films, and fluctuating vision, to possibly improving lens surgery outcomes which will be investigated in chapter four. The LipiView II incorporates meibography for assessment of Meibomian gland dropout and duct dilation, and analyses blink patterns and quantifies the number of complete and partial blinks. All of these tests in addition to symptom assessment, appeared as important tests in DTA and PCA with questions regarding frequency of soreness or irritation, and the effect on visual functioning for everyday tasks, such as reading identified as the most valuable.

CHAPTER 4 ABSTRACT
Tear homeostasis and lens surgery outcomes

PURPOSE: Patients considering private lens replacement surgery represent a segment of the patient population who may benefit from an optometric dry eye service. Lens replacement surgery can be postponed, with reported same day cancellations, until the ocular surface is deemed healthy in order to reduce the chance of infection following surgery. The aim of this chapter was to retrospectively explore the possible effect of dry eye on visual and clinical outcomes for patients managed at a private hospital. Specifically, at a hospital where optometrists from BBR Optometry Ltd. frequently refer patients for private lens replacement surgery.

METHODS: The clinical manager generated a list of private lens replacement surgery consultations with operations carried out by one ophthalmologist from January 1st 2017 to April 14th 2018 who began requesting preoperative tear measures in 2017, namely TearLab tear osmolarity and fluorescein tear break-up time (TBUT). Patients were classified as having normal or abnormal tears based on their pre-surgery tear metrics in line with the recommended Tear Film and Ocular Surface Society (TFOS) Dry Eye Workshop (DEWS) II dry eye disease diagnostic test battery for homeostasis markers (Wolffsohn et al., 2017). If one of the operated eyes had a TBUT < 10 seconds and/or tear osmolarity ≥ 308 mOsm/L or interocular difference > 8 mOsm/L, the patient was classified as having abnormal tears. Multiple Mann-Whitney U tests were conducted to determine if there were differences in dependent variables between the abnormal tears and normal tears groups. The dependent variables were: age, spherical equivalent refraction and logMAR equivalent distance visual acuity (VA) before and after surgery for both eyes, and baseline fluorescein TBUT and TearLab tear osmolarity.

RESULTS: There were no statistically significant differences in pre-operative distance VAs with most patients not having a distance logMAR VA worse than 0.5 (6/19), perhaps reflecting how patients attending the private clinic valued a spectacle or contact lens free option versus demonstrating a clinical need or visual impairment for cataract surgery. Visual outcomes (spherical equivalent refraction and logMAR equivalent distance VA) after surgery were not affected by dry eye status with no statistically significant difference found between the two groups. There were new cases of dry eye following lens surgery in the normal (42%) and abnormal (32%) tears group as determined by notes from the clinician conducting the pre- and post-operative assessments. Complications in both tear groups were infrequent. There were no cases of ocular infection post-lens surgery for either groups.

CONCLUSIONS: Although the study was inconclusive, it does show dry eye needs to be managed at least following anterior eye surgery, and protocols for post-operative care should involve dry eye management advice.

CHAPTER 4
Tear homeostasis and lens surgery outcomes

4.1: Introduction

Cataract surgery is the most commonly performed operation in the National Health Service (NHS) with more than 400, 000 procedures undertaken annually (RCOphth, 2017). The Way Forward project commissioned by the Royal College of Ophthalmologists (RCOphth) predicts that the demand for cataract surgery will rise by 25% over the next 10 years and by 50% over the next 20 years using the National Eye Health Epidemiological Model (NEHEM), population projections derived from the Office of National Statistics (ONS), and after making several assumptions (RCOphth, 2017). The increase in number of cataract operations performed are based on assumptions that diagnosis and referral will continue to take place in primary care, thresholds for surgical eligibility remain unchanged, and the proportion of patients wishing to proceed are stable (RCOphth, 2017). Refractive Lens Exchange or Clear Lens Extraction (CLE) also involves replacing the natural crystalline lens with an intraocular lens (IOL) but for the purpose of reducing the need for spectacles or contact lenses rather than to correct blur or light scatter.

RCOphth guidelines on cataract surgery (2010) have been supplemented by guidance from the National Institute for Health and Care Excellence (NICE) for the management of cataracts in adults on 26 October 2017. Recommendations for on the day of cataract surgery previously included an external eye examination and delaying surgery if concurrent infection existed (RCOphth, 2010). Current guidance simply states "the eye to be operated on has been checked and clearly marked." (NICE, 2017). Surgery can be postponed until the ocular surface is optimised in order to reduce the risk of infection. Endophthalmitis is a serious complication of cataract surgery with the patient's own external microbial flora a frequent source of the infecting organism, suggesting an emphasis on efforts in infection control and interventions for prevention (Speaker et al, 1991). Same day cancellation of lens surgey due to concurrent infection is distressing for patients, and further increases the workload and financial burden for NHS trusts. Stead et al. (2010) determined that introducing a blanket policy of lid hygiene advice to all pre-operative cataract patients led to a significant reduction in the incidence of cancellations due to blepharitis, and an estimated saving of £11, 000 over a four-month period.

Dry eye is not listed as a possible post-operative complication of cataract surgery in consent and information for patients in Appendix B but does mention how it is normal to feel mild discomfort, fluid discharge, itching and sticky eyelids for a non-specified period of time ("few days") that will self-resolve (RCOphth, 2010). The new guidance on pre-operative assessment and biometry for cataract surgery does not include dry eye metrics or external examination of the lids and lashes (NICE, 2017). Lens surgery can induce or exacerbate dry eye, and tends to be performed on older

patients who represent a segment of the populaiton with a higher incidence of pre-exisitng dry eye (Moss et al., 2004). Tear film lipid layer thickness measured using the LipiView interferometer and meibomian gland (MG) expressibility have shown to be reduced at one and three months post-cataract surgery respectively, reflecting an alteration to MG function but not structure (Kim et al., 2018; Han et al., 2014). Reduction in tear film stability using tear breakup time (TBUT) and ocular surface staining measures demonstrating a worsening of dry eye signs post-operatively have been observed with resolution or return to pre-operative values after about three months (Cetinkaya et al., 2015; Li et al., 2007; Cho et al., 2009; Kasetsuwan et al., 2013). The hypothesized pathophysiological mechanisms underlying cataract surgery-related dry eye are (Sutu et al., 2016; Cho & Kim, 2009; El-Harazi & Feldman, 2001; Chee et al., 1999; Oh et al., 2012; Donnenfeld et al., 2003; Kohlhaas, 1998; Han et al. 2014; Ipek et al., 2018):

- Use of topical eyedrops with and without preservatives and topical anaesthetics, and exposure dessication
- Possible light toxicity from the operating microscope
- Intraoperative sterilisation of the surgical field with povidone- iodine solution
- Transection and denervation of the corneal nerves by corneal incisions leading to abnormal blinkng and tear reflexes
- Vigorous irrigation intraoperatively and damage to the corneal epithelium
- Elevation of inflammatory factors following surgical trauma and ocular surface damage
- Loss of goblet cell density and associated conjunctival cell squamous metaplasia
- Meibomian Gland Dysfunction (MGD)

Tear film instability can affect ocular biometry and IOL power calculation resulting in higher likelihood of unexpected refractive error, suboptimal refraction and patient dissatisfaction post-operatively. Epitropoulos et al. (2015) found that subjects presenting for cataract surgery with "hyperosmolar" tears (≥ 316 mOsm/L in at least one eye) versus "normal" tears (≤ 308 mOsm/L in both eyes) had statistically significant higher variability in average keratometry measurements and greater proportion of eyes with a one diopter (D) or more difference in the measured anterior corneal astigmatism between two visits, which in turn affected IOL power calculations. The purpose of the current retrospective analysis was to determine whether patients with clinically observable signs of dry eye indicating a loss of homeostasis, had poorer early visual outcomes and more post-operative complications compared to patients without signs of dry eye following lens replacement surgery in a private ophthalmic clinic.

4.2: Method

This retrospective analysis was conducted at a private eye hospital in Solihull, UK. The clinical manager generated a list of private lens replacement surgery consultations with operations carried out by one ophthalmologist from January 1st 2017 to April 14th 2018 who began requesting pre-operative tear measures in 2017, namely TearLab tear osmolarity and fluorescein TBUT. These clinical tests were described in chapter one. The age was derived from the date of birth to the date of analysis (May 1st 2018), and the patient records were anonymised. There were 29 CLE and 39 cataract surgery procedures conducted. Over half of patients (65%) were fitted with a multifocal intraocular implant (MF), which allow two or three separate areas in focus simultaneously and reduced dependency on reading spectacles post-operatively.

Patients were classified as having normal or abnormal tears based on their pre-surgery tear metrics in line with the recommended Tear Film and Ocular Surface Society (TFOS) Dry Eye Workshop (DEWS) II dry eye disease diagnostic test battery for homeostasis markers (Wolffsohn et al., 2017). If one of the operated eyes had a TBUT < 10 seconds and/or tear osmolarity ≥ 308 mOsm/L or interocular difference > 8 mOsm/L, the patient was classified as having abnormal tears. Surgeries were performed using standard phacoemulsification or the LENSAR femtosecond laser system. The target refraction was not consistently documented and assumptions of plano (0 D) to achieve emmetropia were not made. This study received approval from the Life and Health Sciences Ethics Committee at Aston University (Project #1276) and adhered to the tenets of the Declaration of Helsinki. Analyses were deemed as clinical audits, and full hospital ethical approval was not required. However, tenants of Helsinki were adhered to and anonymised information was audited. The online decision tool from the NHS Health Research Authority also determined that approval from the NHS Research Ethics Committee was not required.

4.2.1: Pre- and post-operative examinations

Refraction and distance visual acuities (VA) before and after lens surgery were noted in the patient records. The spherical equivalent refraction was determined using the formula: half of cylindrical power + spherical power. Snellen VA was converted to Logarithm of the Minimum Angle of Resolution (logMAR) VA using a VA comparison chart (NHS, 2018). All post-operative details were taken from the latest post-operative appointment. It is conventional for patients seen at the clinic to have five follow-up visits at the following time intervals: one to five days, one week, one month, three months and six months post-surgery. If the surgeon deemed necessary, intense regulated pulsed light (IRPL) treatment (E > Eye, E-Swin, Paris, France) was recommended at the time of the consultation, and two further treatments separated by one to two weeks with a view to perform the last treatment on the day of lens surgery. IRPL is a non-invasive treatment developed

in 2014 for the management of MGD that has demonstrated therapeutic potential (Craig et al., 2015; Rong et al., 2018; X. Jiang et al., 2016). Following uncomplicated cataract surgery, patients are issued a prescription for Tobradex (0.3% tobramycin and 1% dexamethasone, Alcon, Fort Worth, USA) eyedrops to be used four times daily, and Yellox (0.9 mg/ml bromfenac sodium sesquihydrate, Bausch & Lomb, Surrey, UK) eyedrops to be used twice daily for 21 days. Details for optometrists performing post-operative care can be seen in appendix 4.2.

4.2.2: Statistical analysis

Statistical analysis was performed using SPSS version 24.0 (IBM SPSS Statistics, Chicago, IL). The Independent-samples t-test was not conducted because there were either outliers in the two groups that were genuinely unusual, and/or the dependent variables were not approximately normally distributed for each group of the independent variable (Laerd Statistics, 2015a). The first three assumptions in order to run a Mann-Whitney U test that relate to study design were met as well as the fourth assumption reflecting the nature of the data (Laerd Statistics, 2015b). A statistical significance level of 0.05 and 95% confidence intervals equating to declaring statistical significance at the $p < 0.05$ level was chosen. The option of "exclude cases test by test" option was selected meaning that only dependent variable values that are missing for a given Mann-Whitney U test were removed from the analysis (Laerd Statistics, 2015b). The dependent variables were: age, spherical equivalent refraction and logMAR equivalent distance VA before and after surgery for both eyes, and baseline fluorescein TBUT and TearLab tear osmolarity for both eyes. Multiple Mann-Whitney U tests were conducted to determine if there were differences in dependent variables between the abnormal tears and normal tears groups.

4.3: Results

Data analysis was carried out on 68 anonymised records and 32 records were excluded for several reasons represented in figure 4.1. Records were excluded if there were no tear metrics taken (n=9), if the patient did not proceed with lens surgery following a consultation (n=5), if the post-operative care was performed elsewhere (n=5), if the record from the clinical list was not available (n=12), or if the case was too complex (n=1; complicated surgery requiring Artisan lens insertion and IOL exchange). The analysis consisted of 35 females and 32 males (one unknown). The mean ± standard deviation age was 64.8 ± 9.9 years and age range 50 to 90.2 years at the time of the analysis. The average time frame between the date of the operation and the latest appointment from which results were reported was 2.2 ± 2.2 months for the entire sample.

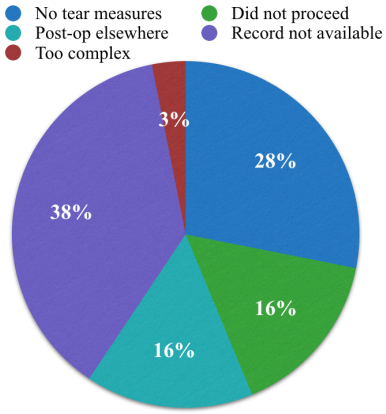


Figure 4.1: Reasons for excluding data from 32 records in the current analysis.

There were 20 patients in the normal tears group and 48 in the abnormal tears groups, and the distribution of surgeries conducted can be seen in table 4.1 and 4.2. There were three monocular surgeries for the normal tears group and six for the abnormal tears group. IRPL was conducted for three patients in the normal tear group and six patients in the abnormal tears group pre-operatively. Only 17% (4/23) of patients who had both baseline TearLab tear osmolarity and TBUT recorded were positive for both homeostasis markers indicating dry eye. 29% (14/48) of patients were categorised into the abnormal tears group based on abnormal TearLab tear osmolarity measures and 63% (30/48) based on reduced TBUT alone.

NORMAL TEARS	CLE	Cataract	Total
Standard phacoemulsification surgery	5 MF	3 MF 3 Monofocal	11
Femtosecond laser-assisted surgery	4 MF 1 Monofocal	1 Toric 3 Monofocal	9
Total	10	10	20

Table 4.1: Distribution of private lens surgeries for the normal tears group (CLE= clear lens extraction; MF= multifocal).

ABNORMAL TEARS	CLE	Cataract	Total
Standard phacoemulsification surgery	8 MF	4 MF 1 Toric 12 Monofocal	25
Femtosecond laser-assisted surgery	11 MF	8 MF 1 Toric MF 2 Toric 1 Monofocal	23
Total	19	29	48

Table 4.2: Distribution of private lens surgeries for the abnormal tears group (CLE= clear lens extraction; MF= multifocal).

The average baseline TearLab tear osmolarity and TBUT were 291.7 ± 8.2 and 10.6 ± 1.2 for the normal tear group, and 301.1 ± 17.4 and 8.0 ± 2.3 for the abnormal tear group respectively. The results of multiple Mann-Whitney U tests to determine if there were differences in dependent variables between the abnormal tears and normal tears group can be found in table 4.3.

Dependent variable	Mann-Whitney U (U)	Standardized test statistic (z)	Asym Sig. (2-sided test (p)	Decision	Mean rank	
					Abnormal	Normal
Age	484	0.054	0.957	Retain null hypothesis	34.58	34.30
RE SER Before	421.50	-0.788	0.431	Retain null hypothesis	33.28	37.42
LE SER Before	464.50	-0.209	0.835	Retain null hypothesis	34.18	35.27
RE DVA Before	388.50	-1.004	0.315	Retain null hypothesis	31.95	37.08
LE DVA Before	314	-2.247	0.025	**Reject the null hypothesis**	31.04	442.80
RE TBUT	42	-3.042	0.002	**Reject the null hypothesis**	22.50	40.00
LE TBUT	32.50	-3.303	0.001	**Reject the null hypothesis**	21.79	40.36
RE SER After	435	1.149	0.250	Retain null hypothesis	32.12	26.41
RE DVA After	237.50	-0.464	0.642	Retain null hypothesis	25.42	27.54
LE DVA After	310	0.347	0.728	Retain null hypothesis	27.95	26.33

Table 4.3: Results of Mann-Whitney U tests where distributions of the dependent variables for both groups were not similar as assessed by visual inspection. The null hypothesis is that the distribution of variables for the two groups are equal. (Asym= Asymptotic; RE= right eye; LE= left eye; SER= spherical equivalent refraction; Before= before surgery; After= after surgery; DVA= logMAR equivalent distance visual acuity; TBUT= fluorescein tear break up time).

As seen in table 4.3, there were only statistically significant differences in left eye (LE) logMAR equivalent distance VA before surgery, and baseline TBUT for both eyes between the two groups. In the normal tears group, entries for baseline right eye (RE) and LE TBUT entered as >10 were not registered by SPSS statistics (n=12 for both dependent variables). Distributions of the LE spherical equivalent refraction after surgery for both groups were similar, as assessed by visual inspection. LE spherical equivalent refraction after surgery was not statistically significantly different between the normal (*Mdn*= -0.13) and abnormal (*Mdn*= 0.07) tear groups, *U*= 362, *z*= 0.168, *p*= .867.

Distributions of the RE and LE TearLab tear osmolarity readings for the abnormal and normal tear group were not similar, as assessed by visual inspection. RE TearLab tear osmolarity readings for abnormal tears (mean rank= 18.54) and normal tears (mean rank= 14.61) were not statistically

significantly different, U= 138.50, z= 1.016, p= .316, using an exact sampling distribution for U (Dineen & Blakesley, 1973). LE TearLab tear osmolarity readings for abnormal tears (mean rank= 20.33) and normal tears (mean rank= 13.00) were not statistically significantly different, U= 171, z= 1.812, p= .073, using an exact sampling distribution for U (Dineen & Blakesley, 1973). It is generally considered that the asymptotic p-value is a good enough approximation to the real p-value when both groups have more than 20 cases, where "asymptotic" means that the p-value approaches the real value as the sample size increases. SPSS Statistics will run an exact p-value test if there are 20 or less cases in each group (Laerd Statistics, 2015b). It is recommended to report the asymptotic significance level in cases when two or more participants have identical values on the dependent variable, referred to as ties in the data (Laerd Statistics, 2015b). The method used to calculate the exact p-value or exact statistical significance level does not correct for ties in the data, and so the exact p-value can be inflated in these situations (Laerd Statistics, 2015b). Thus, for the dependent variable, baseline TBUT, the asymptotic significance level was reported. The post hoc statistical power calculation of the presented sample size was 82% (appendix 4.1; Faul et al., 2009). Therefore, despite uneven sample sizes between groups, the study had high statistical power for rejecting the null hypothesis.

Considering there were no statistically significant differences in spherical equivalent refraction following lens surgery for RE and LE data between groups, the residual post-operative refractive error of eyes was analysed for the entire sample and the distribution can be seen in figure 4.2.

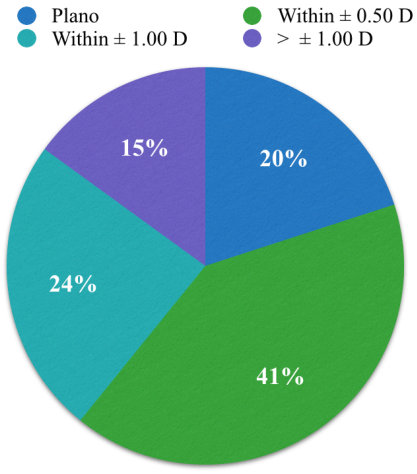


Figure 4.2: Distribution of residual post-operative refractive error for the sample. (D= Dioptres).

There were on average 3.5 ± 2.0 and 3.2 ± 1.3 number of follow-up visits for the normal and abnormal tears groups respectively. Post-operatively, there were instances of refraction fine-tuning with monocular or binocular Laser Assisted Sub-Epithelial Keratectomy (LASEK) and Yttrium-

Aluminium-Garnet (YAG) laser capsulotomy performed on patients in both groups. Complications in both tear groups were infrequent and included post-operative inflammation, and cystoid macular oedema leading to one case of subsequent small full thickness macular hole from the normal tears group and one case of retinal detachment from the abnormal tears group. In the normal tears group, there was one case of allergic conjunctivitis and eight records indicating a need for dry eye management. In the abnormal tears group, there were few cases requiring IOL rotation, repositioning and exchange, one case of raised intraocular pressure, and 16 records indicating a need for dry eye management. There were no cases of ocular infection post-lens surgery for either groups.

Pre-operative dry eye was indicated in the clinical records by use of the terms "demodex, telangiectasia, IRPL, Blephex^{TM}, Cliradex, meibomitis, dry eye and blepharitis." 30% and 42% of patients were identified as having pre-operative dry eye in the normal and abnormal tears groups respectively. Where both pre- and post-operative data were available to indicate dry eye status for both tear groups, an analysis was run to determine the proportion of new cases of dry eye following surgery where there was no pre-existing dry eye noted, cases suggesting no dry eye issues, cases where patients had continued to experience dry eye related issues following surgery, and cases where there was pre-existing dry eye but no dry eye noted at the latest post-operative appointment. The results can be seen in figure 4.3. Post-operative dry eye was deemed existent if the clinical notes stated the diagnosis explicitly or if dry eye management options were recommended including IRPL, lid hygiene techniques, and use of specific ocular lubricants or heating masks.

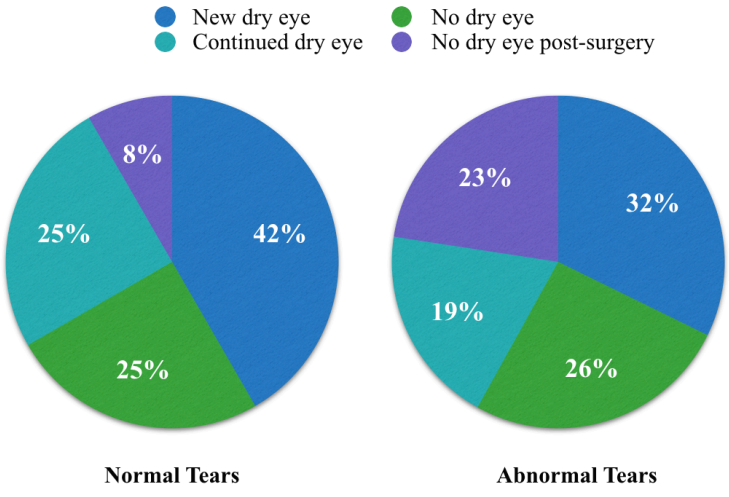


Figure 4.3: Documented cases of dry eye where both pre- and post- operative details were available.

4.4: Discussion

The majority of abnormal tear cases were categorised based on reduced TBUT (63%), and a statistically significant difference in baseline TBUT between groups, but not TearLab tear osmolarity was found. There were no statistically significant differences in pre-operative distance VAs with most patients not having a distance logMAR VA worse than 0.5, perhaps reflecting how patients attending the private clinic valued a spectacle or contact lens free option versus demonstrating a clinical need or visual impairment for cataract surgery. Visual outcomes (spherical equivalent refraction and logMAR equivalent distance VA) after surgery were not affected by dry eye status with no statistically significant difference found between the two groups. Pre- and post-operative VAs measured in this study were recorded at one point in time, and there is no indication of whether the vision recorded was stable or fluctuated. The morphological cataract type was not recorded, and measures of visual function including contrast sensitivity and glare sensitivity were not assessed before or after surgery that can affect the intention for cataract surgery and patient satisfaction with an operation (Elliott et al., 1989). The majority of patients from the entire sample had small myopic residual postoperative refractive errors (65% had ≤1.00D), and 20% had no residual refractive error. At the study site, it is common for patients to be left slightly myopic to help with reading unaided with patients expecting to be out of spectacle wear 80% to 90% of the time. It is clinic policy that LASEK can be considered at six to 12 weeks post-surgery if the visual outcome is disappointing to the patient and if the uncorrected logMAR distance VA is < 0.30 for laser fine tuning. LASEK was conducted postoperatively in patients from both groups. Previous studies have assessed corneal refractive surgery induced dry eye focusing mainly on laser in situ keratomileusis (LASIK) surgery (Gomes et al., 2017).

Patient compliance in terms of attendance for the recommended five postoperative visits was good especially for patients having CLE operations. Lens surgery fees to patients at the clinic cost over £2800.00 per eye with additional fees if it is a CLE versus cataract operation or the patient chooses femtosecond laser-assisted surgery, and if the patient proceeds with dry eye testing and IRPL treatment. Perhaps patients attended as directed because they wanted to achieve the best visual results having invested in their lens surgery, and recognised the value of close monitoring post-surgery. Some patients had fewer follow-up visits because they preferred to be seen for later stage review appointments by their local optometrist for convenience as they did not live in close proximity to the ophthalmic clinic.

Dry eye symptom questionnaire scores were not recorded in the clinical notes analysed, and about 30% of patients with normal tears according to this study's criteria had annotations indicative of dry eye. Despite notes of dry eye for patients in the normal tears groups and in patients classified as having abnormal tears, surgery continued in all cases suggesting these represented mild rather than

severe forms of dry eye. Previous studies with a focus on dry eye symptoms measured with the Ocular Surface Disease Index (OSDI) described in chapter two, have found symptoms increased for a duration of approximately three months following uncomplicated phacoemulsification (Cetinkaya et al., 2015; Oh et al., 2012; Li et al., 2007; Cho & Kim, 2009). Ocular symptoms have been shown to generally worsen over a prolonged time period in diabetic patients undergoing cataract surgery (Liu et al., 2008; D. Jiang et al., 2016). There were no notes regarding diabetic status in this study.

An observational study by Trattler et al. (2017) found > 80% of patients with visually significant cataracts had a TBUT ≤ 7 seconds, and 76.8% of patients were positive for fluoerscein staining with 50% showing central staining prior to cataract surgery, suggesting a higher anticipated incidence of undiagnosed pre-operative dry eye. Interestingly, only 30% of patients from the Trattler et al. (2017) study population experienced at least occasional dry eye symptoms. Ocular signs of dry eye in the absence of symptoms noted pre-operatively may signify early dry eye that may develop into symptomatic dry eye following lens surgery (Gomes et al., 2017). Gibbons et al. (2016) found the most common causes of patient dissatisfaction after cataract surgery were residual refractive error (57%) and both aqueous-deificient and evaporative forms of dry eye (35%). Szakats et al. (2017) found that there were no statisically significant differences in postoperative uncorrected VA, best-corrected VA, and four dry eye parameters with the exception of TBUT between patients who were unsatisified and satisfied with their post-operative outcome two months after uneventful phacoemulsificaiton. Although the sample size was small and results cannot be generalised to the general popultion, health anxiety, dry eye symptoms and patient-reported visual functioning were shown to be more closely associated with post-operative satisfaction (Szakats et al., 2017).

There were new cases of dry eye following lens surgery in the normal (42%) and abnormal (32%) tears group as determined by notes from the clinician conducting the pre- and post-operative assessments. The average timeframe between the operation and the latest follow-up appointment from which outcomes were noted in the current study was 6.3 ± 2.5 weeks for the normal tears group and 3.6 ± 2.7 weeks for the abnormal tears group. Dry eye metrics at each of the follow-up visits were not recorded consistently and some patients decided to have their one-month review appointments conducted by their local optometrist, and so information was not available. The incidence of dry eye post-operatively amongst patients undergoing phacoemulsification and considered to have no dry eye pre-operatively has been reported at 10% and 30% at one week and four weeks respectively after surgery (Kasetsuwan et al., 2013; Miyake & Yokoi, 2017). Iglesias et al. (2018) noted a prevalence of approximately 32% for dry eye symptoms at six months post-cataract surgery, and therefore considered to have persistent post-surgical pain although it is not known what proportion of patients had new or worse symptoms. Patients may attribute newly

deveopled dry eye symptoms post-operatively such as foreign body sensation to the operation rather than pre-exisintg ocular surface disease. Surgeons should inform patients prior to surgery about the possibility of dry eye symptoms following surgery and give an indication of when they will likely diminish or disappear. Xue et al. (2019) found that dry eye symptoms persisted for more than three months post-cataract surgery with OSDI scores still higher than pre-operative scores, though subsiding, at the end of six months.

There were cases in both tear groups that had no pre- or post-operative dry eye noted. However, mild ocular discomfort may be accepted or tolerated by patients especially post-operatively if they are advised of an approximate one-month settling period before spectacles can be considered to enhance distance or near vision where necessary. Kohli et al. (2019) suspect the observed transient nature of post-surgical dry eye with a recovering trend starting from the sixth week could be due to the presence of inflammatory cytokines that induce the synthesis of neurotrophic factors, and stimulate corneal nerve regeneration. Others have detected dry eye on the seventh day following cataract surgery and improvement within 30 days of the operation, offering a similar explanation that the recovery process of the corneal nerves from corneal incisions and neurogenic inflammation is responsible for the observation (Kasetsuwan et al., 2013).

A comparison of visual outcomes for patients having standard phacoemulsification or femtosecond laser-assisted surgery was not conducted. Conrad-Hengerer et al. (2015) found that femtosecond laser-assisted cataract surgery compared to conventional phacoemulsification using pulsed ultrasound energy in the fellow eye had faster visual recovery, less deviation from the target refraction and earlier stabilization of refraction. Other studies have shown no statistically significant differences in uncorrected and correct distance VA, and refraction between the two groups (Lawless et al., 2012; Mihaltz et al., 2011). Both forms of surgeries have been shown to reduce TBUT and tear volume (Schirmer testing I) values with a maximum impact of one week that fail to resolve one month following surgery (Yu et al., 2015). In cases of pre-existing dry eye, increased ocular surface staining and symptoms were worse in patients having femtosecond laser-assisted surgery (Yu et al., 2015). It is unknown as to whether an aspirating speculum was used by the surgeon in the procedures analysed retrospectively, which could account for continued or new cases of dry eye. Moon et al. (2014) showed that use of an aspirating speculum aggravated dry eye parameters during the early post-operative period, which returned to pre-operative values after one month. Negative pressure through sectional holes of the aspirating speculum in contact with the conjunctiva can cause damage to the conjunctiva leading to decreased mucin secretion, and increased inflammation on the ocular surface (Moon et al., 2014).

There were cases of dry eye conversions to no dry eye noted post-operatively for both tear groups. Miyake & Yokoi (2017) also note a change of dry eye classification four weeks after cataract surgery from definite or probable dry eye to non- dry eye at 22.4% and 38.2% respectively. The application of topical steroids and nonsteroidal anti-inflammatory drugs, which have an anesthesia and anti-inflammatory effect, and antibacterial drugs for four weeks post-operatively may account for the improvement in dry eye status (Miyake & Yokoi, 2017). Post-operative dry eye metrics were not available in the current study to comment on whether dry eye metrics remained the same, worsened or returned to pre-operative values at each of the five recommended visits. Cases of no conversion in dry eye status were noted in both tears groups wherein patients were recorded to have dry eye pre- and post- operatively despite excellent visual acuity following cataract surgery. Choi et al. (2018) identified a high OSDI score at baseline, and increased MG dropout, MG orifice obstruction and reduced TBUT at one month post-operative as risk factors for persistent dry eye symptoms after cataract surgery. El-Ameen et al. (2018) showed MG loss in the upper eyelid pre-operatively was associated with an increased early post-operative OSDI score, and that MG expressibility and TBUT changes persisted for up to three months following cataract surgery. The suggesstion is that clinicians should monitor these dry eye parameters and consider directed treatment of those patients with risk factors to improve satisfaction following surgery and to improve dry eye symptoms.

Impaired epithelial wound healing and decreased epithelial metabolic acitivity can result from transection of corneal nerves in cataract surgery, seen clinically as a decrease in corneal sensitivity and tear production (Sutu & Afshari, 2016). Corneal sensitivity can recover to pre-operative levels with recovery time lengthened by larger incision size and a grooved incision in patients without pre-existing dry eye (Oh et al., 2012; Cho & Kim, 2009). The location of the corneal incision, wherein the steeper meridian may be chosen to neutralise astigmatism, has not been shown to induce dry eye post-operatively (Kohli et al., 2019; Cho & Kim, 2009). Sutu and Fukuoka (2016) suggest that each etiological factor contributing to the development or exacerbation of dry eye symptoms post-operatively, such as injury from the corneal incision or ocular surface manipulation and resulting inflammation may have its own recovery time along with individual differences in the return to homeostasis. Interventions shown to improve dry eye symptoms and signs post-operatively:

- Management of ocular rosacea and blepharitis with lid hygiene, manual compression, and oral or topical antibiotic with an anti-inflammatory effect such as doxycycline (El-Harazi & Feldman, 2001; Chee et al., 1999).
- Hyaluronate and carboxymethylcellulose based artifcial tears can improve TBUT, corneal staining and symptoms (Mencucci et al., 2015; Yao et al., 2015)
- Preservative-free sodium hyaluronate 0.1% and fluorometholone 0.1% eyedrops in patients with pre-existing dry eye (Jee et al., 2015)

- Hydroxypropyl (HP)- Guar used in addition to steroid and antibiotic eye drops (Sanchez et al., 2010)
- Diquafosol 3% topical ophthalmic solution can improve TBUT, corneal staining, higher order abberations and Schirmer I test at 12 weeks post-surgery (Park et al., 2016)
- Topical cyclosporine 0.05% in comparison to artificial tears alone can improve dry eye symptoms and signs (Chung et al., 2013; Donnenfeld et al., 2010; Hamada et al., 2016)

The ophthalmic advice to optometrists involved in post-operative care at the study site is that ocular lubrication may be required for up to three months. The sample size was too small and measures of post-operative dry eye were too limited in the current study to determine whether patients having IRPL had better clinical outcomes following surgery stratified by type (cataract or CLE surgery), and by method (phacoemulsification or femtosecond laser-assisted surgery).

4.5: Conclusion

Visual acuity is the traditional biomedical indicator for satisfaction or success regarding cataract surgery outcomes (Xue et al., 2019). Considering there was no difference in visual outcomes post-lens surgery between the abnormal and normal tears groups, it may not be necessary to delay an operation based on visual outcomes. Ocular surface preparation may be beneficial to patients with minimal signs or no symptoms of dry eye in addition to those with established or diagnosed dry eye in order to achieve satisfactory ocular comfort or well-being outcomes. The current study did not analyse the changes in dry eye metrics pre-operatively, and at each of the post-operative visits for the two groups of patients as this information was not available given the retrospective nature of the study but could be explored in future studies. Future longitudinal research with larger cohorts of patients is required to evaluate the long-term impact of surgery (both phacoemulsification and femtosecond laser-assisted) on clinical outcomes, ocular surface health metrics and patient reported outcomes. Individuals considering private lens surgery especially with implantation of costly premium IOLs could benefit from BBR Optometry Ltd.'s dry eye service for management of symptoms and signs, to optimize the ocular surface and to potentially prevent persistent dry eye following surgery. Another significantly large subset of patients from private optometric practice that could benefit from a dry eye service are contact lens wearers given contact lens wear is considered a consistent modifiable risk factor for dry eye.

CHAPTER 5 ABSTRACT
A profile of contact lens dropout in an independent optometric practice

PURPOSE: Contact lens (CL) wearers represent a segment of the patient population who may benefit from a dry eye service. The aim of this chapter was to determine retrospectively at a local level whether dryness and ocular discomfort were main reasons for discontinuing CL wear, commonly referred to as CL dropout (CLDO), for patients at BBR Optometry Ltd.

METHODS: Two strategies using the practice management software I-clarity (I-clarity, Radyr, Cardiff) were employed to extract records of patients who potentially discontinued CL wear. The suspected reason for CLDO was recorded in addition to age at the time of CLDO, sex, date of last CL check, and lens parameters for the latest CL specification issued, such as product name, type, manufacturer, material, and replacement frequency.

RESULTS: Over half of patients from the sample where discontinuation of CL wear was suspected were classified as "false" CLDOs (54.2%), that is not ceasing lens wear due to issues associated with CLs. The primary reason for CLDO in this subgroup was no longer requiring CL wear following surgical intervention (42%). Customer switching (29%) and relocation (19%) were other reasons to explain "false" CLDOs. When multifocal and monovision CL correction were trialed and unsuccessful, patients reverted to full time spectacle wear rather than single vision distance CL correction and use of over readers to enhance near vision. Poor vision was found to be a reason for CLDO in this sample of presbyopic patients despite being fitted with current multifocal designs. The proportion of dropouts due to poor vision were similar between lens types (31.6% multifocal, 26.3% toric, 36.8% spherical). There were no strong patterns to link CLDO to dry eye or to a particular CL product or product range.

CONCLUSIONS: In order to benchmark performance and improve CL service, practitioners should aim to identify CLDOs and determine the retention rate at their practice. There was a large subset of patients in the analysis who discontinued CL wear for unknown reasons, which highlighted a need to improve CL record keeping at the practice. A large proportion of patients who discontinued using CL services at the practice did not necessarily discontinue CL wear permanently. It is possible some people may adapt CL wear to suit their lifestyle.

CHAPTER 5
A profile of contact lens dropout in an independent optometric practice

5.1: Introduction

According to a market data report by the European contact lens (CL) and lens care industry, Euromcontact, which compared CL uptake for seven participating companies across 33 countries, the European CL market grew by 4.5% and daily disposable replacement CLs were found to be a strong growth driver in the market. Sweden had the largest penetration rates for the population aged 15 to 64 at 14.2%, followed by Denmark (13.5%), Norway (10.9%), and the UK and Ireland (8.7%). The most commonly used CLs were weekly/bi-weekly and monthly replacement lenses with an increase in the silicone hydrogels market share in reusable lenses across all 33 countries (Euromcontact, 2018). Discontinuation from CL wear referred to as CL dropout (CLDO) is one of the costly challenges facing CL practice and limits growth in the market (Nichols et al., 2013). Sulley et al. (2017) report that the estimated rate of permanent CLDO has remained high over the past two decades despite advancements in CL designs, materials and modalities of wear ranging from 12% to 43%.

Early soft CL materials in the mid-1980s were made from low water content hydrogel such as hydroxyethyl methacrylate that had low oxygen transmissibility resulting in reports of corneal oedema (Bailey & Carney, 1973; Swarbrick et al., 1985; Morgan & Efron, 1998). Lens replacement was based on discomfort usually caused by the accumulation of deposits that could not be easily removed with cleaning solutions (Efron & Morgan, 2017). Compared to conventional hydrogel materials, silicone hydrogel materials have a greater oxygen permeability resulting in fewer hypoxic complications but not fewer rates of infiltrative events or cases of microbial keratitis (Covey et al., 2001; Morgan et al., 2005; Stapleton et al., 2008). Lysozyme deposits more readily on conventional hydrogels than silicone hydrogels, and is thought to have a protective effect accounting for the observed lower rate of infiltrative complications in hydrogel lens wearers (Omali et al., 2015). The introduction of single use daily disposables has meant a reduction in the risk of adverse reactions such as corneal infiltrative events associated with CL cleaning solutions and reusable lenses (Chalmers et al., 2012; Carnt et al., 2009). CL manufacturers' product lines continue to evolve incrementally with changes to lens design availability, parameter range expansion, and new formulations of silicone hydrogel materials.

The compartmentalisation of the tear film induced by CL insertion leads to biophysical and biochemical changes of tear film properties (Craig et al., 2013). Biophysical changes to the tear film include a reduction in tear film stability, pre-lens lipid layer thickness and tear volume, and increased tear evaporation (Craig et al., 2013). The insertion of a CL divides the pre-corneal tear film into a pre- and post- CL tear film, and decreases the overall pre-corneal tear film thickness once reflex

tearing subsides (Nichols & King-Smith, 2003; King-Smith et al., 2004; Chen et al., 2010). Disruption to the lipid layer of the tear film affecting tear film stability as measured by a reduction in tear break up time, and an increase in evaporation rate have been reported with CL wear (Guillon et al., 1997; Faber et al., 1991; Guillon & Guillon, 1989; Young & Efron, 1991; Morris et al., 1998; Guillon & Maissa, 2008; Thai et al., 2004).

The insertion of a CL is also thought to impact the blink reflex mechanism due to differences in pre- and post- CL tear film temperature (Ooi et al., 2007; Purslow et al., 2005). Corneal surface cooling and increased tear osmolarity following tear evaporation are detected by corneal cold neuroreceptors leading to reflex blinking, which in turn may be affected by the insultating effect of the CL on the post-CL tear film (Hirata et al., 2012; Kovacs et al., 2016; Li et al., 2015). Guillon et al. (2019) determined that tear film kinetics or deviations in the tear film at the time of break-up and the length of time during which the tear film is compromised over a spontaneous interblink period, were significantly inferior in CL wearers when compared to non- CL wearers. It is possible that the presence of a non-continuous tear film over a CL surface could be associated with CL discomfort (CLD) (Guillon et al., 2019). A thick aqueous layer is required for tear film lipid layer spread over the ocular surface, and reduces the interaction between tear film lipids and the CL surface that can lead to lipid deposition and consequent impaired optical quality seen in continuous wear silicone hydrogel CLs (Craig et al., 2013). Best et al. (2013) determined that wettability of the ocular surface was a main factor impacting CLDO in new CL patients fitted with silicone hydrogel CLs, and suggested predictors for those likely to discontinue lens wear within the first six months were a non-invasive tear breakup time < 10 seconds or an OSDI score > 4.2.

The physical presence of a CL in the eye induces factors that may be related to CLD including having a suspected fatiguing effect on ocular tissues linked to frictional aetiology or stimulation of cold nociceptors on the ocular surface (Papas et al., 2014). Papas et al. (2014) found that hydrogel and silicone hydrogel daily disposable lens replacement midway through a 10-hour wearing period with the same or new lens did not influence final perceptions of comfort suggesting comfort decrements experienced by CL wearers at the later part of the wearing period may not be associated with short-term changes occurring to the lenses. Stahl et al. (2016) also found that silicone hydrogel CL- free recovery periods of up to 80 minutes over a 12-hour lens wear day did not positively impact end of day comfort.

Current research into CL properties such as design and material to improve CL adaptation and retention rates propose that lubricity, which is the friction between the lens surface and lid margin, is a key factor in lens wettabilty and comfort (Jones et al., 2013). Vidal-Rohr et al. (2018) showed that enhancing the physical surface property of a monthly disposable standard silicone hygrogel lens

with nanometer thickness coating technology resulted in subjective improvement of CL comfort. Pult et al. (2019) found that ceasing CL wear or refitting experienced CL wearers with a low coeffcient of friction CL material led to improved indirect in-vivo measures of ocular surface friction or indicators of mechanical forces during blinks, namely lid parallel conjunctival folds and lid wiper epitheliopathy, as well as dryness symptoms over a period of 12 weeks.

Lens modulus is an indicator of the material's resistance to deformation, and is two to three times higher in second generation silicone hydrogels compared to conventional hydrogels (Young et al., 2010). High modulus CLs can reduce comfort due to the effect on lens fit such as tighter fit and edge fluting, and the association with changes in ocular physiology (Young et al., 2010). An in vitro study evaluating the effect of CL care products on soft CL modulus, found multi-purpose care solutions were related to decreases in modulus from probable uptake of formulation components, and use of hydrogen peroxide solutions resulted in increased modulus with two CL materials thought due to chemical changes in the CL polymer (Young et al., 2010).

Although a causal relationship has not been found due to the lack of longitudinal studies, there have been reports of structural and functional changes to the Meibomian glands, and associations with CLD in CL wearers including greater acini reflectivity which measures secretion quality, meibomian gland duct dilation, lid margin redness and lid thickness (Siddireddy et al., 2018; Villani et al., 2011; Machalinska et al., 2015; Arita et al., 2009). Whilst other studies have failed to find an association between Meibomian gland atrophy and CLDO (Pucker et al., 2019; Machalinska et al., 2015; Pucker et al., 2015), Alghamdi et al. (2016) observed CL-induced atrophy within the first two years of wear which then stabilises and does not resolve six months following cessation of wear.

Conventional hydrogels incorporate higher water content materials to achieve higher oxygen permeability and corneal oxygenation, and innovations in introducing an internal surfactant could help maintain the hydration of these lens materials rather than designing thicker lenses (Ruiz-Alcocer et al., 2018). Silicone hydrogel lens materials provide a significant increase in oxygen permeability without having to increase the water content of the lens, but their performance is affected by the intrinsic higher modulus and hydrophobic nature (Ruiz-Alcocer et al., 2018). Manufacturers are continually striving to develop products that increase comfort and minimise complications in order to reduce CLDO. In their crossover study assessing in vivo changes in CL thickness of a new daily disposable hydrogel lens with a water content of 78% (Biotrue ONEday, Bausch & Lomb, Kingston upon Thames, UK) compared to two silicone hydrogel lenses (Dailies Total 1, Alcon, Camberley, UK & MyDay, Coopervision, Fareham, UK) of lower water content, Ruiz-Alcocer et al. (2018) found no significant impact of the lens materials on the tear film or corneal swelling after one day of wear in a sample of infrequent CL wearers.

CLD is experienced by up to 50% of CLs wearers, and is characterised by a reduction in the compatibility between CLs and the ocular enviroment that leads to consequent adverse ocular sensations of varying frequency and magnitude (Nichols et al., 2013). Nichols et al. (2013) outline the temporal progression of CLD whereby patients begin to struggle with physical awareness or visual disturbance associated with CL wear, and adopt management strategies such as reducing wearing time and using artificial tears or rewetting drops before eventualy discontinuing CL wear permanently.

Discomfort and dryness have been identified as the main reasons for CLDO followed by vision and handling problems (Dumbleton et al., 2013; Rumpakis, 2010; Richdale et al., 2007; Jutai et al., 2003; Young et al., 2002; Harknett et al., 2001). Dumbleton et al. (2013) conducted an online survey of 4207 Canadian residents who were current or lapsed CLs wearers, and found that the main reason for CLDO was due to discomfort and dryness with lower dropout rates in silicone hydrogel wearers and 23% of respondents discontinuing CL wear permanently. Studies carried out prior to the introduction of silicone hydogels and daily disposable CLs to the market, also found that the most common reason reported for CLDO were discomfort and dryness albeit this may have been due to the fitting of older lens materials and designs (Weed et al., 1993; Pritchard et al., 1999).

The aims of the current analysis were to determine the main reasons and common trends for CLDO at a single optometric practice, and whether CLDO was due to discomfort and reports of dryness or due to fitting of certain CL products.

5.2: Method

This single site study conducted at an independent optometric practice (BBR Optometry Ltd.) was a retrospective record review of patients who had discontinued CL wear. Those eligible for CLs under the National Health Service for medical or other reasons, or utilising myopia control services at the practice were excluded from the study. The author conducted the retrospective review of practice records.

Two methods were employed to identify CLDOs. The first method involved using the practice management software I-clarity (I-clarity, Radyr, Cardiff) to access records of patients who had multiple reminder letters to return for CL aftercare appointments between January 2nd 2017 and March 2nd 2018 having been placed on a two-, three-, six- or twelve- month recall and receiving three to five reminder letters. It is practice protocol for patients to be sent a maximum of five appointment reminder letters and a maximum of three if the recall period is two-months. The second method involved using the “marketing communication” function on I-clarity whereby CLDOs were

identified by generating a list of CL patients who had not attended a CL check for one year prior to the date of list generation.

Strategies used to determine whether patients had discontinued CLs and why included reviewing the CL and eye examination clinical notes, practice communication notes, and CL-related products transaction history. The practice protocol is to record any interactions with patients or changes in patient circumstances in the "practice communication" section of I-clarity. Detailed information on the age at the time of CLDO, sex, date of last CL check, and lens parameters such as product name, type, manufacturer, material, and replacement frequency were recorded for each patient identified as having discontinued CL wear. For method one, the time period lapsed before CL dropout could not be determined accurately with the given information. An assumption for method two data, after scrutinising clinical notes and order history, was that entries for "date of next CL aftercare" generated by I-clarity as "01-Jan-00" meant patient were not assigned a recall period because the CL trial or CL wear was abandoned. All anonymised data was inputted into Microsoft Excel (Microsoft Corporation, Redmond, Washington, USA) for analysis. Duplicate entries from the two methods were removed. This study received approval from the Life and Health Sciences Ethics Committee at Aston University (Project #1276) and adhered to the tenets of the Declaration of Helsinki.

5.3: Results

In total, 214 records of patients suspected of discontinuing CL wear were analysed. There were 123 out of a possible 123 records derived using method one, and 91 from a possible 659 records using method two. There were no clinical notes available for 568 patient identifiers obtained from method two.

There were 116 records excluded from product analysis because they were deemed not to be true or "false" CLDOs. Reasons for CLDO in these cases and the patient demographics for these subgroups can be seen in table 5.1 and figure 5.1, and include patients who no longer required CL correction following cataract, clear lens extraction (CLE) or Laser Assisted in Situ Keratomileusis (LASIK) refractive surgery. Some patients had the intention of continuing CL wear but moved from the local area as far as Europe due to changes in circumstances including pursuing higher education or moving closer to family.

Unfortunately, there were instances of customer switching behaviour discussed in chapter two, which made up the largest proportion of false CLDOs. Clinical notes revealed patients were unhappy with service at BBR Optometry Ltd. due to issues with being charged an incorrect fee for CL care

and products, errors or delays with CL ordering, and expressions that did not want to subscribe to a monthly direct debit for clinical care and product payments at the practice. BBR Optometry Ltd.'s monthly payment plan EyeLife™ was described in chapter two, and BBR Optometry Ltd. require enrolment in EyeLife™ for any new CL wearer. There were notes stating the patient cancelled their direct debit at the bank, and notations stating that the patient admitted purchasing CL elsewhere or the patient's CL specification had been requested by the patient or local competition. The remaining subgroup of patients ("Failure to attend") were those who were most likely overdue a CL check given previous history of attending CL aftercares at the same time as yearly eye examinations rather than in accordance with recommended recalls for CL care typically set at six months at the practice.

Reason for CLDO	No. of pxs	No. Males	No. Females	Average Age (years)	Std Dev Age (years)	Min. Age (years)	Max. Age (years)
Cataract surgery	30	4	26	66.0	10.4	31	83
CLE surgery	8	0	8	61.0	6.3	52	71
Refractive surgery	10	3	7	44.5	11.9	23	62
Relocation	22	11	11	36.2	18.1	17	74
Cx switching	34	9	25	38.9	16.0	16	66
Failure to attend	12	4	8	41.9	16.0	21	68

Table 5.1: Profile for subgroups of patients who were not true contact lens dropouts (CLDOs) and excluded from CL product analysis (CLE= Clear Lens Extraction; Cx= Customer; No.= number; pxs= patients; Std Dev= standard deviation; Min.= minimum; Max= maximum).

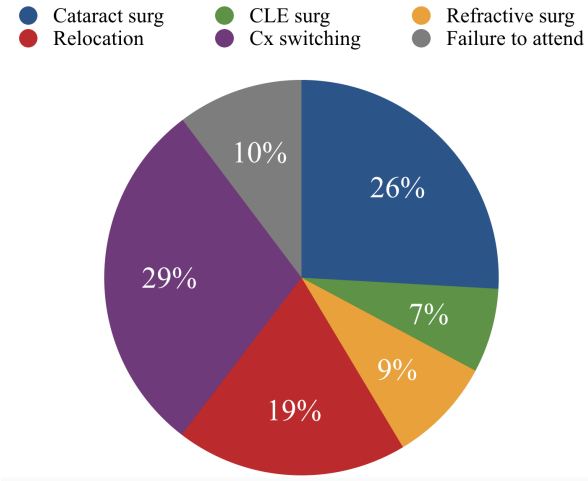


Figure 5.1: Proportion of subgroups of patients who were not true contact lens dropouts (CLDOs) and excluded from CL product analysis (CLE= Clear Lens Extraction; Cx= Customer; Surg= Surgery).

Overall, 98 records were analysed with 52 found using method one and 46 found using method two. There were six entries from method one where there were different lens products for right and left eyes with one case of enhanced monovision with one eye having a spherical distance vision lens and

the fellow eye a multifocal lens. In the other cases, one eye had a spherical correction and the fellow eye had a toric correction (n=5). There was one case of enhanced monovision with different lens products for each eye found using method two.

From method two data where such analysis was possible, 85% (n=39) of CLDOs were active CL wearers for < one year, and 15% (n=7) were active CL wearers for ≥ one year. The reasons for CLDO in those wearing CL for ≥ one year included ceased CL wear following infection (n=2), unknown (n=3), dryness (n=1) and poor vision (n=1). The distributions of reasons for CLDO in those wearing CL for < one year can be seen in figure 5.2.

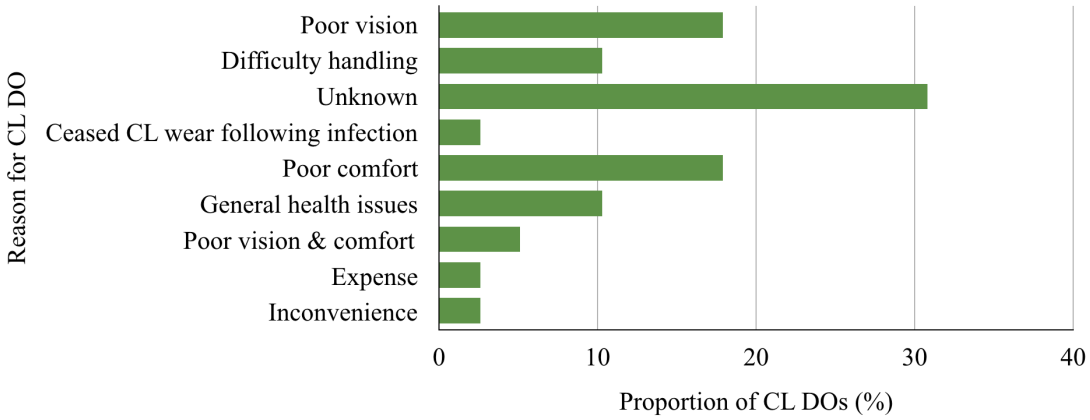


Figure 5.2: Distribution of reasons for contact lens dropout (CLDO) amongst BBR Optometry Ltd patients derived from method two who wore CLs for < one year.

After compiling data from methods one and two, it was found that 18 patients wore rigid gas permeable (RGP) lenses and 80 wore soft contact (SCL) lenses. There were 66 female and 31 male CLDOs. Sex and age were unknown for one entry using method one. The average age of CLDOs was 51.4 ± 15.2 and the average duration for time of dropout (year) was 2012 ± 4.7. At the time of CLDO, the majority of CL recommended were manufactured by Coopervision and Johnson & Johnson, and were either daily or monthly disposable SCLs. Motivations for first choice CL by a practitioner may be sales driven in choosing a certain manufacturer due to cost and efficient delivery or experience driven in choosing a product based on familiarity and previous successes. The distribution of CL manufacturers, and of CL replacement frequencies and lens types can be seen in figures 5.3 and 5.4.

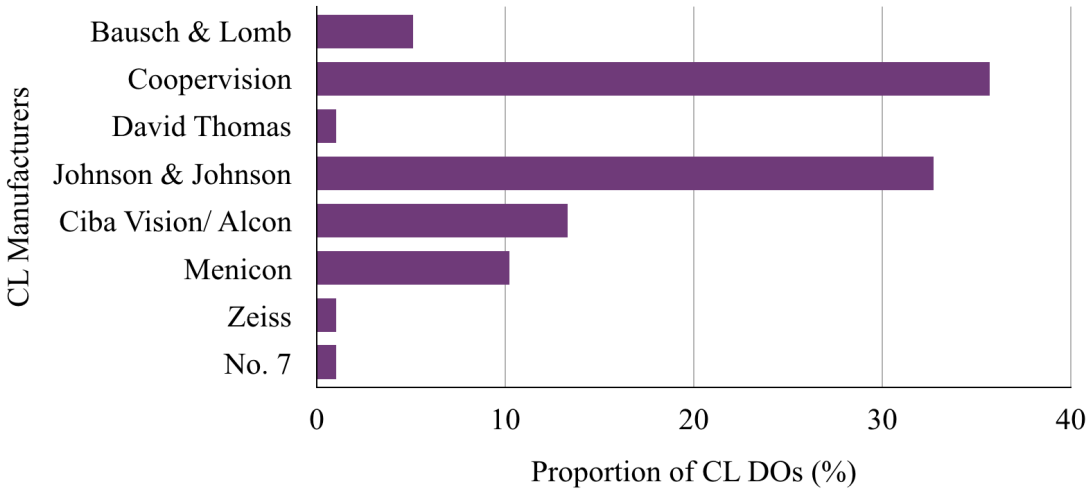


Figure 5.3: The distribution of CL manufacturers for CLs recommended and noted at the time of CLDO for a subgroup of patients at BBR Optometry Ltd. (CL= contact lens; CLDO= contact lens dropout).

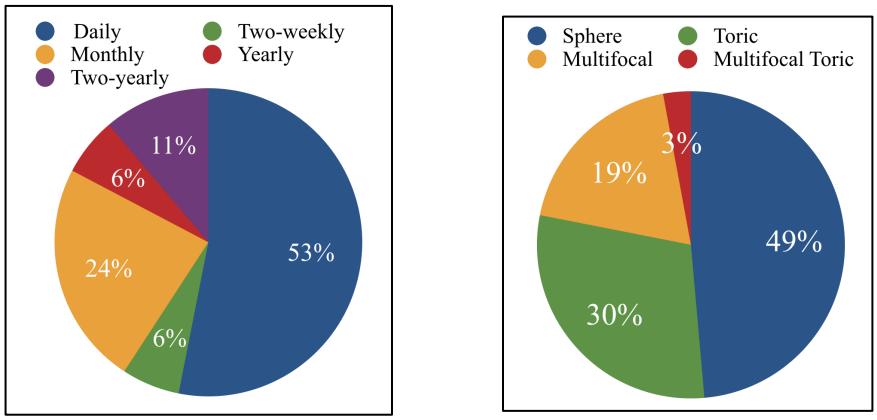


Figure 5.4: The distribution of CL replacement frequencies and lens types for CLs recommended and noted at the time of CLDO for a subgroup of patients at BBR Optometry Ltd. (CL= contact lens; CLDO= contact lens dropout).

The main reasons for CLDO was the unknown group (37.8%), followed by poor vision and poor comfort both at the same proportion of 17.3%. Interestingly, 58.8% of CLDO due to poor comfort explicitly stated that there were symptoms of dryness. The patient demographics for groups arranged according to reasons for CLDO and proportion of CLDOs in each group can be seen in table 5.2 and figure 5.5. Patient records assigned a reason for CLDO as unknown often had notes of "lapsed," "discontinued," "ceased CL wear," "abandoned CL wear," and "CL trial not a success" but did not include any explanation. There were also cases where notes in the eye examination stated "no longer wearing lenses" or "wants to leave multifocal CL trial for now" but no explanation recorded as to why the patient had decided to cease CL wear.

Reason for CLDO	No. of pxs	No. Males	No. Females	No. SCLs	No. RGPs	Average Age (years)	Std Dev Age (years)	Min. Age (years)	Max. Age (years)
Poor vision	17	6	11	14	3	58.2	9.2	41	76
Difficulty handling	7	2	5	6	1	58.4	13.3	28	72
Unknown	37	17	20	29	8	49.5	14.9	17	80
Ceased CL following infection	4	1	3	2	2	54.8	4.8	49	60
Poor comfort	17	1	15	13	4	50.6	13.1	16	75
General health issues	4	1	3	4	0	63.5	10.7	49	79
Poor vision & comfort	3	0	3	3	0	59.7	14.8	39	73
Expense	2	1	1	2	0	29.0	11.0	18	40
Inconvenience	7	2	5	7	0	32.4	15.3	18	65

Table 5.2: Profile for subgroups of patients who were deemed contact lens dropouts (CLDOs) and included in CL product analysis (No.= number; pxs= patients; Std Dev= standard deviation; Min.= minimum; Max= maximum).

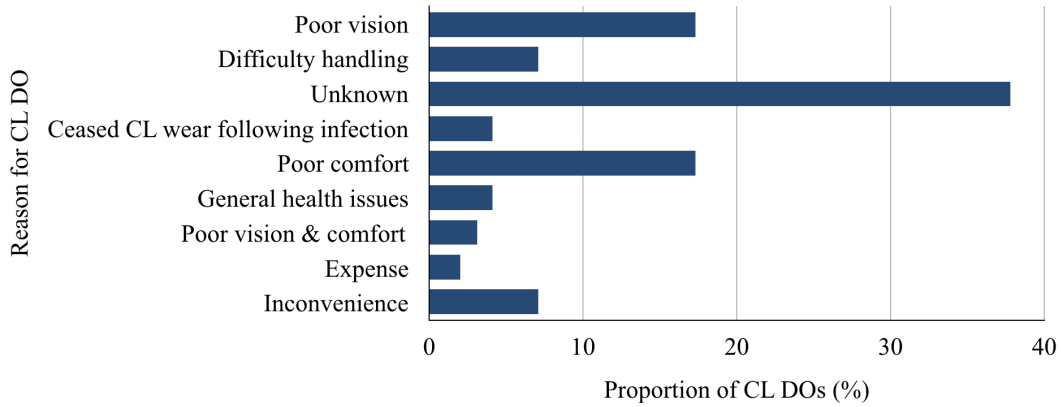


Figure 5.5: Proportion of subgroups of patients who were deemed contact lens dropouts (CLDOs) and included in CL product analysis.

Patient records assigned a reason for CLDO as poor vision often were due to poor near vision, and all were of presbyopic age. There were cases where perhaps patients' needs and expectations were not met with complaints of poor near vision for patients fitted with single vision distance correction although they were presbyopic, and for specific activities such as skiing. There was a trend of patients initially being fitted with multifocal CLs with notes of "jumpy" or "foggy" vision, and then subsequently monovision correction. When multifocal and monovision CL correction were trialled

and unsuccessful, patients reverted to full time spectacle wear rather than single vision distance CL correction and use of over readers to enhance near vision.

Patient records assigned a reason for CLDO as poor comfort had notes such as "reduced wearing time due to discomfort", "dryness" or simply "CL discomfort." There were two instances of recommendations for dry eye work-up and management via BBR Optometry Ltd.'s Tear Clinic dry eye service. There were three cases where both poor vision and poor comfort were determined as reasons for CLDO. "Fluctuating vision," "blurring and tired eyes," and "a combination of dryness and vision perceived as not good enough to drive" were noted in the patient records for this group. One of these cases was booked in for a dry eye consultation at the practice but failed to attend.

Patient records assigned a reason for CLDO as difficulty handling and inconvenience had the same proportion of CLDOs (7.1%). There were notes of "difficulty with insertion and removal," and "problems with handling." One record indicated that a reteach on insertion and removal of CLs with support staff was declined. CLDO patients in the inconvenience group had notes of "prefers specs" and "can't be bothered to put in CLs" for a new mother post-partum. Patient records assigned a reason for CLDO as ceased CL wear following infection and general health issues had the same proportion of CLDOs (4.1%). Patients with recurrent viral infections included two SCL wearers who were fitted with daily disposables and two RGP lens wearers. General health issues leading to CLDO were due to patients wanting to be more cautious overall and averting any perceived risks to their health. One patient was undergoing a course of chemotherapy for lung cancer and decided to cease CL wear, and another had a stroke which affected the ability to handle CLs. The remaining cases stated the patients were "unwell" and ceased CL wear. There were two cases where CL wear became temporarily infrequent due to treatment in hospital for a broken leg, and for anterior uveitis with the subsequent decision for these patients to cease CL wear but due to cost.

Table 5.3 presents the CL products that the sample of BBR Optometry Ltd.'s CLDO patients were wearing at the time of CLDO, organised by reason for CLDO. The product names bolded indicate that the CL material is silicone hydrogel and the asterisk that the CL material is water gradient. The number of patients from the sample in each group can be found in parentheses, and where a patient was fitted with two different products has been indicated. In regards to reason for CLDO due to poor vision, one patient was fitted with a multifocal toric lens, and 31.6%, 26.3% and 36.8% of patients were fitted with multifocal, toric and spherical CLs respectively. About one third of these patients were trialling a silicone hydrogel lens. When analysing CL products trialled for those where reason for DO was due to poor comfort, 16.7% of these patients were wearing CLs with silicone hydrogel formulations. Two-thirds of patients identified as discontinuing CL wear due to both poor vision

and comfort were wearing toric silicone hydrogel lenses, whilst the remaining patient in this group was wearing a daily multifocal.

CLDO Reason (n=98)	CL Product Name
Poor vision (n=17)	1-day Acuvue Moist (n=1) 1-day Acuvue Moist for Astigmatism (n=2) 1-day Acuvue Moist Multifocal (n=2) **1-day Acuvue Trueye** (n=2) **Acuvue Oasys for Astigmatism** (n=1) **Clariti 1day** (n=1) Proclear 1 Day Multifocal (n=2) **Biofinity Toric** (n=1) Frequency 55 Toric (n=1) **Biofinity Multifocal** (n=1) Proclear Multifocal (n=1) Proclear Multifocal toric (n=1) Menicon Z Alpha (n=1) Maxim Ultra (n=2) For one customer, RE **1-day Acuvue Trueye** LE 1-day Acuvue Moist for Astigmatism. For one customer, RE 1-day Acuvue Moist for Astigmatism LE 1-day Acuvue Moist.
Difficulty handling (n=7)	1-day Acuvue Moist (n=1) 1-day Acuvue Moist for Astigmatism (n=1) Focus Dailies All Day Comfort (n=1) Dailies Aquacomfort Plus Toric (n=1) Proclear 1 Day Multifocal (n=1) Proclear Multifocal toric (n=1) Menicon Z Progressive BTC (n=1)
Unknown (n=37)	Dailies Total 1* (n=1) Focus Dailies All Day Comfort (n=3) Dailies Aquacomfort Plus (n=1) Dailies Aquacomfort Plus Toric (n=3) Dailies Aquacomfort Plus Multifocal (n=1) **Air Optix Aqua** (n=1) 1-day Acuvue Moist (n=4) 1-day Acuvue Moist for Astigmatism (n=2) 1-day Acuvue Moist Multifocal (n=2) **Acuvue Oasys 1-day with HydraLuxe** (n=2) **Acuvue Oasys with Hydraclear Plus** (n=1) **Acuvue Advance for Astigmatism** (n=1) Proclear 1 Day (n=2) **Clariti 1day** (n=1) Proclear 1 Day Multifocal (n=1) Proclear toric (n=1) **Biofinity** (n=1) **Biofinity toric** (n=2) **Biofinity Multifocal** (n=1) Menicon Z Alpha (n=1) Maxim (n=2) Fluorolens 90 (n=1) Boston ES (n=2) Quantum 1 (n=1) Quasar FS Multifocal (n=1) For one customer, RE Dailies Aquacomfort Plus Toric LE Focus Dailies All Day Comfort. For one customer, RE 1-day Acuvue Moist for Astigmatism LE 1-day Acuvue Moist Multifocal.
Ceased CL following infection (n=4)	Proclear 1 Day (n=1) 1-day Acuvue Moist for Astigmatism (n=1) Boston IV (n=1) Conflex-Air (n=1)

Poor comfort (n=17)	1-day Acuvue Moist (n=1) 1-day Acuvue Moist for Astigmatism (n=3) 1-day Acuvue Moist Multifocal (n=2) **Acuvue Advance for astigmatism** (n=1) Proclear 1 Day (n=1) Proclear 1 Day Multifocal (n=1) Biomedics toric (n=1) **Biofinity toric** (n=1) **Biofinity Multifocal** (n=1) Dailies Total 1* (n=1) Dailies Aquacomfort Plus Toric (n=1) Menicon Z Alpha (n=1) Menicon Z Progressive BTC (n=1) Boston XO (n=1) Boston IV (n=1) For one customer, RE 1-day Acuvue Moist for Astigmatism LE 1-day Acuvue Moist.
General health issues (n=4)	Proclear 1 Day (n=1) **Clariti 1day multifocal** (n=1) **Biofinity** (n=1) **Biofinity toric** (n=2) For one customer, RE Proclear 1 Day LE **Clariti 1 day multifocal.**
Poor vision & comfort (n=3)	Proclear 1 Day Multifocal (n=1) **Biofinity toric** (n=1) **Acuvue Oasys for Astigmatism** (n=1)
Expense (n=2)	**1-day Acuvue Trueye** (n=1) Proclear (n=1)
Inconvenience (n=7)	1-day Acuvue Moist (n=2) 1-day Acuvue Moist for Astigmatism (n=1) **Acuvue Oasys for Astigmatism** (n=1) Proclear 1 Day (n=1) **Biofinity** (n=1) **Biofinity toric** (n=2) For one customer, RE **Biofinity** LE **Biofinity toric.**

Table 5.3: Contact lens product names that patients were wearing at the time of contact lens dropout (CLDO) categorised based on reason for dropout in a sample of patients at BBR Optometry Ltd. (in bold= Silicone Hydrogel; *= Water Gradient; RE= right eye; LE= left eye).

5.4: Discussion

The proportion or rate of CLDO in the first year of wear for all CL wearers from a sample or those patients recenlty fitted are influenced by the CL products available at the time of fitting. Historical dropout rates estimated from studies in the 1990s are of limited value today due to the discontinuation of most CL products used at that time. A retrospective chart review of 524 records across 29 UK optometric practices conducted by Sulley et al. (2017) found a 74% first-year retention rate for patients fitted with CLs. A high proportion of patients who discontinued CL wear did so within the first two months of wear (47%) with handling and comfort issues cited as common reasons for DO in spherical lens wearers, and visual problems amongst new toric and multifocal CL wearers (Sulley et al., 2017). A prospective evaluation of new CL wearers within the first year of fitting by Sulley et al. (2018) found a 25% CLDO rate due to problems with vision (41%), comfort (36%) and

handling (25%). The shift away from poor comfort as the prime reason for CLDO may be due to the continual improvement in CL products, and the comparison new CL wearers make of vision that is achieveable in spectacle lenses versus CLs.

In the current sample with the average age of CLDO 51.4 ± 15.2 years, an equal proportion of patients discontinued CL wear due to poor vision and poor comfort (17.3%). A survey of 496 presbyopic CL wearers with a mean age of 57 ± 9 years also found that dissatisfaction with vision at all distances and discomfort were equally reported as primary motivations for CLDO, and years of CL wear was not associated with a tendency to cease lens wear (Rueff et al., 2016). Contrary to previous studies involving younger CL populations, Rueff et al. (2016) found that the age of beginning CL wear and CL material did not have a significant influence on CLDO. Previous studies predating the availability of multifocal CLs have shown the onset of visual problems associated with presbyopia as a reason for CLDO (Schlanger, 1993). Poor vision was still found to be a reason for CLDO in this sample of presbyopic patients despite being fitted with current multifocal designs. The proportion of dropouts due to poor vision were similar between lens types (31.6% multifocal, 26.3% toric, 36.8% spherical), although previous studies have shown greater dropout for patients fitted with multifocals suggesting required improvement for fitting procedures and designs to optimise vision (Sulley et al., 2017).

As presbyopia progresses, practitioners can make incremental changes to monovision correction of up to 0.25 Dioptres, and to multifocal CLs due to the availibility of CL brands offering more than one near addition power to improve near vision (Kerr & Chauhan, 2019). Monovision correction can compromise visual performance by introducing interocular rivalry, and multifocal correction can introduce a form of intraocular rivalry whereby distance and near visual inputs are superimposed on each retina (Morgan et al., 2011). Although less convenient, presbyopic patients may choose to wear distance vision CL correction and spectacles with additional strength for near tasks. An observed pattern in this study was the initial fitting of multifocals and subsequent monovision correction if multifocal wear was not successful, and then the use of overreaders with distance correction if monovision failed. In this sample, there were greater issues with poor near vision rather than poor distance vision for multifocal and toric lens wearers seen in the study by Sulley et al. (2017). The prescriptions for patients in this subgroup of CLDO were not recorded to determine if limitations in available parameters was a factor in CLDO. In addition to the possible requirement for specialist CLs ordering for higher prescriptions, patients with complex prescriptions may require multiple fit appointments to optimise vision, and face higher costs and order delays due to the need to order specialist CLs from outside suppliers. Sully et al. (2017) found that factors associated with

retentions rates included higher lens power perhaps for improved cosmesis in those image-conscious, spherical versus multifocals CLs, and quarterly versus adhoc suppling of CLs.

A higher incidence of end of day dryness symptoms has been reported amongst CL wearers versus non- CL wearers that resolve following lens removal (Chalmers & Begley, 2006; Begley et al., 2001; Guillon & Maissa, 2005b; Nichols et al., 2005). The types of discomfort associated with CLDO include dryness, general awareness, edge sensation and burning or stinging (Young et al., 2002). Pucker et al. (2019) found that self-reported symptoms of discomfort and clinical signs of Meibomian gland dysfunction including worsening grade of meibum expressibility and quality, and Meibomian gland tortuosity had predictive value for CL dropout amongst subjects, albeit recruited from academic settings and aged 18 to 45 years. The current study did not assess dry eye in CL patients as dry eye metrics including fluorescein tear break-up time were not routinely carried out or recorded within the patient records.

Another factor that was not recorded was the type of CL cleaning solution used for reusable CLs, which can impact comfort. CL solutions containing polyhexadine and polyquaternium-1 when used to clean various silicone hydrogel materials have been linked with increased rates of ocular surface staining compared with use of hydrogen peroxide disinfecting solution (Carnt et al., 2009). It is possible that varying reusable silicone hydrogel CL and lens solution combinations could have been contributing factors to CLDO due to solution- lens interactions precipitating as poor comfort. Sulley et al. (2017) found that no alternative lens or management strategy had been tried for 71% of CLDOs, which represents missed opportunities for a practice to grow their CL business, and was also seen in the current sample. For a practice that also offers a dry eye service, the incorporation of an avenue for new or lapsed CL wearers may result in retention of CL patients who dropout of CLs due to discomfort.

Over half of patients from the sample where discontinuation of CL wear was suspected were classified as “false” CLDOs (54.2%), that is not ceasing lens wear due to issues associated with CLs. The primary reason for CLDO in this subgroup was no longer requiring CL wear following surgical intervention (42%). Customer switching (29%) and relocation (19%) were other reasons to explain “false” CLDOs. A series of process errors and areas of improvement were identified after analysing patient records including a means to easily record a reason for CLDO and template to record dry eye metrics for CL patients. CL appointment reminders were still being generated for patients who had communicated relocation or who had ceased CL wear due to surgical intervention for up to three years following notification of changes, representing a waste of resources.

The General Optical Council (GOC), which regulates the optical profession in the UK, commissioned consumer research by the Bostock Marketing Group Ltd. to understand the behaviour of UK adult CL wearers (Turner, 2016). A total of 2043 people took part in an online survey with 68% of respondents having only ever bought CL in-store, 8% having only ever bought online, and 22% having bought CLs both in-store and online (Turner, 2016). The latter group may represent customers prone to switching service providers, and so it is important to understand the profile of this segment of patients and what can be done to retain them as customers. In the current study, 29% of "false" CLDOs were due to customer switching with an average age of 38.9 ± 16.0 years with some records stating that CLs were purchased elsewhere although it is unclear if they were purchased online. Approximately half of respondents from the online survey who viewed CLs as a cosmetic rather than healthcare or lifestyle product were more likely to shop around for competitively priced CLs and were less likely to attend for CL check-ups at least once a year (Turner, 2016).

Socio-economic and demographic variance has been found in CL in-store and CL online buyers (Turner, 2016). In the GOC 2015 CL Survey, online buyers were more likely to be aged between 25 and 44, in part-time employment and more likely to live in London and "multicultural metropolitans" (Turner, 2016). The reasons behind decision-making for primarily online buyers included price (37%), convenience (23%), and value for money (19%) (Turner, 2016). CLs are a significant part of optometric business and practitioners could learn from these insights by simplifying their processes for CL ordering, and offering an online platform for CL supply and home delivery plans via their practice. In-store buyers were more likely to be aged 45 and over, and retired or long-term unemployed, choosing to purchase CL in-store because of the relationship with their practitioner (23%), convenience (16%) and habit (13%) (Turner, 2016). Barriers to this group of patients in buying CL online included not knowing their CL specification or how to find the specific CL they needed (Turner, 2016). The remaining respondents in the CL in-store buyer group chose to not purchase CL online because they were satisfied with the level of customer service in-store, they preferred to buy CL in person or would not trust an online supplier (Turner, 2016). Overall, good customer service and the retailer's reputation were attributes valued greater by those buying their CLs in-store, and convenience and product availability were held in higher regard for those buying CLs online (Turner, 2016).

Understanding priorities in CL purchasing from the patient's or customer's point of view can help practitioners in enhancing their CL service offerings and aid in developing strategies to retain customers. At the time of the analysis, BBR Optometry Ltd. had decided to trial the services of Adaro Optics who provide CL product supply chain solutions to manufacturers, practitioners and patients. Through practice-controlled home delivery, a preferred combination of CLs from one supplier and CL solutions from another can be delivered to patients in one single convenient package

designed to fit through letterboxes. Adaro Optics adopt the practice's brand identity to facilitate an association of the products with the practice and serves to enhance customer loyalty. Utilisation of a service such as Adaro Optics enables practices to achieve time efficiencies by enabling CL product ordering through one versus multiple suppliers, and can support direct debit payments for regular deliveries to patients.

In the GOC 2015 CL Survey, the majority of CL wearing respondents said they attended for CL check appointments yearly (54%), whilst 21% attended more than once a year, and 16% attended every two years (Turner, 2016). The subgroup of patients likely to be overdue for a CL check rather than represent a true CLDO made up 10% of the "false" CLDO sample at BBR Optometry Ltd. These patients had a previous history of attending CL checks at the same time as their yearly eye examinations rather than in accordance with recommended recalls of six months set at BBR Optometry Ltd. for Eyelife^{TM} members. With convenience at the forefront of attributes important to CL wearers especially those purchasing CLs online, the frequency of aftercare visits needs to be considered to avoid unduly inconveniencing CL wearers whilst allowing early detection and successful management of any adverse changes related to CL wear.

British legislation allows the optometrist to set the period of validity of a CL prescription (GOC, 1989; BCLA & GOC). In the early days of CL dispensing, there was a cautious approach with CL check intervals set frequently due to previous experiences with rigid CLs that required numerous review visits to refine lens fitting and monitor adverse reaction such as central corneal oedema (Efron & Morgan, 2017). Efron and Morgan (2017) suggest an appropriate aftercare schedule and rationale based on lens replacement frequency, lens type, wearing modality and predicted rate of refractive change. For neophytes, an aftercare within one to two weeks of CL dispensing is advised followed by a further appointment within the first two months (Efron & Morgan, 2017). Thereafter, a two-year recall is recommended for soft daily disposable CL wearers due to the lower associated risk of keratitis (Efron & Morgan, 2017). A yearly CL check is recommended for soft daily reusable CLs, rigid CLs daily wearers and presbyopic changes to address solution reactions and compliance issues, eyelid ptosis and corneal deformation risk, and progressive accomodative loss respectively (Efron & Morgan, 2017). A six-monthly CL check is recommended for soft and rigid CL extended wearers to reduce the risk of keraitis, and overnight lens mucus adhesion specifically for RGP wearers (Efron & Morgan, 2017). Young myopes aged between five and 15 years old are also recommended to be seen for CL checks six-monthly due to possible myopic advances of -0.50 Dioptres annually (Efron & Morgan, 2017). BBR Optometry Ltd. offer myopia control services including Orthokeratology and the fitting of MiSight 1-day CLs. The CLDO rate for patients using CLs for myopia management was not reported in the current analysis.

The sample of CLDOs at BBR Optometry Ltd. may not be representative of the general UK prospective CL wearing population, and may be more reflective of the population of patients seen at BBR Optometry Ltd. who often have complex needs and are presbyopic. The practice setting may also influence the subset of CLs patients seen. Morgan & Efron (2015) found that compared to national group practices throughout the UK, independent practices fit CLs to older patients, and undertake a higher proportion of rigid, soft extended wear and multifocal lens fits. Perhaps the requirement for more frequent fitting visits and need for specialist equipment for efficient rigid lens fittings such as topographers, radiuscopes and lens modification tools are more attuned to independent practice. The sample of CLDO at BBR Optometry Ltd. were mostly female (68.0%), aged 45 or older (72.2%), and 91.8% were fitted with soft CLs. There was a narrow age range compared to other CL discontinuation studies that specified age and found that patients aged < 16 years had an 83% first-year retention rate with motivation suspected as a reason for retention (Sulley et al., 2017). A trend of increase in rate of CLDO with increasing age has previously been shown (Dumbleton et al., 2013; Pritchard et al., 1999; Richdale et al., 2007).

In retrospective chart reviews, there may be selection bias whereby assumptions regarding lens wearing success are filtered through the practitioner, and no means to extract patient attitude data that could be collected directly in a prospective study design. This study relied on the author's interpretation of the outcomes recorded at the single site. It was not possible to comment on whether patients in this sample of CLDOs were new to or revisiting CL wear, and there were similar results to Sulley et al. (2017) where about one-third of wearers discontinued CL wear for unknown reasons. A proportion of the unknown reasons for CLDO could potentially be due to poor comfort or dryness, and therefore not captured as these patients would be less likely to return. In order to benchmark performance and improve CL service, practitioners should aim to identify CLDOs and determine the retention rate at their practice.

Considering nearly half of new CL wearers have been shown to dropout within the first two months of CL fitting (Sulley et al., 2017) and within the first year as seen in the current analysis, strategies to check on early patient progress should be employed to retain patients. Young et al (2002) determined that lapsed CLs wearers mainly due to self-reported discomfort, could be successfully refitted with CL (77 ± 6%) and that the prime reason for subsequent dropout was dissatisfaction with visual performance. Short term success rates in CL retention were greatest for spherical and daily disposable soft CLs, and it is plausible that uncorrected astigmatism was a contributory factor to CLDO (Young et al., 2002). Future work could include blueprinting the CL service at BBR Optometry Ltd. as outlined in chapter two, to develop processes to monitor and minimize CLDO. BBR Optometry Ltd. patients who discontinued CL wear could be invited to trial new CL products

that may address their initial reason for dropout such as poor vision due to limitations in available parameters at the time of fitting, or discomfort.

In terms of strategies to grow a practice's CL business, Mayers et al. (2019) found that offering CLs to patients who only wore spectacles at the time of frame selection positively impacted conversion rate and eyewear spend (20% more), and the likelihood of proceeding with CL fitting compared to patients not given the option. Some patients assigned to the test group declined participation in the market research survey because they were happy with their spectacles (45%), there was a fear associated with lens insertion (26%), there was a prior negative experience with CLs (14%) or lack of time (8%) (Mayers et al., 2019). All participating subjects were able to wear CL successfully during the eyewear selection process with two-thirds being aged 40 years or older, 50% requiring presbyopic correction and 30% requiring correction for astigmatism (Mayers et al., 2019). A complimentary in-practice limited time trial allows an opportunity for the practitioner to demonstrate the benefits of new CL designs and materials, and for patients to move beyond concerns associated with CL wear. This attempt to close provider gap four or the communication gap referenced in chapter two, could help in situations where the practitioner is reluctant to promote CL wear for fear of being perceived as being forceful, whilst the patient may be reluctant to ask about their suitability for CL wear if not mentioned by the practitioner. Another approach would be to apply the EASE method as outlined by Atkins et al. (2009), which has shown to increase the uptake of CLs wear by 33%.

There were no large dominant groups to categorise reasons for dropout or trends in which CL products were worn at the time of CLDO in this study. For some patients, the benefits of CL wear in comparison to spectacle wear presumably do no outweigh factors such as cost and convenience. Cost or expense has been shown to be a reason for CLDO three months or more after fitting (Sulley et al., 2017). There were a large proportion of patients who discontinued using CL services at the practice but did not necessarily discontinue CL wear permanently. It is possible some people may dip in and out of CL wear to suit their lifestyle. Patients have been shown to resume or revisit CL wear for reasons such as resolved discomfort and irritation, cosmetic appearance, for work or leisure pursuits, simpler care regime, improved finances, and changes to general and ocular health (Pritchard et al., 1999). The development of drug eluting CLs and utlisation of CL as drug delivery systems with biosensing capabilities may further transform the profile of CL wearers with CL being worn to address therapeutic needs in addition to offering spectacle-free options to enhance vision (Alvarez-Lorenzo et al., 2019; Choi et al., 2019). Mariño-López et al. (2019) have synthesized a hybrid hydrogel-based soft CL that features the integration of gold-based plasmonic silica-shelled nanocapsules for applications in electromagnetic shielding. The hybrid lens material has high optical density while permitting visible light transmittance, and so could change the current market for

safety eyewear (Mariño-López et al., 2019). A new motivation for CL wear could be to provide daily protection whilst working in an enviroment where high-powered light sources are operated.

5.5: Conclusion

It is important to stress that the findings in the current analysis are specific to a sample of CLDOs from a single site with an older demographic, and are not generalizable across the UK population. Larger studies involving multiple sites would be required for comments on general trends observed amongst CLDOs. There were no strong patterns to link CLDO to dry eye or to a particular CL product or product range. Perhaps the observation of no clear trend in reasons for CLDO and the greater number of "false CLDOs" suggests that the profile of the CL patient has changed. Rather than losing CL patients due to dry eye, patients may be more inclined to shop around and/or flexible in their CL wearing schedule. Patients may prefer a mixture of spectacle and CL wear, deciding to wear CLs when it suits them with daily disposables a viable choice for infrequent wear. Patients with dry eye have been known to present to eye casualty, and represent a subset of people that could be managed and potentially served better within community private practice. The proportion of people presenting to eye casualty that could have been managed in private practice will be explored in chapter six.

CHAPTER 6 ABSTRACT
Retrospective analysis of first-time presentations to a hospital eye casualty department

PURPOSE: To demonstrate the role of optometrists in alleviating the burden on NHS ophthalmology services through local schemes and perhaps private optometric services in the future, such as a dry eye clinic.

METHODS: Records of first-time presentations to the eye casualty department at Hereford County Hospital in January 2018 were analysed sequentially. After grouping patients based on condition diagnosed by the practitioner in eye casualty, and using the reason for visit and College of Optometrist guidance on urgency of referrals list by conditions as reference material, the quality or appropriateness of the optometrist referral was assessed and deemed warranting emergency or same day referral. After grouping conditions diagnosed in eye casualty as a result of referrals from general practitioners (GPs), the patient's reported reason for visit including history and symptoms were compared to the Primary Eye-care Assessment and Referral Service (PEARS) criteria for inclusion. After grouping conditions diagnosed in eye casualty as a result of self-referrals in a similar manner to the College of Optometrists clinical management guidelines (CMGS), the patient's reported reason for visit was compared with the PEARS criteria for inclusion. Cases that were reviewed in eye casualty were grouped into those conditions that were suitable to be seen by an ophthalmologist, optometrist or IP-optometrist.

RESULTS: There were 207 (49.2%) females and 214 (50.8%) male first-time presentations to the department. The mean, median and mode ages respectively were 53.7 ± 22.5, 58 and 68 years, and patients' ages ranged from six months to 102 years. 69% of optometrist referrals were appropriate for same day, and the others were appropriate but not for same day referral. 92% of patients presenting from GP referrals could have been assessed via PEARS with only 30% requiring onwards referral to ophthalmology. 83% of patients could have been assessed via PEARS with only 17% of cases requiring onwards referral to ophthalmology. 66% of patients attending eye casualty for follow-up could be seen within the community, although nearly half of conditions seen would potentially require an IP qualification to manage.

CONCLUSIONS: Considering the total number of cases in January 2018 that could have been seen within the community via PEARS from a GP or self-referral either as a first-time presentation or for review, the amount of savings to the Wye Valley NHS Trust would have been approximately £46, 405.00. The retrospective analysis highlights the value of local optometric community services to address acute ocular symptoms or eye-related concerns, and the value of an IP- qualification in helping to further alleviate the burden on hospital emergency eye services.

CHAPTER 6
Retrospective analysis of first-time presentations to a hospital eye casualty department

6.1: Introduction

According to the annual publication on Accident and Emergency (A&E) activity in English National Health Service (NHS) hospitals and English NHS-commissioned activity in the independent sector, there were 23.8 million attendances in A&E covering the financial year ending March 2018, which has increased by 22% when compared to the period ending 2009. Approximately 3.2% of A&E diagnoses reported in the periods September 2017 to March 2018 were ophthalmology-related (NHS Digital, 2018). General A&E departments and dedicated eye casualty departments both provide emergency eye care for ophthalmic complaints in the UK with variations in the way they operate based on the needs of the local community, size of the population and the resources available to the local clinical commissioning groups (CCGs). London's two largest emergency eye units, Moorfields Eye Hospital and the Western Eye Hospital, have seen annual attendances rise by 7.9% and 9.6% per year respectively (Smith et al., 2013). Alongside the increasing demand for urgent eye care is the risk of delays and poor visual outcomes for those waiting for treatment or monitoring as seen in the management of chronic ocular conditions demonstrating a lack of capacity within the hospital eye service (Foot & MacEwen, 2017).

The Way Forward project commissioned by the Royal College of Ophthalmologists highlights the growing demand for emergency eye care with rising attendances thought to be due in part to an ageing population with higher life expectancy and a shift in health seeking behaviour to favour emergency secondary care (RCOphth, 2017). It is thought that the 2004 change to the General Practice out-of-hours contract and the implementation of the A&E 4-hour wait target contributed to A&E becoming the perceived primary route for emergency care by patients (RCOphth, 2017). There are different models of dealing with emergencies that suit different volumes of patient flow including slotting acute patients into clinic, acute referral clinics, daytime walk-in services and 24 hours walk in emergency eye services (RCOphth, 2017). Daytime eye casualty services offered by many NHS trusts distinct from the main emergency department or minor injuries units are potentially open to abuse with frequent attenders or those with chronic ocular conditions circumventing the wait for an outpatient appointment in general clinic by attending inappropriately.

Herefordshire is a predominately rural county located in the south-west of the West Midlands region bordering Wales with the fourth lowest population density in England (0.87 persons per hectare) and a current estimated resident population of 189,500 (Herefordshire Council, 2018). Herefordshire in particular has an older age structure than England & Wales as a whole, with 24% of the population aged over 65, compared to 18% nationally in 2017 (Herefordshire Council, 2018). The city of

Hereford is situated in the middle of the county where almost one third of the county's residents live, and is the centre for most amenities (Herefordshire Council, 2018). The Hereford County hospital part of the Wye Valley NHS trust is one of the smallest rural district general hospitals in England and has seen an average of 5664 eye casualty attendances each year over the last five years (EMIS health, UK).

The current service design in Hereford is a daytime walk-in service and has taken on the organisational strategy to manage demand by recognising the benefits of utilising optometrists within the community who demonstrate the initiative to upskill. Community optometrists in the department act as the primary reference point for acute eye problems and help to reserve secondary care for higher complexity cases. The department also utilises nurses with experience in ophthalmology who triage and prioritise cases on arrival to ensure emergency cases and complex clinical problems are seen first, and non-urgent cases redirected to their general practitioner (GP) or optometrist to reduce waiting times. The nurses take the initial ophthalmic and general medical history, undertake testing of visual acuity and other initial investigations such as pupil responses and instil dilating drops when required. It has been suggested that ophthalmic nurse practitioners (ONPs) may be better suited to assess emergency ophthalmic complaints than junior doctors in A&E departments, and are effective in reducing the workload of eye casualty departments (Jones et al., 1986; Banerjee et al., 1998; Read & George, 1994; Ezra et al., 2005). In Hereford, there are opportunities for optometrists to have case-based discussions with consultants via NHS email and telephone, and to sit in with consultants during clinics to improve their clinical decision-making skills and ultimately reduce the demand on emergency eye care. The emergency ophthalmology consultant lead holds one-to-one sessions with optometrists in an emergency clinic one half day per week in three-month blocks.

The role of optometrists is changing with referral refinement schemes, pre- and post- operative cataracts schemes and independent prescribing taking the pressure off secondary care. Hospital optometrists have proven to be competent in working in an A&E setting (Hau et al., 2007), and eye health care in community practice has evolved so that optometrists can diagnose and manage more ocular conditions (Parkins et al., 2014). The Department of Health in the UK has granted suitably trained optometrists the rights to extend their therapeutic prescribing capabilities in the form of independent prescribing (Buckley et al., 2005) allowing them to prescribe any drug from the British National Formulary for any condition affecting the eye and adnexa as long as it is not a controlled drug or requires parenteral administration, and providing it is within the prescriber's scope of practice. Non-medical prescribing is seen across the NHS in all four countries, and in other professions including nursing, pharmacy, podiatry, physiotherapy and radiography (National Prescribing Centre 2010). Currently, there are five independent prescribing (IP) optometrists in

Herefordshire based on the General Optical Council register at the time of this analysis who can prescribe any licensed medication except for controlled drugs or medication for injected medication for conditions affecting the eye and the tissues surrounding the eye within the practitioner's recognised area of expertise and competence. Independent prescribing for optometrists was introduced in June 2008 with the Commission on Human Medicines making it clear that the extent of IP for optometrists would be supported by clinical management guidelines from the College of Optometrists, which are regularly updated (College of Optometrists, 2018). Prior to the March 2017 renewal period, there were 499 optometrists listed on the General Optical Council's (GOC) IP specialty register representing 3.3% of all GOC registered optometrists with around 57% of IP optometrists based in England (GOC, 2017). An NHS Education for Scotland initiative to shift the balance of care out of hospitals and into the community has led the issuing of NHS prescribing pads to trained IP optometrists in 2013, who can manage patients in primary care at no cost to the patient (Parkins et al., 2014). The Hereford County hospital ophthalmology department support optometrists in becoming IP qualified by offering clinical placements that makes up the second stage of qualification. In this phase, optometrists have exposure to different ocular complaints, which will aid future referral decisions from community practice and direct clinical decision making in the community. In order to register as an IP optometrist, the optometrist must have been qualified and practicing in the UK for at least two years, complete a course offered from one of five universities, complete a 24-session clinical placement of not less than three hours (12 days) documented in an online logbook to be verified by the supervising ophthalmic consultant, and pass the College of Optometrists' therapeutics common final assessment which is made up of 75 multiple choice questions grouped into patient scenarios.

The Primary Eye-care Assessment and Referral Service (PEARS) is an NHS-funded intermediate-tier service providing timely optometric assessments of those presenting with acute eye conditions. The aim of PEARS is to reduce unnecessary referrals to the hospital eye service, increase capacity within the overburdened hospital eye health services and provide a more cost-effective service with a greater number of patients being retained and managed appropriately within the community (LOCSU, 2016). Patients presenting to their GP with an eye problem and satisfying specific inclusion criteria are referred to accredited community optometrists. There is no requirement for the optometrists participating in PEARS to be IP qualified. Under the Entry Level Medicines Act exemptions, registered optometrists without an IP qualification can sell or supply all medicinal products on a General Sale List and all pharmacy medicines including ocular lubricants, topical and systemic anti-allergy agents, and freely prescribe certain topical antibiotic drugs via a signed order (College of Optometrists, 2018). Large numbers of community optometrists commonly supply and recommend over-the-counter drugs, particularly ocular lubricants, topical anti-histamines and mast cell stabilisers (Needle et al., 2008). The scheme also allows patients direct access to an accredited

optometrist without a GP referral. In order to participate in PEARS, optometrists must complete two parts of training and accreditation, which is based on the course used to train PEARS providers in Wales. Part one is a series of distant learning lectures for theoretical training that involves online multiple-choice testing, and part two is the practical station assessment organised by the participating local optical committee and the Wales Optometry Postgraduate Education Centre (WOPEC). Successful completion allows accreditation to PEARS and a total of 14 continuing education and training (CET) points, which help practitioners earn the number of CET points required in a three-year cycle that is a statutory requirement for all fully-qualified optometrists and dispensing opticians. The service was renamed to the Minor Eye Conditions Service (MECS) but will be referred to as PEARS throughout this chapter as it continues to be referred to by local Herefordshire practitioners. A number of PEARS and similar schemes have been introduced across the UK demonstrating clinical safety, easing overstretched hospital eye services by reducing referrals, and increasing patient's accessibility resulting in high patient satisfaction (Cottier, 2015; Craven, 2015; McCracken, 2013; Sheen et al., 2009; Greenwood, 2013). The purpose of this retrospective analysis was to determine how many people presenting to the Hereford County Hospital Eye Casualty department could be managed in community optometric practice under PEARS, and how many people presenting to eye casualty could be reviewed within the community.

6.2: Method

Records of first-time presentations to the eye casualty department at Hereford County Hospital in January 2018 were analysed sequentially. Triage nurses in the eye casualty department document by hand all presentations to the clinic in a large binded book including details such as date seen, source of referral, the patient name, the patient identifier number and consultation outcome, that is not removed from the unit. The month of January was chosen as using this binded book did not interfere with the activity of the clinic. All completed hand written eye casualty records documenting details of the visit are scanned by administrative staff to the patient's electronic record using Symphony software (EMIS health, UK). The scanned records are accessible after searching for any given patient using their patient identifier number referred to as the RLQ. The patient's age was calculated from their date of birth and the date of their visit to eye casualty. Data collection spreadsheets with patient identifiable information are confidential and are stored in line with information governance requirements and remain within the Wye Valley trust firewall. Patient details were not included in the data analysis file. A decoding file with the relationship between audit identification number and patient identification is held separately from the data analysis file to minimise information governance risk and provides a mechanism for returning back to the patient in the event of requiring clarification.

This analysis received approval from the Life and Health Sciences Ethics Committee at Aston University (Project #1276) and adhered to the tenets of the Declaration of Helsinki. Analyses were deemed as clinical audits, and full hospital ethical approval was not required. However, tenants of Helsinki were adhered to and anonymised information was audited. The online decision tool from the NHS Health Research Authority also determined that approval from the NHS Research Committee was not required.

6.3: Results

In January 2018, there were 581 presentations to the Hereford County eye casualty department according to the triage nurses' records. Data analysis was carried out on 421 records and 160 records were excluded for several reasons represented in figure 6.1. Records were excluded if they were not first-time presentations to the department and were follow-up appointments (n=128), and if there were administrative errors such as incomplete notes, no scanned notes available or repeat entries (n=15). Other entries were excluded from analysis because they were illegible (n=12) or because the patient did not wait to be seen (n=4). One record was excluded because it represented an existing glaucoma patient attending eye casualty to enquire about the use of prescribed hypotensive eye drops.

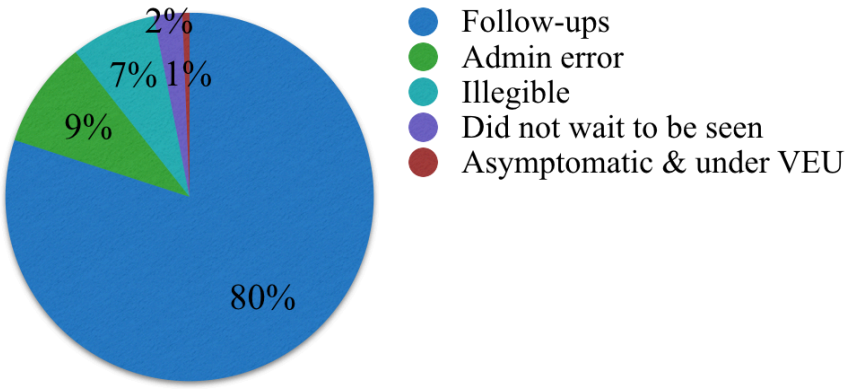


Figure 6.1: Reasons for excluding data from 160 records in analysis of first-time presentations to Hereford County hospital eye casualty department in January 2018.

There were 207 (49.2%) females and 214 (50.8%) male first-time presentations to the department. The mean, median and mode ages respectively were 53.7 ± 22.5, 58 and 68 years, and patients' ages ranged from six months to 102 years (figure 6.2). There were 32 cases under the age of 16, and a similar number of cases aged 16-60 (n=193) and those aged over 60 (n=196).

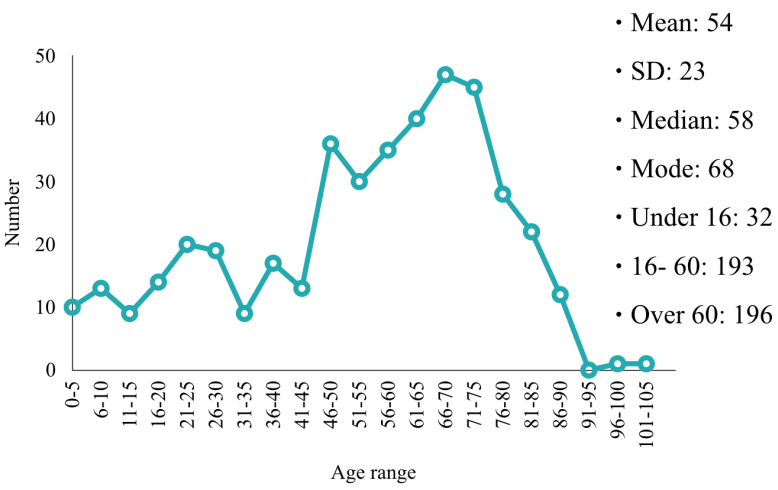


Figure 6.2: Age demographics for first-time presentations to Hereford County hospital eye casualty department in January 2018.

A large proportion of presentations were self-referrals (n=300), with GPs (n=50) and optometrists (n=51) accounting for about 12% each of emergency referrals (figure 3). The remaining sources of referrals were from Hereford County hospital's general accident and emergency (n=11) department, other Hereford County hospital wards (n=4; paediatrics, clinical assessment unit, neurology) and other hospitals (n=5). The majority of cases were seen by ophthalmologists not in training (n=222), followed by ophthalmologists in training (n=140), independent prescribing optometrists (n=42) and consultant ophthalmologists (n=16) (figure 6.3).

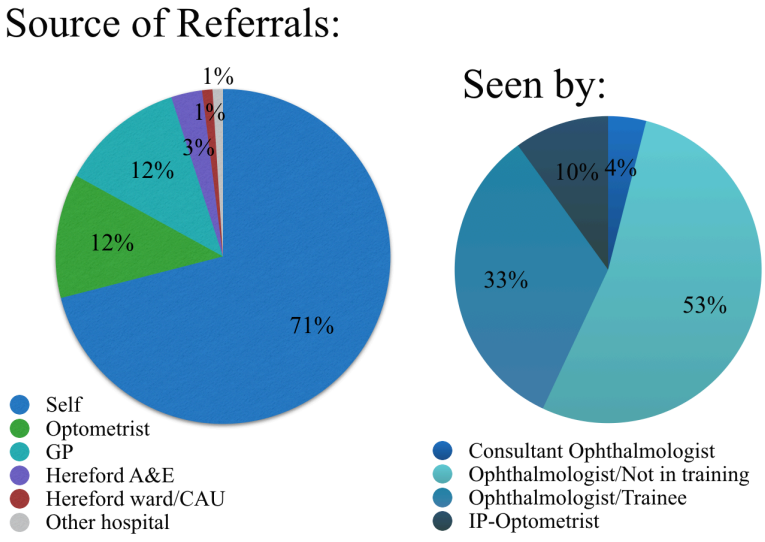


Figure 6.3: Distribution of source of referrals to Hereford County hospital eye casualty department in January 2018 and of the eye care practitioners managing first-time presentations to the department.

One of the records did not specify who saw the patient. During the time period for which the analysis was conducted, there were seven ophthalmologists not in training, seven ophthalmologists in training, two independent optometrists working in eye casualty under the supervision of ophthalmology staff, and four consultants. Some records were annotated to include details of whether the case was discussed with a more senior member of staff. Of the cases seen by ophthalmology trainees, 10 records (7%) were annotated to say that the patient was also discussed with or seen by a more senior colleague. Of the cases seen by ophthalmologists, 11 records (5%) were annotated to say that the patient was also discussed with or seen by a colleague. Of the cases seen by independent prescribing optometrists, nine records (21%) were annotated to say that the patient was also discussed with or seen by a consultant. At the time of the analysis, one of the optometrists had been IP qualified for nine months and the other for one month perhaps accounting for the larger number of cases where a colleague was consulted. It is also possible that more cases were seen by consultants who were acting as mentors for the IP optometrists.

The data collected was organised by source of referral. The conditions seen and diagnosed in eye casualty as a result of optometric referral are shown rather than the provisional diagnoses from optometrist referrals as the original referral letters were not scanned to the records and the suspected diagnosis from the optometrist was not always listed (figure 4). Identified with spectacle icons in figure 6.4 are the conditions that could be treated with pharmacological intervention, which an IP optometrist could initiate according to the College of Optometrists clinical management guidelines (CMGs) at the time of the analysis, and this made up 33% (17/51) of cases. That is not to say that contact lens related ulcers could not be managed by an optometrist or IP optometrist but depending on the location and size of the infiltrate, it may be more appropriate to refer suspect microbial keratitis cases in contact lens wearers to eye casualty for a corneal scrape for culture and determination of antibiotic sensitivities. A foreign body could also be managed in the community by an optometrist or IP optometrist if they are confident to do so, have a means to dispose of sharps if hypodermic needles are used, and the foreign body has not penetrated into the stroma. Following removal of the foreign body the optometrist could advise on the use of ointment for ocular lubrication or consider over-the-counter topical antibiotic prophylaxis which would not require an IP qualification. The purpose of the College of Optometrist CMGs is for optometrists to ensure that any referral decision falls within accepted advice, and are referred to if any investigation into practice is instigated. The CMGs were created in 2008 when optometrists first gained independent prescribing status. The information on the CMGs is succinct covering aetiology, predisposing factors, symptoms, signs, differential diagnosis, management by an optometrist (non-pharmacological and pharmacological), management category, possible management by an ophthalmologist, evidence base and lay summary.

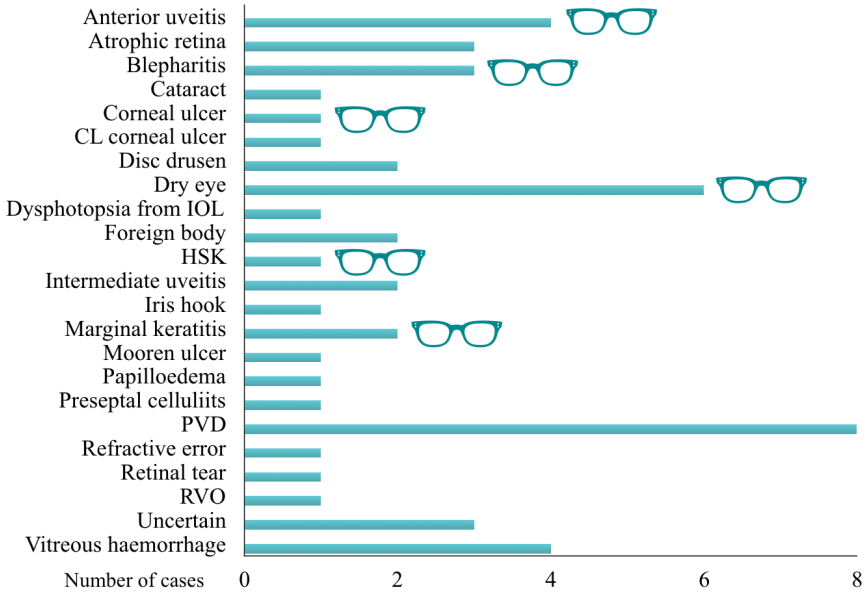


Figure 6.4: Conditions diagnosed in Hereford County hospital eye casualty department in January 2018 as a result of optometric referral. Identified with spectacle icons ( ) are the conditions that could be managed with pharmacological intervention potentially by an IP optometrist, making up 33% (17/51) of cases. HSK= herpes simplex keratitis, PVD= posterior vitreous detachment, RVO= retinal vein occlusion.

Of the conditions that could have been treated by an IP optometrist assuming agreeance on diagnoses between hospital and community practitioners, 59% (10/17) of cases were actually treated with prescription medication. The conditions treated were blepharitis, anterior uveitis, non- contact lens related corneal ulcer, herpes simplex keratitis, and marginal keratitis. Perhaps the non-contact lens related corneal ulcer case could have been categorized as a marginal keratitis, however, the diagnosis was not recorded as such and there were no notes to make this assumption. Also, there were no medications prescribed for dry eye that were not available over-the-counter aside from one case where Pilocarpine 1% was prescribed for a secondary eye condition.

After grouping patients based on condition diagnosed by the practitioner in eye casualty, and using the reason for visit and College of Optometrist guidance on urgency of referrals list by conditions as reference material, the quality or appropriateness of the optometrist referral was assessed and deemed warranting emergency or same day referral. I found about 69% were appropriate for same day referral and the others were appropriate but not for same day referral. A limitation to the retrospective analysis is knowing whether or not the patient was actually referred same day due to lack of original referral letters from optometrists or whether the patient admitted themselves to eye casualty rather than waiting for an appointment in the general eye clinic. Additionally, patients presenting to their local optometric practice participating in the PEARS scheme may have failed to receive an appointment and had been advised by reception staff to attend eye casualty. Although the

patient may not have been seen by an optometrist, the source of referral in the nurse triage book may still have been recorded as "optometrist."

Conditions that did not require emergency referral may have presented to the optometrist with an air of urgency by the patient, or the suspected diagnosis was different from the final diagnosis in eye casualty. For instance, a four-year-old female patient was referred with "query phylenticular conjunctivitis requiring steroid treatment" who was later diagnosed with blepharitis and discharged. It is suspected the age of the patient and presentation although there are no notes on symptoms or signs, dictated the optometrist's decision to refer. The number of PEARS appointments allocated for dry eye and blepharitis patients in the county is limited in order to avoid the scheme being used as a dry eye management service with one follow-up appointment permitted for dry eye patients and no follow-up appointments for anterior blepharitis. The College of Optometrists CMG for dry eye (2018) only recommend an urgent (i.e. within one week) if Stevens-Johnsons syndrome or Ocular cicatricial pemphigoid are suspected but not a same day, emergency referral. From the two blepharitis cases that did not require emergency referral, it would seem first line non-pharmacological management did not offer improvement in symptoms and onwards referral to ophthalmology led to the prescribing of systemic tetracyclines. One case diagnosed with dry eye was actually referred to eye casualty for unexplained bilateral blurred vision and poorly reacting pupils. The patient was also awaiting surgery for bowel and liver cancer, and was issued with ocular lubrication and booked in to general clinic for visual field testing reflecting the complexity of the presentation.

Other conditions diagnosed in eye casualty that did not require same day referral included atrophic hole, cataract, marginal keratitis, and a retinal vein occlusion. In both atrophic hole cases, the patients were asymptomatic and discharged but one could justify the referral if a retinal hole was suspected. Superficially, a diagnosis of cataract from an emergency optometric referral would raise criticism given established pre- and post-operative cataract referral schemes in the county, however, this one case was not straightforward. The reported reason for referral listed a dull ache, blurred vision and raised macula in the operated eye two months post-cataract surgery, with a note of bilateral glaucoma and previous retinopexy for a retinal tear in the fellow eye. One could assume that the optometrist did not have access to OCT imaging to rule out cystoid macula oedema and it may have been more appropriate to refer the patient urgently on the wet age-related macular degeneration rapid access scheme. The record for this indicates the patient required fellow eye cataract surgery and was discharged, so one can only assume the eye casualty practitioner determined there was no intraretinal fluid and the achiness reported was due to induced anisometropia. According to the College of optometrist CMGs (2018), marginal keratitis is self-limiting although it is conventional to give pharmacological treatment with a view to relieve

symptoms and shorten the clinical course, and can be referred to ophthalmology if persistent or recurrent but no level of urgency for the referral is indicated. The assumption would be that the cases noted here were not resolving and pharmacological intervention was prescribed in eye casualty for both cases. The retinal vein occlusion case was referred onwards for fundus fluorescein angiography from eye casualty, however, the College of Optometrists guidance C205a and C205b (2018) indicate an urgent versus emergency referral for a central retinal vein occlusion where the intraocular pressure is less than 40 mmHg and in this particular case, the patient presented over 12 hours from the onset of symptoms (table 6.1). There were two cases with uncertain diagnoses that both were appropriate referrals but perhaps as urgent versus same day referrals according to the College of Optometrist guidance. They were query suspect retrobulbar optic neuritis and sudden onset diplopia following a sports-related concussion.

Conditions that did require emergency referral were warranted where, pharmacological intervention could not be initiated by an optometrist in the cases of anterior uveitis or Herpes simplex keratitis, patients were symptomatic in the presence of a suspect retinal hole, corneal scrapes were carried out in the presence of contact lens related corneal ulcers, suspected papilloedema in symptomatic patients later diagnosed with disc drusen, and foreign body removal. Other appropriate referrals included conditions suggesting a retinal tear including a case of dysphotpsia post-cataract surgery and posterior vitreous detachments, actual retinal tears, intermediate uveitis, the appearance of an iris hook in the anterior chamber of a patient with history of bilateral intraocular lens subluxation, a case diagnosed as Mooren ulcer following presentation of severe ocular pain, preseptal cellulitis in a child, and vitreous haemorrhages. There was an odd diagnosis of refractive error where sudden loss of vision was noted and therefore suggestive of an emergency. There is mention of a two-line drop in visual acuity following a head injury five weeks prior to the onset of symptoms by the optometrist. Perhaps due to the unexplained reduction in visual acuity and recent trauma, the optometrist referred to secondary care where no sight threatening pathology was found. Similarly, in a case diagnosed in eye casualty as uncertain, there were notes of unexplained reduction in visual acuity and headaches with the patient reporting onset of new floaters. This patient was referred by ophthalmology to a specialist clinic for visual field testing.

Table 6.1: Urgency of referrals from College of Optometrist's guidance C205a and C205b if symptoms or signs suggest the conditions listed (https://guidance.college-optometrists.org/guidance-contents/communication-partnership-and-teamwork-domain/working-with-colleagues/urgency-of-referrals/ accessed 11/10/2018).

After grouping conditions diagnosed in eye casualty as a result of referrals from GPs, the patient's reported reason for visit including history and symptoms were compared to the PEARS criteria for inclusion, and it was determined 92% could have been seen by an optometrist on the scheme. Based on the diagnosis in secondary care against the College of Optometrists' CMGs, it was determined that 57% of the 92% could have been managed by an optometrist and a further 13% if pharmacological intervention was required and the optometrist was IP qualified (figure 6.5). An additional 30% would have been referred to ophthalmology although perhaps not on the same day. At the time of the analysis, the Local Optical Committee Support Unit outlined the criteria for

inclusion onto PEARS renamed to MECS (LOCSU, 2016). Presentations were PEARS appropriate if the following symptoms were experienced within the last two weeks: loss of vision including transient loss, foreign body and emergency contact lens removal (not by the fitting practitioner), sudden onset of blurred vision but always consider if a sight test would be more appropriate, ocular pain or discomfort, systemic disease affecting the eye, differential diagnosis of red eye, dry eye, epiphora, trichiasis, differential diagnosis of lumps and bumps in the vicinity of the eye, recent onset diplopia, retinal lesions, and patient reported field defects. If symptoms of flashes and floaters were experienced within the last six weeks, these cases could also be claimed on PEARS. GPs can also refer into the scheme whereby participating optometrists must be able to offer an eye examination within 48 hours or within two weeks if it is a routine referral. If the participating optometrist does not have an appointment available, then they must refer to their nearest colleague. PEARS exclusions include use of the scheme to claim for cases of diabetic retinopathy, adult squints, longstanding diplopia, and repeat field tests to aid diagnosis following an eye examination.

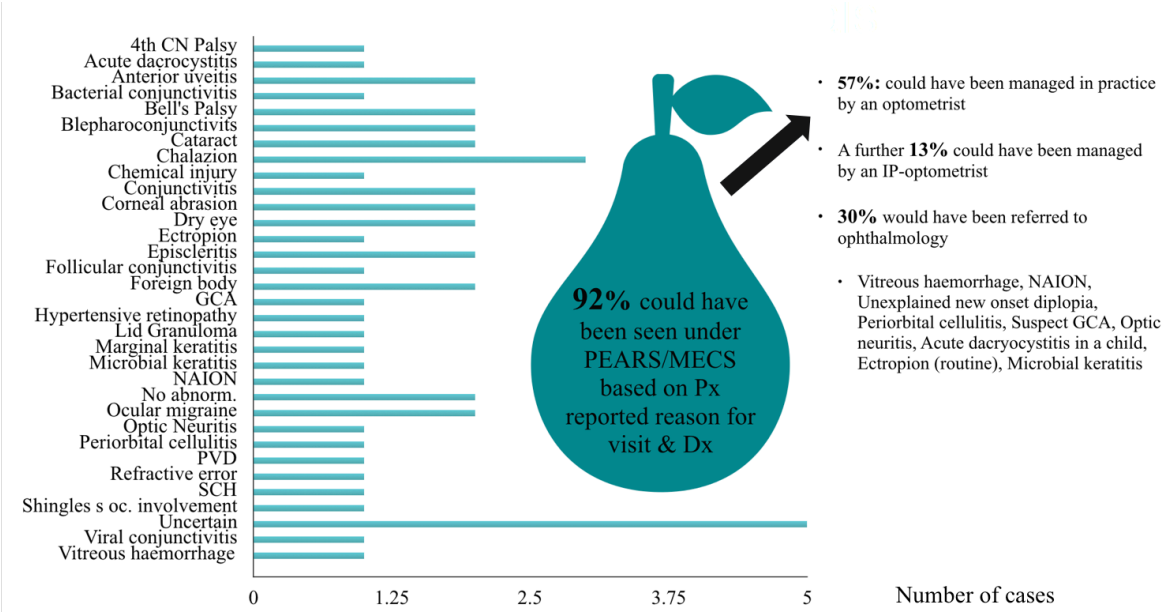


Figure 6.5: Conditions diagnosed in Hereford County hospital eye casualty department in January 2018 as a result of GP referral. Analysing the patient reported reason for visit and diagnosis in eye casualty against criteria for PEARS inclusion revealed 92% of first-time presentations could have been seen by an optometrist in the community first. Of the 92%, 70% could have been managed by an optometrist and 30% would have been referred to ophthalmology although not all same day referrals. CN= cranial nerve, GCA= giant cell arteritis, NAION= non-arteritis anterior ischemic optic neuropathy, No abnorm= no abnormality, PVD= posterior vitreous detachment, SCH= subconjunctival haemorrhage, s oc.= without ocular.

After grouping conditions diagnosed in eye casualty as a result of self-referrals in a similar manner to the College of Optometrists CMGs, the patient's reported reason for visit was compared with the PEARS criteria for inclusion. It was determined 83% of patients could have been seen on the PEARS scheme as a first-port of call with only 17% of cases requiring onwards referral to ophthalmology

after considering the diagnosis in secondary care against the College of Optometrists' CMGs (figure 6.6). Disorders of the cornea (n=52) made up the majority of cases followed by trauma (n=42), the miscellaneous category (n=30), disorders of eyelids (n=29) and posterior vitreous detachment (n=29). The miscellaneous category included the following diagnoses from eye casualty: vitreous haemorrhage, wet and dry age-related macular degeneration, toxoplasmosis, shingles, skin rash, third nerve palsy, Bell's palsy, bilateral diplopia, branched retinal vein occlusion, cataract, Cobb's tufts, conformer replacement, diabetic maculopathy, intradermal naevus, iris naevus, ocular migraine, papilloedmea, and retrobulbar haemorrhage. Notably there were 22 cases (7.3%) that showed no abnormality with presenting symptoms ranging from intermittent headaches, intermittent loss of vision, requesting for prescription of repeat glaucoma drops, and ocular discomfort.

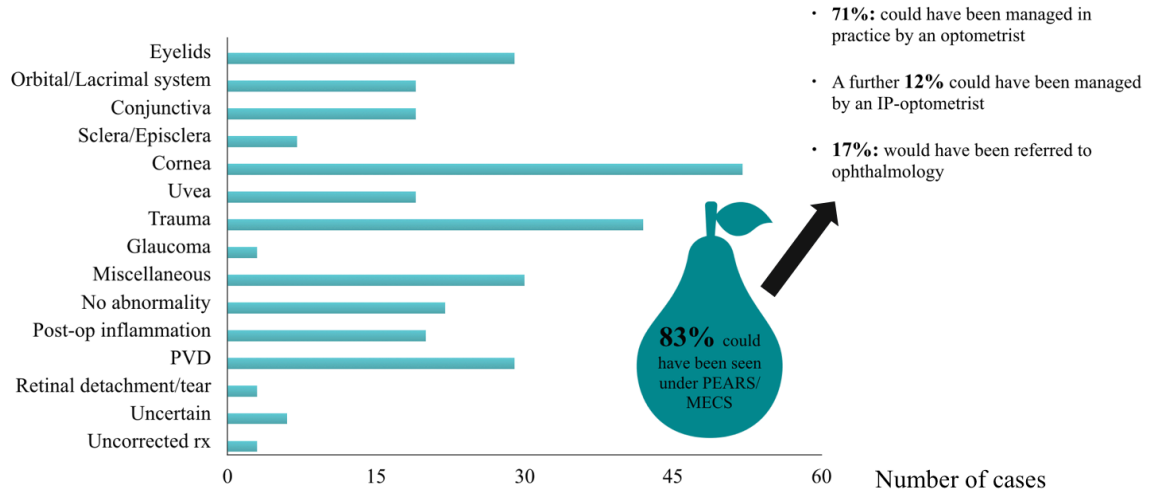


Figure 6.6: Conditions diagnosed in Hereford County hospital eye casualty department in January 2018 as a result of self-referral. Analysing the patient reported reason for visit and diagnosis in eye casualty against criteria for PEARS inclusion revealed 83% of first-time presentations could have been seen by an optometrist in the community first. Of the 83%, 83% could have been managed by an optometrist and 17% would have been referred to ophthalmology although not all same day referrals.

There were two referrals from Hereford County hospital's paediatric ward, one from neurology and one from the clinical assessment unit. One patient had received an MRI scan and was referred to eye casualty to rule out causes of retrobulbar inflammation noted. The patient was seen by the lead consultant ophthalmologist for the department where venous malformation behind the right eye was suspected following interpretation of the MRI and valsalva movement. The patient was experiencing more frequent headaches and migraines and this diagnosis and explanation to the patient warranted a senior ophthalmologist, which was able to take place on this occasion. Perhaps this highlights the need for senior input availability during emergency service hours and potentially better communication within the hospital to direct patients to the most appropriate clinic. Locally, there was a referral from Brecon hospital for anterior uveitis and foreign body removal, and from Neville

hall hospital in Abergavenny for chemical trauma. Birmingham hospital also requested ophthalmologic review of a child following head injury and skin graft application, and of a patient post-vitreoretinal surgery.

After being assessed and managed by the eye casualty practitioner, patients were either discharged, a follow-up appointment in eye casualty was arranged or they were referred to another subspecialty service. In analysing the outcomes, it was found that 59% of first-time presentations to eye casualty were discharged after their initial visit, 22% were referred for follow-up to a specialist or general clinic and 20% were given appointments for follow-up in eye casualty. Conditions that were discharged included chalazion, blepharitis, dry eye and Meibomian gland dysfunction, subconjunctival haemorrhage, episcleritis, viral and bacterial conjunctivitis, corneal abrasion, recurrent uveitis, mild post-operative inflammation, and posterior vitreous detachment. Other cases discharged were those relating to chemical trauma due to hair dye and nail glue, blunt trauma, and foreign body and rust ring removal.

Cases that were reviewed in eye casualty were grouped into those conditions that were suitable to be seen by an ophthalmologist, optometrist or IP-optometrist. It was determined that about 66% of patients attending eye casualty for follow-up could be seen within the community for example, review of resolving recurrent uveitis (figure 6.7). Subdividing review cases that could be seen within optometric community practice into IP and non-IP optometrists as well as considering cases where repeat prescriptions and co-management with ophthalmology may be required, 49% of conditions would potentially require an IP qualification to manage. The conditions requiring follow-up in eye casualty that could potentially be managed in the community were anterior uveitis, corneal abrasions for example following foreign body removal, corneal ulcer, episcleritis, and marginal keratitis. On average, the recommended timing for follow-up in eye casualty was 7.8 ± 6.8 days.

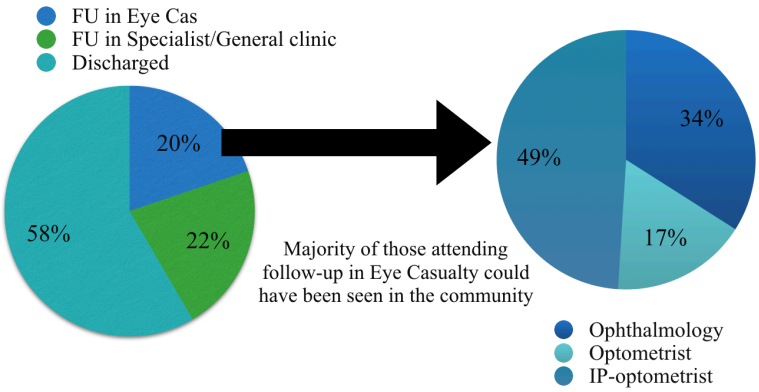


Figure 6.7: Distribution of outcomes of first-time presentations to the Hereford County hospital eye casualty department in January 2018. The majority of cases (66%) could potentially be followed up in the community.

6.4: Discussion

The current analysis highlights the value of local optometric community services to address acute ocular symptoms, and the value of an IP- qualification in helping to further alleviate the burden on hospital emergency eye services. Pharmacological treatment could have been initiated by an IP-optometrist in about one fifth of cases referred by optometrists, and about half of follow-up appointments scheduled in eye casualty could be reviewed by an IP-optometrist within the community. Assessing GP and self-referrals to eye casualty together showed that approximately 85% of cases could have been managed under PEARS. Studies monitoring the activity and evaluating the clinical safety of a minor eye conditions enhanced service schemes similar to PEARS have shown that over 66% of patients could be retained in community optometric practice (Sheen et al., 2009; Konstantakopoulou et al., 2018; McCracken, 2013; Greenwood, 2013).

Criticism to the current analysis of PEARS appropriateness and management by an optometrist within the community may include questioning whether in reality, the optometrist would arrive at the same diagnosis determined in secondary care and manage the patient appropriately. Provisional diagnoses were not always documented from optometrist referrals to eye casualty, and same day referral letters were not scanned to allow an analysis of potential areas for further optometric training or areas where optometrists lack confidence. Variations in presenting signs of cases affect the final clinical decisions on suspected diagnosis and management, which in turn is a reflection of one's clinical expertise, and this could not be captured in the current analysis. Management decisions may also differ between secondary care and community optometrists based on the level of additional training, experience, and actual or perceived level of competence.

There is evidence to suggest that optometrists and ophthalmologists may arrive at similar diagnoses and management plans. A prospective observational study carried out in the A&E department at Moorfields eye hospital in London over six months, showed that there was good agreement using weighted kappa statistics in both the diagnosis and management plan between two senior hospital optometrists and a consultant ophthalmologist with no sight threatening conditions being misdiagnosed by the optometrist (Hau et al., 2007). There were three cases where there was an agreement in primary diagnosis but disagreement in referral management due to the limited therapeutic prescribing power of the optometrists where prescriptions for topical steroids were indicated (Hau et al., 2007). The optometrists without IP- qualifications in these cases referred the patient to be seen same day by the consultant. A service evaluation audit conducted by Bailie et al. (2018), also showed a trend of fair levels of agreement in management decisions for a chronic condition made by specialist trained optometrists and a consultant ophthalmologist within Belfast Health and Social Care Trust's virtual glaucoma clinic. In all cases of disagreement, the optometrists were overly cautious in diagnosing suspect glaucoma (Bailie et al., 2018), which is a tendency noted

in other studies where the consultant clinician is more willing to accept uncertainty (Clarke et al., 2017).

There is no information on the concordance between hospital and community optometrists' clinical decision making, which could reveal areas of further training and opportunities for community service improvement. Community optometrists have challenges that may affect their clinical decision making including time constraints related to clinical chair time, and commercial pressures especially when working in multiple practices with traditional loss leading models that rely on high margin spectacle sales. Conversely, these challenges alongside more exposure to acute pathology and appropriate funding, may make a community optometrist well suited for emergency eye care, and perhaps in a dual role in hospital or within a GP surgery or pharmacy. Hospital optometrists may have greater scope of practice due to the advantage of working closely with ophthalmologists, and avoiding the discussion of professional fees with patients for services beyond PEARS criteria.

6.4.1: Optometrist referrals

Participation in enhanced service schemes provides exposure to more challenging clinical cases, allowing optometrists to utilise clinical skills to a greater extent. A qualitative study found further professional development was noted as the most common reason given by optometrists for participating in enhanced schemes whilst non-participation was due to perceived incompatibility of the service with the business model in a retail-focused practice and potential negative impact on the profitability of their business (Konstantakopoulou et al., 2014). PEARS is designed to reduce ophthalmology referrals with an average referral rate of about 19% reported in the UK (Cottier, 2015; Konstantakopoulou et al., 2018). From the current analysis, 12% of emergency referrals were from community optometrists although it is unclear as to whether these referrals resulted from PEARS assessments. Optometrists are trained to differentiate between various ocular pathologies, assess risk, and understand the limitations of an enhanced service scheme. Differences of opinion between ophthalmologists and optometrists regarding PEARS referral urgency with optometrists tending to refer patients with greater urgency may be due to disparities in knowledge of evolving treatment options for certain pathologies and clinical experience (Konstantakopoulou et al., 2018).

The appropriateness of the optometrist referrals and the consistency in pharmacological interventions were also assessed in this analysis. Evidence-based medicine is an approach to clinical practice intended to optimise decision-making by using evidence from well designed and conducted research (Sackett et al., 1996). The Oxford centre for evidence-based medicine has created a grading scheme to classify the quality of scientific evidence with stronger types from systematic review of randomised controlled trials and randomized controlled trials at level one, forming the highest level

of evidence and yielding strong recommendations (CEBM, 2009). Case reports (level four) and expert opinion (level five) form the lowest level of evidence and yield weaker recommendations (CEBM, 2009). A prospective observational study surveyed the extent to which the activity of the ophthalmic A&E department in a large district general hospital (Wolverhampton & Midland Counties Eye Infirmary) was evidence-based by assessing the level of evidence provided for each diagnosis-intervention pair for new patients over the period of one week (Bhatt & Sandramouli, 2007). Overall, 89.7% of patient interventions were based on some scientific evidence comparable to similar studies in an emergency ophthalmic unit (Bhatt & Sandramouli, 2007; Lai et al., 2003).

A retrospective audit of diagnosis-intervention pairs at an eye casualty facility in the ophthalmic department of North Middlesex University hospital in London led to development of locally agreed guidelines and protocols (Sagoo & Raina, 2009). The study was repeated prospectively the following year and the authors found a decrease in the proportion of interventions with no evidence or against evidence, and a reduction in the number of re-attendances compared to their initial audit results (Sagoo & Raina, 2009). Medical versus surgical interventions accounted for a greater number of cases in the studies showing the value of an IP qualification for optometrists encountering acute ocular conditions, and the studies demonstrated that evidence-based medicine can be used to improve the quality of ophthalmic care in refining the standard of interventions and reducing the number of hospital visits (Sagoo & Raina, 2009). Table 6.2 shows conditions diagnosed in Hereford County hospital's eye casualty department in January 2018 as a result of optometric referral that could have pharmacological intervention initiated by an optometrist, and were actually issued with a prescription. The numbers allocated in the second column correspond to the individual cases that were treated sharing the same primary diagnosis. The College of Optometrists' suggested pharmacological interventions for each condition as viewed 18 October 2018 are also listed, and include the level of evidence and strength of recommendations according to the grading system developed by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group. Evidence from randomised controlled trials for interventions to manage rare conditions may be difficult to achieve and so a proportion of clinical practice will exist that has little published backing. Of the conditions that could have been treated by an IP optometrist assuming agreeance on diagnoses between hospital and community practitioners, 59% (10/17) of cases were actually treated with prescription medication.

Other than the management of Herpes Simplex Keratitis, there was no consistency between what was prescribed and the College of Optometrist pharmacological management guidelines nor with what was recommended for each condition. In reality, each individual case may present differently with varying levels of severity and the clinician needs to use their best judgment, experience and evidence-base when initiating treatment. Using evidence-based practice equates to clinical decision

making based on published evidence, the wishes and circumstances of patients, and the practitioner's professional judgment (College of Optometrists, 2018). There are resources such as the College of Optometrists' Optometrists' Formulary and the British National Formulary to aid in advice regarding dosage. It can be difficult for a newly qualified IP community optometrist to develop a formulary including recommended dosing and review timings, with limited exposure to acute eye conditions and their management to full resolution. Clinicians may differ in their administration of first-line treatment as reflected in table 6.2. Practitioners must also be aware of the eye formulary funded by their CCG.

Condition	**Prescribed in secondary care**	**College of Optometrists' intervention advice**	**Interventions based on systemic reviews/meta-analysis, randomised controlled trials and prospective case series**
Blepharitis	1. Blephasol od 2. Ocular lubricant+ Heat Compress+ p.o. doxycycline 100mg od for 3/12 3. Hyloforte 4-6x/day BE + prn long-term via GP. GP can consider doxycycline 100mg od for 3/12 or azithromycin 500 mg od for 1 week then 250 mg od for 4/7 if continues to have problems	Staphylococcal and seborrhoeic blepharitis may benefit from topical antibiotics if not controlled by first-line management • Antibiotic ointment (e.g. chloramphenicol) twice daily; place in eyes or rub into lid margin with fingertip • topical azithromycin (NB off-label use) *Level of evidence = moderate, Strength of recommendation = weak* In patients with posterior blepharitis, systemic antibiotics may be effective as a second line treatment • Consider prescribing a systemic tetracycline, such as oxytretracycline, doxycycline, or minocycline (contraindicated in pregnancy, lactation and in children under 12 years; various adverse effects have been reported). Such treatment will need to be continued for several weeks or months and the dosage may need to be varied from time to time *Level of evidence = low, Strength of recommendation = weak* For suspect Demodex blepharitis consider weekly lid cleansing with 50% tea tree oil (see evidence base), but this should be undertaken only by experienced practitioners as such preparations are toxic to the ocular surface. Preparations containing 4-terpineol (an active ingredient of tea tree oil) are commercially available for patient use. *Level of evidence = low, Strength of recommendation = weak*	Topical Maxitrol i.e. steroid & antibiotic (Shulman et al., 1996; Jones et al., 2017) Topical Ofloxacin (Bron et al., 1991) Topical Chloramphenicol (Power et al., 1993) Topical Fusidic acid gel (Seal et al., 1995) Lid hygiene (Key, 1996; Lindsley, 2012; Sung et al., 2018) Tea tree oil (Jones et al., 2017)

Anterior uveitis	1. RE Predforte qds then weekly tapering dose 2. Chloramphenicol 1% RE qds for 7/7 + g Maxidex 0.1% PF RE hourly for 3/7, 2 hourly for 3/7 and 6x/day for 1 week + cyclopentolate 1% RE bd 3. Predforte 1% hourly BE for 2 days and 6x/day BE until review (1 week) 4. Cyclopentolate 1% RE bd for 1/52, Maxidex 0.1% hourly for 3/7, 2 hourly for 3/7, and 6x/day for 1 week then weekly tapering	First episode: • Topical steroid (first exclude herpes): e.g. gutt. Prednisolone acetate 1% hourly until eye is white or inflammation controlled • Topical cycloplegic (NB first check for possibility of angle closure): gutt. cyclopentolate 1% tds • Review frequently, tapering off treatment as possible; if no improvement at one week, refer to ophthalmologist Second or subsequent episode: • Reinstate uveitic therapies as above • Refer to an ophthalmologist for systemic review and possible onward referral to rheumatologist **NB:** do not commence treatment if patient is known to have a history of corticosteroid-induced ocular hypertension or has had an episode of hypertensive uveitis *Level of evidence=low, Strength of recommendation=strong*	Topical steroids (Dunne & Travers, 1979; Young et al., 1982)
Non CL-related corneal ulcer	1. Ofloxacin 2 hourly RE until review in 1 week	See Marginal keratitis below	Corneal scrapes & topical ofloxacin (Prajna et al., 2001) Topical antibiotics (Bennett et al., 1998)
Dry eyes	1. No treatment 2. Chloramphenicol 0.5% qds LE 7/7, g. Hyloforte qds 7 prn BE 3. Hyloforte 4-6x/day BE, Viscotears 3-4x/day BE, Xailin night nocte BE, lid hygiene advice, Pilocarpine 1% BE qds until laser due to incidental finding of bilateral narrow angles 4. Hyloforte 4-6x/day BE, Viscotears prn BE, lid hygiene advice, limit contact lens wear/consider refit 5. Lubricants (does not specify) 6. Hyloforte 4-6x daily & Xailin nocte	• Tear supplements (preferably unpreserved) for use during the day ± unmedicated ointment for use at bedtime • Recent systematic review found no evidence to support the superiority of any particular tear supplement • Liposomal sprays in evaporative dry eye *Level of evidence=moderate, Strength of recommendation=strong* • Patients on long-term medication may develop sensitivity reactions which may be to active ingredients or to preservative systems (see Clinical Management Guideline on Conjunctivitis Medicamentosa). They should be switched to unpreserved preparations • Topical steroids (such as fluorometholone or loteprednol) may be considered for short-term use in some cases.	Moderate dry eye- Viscotears (Sullivan et al., 1997) Severe keratoconjunctivitis sicca- Celluvisc (Grene et al., 1992) Mild dry eye- Hypotears (Norn, 1977) Ocular lubricant (McDonald et al., 2002) Topical corticosteroids (Jones et al., 2017) Topical non-glucocorticoid immunimodulary drugs such as cyclosporine (Jones et al., 2017)

		The usual precautionary surveillance is required. *Level of evidence=moderate, Strength of recommendation=weak*	
Herpes Simplex Keratitis	1. Aciclovir 3% 5x/day LE for 2/52	In non-contact lens wearing adults and where HSK is confined to the epithelium, commence antiviral therapy with one of the following: • oc. aciclovir 3%, e.g. Zovirax, ophthalmic preparation, 5x daily • ganciclovir 0.15% ophthalmic gel (Virgan), 5x daily **NB:** HSK is a potentially blinding disease and optometrists should consistently apply a low threshold for referral for this condition *Level of evidence=moderate, Strength of recommendation=strong)*	Topical aciclovir (Wilhelmus, 2015) Herpes Simplex dendritic ulcer- topical antiviral (Coster et al., 1980) Herpes Simplex stromal keratitis- topical antiviral and topical steroid (Wilhelmus et al., 1994)
Marginal keratitis	1. Maxitrol tds RE for 5 days 2. Exocin 0.3% hourly for 3/7 then 2 hourly, Predforte 0.5% PF bd, lid hygiene + Systane Balance	Ocular lubricants for symptomatic relief (drops for use during the day, unmedicated ointment for use at bedtime) • Systemic analgesia if needed: paracetamol, aspirin or ibuprofen • Regular lid hygiene for associated blepharitis (with a view to limiting recurrence) *Level of evidence=low, Strength of recommendation=strong* • Marginal keratitis is a self-limiting condition. Nevertheless it is conventional to give pharmacological treatment with a view to relieving symptoms and shortening the clinical course. • The concurrent use of topical antibiotic (e.g. chloramphenicol) to reduce bacterial load, in addition to topical steroid (e.g. prednisolone) to reduce inflammation, is theoretically justified. However, the immunosuppressive effect of the steroid enhances the risk of infection *Level of evidence=low, Strength of recommendation=weak*	Topical steroid & antibiotic (Chignell et al., 1970; McGill et al., 1971) Topical antibiotic (Bennett et al., 1998)

Table 6.2: Analysis of conditions diagnosed in Hereford County hospital eye casualty department in January 2018 as a result of optometric referral that could have pharmacological intervention initiated by an optometrist and were actually issued a prescription. College of Optometrist management guidance viewed 18 October 2018. (p.o.= oral medication, o.d.= once daily; bd= twice daily; prn= when necessary; tds= three times daily; qds= four times daily; BE= both eyes; PF= preservative free; RE= right eye; LE= left eye; nocte= at night; gutt= drops; oc= eye ointment)

The Health and Social Care Act 2012 introduced significant structural changes to the NHS including the establishment of 200-plus CCGs, replacing the previous private care trust, who commission enhancements to the NHS England sight test (Parkins et al., 2014). Therefore, there are protocols for local variations in primary eye health care across the country, which can be confusing for practices on the border of a number of CCG areas such as the case in Herefordshire. Practices are under no obligation to participate in CCG commissioned services and patients do not always remain within their CCG boundaries albeit unknowingly for their care. For self-employed optometrists referred to as locums who are working in a number of different practices, the criteria requirements, referral pathways and obligations in relation to those may vary widely. The local optical committee support unit can provide specific advice to locums, and it is also the responsibility of the practice to assist in providing information on local schemes. The fear of litigation and accusations of inappropriate referral leading to avoidable delay may underlie the decision for emergency referrals. This analysis did not include the proportion of optometrist referrals from self-employed versus resident optometrists working in local multiple or independent practices. This analysis could have been redundant given self-employed optometrists can also work regularly in set practices. In cases where locums provide one-off cover it can be difficult to follow-up repeat tests and advice from the Association of Optometrists (AOP) is to refer on the basis of the findings on the day (AOP, 2018).

Posterior vitreous detachment (PVD) was the most common condition diagnosed at eye casualty as a result of optometrist referrals (n=8; 15.7%). Locum optometrists unfamiliar with local schemes may follow advice from the AOP if there is any uncertainty in the diagnosis, and refer patients to eye casualty on the day of presentation as a default option. The mean age of people diagnosed with PVD in this analysis was 69.3 ± 6.7 and there was an even split between males and females. The reasons for visit associated with the PVD diagnoses in eye casualty included recent onset of flashes and floaters, and the assumption is that the optometrist did not feel competent to examine the patient or could not definitively rule out a retinal break. It is also possible that the patient was triaged by reception, where a PEARS appointment was unavailable and the patient was instructed to attend eye casualty on the basis of their symptoms suggesting a retinal break. The ONP could have potentially still recorded “optometrist” as the source of referral.

If a retinal break is present the patient can be referred for prophylactic treatment before a retinal detachment occurs and threatens sight. PVD is an ageing process of the vitreous and its prevalence increases proportionally with age and degree of myopia often with patients over the age of 40 presenting with classical symptoms of monocular floaters and or flashing lights under dim rather than bright illumination (Tanner et al., 2000). Tractional forces between the retina and vitreous at sites of vitreoretinal adhesion cause mechanical stimulation of the retina photoreceptors, which is perceived by the occipital cortex as a flash of light, and floaters are vitreous opacities casting

shadows on the retina during eye movement (Alwitry et al., 2002). An increase in floaters could indicate a general condensation of collagen fibres in the vitreous or a vitreous haemorrhage secondary to peripheral tearing of a retinal blood vessel as the vitreous collapses, which requires attention. The flashes of light usually cease when the vitreous has separated from a point of adhesion and the floaters may slowly disappear over time as the vitreous opacities move into the anterior vitreous (Serpetopoulos, 1997). A visual field defect and loss of vision are also common presenting symptoms relating to a PVD, retinal break or retinal detachment and can be the result of accumulation of subretinal fluid in the posterior pole (Tanner et al., 2000). It has been reported that the prevalence of a retinal break following acute PVD ranges from 8- 46% (Novak & Welch, 1984).

The College of Optometrists guidance document titled "examining patients who present with flashes and floater" recommend referring a patient with such symptoms if the optometrist does not feel confident to manage (2018). If the optometrist carries out an examination, as a minimum it should include a detailed history and symptoms looking for particular risk factors, examining the anterior vitreous for pigment cells, a dilated fundal examination using an indirect viewing technique and providing written and verbal advice (College of Optometrists, 2018). An emergency referral would be warranted for findings of a retinal detachment, pigment in the anterior vitreous (tobacco dust), and a vitreous, retinal or pre-retinal haemorrhage, or lattice generation or retinal break with symptoms in line with guidance from the National Institute for Health and Care excellence (College of Optometrists, 2018; NICE, 2015c).

In an application of theory-informed implementation research within community optometry, Duncan et al. (2018) engaged with stakeholders and health professional to identify 'patients presenting with flashes and floaters' as an important priority for practice improvement and the decision about whether or not to refer patients to secondary care as the target behaviour. A systematic search, review and appraisal of 28 documents relating to the management of patients with flashing lights and floater symptoms including international guidance and UK protocols indicated that where recommendations were present they were poorly supported by evidence and noted how instructions for readers to 'refer to local protocols if available' as in the College of Optometrists guidance, undermined the credibility of the document as standalone guidance (Duncan et al., 2018). The National Institute for Health and Care Excellence (NICE) clinical knowledge summary on retinal detachment amended in March 2015 was the only document identified as potentially being of sufficient quality for use with a requirement for modification before use within community optometry. The document provides advice that any practitioners who are competent in the use of slit lamp examination and indirect ophthalmoscopy can examine patients with new onset flashes and floater symptoms without visual loss, reducing the burden to refer patients unnecessarily (Duncan et al., 2018). Barriers to appropriate referrals following a survey of 184 Scottish community

optometrists included social influences in the form of patients experiencing symptoms and think they should be referred to secondary care, lack of feedback from secondary care about patients that have been referred, and a belief that one was likely to be sued if they did not refer a patient with flashes and floaters who needs to be seen (Duncan et al., 2018). Duncan et al. (2018) also suggest that having a clear plan of steps that need to be taken once the decision not to refer has been made can facilitate an appropriate referral, and suggest enhancing practitioner confidence with access to video presentations of simulated patient-optometrist consultations and conversations with patients who expect to be referred.

Scleral indentation used in conjunction with head mounted binocular indirect ophthalmoscopy is the best technique for examining the peripheral retina up to the ora serrata for peripheral retinal breaks (Alwitry et al., 2002), however, routinely performed fundus imaging (Mackenzie et al., 2007) and slit lamp binocular indirect ophthalmoscopy (Natkunarajah et al., 2003) also give good results. Given 8% of all patients attending for eye examinations present with symptoms of flashes and or floaters (Alwitry et al., 2002), it would be impractical to refer all of these patients to eye casualty for indirect ophthalmoscopy with scleral depression. A proportion of retinal breaks will not be visualised despite performing a dilated fundus examination (Alwitry et al., 2002) although in terms of quadrantic distribution of breaks in eyes with retinal detachments, 60% occur in the upper temporal quadrant (Alwitry et al., 2002). It is important to educate patients on the dynamic nature of a PVD and for the warning signs should a retinal break be undetected and lead to a sight threatening retinal detachment. The presence of retinal pigment granules (tobacco dust) in the anterior vitreous referred to as Shafer's sign, following dilated high magnification biomicroscopy, is a reliable indicator of a retinal break and is a simpler technique used in clinical optometric practice (Brod et al., 1991; Lightman & Brod, 1994; Tanner et al., 2000).

Shah et al. (2009) used unannounced standardised patients as the golden standard methodology for evaluating quality of clinical care to investigate the content of a typical optometric eye examination for a person presenting with symptoms suggestive of a PVD. There was variation in the standards of different optometrists. Interestingly, none of the optometrists visited by the standardised patient carried out a purely symptom-led assessment once the presenting symptom of recent onset flashing lights in one eye in the dark was identified, and 99% performed a routine sight test including refraction and binocular vision tests rather than concentrate on posterior segment investigation (Shah et al., 2009). The one practitioner who did not carry out a routine eye examination advised the patient to attend eye casualty immediately at the local hospital without a referral letter, and results showed that of the 102 optometrists visited by the standardised patient, 13% advised the patient to attend eye casualty on the same day (Shah et al., 2009). Perhaps results would have been different if the standardised patient had presented for a PEARS rather than a private eye examination, and further

training in techniques such as detection of tobacco dust in the anterior vitreous and head mounted binocular indirect ophthalmoscopy with scleral indentation should be carried out to enhance the clinical confidence of optometrists especially if the response to the rising demand for healthcare is to extend the role of health professionals and the range of their service provision.

Overall 69% of optometrists' referrals were appropriate for same day referral, and 33% of cases could have remained in primary care had the optometrist been IP- qualified. There was no way retrospectively to determine if any of the referring optometrists were IP-qualified and the assumption was that the 33% of cases identified would have been treated in the community if they were seen by an IP optometrist in accordance with the College of Optometrists CMGs. Anecdotally, there is a large learning curve for newly qualified IP optometrists for initiating pharmacological intervention that can be improved with hands on experience, regular review of the literature, and ongoing feedback and communication with ophthalmology colleagues. There are many reasons for inappropriate referrals including fear of litigation and lack of standalone guidance for certain conditions, which may explain the many cases of PVD referred to eye casualty. Future work is needed to develop materials to enhance practitioner confidence including videos of simulated consultations to carry out symptom-led assessments for various acute presentations.

6.4.2: General Practitioner referrals

An urgent eye condition is defined as "any eye condition that is of recent onset and is distressing or is believed by the patient, carer or referring health professional to present an imminent threat to vision or to the general health." (Smith & Tromans, 2013) Occasionally, the referring practitioner cannot establish serious pathology, and so caution should be taken when labelling a referral as inappropriate and more should be done to empower primary care colleagues to prevent low value attendances to secondary care. It has been shown that more than 50% of GP referrals to eye casualty departments do not constitute true emergencies (Kheterpal et al., 1995). There was a high proportion of non-urgent referrals to eye casualty from GPs noted in this analysis, although GP referrals made up a similar proportion to optometrist referrals in terms of source of referral for first-time eye casualty presentations (12%). It is estimated that approximately 2% to 4% of GP consultations relate to ophthalmic concerns with more than 70% representing cases of bacterial conjunctivitis, allergic conjunctivitis, meibomian cyst and blepharitis (McDonnell, 1988; Sheldrick et al., 1993; Sheldrick et al., 1992). The need for further ophthalmic training is still under debate despite GPs expressing a lack of confidence in ophthalmology as a subject, and in the diagnosis and management of specific eye conditions (Sheth et al., 2008; Featherstone et al., 1992). Conditions affecting the lids, tear ducts, and conjunctiva were the most common cases referred to ophthalmology by GPs with GPs referring more false positive cases than did optometrists (Pierscionek et al., 2009), and having a higher

prescribing rate (Sheldrick et al., 1993; Burns et al., 2002). The traditional relationship between GPs and optometrists was a one-way flow with optometrists referring to GPs who would coordinate onwards referral to ophthalmology. Enhanced eye care services are helping to change the direction towards optometrists as the first-port of call for eye problems considering the lack of specialist ophthalmic equipment in GP surgeries, for example slit- lamp bio-microscopy, and generalist training preventing GPs from managing a wide range of ocular conditions.

Greater levels of GP engagement in enhanced service schemes could result in a higher proportion of patients being retained in community optometric practice. The level of GP engagement in enhanced optometric services is varied with an evaluation of the Somerset Acute Community Eye-care Services (ACES) reporting GP confidence at 89.4% whilst an audit in Bromley showed a significant number of GPs were not engaging with a total of 62.5% of GP practices using the service 10 times or less (Cottier, 2015). An understanding of reservations from GPs about using PEARS would be useful considering it's been shown that despite scientific evidence, it is challenging to change a GP's beliefs and prescribing habits (Petricek et al., 2006; Sekimoto et al., 2006). A survey of GPs in South London which focused on the minor eye condition scheme found the majority favoured assessment of patients presenting with ophthalmic complaints by an optometrist especially for diagnoses of presentations with red eyes, flashes and floaters where use of specialist skills with slit lamp and fundoscopy were required (Konstantakopoulou et al., 2014). The GPs surveyed also saw the value of the scheme in improving care and accessibility, reducing waiting times, and potentially reducing their workload (Konstantakopoulou et al., 2014). Red eye, painful white eye, flashes and floaters and loss of vision have been reported as the commonest reasons for a MECS assessment (Konstantakopoulou et al., 2016).

In order to maximise the benefits of schemes such as PEARS, GPs require training on the referral procedure to avoid situations where GPs from outside the participating area refer patients into the scheme resulting in patients taking up optometric consulting room time for which the optometrist receives no remuneration. Optometrists may charge an appropriate fee for emergency examinations if the patient presenting does not meet PEARS criteria. There was a case in this analysis where a patient attended with a PEARS GP referral letter from South Worcestershire and Wyre forest, which is outside of Herefordshire clinical commissioning. There is no way to determine if the patient was instructed by their GP to attend eye casualty rather than a local participating practice, or whether the patient misunderstood where to attend for further assessment or had difficulty booking an appointment in the community and found it more accessible to attend eye casualty. Additionally, if GPs refer patients to optometrists inappropriately, the expectations of these patients can be difficult to manage by the optometrist. An outcome of a PEARs assessment could be a referral to a GP surgery for systemic investigations with referral rates reported at 5.7%, 8.63%, and up to 16%

(Konstantakopoulou et al, 2018; Cottier, 2015; Sheen et al, 2009). Engagement of GPs in communicating follow-on management decisions from optometric PEARS referrals would help enhance the quality of future referrals and aid practitioner confidence for better patient care.

6.4.3: Self-referrals

Self-referrals accounted for the largest source of referrals to eye casualty in this analysis at 71%. In 2018, 59% of women and 50% of men in Great Britain used the internet to search for health-related information (Prescott, 2018). Health-related information is free to access online anonymously and at any time allowing new opportunities for seeking such material for learning purposes. Cyberchondria is the term applied to heightened anxiety or distress associated with excessive or repeated searches online for health-related information, and is an abnormal behavioural pattern that can develop when the internet is used to self-diagnose or obtain reassurance (Starcevic & Berle, 2013; McMullan et al., 2018). Sources of online health information can vary in their accuracy and completeness leading individuals to carry out multiple searches in an attempt to determine their validity, which can in turn lead to increased levels of distress and anxiety. A systematic review and meta-analysis conducted by McMullan et al. (2018) found a positive correlation between health anxiety and online health information seeking, and a strong positive association between health anxiety and cyberchondria.

The rise of people searching for symptoms on the internet has led to greater awareness of health conditions, but perhaps also heightened health anxiety and an increase in health seeking behaviour in primary and secondary care. Studies have shown 50-70% of people attending eye casualty departments are non-urgent cases (Jones et al., 1986; Kheterpal et al., 1995; Fenton et al., 2001; Bhopal et al., 1993). Reasons cited for patients deciding to present at A&E rather than their GP surgery in line with the previous one-way referral system from primary to secondary care include anxiety, depression, convenience and accessibility (Martin et al., 2002; Sempere-Selva et al., 2001). One of the records excluded from the analysis of first-time presentations to eye casualty at Hereford County hospital represented an existing glaucoma patient who wanted clarification regarding use of prescribed hypotensive eye drops. This case was non-urgent and perhaps reflects areas of improvements to be made regarding communication with patients including providing written information and creating points of contact to allow opportunities for clarification on recommended treatment.

Actual trauma in this analysis accounted for about 14% of self-referral cases and included orbital fracture, chemical injury and mainly foreign body removal crediting for over three quarters of cases. All but two cases requiring foreign body removal were discharged same day with the average patient

being 38 ± 16.6 years old and predominantly male (90.6%). Optometrists have the skills and dexterity to remove non-penetrating foreign bodies and manage corneal abrasions although there may be a lack of confidence given the two cases of optometrist referrals for foreign body removal. Corneal problems were the main condition category for self-referrals with over half of cases representing corneal abrasions that could be managed with over-the-counter topical antibiotics and optometric monitoring. Only 20% (6/30) of corneal abrasion cases were reviewed in eye casualty at the request of a consultant ophthalmologist and ophthalmologists not in training presumably due to the size of the abrasion. The miscellaneous category encompassed a wide range of conditions from retinal vascular disease, acquired macular disorders and neuro-ophthalmology.

A prospective questionnaire-based survey of consecutive patients attending the A&E department at Moorfields eye hospital over a seven-day period investigated the numbers of patients with ophthalmic complaints and interestingly, the reason for attending from the patient's perspective (Hau et al., 2008). In contrast to the Hereford County hospital, Moorfields is an urban specialist eye hospital with a 24-hour walk-in A&E department seeing on average more than 60 000 patients each year, and receiving referrals not only from local CCGs in the London region but from hospitals within the UK and abroad (Hau et al., 2008). Demographic data was collected from 560 patients in May 2005 with the proportion of source of referrals similar to what was found in this analysis. The median age was younger at 35 with a similar split between men and women (51.9% and 48.1% respectively) and with the greatest source of referrals to eye casualty being self at 76.9%, followed by community optometrist accounting for 10% of referrals and 8.1% being GP referrals (Hau et al., 2008). Of the completed questionnaires, 46.9% of respondents had attended the eye casualty department previously and were not first-time presentations, however, data on reasons for re-attending such as due to previous advice if had new symptoms, and not having their chronic condition explained to a satisfactory level allowing self-management were not collected (Hau et al., 2008). Only first-time presentations were considered in the current analysis but consideration of potential reasons for frequent attenders, that is those with more than three visits in a 12-month period (Murphy et al., 1999), could help with understanding the patient perspective. Factors in frequent attending have been thought to include increasing age, living locally and psychiatric comorbidity (Murphy et al., 1999; Sheth & Sheth, 2007)

A large proportion of cases in the Moorfields prospective study were discharged on the day of presentation (62.5%) as seen in the current analysis at 58% (Hau et al., 2008). The authors of the Moorfields study determined 30.6% of cases could be categorised as non-acute, and that 28.6% with non-acute diagnoses and 8.9% with acute diagnoses of conjunctivitis could be seen by an optometrist or specialist trained GP (Hau et al., 2008). In the study, PVD was considered not suitable to be seen by primary care practitioners perhaps reflecting the views of the authors at the time of publishing

which pre-dates amendments to the NICE clinical knowledge summary on retinal detachment (NICE, 2015c). Other conditions that were deemed to be unsuitable for primary care management were acute corneal problems, anterior uveitis, macular disease, herpes simplex virus infections, trauma, conjunctival disorders, neuro-ophthalmology and oculoplastic related diagnoses, vitreoretinal emergencies, glaucoma and scleritis (Hau et al., 2008). Conditions that were deemed suitable to be seen by optometrists or specialist trained GPs included blepharitis, conjunctivitis, chalazion, dry eye, contact-lens related problems, cataract and episcleritis (Hau et al., 2008). PEARS inclusion criteria time frame permits acute symptoms of less than two weeks (LOCSU, 2016), and it was interesting from the Moorfields study to see that 62.8% of patients self-reported the duration of symptoms to span the last one to six days and 25.7% reported symptoms experienced over the last one to four weeks (Hau et al., 2008). Perhaps work should be carried out to educate patients on seeking advice from optometrists for ocular problems via their local primary care services.

From the patients' perspective, the most common overall reason for attending eye casualty was "great concern", whilst "convenience" and "unable to wait for a GP appointment" were also common justifications in the cases deemed non-acute by the authors of the Moorfields study (Hau et al., 2008). The stress and anxiety associated with the prospect of visual loss, blindness and the possible disfiguring nature of inflammatory eye conditions can evoke levels of anxiety seen in patients with diagnoses of melanoma, acquired immunodeficiency syndrome and requiring bone marrow transplantation (Williams et al., 1998). The findings from Hau et al. (2008) suggest that patients view eye casualty not only as a place for emergencies but for obtaining prompt treatment and second opinions for non-sight threatening complaints because of 24-hour accessibility and the convenience of not requiring a scheduled appointment. Ocular symptoms often induce in the patient a fear that does not match the severity of the condition that leads the patient to seek rapid reassurance. In the current analysis, there was a self-referral case where the patient had a future appointment scheduled in secondary care as a result of an optometric referral. The final diagnosis for this case was episcleritis, however, the persistent redness and irritation noted may have led the optometrist to question the original diagnosis and refer to ophthalmology. The patient may have attended eye casualty due to the uncertainty surrounding the cause of their ongoing symptoms or because they had been instructed to attend eye casualty if their symptoms failed to improve. In the current analysis 7.3% of self-referrals showed no abnormality and attended eye casualty due to symptoms of intermittent headaches, blur and ocular discomfort highlighting the use of the walk-in service for reassurance regarding sporadic concerns. There was one case wherein a patient attended eye casualty to request a repeat prescription for hypotensive eye drops.

It was determined from the current analysis that 83% of self-referrals could have been seen on the PEARS scheme as a first-port of call for ophthalmic concerns. In the age of "Dr Google" there may

be an increase in health seeking behaviour, however, signposting by ONPs, GPs, nurses and pharmacists could help alleviate the pressure from eye casualty services, reserving time for the management of complex cases and refined referrals from optometrists.

6.4.4: Managing follow-up appointments within the community

Referrals to PEARS and PEARS scheme follow-up appointments for eye casualty provide an opportunity for community optometric practices to gain new patients, and the overall cost effectiveness and patient satisfaction in relation to enhanced service optometric schemes have been reported (Konstantakopoulou et al., 2014; Baker et al., 2016; Mason et al., 2017). Studies monitoring the activity of PEARS schemes have shown that 8.7% and up to 22.13% of patients are followed up within the community predominately for reviewing cases of minor trauma, and red eye (Konstantakopoulou et al., 2018; Cottier, 2015). From the current analysis, it was determined that about 66% of patients attending eye casualty for follow-up could have been seen by an optometrist within the community for example, to monitor resolving recurrent uveitis. In a retrospective analysis of attendances to a 24-hour access casualty department over a 6-month period at Southampton eye hospital, acute or recurrent uveitis accounted for 7.1% of all cases of inflammatory disease requiring on average about four visits per patient (Jones et al., 1986). An IP qualification could help in these cases where a repeat prescription may be required and monitoring of the condition to resolution could be managed by a community optometrist. There are existing services that utilise the skills of optometrists including the Grampian Eye Health Network established in 2010 that allows co-prescribing with GPs for non-IP optometrists to provide treatment for patients with anterior uveitis, herpes simplex keratitis, marginal keratitis and corneal foreign body removal (Kearney, 2017). The Fife Uveitis Shared-Care Scheme (FUSS) initiated in November 2016 involves IP optometrists who diagnose and treat anterior uveitis, and carry out four monthly uveitis screening for children with Juvenile Idiopathic Arthritis (Kearney, 2017). In West Kent since 2010, the Acute Primary Care Ophthalmology Service (APCOS) involves IP optometrists who are given an NHS FP10 prescription pad for the management of acute eye conditions within the community. The overall cost effectiveness and patient satisfaction for these predominately IP- optometrist led schemes are yet to be reported in the literature.

At the time of the analysis, Symphony software (EMIS health, UK) was used to manage initial presentations and IMS MAXIMS software (IMS MAXIMS, Dublin) was used to manage eye casualty follow-up appointments at the Hereford County hospital. According to reports generated by Symphony software (EMIS health, UK), there were on average 5617.7 ± 69.9 eye casualty attendances each year from 2015- 2017. The tariff cost of an eye casualty attendance at Hereford County hospital is £125.00, which means the cost per month of first-time attendances from 2015-

2017 would equate to about £58,517.36. If one considers the total number of cases in January 2018 that could have been seen within the community on the PEARs scheme from a GP or self-referral either as a first-time presentation or for review, the amount of savings to the Wye Valley NHS Trust would have been approximately £46, 405.00 (table 6.3).

	Appointments	Cost
No. of eye cas first-time attendances	421	£56, 625.00
No. of eye cas presentations from GP & Self-referrals that could have been seen in the community	245	£14,700.00
	Potential Cost saving:	£41, 925.00
No. of eye cas presentations that were booked for follow-up in eye cas	83	£6, 640.00
No. of eye cas presentations booked for follow-up in eye cas that could have been seen in the community	54	£2, 160.00
	Potential Cost saving:	£4, 480.00

Table 6.3: Cost analysis comparing appointments at the hospital and within the community in January 2018. This analysis assumes Wye Valley NHS Trust tariff costs of £125/ appointment and £80/appointment at the Hereford County Hospital eye casualty for first-time presentations and follow-ups respectively. This analysis assumes £60/ appointment and £40/appointment paid by NHS Herefordshire CCG for first-time PEARS presentations and PEARS follow-ups respectively, and that the presentations would have met PEARS inclusion. Eye cas= eye casualty.

There is evidence to suggest that the reported rise in eye casualty attendances is due to new attendances rather than review appointments, and contrary evidence attributing a rise in numbers to an increase in follow-up appointments and limited access to sub-specialty and general clinics for hospital review appointments (RCOphth, 2017). It is thought that ophthalmology trainees are slower and more cautious than previous generations, seeing fewer patients per hour and tend to schedule more follow-up appointments (Armstrong et al., 2010). The eye casualty clinic at the Hereford County hospital is organised to offer four morning and four afternoon appointments for the purpose of follow-up during the working week. In the current analysis, 36.6% of decisions to follow-up patients in eye casualty were made by ophthalmologists in training and 8.5% by IP optometrists. In addition to discharging to community optometry monitoring and restricting the number of follow-ups appointments available in eye casualty, the presence of a consultant ophthalmologist during eye casualty service hours could help reduce the burden on secondary care. The consultant accessible to eye casualty practitioners from IP-optometry or other grades of ophthalmology could offer same day advice leading to a reduction in the number of follow-up appointments scheduled in eye casualty, and enhance the practitioner's clinical knowledge for future decision making.

6.5: Conclusion

In Herefordshire, the Ophthalmology Transformation Group involving the Wye Valley Trust, the Local Optical Committee and the CCG intends to expand the existing optometric schemes to decompress the demand on secondary care services into the community. Progress has been made with the local CCG agreeing to directly fund optometric monitoring of stable glaucoma and PEARS scheme follow-up appointments for eye casualty. More research is required to investigate how PEARS affects demand and supply in the wider healthcare system, and concerns regarding overcapacity and inadequate remuneration. Perhaps community IP optometry needs a specific funding source within the NHS, and a means of referring to IP optometrists by other optometrists, GPs and pharmacists in order to build competence that could weaken if patient numbers are low, increase scope of practice and avoid overburdening secondary care. Ongoing structured training is important in producing and maintaining a high standard of care on the scheme.

Feedback on referrals from GPs and ophthalmologists is essential to improve optometrists' diagnostic skills, and good systems of communication are important for effective inter-professional co-operation. Optometrists are capable of managing common non-sight threatening conditions in community practice that would otherwise present to eye casualty as a GP or self-referral, with or without therapeutic agents accessible through Medicines Act exemptions. Extended prescribing with an IP qualification allows an optometrist to use and develop their skills to a greater extent, and provide efficient clinical services to their patients with quicker access to required medication. The expanding role of optometrists was discussed in section 1.3. Dry eye was the second most common diagnosis from optometrist referrals to eye casualty in this analysis, and accounted for approximately 4% and 6% of conditions diagnosed from GP and self-referrals respectively.

CHAPTER 7
Conclusions

7.1: Summary of previous chapters

The study outlined in chapter two determined that a proportion of patients attending BBR Optometry Ltd. self-reported some degree of dry eye, and that there was a local demand and business case for a dry eye service. Findings from chapter two suggest that service blueprinting can help facilitate the design of new community optometric services, and that customers prefer to purchase dry eye products when required, and need to understand and be reminded that dry eye is a chronic condition requiring long-term management. Amendments were made to internal processes at BBR Optometry Ltd. as a result of the study, such as utilizing practice management software to remind customers using the dry eye service to replenish those products recommended for ongoing care.

The results of the study presented in chapter three suggest that a fluorescein tear breakup time ≤ to nine seconds and/or between nine and 12 seconds in women, and changes to Meibomian gland structure and function with a total Meibomian gland expressibility score cut-off value that is between one and nine are clinical tests predictive of predominately evaporative dry eye status. Important predictive questions for dry eye included those relating to frequency of soreness or irritation, and the impact on visual functioning for daily tasks. These results derived objectively using statistical means suggest that asking certain questions regarding dry eye symptoms, performing an accessible, quick test of fluorescein tear breakup time, and utilising technology invested in by the practice could deliver a sufficient level of clinical testing to identify evaporative dry eye.

In addition to diagnostic technology, BBR Optometry Ltd. has also invested in in-practice dry eye treatment options to differentiate from competitors in the market, and to optimize the tear film for refractive surgery and contact lens fittings for presumed potential benefits. Results from chapter four showed that there were no differences in visual outcomes post-lens surgery between patients with abnormal and normal tears but that there were new cases of symptomatic dry eye in both groups. The author suggests that optimization of the ocular surface prior to surgery could prevent new or persistent dry eye following lens surgery.

There were no strong trends to link CLDO to dry eye or to a particular contact lens (CL) product or product range in the sample of BBR Optometry Ltd. patients. The high proportion of "false dropouts" found suggests that patients may be more flexible in their CL wearing schedule and may be motivated to change service providers for reasons other than the availability of modern CL products. The commonly reported CLDO rates are probably not as bad as reported but this would need further investigation to be conclusive. There was a large subset of patients in the study who discontinued CL wear for unknown reasons, which highlighted a need to improve CL record keeping

at the practice. Dryness related to CL wear was a reason for CLDO in the sample presented in chapter five, and dry eye symptoms were also seen in chapter six as a reason for referral to the local hospital's eye casualty department. The largest proportion of presentations to the Hereford County hospital's eye casualty department were self-referrals (71%), and it was determined that the majority of self and general practitioner referrals could have been managed or reviewed by an optometrist in the community with even greater proportions treatable by an IP optometrist.

7.2: Concluding remarks

The final achieved objective for the KTP project was to embed a service for the non-routine patient to establish BBR Optometry Ltd. as capable of diagnosing and managing complex, chronic eye conditions at the highest level whilst introducing new revenue streams. In order to ensure continued success, a recommendation of the KTP project was to allow time for optometrists' professional development as well as time for reflection and regular review of current services for improvements and identification of patient needs not met by existing services. The dry eye service is now well embedded at BBR Optometry Ltd., and the practice directors have reported increased activity. This research is relevant to practice owners, managers, eye healthcare stakeholders, and NHS clinical commissioners. Furthermore, due to the impact of this research, the KTP project was voted second place in Aston University's Knowledge exchange poster competitions in 2016 and 2017 for best new and established projects respectively. The author received a rating of 'Very Good' on completion of the KTP project (see Appendix 1.4).

7.3: Limitations and future work

This research demonstrated that service blueprinting (chapter two) could be applied to improve or build-on existing optometric services, and could potentially be used to roll out new services where there is a local need. The service performance and practice capabilities following introduction of the service blueprint could be audited using the Service Quality Gaps model audit shown in appendix 2.9, and metrics to monitor service activity, such as conversion to dry eye treatment from consultation or telephone call and digital KPIs, could be measured. Future work is required on the development of customer-defined service standards to provide feedback on the operational performance of new services, and metrics that document the customers' opinions on the delivery of new services. A SERVQUAL audit could be conducted to understand the customer's view on private optometric services. Customer's opinions on a service affect the willingness to recommend and return to the same service providers, which are indicators of customer loyalty (Lonial & Raju, 2015). Further studies could investigate reasons customers choose to become Eyelife^{TM} members at the varying tiers of membership or not.

A larger sample of dry eye patients and wider variety of questionnaires and tests could be used to determine the possibility of objectively identifying clinical tests for predicting dry eye of evaporative, aqueous-deficient and mixed aetiology. In regards to the impact of tear homeostasis on lens surgery outcomes studied in chapter four, future longitudinal research with larger cohorts of patients is required to evaluate the long-term impact of both femtosecond laser-assisted or standard phacoemulsification surgery on clinical outcomes and ocular surface health metrics. A similar analysis could also be carried out for patients having implantable contact lens treatment (ICL) or laser refractive surgery having had TearLab tear osmolarity measures taken to determine the impact of tear osmolarity on surgical outcomes. Comparison of pre- and post-operative tear homeostatic markers and symptoms would also provide valuable information in regards to the justification of prophylactic measures to optimise the ocular surface in preparation for and following lens surgery. Future work comparing outcomes between patients having intense regulated pulsed light (IRPL) treatment and those not receiving in-practice dry eye treatment prior to lens surgery could also help practitioners make evidence-based recommendations, especially where cost is a factor.

In terms of implications from a business point of view in retaining patients, future work could investigate, via interview or survey, reasons why patients discontinue CL wear and determine whether patients dropout of CL wear again following an invitation to revisit CL wear at BBR Optometry Ltd. Larger studies involving multiple sites would be required for comments on general trends observed amongst CLDOs. There was missing information on the average amount of CL products trialled for each person who ceased CL wear in chapter five to highlight possible training requirements for practitioners in their approach to CL fitting, especially for presbyopic patients fitted with multifocal lenses. Future interventional prospective longitudinal studies could inform practitioners whether proactively treating Meibomian gland dysfunction (MGD) prior to trialling CLs for new users and lapsed CLs wears intending to revisit CL wear could help prevent CLDO.

In regards to chapter six, a new prospective design study could investigate whether provisional diagnoses from optometrists referring patients to eye casualty hospital services are appropriate to demonstrate the safety and effectiveness of current acute optometric services. The suspected diagnoses from optometrist referrals were not always listed, and so chapter six presents diagnoses from eye casualty that are organised by the source of referral. Further research is required to investigate how existing optometric schemes impact demand and supply in the wider healthcare system in order to prevent overcapacity and inadequate remuneration, especially considering the uptake of IP qualifications for extended prescribing by community optometrists. The major weaknesses of all of these studies are that they are based on a single site, and so findings are not necessarily representative of the UK as a whole.

There are opportunities for independent optometrists to grab the low-hanging fruit by implementing private specialist services for conditions such as dry eye that are highly prevalent. SWOT (strengths, weaknesses, opportunities and threats) analysis carried out for the consideration of new private optometric services, is a tool that is used to evaluate how an organisation or business compares to its competition and can establish a position within the broader market (Teoli & An, 2019). Firstly, a strength would be the financial gain through introducing a new revenue stream, and a weakness would be the time required to develop and trial a new service. However, business models successfully applied in optometric practice (Patel, 2015) provide guidance on how to set appropriate fees, and service blueprinting described in chapter two provides a framework for the design of new services. The offering of specialist optometric services where there is a local need, introduces convenient access to those who would benefit and value from the service within the community, which may then lead to customer loyalty and use of other practice services. Other opportunities associated with offering high quality care include a chance to build a reputation for clinical and customer service excellence, and to enhance professional credibility.

A threat to new optometric services may be the replication of similar services and so there is a need for providers to stay ahead of the curve. There have been threats to traditional optometric care noted 15 years ago with the introduction of automated subjective refractive systems that were found to be accurate and repeatable (Dave & Fukuma, 2004). Recent advances in technology have also meant that people can have "prescription renewal tests" online through their smartphones, tablets and computers in the US (Scott, 2019). In terms of the clinical aspect of traditional optometric services, rapid non-invasive techniques have been evaluated and continue to be developed for monitoring subtle changes, progression of ocular disease, and the response to therapeutic interventions (Acton et al., 2011). Despite the emergence of new technologies and care delivery models, the optometrist's role in patient education, and patients' trust in optometrists as professional clinicians could help reduce the impact of these threats. In the context of a dry eye service, staying ahead of the curve would equate to offering the latest diagnostics, modern in-practice treatment options, and the possibility of pharmacological intervention for advanced dry eye care via the utilisation of IP optometrists.

List of References

Abelson, M. B., & Holly, F. J. (1977). A tentative mechanism for inferior punctate keratopathy. *Am J Ophthalmol, 83*(6), 866-869.

Abelson, M. B., Ousler, G. W., 3rd, Nally, L. A., Welch, D., & Krenzer, K. (2002). Alternative reference values for tear film break up time in normal and dry eye populations. *Adv Exp Med Biol, 506*(Pt B), 1121-1125.

Abelson, R., Lane, K. J., Rodriguez, J., Johnston, P., Angjeli, E., Ousler, G., & Montgomery, D. (2012). A single-center study evaluating the effect of the controlled adverse environment (CAE(SM)) model on tear film stability. *Clin Ophthalmol, 6*, 1865-1872.

Acera, A., Rocha, G., Vecino, E., Lema, I., & Duran, J. A. (2008). Inflammatory markers in the tears of patients with ocular surface disease. *Ophthalmic Res, 40*(6), 315-321.

Acosta, M. C., Alfaro, M. L., Borras, F., Belmonte, C., & Gallar, J. (2006). Influence of age, gender and iris color on mechanical and chemical sensitivity of the cornea and conjunctiva. *Exp Eye Res, 83*(4), 932-938.

Acs, M., Caffery, B., Barnett, M., Edmonds, C., Johnson-Tong, L., Maharaj, R., Pemberton, B., Papinski, D., Harthan, J., Srinivasan, S. (2018). Customary practices in the monitoring of dry eye disease in Sjögren's syndrome. *J Optom, 11*(4), 232-241.

Acton, J. H., Cubbidge, R. P., King, H., Galsworthy, P., & Gibson, J. M. (2011). Drusen detection in retro-mode imaging by a scanning laser ophthalmoscope. *Acta Ophthalmol*, 89(5), e404-411.

Adil, M. Y., Xiao, J., Olafsson, J., Chen, X., Lagali, N. S., Raeder, S., Utheim, O., Dartt, D.A., Utheim, T. P. (2018). Meibomian Gland Morphology is a Sensitive Early Indicator of Meibomian Gland Dysfunction. *Am J Ophthalmol*., 200, 16-25.

Age UK (2019). Hearing loss. Retrieved July 31, 2019, https://www.ageuk.org.uk/information-advice/health-wellbeing/conditions-illnesses/hearing-loss/

Ahn, J. M., Lee, S. H., Rim, T. H., Park, R. J., Yang, H. S., Kim, T. I., Yoon, K,C., Seo, K. Y. (2014). Prevalence of and risk factors associated with dry eye: the Korea National Health and Nutrition Examination Survey 2010-2011. *Am J Ophthalmol, 158*(6), 1205-1214.

Ahnood, D., Souriti, A., & Williams, G. S. (2018). Assessing patient acceptance of virtual clinics for diabetic retinopathy: a large scale postal survey. *Can J Ophthalmol*, 53(3), 207-209.

Alghamdi, W. M., Markoulli, M., Holden, B. A., & Papas, E. B. (2016). Impact of duration of contact lens wear on the structure and function of the meibomian glands. *Ophthalmic Physiol Opt, 36*(2), 120-131.

Alkhaffaf, B., Bruce, I., Glenny, A.-M., Williamson, P., Blazeby, J., & Morris, R. (2017). Are the priorities of patients & researchers aligned in the reporting of outcomes in gastric cancer surgery trials? *European Journal of Surgical Oncology, 43*(11), 2225.

Alvarez-Lorenzo, C., Anguiano-Igea, S., Varela-Garcia, A., Vivero-Lopez, M., & Concheiro, A. (2019). Bioinspired hydrogels for drug-eluting contact lenses. *Acta Biomater*, 84, 49-62.

Alwitry, A., Chen, H., & Wigfall, S. (2002). Optometrists' examination and referral practices for patients presenting with flashes and floaters. *Ophthalmic Physiol Opt, 22*(3), 183-188.

Amparo, F., Wang, H., Emami-Naeini, P., Karimian, P., & Dana, R. (2013). The Ocular Redness Index: a novel automated method for measuring ocular injection. *Invest Ophthalmol Vis Sci, 54*(7), 4821-4826.

Apter, A. J., Boston, R. C., George, M., Norfleet, A. L., Tenhave, T., Coyne, J. C., Birck, K., Reisine, S.T., Cucchiara, A.J., Feldman, H. I. (2003). Modifiable barriers to adherence to inhaled steroids among adults with asthma: it's not just black and white. *J Allergy Clin Immunol, 111*(6), 1219-1226.

Arita, R., Itoh, K., Inoue, K., & Amano, S. (2008). Noncontact infrared meibography to document age-related changes of the meibomian glands in a normal population. *Ophthalmology, 115*(5), 911-915.

Arita, R., Itoh, K., Inoue, K., Kuchiba, A., Yamaguchi, T., & Amano, S. (2009). Contact lens wear is associated with decrease of meibomian glands. *Ophthalmology, 116*(3), 379-384.

Arita, R., Itoh, K., Maeda, S., Maeda, K., Furuta, A., Fukuoka, S., Tomidokoro, A., Amano, S. (2009). Proposed diagnostic criteria for obstructive meibomian gland dysfunction. *Ophthalmology, 116*(11), 2058-2063.

Arita, R., Itoh, K., Maeda, S., Maeda, K., Tomidokoro, A., & Amano, S. (2010). Efficacy of diagnostic criteria for the differential diagnosis between obstructive meibomian gland dysfunction and aqueous deficiency dry eye. *Jpn J Ophthalmol, 54*(5), 387-391.

Arita, R., Morishige, N., Koh, S., Shirakawa, R., Kawashima, M., Sakimoto, T., Suzuki, T., Tsubota, K. (2015). Increased Tear Fluid Production as a Compensatory Response to Meibomian Gland Loss: A Multicenter Cross-sectional Study. *Ophthalmology, 122*(5), 925-933.

Armstrong, P. A., White, A. L., & Thakore, S. (2010). Reduced productivity among junior trainees in the emergency department and the impact on senior clinicians. *Emerg Med J, 27*(2), 97-99.

Armstrong, R. A., & Eperjesi, F. (2008). Data analysis methods in optometry Part 8: Principal components analysis (PCA) and factor analysis (FA). *Optometry Today*, *2008*(March), 40-44.

Armstrong, R.A., Hilton, A.C. (2011). Statistical analysis in biology. StatNotes. Wiley-Blackwell, New Jersey (appendix 4, summary of sample size procedures for different statistical tests).

Armstrong, R. A., Nochlin, D., & Bird, T. D. (2000). Neuropathological heterogeneity in Alzheimer's disease: a study of 80 cases using principal components analysis. *Neuropathology, 20*(1), 31-37.

Armstrong, R. A. (2013). Statistical guidelines for the analysis of data obtained from one or both eyes. *Ophthalmic Physiol Opt, 33*(1), 7-14.

Armstrong, R.A. (2014) When to use the Bonferroni correction. *Ophthalmic Physiol Opt,* 34, 502-508.

Arnould, E. J., Price, L. L., & Tierney, P. (1998). Communicative Staging of the Wilderness Servicescape. *Service Industries Journal,* 18(3), 90–115.

Arora, A., Poudel, P., Manohar, N., Bhole, S., & Baur, L. A. (2019). The role of oral health care professionals in preventing and managing obesity: A systematic review of current practices and perceived barriers. *Obes Res Clin Pract*, 13(3), 217-225.

Arora, R. (2008). Price bundling and framing strategies for complementary products. *Journal of Product & Brand Management*,17 (7), 475-484.

Arrua, M., Samudio, M., Farina, N., Cibils, D., Laspina, F., Sanabria, R., Carpinelli, L., Mino de Kaspar, H. (2015). Comparative study of the efficacy of different treatment options in patients with chronic blepharitis. *Arch Soc Esp Oftalmol, 90*(3), 112-118.

Asbell, P. A., Maguire, M. G., Pistilli, M., Ying, G. S., Szczotka-Flynn, L. B., Hardten, D. R., Lin, M.C., Shtein, R. M. (2018). n-3 Fatty Acid Supplementation for the Treatment of Dry Eye Disease. *N Engl J Med, 378*(18), 1681-1690.

Ashraf, Z., Pasha, U., Greenstone, V., Akbar, J., Apenbrinck, E., Foulks, G. N., & Borchman, D. (2011). Quantification of human sebum on skin and human meibum on the eye lid margin using Sebutape(R), spectroscopy and chemical analysis. *Curr Eye Res, 36*(6), 553-562.

Asiedu, K. (2017). Rasch Analysis of the Standard Patient Evaluation of Eye Dryness Questionnaire. *Eye Contact Lens, 43*(6), 394-398.

Asiedu, K., Kyei, S., Boampong, F., & Ocansey, S. (2017). Symptomatic Dry Eye and Its Associated Factors: A Study of University Undergraduate Students in Ghana. *Eye Contact Lens, 43*(4), 262-266.

Asiedu, K., Kyei, S., Mensah, S. N., Ocansey, S., Abu, L. S., & Kyere, E. A. (2016). Ocular Surface Disease Index (OSDI) Versus the Standard Patient Evaluation of Eye Dryness (SPEED): A Study of a Nonclinical Sample. *Cornea, 35*(2), 175-180.

Association of Optometrists (AOP) (2018). Clinical governance- referring a patient. Retrieved November 11, 2018, https://www.aop.org.uk/advice-and-support/clinical/clinical-governance/referring-a-patient

Atkins, N. P., Morgan, S. L., & Morgan, P. B. (2009). Enhancing the approach to selecting eyewear (EASE): a multi-centre, practice-based study into the effect of applying contact lenses prior to spectacle dispensing. *Cont Lens Anterior Eye, 32*(3), 103-107.

Averett, P. (2001). People: The human side of systems technology. *Journal for Quality and Participation*, 24(2), 34–37.

Awobem, J. F., Cassels-Brown, A., Buchan, J. C., & Hughes, K. A. (2009). Exploring glaucoma awareness and the utilization of primary eye care services: community perceived barriers among elderly African Caribbeans in Chapeltown, Leeds. *Eye*, 23(1), 243.

Bailey, I. L., & Carney, L. G. (1973). Corneal changes from hydrophilic contact lenses. *Am J Optom Arch Am Acad Optom, 50*(4), 299-304.

Bailie, M., Jackson, A.J., Logan, J., Knox, A., & Azuara-Blanco, A. (2018). The agreement between optometrists and consultant ophthalmologists on the glaucoma management of patients attending a first-contact glaucoma clinic. Optometry in practice (online), 19(2), 1-7.

Baird, K.M., Harrison, G.L. and Reeve, R.C. (2004). Adoption of activity management practices: a note on the extent of adoption and the influence on organizational and cultural factors. *Management Accounting Research*, 15 (4), 383-399.

Baker, H., Harper, R. A., Edgar, D. F., & Lawrenson, J. G. (2016). Multi-stakeholder perspectives of locally commissioned enhanced optometric services. *BMJ Open, 6*(10), e011934.

Baker, H., Ratnarajan, G., Harper, R. A., Edgar, D. F., & Lawrenson, J. G. (2016). Effectiveness of UK optometric enhanced eye care services: a realist review of the literature. *Ophthalmic Physiol Opt, 36*(5), 545-557.

Baldini, C., Ferro, F., Luciano, N., Bombardieri, S., & Grossi, E. (2018). Artificial neural networks help to identify disease subsets and to predict lymphoma in primary Sjögren's syndrome. *Clin Exp Rheumatol, 36 Suppl 112*(3), 137-144.

Bambauer-Sachse, S., & Grewal, D. (2011). Temporal Reframing of Prices: When Is It Beneficial? *Journal of Retailing*, *87*(2), 156–165.

Bambauer-Sachse, S., & Mangold, C.S. (2009). Are temporally reframed prices really advantageous? A more detailed look at the processes triggered by temporally reframed prices. *Journal of Retailing and Consumer Services*, *16*(6), 451–457.

Banerjee, S., Beatty, S., Tyagi, A., & Kirkby, G. R. (1998). The role of ophthalmic triage and the nurse practitioner in an eye-dedicated casualty department. *Eye (Lond), 12 (Pt 5)*, 880-882.

Barabino, S., Labetoulle, M., Rolando, M., & Messmer, E. M. (2016). Understanding Symptoms and Quality of Life in Patients With Dry Eye Syndrome. *Ocul Surf, 14*(3), 365-376.

Barker, G. T., & Mansberger, S. L. (2019). Psychometric Properties of the Reduced Version of the Glaucoma Treatment Compliance Assessment Tool (GTCAT). *Ophthalmic Epidemiol, 26*(1), 55-62.

Basak, S. K., Pal, P. P., Basak, S., Bandyopadhyay, A., Choudhury, S., & Sar, S. (2012). Prevalence of dry eye diseases in hospital-based population in West Bengal, Eastern India. *J Indian Med Assoc, 110*(11), 789-794.

Baudouin, C., Aragona, P., Messmer, E. M., Tomlinson, A., Calonge, M., Boboridis, K. G., Akova, Y.A., Geerling, G., Labetoulle, M., Rolando, M. (2013). Role of hyperosmolarity in the pathogenesis and management of dry eye disease: proceedings of the OCEAN group meeting. *Ocul Surf, 11*(4), 246-258.

Baudouin, C., Aragona, P., Setten, G.V., Rolando, M., Irkec, M., de Castillo, J.B., Geerling, G., Labetoulle, M., Bonini, S. (2014). Diagnosing the severity of dry eye: a clear and practical algorithm. *Br J Ophthalmol, 98*(9), 1168-1176.

Baudouin, C., Messmer, E. M., Aragona, P., Geerling, G., Akova, Y. A., Benitez-del-Castillo, J., Boboridis, K.G., Merayo-Lloves, J., Rolando, M., Labetoulle, M. (2016). Revisiting the vicious circle of dry eye disease: a focus on the pathophysiology of meibomian gland dysfunction. *Br J Ophthalmol, 100*(3), 300-306.

Bayraktar, E., Tatoglu, E., Turkyilmaz, A., Delen, D., & Zaim, S. (2012). Measuring the efficiency of customer satisfaction and loyalty for mobile phone brands with DEA. *Expert Systems With Applications*, 39(1), 99–106.

Beatty, S. E., & Lee, J. (1996). Customer-Sales Associate Retail Relationships. *Journal of Retailing*, 72(3), 223–247.

Beavers, A.S., Lounsbury, J.W., Richards, J.K., Huck, S.W., Skolits, G.J., Esquivel, S.L. (2013). Practical considerations for using exploratory factor analysis in educational research. *Practical assessment, research & evaluation*, 18(6), 1-13. Retrieved February 2, 2019, https://www.pareonline.net/getvn.asp?v=18&n=6

Begley, C. G., Caffery, B., Chalmers, R. L., & Mitchell, G. L. (2002). Use of the dry eye questionnaire to measure symptoms of ocular irritation in patients with aqueous tear deficient dry eye. *Cornea, 21*(7), 664-670.

Begley, C. G., Chalmers, R. L., Abetz, L., Venkataraman, K., Mertzanis, P., Caffery, B. A., Snyder, C., Edrington, T., Nelson, D., Simpson, T. (2003). The relationship between habitual patient-reported symptoms and clinical signs among patients with dry eye of varying severity. *Invest Ophthalmol Vis Sci, 44*(11), 4753-4761.

Begley, C. G., Chalmers, R. L., Mitchell, G. L., Nichols, K. K., Caffery, B., Simpson, T., Du Toit, R., Portello, J., Davis, L. (2001). Characterization of ocular surface symptoms from optometric practices in North America. *Cornea, 20*(6), 610-618.

Behrens, A., Doyle, J. J., Stern, L., Chuck, R. S., McDonnell, P. J., Azar, D. T., Dua, H.S., Hom, M., Karpecki. P.M. (2006). Dysfunctional tear syndrome: a Delphi approach to treatment recommendations. *Cornea, 25*(8), 900-907.

Bell, R. W., & O'Brien, C. (1997). Accuracy of referral to a glaucoma clinic. *Ophthalmic Physiol Opt, 17*(1), 7-11.

Belmonte, C., Acosta, M. C., & Gallar, J. (2004a). Neural basis of sensation in intact and injured corneas. *Exp Eye Res, 78*(3), 513-525.

Belmonte, C., Aracil, A., Acosta, M. C., Luna, C., & Gallar, J. (2004b). Nerves and sensations from the eye surface. *Ocul Surf, 2*(4), 248-253.

Bender, B. G., & Bender, S. E. (2005). Patient-identified barriers to asthma treatment adherence: responses to interviews, focus groups, and questionnaires. *Immunol Allergy Clin North Am, 25*(1), 107-130.

Bennett, H. G., Hay, J., Kirkness, C. M., Seal, D. V., & Devonshire, P. (1998). Antimicrobial management of presumed microbial keratitis: guidelines for treatment of central and peripheral ulcers. *Br J Ophthalmol, 82*(2), 137-145.

Berry, M., Pult, H., Purslow, C., & Murphy, P. J. (2008). Mucins and ocular signs in symptomatic and asymptomatic contact lens wear. *Optom Vis Sci, 85*(10), E930-938.

Best, N., Drury, L., & Wolffsohn, J. S. (2012). Clinical evaluation of the Oculus Keratograph. *Cont Lens Anterior Eye, 35*(4), 171-174. doi:10.1016/j.clae.2012.04.002

Best, N., Drury, L., & Wolffsohn, J. S. (2013). Predicting success with silicone-hydrogel contact lenses in new wearers. *Cont Lens Anterior Eye, 36*(5), 232-237.

Bhatt, R., & Sandramouli, S. (2007). Evidence-based practice in acute ophthalmology. *Eye (Lond), 21*(7), 976-983.

Bhopal, R. S., Parkin, D. W., Gillie, R. F., & Han, K. H. (1993). Pattern of ophthalmological accidents and emergencies presenting to hospitals. *J Epidemiol Community Health, 47*(5), 382-387.

Bigné, J.E., Anna, S., Mattila, A.S., Andreu, L. (2008). The impact of experiential consumption cognitions and emotions on behavioral intentions. *Journal of Services Marketing*, 22(4), 303-315.

Bitner, M. J., Ostrom, A. L., & Morgan, F. N. (2008). Service Blueprinting: A practical technique for service innovation. *California Management Review*, 50(3), 66–94.

Blackie, C. A., Carlson, A. N., & Korb, D. R. (2015). Treatment for meibomian gland dysfunction and dry eye symptoms with a single-dose vectored thermal pulsation: a review. *Curr Opin Ophthalmol, 26*(4), 306-313.

Blackie, C. A., Coleman, C. A., & Holland, E. J. (2016). The sustained effect (12 months) of a single-dose vectored thermal pulsation procedure for meibomian gland dysfunction and evaporative dry eye. Clin Ophthalmol, 10, 1385-1396.

Blackie, C. A., & Korb, D. R. (2010). The diurnal secretory characteristics of individual meibomian glands. *Cornea, 29*(1), 34-38.

Blackie, C. A., Korb, D. R., Knop, E., Bedi, R., Knop, N., & Holland, E. J. (2010). Nonobvious obstructive meibomian gland dysfunction. *Cornea, 29*(12), 1333-1345.

Blackie, C. A., Solomon, J. D., Scaffidi, R. C., Greiner, J. V., Lemp, M. A., & Korb, D. R. (2009). The relationship between dry eye symptoms and lipid layer thickness. *Cornea, 28*(7), 789-794.

Blaschke, T. F., Osterberg, L., Vrijens, B., & Urquhart, J. (2012). Adherence to medications: insights arising from studies on the unreliable link between prescribed and actual drug dosing histories. *Annu Rev Pharmacol Toxicol, 52*, 275-301.

Blut, M., Beatty, S. E., Evanschitzky, H., & Brock, C. (2014). The Impact of Service Characteristics on the Switching Costs–Customer Loyalty Link. *Journal of Retailing*, 90(2), 275–290.

Borchman, D., Foulks, G. N., Yappert, M. C., Bell, J., Wells, E., Neravetla, S., & Greenstone, V. (2011). Human meibum lipid conformation and thermodynamic changes with meibomian-gland dysfunction. *Investigative ophthalmology & visual science*, *52*(6), 3805-17.

Borchman, D., Foulks, G. N., Yappert, M. C., Mathews, J., Leake, K., & Bell, J. (2009). Factors affecting evaporation rates of tear film components measured in vitro. *Eye Contact Lens, 35*(1), 32-37.

Borchman, D., Foulks, G. N., Yappert, M. C., & Milliner, S. E. (2012). Differences in human meibum lipid composition with meibomian gland dysfunction using NMR and principal component analysis. *Invest Ophthalmol Vis Sci, 53*(1), 337-347.

Boulding, W., Kalra, A., Staelin, R., & Zeithaml, V. A. (1993). A Dynamic Process Model of Service Quality: From Expectations to Behavioral Intentions. *Journal of Marketing Research*, *30*(1), 7–27.

Bourcier, T., Acosta, M. C., Borderie, V., Borras, F., Gallar, J., Bury, T., Laroche, L., Belmonte, C. (2005). Decreased corneal sensitivity in patients with dry eye. *Invest Ophthalmol Vis Sci, 46*(7), 2341-2345.

Bowen, D. E. (1986). Managing Customers as Human Resources in Service Organizations. *Human Resource Management*, *25*(3), 371–383.

Bowes, O. M. B., Shah, P., Rana, M., Farrell, S., & Rajan, M. S. (2018). Quality indicators in a community optometrist led cataract shared care scheme. *Ophthalmic Physiol Opt*, 38(2), 183-192.

Bradley, F., Ashcroft, D.M., Noyce, P.R. (2012). Integration and differentiation: a conceptual model of general practitioner and community pharmacist collaboration. *Research in Social & Administrative Pharmacy*, 8(1), 36–46.

Bradley, J. L., Ozer Stillman, I., Pivneva, I., Guerin, A., Evans, A. M., & Dana, R. (2019). Dry eye disease ranking among common reasons for seeking eye care in a large US claims database. *Clin Ophthalmol, 13*, 225-232.

British Contact Lens Association (BCLA) and General Optical Council (GOC). Buying contact lenses. Retrieved July 8, 2019, https://www.optical.org/download.cfm?docid=0C986F53-097D-4D39-B7FD5CF074BC0EB6

Brod, R. D., Lightman, D. A., Packer, A. J., & Saras, H. P. (1991). Correlation between vitreous pigment granules and retinal breaks in eyes with acute posterior vitreous detachment. *Ophthalmology, 98*(9), 1366-1369.

Bron, A. J., Leber, G., Rizk, S. N., Baig, H., Elkington, A. R., Kirkby, G. R., Neoh, C., Harden, A., Leong, T. (1991). Ofloxacin compared with chloramphenicol in the management of external ocular infection. *Br J Ophthalmol, 75*(11), 675-679.

Bron, A. J., & Tiffany, J. M. (2004). The contribution of meibomian disease to dry eye. *Ocul Surf, 2*(2), 149-165.

Bron, A. J., Tiffany, J. M., Gouveia, S. M., Yokoi, N., & Voon, L. W. (2004). Functional aspects of the tear film lipid layer. *Exp Eye Res, 78*(3), 347-360.

Bron, A. J., Tomlinson, A., Foulks, G. N., Pepose, J. S., Baudouin, C., Geerling, G., Nichols, K.K., Lemp, M.A. (2014). Rethinking dry eye disease: a perspective on clinical implications. *Ocul Surf, 12*(2 Suppl), S1-31.

Bron, A. J., Yokoi, N., Gafney, E., & Tiffany, J. M. (2009). Predicted phenotypes of dry eye: proposed consequences of its natural history. *Ocul Surf, 7*(2), 78-92.

Brown, E. M., Hayes, K. A., Olson, L. T., Battles, H., & Ortega-Peluso, C. (2019). Dentist and hygienist smoking cessation counseling and awareness of Medicaid benefits. *J Public Health Dent.* [Epub ahead of print]

Buckley, R., Lawrenson, J., Hennelly, M. (2005). Therapeutics in clinical practice: recent developments in drug legislation for optometrists. *Optometry Today*, 45, 40–47.

Bunya, V. Y., Fernandez, K. B., Ying, G. S., Massaro-Giordano, M., Macchi, I., Sulewski, M. E., Hammersmith, K.M., Nagra, P.K., Rapuano, C.J., Orlin, S. E. (2018). Survey of Ophthalmologists Regarding Practice Patterns for Dry Eye and Sjögren's Syndrome. *Eye Contact Lens, 44 Suppl 2*, 196-201.

Bunya, V. Y., Fuerst, N. M., Pistilli, M., McCabe, B. E., Salvo, R., Macchi, I., Ying, G., Massaro-Giordano, M. (2015). Variability of Tear Osmolarity in Patients With Dry Eye. *JAMA Ophthalmol, 133*(6), 662-667.

Burnier, M., Santschi, V., Favrat, B., & Brunner, H. R. (2003). Monitoring compliance in resistant hypertension: an important step in patient management. *J Hypertens Suppl, 21*(2), S37-42.

Burns, D.H., Dart, J.K, Edgar, D.F. (2002). Review of the Camden and Islington anterior segment disease scheme. *Optometry in Practice*, 3, 55-60.

Buttle, F. (1996). SERVQUAL: review, critique, research agenda. *European Journal of Marketing*, 30(1), 8-32.

Cadwallader, S., Jarvis, C. B., Bitner, M. J., & Ostrom, A. L. (2010). Frontline employee motivation to participate in service innovation implementation. *Journal of the Academy of Marketing Science*, 38(2), 219–239.

Caffery, B., Srinivasan, S., Reaume, C. J., Fischer, A., Cappadocia, D., Siffel, C., & Chan, C. C. (2019). Prevalence of dry eye disease in Ontario, Canada: A population-based survey. *Ocul Surf.* [Epub ahead of print]

Cardona, G., Marcellan, C., Fornieles, A., Vilaseca, M., & Quevedo, L. (2010). Temporal stability in the perception of dry eye ocular discomfort symptoms. *Optom Vis Sci, 87*(12), 1023-1029.

Cardona, G., Seres, C., Quevedo, L., & Auge, M. (2011). Knowledge and use of tear film evaluation tests by spanish practitioners. *Optom Vis Sci, 88*(9), 1106-1111.

Carlson, J. P., Bearden, W. O., & Hardesty, D. M. (2007). Influences on what consumers know and what they think they know regarding marketer pricing tactics. *Psychology & Marketing*, 24(2), 117–142.

Carney, L. G., & Hill, R. M. (1982). The nature of normal blinking patterns. *Acta Ophthalmol (Copenh), 60*(3), 427-433.

Carnt, N. A., Evans, V. E., Naduvilath, T. J., Willcox, M. D., Papas, E. B., Frick, K. D., & Holden, B. A. (2009). Contact lens-related adverse events and the silicone hydrogel lenses and daily wear care system used. *Arch Ophthalmol, 127*(12), 1616-1623.

Caterina, M. J. (2007). Transient receptor potential ion channels as participants in thermosensation and thermoregulation. *Am J Physiol Regul Integr Comp Physiol, 292*(1), R64-76.

Centre for Evidence-Based Medicine (CEBM) (2009). Oxford centre for evidence-based medicine-levels of evidence (March 2009). Retrieved November 28, 2018, https://www.cebm.net/2009/06/oxford-centre-evidence-based-medicine-levels-evidence-march-2009/

Cetinkaya, S., Mestan, E., Acir, N. O., Cetinkaya, Y. F., Dadaci, Z., & Yener, H. I. (2015). The course of dry eye after phacoemulsification surgery. *BMC Ophthalmol, 15*, 68.

Chaganti, S., Nelson, K., Mundy, K., Harrigan, R., Galloway, R., Mawn, L. A., & Landman, B. (2018). Imaging biomarkers in thyroid eye disease and their clinical associations. *J Med Imaging (Bellingham), 5*(4), 044001.

Chalmers, I., & Glasziou, P. (2009). Avoidable waste in the production and reporting of research evidence. *Lancet, 374*(9683), 86-89.

Chalmers, R. L., & Begley, C. G. (2006). Dryness symptoms among an unselected clinical population with and without contact lens wear. *Cont Lens Anterior Eye, 29*(1), 25-30.

Chalmers, R. L., Begley, C. G., & Caffery, B. (2010). Validation of the 5-Item Dry Eye Questionnaire (DEQ-5): Discrimination across self-assessed severity and aqueous tear deficient dry eye diagnoses. *Cont Lens Anterior Eye, 33*(2), 55-60.

Chalmers, R. L., Keay, L., McNally, J., & Kern, J. (2012). Multicenter case-control study of the role of lens materials and care products on the development of corneal infiltrates. *Optom Vis Sci*, 89(3), 316-325.

Chan, G. C. Y., Kamble, R., Muller, H., Shah, S. A. A., Tang, T. B., & Meriaudeau, F. (2018). Fusing Results of Several Deep Learning Architectures for Automatic Classification of Normal and Diabetic Macular Edema in Optical Coherence Tomography. *Conf Proc IEEE Eng Med Biol Soc, 2018*, 670-673.

Chan, K. W., Yim, C. K., & Lam, S. S. K. (2010). Is Customer Participation in Value Creation a Double-Edged Sword? Evidence from Professional Financial Services Across Cultures. *Journal of Marketing*, 74(3), 48-64.

Chan, W. Y., To, C. K. M., & Chu, W. C. (2015). Materialistic consumers who seek unique products: How does their need for status and their affective response facilitate the repurchase intention of luxury goods? *Journal of Retailing and Consumer Services*, *27*, 1–10.

Charafaray, A. (2006). Service Quality expectations and perceptions held by CIBA Vision's customers. *MBA thesis*, University of Kwa-Zulu Natal.

Chee, S. P., Ti, S. E., Sivakumar, M., & Tan, D. T. (1999). Postoperative inflammation: extracapsular cataract extraction versus phacoemulsification. *J Cataract Refract Surg, 25*(9), 1280-1285.

Chen, C.-C. V., & Chen, C.-J. (2017). The role of customer participation for enhancing repurchase intention. *Management Decision*, 55(3), 547–562.

Chen, Q., Wang, J., Tao, A., Shen, M., Jiao, S., & Lu, F. (2010). Ultrahigh-resolution measurement by optical coherence tomography of dynamic tear film changes on contact lenses. *Invest Ophthalmol Vis Sci, 51*(4), 1988-1993.

Cheng, A. M., Sheha, H., & Tseng, S. C. (2015). Recent advances on ocular Demodex infestation. *Curr Opin Ophthalmol, 26*(4), 295-300.

Chia, E. M., Mitchell, P., Rochtchina, E., Lee, A. J., Maroun, R., & Wang, J. J. (2003). Prevalence and associations of dry eye syndrome in an older population: the Blue Mountains Eye Study. *Clin Exp Ophthalmol, 31*(3), 229-232.

Chiang, P. P., Xie, J., & Keeffe, J. E. (2011). Identifying the critical success factors in the coverage of low vision services using the classification analysis and regression tree methodology. *Invest Ophthalmol Vis Sci, 52*(5), 2790-2795.

Chignell, A. H., Easty, D. L., Chesterton, J. R., & Thomsitt, J. (1970). Marginal ulceration of the cornea. *Br J Ophthalmol, 54*(7), 433-440.

Cho, P., & Brown, B. (1993). Review of the tear break-up time and a closer look at the tear break-up time of Hong Kong Chinese. *Optom Vis Sci, 70*(1), 30-38.

Cho, Y. K., & Kim, M. S. (2009). Dry eye after cataract surgery and associated intraoperative risk factors. Korean J Ophthalmol, 23(2), 65-73.

Choi, J. H., Li, Y., Jin, R., Shrestha, T., Choi, J. S., Lee, W. J., Moon, M.J., Ju, H.T., Choi, W., Yoon, K. C. (2019). The Efficiency of Cyclosporine A-Eluting Contact Lenses for the Treatment of Dry Eye. *Curr Eye Res, 44*(5), 486-496.

Choi, Y. J., Park, S. Y., Jun, I., Choi, M., Seo, K. Y., Kim, E. K., & Kim, T. I. (2018). Perioperative Ocular Parameters Associated With Persistent Dry Eye Symptoms After Cataract Surgery. *Cornea, 37*(6), 734-739.

Chono, I., Miyazaki, D., Miyake, H., Komatsu, N., Ehara, F., Nagase, D., Kawamoto, Y., Shimizu, Y., Ideta, R., Inoue, Y. (2018). High interleukin-8 level in aqueous humor is associated with poor prognosis in eyes with open angle glaucoma and neovascular glaucoma. *Sci Rep, 8*(1), 14533.

Chotikavanich, S., de Paiva, C.S., Li de, Q., Chen, J.J., Bian, F., Farley, W.J., et al. (2009). Production and activity of matrix metalloproteinase-9 on the ocular surface increase in dysfunctional tear syndrome. *Invest Ophthalmol Vis Sci*, 50, 3203e9.

Chung, Y. W., Oh, T. H., & Chung, S. K. (2013). The effect of topical cyclosporine 0.05% on dry eye after cataract surgery. *Korean J Ophthalmol, 27*(3), 167-171.

Clarke, J., Puertas, R., Kotecha, A., Foster, P. J., & Barton, K. (2017). Virtual clinics in glaucoma care: face-to-face versus remote decision-making. *Br J Ophthalmol, 101*(7), 892-895.

Clegg, J. P., Guest, J. F., Lehman, A., & Smith, A. F. (2006). The annual cost of dry eye syndrome in France, Germany, Italy, Spain, Sweden and the United Kingdom among patients managed by ophthalmologists. *Ophthalmic Epidemiol, 13*(4), 263-274.

Clemons, T. E., Rankin, M. W., & McBee, W. L. (2006). Cognitive impairment in the Age-Related Eye Disease Study: AREDS report no. 16. *Arch Ophthalmol*, 124(4), 537-543.

Clinical Knowledge Summaries (CKS) (2015). Blepharitis. Retrieved May 15, 2019, from https://cks.nice.org.uk/blepharitis#!scenario

College of Optometrists (2018). A short guide to hay fever infograph. Retrieved April 2, 2019, https://www.college-optometrists.org/resourceLibrary/a-short-guide-to-hay-fever-infographic.html

College of Optometrists (2018). How to use the clinical management guidelines. Retrieved Novemeber 28, 2018, https://www.college-optometrists.org/guidance/clinical-management-guidelines/what-are-clinical-management-guidelines.html

College of Optometrists (2018). Use and supply of drugs or medicines in optometric practice. Retrieved November 28, 2018, https://guidance.college-optometrists.org/guidance-contents/knowledge-skills-and-performance-domain/use-and-supply-of-drugs-or-medicines-in-optometric-practice/

Collins, M. J., Iskander, D. R., Saunders, A., Hook, S., Anthony, E., & Gillon, R. (2006). Blinking patterns and corneal staining. *Eye Contact Lens, 32*(6), 287-293.

Conrad-Hengerer, I., Al Sheikh, M., Hengerer, F. H., Schultz, T., & Dick, H. B. (2015). Comparison of visual recovery and refractive stability between femtosecond laser-assisted cataract surgery and standard phacoemulsification: six-month follow-up. *J Cataract Refract Surg, 41*(7), 1356-1364.

Copay, A. G., Subach, B. R., Glassman, S. D., Polly, D. W., Jr., & Schuler, T. C. (2007). Understanding the minimum clinically important difference: a review of concepts and methods. *Spine J, 7*(5), 541-546.

Coster, D.J., Wilhelmus, K.R., Michaud, R., Jones, B.R. (1980). A comparison of acyclovir and idoxuridine as treatment for ulcerative herpetic keratitis. *Br J Ophthalmol*, 64(10), 763-765.

Coston, T.O. (1967). Demodex folliculorum blepharitis. Trans Am Ophthalmol Soc, 65, 361–392.

Cottier, K. (2015). An audit of the Primary Eye-care Acute Referral Scheme (PEARS) within NHS Bromley Clinical Commissioning Group (CCG). *Optometry in Practice*, 16, 21–32.

Court, J. H., & Austin, M. W. (2015). Virtual glaucoma clinics: patient acceptance and quality of patient education compared to standard clinics. *Clin Ophthalmol*, 9, 745-749.

Covey, M., Sweeney, D. F., Terry, R., Sankaridurg, P. R., & Holden, B. A. (2001). Hypoxic effects on the anterior eye of high-Dk soft contact lens wearers are negligible. *Optom Vis Sci*, 78(2), 95-99.

Craig, J. P., Chen, Y. H., & Turnbull, P. R. (2015). Prospective trial of intense pulsed light for the treatment of meibomian gland dysfunction. *Invest Ophthalmol Vis Sci, 56*(3), 1965-1970.

Craig, J. P., Nichols, K. K., Akpek, E. K., Caffery, B., Dua, H. S., Joo, C. K., Liu, Z., Nelson, J.D., Nichols, J.J., Tsubota, K., Stapleton, F. (2017). TFOS DEWS II Definition and Classification Report. *Ocul Surf, 15*(3), 276-283.

Craig, J. P., Wang, M. T., Kim, D., & Lee, J. M. (2016). Exploring the Predisposition of the Asian Eye to Development of Dry Eye. *Ocul Surf, 14*(3), 385-392.

Craig, J. P., Willcox, M. D., Argueso, P., Maissa, C., Stahl, U., Tomlinson, A., Wang, J., Yokoi, N., Stapleton, F. (2013). The TFOS International Workshop on Contact Lens Discomfort: report of the contact lens interactions with the tear film subcommittee. *Invest Ophthalmol Vis Sci,* 54(11), 123-156.

Cramer, J. A., Scheyer, R. D., & Mattson, R. H. (1990). Compliance declines between clinic visits. *Arch Intern Med, 150*(7), 1509-1510.

Craven, W. *(2015).* Monitoring activity in a minor eye conditions service. *Optometry Today,* 4, 39– 41.

Cronin Jr., J. J., & Taylor, S. A. (1992). Measuring Service Quality: A Re-examination and Extension. *Journal of Marketing*, 56(3), 55–68.

Cross, V., Shah, P., Bativala, R., & Spurgeon, P. (2007). ReGAE 2: glaucoma awareness and the primary eye-care service: some perceptions among African Caribbeans in Birmingham UK. *Eye*, 21(7), 912-920.

Cruz, A. A., Garcia, D. M., Pinto, C. T., & Cechetti, S. P. (2011). Spontaneous eyeblink activity. *Ocul Surf, 9*(1), 29-41.

Cuevas, M., Gonzalez-Garcia, M. J., Castellanos, E., Quispaya, R., Parra Pde, L., Fernandez, I., & Calonge, M. (2012). Correlations among symptoms, signs, and clinical tests in evaporative-type dry eye disease caused by Meibomian gland dysfunction (MGD). *Curr Eye Res, 37*(10), 855-863.

Cummings, K. M., Kirscht, J. P., Binder, L. R., & Godley, A. J. (1982). Determinants of drug treatment maintenance among hypertensive persons in inner city Detroit. *Public Health Rep, 97*(2), 99-106.

Dabasia, P. L., Edgar, D. F., Garway-Heath, D. F., & Lawrenson, J. G. (2014). A survey of current and anticipated use of standard and specialist equipment by UK optometrists. *Ophthalmic Physiol Opt*, 34(5), 592-613.

Dana, R., Bradley, J. L., Guerin, A., Pivneva, I., Evans, A. M., & Stillman, I. O. (2019a). Comorbidities and Prescribed Medications in Patients With or Without Dry Eye Disease: A Population-Based Study. *Am J Ophthalmol, 198*, 181-192.

Dana, R., Bradley, J. L., Guerin, A., Pivneva, I., Stillman, I. O., Evans, A. M., & Schaumberg, D. A. (2019b). Estimated Prevalence and Incidence of Dry Eye Disease Based on Coding Analysis of a Large, All-age United States Health Care System. *Am J Ophthalmol*. [Epub ahead of print]

Dave, T., & Fukuma, Y. (2004). Clinical evaluation of the Topcon BV-1000 automated subjective refraction system. *Optom Vis Sci*, 81(5), 323-333.

Deber, R. B., Kraetschmer, N., Urowitz, S., & Sharpe, N. (2005). Patient, consumer, client, or customer: what do people want to be called? *Health Expect, 8*(4), 345-351.

Dedeoglu, B. B., Bilgihan, A., Ye, B. H., Buonincontri, P., & Okumus, F. (2018). The impact of servicescape on hedonic value and behavioral intentions: The importance of previous experience. *International Journal of Hospitality Management*, *72*, 10–20.

Den, S., Shimizu, K., Ikeda, T., Tsubota, K., Shimmura, S., & Shimazaki, J. (2006). Association between meibomian gland changes and aging, sex, or tear function. *Cornea, 25*(6), 651-655.

De Paiva, C. S., & Pflugfelder, S. C. (2004). Corneal epitheliopathy of dry eye induces hyperesthesia to mechanical air jet stimulation. *Am J Ophthalmol, 137*(1), 109-115.

Dineen, L. C., & Blakesley, B. C. (1973). Algorithm AS 62: Generator for the sampling distribution of the Mann-Whitney U statistic. *Applied Statistics*, *22*, 269-273.

Doane, M. G. (1980). Interactions of eyelids and tears in corneal wetting and the dynamics of the normal human eyeblink. *Am J Ophthalmol, 89*(4), 507-516.

Doane, M. G. (1981). Blinking and the mechanics of the lacrimal drainage system. *Ophthalmology, 88*(8), 844-851.

Dodd, N. G., & Ganster, D. C. (1996). The interactive effects of variety, autonomy, and feedback on attitudes and performance. *Journal of Organizational Behavior*, 17, 329–347.

Dogru, M., Asano-Kato, N., Tanaka, M., Igarashi, A., Shimmura, S., Shimazaki, J., Okada, N., Takano, Y., Fukagawa, K., Tsubota, K., Fujishima, H. (2005). Ocular surface and MUC5AC alterations in atopic patients with corneal shield ulcers. *Curr Eye Res, 30*(10), 897-908.

Dogru, M., Matsumoto, Y., Okada, N., Igarashi, A., Fukagawa, K., Shimazaki, J., Tsubota, K., Fujishima, H. (2008). Alterations of the ocular surface epithelial MUC16 and goblet cell MUC5AC in patients with atopic keratoconjunctivitis. *Allergy, 63*(10), 1324-1334.

Donaldson, L., Subramanian, A., & Conway, M. L. (2018). Eye care in young children: a parent survey exploring access and barriers. *Clin Exp Optom, 101*(4), 521-526.

Donnenfeld, E. D., Solomon, K., Perry, H. D., Doshi, S. J., Ehrenhaus, M., Solomon, R., & Biser, S. (2003). The effect of hinge position on corneal sensation and dry eye after LASIK. *Ophthalmology, 110*(5), 1023-1029; discussion 1029-1030.

Donnenfeld, E. D., Solomon, R., Roberts, C. W., Wittpenn, J. R., McDonald, M. B., & Perry, H. D. (2010). Cyclosporine 0.05% to improve visual outcomes after multifocal intraocular lens implantation. *J Cataract Refract Surg, 36*(7), 1095-1100.

Doughty, M. J., Fonn, D., Richter, D., Simpson, T., Caffery, B., & Gordon, K. (1997). A patient questionnaire approach to estimating the prevalence of dry eye symptoms in patients presenting to optometric practices across Canada. *Optom Vis Sci, 74*(8), 624-631.

Downie, L. E., & Keller, P. R. (2015). A Pragmatic Approach to Dry Eye Diagnosis: Evidence into Practice. *Optom Vis Sci, 92*(12), 1189-1197.

Downie, L. E., Keller, P. R., & Vingrys, A. J. (2013). An evidence-based analysis of Australian optometrists' dry eye practices. *Optom Vis Sci, 90*(12), 1385-1395.

Downie, L. E., Rumney, N., Gad, A., Keller, P. R., Purslow, C., & Vingrys, A. J. (2016). Comparing self-reported optometric dry eye clinical practices in Australia and the United Kingdom: is there scope for practice improvement? *Ophthalmic Physiol Opt, 36*(2), 140-151.

Dray, S., Josse, J. (2015). Principal component analysis with missing values: a comparitive survey of methods. *Plan Ecol*, 216: 657- 667.

Dudley Local Optical Committee (LOC) (2019). Dudley Healthy Living Optician Scheme. Retrieved August 12, 2019, http://dudleyloc.co.uk/hlo/

Dumbleton, K., Caffery, B., Dogru, M., Hickson-Curran, S., Kern, J., Kojima, T., Morgan, P.B., Purslow, C., Robertson, D.M., Nelson, J. D. (2013). The TFOS International Workshop on Contact Lens Discomfort: report of the subcommittee on epidemiology. *Invest Ophthalmol Vis Sci, 54*(11), Tfos20-36.

Dumbleton, K., Woods, C. A., Jones, L. W., & Fonn, D. (2013). The impact of contemporary contact lenses on contact lens discontinuation. *Eye Contact Lens, 39*(1), 93-99.

Duncan, A. K., Breslin, M. A. (2009). Innovating health care delivery: the design of health services. *Journal of Business Strategy,* 30(2/3), 13-20.

Duncan, E. M., Cassie, H., Pooley, J., Elouafakoui, P., Prior, M., Gibb, E., Ramsay, C., Young, L. (2018). Areas for improvement in community optometry: flashes and floaters take priority. *Ophthalmic Physiol Opt, 38*(4), 411-421.

Dunn, O. J. (1964). Multiple comparisons using rank sums. *Technometrics*, *6*, 241-252.

Dunne, J.A., Traver, J.P. (1979). Double-blind clinical trial of topical steroids in anterior uveitis. *Br J Ophthalmol*, 63, 762–767.

Dunstone, D., Armstrong, R., Dunne, M. (2013). Survey of habits and attitudes to retinoscopy by optometrists in the UK. Optometry in Practice, 14, 45-54.

du Toit, R., Situ, P., Simpson, T., & Fonn, D. (2001). The effects of six months of contact lens wear on the tear film, ocular surfaces, and symptoms of presbyopes. *Optom Vis Sci, 78*(6), 455-462.

Edvardsson, B., Haglund, L., Mattsson, J. (1995). Analysis, planning, improvisation and control in the development of new services. *International Journal of Service Industry Management*, *6*(2), 24.

Efron, N., & Morgan, P. B. (2017). Rethinking contact lens aftercare. *Clin Exp Optom, 100*(5), 411-431.

Eisner, A. (2015). Sex, eyes, and vision: male/female distinctions in ophthalmic disorders. *Curr Eye Res, 40*(2), 96-101.

El Ameen, A., Majzoub, S., Vandermeer, G., & Pisella, P. J. (2018). Influence of cataract surgery on Meibomian gland dysfunction. *J Fr Ophtalmol*, 41(5), e173-e180.

El-Harazi, S. M., & Feldman, R. M. (2001). Control of intra-ocular inflammation associated with cataract surgery. *Curr Opin Ophthalmol, 12*(1), 4-8.

Elliott, D. B., Gilchrist, J., & Whitaker, D. (1989). Contrast sensitivity and glare sensitivity changes with three types of cataract morphology: are these techniques necessary in a clinical evaluation of cataract? *Ophthalmic Physiol Opt, 9*(1), 25-30.

English, F.P. (1971). Demodex folliculorum and oedema of the eyelash. Br J Ophthalmol, 55, 742–746.

Eom, Y., Lee, J. S., Kang, S. Y., Kim, H. M., & Song, J. S. (2013). Correlation between quantitative measurements of tear film lipid layer thickness and meibomian gland loss in patients with obstructive meibomian gland dysfunction and normal controls. *Am J Ophthalmol, 155*(6), 1104-1110.e1102.

Epitropoulos, A.T., Goslin, K., Bedi, R., Blackie, C.A. (2017). Meibomian gland dysfunction patients with novel Sjögren's syndrome biomarkers benefit significantly from a single vectored thermal pulsation procedure: a retrospective analysis. Clin Ophthalmol, 11, 701–706.

Epitropoulos, A. T., Matossian, C., Berdy, G. J., Malhotra, R. P., & Potvin, R. (2015). Effect of tear osmolarity on repeatability of keratometry for cataract surgery planning. *J Cataract Refract Surg, 41*(8), 1672-1677.

Ervin, A. M., Law, A., & Pucker, A. D. (2017). Punctal occlusion for dry eye syndrome. *Cochrane Database Syst Rev, 6*, Cd006775.

Ervin, A. M., Law, A., & Pucker, A. D. (2019). Punctal occlusion for dry eye syndrome: summary of a Cochrane systematic review. *Br J Ophthalmol, 103*(3), 301-306.

Ervin, A. M., Wojciechowski, R., & Schein, O. (2010). Punctal occlusion for dry eye syndrome. *Cochrane Database Syst Rev*(9), Cd006775.

Esteva, A., Kuprel, B., Novoa, R. A., Ko, J., Swetter, S. M., Blau, H. M., & Thrun, S. (2017). Dermatologist-level classification of skin cancer with deep neural networks. *Nature, 542*(7639), 115-118.

Euromcontact (2018). A comparison of European soft contact lens and lens care markets in 2018. Retrieved July 7, 2019, https://euromcontact.org/2019/03/14/euromcontact-2018-market-data-report-sales-contact-lenses-lens-care-products-31-countries-now-available/

Ezra, D. G., Mellington, F., Cugnoni, H., & Westcott, M. (2005). Reliability of ophthalmic accident and emergency referrals: a new role for the emergency nurse practitioner? *Emerg Med J, 22*(10), 696-699.

Faber, E., Golding, T. R., Lowe, R., & Brennan, N. A. (1991). Effect of hydrogel lens wear on tear film stability. *Optom Vis Sci, 68*(5), 380-384.

Fabrigar, L.R., Wegener, D.T., MacCallum, R.C. & Strahan, E.J. (1999). Evaluating the use of exploratory factor analysis in psychological research. *Psychological Methods*, 4, 272-299.

Farrand, K. F., Fridman, M., Stillman, I. O., & Schaumberg, D. A. (2017). Prevalence of Diagnosed Dry Eye Disease in the United States Among Adults Aged 18 Years and Older. *Am J Ophthalmol, 182*, 90-98.

Faul, F., Erdfelder, E., Buchner, A., & Lang, A.-G. (2009). Statistical power analyses using G*Power 3.1: Tests for correlation and regression analyses. *Behavior Research Methods*, *41*, 1149-1160.

Featherstone, P. I., James, C., Hall, M. S., & Williams, A. (1992). General practitioners' confidence in diagnosing and managing eye conditions: a survey in south Devon. *Br J Gen Pract, 42*(354), 21-24.

Feinstein, A. R. (1990). On white-coat effects and the electronic monitoring of compliance. *Arch Intern Med, 150*(7), 1377-1378.

Feng, Y., Gao, Z., Feng, K., Qu, H., & Hong, J. (2014). Meibomian gland dropout in patients with dry eye disease in China. *Curr Eye Res, 39*(10), 965-972.

Fenga, C., Aragona, P., Cacciola, A., Spinella, R., Di Nola, C., Ferreri, F., & Rania, L. (2008). Meibomian gland dysfunction and ocular discomfort in video display terminal workers. *Eye (Lond), 22*(1), 91-95.

Fenton, S., Jackson, E., & Fenton, M. (2001). An audit of the ophthalmic division of the accident and emergency department of the Royal Victoria Eye and Ear Hospital, Dublin. *Ir Med J, 94*(9), 265-266.

Fieguth, P., & Simpson, T. (2002). Automated measurement of bulbar redness. *Invest Ophthalmol Vis Sci, 43*(2), 340-347.

Fillingim, R. B., King, C. D., Ribeiro-Dasilva, M. C., Rahim-Williams, B., & Riley, J. L., 3rd. (2009). Sex, gender, and pain: a review of recent clinical and experimental findings. *J Pain, 10*(5), 447-485.

Finis, D., Ackermann, P., Pischel, N., Konig, C., Hayajneh, J., Borrelli, M., Schrader, S., Geerling, G. (2015). Evaluation of Meibomian Gland Dysfunction and Local Distribution of Meibomian Gland Atrophy by Non-contact Infrared Meibography. *Curr Eye Res, 40*(10), 982-989.

Finis, D., Hayajneh, J., Konig, C., Borrelli, M., Schrader, S., Geerling, G. (2014c) Evaluation of an automated thermodynamic treatment (LipiFlow®) system for Meibomian gland dysfunction: a prospective, randomized, observer-masked trial. *Ocul Surf*, 12(2),146-154.

Finis, D., Konig, C., Hayajneh, J., Borrelli, M., Schrader, S., Geerling, G. (2014b). Six-month effects of a thermodynamic treatment for MGD and implications of Meibomian gland atrophy. *Cornea,* 33(12), 1265-1270.

Finis, D., Pischel, N., Konig, C., Hayajneh, J., Borrelli, M., Schrader, S., & Geerling, G. (2014a). [Comparison of the OSDI and SPEED questionnaires for the evaluation of dry eye disease in clinical routine]. *Ophthalmologe, 111*(11), 1050-1056.

Finis, D., Pischel, N., Schrader, S., & Geerling, G. (2013). Evaluation of lipid layer thickness measurement of the tear film as a diagnostic tool for Meibomian gland dysfunction. *Cornea, 32*(12), 1549-1553.

Fisk, R. P., Brown, S. W., & Bitner, M. J. (1993). Tracking the Evolution of Services Marketing Literature. *Journal of Retailing*, 69(1), 61.

Fleming, J. H., Coffman, C., & Harter, J. K. (2005). Manage your human sigma. *Harvard Business Review*, 83(7/8), 106–114.

Fließ, S., & Kleinaltenkamp, M. (2004). Blueprinting the service company: Managing service processes efficiently. *Journal of Business Research*, 57(4), 392–404.

Foot, B., & MacEwen, C. (2017). Surveillance of sight loss due to delay in ophthalmic treatment or review: frequency, cause and outcome. *Eye (Lond), 31*(5), 771-775.

Forst, G. (1987). Structure of the tear film during the blinking process. *Ophthalmic Physiol Opt, 7*(1), 81-83.

Foulks, G. N. (2003). Challenges and pitfalls in clinical trials of treatments for dry eye. *Ocul Surf, 1*(1), 20-30.

Foulks, G.N., Bron, A.J. (2003). Meibomian-gland dysfunction: a clinical scheme for description, diagnosis, classification and grading. *Ocul Surf.*, 1:17–36.

Foulks, G. N., Nichols, K. K., Bron, A. J., Holland, E. J., McDonald, M. B., & Nelson, J. D. (2012). Improving awareness, identification, and management of meibomian gland dysfunction. *Ophthalmology, 119*(10 Suppl), S1-12.

Frick, K. D., Riva-Clement, L., & Shankar, M. B. (2009). Screening for refractive error and fitting with spectacles in rural and urban India: cost-effectiveness. *Ophthalmic Epidemiol, 16*(6), 378-387.

Fuentes-Paez, G., Herreras, J. M., Cordero, Y., Almaraz, A., Gonzalez, M. J., & Calonge, M. (2011). [Lack of concordance between dry eye syndrome questionnaires and diagnostic tests]. *Arch Soc Esp Oftalmol, 86*(1), 3-7.

Gallar, J., Acosta, M. C., Moilanen, J. A., Holopainen, J. M., Belmonte, C., & Tervo, T. M. (2004). Recovery of corneal sensitivity to mechanical and chemical stimulation after laser in situ keratomileusis. *J Refract Surg, 20*(3), 229-235.

Galor, A., Feuer, W., Lee, D. J., Florez, H., Carter, D., Pouyeh, B., Prunty, W.J., Perez, V. L. (2011). Prevalence and risk factors of dry eye syndrome in a United States veterans affairs population. *Am J Ophthalmol, 152*(3), 377-384.

Gao, Y. Y., Di Pascuale, M. A., Elizondo, A., & Tseng, S. C. (2007). Clinical treatment of ocular demodecosis by lid scrub with tea tree oil. *Cornea, 26*(2), 136-143.

Gao, Y. Y., Di Pascuale, M. A., Li, W., Baradaran-Rafii, A., Elizondo, A., Kuo, C. L., Raju, V.K., Tseng, S. C. (2005b). In vitro and in vivo killing of ocular Demodex by tea tree oil. *Br J Ophthalmol, 89*(11), 1468-1473.

Gao, Y. Y., Di Pascuale, M. A., Li, W., Liu, D. T., Baradaran-Rafii, A., Elizondo, A., Kawakita, T., Raju, V.K., Tseng, S. C. (2005a). High prevalence of Demodex in eyelashes with cylindrical dandruff. *Invest Ophthalmol Vis Sci, 46*(9), 3089-3094.

Gascon, J.J., Sanchez-Ortuno M., Llor, B, Skidmore, D, Saturno, P.J. (2004). Why hypertensive patients do not comply with the treatment: results from a qualitative study. *Family Practice*, 21(2),125–130.

Gazzard, G., Konstantakopoulou, E., Garway-Heath, D., Garg, A., Vickerstaff, V., Hunter, R., Ambler, G., Bunce, C., Wormald, R., Nathwani, N., Barton, K., Rubin, G., Buszewicz, M. (2019). Selective laser trabeculoplasty versus eye drops for first-line treatment of ocular hypertension and glaucoma (LiGHT): a multicentre randomised controlled trial. *Lancet*, 393(10180), 1505-1516.

General Optical Council (GOC). Opticians Act 1989. Retrieved July 8, 2019, https://www.optical.org/en/about_us/legislation/opticians_act.cfm

General Optical Council (2017). Freedom of Information requests 1 January 2017- 31 March 2017. Retreived November 26, 2018, file:///Users/macisaaj/Downloads/goc_foi_requests_quarter_4_2016_17_pdf.pdf

Gerges, S., Peter, E., Bowles, S. K., Diamond, S., Bucci, L. M., Resnick, A., & Taddio, A. (2018). Pharmacists as vaccinators: An analysis of their experiences and perceptions of their new role. Hum Vaccin Immunother, 14(2), 471-477.

Gibbons, A., Ali, T. K., Waren, D. P., & Donaldson, K. E. (2016). Causes and correction of dissatisfaction after implantation of presbyopia-correcting intraocular lenses. *Clin Ophthalmol, 10*, 1965-1970.

Gilbard, J. P., Farris, R. L., & Santamaria, J., 2nd. (1978). Osmolarity of tear microvolumes in keratoconjunctivitis sicca. *Arch Ophthalmol, 96*(4), 677-681.

Gilbard, J. P., Rossi, S. R., & Heyda, K. G. (1989). Tear film and ocular surface changes after closure of the meibomian gland orifices in the rabbit. *Ophthalmology, 96*(8), 1180-1186.

Glasziou, P., Altman, D. G., Bossuyt, P., Boutron, I., Clarke, M., Julious, S., Michie, S., Moher, D., Wager, E. (2014). Reducing waste from incomplete or unusable reports of biomedical research. *Lancet, 383*(9913), 267-276.

Golebiowski, B., Papas, E. B., & Stapleton, F. (2008). Factors affecting corneal and conjunctival sensitivity measurement. *Optom Vis Sci, 85*(4), 241-246.

Golebiowski, B., Papas, E. B., & Stapleton, F. (2012). Corneal and conjunctival sensory function: the impact on ocular surface sensitivity of change from low to high oxygen transmissibility contact lenses. *Invest Ophthalmol Vis Sci, 53*(3), 1177-1181.

Gomes, J. A. P., Azar, D. T., Baudouin, C., Efron, N., Hirayama, M., Horwath-Winter, J., Kim, T., Mehta, J.S., Messmer, E.M., Pepose, J.S., Sangwan, V.S., Weiner, A.L., Wilson, S.E., Wolffsohn, J. S. (2017). TFOS DEWS II iatrogenic report. *Ocul Surf, 15*(3), 511-538.

Goto, T., Zheng, X., Klyce, S. D., Kataoka, H., Uno, T., Karon, M., Tatematsu, Y., Bessyo, T., Ohashi, Y. (2003). A new method for tear film stability analysis using videokeratography. *Am J Ophthalmol, 135*(5), 607-612.

Goto, T., Zheng, X., Okamoto, S., & Ohashi, Y. (2004). Tear film stability analysis system: introducing a new application for videokeratography. *Cornea, 23*(8 Suppl), S65-70.

Gourville, J. T. (1998). Pennies-a-Day: The Effect of Temporal Reframing on Transaction Evaluation. *Journal of Consumer Research*, *24*(4), 395–408.

Graham, J. E., McGilligan, V. E., Berrar, D., Leccisotti, A., Moore, J. E., Bron, A. J., & Moore, T. C. (2010). Attitudes towards diagnostic tests and therapies for dry eye disease. *Ophthalmic Res, 43*(1), 11-17.

Greenwood, L. (2013). Auditing of a referral refinement service in Hull. *Optometry Today*, 25, 24–26.

Greiner, J.V. (2016). Long-term (3 year) effects of a single thermal pulsation system treatment on meibomian gland function and dry eye symptoms. *Eye Contact Lens*, 42(2), 99–107.

Grene, R. B., Lankston, P., Mordaunt, J., Harrold, M., Gwon, A., & Jones, R. (1992). Unpreserved carboxymethylcellulose artificial tears evaluated in patients with keratoconjunctivitis sicca. *Cornea, 11*(4), 294-301

Griffin, A. (1997). PDMA Research on New Product Development Practices: Updating Trends and Benchmarking Best Practices. *Journal of Product Innovation Management*, *14*(6), 429–458.

Grönroos, C. (1984). A Service Quality Model and its Marketing Implications. *European Journal of Marketing*, 18(4), 36-44.

Guadagnoli, E. & Velicer, W.F. (1988). Relation of sample size to the stability of component patterns. *Psychological Bulletin*, 103, 265-275.

Guillemin, I., Begley, C., Chalmers, R., Baudouin, C., & Arnould, B. (2012). Appraisal of patient-reported outcome instruments available for randomized clinical trials in dry eye: revisiting the standards. *Ocul Surf, 10*(2), 84-99.

Guillon, M., & Guillon, J. P. (1989). Hydrogel lens wettability during overnight wear. *Ophthalmic Physiol Opt, 9*(4), 355-359.

Guillon, M., & Maissa, C. (2005a). Bulbar conjunctival staining in contact lens wearers and non lens wearers and its association with symptomatology. *Cont Lens Anterior Eye, 28*(2), 67-73.

Guillon, M., & Maissa, C. (2005b). Dry eye symptomatology of soft contact lens wearers and nonwearers. *Optom Vis Sci, 82*(9), 829-834.

Guillon, M., & Maissa, C. (2008). Contact lens wear affects tear film evaporation. *Eye Contact Lens, 34*(6), 326-330.

Guillon, M., Styles, E., Guillon, J. P., & Maissa, C. (1997). Preocular tear film characteristics of nonwearers and soft contact lens wearers. *Optom Vis Sci, 74*(5), 273-279.

Guillon, M., Theodoratos, P., Patel, K., Gupta, R., & Patel, T. (2019). Pre-contact lens and pre-corneal tear film kinetics. *Cont Lens Anterior Eye, 42*(3), 246-252.

Gulshan, V., Peng, L., Coram, M., et al. (2016) Development and Validation of a Deep Learning Algorithm for Detection of Diabetic Retinopathy in Retinal Fundus Photographs. *JAMA,* 316(22):2402–2410.

Gumus, K., Crockett, C. H., Rao, K., Yeu, E., Weikert, M. P., Shirayama, M., Hada, S., Pflugfelder, S.C. (2011). Noninvasive assessment of tear stability with the tear stability analysis system in tear dysfunction patients. *Invest Ophthalmol Vis Sci, 52*(1), 456-461.

Guo, B., Lu, P., Chen, X., Zhang, W., & Chen, R. (2010). Prevalence of dry eye disease in Mongolians at high altitude in China: the Henan eye study. *Ophthalmic Epidemiol, 17*(4), 234-241.

Gutgesell, V. J., Stern, G. A., & Hood, C. I. (1982). Histopathology of meibomian gland dysfunction. *Am J Ophthalmol, 94*(3), 383-387.

Hadassah, J., Bhuvaneshwari, N., Rao, U., Sehgal, P.K. (2009). Evaluation of succinylated collagen bandage lenses in corneal healing by the expression of matrix metalloproteinases (MMP-2 and MMP-9) in tear fluid. *Ophthalmic Res*, 42, 64e72.

Hagen, K. B., Bedi, R., Blackie, C. A., & Christenson-Akagi, K. J. (2018). Comparison of a single-dose vectored thermal pulsation procedure with a 3-month course of daily oral doxycycline for moderate-to-severe meibomian gland dysfunction. *Clin Ophthalmol, 12*, 161-168.

Hall, N.J., Donovan, G., Wilkes, S. (2018). A qualitative synthesis of pharmacist, other health professional and lay perspectives on the role of community pharmacy in facilitating care for people with long-term conditions. *Research in Social & Administrative Pharmacy*, 14(11), 1043-1057.

Hamada, S., Moore, T. C., Moore, J. E., Al-Dreihi, M. G., Anbari, A., & Shah, S. (2016). Assessment of the effect of cyclosporine-A 0.05% emulsion on the ocular surface and corneal sensation following cataract surgery. *Cont Lens Anterior Eye, 39*(1), 15-19.

Han, K. E., Yoon, S. C., Ahn, J. M., Nam, S. M., Stulting, R. D., Kim, E. K., & Seo, K. Y. (2014). Evaluation of dry eye and meibomian gland dysfunction after cataract surgery. Am J Ophthalmol, 157(6), 1144-1150.

Han, R. C., Jefferis, J. M., Taylor, J. P., Archibald, N. K., & Clarke, M. P. (2012). A novel, multidisciplinary clinic for complex visual problems in older people. *Eye (London, England)*, 26(12), 1536–1541.

Han, S. B., Hyon, J. Y., Woo, S. J., Lee, J. J., Kim, T. H., & Kim, K. W. (2011). Prevalence of dry eye disease in an elderly Korean population. *Arch Ophthalmol, 129*(5), 633-638.

Han, S. B., Yang, H. K., Hyon, J. Y., & Wee, W. R. (2017). Association of dry eye disease with psychiatric or neurological disorders in elderly patients. *Clin Interv Aging, 12*, 785-792.

Hansemark, O.C., Albinsson, M. (2004). Customer satisfaction and retention: the experiences of individual employees. *Managing Service Quality: An International Journal*, 14(1), 40-57.

Hardesty, D. M., Bearden, W. O., & Carlson, J. P. (2007). Persuasion knowledge and consumer reactions to pricing tactics. *Journal of Retailing*, 83(2), 199–210.

Harknett, T., Bowden, T., Shadbolt, H., & Mian, S. (2001). Five years after dispensing--are contact lenses a success? *Cont Lens Anterior Eye, 24*(3), 127-128.

Harvey, J. (1998). Service quality: a tutorial. *Journal of Operations Management,* 16(5), 583- 597.

Hashemi, H., Khabazkhoob, M., Kheirkhah, A., Emamian, M. H., Mehravaran, S., Shariati, M., & Fotouhi, A. (2014). Prevalence of dry eye syndrome in an adult population. *Clin Exp Ophthalmol, 42*(3), 242-248.

Hau, S., Ehrlich, D., Binstead, K., & Verma, S. (2007). An evaluation of optometrists' ability to correctly identify and manage patients with ocular disease in the accident and emergency department of an eye hospital. *Br J Ophthalmol, 91*(4), 437-440.

Hau, S., Ioannidis, A., Masaoutis, P., & Verma, S. (2008). Patterns of ophthalmological complaints presenting to a dedicated ophthalmic Accident & Emergency department: inappropriate use and patients' perspective. *Emerg Med J, 25*(11), 740-744.

Hay, E. M., Thomas, E., Pal, B., Hajeer, A., Chambers, H., & Silman, A. J. (1998). Weak association between subjective symptoms or and objective testing for dry eyes and dry mouth: results from a population based study. *Ann Rheum Dis, 57*(1), 20-24.

Hazel, C. A., Petre, K. L., Armstrong, R. A., Benson, M. T., & Frost, N. A. (2000). Visual function and subjective quality of life compared in subjects with acquired macular disease. *Invest Ophthalmol Vis Sci, 41*(6), 1309-1315.

Hazen, A. C. M., de Bont, A. A., Leendertse, A. J., Zwart, D. L. M., de Wit, N. J., de Gier, J. J., & Bouvy, M. L. (2019). How Clinical Integration of Pharmacists in General Practice has Impact on Medication Therapy Management: A Theory-oriented Evaluation. *Int J Integr Care*, 19(1), 1.

Henriquez, A. S., & Korb, D. R. (1981). Meibomian glands and contact lens wear. *Br J Ophthalmol, 65*(2), 108-111.

Henson, R.K. & Roberts, J.K. (2006). Use of exploratory factor analysis in published research: common errors and some comment on improved practice. *Educational and Psychological Measurement*, 66, 393-416.

Herefordshire Council (2018). The Population of Herefordshire 2018- Version 1.0, June 2018. Retrieved October 14, 2018, https://factsandfigures.herefordshire.gov.uk/media/60636/population-of-herefordshire-2018-v10.pdf

Hernandez-Ronquillo, L., Tellez-Zenteno, J. F., Garduno-Espinosa, J., & Gonzalez-Acevez, E. (2003). Factors associated with therapy noncompliance in type-2 diabetes patients. *Salud Publica Mex, 45*(3), 191-197.

Himebaugh, N. L., Begley, C. G., Bradley, A., & Wilkinson, J. A. (2009). Blinking and tear break-up during four visual tasks. *Optom Vis Sci, 86*(2), E106-114.

Hindi, A.M.K., Jacobs, S., Schafheutle, E.I. (2019a). Solidarity or dissonance? A systematic review of pharmacist and GP views on community pharmacy services in the UK. *Health & Social Care in the Community*, 27(3), 565-598.

Hindi, A.M.K., Schafheutle, E.I., Jacobs, S. (2019b). Community pharmacy integration within the primary care pathway for people with long-term conditions: a focus group study of patients', pharmacists' and GPs' experiences and expectations. *BMC Family Practice*, 20(1), 1-15.

Hirata, H., Fried, N., & Oshinsky, M. L. (2012). Quantitative characterization reveals three types of dry-sensitive corneal afferents: pattern of discharge, receptive field, and thermal and chemical sensitivity. *J Neurophysiol, 108*(9), 2481-2493.

Hirata, H., Mizerska, K., Marfurt, C.F., Rosenblatt, M.I. (2015). Hyperosmolar tears induce functional and structural alterations of corneal nerves: electrophysiological and anatomical evidence toward neurotoxicity. *Investigative Ophthalmology & Visual Science*, 56 (13), 8125–8140.

Hirnschall, N., Leisse, C., Radda, S., Maedel, S., Findl, O. (2016). Macular disease detection with a swept-source optical coherence tomography-based biometry device in patients scheduled for cataract surgery. *J Cataract Refract Surg,* 42(4), 530–536.

Hirota, M., Uozato, H., Kawamorita, T., Shibata, Y., & Yamamoto, S. (2013). Effect of incomplete blinking on tear film stability. *Optom Vis Sci, 90*(7), 650-657.

Hogarty, K.Y., Hines, C.V., Kromrey, J.D., Ferron, J.M & Mumford, K.R. (2005). The quality factor solutions in exploratory factor analysis: the influence of sample size, communality, and overdetermination. *Educational and Psychological Measurement*, 65, 202-226.

Holly, F. J. (1985). Physical chemistry of the normal and disordered tear film. *Trans Ophthalmol Soc U K, 104 (Pt 4)*, 374-380.

Hong, J., Sun, X., Wei, A., Cui, X., Li, Y., Qian, T., Wang, W., Xu, J. (2013). Assessment of tear film stability in dry eye with a newly developed keratograph. *Cornea, 32*(5), 716-721.

Hsieh, A., & Yen, C. (2005). The effect of customer participation on service providers' job stress. *Service Industries Journal*, *25*(7), 891–905.

Hu, F. B., & Willett, W. C. (2002). Optimal diets for prevention of coronary heart disease. *Jama, 288*(20), 2569-2578.

Hungin, A. P., Rubin, G., & O'Flanagan, H. (1999). Factors influencing compliance in long-term proton pump inhibitor therapy in general practice. *Br J Gen Pract, 49*(443), 463-464.

Hykin, P. G., & Bron, A. J. (1992). Age-related morphological changes in lid margin and meibomian gland anatomy. *Cornea, 11*(4), 334-342.

IBM Knowledge Center (2016). IBM SPSS Decision Trees 24. User guide to IBM SPSS. Retrieved January 14, 2019, ftp://public.dhe.ibm.com/software/analytics/spss/documentation/statistics/24.0/en/client/Manuals/IBM_SPSS_Decision_Trees.pdf

IBM Support (2019). Pairwise vs. listwise deletion: what are they and when should I use them? Retrieved 07/02/2019, http://www-01.ibm.com/support/docview.wss?uid=swg21475199

Iglesias, E., Sajnani, R., Levitt, R. C., Sarantopoulos, C. D., & Galor, A. (2018). Epidemiology of Persistent Dry Eye-Like Symptoms After Cataract Surgery. *Cornea, 37*(7), 893-898.

Interaction Design Foundation. Service Blueprints: Communicating the design of services. Retrieved 28 April 2019 from https://www.interaction-design.org/literature/article/service-blueprints-communicating-the-design-of-services

Ipek, T., Hanga, M. P., Hartwig, A., Wolffsohn, J., & O'Donnell, C. (2018). Dry eye following cataract surgery: The effect of light exposure using an in-vitro model. *Cont Lens Anterior Eye, 41*(1), 128-131.

Jackson, G. R., & Owsley, C. (2003). Visual dysfunction, neurodegenerative diseases, and aging. *Neurol Clin,* 21(3), 709-728.

Jacobi, C., Jacobi, A., Kruse, F. E., & Cursiefen, C. (2011). Tear film osmolarity measurements in dry eye disease using electrical impedance technology. *Cornea, 30*(12), 1289-1292.

Jaeschke, R., Singer, J., & Guyatt, G. H. (1989). Measurement of health status. Ascertaining the minimal clinically important difference. *Control Clin Trials, 10*(4), 407-415.

Jani, D., & Han, H. (2015). Influence of environmental stimuli on hotel customer emotional loyalty response: Testing the moderating effect of the big five personality factors. *International Journal of Hospitality Management*, 44, 48–57.

Jee, D., Park, M., Lee, H. J., Kim, M. S., & Kim, E. C. (2015). Comparison of treatment with preservative-free versus preserved sodium hyaluronate 0.1% and fluorometholone 0.1% eyedrops after cataract surgery in patients with preexisting dry-eye syndrome. *J Cataract Refract Surg, 41*(4), 756-763.

Jester, J. V., Nicolaides, N., Kiss-Palvolgyi, I., & Smith, R. E. (1989). Meibomian gland dysfunction. II. The role of keratinization in a rabbit model of MGD. *Invest Ophthalmol Vis Sci, 30*(5), 936-945.

Jester, J. V., Nicolaides, N., & Smith, R. E. (1981). Meibomian gland studies: histologic and ultrastructural investigations. *Invest Ophthalmol Vis Sci, 20*(4), 537-547.

Jiang, D., Xiao, X., Fu, T., Mashaghi, A., Liu, Q., & Hong, J. (2016). Transient Tear Film Dysfunction after Cataract Surgery in Diabetic Patients. *PLoS One, 11*(1), e0146752.

Jiang, X., Lv, H., Song, H., Zhang, M., Liu, Y., Hu, X., Li, X., Wang, W. (2016). Evaluation of the Safety and Effectiveness of Intense Pulsed Light in the Treatment of Meibomian Gland Dysfunction. *J Ophthalmol, 2016*, 1910694.

Jie, Y., Xu, L., Wu, Y. Y., & Jonas, J. B. (2009). Prevalence of dry eye among adult Chinese in the Beijing Eye Study. *Eye (Lond), 23*(3), 688-693.

Jin, J., Sklar, G.E., Oh, V.M.S., Li, S.H. (2008). Factors affecting therapeutic compliance: A review from the patient's perspective. *Therapeutics and Clinical Risk Management*, 4(1), 269- 286

Johnson, M. E. (2009). The association between symptoms of discomfort and signs in dry eye. *Ocul Surf, 7*(4), 199-211.

Johnston, R. (1995). The zone of tolerance: Exploring the relationship between service transactions and satisfaction with the overall service. *International Journal of Service Industry Management*, 6(2), 46-61.

Jones, L., Brennan, N. A., Gonzalez-Meijome, J., Lally, J., Maldonado-Codina, C., Schmidt, T. A., Subbaraman, L., Young, G., Nichols, J. J. (2013). The TFOS International Workshop on Contact Lens Discomfort: report of the contact lens materials, design, and care subcommittee. *Invest Ophthalmol Vis Sci*, 54(11), 37-70.

Jones, L., Downie, L.E., Korb, D., Benitez-Del-Castillo, J.M., Dana, R., Deng, S.X., Dong, P.N., Geerling, G., Hida, R.Y., Liu, Y., Seo, K.Y., Tauber, J., Wakamatsu, T.H., Xu, J., Wolffsohn, J.S., Craig, J.P. (2017). TFOS DEWS II Management and Therapy Report. *Ocul Surf* 15(3), 575-628.

Jones, M. A., Mothersbaugh, D. L., & Beatty, S. E. (2000). Switching barriers and repurchase intentions in services. *Journal of Retailing*, 76(2), 259-274.

Jones, N. P., Hayward, J. M., Khaw, P. T., Claoue, C. M., & Elkington, A. R. (1986). Function of an ophthalmic "accident and emergency" department: results of a six month survey. *Br Med J (Clin Res Ed), 292*(6514), 188-190.

Jung, J. W., Park, S. Y., Kim, J. S., Kim, E. K., Seo, K. Y., & Kim, T. I. (2016). Analysis of Factors Associated With the Tear Film Lipid Layer Thickness in Normal Eyes and Patients With Dry Eye Syndrome. *Invest Ophthalmol Vis Sci, 57*(10), 4076-4083.

Jutai, J., Day, H., Woolrich, W., & Strong, G. (2003). The predictability of retention and discontinuation of contact lenses. *Optometry, 74*(5), 299-308.

Kallarackal, G. U., Ansari, E. A., Amos, N., Martin, J. C., Lane, C., & Camilleri, J. P. (2002). A comparative study to assess the clinical use of Fluorescein Meniscus Time (FMT) with Tear Break up Time (TBUT) and Schirmer's tests (ST) in the diagnosis of dry eyes. *Eye (Lond), 16*(5), 594-600.

Kanellopoulos, A. J., & Asimellis, G. (2016). In pursuit of objective dry eye screening clinical techniques. *Eye Vis (Lond), 3*, 1.

Kang, Y. S., Lee, H. S., Li, Y., Choi, W., & Yoon, K. C. (2018). Manifestation of meibomian gland dysfunction in patients with Sjögren's syndrome, non- Sjögren's dry eye, and non-dry eye controls. *Int Ophthalmol, 38*(3), 1161-1167.

Karson, C. N., Burns, R. S., LeWitt, P. A., Foster, N. L., & Newman, R. P. (1984). Blink rates and disorders of movement. *Neurology, 34*(5), 677-678.

Kasetsuwan, N., Satitpitakul, V., Changul, T., & Jariyakosol, S. (2013). Incidence and pattern of dry eye after cataract surgery. *PLoS One, 8*(11), e78657.

Kass, G. V. (1980). An Exploratory Technique for Investigating Large Quantities of Categorical Data. *Journal of the Royal Statistical Society. Series C (Applied Statistics), 29*(2), 119-127.

Kassan, S. S., & Moutsopoulos, H. M. (2004). Clinical manifestations and early diagnosis of Sjögren's syndrome. *Arch Intern Med, 164*(12), 1275-1284.

Kaufman, H.E. (2013). The practical detection of mmp-9 diagnoses ocular surface disease and may help prevent its complications. *Cornea*, 32, 211e6.

Kearney, Liam (2017). Scottish government community eyecare services: review. Retrieved August 21, 2018, https://www.gov.scot/publications/community-eyecare-services-review/

Keaveney, S., Parthasarathy, M. (2001). Customer switching behavior in online services: an exploratory study of the role of selected attitudinal, behavioural and demographic factors. *Journal of Academy of Marketing Science*, 29(4), 374-390.

Keech, A., Senchyna, M., & Jones, L. (2013). Impact of time between collection and collection method on human tear fluid osmolarity. *Curr Eye Res, 38*(4), 428-436.

Kerr, C., Chauhan, K. (2019). The ACLM Contact Yearbook 2019. Devises: Association of Contact Lens Manufacturers.

Key, J. E. (1996). A comparative study of eyelid cleaning regimens in chronic blepharitis. *Clao j, 22*(3), 209-212.

Khaireddin, R., & Hueber, A. (2013). [Eyelid hygiene for contact lens wearers with blepharitis. Comparative investigation of treatment with baby shampoo versus phospholipid solution]. *Ophthalmologe, 110*(2), 146-153.

Khanal, S., Tomlinson, A., McFadyen, A., Diaper, C., & Ramaesh, K. (2008). Dry eye diagnosis. *Invest Ophthalmol Vis Sci, 49*(4), 1407-1414.

Kheirkhah, A., Dohlman, T. H., Amparo, F., Arnoldner, M. A., Jamali, A., Hamrah, P., & Dana, R. (2015). Effects of corneal nerve density on the response to treatment in dry eye disease. *Ophthalmology, 122*(4), 662-668.

Kheterpal, S., Perry, M. E., & McDonnell, P. J. (1995). General practice referral letters to a regional ophthalmic accident and emergency department. *Eye (Lond), 9 (Pt 6 Su)*, 67-69.

Kim, J. S., Lee, H., Choi, S., Kim, E. K., Seo, K. Y., & Kim, T. I. (2018). Assessment of the Tear Film Lipid Layer Thickness after Cataract Surgery. *Semin Ophthalmol, 33*(2), 231-236.

Kim, K. W., Han, S. B., Han, E. R., Woo, S. J., Lee, J. J., Yoon, J. C., & Hyon, J. Y. (2011). Association between depression and dry eye disease in an elderly population. *Invest Ophthalmol Vis Sci, 52*(11), 7954-7958.

Kim, Y. S., Kwak, A. Y., Lee, S. Y., Yoon, J. S., & Jang, S. Y. (2015). Meibomian gland dysfunction in Graves' orbitopathy. *Can J Ophthalmol, 50*(4), 278-282.

King-Smith, P. E., Fink, B. A., Hill, R. M., Koelling, K. W., & Tiffany, J. M. (2004). The thickness of the tear film. *Curr Eye Res, 29*(4-5), 357-368.

Klein, B.R., Brown, E.N., Casden, R.S. (2016). Preoperative macular spectral-domain optical coherence tomography in patients considering advanced technology intraocular lenses for cataract surgery. *J Cataract Refract Surg*, 42(4), 537–541.

Knop, E., Knop, N., Millar, T., Obata, H., & Sullivan, D. A. (2011). The international workshop on meibomian gland dysfunction: report of the subcommittee on anatomy, physiology, and pathophysiology of the meibomian gland. *Invest Ophthalmol Vis Sci, 52*(4), 1938-1978.

Knop, E., Knop, N., & Schirra, F. (2009). [Meibomian glands. Part II: physiology, characteristics, distribution and function of meibomian oil]. *Ophthalmologe, 106*(10), 884-892.

Knop, N., & Knop, E. (2009). [Meibomian glands. Part I: anatomy, embryology and histology of the Meibomian glands]. *Ophthalmologe, 106*(10), 872-883.

Koenig-Lewis Nicole, Palmer Adrian, & Martin Charles. (2014). The effects of anticipatory emotions on service satisfaction and behavioral intention. *Journal of Services Marketing*, 28(6), 437-451.

Kohlhaas, M. (1998). Corneal sensation after cataract and refractive surgery. J Cataract Refract Surg, 24(10), 1399-1409.

Kohli, P., Arya, S. K., Raj, A., & Handa, U. (2019). Changes in ocular surface status after phacoemulsification in patients with senile cataract. *Int Ophthalmol, 39*(6), 1345-1353.

Kojima, T., Ibrahim, O. M., Wakamatsu, T., Tsuyama, A., Ogawa, J., Matsumoto, Y., Dogru, M., Tsubota, K. (2011). The impact of contact lens wear and visual display terminal work on ocular surface and tear functions in office workers. *Am J Ophthalmol, 152*(6), 933-940.

Kojima, T., Ishida, R., Dogru, M., Goto, E., Takano, Y., Matsumoto, Y., Kaido, M., Ohashi, Y., Tsubota, K. (2004). A new noninvasive tear stability analysis system for the assessment of dry eyes. *Invest Ophthalmol Vis Sci, 45*(5), 1369-1374.

Konstantakopoulou, E., Edgar, D. F., Harper, R. A., Baker, H., Sutton, M., Janikoun, S., Larkin, G., Lawrenson, J. G. (2016). Evaluation of a minor eye conditions scheme delivered by community optometrists. *BMJ Open, 6*(8), e011832.

Konstantakopoulou, E., Harper, R. A., Edgar, D. F., Larkin, G., Janikoun, S., & Lawrenson, J. G. (2018). Clinical safety of a minor eye conditions scheme in England delivered by community optometrists. *BMJ Open Ophthalmol, 3*(1), e000125.

Konstantakopoulou, E., Harper, R. A., Edgar, D. F., & Lawrenson, J. G. (2014). A qualitative study of stakeholder views regarding participation in locally commissioned enhanced optometric services. *BMJ Open, 4*(5), e004781.

Koo, H., Kim, T. H., Kim, K. W., Wee, S. W., Chun, Y. S., & Kim, J. C. (2012). Ocular surface discomfort and Demodex: effect of tea tree oil eyelid scrub in Demodex blepharitis. *J Korean Med Sci, 27*(12), 1574-1579.

Korb, D., Blackie, C. A. (2014). Single Lipiflow treatment increases soft contact lens wearing time and reduces lid wiper epitheliopathy and dry eye symptoms. American Academy of Optometry's 93rd Annual Meeting, Denver.

Korb, D.R. (2000). Survey of preferred tests for diagnosis of the tear film and dry eye. *Cornea*, 19,483–486.

Korb, D. R., Baron, D. F., Herman, J. P., Finnemore, V. M., Exford, J. M., Hermosa, J. L., Leahy, C.D., Glonek, T., Greiner, J. V. (1994). Tear film lipid layer thickness as a function of blinking. *Cornea, 13*(4), 354-359.

Korb, D. R., & Blackie, C. A. (2008). Meibomian gland diagnostic expressibility: correlation with dry eye symptoms and gland location. *Cornea, 27*(10), 1142-1147.

Korb, D. R., & Henriquez, A. S. (1980). Meibomian gland dysfunction and contact lens intolerance. *J Am Optom Assoc, 51*(3), 243-251.

Kotecha, A., Brookes, J., & Foster, P. J. (2017). A technician-delivered 'virtual clinic' for triaging low-risk glaucoma referrals. *Eye (Lond),* 31(6), 899-905.

Kovacs, I., Luna, C., Quirce, S., Mizerska, K., Callejo, G., Riestra, A., Fernandez-Sanchez, L., Meseguer, V.M., Cuenca, N., Merayo-Lloves, J., Acosta, M.C., Gasull, X., Belmonte, C., Gallar, J. (2016). Abnormal activity of corneal cold thermoreceptors underlies the unpleasant sensations in dry eye disease. *Pain, 157*(2), 399-417.

Kruszka, P., & O'Brian, R. J. (2009). Diagnosis and management of Sjögren's syndrome. *Am Fam Physician, 79*(6), 465-470.

Kuo, W. J., Chang, R. F., Chen, D. R., & Lee, C. C. (2001). Data mining with decision trees for diagnosis of breast tumor in medical ultrasonic images. *Breast Cancer Res Treat, 66*(1), 51-57.

Kwortnik, R. J., Jr., Creyer, E. H., & Ross, W. T., Jr. (2006). Usage-based versus measure-based unit pricing: is there a better index of value? *Journal of Consumer Policy*, 29(1), 37-66.

Kyngas, H., & Lahdenpera, T. (1999). Compliance of patients with hypertension and associated factors. *J Adv Nurs, 29*(4), 832-839.

Ladhari, R. (2009). Service quality, emotional satisfaction, and behavioural intentions: A study in the hotel industry. *Managing Service Quality: An International Journal*, 19(3), 308-331.

Ladhari, R., Souiden, N., & Dufour, B. (2017). The role of emotions in utilitarian service settings: The effects of emotional satisfaction on product perception and behavioral intentions. *Journal of Retailing and Consumer Services*, *34*, 10–18.

Laerd Statistics (2017). One-way ANOVA using SPSS Statistics. *Statistical tutorials and software guides*. Retrieved 03/04/2019 from https://statistics.laerd.com/

Laerd Statistics (2015a). Independent-samples t-test using SPSS Statistics. *Statistical tutorials and software guides*. Retrieved 31 May 2019 from https://statistics.laerd.com/

Laerd Statistics (2015b). Mann-Whitney U test using SPSS Statistics. *Statistical tutorials and software guides*. Retrieved 31 May 2019 from https://statistics.laerd.com/

Lai, T.Y.Y., Wong, V.W.Y., Leung, G.M. (2003). Is ophthalmology evidence based? A clinical audit of emergency unit of a regional eye hospital. *Br J Ophthalmol*, 87, 385–390.

Lane, S. S., DuBiner, H. B., Epstein, R. J., Ernest, P. H., Greiner, J. V., Hardten, D. R., Holland, E.J., Lemp, M.A., McDonald, J.E. 2nd, Silbert, D.I., Blackie, C.A., Stevens, C.A., Bedi, R. (2012). A new system, the LipiFlow, for the treatment of meibomian gland dysfunction. *Cornea, 31*(4), 396-404.

Lariviere, B., Keiningham, T. L., Aksoy, L., Yalcin, A., Morgeson, F. V., & Mithas, S. (2016). Modeling heterogeneity in the satisfaction, loyalty intention, and shareholder value linkage: a cross-industry analysis at the customer and firm levels. *Journal of Marketing Research*, 53(1), 91-109.

Lawless, M., Bali, S. J., Hodge, C., Roberts, T. V., Chan, C., & Sutton, G. (2012). Outcomes of Femtosecond Laser Cataract Surgery With a Diffractive Multifocal Intraocular Lens. *Journal of Refractive Surgery*, 28(12), 859-864.

Lawrenson, J. G., Birhah, R., & Murphy, P. J. (2005). Tear-film lipid layer morphology and corneal sensation in the development of blinking in neonates and infants. *J Anat, 206*(3), 265-270.

Lawson, V.L., Lyne, P.A., Harvey, J.N., Bundy, C.E. (2005). Understanding why people with type 1 diabetes do not attend for specialist advice: a qualitative analysis of the views of people with insulin-dependent diabetes who do not attend diabetes clinic. *Journal of Health Psychology*, 10(3), 409–423.

Le, J. T., Viswanathan, S., Tarver, M. E., Eydelman, M., & Li, T. (2016). Assessment of the Incorporation of Patient-Centric Outcomes in Studies of Minimally Invasive Glaucoma Surgical Devices. *JAMA Ophthalmol, 134*(9), 1054-1056.

Leamon, S., Hayden, C., Lee, H., Trudinger, D., Appelbee, E., Hurrell, D. L., & Richardson, I. (2014). Improving access to optometry services for people at risk of preventable sight loss: a qualitative study in five UK locations. *J Public Health (Oxf), 36*(4), 667-673.

Lee, A. J., Lee, J., Saw, S. M., Gazzard, G., Koh, D., Widjaja, D., & Tan, D. T. (2002). Prevalence and risk factors associated with dry eye symptoms: a population based study in Indonesia. *Br J Ophthalmol, 86*(12), 1347-1351.

Lee, H., & Caterina, M. J. (2005). TRPV channels as thermosensory receptors in epithelial cells. *Pflugers Arch, 451*(1), 160-167.

Lee, J. H., & Hyun, P. M. (1988). The reproducibility of the Schirmer test. *Korean J Ophthalmol, 2*(1), 5-8.

Lemp, M. A., Bron, A. J., Baudouin, C., Benitez Del Castillo, J. M., Geffen, D., Tauber, J., Foulks, G.N., Pepose, J.S., Sullivan, B. D. (2011). Tear osmolarity in the diagnosis and management of dry eye disease. *Am J Ophthalmol, 151*(5), 792-798.

Lemp, M. A., Crews, L. A., Bron, A. J., Foulks, G. N., & Sullivan, B. D. (2012). Distribution of aqueous-deficient and evaporative dry eye in a clinic-based patient cohort: a retrospective study. *Cornea, 31*(5), 472-478.

Lemp, M. A., & Hamill, J. R., Jr. (1973). Factors affecting tear film breakup in normal eyes. *Arch Ophthalmol, 89*(2), 103-105.

Lemp, M. A., Holly, F. J., Iwata, S., & Dohlman, C. H. (1970). The precorneal tear film. I. Factors in spreading and maintaining a continuous tear film over the corneal surface. *Arch Ophthalmol, 83*(1), 89-94.

Lemp, M. A., & Nichols, K. K. (2009). Blepharitis in the United States 2009: a survey-based perspective on prevalence and treatment. *Ocul Surf, 7*(2 Suppl), S1-s14.

Li, J., Zheng, K., Deng, Z., Zheng, J., Ma, H., Sun, L., & Chen, W. (2015). Prevalence and risk factors of dry eye disease among a hospital-based population in southeast China. *Eye Contact Lens, 41*(1), 44-50.

Li, W., Graham, A. D., Selvin, S., & Lin, M. C. (2015). Ocular Surface Cooling Corresponds to Tear Film Thinning and Breakup. *Optom Vis Sci, 92*(9), e248-256.

Li, X. M., Hu, L., Hu, J., & Wang, W. (2007). Investigation of dry eye disease and analysis of the pathogenic factors in patients after cataract surgery. *Cornea, 26*(9 Suppl 1), S16-20.

Liao, C., Lin, H.-N., Luo, M. M., & Chea, S. (2017). Factors influencing online shoppers' repurchase intentions: The roles of satisfaction and regret. *Information & Management*, 54(5), 651–668.

Lienert, J. P., Tarko, L., Uchino, M., Christen, W. G., & Schaumberg, D. A. (2016). Long-term Natural History of Dry Eye Disease from the Patient's Perspective. *Ophthalmology, 123*(2), 425-433.

Lightman, D. A., & Brod, R. D. (1994). Relationship between floaters, light flashes, or both, and complications of posterior vitreous detachment. *Am J Ophthalmol, 118*(5), 683-684.

Lim, T.O., Ngah, B.A. (1991). The Mentakab hypertension study project. Part II – why do hypertensives drop out of treatment? *Singapore Medical Journal*, 32(4), 249–251.

Lin, P. Y., Cheng, C. Y., Hsu, W. M., Tsai, S. Y., Lin, M. W., Liu, J. H., & Chou, P. (2005). Association between symptoms and signs of dry eye among an elderly Chinese population in Taiwan: the Shihpai Eye Study. *Invest Ophthalmol Vis Sci, 46*(5), 1593-1598.

Lin, P. Y., Tsai, S. Y., Cheng, C. Y., Liu, J. H., Chou, P., & Hsu, W. M. (2003). Prevalence of dry eye among an elderly Chinese population in Taiwan: the Shihpai Eye Study. *Ophthalmology, 110*(6), 1096-1101.

Lin, S., Mihailovic, A., West, S. K., Johnson, C. A., Friedman, D. S., Kong, X., & Ramulu, P. Y. (2018). Predicting Visual Disability in Glaucoma With Combinations of Vision Measures. *Transl Vis Sci Technol, 7*(2), 22.

Lindsley, K., Matsumura, S., Hatef, E., & Akpek, E. K. (2012). Interventions for chronic blepharitis. *Cochrane Database Syst Rev*(5), Cd005556.

Linton, R. G., Curnow, D. H., & Riley, W. J. (1961). The meibomian glands: an investigation into secretions and some aspects of the physiology. *Br J Ophthalmol, 45*(11), 718-723.

Little, R.J.A., Rubin, D.B. (2002). Statistical analysis with missing data. Wiley series in probability and statistics. Wiley, Hoboken, NJ

Liu, H., Begley, C., Chen, M., Bradley, A., Bonanno, J., McNamara, N. A., Nelson, J.D., Simpson, T. (2009). A link between tear instability and hyperosmolarity in dry eye. *Invest Ophthalmol Vis Sci, 50*(8), 3671-3679.

Liu, J., Sheha, H., & Tseng, S. C. (2010). Pathogenic role of Demodex mites in blepharitis. *Curr Opin Allergy Clin Immunol, 10*(5), 505-510

Liu, X., Gu, Y. S., & Xu, Y. S. (2008). Changes of tear film and tear secretion after phacoemulsification in diabetic patients. *J Zhejiang Univ Sci B, 9*(4), 324-328.

Lloyd, C., King, R., Bassett, H., Sandland, S., Savige, G. (2001). Patient, client or consumer? A survey of preferred terms. *Australasian Psychiatry,* 9, 321–324.

Local Optical Committee Support Unit (LOCSU) community services (2016). Minor eye conditions service pathway. Retrieved October 25, 2018, http://www.locsu.co.uk/community-services-pathways/primary-eyecare-assessment-and-referral-pears/

Lonial, S., Raju, P.S. (2015). Impact of service attributes on customer satisfaction and loyalty in a healthcare context. *Leadership in Health Services*, 28(2), 149- 166.

Lovelock, C., & Gummesson, E. (2004). Whither Services Marketing?: In Search of a New Paradigm and Fresh Perspectives. Journal of Service Research, 7(1), 20–41.

Lovelock, C. H., & Young, R. F. (1979). Look to consumers to increase productivity. *Harvard Business Review,* 57(3), 168–178

Lu, P., Chen, X., Liu, X., Yu, L., Kang, Y., Xie, Q., Ke, L., Wei, X. (2008). Dry eye syndrome in elderly Tibetans at high altitude: a population-based study in China. *Cornea, 27*(5), 545-551.

MacCallum, R.C., Widaman, K.F., Preacher, K.J & Hong, S. (2001). Sample size in factor analysis: the role of model error. *Multivariate Behavioral Research*, 36, 611-637.

Machalinska, A., Zakrzewska, A., Adamek, B., Safranow, K., Wiszniewska, B., Parafiniuk, M., & Machalinski, B. (2015). Comparison of Morphological and Functional Meibomian Gland Characteristics Between Daily Contact Lens Wearers and Nonwearers. *Cornea, 34*(9), 1098-1104.

Mackenzie, P. J., Russell, M., Ma, P. E., Isbister, C. M., & Maberley, D. A. (2007). Sensitivity and specificity of the optos optomap for detecting peripheral retinal lesions. *Retina, 27*(8), 1119-1124.

Macri, A., Scanarotti, C., Bassi, A. M., Giuffrida, S., Sangalli, G., Traverso, C. E., & Iester, M. (2015). Evaluation of oxidative stress levels in the conjunctival epithelium of patients with or without dry eye, and dry eye patients treated with preservative-free hyaluronic acid 0.15 % and vitamin B12 eye drops. *Graefes Arch Clin Exp Ophthalmol, 253*(3), 425-430.

Malet, F., Le Goff, M., Colin, J., Schweitzer, C., Delyfer, M. N., Korobelnik, J. F., Rougier, M.B., Radeau, T., Dartigues, J.F., Delcourt, C. (2014). Dry eye disease in French elderly subjects: the Alienor Study. *Acta Ophthalmol, 92*(6), e429-436.

Manthorpe, R., Asmussen, K., & Oxholm, P. (1997). Primary Sjögren's syndrome: diagnostic criteria, clinical features, and disease activity. *J Rheumatol Suppl, 50*, 8-11.

Mariño-López, A., Sousa-Castillo, A., Carbó-Argibay, E., Otero-Espinar, F., Alvarez-Puebla, R. A., Pérez-Lorenzo, M., & Correa-Duarte, M. A. (2019). Laser-protective soft contact lenses: Keeping an eye on the eye through plasmonics. *Applied Materials Today*, 15, 1–5.

Market Research Future (MRF) (2019). False eyelashes market research report- global forecast. Retrieved July 31, 2019, https://www.marketresearchfuture.com/reports/false-eyelashes-market-2921

Martin, A., Martin, C., Martin, P. B., Martin, P. A., Green, G., & Eldridge, S. (2002). 'Inappropriate' attendance at an accident and emergency department by adults registered in local general practices: how is it related to their use of primary care? *J Health Serv Res Policy, 7*(3), 160-165.

Mason, T., Jones, C., Sutton, M., Konstantakopoulou, E., Edgar, D. F., Harper, R. A., Birch, S., Lawrenson, J. G. (2017). Retrospective economic analysis of the transfer of services from hospitals to the community: an application to an enhanced eye care service. *BMJ Open, 7*(7), e014089.

Mathers, W. D., & Lane, J. A. (1998). Meibomian gland lipids, evaporation, and tear film stability. *Adv Exp Med Biol, 438*, 349-360.

Mathers, W. D., Lane, J. A., Sutphin, J. E., & Zimmerman, M. B. (1996). Model for ocular tear film function. *Cornea, 15*(2), 110-119.

Mathers, W. D., Lane, J. A., & Zimmerman, M. B. (1996). Tear film changes associated with normal aging. *Cornea, 15*(3), 229-234.

Mathers, W. D., Shields, W. J., Sachdev, M. S., Petroll, W. M., & Jester, J. V. (1991). Meibomian gland dysfunction in chronic blepharitis. *Cornea, 10*(4), 277-285.

Mathers, W. D., Stovall, D., Lane, J. A., Zimmerman, M. B., & Johnson, S. (1998). Menopause and tear function: the influence of prolactin and sex hormones on human tear production. *Cornea, 17*(4), 353-358.

Mathews, P. M., Ramulu, P. Y., Swenor, B. S., Utine, C. A., Rubin, G. S., & Akpek, E. K. (2017). Functional impairment of reading in patients with dry eye. *Br J Ophthalmol, 101*(4), 481-486.

Mayers, M., Jansen Bishop, M., Walerius, D., Conway, K., Usseglio, M., Hasty, S., & Allison, S. (2019). Improving your spectacle patients' in-practice experience with contact lenses during frame selection. *Cont Lens Anterior Eye, 42*(4), 406-410.

Maze Feedback Ltd. Case Studies: Specsavers. Retrieved 28 April 2019 from: https://en.mymaze.com/casestories/specsavers/

McAlinden, C., Gao, R., Wang, Q., Zhu, S., Yang, J., Yu, A., Bron, A.J., Huang, J. (2017). Rasch analysis of three dry eye questionnaires and correlates with objective clinical tests. *Ocul Surf, 15*(2), 202-210.

McCarter, R. V., Neville, C. E., Silvestri, G., Montgomery, S., Moore, E., Silvestri, V., Cardwell, C.R., Hogg, R.E., Woodside, J.V., McKay, G. J. (2019). Dietary patterns were not associated with age-related macular degeneration: a cross-sectional analysis in the Irish Nun Eye Study. *Ir J Med Sci*., 188(3): 1005-1012.

McCarty, C. A., Bansal, A. K., Livingston, P. M., Stanislavsky, Y. L., & Taylor, H. R. (1998). The epidemiology of dry eye in Melbourne, Australia. *Ophthalmology, 105*(6), 1114-1119.

McColl-Kennedy, J. R., Danaher, T. S., Gallan, A. S., Orsingher, C., Lervik-Olsen, L., & Verma, R. (2017). How do you feel today? Managing patient emotions during health care experiences to enhance well-being. *Journal of Business Research*, 79, 247–259.

McCracken, M. (2013). Auditing an acute eye pathway. *Optometry Today*, 22, 34–37.

McDonald, C.C., Kaye, S.B., Figueiredo, F.C., Macintosh, G., Lockett, C. (2002). A randomised, crossover, multicentre study to compare the performance of 0.1% (w/v) sodium hyaluronate with 1.4% (w/v) polyvinyl alcohol in the alleviation of symptoms associated with dry eye syndrome. *Eye*, 16(5), 601–607.

McDonnell, P. J. (1988). How do general practitioners manage eye disease in the community? *Br J Ophthalmol, 72*(10), 733-736.

McDonnell, P. J., Pflugfelder, S. C., Stern, M. E., Hardten, D. R., Conway, T., Villanueva, L., & Hollander, D. A. (2017). Study design and baseline findings from the progression of ocular findings (PROOF) natural history study of dry eye. *BMC Ophthalmol, 17*(1), 265.

McDougall, G.H.G, Levesque, T. (2000). Customer satisfaction with services: putting perceived value into the equation. *Journal of Services Marketing*, 14(5), 392-410.

McGill, J.I., Easty, D.L., Levy, I., Holt-Wilson, A.D., Shilling, J. (1971). The aetiology and treatment of marginal corneal ulcers. *Trans Ophthalmol Soc UK*, 91, 501–507.

McKenzie, R. W., Jumblatt, J. E., & Jumblatt, M. M. (2000). Quantification of MUC2 and MUC5AC transcripts in human conjunctiva. *Invest Ophthalmol Vis Sci, 41*(3), 703-708.

McMonnies, C. W. (1986). Key questions in a dry eye history. *J Am Optom Assoc, 57*(7), 512-517.

McMonnies, C. W. (2007). Incomplete blinking: exposure keratopathy, lid wiper epitheliopathy, dry eye, refractive surgery, and dry contact lenses. *Cont Lens Anterior Eye, 30*(1), 37-51.

McMonnies, C. W. (2011). Blink efficiency: a neglected area of ocular surface disease management? *Invest Ophthalmol Vis Sci, 52*(7), 4484.

McMonnies, C. W., & Ho, A. (1987). Responses to a dry eye questionnaire from a normal population. *J Am Optom Assoc, 58*(7), 588-591.

McMonnies, C.W., Ho, A.(1986). Marginal dry eye diagnosis: history versus biomicroscopy. In: Holly FJ, ed. The Pre-Ocular Tear Film in Health, Disease and Contact Lens Wear. Lubbock, TX: Dry Eye Institute, 32-40.

McMullan, R. D., Berle, D., Arnaez, S., & Starcevic, V. (2018). The relationships between health anxiety, online health information seeking, and cyberchondria: Systematic review and meta-analysis. *J Affect Disord, 245*, 270-278.

Mencucci, R., Boccalini, C., Caputo, R., & Favuzza, E. (2015). Effect of a hyaluronic acid and carboxymethylcellulose ophthalmic solution on ocular comfort and tear-film instability after cataract surgery. *J Cataract Refract Surg, 41*(8), 1699-1704.

Mengher, L. S., Bron, A. J., Tonge, S. R., & Gilbert, D. J. (1985a). Effect of fluorescein instillation on the pre-corneal tear film stability. *Curr Eye Res, 4*(1), 9-12.

Mengher, L. S., Bron, A. J., Tonge, S. R., & Gilbert, D. J. (1985b). A non-invasive instrument for clinical assessment of the pre-corneal tear film stability. *Curr Eye Res, 4*(1), 1-7.

Mihaltz, K., Knorz, M. C., Alio, J. L., Takacs, A. I., Kranitz, K., Kovacs, I., & Nagy, Z. Z. (2011). Internal Aberrations and Optical Quality After Femtosecond Laser Anterior Capsulotomy in Cataract Surgery. *Journal of Refractive Surgery*, 27(10), 711-716.

Miljanovic, B., Dana, R., Sullivan, D. A., & Schaumberg, D. A. (2007). Impact of dry eye syndrome on vision-related quality of life. *Am J Ophthalmol, 143*(3), 409-415.

Miller, K. L., Walt, J. G., Mink, D. R., Satram-Hoang, S., Wilson, S. E., Perry, H. D., Asbell, P.A., Pflugfelder, S. C. (2010). Minimal clinically important difference for the ocular surface disease index. *Arch Ophthalmol, 128*(1), 94-101.

Mintel (2017). Optical Goods and Retailing, Mintel Group, London. Retrieved 2 May 2019, https://store.mintel.com/optical-goods-retailing-uk-february-2017

Mintel (2019). Optical Goods and Retailing, Mintel Group, London. Retrieved 2 May 2019, https://store.mintel.com/optical-goods-retailing-uk-february-2019

Mishima, S., & Maurice, D. M. (1961). The oily layer of the tear film and evaporation from the corneal surface. *Exp Eye Res, 1*, 39-45.

Mittal, B., Lassar, W.M. (1998). Why do customers switch? The dynamics of satisfaction versus loyalty. *Journal of Services Marketing*, 12(3), 177- 192.

Mittal, V., Kamakura, W.A. (2001). Satisfaction, Repurchase Intent, and Repurchase Behavior: Investigating the Moderating Effect of Customer Characteristics. *Journal of Marketing Research*, 38(1), 131- 142.

Miyake, K., & Yokoi, N. (2017). Influence on ocular surface after cataract surgery and effect of topical diquafosol on postoperative dry eye: a multicenter prospective randomized study. Clin Ophthalmol, 11, 529-540.

Mizuno, Y., Yamada, M., & Miyake, Y. (2010). Association between clinical diagnostic tests and health-related quality of life surveys in patients with dry eye syndrome. *Jpn J Ophthalmol, 54*(4), 259-265.

Mooi, J. K., Wang, M. T. M., Lim, J., Muller, A., & Craig, J. P. (2017). Minimising instilled volume reduces the impact of fluorescein on clinical measurements of tear film stability. *Cont Lens Anterior Eye, 40*(3), 170-174.

Moon, H., Yoon, J. H., Hyun, S. H., & Kim, K. H. (2014). Short-term influence of aspirating speculum use on dry eye after cataract surgery: a prospective study. *Cornea*, 33(4), 373-375.

Moore, J. E., Graham, J. E., Goodall, E. A., Dartt, D. A., Leccisotti, A., McGilligan, V. E., & Moore, T. C. (2009). Concordance between common dry eye diagnostic tests. *Br J Ophthalmol, 93*(1), 66-72.

Moore, P.J., Sickel, A.E., Malat, J., Williams, D., Jackson, J., Adler, N.E. (2004). Psychosocial factors in medical and psychological treatment avoidance: the role of the doctor-patient relationship. *Journal of Health Psychology*, 9(3), 421–433.

Moorfields Eye Hospital (MEH) (2017). GP handbook: common eye condition management. Retrieved 15 May 2019 from: https://www.moorfields.nhs.uk/content/gp-handbook

Morejon, A., Mayo-Iscar, A., Martin, R., & Ussa, F. (2019). Development of a new algorithm based on FDT Matrix perimetry and SD-OCT to improve early glaucoma detection in primary care. *Clin Ophthalmol, 13*, 33-42.

Morgan, P.B., Efron, N. (1998). The oxygen performance of contemporary hydrogel contact lenses. *Cont Lens Anterior Eye*, 21, 3–6.

Morgan, P. B., & Efron, N. (2015). Influence of practice setting on contact lens prescribing in the United Kingdom. *Cont Lens Anterior Eye*, 38(1), 70-72.

Morgan, P. B., Efron, N., Hill, E. A., Raynor, M. K., Whiting, M. A., & Tullo, A. B. (2005). Incidence of keratitis of varying severity among contact lens wearers. *Br J Ophthalmol*, 89(4), 430-436.

Morgan, P. B., Efron, N., & Woods, C. A. (2011). An international survey of contact lens prescribing for presbyopia. *Clin Exp Optom, 94*(1), 87-92.

Mori, A., Oguchi, Y., Okusawa, Y., Ono, M., Fujishma, H., Tsubota, K. (1997). Application of High-speed high resolution thermography for evaluation of tear film layer. *Am J Ophthalmol.*, 124, 729–735.

Morris, C. A., Holden, B. A., Papas, E., Griesser, H. J., Bolis, S., Anderton, P., & Carney, F. (1998). The ocular surface, the tear film, and the wettability of contact lenses. *Adv Exp Med Biol, 438*, 717-722.

Moss, S. E., Klein, R., & Klein, B. E. (2000). Prevalence of and risk factors for dry eye syndrome. *Arch Ophthalmol, 118*(9), 1264-1268.

Moss, S. E., Klein, R., & Klein, B. E. (2004). Incidence of dry eye in an older population. *Arch Ophthalmol, 122*(3), 369-373.

Moss, S. E., Klein, R., & Klein, B. E. (2008). Long-term incidence of dry eye in an older population. *Optom Vis Sci, 85*(8), 668-674.

Murphy, A. L., Gardner, D. M., & Jacobs, L. M. (2018). Patient care activities by community pharmacists in a capitation funding model mental health and addictions program. *BMC Psychiatry*, 18(1), 192.

Murphy, A. W., Leonard, C., Plunkett, P. K., Brazier, H., Conroy, R., Lynam, F., & Bury, G. (1999). Characteristics of attenders and their attendances at an urban accident and emergency department over a one year period. *J Accid Emerg Med, 16*(6), 425-427.

Nagy, N., Decaestecker, C., Kiss, R., Rypens, F., Van Gansbeke, D., Mockel, J., Rocmans, P., Salmon, I. (1999). A pilot study for identifying at risk thyroid lesions by means of a decision tree run on clinicocytological variables. *Int J Mol Med, 4*(3), 299-308.

Nair, B.R. (1998). Patient, client or customer? *Medical Journal of Australia*, 169, 593.

Nakamori, K., Odawara, M., Nakajima, T., Mizutani, T., & Tsubota, K. (1997). Blinking is controlled primarily by ocular surface conditions. *Am J Ophthalmol, 124*(1), 24-30.

Nasir, S., Nasir, V.A. (2005). Analyzing the role of customer-base differences in developing customer relationship management strategies. *Journal of American Academy of Business, Cambridge*, 7(2), 32-38.

National Health Service (NHS) (2016). Common health questions: how often can I have a free NHS eye test. Retrieved 9 May 2019 from: https://www.nhs.uk/common-health-questions/nhs-services-and-treatments/

National Institute for Health and Care Excellence (NICE) (2015a). LipiFlow thermal pulsation treatment for dry eyes caused by blocked Meibomian glands. Medtech Innovation briefing [MI29]. Retrieved 15 May 2019 from https://www.nice.org.uk/advice/mib29/chapter/About-this-briefing

National Institute for Health and Care Excellence (NICE) (2015b). TearLab osmolarity system for diagnosing dry eye disease. Medtech Innovation briefing [MIB47]. Retrieved 20 May 2019 from https://www.nice.org.uk/advice/mib47

National Institute for Health and Care excellence (NICE) (2015c). Clinical Knowledge Summaries: Retinal detachment. Retrieved November 1, 2018, https://cks.nice.org.uk/retinal-detachment#!scenario

National Institute for Health and Care Excellence (NICE) (2017). Cataracts in adults: management. Retrieved 9 June 2019 from: https://www.nice.org.uk/guidance/ng77/chapter/Recommendations

National Prescribing Centre (2010). Non-medical Prescribing. A Quick Guide for Commissioners. NHS National Prescribing Centre, Liverpool. Retrieved November 25, 2018, http://www.npc.nhs.uk/non_medical/resources/NMP_QuickGuide.pdf

Natkunarajah, M., Goldsmith, C., & Goble, R. (2003). Diagnostic effectiveness of noncontact slitlamp examination in the identification of retinal tears. *Eye (Lond), 17*(5), 607-609.

Needle, J. J., Petchey, R., & Lawrenson, J. G. (2008). A survey of the scope of therapeutic practice by UK optometrists and their attitudes to an extended prescribing role. *Ophthalmic Physiol Opt, 28*(3), 193-203.

Nelson, J. D., Craig, J. P., Akpek, E. K., Azar, D. T., Belmonte, C., Bron, A. J., Clayton, J.A., Dogru, M., Dua, H.S., Foulks, G.N., Gomes, J.A.P., Hammitt, K.M., Holopainen, J., Jones, L., Joo, C.K., Liu, Z., Nicholls, J.J., Nichols, K.K., Novack, G.D., Sangwan, V., Stapleton, F, Tomlinson, A., Tsubota, K., Wilcox, M.D.P., Wolffsohn, J.S., Sullivan, D. A. (2017). TFOS DEWS II Introduction. *Ocul Surf*, 15(3), 269-275.

Neville, C. E., Montgomery, S., Silvestri, G., McGowan, A., Moore, E., Silvestri, V., Cardwell, C., McEvoy, C.T., Maxwell, A.P., Woodside, J.V., McKay, G. J. (2018). Dietary Patterns and Retinal Vessel Caliber in the Irish Nun Eye Study. *J Nutr Health Aging, 22*(7), 751-758.

Newby, P. K., & Tucker, K. L. (2004). Empirically derived eating patterns using factor or cluster analysis: a review. *Nutr Rev, 62*(5), 177-203.

Ng, S., Russell-Bennett, R. (2015). The Role of Affect in Consumer Evaluation of Health Care Services. *Health Marketing Quarterly*, 32(1), 31–47.

Ngo, W., Situ, P., Keir, N., Korb, D., Blackie, C., & Simpson, T. (2013). Psychometric properties and validation of the Standard Patient Evaluation of Eye Dryness questionnaire. *Cornea, 32*(9), 1204-1210.

NHS Central Mersey Diabetic Retinopathy Screening Programme (NHS) (2018). VA comparison chart. Retrieved 1 May 2018 from: http://www.locnet.org.uk/media/1266/va_comparison_chart.pdf

NHS Digital (2018). Hospital outpatient activity 2017-18. Retrieved November 1, 2018, https://digital.nhs.uk/data-and-information/publications/statistical/hospital-outpatient-activity/2017-18

Nichols, J. J., & King-Smith, P. E. (2003). Thickness of the pre- and post-contact lens tear film measured in vivo by interferometry. *Invest Ophthalmol Vis Sci, 44*(1), 68-77.

Nichols, J. J., Willcox, M. D., Bron, A. J., Belmonte, C., Ciolino, J. B., Craig, J. P., Dogru, M., Foulks, G.N., Jones, L., Nelson, J.D., Nichols, K.K., Purslow, C., Schaumberg, D.A., Stapleton, F., Sullivan, D. A. (2013). The TFOS International Workshop on Contact Lens Discomfort: executive summary. *Invest Ophthalmol Vis Sci*, 54(11), 7-13.

Nichols, J. J., Ziegler, C., Mitchell, G. L., & Nichols, K. K. (2005). Self-reported dry eye disease across refractive modalities. *Invest Ophthalmol Vis Sci, 46*(6), 1911-1914.

Nichols, K. K., Begley, C. G., Caffery, B., & Jones, L. A. (1999). Symptoms of ocular irritation in patients diagnosed with dry eye. *Optom Vis Sci, 76*(12), 838-844.

Nichols, K. K., Mitchell, G. L., & Zadnik, K. (2004a). The repeatability of clinical measurements of dry eye. *Cornea, 23*(3), 272-285.

Nichols, K. K., Nichols, J. J., & Mitchell, G. L. (2004b). The lack of association between signs and symptoms in patients with dry eye disease. *Cornea, 23*(8), 762-770.

Nichols, K.K., Nichols, J.J., Zadnik, K. (2000). Frequency of dry eye diagnostic test procedures used in various modes of ophthalmic practice. *Cornea*, 19, 477–482.

Nichols, K. K., Redfern, R. L., Jacob, J. T., Nelson, J. D., Fonn, D., Forstot, S. L., Huang, J.F., Holden, B.A., Nichols, J.J. (2013). The TFOS International Workshop on Contact Lens Discomfort: report of the definition and classification subcommittee. *Invest Ophthalmol Vis Sci*, 54(11), 14-19.

Noble, C. H., & Mokwa, M. P. (1999). Implementing marketing strategies: Developing and testing a managerial theory. *Journal of Marketing*, 63(4), 57–73.

Normann, R. (2000). *Service management : strategy and leadership in service business,* 3rd edn. Chichester : John Wiley & Sons, 2000.

Norn, M. (1987). Expressibility of meibomian secretion. Relation to age, lipid precorneal film, scales, foam, hair and pigmentation. *Acta Ophthalmol (Copenh), 65*(2), 137-142

Norn, M. S. (1969). Desiccation of the precorneal film. I. Corneal wetting-time. *Acta Ophthalmol (Copenh), 47*(4), 865-880.

Norn, M.S. (1970). Demodex folliculorum. Incidence and possible pathogenic role in the human eyelid. *Acta Ophthalmol Suppl*, 108, 7–85.

Norn, M. S. (1977). Treatment of keratoconjunctivitis sicca with liquid paraffin or polyvinyl alcohol in double-blind trial. *Acta Ophthalmol (Copenh), 55*(6), 945-950.

Nosch, D. S., Foppa, C., Toth, M., & Joos, R. E. (2015). Blink Animation Software to Improve Blinking and Dry Eye Symptoms. *Optom Vis Sci, 92*(9), e310-315.

Novack, G. D., Asbell, P., Barabino, S., Bergamini, M. V. W., Ciolino, J. B., Foulks, G. N., . . . Stapleton, F. (2017). TFOS DEWS II Clinical Trial Design Report. *Ocul Surf, 15*(3), 629-649.

Novak, M. A., & Welch, R. B. (1984). Complications of acute symptomatic posterior vitreous detachment. *Am J Ophthalmol, 97*(3), 308-314.

Office for National Statistics (ONS) (2018). Overview of the UK population: November 2018. Retrieved July 31, 2019, https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationestimates/articles/overviewoftheukpopulation/november2018

Oh, T., Jung, Y., Chang, D., Kim, J., & Kim, H. (2012). Changes in the tear film and ocular surface after cataract surgery. *Jpn J Ophthalmol, 56*(2), 113-118.

Omali, N. B., Subbaraman, L. N., Coles-Brennan, C., Fadli, Z., & Jones, L. W. (2015). Biological and Clinical Implications of Lysozyme Deposition on Soft Contact Lenses. *Optom Vis Sci*, 92(7), 750-757.

Onwubiko, S. N., Eze, B. I., Udeh, N. N., Arinze, O. C., Onwasigwe, E. N., & Umeh, R. E. (2014). Dry eye disease: prevalence, distribution and determinants in a hospital-based population. *Cont Lens Anterior Eye, 37*(3), 157-161.

Ooi, E. H., Ng, E. Y., Purslow, C., & Acharya, R. (2007). Variations in the corneal surface temperature with contact lens wear. *Proc Inst Mech Eng H, 221*(4), 337-349

Optometry Today (OT) (2019). In practice: Hearing the benefits. *Journal of the Association of Optometrists*, 59 (8), 43-45.

Ordanini, A., & Parasuraman, A. (2011). Service Innovation Viewed Through a Service-Dominant Logic Lens: A Conceptual Framework and Empirical Analysis. *Journal of Service Research*, 14(1), 3-23.

Ozdemir, M., & Temizdemir, H. (2010). Age- and gender-related tear function changes in normal population. *Eye (Lond), 24*(1), 79-83.

Pacheco, N. A., Becker, L. C. B., & Brei, V. A. (2017). A light in the dark: The benefits of co-production in service failures. *Journal of Retailing and Consumer Services*, 34, 95–101.

Pallant, J. SPSS survival manual. A step by step guide to data analysis using SPSS. 6th Edition. McDraw-Hill, Berkshire. 2016. (chapter 15, p182-203)

Pancholi, B.R., Dunne, M.C.M. (2018). Virtual patient instruction and self-assessment accuracy in optometry students. Optometric Education. Retrieved January 17, 2019, https://journal.opted.org/article/virtual-patient-instruction-and-self-assessment-accuracy-in-optometry-students/

Papas, E. B. (2000). Key factors in the subjective and objective assessment of conjunctival erythema. *Invest Ophthalmol Vis Sci, 41*(3), 687-691.

Papas, E. B., Tilia, D., Tomlinson, D., Williams, J., Chan, E., Chan, J., & Golebiowski, B. (2014). Consequences of wear interruption for discomfort with contact lenses. *Optom Vis Sci*, 91(1), 24-31.

Parasuraman, A. (2004). Assessing and improving service performancefor maximum impact: insights from a two-decade-long research journey. *Performance Measurement and Metrics*, 5(2), 45-52.

Parasuraman, A., Zeithaml, V. A., & Berry, L. L. (1985). A Conceptual Model of Service Quality and Its Implications for Future Research. *Journal of Marketing*, 49(4), 41–50.

Parasuraman, A., Zeithaml, V., Berry, L. (1994). Reassessment of Expectations as a Comparison Standard in Measuring Service Quality: Implications for further research. *Journal of Marketing,* 58(1), 111-124.

Parasuraman, A., Zeithaml, V. A., & Berry, L. L. (1988). SERVQUAL: A Multiple-Item Scale for Measuring Consumer Perceptions of Service Quality. *Journal of Retailing*, *64*(1), 5–6.

Park, D. H., Chung, J. K., Seo, D. R., & Lee, S. J. (2016). Clinical Effects and Safety of 3% Diquafosol Ophthalmic Solution for Patients With Dry Eye After Cataract Surgery: A Randomized Controlled Trial. *Am J Ophthalmol, 163*, 122-131.e122.

Parkins, D.J.C.R., Pooley, J.E. & Ryan, B. (2014). The developing role of optometrists as part of the NHS primary care team. *Optom Pract*, 15, 177–184.

Patel, D., Baker, H., & Murdoch, I. (2006). Barriers to uptake of eye care services by the Indian population living in Ealing, west London. *Health Educ J*, 65(3), 267-276.

Patel, N.I. (2015). Exploring Business Models to provide a foundation for enhanced eye care services in high street optometric practice. *DOptom thesis*, Aston University.

Patel, N. I., Naroo, S. A., Eperjesi, F., & Rumney, N. J. (2015). Customer loyalty among daily disposable contact lens wearers. *Cont Lens Anterior Eye, 38*(1), 15-20.

Patel, S., Henderson, R., Bradley, L., Galloway, B., & Hunter, L. (1991). Effect of visual display unit use on blink rate and tear stability. *Optom Vis Sci, 68*(11), 888-892.

Patricio, L., Fisk, R. P., & e Cunha, J. F. (2008). Designing Multi-Interface Service Experiences: The Service Experience Blueprint. *Journal of Service Research*, 10(4), 318-334.

Patterson, P. G., & Smith, T. (2003). A cross-cultural study of switching barriers and propensity to stay with service providers. *Journal of Retailing*, 79(2), 107–120.

Paulsen, A. J., Cruickshanks, K. J., Fischer, M. E., Huang, G. H., Klein, B. E., Klein, R., & Dalton, D. S. (2014). Dry eye in the beaver dam offspring study: prevalence, risk factors, and health-related quality of life. *Am J Ophthalmol, 157*(4), 799-806.

Peng, C. C., Cerretani, C., Braun, R. J., & Radke, C. J. (2014). Evaporation-driven instability of the precorneal tear film. *Adv Colloid Interface Sci, 206*, 250-264.

Petricek, I., Prost, M., & Popova, A. (2006). The differential diagnosis of red eye: a survey of medical practitioners from Eastern Europe and the Middle East. *Ophthalmologica, 220*(4), 229-237.

Pett, M., Lackey, N. & Sullivan, J. (2003). Making sense of factor analysis. Thousand Oaks: Sage Publications, Inc.

Petty, R. E., & Cacioppo, J. T. (1984). Source Factors and the Elaboration Likelihood Model of Persuasion. *Advances in Consumer Research*, *11*(1), 668–672.

Pflugfelder, S. C., Tseng, S. C., Sanabria, O., Kell, H., Garcia, C. G., Felix, C., Feuer, W., Reis, B. L. (1998). Evaluation of subjective assessments and objective diagnostic tests for diagnosing tear-film disorders known to cause ocular irritation. *Cornea, 17*(1), 38-56.

Pierscionek, T. J., Moore, J. E., & Pierscionek, B. K. (2009). Referrals to ophthalmology: optometric and general practice comparison. *Ophthalmic Physiol Opt, 29*(1), 32-40.

Poon, K. H., Yeo, S., & Tong, L. (2014). Lost to follow-up for appointments in a dedicated dry eye clinic. *Patient Prefer Adherence, 8*, 1409-1418.

Poplin, R., Varadarajan, A. V., Blumer, K., Liu, Y., McConnell, M. V., Corrado, G. S., Peng, L., Webster, D. R. (2018). Prediction of cardiovascular risk factors from retinal fundus photographs via deep learning. *Nature Biomedical Engineering, 2*(3), 158-164.

Portello, J. K., Rosenfield, M., & Chu, C. A. (2013). Blink rate, incomplete blinks and computer vision syndrome. *Optom Vis Sci, 90*(5), 482-487.

Potvin, R., Makari, S., & Rapuano, C. J. (2015). Tear film osmolarity and dry eye disease: a review of the literature. *Clin Ophthalmol, 9*, 2039-2047.

Pouyeh, B., Viteri, E., Feuer, W., Lee, D. J., Florez, H., Fabian, J. A., Perez, V.L., Galor, A. (2012). Impact of ocular surface symptoms on quality of life in a United States veterans affairs population. *Am J Ophthalmol, 153*(6), 1061-1066.

Power, W. J., Collum, L. M., Easty, D. L., Bloom, P. A., Laidlaw, D. A., Libert, J., Sangers, D., Wuokko, M., Saksela, T. (1993). Evaluation of efficacy and safety of ciprofloxacin ophthalmic solution versus chloramphenicol. *Eur J Ophthalmol, 3*(2), 77-82.

Prahalad, C. K., & Ramaswamy, V. (2004). Co-Creation Experiences: The Next Practice in Value Creation. *Journal of Interactive Marketing*, 18(3), 5-14.

Prajna, N. V., George, C., Selvaraj, S., Lu, K. L., McDonnell, P. J., & Srinivasan, M. (2001). Bacteriologic and clinical efficacy of ofloxacin 0.3% versus ciprofloxacin 0.3% ophthalmic solutions in the treatment of patients with culture-positive bacterial keratitis. *Cornea, 20*(2), 175-178.

Prescott, C. (2018). Internet access – households and individuals, Great Britain: 2018. Retrieved November 18, 2018, https://www.ons.gov.uk/peoplepopulationandcommunity/householdcharacteristics/homeinternetandsocialmediausage/bulletins/internetaccesshouseholdsandindividuals/2018

Pritchard, N., Fonn, D., & Brazeau, D. (1999). Discontinuation of contact lens wear: a survey. *Int Contact Lens Clin, 26*(6), 157-162.

Public Health England (PHE) (2017). Health and social care: Child vision screening guidance. Retrieved 25 May 2019 from, https://www.gov.uk/government/publications/child-vision-screening

Pucker, A. D., Jones-Jordan, L. A., Li, W., Kwan, J. T., Lin, M. C., Sickenberger, W., Marx, S., Srinivasan, S., Jones, L. W. (2015). Associations with Meibomian Gland Atrophy in Daily Contact Lens Wearers. *Optom Vis Sci, 92*(9), e206-213.

Pucker, A. D., Jones-Jordan, L. A., Marx, S., Powell, D. R., Kwan, J. T., Srinivasan, S., Sickenberger, W., Jones, L. (2019). Clinical factors associated with contact lens dropout. *Cont Lens Anterior Eye, 42*(3), 318-324.

Pult, H. (2014). Dry eye tool box. Retrieved March 10, 2019, https://www.heiko-pult.de/international.html

Pult, H., & Riede-Pult, B. H. (2012). Non-contact meibography: keep it simple but effective. *Cont Lens Anterior Eye, 35*(2), 77-80.

Pult, H., & Riede-Pult, B. H. (2019). Impact of soft contact lenses on lid- parallel conjunctival folds. *Cont Lens Anterior Eye, 42*(4), 415-419.

Pult, H., Riede-Pult, B. H., & Murphy, P. J. (2013). The relation between blinking and conjunctival folds and dry eye symptoms. *Optom Vis Sci, 90*(10), 1034-1039.

Purslow, C., Wolffsohn, J. S., & Santodomingo-Rubido, J. (2005). The effect of contact lens wear on dynamic ocular surface temperature. *Cont Lens Anterior Eye, 28*(1), 29-36.

Quinto, G. G., Campos, M., & Behrens, A. (2008). Autologous serum for ocular surface diseases. *Arq Bras Oftalmol, 71*(6 Suppl), 47-54.

Rambold, H., Sprenger, A., & Helmchen, C. (2002). Effects of voluntary blinks on saccades, vergence eye movements, and saccade-vergence interactions in humans. *J Neurophysiol, 88*(3), 1220-1233.

Ramos-Casals, M., Brito-Zeron, P., Siso-Almirall, A., & Bosch, X. (2012). Primary Sjögren's syndrome. *Bmj, 344*, e3821.

Read, S. M., & George, S. (1994). Nurse practitioners in accident and emergency departments: reflections on a pilot study. *J Adv Nurs, 19*(4), 705-716.

Reichheld, F. F., & Schefter, P. (2000). E-Loyalty: Your Secret Weapon on the Web. Harvard Business Review, 78(4), 105-113.

Reimer, A., Kuehn, R. (2005). The impact of servicescape on quality perception. *European Journal of Marketing*, 39 (7/8), 785-808.

Richdale, K., Sinnott, L. T., Skadahl, E., & Nichols, J. J. (2007). Frequency of and factors associated with contact lens dissatisfaction and discontinuation. *Cornea, 26*(2), 168-174.

Rigby, D., & Zook, C. (2002). Open-Market Innovation. *Harvard Business Review*, *80*(10), 80–89.

Roberts, C. W., Carniglia, P. E., & Brazzo, B. G. (2007). Comparison of topical cyclosporine, punctal occlusion, and a combination for the treatment of dry eye. *Cornea, 26*(7), 805-809.

Robin, J. B., Jester, J. V., Nobe, J., Nicolaides, N., & Smith, R. E. (1985). In vivo transillumination biomicroscopy and photography of meibomian gland dysfunction. A clinical study. *Ophthalmology, 92*(10), 1423-1426.

Robledo M.A. (2001). Measuring and managing service quality: integrating customer expectations. *Managing Service Quality*; 11(1), 22-31.

Rong, B., Tang, Y., Liu, R., Tu, P., Qiao, J., Song, W., & Yan, X. (2018). Long-Term Effects of Intense Pulsed Light Combined with Meibomian Gland Expression in the Treatment of Meibomian Gland Dysfunction. *Photomed Laser Surg, 36*(10), 562-567.

Rosenthal, P., & Borsook, D. (2012). The corneal pain system. Part I: the missing piece of the dry eye puzzle. *Ocul Surf, 10*(1), 2-14.

Rothman, A. J., & Salovey, P. (1997). Shaping Perceptions to Motivate Healthy Behavior: The Role of Message Framing. *Psychological Bulletin*, 121(1), 3-19.

Royal College of Ophthalmologists (RCOphth) (2010). Cataract Surgery Guidelines September 2010. Retrieved 10 June 2019 from: https://www.rcophth.ac.uk/wp-content/uploads/2014/12/2010-SCI-069-Cataract-Surgery-Guidelines-2010-SEPTEMBER-2010-1.pdf

Royal College of Ophthalmologists (RCOphth) (2017). The Way Forward Cataract Report. Retrieved May 29, 2019, https://www.rcophth.ac.uk/wp-content/uploads/2018/10/RCOphth-Way-Forward-Cataract.pdf

Royal College of Ophthalmologists (RCOphth) (2017). The Way Forward Emergency Eye Care Report. Retrieved September 10, 2018, https://www.rcophth.ac.uk/wp-content/uploads/2015/10/RCOphth-The-Way-Forward-Emergency-Eye-Care-300117.pdf

Rueff, E. M., Varghese, R. J., Brack, T. M., Downard, D. E., & Bailey, M. D. (2016). A Survey of Presbyopic Contact Lens Wearers in a University Setting. *Optom Vis Sci, 93*(8), 848-854.

Ruiz-Alcocer, J., Monsalvez-Romin, D., Garcia-Lazaro, S., Albarran-Diego, C., Hernandez-Verdejo, J. L., & Madrid-Costa, D. (2018). Impact of contact lens material and design on the ocular surface. *Clin Exp Optom*, 101(2), 188-192.

Rumpakis, J. (2010). New data on contact lens dropouts: an international perspective. *Rev. Optom*, 147 (1), 37–40.

Rushton, R. M., Armstrong, R. A., & Dunne, M. C. (2016). The influence on unaided vision of age, pupil diameter and sphero-cylindrical refractive error. *Clin Exp Optom, 99*(4), 328-335.

Russ, M. (2008). Professional Fees: Part 2 – Fee and product pricing calculations. Optician (issue 28/03/2008). Retrieved 18 April 2019 from: http://www.opticianonline.net/professional-fees-part-2-fee-and-product-pricingcalculations/.

Rychalski, A., Hudson, S. (2017). Asymmetric effects of customer emotions on satisfaction and loyalty in a utilitarian service context. *Journal of Business Research*, *71*, 84–91.

Rynerson, J. M., & Perry, H. D. (2016). DEBS - a unification theory for dry eye and blepharitis. *Clinical ophthalmology,10*, 2455–2467.

Saavedra, R., & Kwun, S. K. (2000). Affective states in job characteristics theory. *Journal of Organizational Behavior*, 21, 131–146.

Sackett, D. L., Rosenberg, W. M., Gray, J. A., Haynes, R. B., & Richardson, W. S. (1996). Evidence based medicine: what it is and what it isn't. *BMJ, 312*(7023), 71-72.

Sagoo, M. S., & Raina, J. (2009). Evidence-based medicine audit as a tool for improving emergency ophthalmology. *Eye (Lond), 23*(2), 368-375.

Sahai, A., & Malik, P. (2005). Dry eye: prevalence and attributable risk factors in a hospital-based population. *Indian J Ophthalmol, 53*(2), 87-91.

Sanchez, M. A., Arriola-Villalobos, P., Torralbo-Jimenez, P., Giron, N., de la Heras, B., Herrero Vanrell, R., Alvarez-Barrientos, A., Benitez-del-Castillo, J. M. (2010). The effect of preservative-free HP-Guar on dry eye after phacoemulsification: a flow cytometric study. Eye (Lond), 24(8), 1331-1337.

Saldanha, I. J., Li, T., Yang, C., Owczarzak, J., Williamson, P. R., & Dickersin, K. (2017). Clinical trials and systematic reviews addressing similar interventions for the same condition do not consider similar outcomes to be important: a case study in HIV/AIDS. *J Clin Epidemiol, 84*, 85-94.

Saldanha, I. J., Petris, R., Han, G., Dickersin, K., & Akpek, E. K. (2018). Research Questions and Outcomes Prioritized by Patients With Dry Eye. *JAMA Ophthalmol, 136*(10), 1170-1179.

Sang, X., Li, Y., Yang, L., Liu, J. H., Wang, X. R., Li, C. Y., Liu, Y., Wang, C.J., He, X.J., Wang, S.B., Wang, Z. C. (2018). Lipid layer thickness and tear meniscus height measurements for the differential diagnosis of evaporative dry eye subtypes. *Int J Ophthalmol, 11*(9), 1496-1502.

Satjawatcharaphong, P., Ge, S., & Lin, M. C. (2015). Clinical Outcomes Associated with Thermal Pulsation System Treatment. Optom Vis Sci, 92(9), e334-341.

Savini, G., Prabhawasat, P., Kojima, T., Grueterich, M., Espana, E., & Goto, E. (2008). The challenge of dry eye diagnosis. *Clin Ophthalmol, 2*(1), 31-55.

Schallhorn, C.S., Schallhorn, J.M., Hannan, S., Schallhorn, S.C. (2017). Effectiveness of an eyelid thermal pulsation procedure to treat recalcitrant dry eye symptoms after laser vision correction. J Refract Surg, 33(1), 30–36.

Schargus, M., Ivanova, S., Kakkassery, V., Dick, H. B., & Joachim, S. (2015a). Correlation of Tear Film Osmolarity and 2 Different MMP-9 Tests with Common Dry Eye Tests in a Cohort of Non-Dry Eye Patients. *Cornea, 34*(7), 739-744.

Schargus, M., Meyer-ter-Vehn, T., Menrath, J., Grigoleit, G. U., & Geerling, G. (2015b). Correlation Between Tear Film Osmolarity and the Disease Score of the International Chronic Ocular Graft-Versus-Host-Disease Consensus Group in Hematopoietic Stem Cell Transplantation Patients. *Cornea, 34*(8), 911-916.

Schaumberg, D. A., Dana, R., Buring, J. E., & Sullivan, D. A. (2009). Prevalence of dry eye disease among US men: estimates from the Physicians' Health Studies. *Arch Ophthalmol, 127*(6), 763-768.

Schaumberg, D. A., Nichols, J. J., Papas, E. B., Tong, L., Uchino, M., & Nichols, K. K. (2011). The international workshop on meibomian gland dysfunction: report of the subcommittee on the epidemiology of, and associated risk factors for, MGD. *Invest Ophthalmol Vis Sci, 52*(4), 1994-2005.

Schaumberg, D. A., Sullivan, D. A., Buring, J. E., & Dana, M. R. (2003). Prevalence of dry eye syndrome among US women. *Am J Ophthalmol, 136*(2), 318-326.

Schaumberg, D. A., Uchino, M., Christen, W. G., Semba, R. D., Buring, J. E., & Li, J. Z. (2013). Patient reported differences in dry eye disease between men and women: impact, management, and patient satisfaction. *PLoS One, 8*(9), e76121.

Schein, O.D., Munoz, B., Tielsch, J.M., et al. (1997). Prevalence of dry eye among the elderly. *Am J Ophthalmol,* 124, 723–728.

Schein, O. D., Tielsch, J. M., Munoz, B., Bandeen-Roche, K., & West, S. (1997). Relation between signs and symptoms of dry eye in the elderly. A population-based perspective. *Ophthalmology, 104*(9), 1395-1401.

Schepers, R. J., & Ringkamp, M. (2009). Thermoreceptors and thermosensitive afferents. *Neurosci Biobehav Rev, 33*(3), 205-212.

Schiffman, R. M., Christianson, M. D., Jacobsen, G., Hirsch, J. D., & Reis, B. L. (2000). Reliability and validity of the Ocular Surface Disease Index. *Arch Ophthalmol, 118*(5), 615-621.

Schindel, T. J., Yuksel, N., Breault, R., Daniels, J., Varnhagen, S., & Hughes, C. A. (2017). Perceptions of pharmacists' roles in the era of expanding scopes of practice. *Res Social Adm Pharm*, 13(1), 148-161.

Schlanger, J. L. (1993). A study of contact lens failures. *J Am Optom Assoc, 64*(3), 220-224.

Scott, C. (2019). Smart moves. *Acuity,* Summer 2019, Retrieved August 9, 2019, https://www.college-optometrists.org/acuity-resource/smart-moves.html

Seal, D.V., Wright, P., Ficker, L., Hagan, K., Troski, M., Menday, P. (1995). Placebo controlled trial of fusidic acid gel and oxytetracycline for recurrent blepharitis and rosacea. *Br J Ophthalmol*, 79(1), 42–45.

Segal, B., Bowman, S. J., Fox, P. C., Vivino, F. B., Murukutla, N., Brodscholl, J., Ogale, S., McLean, L. (2009). Primary Sjögren's Syndrome: health experiences and predictors of health quality among patients in the United States. *Health Qual Life Outcomes, 7*, 46.

Sekimoto, M., Imanaka, Y., Kitano, N., Ishizaki, T., & Takahashi, O. (2006). Why are physicians not persuaded by scientific evidence? A grounded theory interview study. *BMC Health Serv Res, 6*, 92.

Sempere-Selva, T., Peiro, S., Sendra-Pina, P., Martinez-Espin, C., & Lopez-Aguilera, I. (2001). Inappropriate use of an accident and emergency department: magnitude, associated factors, and reasons--an approach with explicit criteria. *Ann Emerg Med, 37*(6), 568-579.

Sen, S., Patil, M., Saxena, R., Kumar, A., Amar, S. P., Das, D., Brar, A.S., Saini, P. (2019). Perceived difficulties and complications in learners of phacoemulsification: A principal component analysis model. *Indian J Ophthalmol, 67*(2), 213-216.

Serpetopoulos, C. (1997). Optical explanation of the gradual disappearance of flying dots in posterior vitreous detachment. *Surv Ophthalmol, 42*(1), 92-94.

Shah, C. T., Blount, A. L., Nguyen, E. V., & Hassan, A. S. (2012). Cranial nerve seven palsy and its influence on meibomian gland function. *Ophthalmic Plast Reconstr Surg, 28*(3), 166-168.

Shah, R., Edgar, D. F., Harle, D. E., Weddell, L., Austen, D. P., Burghardt, D., & Evans, B. J. (2009). The content of optometric eye examinations for a presbyopic patient presenting with symptoms of flashing lights. *Ophthalmic Physiol Opt, 29*(2), 105-126.

Sheen, N. J., Fone, D., Phillips, C. J., Sparrow, J. M., Pointer, J. S., & Wild, J. M. (2009). Novel optometrist-led all Wales primary eye-care services: evaluation of a prospective case series. *Br J Ophthalmol, 93*(4), 435-438.

Sheldrick, J. H., Vernon, S. A., & Wilson, A. (1992). Study of diagnostic accord between general practitioners and an ophthalmologist. *Bmj, 304*(6834), 1096-1098.

Sheldrick, J. H., Wilson, A. D., Vernon, S. A., & Sheldrick, C. M. (1993). Management of ophthalmic disease in general practice. *Br J Gen Pract, 43*(376), 459-462.

Sheskin, D. J. (2011). *Handbook of parametric and nonparametric statistical procedures* (5th ed.). Boca Raton, FL: Chapman & Hall/CRC Press.

Sheth, H. G., Aslam, S. A., Subramanian, S., & Sheth, A. G. (2008). Acute ophthalmic referrals from primary care--an audit and recommendations. *J Eval Clin Pract, 14*(4), 618-620.

Sheth, H. G., & Sheth, A. G. (2007). Frequent attenders to ophthalmic accident and emergency departments. *J Med Ethics, 33*(8), 496.

Shevell, M. I. (2009). What do we call 'them'?: the 'patient' versus 'client' dichotomy. *Dev Med Child Neurol, 51*(10), 770-772.

Shickle, D., Davey, C. J., & Slade, S. V. (2015). Why is the General Ophthalmic Services (GOS) Contract that underpins primary eye care in the U.K. contrary to the public health interest? *Br J Ophthalmol*, 99(7), 888-892.

Shimmura, S., Shimazaki, J., & Tsubota, K. (1999). Results of a population-based questionnaire on the symptoms and lifestyles associated with dry eye. *Cornea, 18*(4), 408-411.

Shirai, M. (2017). Effects of price reframing tactics on consumer perceptions. *Journal of Retailing and Consumer Services*, 34, 82–87.

Shostack, G. L. (1984). Designing services that deliver. *Harvard Business Review*, *62*(1), 133–139.

Shostack, G. L. (1987). Service Positioning Through Structural Change. *Journal of Marketing*, 51(1), 34–43.

Shulman, D. G., Sargent, J. B., Stewart, R. H., & Mester, U. (1996). Comparative evaluation of the short-term bactericidal potential of a steroid-antibiotic combination versus steroid in the treatment of chronic bacterial blepharitis and conjunctivitis. *Eur J Ophthalmol, 6*(4), 361-367.

Siddireddy, J. S., Vijay, A. K., Tan, J., & Willcox, M. (2018). The eyelids and tear film in contact lens discomfort. *Cont Lens Anterior Eye, 41*(2), 144-153.

Silcock, J., Raynor, D. K. T., & Petty, D. (2004). The organisation and development of primary care pharmacy in the United Kingdom. *Health Policy*, 67(2), 207–214.

Simpson, T. L., Situ, P., Jones, L. W., & Fonn, D. (2008). Dry eye symptoms assessed by four questionnaires. *Optom Vis Sci, 85*(8), 692-699.

Skelly, A. C., Dettori, J. R., & Brodt, E. D. (2012). Assessing bias: the importance of considering confounding. *Evid Based Spine Care J, 3*(1), 9-12.

Smith, H. B., Daniel, C. S., & Verma, S. (2013). Eye casualty services in London. *Eye (Lond), 27*(3), 320-328.

Smith, J., Nichols, K. K., & Baldwin, E. K. (2008). Current patterns in the use of diagnostic tests in dry eye evaluation. *Cornea, 27*(6), 656-662.

Smith, J. A., Vitale, S., Reed, G. F., Grieshaber, S. A., Goodman, L. A., Vanderhoof, V. H., Calis, K.A., Nelson, L. M. (2004). Dry eye signs and symptoms in women with premature ovarian failure. *Arch Ophthalmol, 122*(2), 151-156.

Smith, R., Tromans, C. (2013). Commissioning better eye care: Urgent eye care. The Royal College of Ophthalmologists / College of Optometrists.

Smith, S.J. (2011). Delivering optometric care in the UK. *Doctoral thesis*, Aston University.

Speaker, M. G., Milch, F. A., Shah, M. K., Eisner, W., & Kreiswirth, B. N. (1991). Role of external bacterial flora in the pathogenesis of acute postoperative endophthalmitis. *Ophthalmology, 98*(5), 639-649.

Spikmans, F. J., Brug, J., Doven, M. M., Kruizenga, H. M., Hofsteenge, G. H., & van Bokhorst-van der Schueren, M. A. (2003). Why do diabetic patients not attend appointments with their dietitian? *J Hum Nutr Diet, 16*(3), 151-158.

SPSS Inc. PASW Decision Trees 18. Retrieved January 16, 2019, http://www.sussex.ac.uk/its/pdfs/SPSS18_Decision_Trees.pdf

Srinivasan, S., Menzies, K., Sorbara, L., & Jones, L. (2012). Infrared imaging of meibomian gland structure using a novel keratograph. *Optom Vis Sci, 89*(5), 788-794.

Stahl, U., Keir, N. J., Landers, A., & Jones, L. W. (2016). Effect of Short Recovery Periods on Ocular Comfort During Daily Lens Wear. *Optometry and Vision Science American Academy of Optometry*, 93(8), 861-871.

Stapleton, F., Alves, M., Bunya, V. Y., Jalbert, I., Lekhanont, K., Malet, F., Na, K.S., Schaumberg, D., Uchino, M., Vehof, J., Viso, E., Vitale, S., Jones, L. (2017). TFOS DEWS II Epidemiology Report. *Ocul Surf, 15*(3), 334-365.

Stapleton, F., Keay, L., Edwards, K., Naduvilath, T., Dart, J. K., Brian, G., & Holden, B. A. (2008). The incidence of contact lens-related microbial keratitis in Australia. *Ophthalmology*, 115(10), 1655-1662.

Starcevic, V., & Berle, D. (2013). Cyberchondria: towards a better understanding of excessive health-related Internet use. *Expert Rev Neurother, 13*(2), 205-213.

Stead, R. E., Stuart, A., Keller, J., & Subramaniam, S. (2010). Reducing the rate of cataract surgery cancellation due to blepharitis. *Eye (Lond),* 24(4), 742.

Steinbach, Ingeborg (2018). Triple bottom line analysis of eye motility services at Moorfields eye hospital and its satellite clinics. *Centre for Sustainable Healthcare*, Retrieved 5 May 2019 from: https://networks.sustainablehealthcare.org.uk/networks/eyehealth-susnet/triple-bottom-line-analysis-eye-motility-services-moorfields-eye-hospital

Stone, J. L., Robin, A. L., Novack, G. D., Covert, D. W., & Cagle, G. D. (2009). An objective evaluation of eyedrop instillation in patients with glaucoma. *Arch Ophthalmol, 127*(6), 732-736.

Stratford, P. W., Binkley, J. M., Riddle, D. L., & Guyatt, G. H. (1998). Sensitivity to change of the Roland-Morris Back Pain Questionnaire: part 1. *Phys Ther, 78*(11), 1186-1196.

Sudhalkar, A., Vasavada, V., Bhojwani, D., Raju, C. V. G., Vasudev, P., Jain, S., & Praveen, M. R. (2019). Incorporating Optical Coherence Tomography in the Cataract Preoperative Armamentarium: Additional Need or Additional Burden? *Am J Ophthalmol, 198*, 209-214.

Sulley, A., Young, G., & Hunt, C. (2017). Factors in the success of new contact lens wearers. *Cont Lens Anterior Eye, 40*(1), 15-24.

Sulley, A., Young, G., Hunt, C., McCready, S., Targett, M. T., & Craven, R. (2018). Retention Rates in New Contact Lens Wearers. *Eye Contact Lens, 44 Suppl 1*, S273-s282.

Sullivan, B. (2014). Challenges in using signs and symptoms to evaluate new biomarkers of dry eye disease. *Ocul Surf, 12*(1), 2-9.

Sullivan, B. D., Crews, L. A., Messmer, E. M., Foulks, G. N., Nichols, K. K., Baenninger, P., Geerling, G., Figueiredo, F., Lemp, M. A. (2014). Correlations between commonly used objective signs and symptoms for the diagnosis of dry eye disease: clinical implications. *Acta Ophthalmol, 92*(2), 161-166.

Sullivan, B. D., Crews, L. A., Sonmez, B., de la Paz, M. F., Comert, E., Charoenrook, V., de Araujo, A.L., Pepose, J.S., Berg, M.S., Kosheleff, V.P., Lemp, M. A. (2012). Clinical utility of objective tests for dry eye disease: variability over time and implications for clinical trials and disease management. *Cornea, 31*(9), 1000-1008.

Sullivan, B.D., Whitmer, D., Nichols, K.K., Tomlinson, A., Foulks, G.N., Geerling, G., Khanal, S., Ramaesh, K., Diaper, C., McFadyen, A. (2010). Tear film osmolarity: determination of a referent for dry eye diagnosis. *Invest Ophthalmol Vis Sc*, 47: 4309-4315.

Sullivan, D. A., Rocha, E. M., Aragona, P., Clayton, J. A., Ding, J., Golebiowski, B., Hampel, U., McDermott, A.M., Schaumberg, D.A., Srinivasan, S., Versura, P., Willcox, M. D. P. (2017). TFOS DEWS II Sex, Gender, and Hormones Report. *Ocul Surf, 15*(3), 284-333.

Sullivan, L. J., McCurrach, F., Lee, S., Taylor, H. R., Rolando, M., Marechal-Courtois, C., Creuzot-Garcher, C., Easty, D.L., Karabatsas, C., Bingh Hoh, M., Faschinger, C., Laroche, L. (1997). Efficacy and safety of 0.3% carbomer gel compared to placebo in patients with moderate-to-severe dry eye syndrome. *Ophthalmology, 104*(9), 1402-1408.

Sun, M. J., Rubin, G. S., Akpek, E. K., & Ramulu, P. Y. (2017). Impact of Glaucoma and Dry Eye on Text-Based Searching. *Transl Vis Sci Technol, 6*(3), 24.

Sung, J., Wang, M. T. M., Lee, S. H., Cheung, I. M. Y., Ismail, S., Sherwin, T., & Craig, J. P. (2018). Randomized double-masked trial of eyelid cleansing treatments for blepharitis. *Ocul Surf, 16*(1), 77-83.

Sutu, C., Fukuoka, H., & Afshari, N. A. (2016). Mechanisms and management of dry eye in cataract surgery patients. *Curr Opin Ophthalmol, 27*(1), 24-30.

Swarbrick, H., Pye, D.C., Holden, B.A. (1985). Current contact lens practice. *Aust J Optom*, 68, 2–7.

Szakats, I., Sebestyen, M., Toth, E., & Purebl, G. (2017). Dry Eye Symptoms, Patient-Reported Visual Functioning, and Health Anxiety Influencing Patient Satisfaction After Cataract Surgery. *Curr Eye Res, 42*(6), 832-836.

Szczesna-Iskander, DH. (2016). Measurement variability of the TearLab Osmolarity System. *Contact Lens Anterior Eye*, 39(5), 353-358.

Tabachnick, B.G. & Fidell, L.S. (2007) *Using multivariate statistics* (5th edn). Boston: Pearson Eduction.

Takahashi, Y., & Kakizaki, H. (2015). Meibomian Gland Dysfunction in Cranial Nerve VII Palsy. *Ophthalmic Plast Reconstr Surg, 31*(3), 179-181.

Tan, E. C. K., Stewart, K., Elliott, R. A., & George, J. (2014). Pharmacist consultations in general practice clinics: The Pharmacists in Practice Study (PIPS). *Research in Social and Administrative Pharmacy*, 10(4), 623-632.

Tan, L. L., Morgan, P., Cai, Z. Q., & Straughan, R. A. (2015). Prevalence of and risk factors for symptomatic dry eye disease in Singapore. *Clin Exp Optom, 98*(1), 45-53.

Tanner, V., Harle, D., Tan, J., Foote, B., Williamson, T. H. and Chignell, A. H. (2000). Acute posterior vitreous detachment: the predictive value of vitreous pigment and symptomatology. *Br. J. Ophthalmol.* 84, 1264–1268.

Tax, S. S., Brown, S. W., & Chandrashekaran, M. (1998). Customer Evaluations of Service Complaint Experiences: Implications for Relationship Marketing. *Journal of Marketing*, 62(2), 60–76.

TearLab Corp (2017). TearLab Technician In-Service Review, 920107 Rev B, Retrieved 20 May 2019 from: https://www.tearlab.com/resources/TearLab_Technician_In-Service_Review_920107_Rev_B_with_NOTES.pdf

Teoli, D., & An, J. (2019). SWOT Analysis StatPearls. Treasure Island (FL): StatPearls Publishing StatPearls Publishing LLC. Retrieved August 9, 2019, https://www.ncbi.nlm.nih.gov/books/NBK537302/

Teson, M., Calonge, M., Fernandez, I., Stern, M. E., & Gonzalez-Garcia, M. J. (2012). Characterization by Belmonte's gas esthesiometer of mechanical, chemical, and thermal corneal sensitivity thresholds in a normal population. *Invest Ophthalmol Vis Sci, 53*(6), 3154-3160.

Thai, L. C., Tomlinson, A., & Doane, M. G. (2004). Effect of contact lens materials on tear physiology. *Optom Vis Sci, 81*(3), 194-204.

Theobald, A. H., Wong, B. K., Quick, A. N., & Thomson, W. M. (2006). The impact of the popular media on cosmetic dentistry. *N Z Dent J*, 102(3), 58-63.

Thomke, S. (2003). R&D Comes to Services. *Harvard Business Review*, *81*(4), 70–79.

Tighe, S., Gao, Y. Y., & Tseng, S. C. (2013). Terpinen-4-ol is the Most Active Ingredient of Tea Tree Oil to Kill Demodex Mites. *Transl Vis Sci Technol, 2*(7), 2.

Toda, I., Fujishima, H., & Tsubota, K. (1993). Ocular fatigue is the major symptom of dry eye. *Acta Ophthalmol (Copenh), 71*(3), 347-352.

Tomlinson, A., Bron, A. J., Korb, D. R., Amano, S., Paugh, J. R., Pearce, E. I., Yee, R., Yokoi, N., Arita, R., Dogru, M. (2011). The international workshop on meibomian gland dysfunction: report of the diagnosis subcommittee. *Invest Ophthalmol Vis Sci, 52*(4), 2006-2049.

Tomlinson, A., McCann, L. C., & Pearce, E. I. (2010). Comparison of human tear film osmolarity measured by electrical impedance and freezing point depression techniques. *Cornea, 29*(9), 1036-1041.

Tong, L., Chaurasia, S. S., Mehta, J. S., & Beuerman, R. W. (2010). Screening for meibomian gland disease: its relation to dry eye subtypes and symptoms in a tertiary referral clinic in singapore. *Invest Ophthalmol Vis Sci, 51*(7), 3449-3454.

Tong, L., Saw, S. M., Lamoureux, E. L., Wang, J. J., Rosman, M., Tan, D. T., & Wong, T. Y. (2009). A questionnaire-based assessment of symptoms associated with tear film dysfunction and lid margin disease in an Asian population. *Ophthalmic Epidemiol, 16*(1), 31-37.

Toor, T. (2014). Market segmentation for penetrating deeper into the contact lens market. *Strategic Direction*, 30(5), 34-36.

Tran, N., Graham, A. D., & Lin, M. C. (2013). Ethnic differences in dry eye symptoms: effects of corneal staining and length of contact lens wear. *Cont Lens Anterior Eye, 36*(6), 281-288.

Trattler, W. B., Majmudar, P. A., Donnenfeld, E. D., McDonald, M. B., Stonecipher, K. G., & Goldberg, D. F. (2017). The Prospective Health Assessment of Cataract Patients' Ocular Surface (PHACO) study: the effect of dry eye. *Clin Ophthalmol, 11*, 1423-1430.

Trikha, S., Macgregor, C., Jeffery, M., & Kirwan, J. (2012). The Portsmouth-based glaucoma refinement scheme: a role for virtual clinics in the future? *Eye (Lond)*, 26(10), 1288-1294.

Tsaousis, K. T., Empeslidis, T., Konidaris, V. E., Kapoor, B., & Deane, J. (2016). The concept of virtual clinics in monitoring patients with age-related macular degeneration. *Acta Ophthalmol*, 94(5), e353-355.

Tsubota, K., Hata, S., Okusawa, Y., Egami, F., Ohtsuki, T., & Nakamori, K. (1996). Quantitative videographic analysis of blinking in normal subjects and patients with dry eye. *Arch Ophthalmol, 114*(6), 715-720.

Tsubota, K., & Nakamori, K. (1993). Dry eyes and video display terminals. *N Engl J Med, 328*(8), 584.

Tsubota, K., & Nakamori, K. (1995). Effects of ocular surface area and blink rate on tear dynamics. *Arch Ophthalmol, 113*(2), 155-158.

Tung, C. I., Perin, A. F., Gumus, K., & Pflugfelder, S. C. (2014). Tear meniscus dimensions in tear dysfunction and their correlation with clinical parameters. *Am J Ophthalmol, 157*(2), 301-310.e301.

Turner, A. W., Layton, C. J., & Bron, A. J. (2005). Survey of eye practitioners' attitudes towards diagnostic tests and therapies for dry eye disease. *Clin Exp Ophthalmol, 33*(4), 351-355.

Turner, M. (2016). BMG Research GOC 2015 Contact Lens Survey. Retrieved July 7, 2019, https://www.optical.org/en/news_publications/Publications/policy-and-research-papers.cfm

Tutt, R., Bradley, A., Begley, C., & Thibos, L. N. (2000). Optical and visual impact of tear break-up in human eyes. *Invest Ophthalmol Vis Sci, 41*(13), 4117-4123.

Twa, M. D., Parthasarathy, S., Roberts, C., Mahmoud, A. M., Raasch, T. W., & Bullimore, M. A. (2005). Automated decision tree classification of corneal shape. *Optom Vis Sci, 82*(12), 1038-1046.

Uchino, M., Nishiwaki, Y., Michikawa, T., Shirakawa, K., Kuwahara, E., Yamada, M. Dogru, M., Schaumberg, D.A., Kawakita, T., Takebayashi, T., Tsubota, K. (2011). Prevalence and risk factors of dry eye disease in Japan: Koumi study. *Ophthalmology, 118*(12), 2361-2367.

Uchino, M., Schaumberg, D. A., Dogru, M., Uchino, Y., Fukagawa, K., Shimmura, S., Satoh, T., Takebayashi, T., Tsubota, K. (2008). Prevalence of dry eye disease among Japanese visual display terminal users. *Ophthalmology, 115*(11), 1982-1988.

Uchino, M., Yokoi, N., Uchino, Y., Dogru, M., Kawashima, M., Komuro, A., Sonomura, Y., Kato, H., Kinoshita, S., Schaumberg, D.A., Tsubota, K. (2013). Prevalence of dry eye disease and its risk factors in visual display terminal users: the Osaka study. *Am J Ophthalmol, 156*(4), 759-766.

Um, S. B., Kim, N. H., Lee, H. K., Song, J. S., & Kim, H. C. (2014). Spatial epidemiology of dry eye disease: findings from South Korea. *Int J Health Geogr, 13*, 31.

Umashankar, N., Srinivasan, R., & Hindman, D. (2011). Developing Customer Service Innovations for Service Employees: The Effects of NSD Characteristics on Internal Innovation Magnitude. *Journal of Service Research*, 14(2), 164-179.

Urzua, C. A., Vasquez, D. H., Huidobro, A., Hernandez, H., & Alfaro, J. (2012). Randomized double-blind clinical trial of autologous serum versus artificial tears in dry eye syndrome. *Curr Eye Res, 37*(8), 684-688.

Vajdic, C., Holden, B. A., Sweeney, D. F., & Cornish, R. M. (1999). The frequency of ocular symptoms during spectacle and daily soft and rigid contact lens wear. *Optom Vis Sci, 76*(10), 705-711.

van de Graaf, E. S., Felius, J., van Kempen-du Saar, H., Looman, C. W., Passchier, J., Kelderman, H., & Simonsz, H. J. (2009). Construct validation of the Amblyopia and Strabismus Questionnaire (A&SQ) by factor analysis. *Graefes Arch Clin Exp Ophthalmol, 247*(9), 1263-1268.

van Landingham, S. W., West, S. K., Akpek, E. K., Munoz, B., & Ramulu, P. Y. (2014). Impact of dry eye on reading in a population-based sample of the elderly: the Salisbury Eye Evaluation. *Br J Ophthalmol, 98*(5), 639-644.

Vargo, S. L., & Lusch, R. F. (2004). The Four Service Marketing Myths: Remnants of a Goods-Based, Manufacturing Model. Journal of Service Research, 6(4), 324–335.

Vehof, J., Kozareva, D., Hysi, P. G., & Hammond, C. J. (2014). Prevalence and risk factors of dry eye disease in a British female cohort. *Br J Ophthalmol, 98*(12), 1712-1717.

Vehof, J., Sillevis Smitt-Kamminga, N., Nibourg, S. A., & Hammond, C. J. (2018). Sex differences in clinical characteristics of dry eye disease. *Ocul Surf, 16*(2), 242-248.

Vermeire, E., Hearnshaw, H., Van Royen, P., & Denekens, J. (2001). Patient adherence to treatment: three decades of research. A comprehensive review. *J Clin Pharm Ther, 26*(5), 331-342.

Versura, P., Profazio, V., & Campos, E. C. (2010). Performance of tear osmolarity compared to previous diagnostic tests for dry eye diseases. *Curr Eye Res, 35*(7), 553-564.

Vidal-Rohr, M., Wolffsohn, J. S., Davies, L. N., & Cervino, A. (2018). Effect of contact lens surface properties on comfort, tear stability and ocular physiology. *Cont Lens Anterior Eye, 41*(1), 117-121.

Viikki, K., Kentala, E., Juhola, M., & Pyykko, I. (1999). Decision tree induction in the diagnosis of otoneurological diseases. *Med Inform Internet Med, 24*(4), 277-289.

Villani, E., Ceresara, G., Beretta, S., Magnani, F., Viola, F., & Ratiglia, R. (2011). In vivo confocal microscopy of meibomian glands in contact lens wearers. *Invest Ophthalmol Vis Sci, 52*(8), 5215-5219.

Villarosa, A. R., George, D., Ramjan, L. M., Srinivas, R., & George, A. (2018). The role of dental practitioners in addressing overweight and obesity among children: A scoping review of current interventions and strategies. *Obes Res Clin Pract*, 12(5), 405-415.

Viso, E., Gude, F., & Rodriguez-Ares, M. T. (2011). The association of meibomian gland dysfunction and other common ocular diseases with dry eye: a population-based study in Spain. *Cornea, 30*(1), 1-6.

Viso, E., Rodriguez-Ares, M. T., & Gude, F. (2009). Prevalence of and associated factors for dry eye in a Spanish adult population (the Salnes Eye Study). *Ophthalmic Epidemiol, 16*(1), 15-21.

Vitali, C., Bombardieri, S., Jonsson, R., Moutsopoulos, H. M., Alexander, E. L., Carsons, S. E., Daniels, T.E., Fox, P.C., Fox, R.I., Kassan, S.S., Pillemer, S.R., Talal, N., Weisman, M. H. (2002). Classification criteria for Sjögren's syndrome: a revised version of the European criteria proposed by the American-European Consensus Group. *Ann Rheum Dis, 61*(6), 554-558.

Vlasnik, J. J., Aliotta, S. L., & DeLor, B. (2005). Medication adherence: factors influencing compliance with prescribed medication plans. *Case Manager, 16*(2), 47-51.

von Thun Und Hohenstein-Blaul, N., Funke, S., & Grus, F. H. (2013). Tears as a source of biomarkers for ocular and systemic diseases. *Exp Eye Res, 117*, 126-137.

Walker, R. H., Craig-Lees, M., Hecker, R., & Francis, H. (2002). Technology-enabled service delivery: An investigation of reasons affecting customer adoption and rejection. *International Journal of Service Industry Management*, 13(1), 91–106.

Walker, T. W. M., Gately, F., Stagnell, S., Kerai, A., Mills, C., & Thomas, S. (2017). Can UK undergraduate dental programmes provide training in non-surgical facial aesthetics? *Br Dent J*, 222(12), 949-953.

Wan, T., Jin, X., Lin, L., Xu, Y., & Zhao, Y. (2016). Incomplete Blinking May Attribute to the Development of Meibomian Gland Dysfunction. *Curr Eye Res, 41*(2), 179-185.

Wang, M. T. M., Tien, L., Han, A., Lee, J. M., Kim, D., Markoulli, M., & Craig, J. P. (2018). Impact of blinking on ocular surface and tear film parameters. *Ocul Surf, 16*(4), 424-429.

Weed, K., Fonn, D., Potvin, R. (1993). Discontinuation of contact lens wear. *Optom Vis Sci*, 70(12s):140.

Welling, J.D., Mauger, T.F., Schoenfield, L.R., Hendershot, A.J. (2014). Chronic eyelid dermatitis secondary to cocamidopropyl betaine allergy in a patient using baby shampoo eyelid scrubs. *JAMA Ophthalmol,* 132(3), 357-359.

Whitaker, B. G., Dahling, J. J., & Levy, P. (2007). The development of a feedback environment and role clarity model of job performance. *Journal of Management*, 33(4), 570–591.

Wien, A. H., & Olsen, S. O. (2014). Understanding the Relationship between Individualism and Word of Mouth: A Self-Enhancement Explanation. *Psychology & Marketing*, *31*(6), 416–425.

Wilhelmus, K. R. (2015). Antiviral treatment and other therapeutic interventions for herpes simplex virus epithelial keratitis. *Cochrane Database Syst Rev, 1*, Cd002898.

Wilhelmus, K.R., Gee, L., Hauck, W.W., Kurinij, N., Dawson, C.R., Jones, D.B. et al. (1994). Herpetic Eye Disease Study. A controlled trial of topical corticosteroids for herpes simplex stromal keratitis. *Ophthalmology,* 101(12), 1883–1895, discussion 1895–1896.

Willcox, M. D. P., Argueso, P., Georgiev, G. A., Holopainen, J. M., Laurie, G. W., Millar, T. J., Papas, E.B., Rolland, J.P., Schmidt, T.A., Stahl, U., Suarez, T., Subbaraman, L.N., Ucakhan, O.O., Jones, L. (2017). TFOS DEWS II Tear Film Report. *Ocul Surf, 15*(3), 366-403.

Williams, R. A., Brody, B. L., Thomas, R. G., Kaplan, R. M., & Brown, S. I. (1998). The psychosocial impact of macular degeneration. *Arch Ophthalmol, 116*(4), 514-520.

Williamson, J. F., Huynh, K., Weaver, M. A., & Davis, R. M. (2014). Perceptions of dry eye disease management in current clinical practice. *Eye Contact Lens, 40*(2), 111-115.

Wilson, A. M., Zeithaml, V. A., Bitner, M. J., & Gremler, D. D. (2016). Services marketing : integrating customer focus across the firm. Maidenhead, Berkshire : McGraw Hill Education, 2016.

Wing, P.C. (1997). Patient or client? If in doubt, ask. *Canadian Medical Association Journal,* 157, 287–289.

Wojtowicz, J. C., Butovich, I., Uchiyama, E., Aronowicz, J., Agee, S., & McCulley, J. P. (2011). Pilot, prospective, randomized, double-masked, placebo-controlled clinical trial of an omega-3 supplement for dry eye. *Cornea, 30*(3), 308-314.

Wolffsohn, J. S., Arita, R., Chalmers, R., Djalilian, A., Dogru, M., Dumbleton, K., Gupta, P.K., Karpecki, P., Lazreg, S., Pult, H., Sullivan, B.D., Tomlinson, A., Tong, L., Villani, E., Yoon, K.C., Jones, L., Craig, J. P. (2017). TFOS DEWS II Diagnostic Methodology report. *Ocul Surf, 15*(3), 539-574.

Wolffsohn, J. S., Naroo, S. A., Gupta, N., & Emberlin, J. (2011). Prevalence and impact of ocular allergy in the population attending UK optometric practice. *Cont Lens Anterior Eye*, 34(3), 133-138.

Woodall, T. (2001). Six Sigma and Service Quality: Christian Grönroos Revisited. *Journal of Marketing Management*, 17(5–6), 595–607.

Wright, H. R., & Diamond, J. P. (2015). Service innovation in glaucoma management: using a Web-based electronic patient record to facilitate virtual specialist supervision of a shared care glaucoma programme. *Br J Ophthalmol*, 99(3), 313-317.

Xue, A. L., Downie, L. E., Ormonde, S. E., & Craig, J. P. (2017). A comparison of the self-reported dry eye practices of New Zealand optometrists and ophthalmologists. *Ophthalmic Physiol Opt, 37*(2), 191-201.

Xue, W., Zhu, M. M., Zhu, B. J., Huang, J. N., Sun, Q., Miao, Y. Y., & Zou, H. D. (2019). Long-term impact of dry eye symptoms on vision-related quality of life after phacoemulsification surgery. *Int Ophthalmol, 39*(2), 419-429.

Yao, K., Bao, Y., Ye, J., Lu, Y., Bi, H., Tang, X., Zhao, Y., Zhang, J., Yang, J. (2015). Efficacy of 1% carboxymethylcellulose sodium for treating dry eye after phacoemulsification: results from a multicenter, open-label, randomized, controlled study. *BMC Ophthalmol, 15*, 28.

Yap, K. B., & Sweeney, J. C. (2007). Zone-of-tolerance moderates the service quality-outcome relationship. *Journal of Services Marketing*, 21(2), 137-148.

Yavas, U., Benkenstein, M., Holtz, M. (2008). Service provider-customer similarities and disparities: A German study. *Cross Cultural Management: An International Journal*, 15(3), 275-284.

Yeh, T. N., Graham, A. D., & Lin, M. C. (2015). Relationships among Tear Film Stability, Osmolarity, and Dryness Symptoms. *Optom Vis Sci, 92*(9), e264-272.

Yenice, O., Temel, A., Incili, B., & Tuncer, N. (2006). Short-wavelength automated perimetry in patients with migraine. *Graefes Arch Clin Exp Ophthalmol, 244*(5), 589-595.

Yim, C. K. (Bennett), Chan, K. W., & Hung, K. (2007). Multiple reference effects in service evaluations: Roles of alternative attractiveness and self-image congruity. *Journal of Retailing*, *83*(1), 147–157.

Yoon, M.H., Seo, J.H., Yoon, T.S. (2004). Effects of contact employee supports on critical employee responses and customer service evaluation. *Journal of Services Marketing*, 18(5), 395-412.

Young, B.J., Cunningham, W.F., Akingbehin, T. (1982). Double-masked controlled clinical trial of 5% tolmetin versus 0.5% prednisolone versus 0.9% saline in acute endogenous nongranulomatous anterior uveitis. *Br J Ophthalmol,* 66, 389–391.

Young, G., & Efron, N. (1991). Characteristics of the pre-lens tear film during hydrogel contact lens wear. *Ophthalmic Physiol Opt, 11*(1), 53-58.

Young, G., Garofalo, R., Harmer, O., & Peters, S. (2010). The effect of soft contact lens care products on lens modulus. *Cont Lens Anterior Eye, 33*(5), 210-214.

Young, G., Veys, J., Pritchard, N., & Coleman, S. (2002). A multi-centre study of lapsed contact lens wearers. *Ophthalmic Physiol Opt,* 22(6), 516-527.

Yousefi, S., Yousefi, E., Takahashi, H., Hayashi, T., Tampo, H., Inoda, S., Arai, Y., Asbell, P. (2018). Keratoconus severity identification using unsupervised machine learning. *PLoS One, 13*(11), e0205998.

Yu, J., Asche, C. V., & Fairchild, C. J. (2011). The economic burden of dry eye disease in the United States: a decision tree analysis. *Cornea, 30*(4), 379-387.

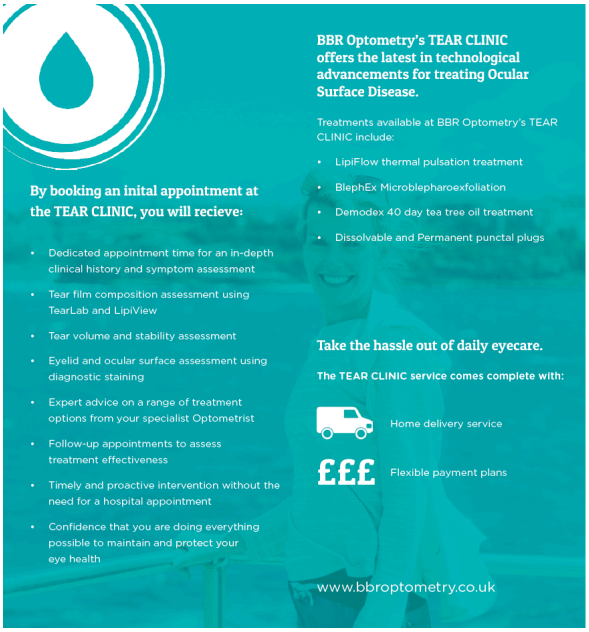
Yu, Y., Hua, H., Wu, M., Yu, Y., Yu, W., Lai, K., & Yao, K. (2015). Evaluation of dry eye after femtosecond laser-assisted cataract surgery. *J Cataract Refract Surg, 41*(12), 2614-2623.

Zeelenberg, M., Dijk, W. W. van, Pligt, J. van der, Manstead, A. S. R., Empelen, P. van, & Reinderman, D. (1998). Emotional reactions to the outcomes of decisions: the role of counterfactual thought in the experience of regret and disappointment. *Organizational Behavior & Human Decision Processes*, 75(2), 117-141.

Zeelenberg, M., & Pieters, R. (2004). Beyond valence in customer dissatisfaction: A review and new findings on behavioral responses to regret and disappointment in failed services. *Journal of Business Research*, 57(4), 445–455.

APPENDICES

Appendix 1.1: BBR Optometry Ltd. Tear Clinic leaflet used at the time of the analysis.



By booking an inital appointment at the TEAR CLINIC, you will recieve:

- Dedicated appointment time for an in-depth clinical history and symptom assessment
- Tear film composition assessment using TearLab and LipiView
- Tear volume and stability assessment
- Eyelid and ocular surface assessment using diagnostic staining
- Expert advice on a range of treatment options from your specialist Optometrist
- Follow-up appointments to assess treatment effectiveness
- Timely and proactive intervention without the need for a hospital appointment
- Confidence that you are doing everything possible to maintain and protect your eye health

BBR Optometry's TEAR CLINIC offers the latest in technological advancements for treating Ocular Surface Disease.

Treatments available at BBR Optometry's TEAR CLINIC include:

- LipiFlow thermal pulsation treatment
- BlephEx Microblepharoexfoliation
- Demodex 40 day tea tree oil treatment
- Dissolvable and Permanent punctal plugs

Take the hassle out of daily eyecare.

The TEAR CLINIC service comes complete with:

Home delivery service

£££ Flexible payment plans

www.bbroptometry.co.uk

TEAR CLINIC

WHAT IS TEAR CLINIC?

TEAR CLINIC is a specialist eye care service to diagnose and manage ocular surface disease, relieving dry eye symptoms and preventing long-term complications.

For more information, ask at reception today!

BBR Optometry

BBR Optometry
Marbury House
38 St Owen Street
Hereford
HR1 2PR

Tel: 01432 265030
Email: enquiries@bbroptometry.co.uk

SUPPORTED BY

SCOPE OPHTHALMICS

BBR Optometry

TEAR CLINIC

DRY, SCRATCHY, RED, SORE OR IRRITATED EYES?

To find out if you have ocular surface disease, make an appointment now with a TEAR CLINIC expert at BBR Optometry for specialist advice and treatment.

www.bbroptometry.co.uk

Ocular surface disease is largely undiagnosed and untreated and affects a significant number of people.

Nearly **50%** of people surveyed with dry eye disease say it affects their work life[1]

1/3 people claim dry eyes impact the amount of time they spend reading, going outdoors or watching a movie[1]

Early intervention is crucial in preventing progressive and possibly permanent damage to the eyes.

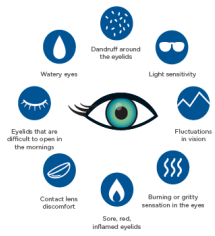
1. Scope Ophthalmics Market Research, 2015

WHAT IS OCULAR SURFACE DISEASE?

Ocular surface disease is a multifactorial disease of the tears and ocular surface. This general term is used to describe a range of conditions that affect the surface of the eye:

- Dry eye disease (DED)—Reduction in the volume and quality of tears
- Blepharitis—Inflammatory condition of the eyelids
- Meibomian gland dysfunction (MGD)—Reduced oil production leading to tear evaporation from the surface of the eye

Common signs and symptoms of ocular surface disease:



TAKE ACTION.

The TEAR CLINIC at BBR Optometry provides expert diagnosis, advice and treatment for ocular surface disease, using advanced techniques.

DO YOU...

- ☐ Wear contact lenses?
- ☐ Use computers for more than 6 hours per day?
- ☐ Take medications (e.g., antibiotics/antihistamines)?

Do you suffer from any of the following?

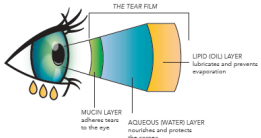
- ☐ Dry eyes
- ☐ Watery eyes
- ☐ Sandy or gritty feeling in your eyes
- ☐ Sore eyes upon waking
- ☐ Blurry or fluctuating vision
- ☐ Stinging or burning eyes
- ☐ Redness of eyes
- ☐ Contact lens discomfort

If so, you could be suffering from ocular surface disease.

Why is tear film important?

The surface of our eyes is coated with a thin layer of tears, called the tear film, which washes, protects, nourishes and lubricates the eye.

Blinking smooths the tear film evenly across the surface of the eye and stimulates the glands to produce more tears.



DON'T LET OCULAR SURFACE DISEASE IMPACT YOUR QUALITY OF LIFE.

A recent survey showed that people with ocular surface disease reported[1]:

- Reduced self confidence due to the impact on their appearance
- Disrupted social activity (e.g., impact on time spent reading/watching TV)
- Decreased productivity at work due to eye fatigue
- Spending less time outdoors due to the effect of the weather (e.g., sun & wind) had on their eyes.

For more information, ask at reception today!

1. Scope Ophthalmics Market Research, 2015

Don't Take Our Word For It. ...Hear What Our Customers Have to Say.

"The service has been useful to help me understand and manage the dryness in my eye"
TONY

"Each stage of my treatment was clearly explained. As always BBR provided an excellent professional service"
SANDRA

"Two months post Lipiflow I am noticing that I can cope without eye drops and my eyes are generally much less dry"
CLARE

Appendix 1.2: Description of in-practice treatment options for dry eye offered at BBR Optometry Ltd.

BBR Optometry Ltd. are one of the early adopters and few providers of the LipiFlow Thermal Pulsation system (TearScience, Morrisville, NC, USA) in the UK. LipiFlow was approved by the Food and Drug Administration in 2011, CE-marked in July 2011 as a Class II a device, and is intended for the application of localised heat and pressure therapy in adult patients with cystic conditions of the eyelids including Meibomian Gland Dysfunction (MGD) (Satjawatcharaphong et al., 2015; NICE, 2015a). Optimal treatment of MGD requires some method of evacuating the Meibomian gland contents and LipiFlow offers an alternative to painful manual expression that may need to be repeated several times a year (Blackie et al., 2016). The LipiFlow treatment itself involves the fitting of disposable eyepieces under the eyelids, which vault the cornea and once activated apply directional therapeutic heat of 42.5°C to the inner eyelid, and pressure to the outer eyelid surfaces (up to 5.5 psi) simultaneously for 12 minutes (Lane et al., 2012; Blackie et al., 2015). These actions are designed to loosen, liquefy and express hardened Meibomian lipids, which have blocked the Meibomian glands (NICE, 2015a). LipiFlow has been shown to be effective in evacuating contents of the Meibomian glands from all four eyelids, and in offering sustained improvement in symptoms and Meibomian gland function over 12 to 36 months following a single treatment (Blackie et al., 2015; Blackie et al., 2016; Greiner et al., 2016). Cohorts of people with MGD, refractory dry eye, refractory dry eye post LASIK, Sjögren's disease and contact lens wearers have benefited from LipiFlow treatment (Blackie et al., 2016; Epitropoulos et al., 2017; Korb & Blackie, 2014; Schallhorn et al., 2017). Adverse effects reported include discomfort during the procedure leading to cessation of treatment, and development of a chalazion on the upper or lower lid which resolved within one month of therapy (NICE, 2015a).

Finis et al. (2014b) found that the effects of a single LipiFlow treatment were sustained over six months and performed at least as well as a robust twice daily hygiene, heat and massage regime over three months (Finis et al., 2014c). It is unclear if compliance rates affected the study outcomes. Hagen et al. (2018) compared the efficacy of a single bilateral LipiFlow treatment versus daily oral doxycycline for three months, which can be prescribed by independent prescribing optometrists, for moderate to severe MGD in a prospective, randomized, parallel-group single masked study involving 28 subjects. Dry eye symptoms were evaluated using the SPEED questionnaire, and dry eye signs were evaluated using the Meibomian gland evaluator to count the number of glands yielding liquid secretion, tear break up time, and corneal and conjunctival staining (Hagen et al., 2018). These clinical tests are used at BBR Optometry Ltd. and are described in chapter one. Results showed LipiFlow at three-months post treatment was more effective at improving symptoms and at least as effective in improving clinical signs when compared to a three-month daily course of oral doxycycline, suggesting LipiFlow provides a more favourable minimal risk profile treatment option for MGD versus long-term antibiotic use (Hagen et al., 2018). The LipiFlow system is currently a private treatment used in primary care by optometrists or in ophthalmology departments in secondary or tertiary care but has not been adopted in the National Health Service (NHS) presumably because alternative, traditional management options such as warm compress or lid massage are available at little or no cost to the NHS.

Use of baby shampoo despite containing known skin irritants and association with ingredients that reduce tear film stability, and use of home-made solutions of water and sodium bicarbonate are the traditional recommendations for lid hygiene methods for blepharitis based largely on expert opinion in current clinical guidance for eye care health professionals and GPs (Maibach, 1986; Zirwas & Moennich, 2009; Wieslander & Norback, 2010; Welling et al., 2014; CKS, 2015; MEH, 2017). There is evidence of improvement in blepharitis signs and symptoms following intervention with eyelid hygiene regimens including commercially available cleanser and diluted baby shampoo (Lindsley et al., 2012; Key, 1996; Khaireddin & Hueber, 2013; Arrua et al., 2015). However, outside of sterile laboratory conditions the precision of at-home preparations may not be reproduced with risks of contamination and insufficient dilution. The length of time for safe storage of these preparations is also not established, which could also lead to undesirable outcomes. In a prospective,

randomised, double-masked, paired eye trial, Sung et al. (2018) found clinical improvements in blepharitis occurred with twice daily use of dedicated eye cleanser (TheraTears® SteriLid®) and diluted baby shampoo (Johnson's® No More Tears®) over four weeks. However, only the dedicated cleanser was effective in reducing ocular surface inflammation quantified using MMP-9 inflammatory markers, and was the preferred treatment amongst participants (Sung et al., 2018). MUC5AC is a goblet cell-specific mucin and its expression levels within the conjunctival epithelium reflects goblet cell density and function (McKenzie et al., 2000; Dogru et al., 2005; Dogru et al., 2008). There was a decrease in level of MUC5AC expression in eyes treated with baby shampoo only, suggesting the presence of pro-inflammatory agents within the formulation given inflammation and hyperosmotic stress can compromise goblet cell integrity (Sung et al., 2018). A study involving contact lens wearers with blepharitis has also reported greater clinical efficacy of a phospholipid-lipsosome solution (Blepha Cura®) compared to baby shampoo (Khaireddin & Hueber, 2013).

BBR Optomery Ltd. offer BlephEx™ microblepharoexfoliation treatment, which uses a patented hand-held electromechanical device to spin a medical grade micro-sponge along the edge of the eyelids and lashes to remove scurf and bacterial debris found in blepharitis. The medical grade, single use sponges are soaked in eyelid cleansing product prior to use and four different sponges are used to exfoliate the upper and lower eyelids. Customers are instructed to maintain their clean eyelids with regular lid hygiene at home, with a view to repeat the procedure every six months to one year depending on the severity of blepharitis. Although the authors are biased, it has been suggested that BlephEx™ should be performed routinely on people after age 50 as commonplace as dental cleaning in order to prevent damage to and loss of the Meibomian glands, given bacterial changes at the lid margin including over-colonization can culminate in inflammation (Rynerson & Perry). BlephEx™ is a standalone treatment, conducted prior to LipiFlow and as part of treatment for Demodex blepharitis over the course of three visits.

Demodex infestation should be suspected in those with chronic blepharitis or refractory ocular surface inflammation, and where cylindrical dandruff at the root of the lashes is present (Gao et al., 2005a; Coston, 1967; English, 1971; Norn, 1970). Demodex mites can be dose-dependently killed with three applications of 50% Tea Tree Oil (TTO) and daily use of TTO preparations up to 10% by customers (Gao et al., 2005b; Gao et al., 2007; Liu et al., 2010; Koo et al., 2012). Cliradex (Cliradex, Miami, FL, USA) is a lid wipe used by customers at home following in-practice tea tree oil TTO treatments (three weekly applications of 50:50, Jojoba oil and 100% TTO) at BBR Optometry Ltd. that contains the active ingredient from TTO, terpinen-4-ol, and has shown promising results for the treatment of Demodex folliculorum blepharitis (Tighe et al., 2013; Cheng et al., 2015; Jones et al., 2017). The recommended regimen for customers is to apply Cliradex twice daily for at least six weeks to cover two life cycles of Demodex, and customers may wish to continue with a maintenance dose of once daily for a longer period of time (Cheng et al., 2015).

Punctal occlusion with temporary absorbable or permanent non-absorbable plugs is another treatment option offered at BBR Optometry Ltd. that conserves tears and retains moisture on the ocular surface by preventing tear drainage (Jones et al., 2017). Typically, temporary plugs are collagen-based and fitted first prior to permanent occlusion in order to assess the efficacy of occlusion (Jones et al., 2017). A systematic review conducted by Ervin et al. (2010) concluded that punctal plugs can offer symptomatic improvement and clinical improvements from baseline metrics, with temporary plugs just as effective as silicone-based permanent plugs on a short-term basis in severe dry eye. The effectiveness of punctal plugs for treating dry eye is inconclusive given the variability in type of plug used across different studies, severity of dry eye being managed and trial methodology (Ervin et al., 2019). There are few studies that show a benefit of punctal plugs over a comparison treatment and it is thought that punctal occlusion may be most effective when combined with other dry eye therapies (Ervin et al., 2010; Roberts et al., 2007). Punctal occlusion is relatively safe although their use has been associated with epiphora and less commonly with inflammatory conditions such as dacryocystitis (Ervin et al., 2017).

Appendix 1.3: Knowledge Transfer Partnership certificate.

Certificate No. **KTP009622-A01**

This is to certify that

Jessica MacIsaac

was an Associate on the Knowledge Transfer Partnership between

Aston University and BBR Optometry Limited

from **13/07/2015** to **30/06/2018** and completed the following project:

To create an easily transferable model for the management and treatment of vulnerable groups of patients within an independent optometry practice.

[redacted]

KTP Programme Manager
Innovate UK

THE AIM OF THE KNOWLEDGE TRANSFER PARTNERSHIP IS TO:

- Strengthen the competitiveness, wealth creation and economic performance of the UK by the enhancement of knowledge and skills and the stimulation of innovation through collaborative projects between business and the knowledge base.

WITH THE OBJECTIVES OF:

- facilitating the transfer of knowledge and the spread of technical and business skills, through innovation projects undertaken by high calibre, recently qualified, people under the joint supervision of personnel from business and the knowledge base;
- providing company-based training for graduates in order to enhance their business and specialist skills;
- stimulating and enhancing business relevant education and research undertaken by the knowledge base;
- increasing the extent of interactions by businesses with the knowledge base and their awareness about the contribution the knowledge base can make to business development and growth.

Knowledge Transfer Partnerships, Innovate UK, Polaris House, North Star Avenue, Swindon, SN2 1FL

Appendix 1.4: Assessment of final Knowledge Transfer Partnership report.

Innovate UK

Our Ref: KTP009622

Mr Martin May
Aston University
Business Partnership Unit
Aston Triangle
Birmingham
B4 7ET

10 September 2018

Dear Mr May

ASSESSMENT OF KNOWLEDGE TRANSFER PARTNERSHIP FINAL REPORT BETWEEN:
Aston University and BBR Optometry Limited

The final report for the above Knowledge Transfer Partnership has been assessed as indicated below:

Grade A (Outstanding)	
Grade B (Very Good)	X
Grade C (Good)	
Grade D (Satisfactory)	
Grade E (Unsatisfactory)	

I regret that we are unable to enter into correspondence about the gradings given.

Please note that a similar letter has been sent to the Lead Academic.

Yours sincerely

[redacted]
Post-Award Team
Email: [redacted]

Innovate UK is the trading name of the Technology Strategy Board
Innovate UK, Polaris House, North Star Avenue, Swindon, SN2 1FL
Tel: +44 (0)1793 442 700
Email: support@innovateuk.gov.uk
www.innovate.gov.uk

Appendix 2.1: SERVQUAL and applications to optometric businesses

The SERVQUAL instrument or scale published by Parauraman et al. in 1988 involves a survey with 21 service attributes grouped into five service quality dimensions that helps to gauge the overall relationship with the customer (Parasuraman, 2004). The five service quality dimensions are:

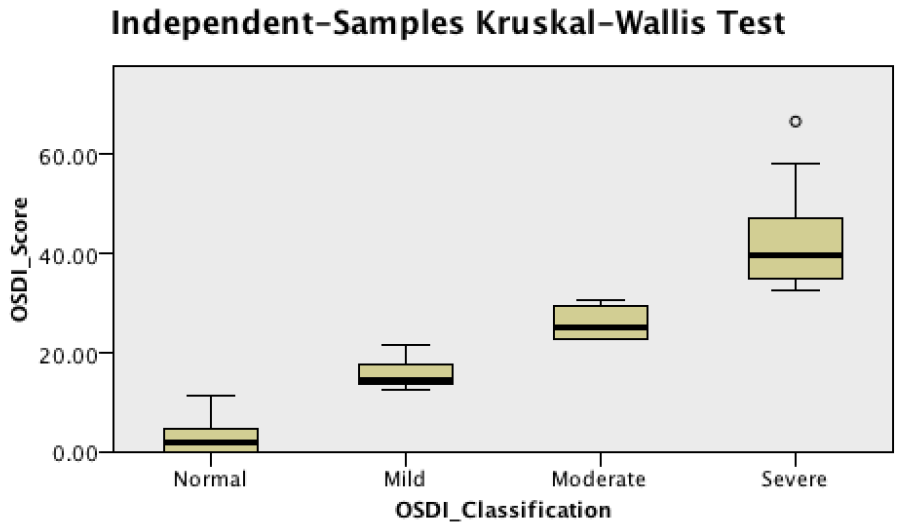
1. *Reliability:* the ability to perform the promised service dependably and accurately (statements 1-5).
2. *Responsiveness:* the willingness to help the customer and provide prompt service (statements 6-10).
3. *Assurance:* the knowledge and courtesy of employees and their ability to convey or inspire trust and confidence (statements 11-13).
4. *Empathy:* the provision of caring, individualised attention to customer (statements 14-17).
5. *Tangibles:* the appearance of the physical facilities, equipment, personnel and communication materials (statements 18-21).

Customers provide two ratings on each attribute at different points in time- one reflecting the level of service they would expect from excellent companies in the industry before the service encounter and the other reflecting their perception of the service delivered by a specific company within the industry after the service encounter. A quantified measure of service quality is derived from the difference between the two ratings. The SERVQUAL is used in many service industries, and has been criticized for failing to capture the dynamics of changing expectations and taking into account whether expectations exist or are clearly formed to serve as a standard for evaluation of a service experience (Buttle, 1996).

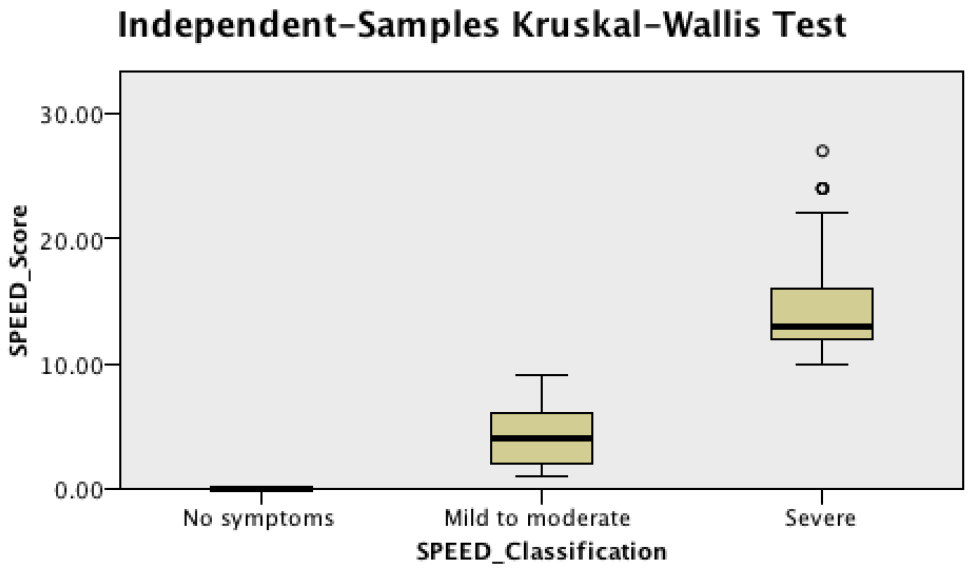
Charafaray (2006) discusses the importance of service quality as a differentiating characteristic for contact lens manufacturers in the South African contact lens industry. The research set out to measure expectations and perceptions of optometrists interacting with Ciba Vision as a contact lens supplier in a business to business interaction using the SERVQUAL instrument (Charafaray, 2006). The study found that the reliability dimension contributed the most to differences between expectations and perceptions suggesting that companies need to keep customers informed with regards to the availability of products, and of any delays or backorders (Charafaray, 2006). Charafaray (2006) recommends that companies provide explicit and implicit service promises in order to improve their customer's perception of the reliability of their service.

SERVQUAL has been shown to be valid for measurement of optometric service quality with good reliability, and correlation between overall quality scores and SERVQUAL gap values in a doctoral thesis by Dr Sarah Joy Smith (2011). Results showed that customers had relatively low expectations as to the appearance of the practice and staff for evaluating service quality in optometric practices but had high expectations that the practice would have modern equipment (Smith, 2011). Indicating modern equipment as particularly relevant to good service quality suggests customers may link access to advanced technology to problem solving and accuracy in relation to producing prompt and reliable diagnoses that are important to the customer. Contact lens wearers had a higher opinion of service quality from their optometrist thought due to the increased level of interaction these customers have with the practice for more regular aftercare appointments or due to the optometrist adding value in the customer's view by introducing an alternative to spectacle wear or managing previous issues with contact lens tolerance (Smith, 2011).

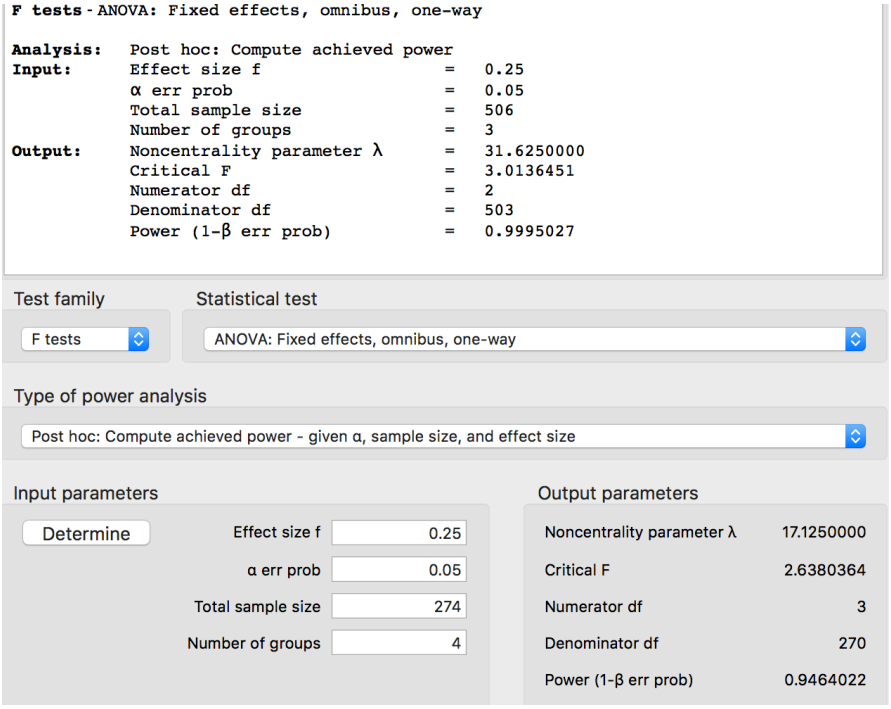
Appendix 2.4: Visualizing distribution shape with a boxplot for OSDI Independent-Samples Kruskal-Wallis test.



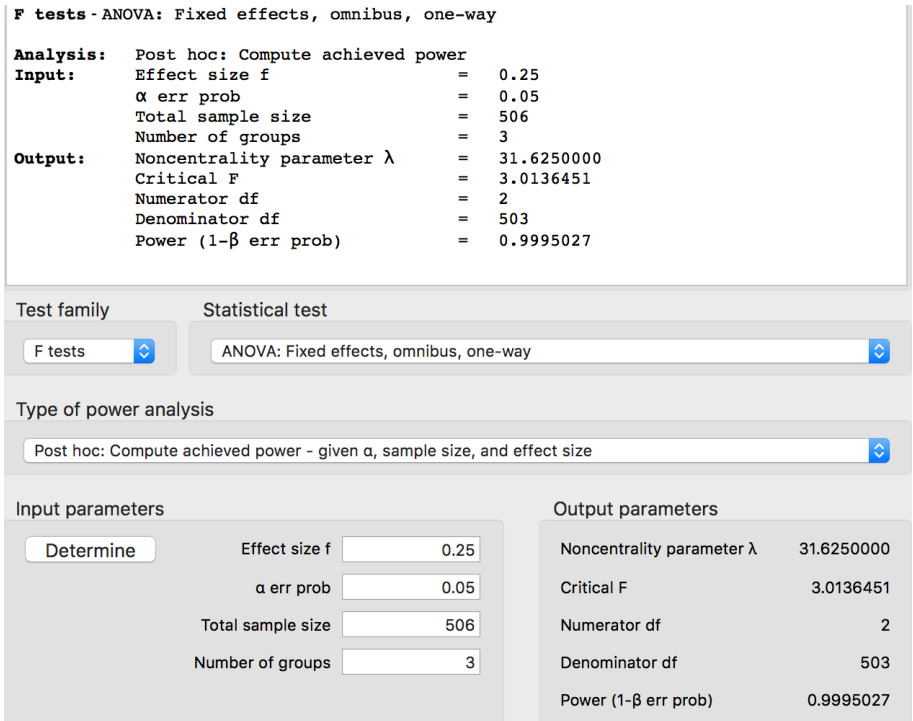
Appendix 2.5: Visualizing distribution shape with a boxplot for SPEED Independent-Samples Kruskal-Wallis test.



Appendix 2.6: G*Power calculation for OSDI chapter two data



Appendix 2.7: G*Power calculation for SPEED chapter two data



Appendix 2.8: Certificates of completion for courses in the W.P. Carey Certificate in Service Experience Management Programme from Arizona State University.

ARIZONA STATE UNIVERSITY

CENTER FOR SERVICES LEADERSHIP

This is to certify that

JESSICA MACISAAC

has participated in the Continuing and Professional Education online course

FOUNDATIONS OF SERVICE EXCELLENCE

and has earned satisfactory scores to complete the course

March 19, 2019

[redacted]

ASU W.P. Carey School of Business
Arizona State University

ARIZONA STATE UNIVERSITY

CENTER FOR SERVICES LEADERSHIP

This is to certify that

JESSICA MACISAAC

has participated in the Continuing and Professional Education online course

DELIVERING SERVICE EXCELLENCE

and has earned satisfactory scores to complete the course

March 20, 2019

[redacted]

ASU W.P. Carey School of Business
Arizona State University

Arizona State University

Center for Services Leadership

This is to certify that

JESSICA MACISAAC

has participated in the Continuing and Professional Education online course

BLUEPRINTING SERVICE EXPERIENCES

and has earned satisfactory scores to complete the course

March 25, 2019

[redacted]

ASU W. P. Carey School of Business
Arizona State University

Arizona State University

Center for Services Leadership

This is to certify that

JESSICA MACISAAC

has participated in the Continuing and Professional Education online course

VOICE OF THE CUSTOMER

and has earned satisfactory scores to complete the course

March 25, 2019

[redacted]

ASU W. P. Carey School of Business
Arizona State University

Appendix 3.1: Relevant evidence where DTA and PCA have been used.

DTA has been used in some of Aston University's ophthalmic postgraduate research. The following is a list of successful theses:

- Dr Derek Dunstone "Habits and attitudes towards retinoscopy and the relative accuracy of dedicated and combined retinoscopes" DOptom thesis, 2013
- Dr Rebecca Rushton "A new algorithm for the relationship between vision and ametropia" DOptom thesis, 2014
- Dr Rajeshwari Sagar "Application of Naïve Bayesian sequential analysis to primary care optometry" DOptom thesis, 2014
- Dr Bhavna Pancholi "A comparison of computer aided learning and traditional didactic lectures for teaching clinical decision-making skills to optometry undergraduates" PhD thesis, 2016
- Dr Anita Morrison-Fokken "Provision of spectacle lens correction to elderly people at risk of falls" PhD thesis, 2017
- Dr Laura Knowles "The prevalence and progression of astigmatism and myopia in children" DOptom thesis, 2017
- Dr Peter Frampton "Tonometry: A Study in Biomechanical Modelling. Appraisal and utility of measurable biomechanical markers" DOptom thesis, 2017

The following are examples of factor analytic techniques used in ophthalmic research.
Relating to Glaucoma:

- A prospective, clinical, and comparative study conducted by Morejon et al. (2019), used PCA to extract the four most important features of Frequency Doubling Technology as a functional test, and spectral domain Optical Coherence Tomography (OCT) as a structural test alongside the variables age, visual acuity and intraocular pressure to discriminate between nonglaucomatous and glaucoma suspect subjects. A logisitc analysis was then applied to obtain objective predictive rules providing a high sensitivity and specificity to detect the earliest stages on glaucoma in a primary care setting.

- Lin et al. (2018) used PCA in a cross-sectional study to investigate the overall dimensionality of vision in glaucoma as pairwise comparisons could not adequately describe the complex matrix of correlations within the sample of glaucoma patients of vision tests including integrated visual field sensitivity, visual acuity, contrast sensitivity (CS), area under the log CS function, stereoacuity and visual acuity with noise. The first principal component positively incorporated multiple vision measures and was not dominated by one element suggesting that no single measure was sufficient to describe the full spectrum of vision loss resulting from glaucoma (Lin et al., 2018).

- A prospective, open cohort study conducted by Chono et al. (2018), used PCA to analyse the complex interaction of intraocular pressure and cytokines, and found a pro-inflammatory and IOP-associated component with interleukin-8 having the strongest loading, suggesting potential candidate molecules that can predict the clinical outcome of surgical interventions in eyes with refractive glaucoma.

Relating to Macular Disease:

- McCarter et al. (2019) used PCA (orthogonal rotation) in a cross-sectional analysis in the Irish Nun Eye Study and identified two major dietary patterns labelled as healthy and unhealthy with no evidence of association with risk of age-related macular degeneration.

- PCA identified a dominant first principal component accounting for 77% of the variation and including all reading items evenly weighted in a psychometric evaluation of a vision-related quality of life questionnaire in a sample of patients with acquired macular disease (Hazel et al., 2000).

- Chan et al. (2018) used PCA to extract features from a proposed detection framework combining AlexNet, VggNet and GoogleNet which are Convolutional Neural Network models or deep learning methods that can classify optical coherence tomography images as normal or having diabetic macular oedema, for dimensionality reduction.

Relating to Cataract Surgery:

- (Sen et al., 2019) used PCA to determine factors resulting in perceived difficulty of each step of phacoemulsification for 12 trainee residents performing 10 surgeries each at a tertiary care center in New Delhi. Steps involved in high amount of binocularity and those involving high precision of hand control accounted for the majority of the variance for the entire set of variables and were the main reasons for perception of difficulty in performing cataract surgery amongst trainees, which may highlight factors that should form part of training modules.

Relating to Keratoconus:

- In a multi-center retrospective study, Yousefi et al. (2018) found keratoconus diagnosis and staging could be determined with high specificity and sensitivity using an automated clustering algorithm, which utilized corneal thickness profiles as well as topographic and tomographic information. Yousefi et al. (2018) used PCA to extract the information that is highly predictable of the corneal status and linearly reduced the dimensionality of the input data rather than feeding approximately 420 corneal parameters to a machine learning algorithm and confusing its prediction.

Relating to Thyroid Eye Disease:

- A retrospective analysis of orbital computed tomography imaging for 85 patients and an automated segmentation tool used PCA of 25 bilateral orbital structural metrics to identify the two most important characteristics of thyroid eye disease that accounted for 60% of the variance, which were the "big volume phenotype" showing large size and volume features and the "stretched optic nerve phenotype" showing longer and thinner optic nerves with increased orbital fat (Chaganti et al., 2018). A Kendall rank correlation between the principal components and clinical data identified associations between the phenotypes and clinical markers.

Relating to Retinal Vessel Caliber:

- In a cross-sectional study of participants from the Irish Nun Eye Study, PCA identified two dietary patterns as healthy or unhealthy using the food frequency questionnaire to assess dietary intake, with subsequent adjusted linear regression analysis revealing an independent association between an unhealthy dietary pattern and an unfavourable retinal profile defined as a widening of retinal venules and narrowing of retinal arterioles (Neville et al., 2018). PCA used in nutritional epidemiological studies to derive dietary patterns empirically has been criticised as a subjective measure involving arbitrary decisions although good reproducibility and validity have been demonstrated (Newby & Tucker, 2004; Hu & Willett, 2002).

Relating to Neurological Conditions:

- Armstrong et al. (2000) used PCA to test proposed hypotheses for the explanation of neuropathological heterogeneity in Alzheimer's disease by studying the variation in the distribution and severity of neuropathological data including the abundance scores of senile plaques and neurofibrillary tangles in 23 brain regions collected from 80 cases. Initially the cases were used as variables in PCA to determine whether differences between patients were continuously distributed or clustered into subtypes, then the neuropathological data were used as variables to determine the most important factors for individual variations (Armstrong et al., 2000). Results from the sample showed the neuropathological variation was continuously distributed, and the presence of lesions in brain areas hypothesized to be

part of the pathway of pathological change spreading were identified as the most important sources of neuropathological variation, which support the phase hypothesis that explains variation in Alzheimer's disease by the rate of spread of the pathology (Armstrong et al., 2000).

Appendix 3.2: Model Summary table, DTA by CHAID method, and Risk & Classification table for LE data

The Model summary table seen in figure 1 confirms the specifications selected, and summarises the results of the left eye DTA by the CHAID method. It was noted that four of the eight independent variables were included. DTA (CHAID) automatically determined that sex, lipid layer thickness, percentage of partial blinks, and Meibomian gland duct dilation were not important predictors of dry eye status. The depth of the resulting tree (four) was less than what was allowed for (eight), so decision tree growth was not artificially restricted.

Model Summary

Specifications	Growing Method	CHAID
	Dependent Variable	Dry_Eye_Status
	Independent Variables	Age, Sex, LE_lipid_layer_thickness, LE_Percentage_of_partial_blinks, LE_Meibomian_gland_evaluator_score, LE_Fluorescein_tear_breakup_time, LE_Meibomian_gland_dropout, LE_Meibomian_gland_duct_dilation
	Validation	None
	Maximum Tree Depth	8
	Minimum Cases in Parent Node	16
	Minimum Cases in Child Node	8
Results	Independent Variables Included	LE_Fluorescein_tear_breakup_time, Age, LE_Meibomian_gland_evaluator_score, LE_Meibomian_gland_dropout
	Number of Nodes	11
	Number of Terminal Nodes	7
	Depth	4

Figure 1: Model summary for left eye DTA by the CHAID method

Figure 2 shows the DTA for left eye data. Fluorescein tear breakup time was the most important predictor of dry eye status: Chi-square (1, n = 162) = 15.89, $p < 0.001$. The other predictors of dry eye status in order of importance included:

- Age: Chi-square (2, n = 143) = 8.67, $p < 0.05$
- Meibomian gland evaluator score: Chi-square (2, n = 119) = 9.33, $p < 0.05$
- Meibomian gland dropout: Chi-square (1, n = 36) = 7.36, $p < 0.05$

The decision tree classified 73% of the subjects correctly, and had seven terminal nodes:

- The first (11.7% of the sample) included those with a fluorescein tear breakup time greater than 11 seconds, and showed 79% of subjects were from the normal subgroup.
- The second (6.8% of the sample) included those with a fluorescein tear breakup time less than or equal to 11 seconds, aged between 74 and 78 years, and showed a greater proportion of normal subjects (72.7%).
- The third (8% of the sample) included those with a fluorescein tear breakup time less than or equal to 11 seconds, aged older than 78 years, and showed a greater proportion of dry eye subjects (69.2%).
- The fourth (8% of the sample) included those with a fluorescein tear breakup time less than or equal to 11 seconds, aged less than or equal to 74 with a total Meibomian gland evaluator score of six or seven, and comprised 100% of dry eye subjects.
- The fifth (43.2% of the sample) included those with a fluorescein tear breakup time less than or equal to 11 seconds, aged less than or equal to 74 with a total Meibomian gland evaluator score greater than seven, and showed a greater proportion of dry eye subjects (67.1%).
- The sixth (9.9% of the sample) included those with a fluorescein tear breakup time less than or equal to 11 seconds, aged less than or equal to 74 with a total Meibomian gland evaluator score less than or equal to six, had no or mild Meibomian gland dropout, and showed an even split between dry eye and normal subjects (50%).
- The seventh (12.3% of the sample) included those with a fluorescein tear breakup time less than or equal to 11 seconds, aged less than or equal to 74 with a total Meibomian gland evaluator score less than or equal to six, had moderate or severe Meibomian gland dropout, and showed predominately dry eye subjects (90%).

It would appear that three of the seven terminal nodes are based on less than 15 observations, which may render the model prone to spurious observations. The risk and classification table for the left eye DTA can be seen in figure 3, showing the model is overall 73% accurate.

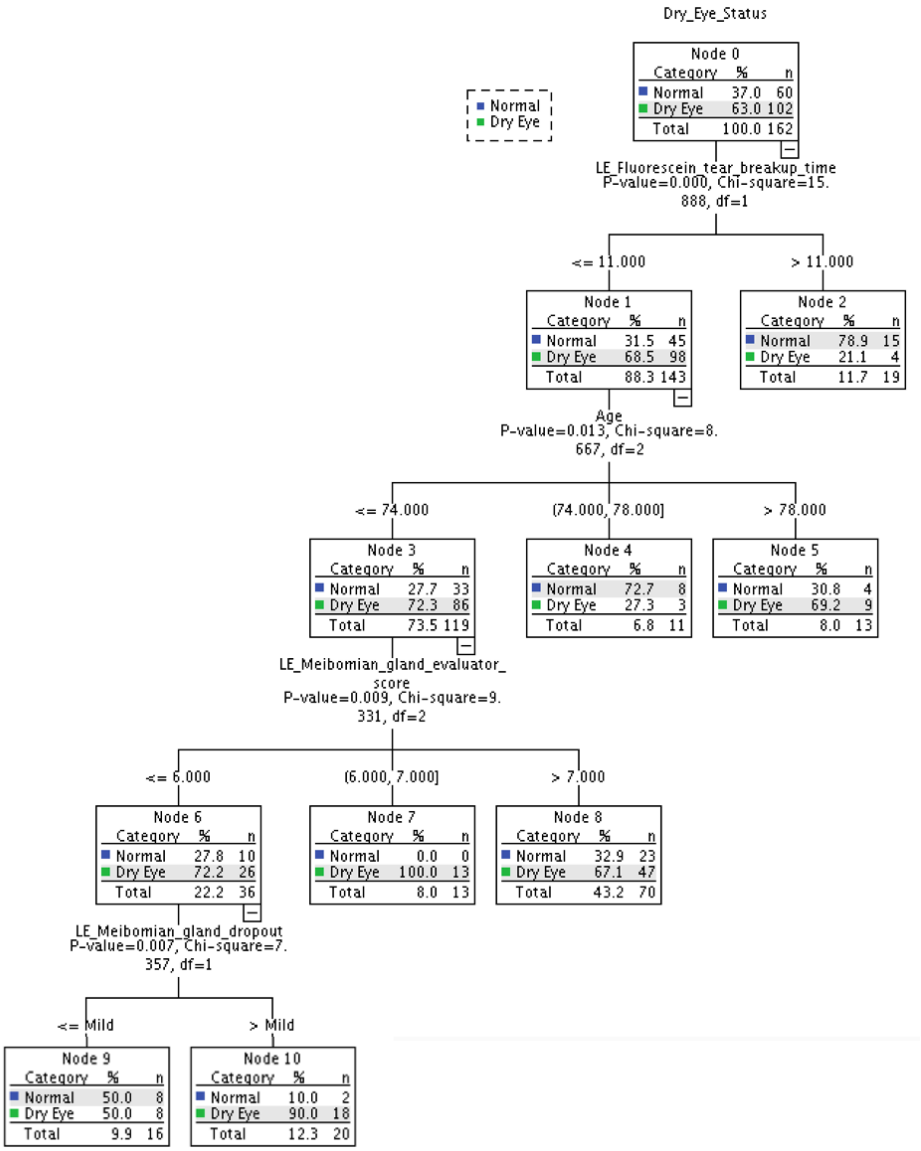


Figure 2: Decision tree for left eye showing which clinical tests can predict dry eye status.

Risk

Estimate	Std. Error
.272	.035

Growing Method: CHAID
Dependent Variable: Dry_Eye_Status

Classification

	Predicted		
Observed	Normal	Dry Eye	Percent Correct
Normal	31	29	51.7%
Dry Eye	15	87	85.3%
Overall Percentage	28.4%	71.6%	72.8%

Growing Method: CHAID
Dependent Variable: Dry_Eye_Status

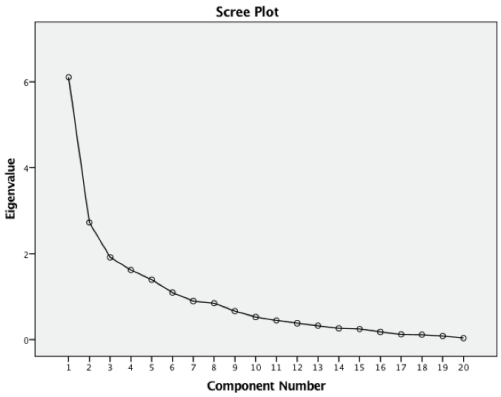
Figure 3: Risk and Classification table for left eye data.

Appendix 3.3: Component matrices, Catell's scree test plots, and Component correlation matrices.

Component Matrix[a]

	Component					
	1	2	3	4	5	6
SPEED_2	.796	-.356				
OSDI_3	.756					
SPEED_4	.690		-.310			
OSDI_2	.685					
SPEED_8	.654		-.392			.314
SPEED_6	.642	-.482				
OSDI_5	.571	.400		-.386		
OSDI_11	.546			.531		
OSDI_7	.303	.696				
OSDI_6	.517	.637		-.300		
OSDI_4	.374	.582		-.427		
OSDI_9	.435	.574				
OSDI_8	.445	.519				-.394
SPEED_7	.366		.715	-.394		
SPEED_3	.389		.704	-.404		
OSDI_10	.537		.601			
OSDI_12	.517			.551		
SPEED_5	.599				.661	
SPEED_1	.587				.643	
OSDI_1					.303	.659

Extraction Method: Principal Component Analysis.
a. 6 components extracted.

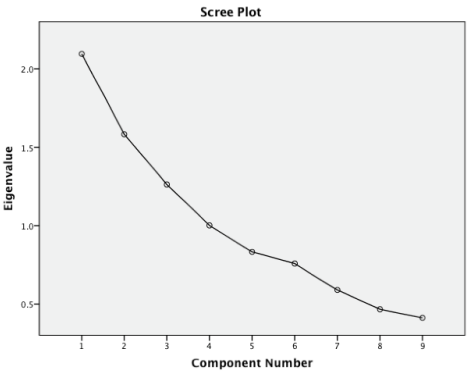


Results from PCA Section 3.3.3: Output generated from SPSS including table of unrotated loadings from the Component Matrix and the Catell's scree test plot.

Component Matrix[a]

	Component			
	1	2	3	4
RE_Meibomian_Gland_Evaluator_score	.755			
RE_Meibomian_Gland_Dropout	-.747			
RE_Lipid_layer_thickness	.577		.501	
Total_OSDI_Score		.846		
Total_SPEED_Score		.837		
RE_Fluorescein_tear_breakup_time			-.665	.400
RE_TearLab_Osmolarity	-.404		.620	
RE_Percentage_of_partial_blinks	.373		.359	.645
RE_Meibomian_Gland_Duct_Dilation	-.505			.547

Extraction Method: Principal Component Analysis.
a. 4 components extracted.



Results from PCA Section 3.3.4: Output generated from SPSS including table of unrotated loadings from the Component Matrix and the Catell's scree test plot for a four-factor solution of right eye data

Component Correlation Matrix

Component	1	2	3	4
1	1.000	-.030	-.096	.179
2	-.030	1.000	.034	-.021
3	-.096	.034	1.000	-.049
4	.179	-.021	-.049	1.000

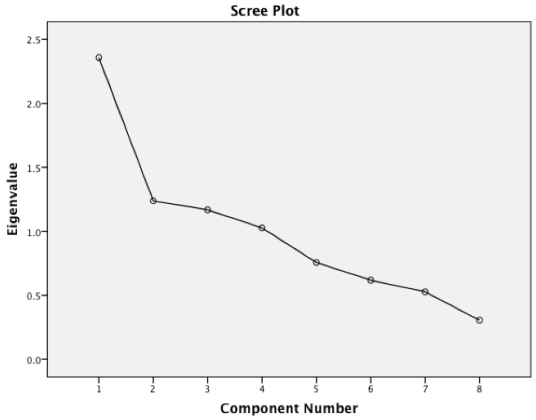
Extraction Method: Principal Component Analysis.
Rotation Method: Oblimin with Kaiser Normalization.

Results from PCA Section 3.3.4: Component Correlation Matrix for the four-factor solution for right eye data.

Component Matrix[a]

	Component			
	1	2	3	4
RE_Meibomian_Gland_Dropout	-.813		.335	
RE_Meibomian_Gland_Evaluator_score	.785			
RE_Meibomian_Gland_Duct_Dilation	-.630			
RE_TearLab_Osmolarity		.607		.456
RE_Lipid_layer_thickness	.577	.589		
RE_Fluorescein_tear_breakup_time		-.343	.757	
RE_Percentage_of_partial_blinks	.324	.590	.593	
Total_Jessica_Score	.329			.848

Extraction Method: Principal Component Analysis.
a. 4 components extracted.



Results from PCA Section 3.3.5: Output generated from SPSS including table of unrotated loadings from the Component Matrix and the Catell's scree test plot for a four-factor solution of right eye data.

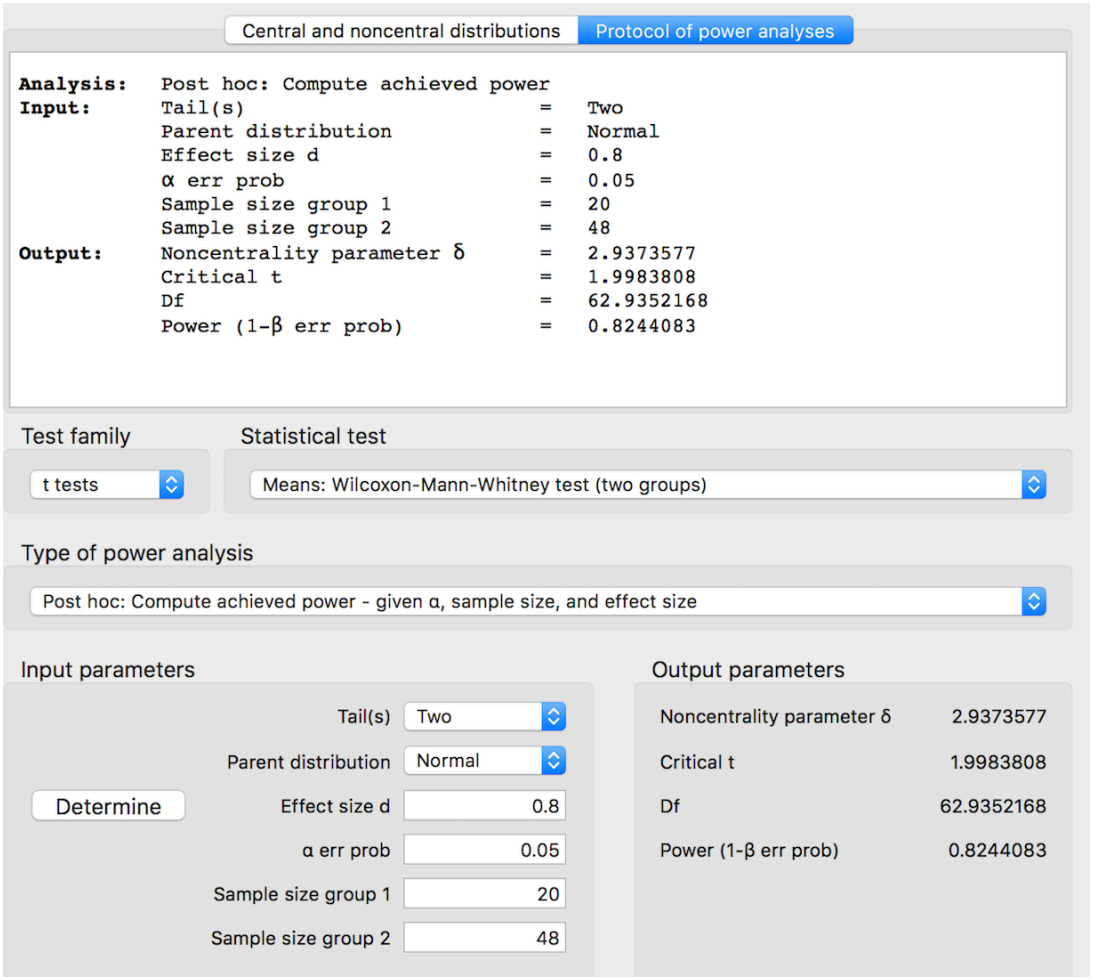
Component Correlation Matrix

Component	1	2	3	4
1	1.000	.133	.103	.026
2	.133	1.000	-.022	.060
3	.103	-.022	1.000	.008
4	.026	.060	.008	1.000

Extraction Method: Principal Component Analysis.
Rotation Method: Oblimin with Kaiser Normalization.

Results from PCA Section 3.3.5: Component Correlation Matrix for the four-factor solution for right eye data.

Appendix 4.1: G*Power calculation for chapter four data



Appendix 4.2: Details for optometrists involved in post-operative care.

- Spectacles can be prescribed at one month post-surgery.
- Optometrist to record: distance and near vision, refraction, distance and near visual acuity, and corneal findings in addition to completing the table below.

Signs to assess	Right	Action	Left
Wound secure	Yes/No	No- refer	Yes/No
AC formed	Yes/No	No- refer	Yes/No
AC cells	Yes/No	>+1 refer	Yes/No
AC flare	Yes/No	>+1 refer	Yes/No
Other signs	Yes/No	Discuss if appropriate	Yes/No
IOL good position	Yes/No	No- refer	Yes/No
IOP	mmHg	>24 discuss	mmHg
Macula dry	Yes/No	No- refer (dilate if poor VA)	Yes/No
PCO	Yes/No	Yes- refer to YAG after 6/52	Yes/No

- Additional protocol:

  "If any evidence of infection/ inflammation, document and refer immediately without increasing antibiotics in case needs a sample. If unsure, better to have it checked. If punctate keratitis, increase lubrication. Lubrication may be needed up to 3 months.

  Advice to patient:

  1. Can go back to normal 4 weeks after surgery.
  2. If has premium IOL
     - Multiofocal intermediate add eg Rezoom: expect near VA of N8-N10
     - Multifocal Near add e.g. Tecnis mutifocal: expect near VA of N5-N8
     - Accommodating eg. Tetraflex : variable from N6-N24
     - Mix + Match (eg Rezoom + Tecnis): different near VA in both eyes but will get used to it
  3. Even with premium lenses, expect to be out of glasses 80-90% of time.
  4. Glasses can be prescribed at 1 month visit
  5. If visual outcome disappointing laser fine tune can be considered at 6-12 weeks but only generally if uncorrected VA <6/12. Typically, with LASEK rather than LASIK. Risk are those with laser."

Ethics approval

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Memo

Life and Health Sciences Ethics Committee's Decision Letter

To: Jessica MacIsaac, Dr Shehzad Naroo

Cc: [redacted]
Administrator, Life and Health Sciences Ethics Committee

From: [redacted]
Chair, Life and Health Sciences Ethics Committee

Date: 13/2/2018

Subject: **Project #1276** Evaluation of dry eye problems in primary eye care

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Thank you for your submission. The additional information for the above proposal has been considered by the Chair of the LHS Ethics Committee.

Please see below for details of the decision and the approved documents.

Reviewer's recommendation: Favourable opinion

Please see the tabled list below of approved documents:

Documentation	Version/s	Date	Approved
Response to reviewers' comments	1	5/2/18	✓
Risk assessment	1	14/11/17	✓
Dry Eye Questionnaire	n/a	n/a	✓
OSDI Questionnaire	n/a	n/a	✓

After starting your research please notify the LHS Research Ethics Committee of any of the following:

Substantial amendments. Any amendment should be sent as a Word document, with the amendment highlighted. The amendment request must be accompanied by all amended documents, e.g. protocols, participant information sheets, consent forms etc. Please include a version number and amended date to the file name of any amended documentation (e.g. "Ethics Application #100 Protocol v2 amended 17/02/12.doc").

New Investigators

The end of the study

Please email all notifications and reports to lhs_ethics@aston.ac.uk and quote the original project reference number with all correspondence.

Ethics documents can be downloaded from: [redacted] Please note that these documents can ONLY be opened using Mozilla Firefox or the latest Internet Explorer version (IE9).

Statement of Compliance

The Committee is constituted in accordance with the Government Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK. In accord with University Regulation REG/11/203(2), this application was considered to have low potential risk and was reviewed by three appropriately qualified members, including the Chair of the Life and Health Sciences Ethics Committee.

Yours sincerely,

[redacted]
Chair, LHS Ethics Committee