THE DESIGN, IMPLEMENTATION AND EVALUATION OF A LABORATORY BASED INTERVENTION TO OPTIMISE SERUM IMMUNOGLOBULIN TEST USE IN PRIMARY CARE

A thesis submitted to the National University of Ireland, Cork for the degree of Doctor of Philosophy in the Department of Epidemiology & Public Health, School of Medicine, September 2016.

SHARON LOUISE CADOGAN (BSc, MPH)

Supervisors

Professor Mary Cahill
Professor John Browne
Professor Colin Bradley

Head of Department

Professor Ivan Perry

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

BCT	Behaviour Change Technique
BGH	Bantry General Hospital
COM-B	Capability, Opportunity and Motivation Behaviour
CUH	Cork University Hospital
CBA	Controlled Before-After
CCT	Controlled Clinical Trial
CREC	Cork Research Ethics Committee
ELE	Electrophoresis
EPOC	Effective Practice of Organisational Care
GP	General Practitioner
GMS	General Medical Scheme
HSE	Health Service Executive
HSE-PCRS	Health Service Executive Primary Care Reimbursement Scheme
IG	Immunoglobulin
IGA	Immunoglobulin A
IGG	Immunoglobulin G
IGM	Immunoglobulin M
INAB	Irish National Accreditation Board
IT	Information Technology
ITS	Interrupted Time Series
LIS	Laboratory Information System
MGH	Mallow General Hospital
MeSH	Medical Subject Headings
MRN	Medical Record Number
MGUS	Monoclonal Gammopathy of Uncertain Significance
NQAIS	National Quality Assurance Intelligence System
NRCT	Non-Randomised Controlled Trial
PARA	Paraprotein
RCT	Randomised Control Trial
RCPI	Royal College of Physicians of Ireland
SIVUH	South Infirmary Victoria University Hospital
SPHeRE	Structured Population and Health-services Research Education
TDF	Theoretical Domains Framework
UHK	University Hospital Kerry
UK	United Kingdom
US	United States

LIST OF PAPERS AND RESEARCH DISEMINATION

PAPERS RELATING TO THESIS

Cadogan SL, Browne JP, Bradley CP, Cahill MR: **The effectiveness of interventions to improve laboratory requesting patterns among primary care physicians: a systematic review**. *Implementation Science* 2015, **10**(1):167.

Cadogan SL, McHugh SM, Bradley CP, Browne JP, Cahill MR: **General practitioner views on the determinants of test ordering: a theory-based qualitative approach to the development of an intervention to improve immunoglobulin requests in primary care**. *Implementation Science* 2016, **11**(1):1-12.

Cadogan SL, Browne JP, Bradley CP, Fitzgerald AP, Cahill MR: **Physician and practice level variation in primary care requesting patterns for laboratory tests.** *Under review at Family Practice (August 2016).*

Cadogan SL, Browne JP, Bradley CP, Fitzgerald AP, Cahill MR: **Evaluation of guidelines combined with automated educational messages for the effective use of laboratory tests among Primary Care physicians: an interrupted time series.** *Submitted to the British Medical Journal Quality and Safety (September 2016).*

OTHER PUBLICATIONS RELATING TO THE THESIS

Cadogan SL. **Testing times ahead? An exploration of laboratory use in primary care**, The Boolean, 2015, pp.37-41

RESEARCH DISSEMINATION

Paper	**Conference proceedings**
Cadogan SL, Browne JP, Bradley CP, Cahill MR: **The effectiveness of interventions to improve laboratory requesting patterns among primary care physicians: a systematic review**. *Implementation Science* 2015, **10**(1):167.	*Oral presentation* European Forum for Primary Care, Amsterdam, Netherlands. August 2015 *Poster presentation* SPHeRE Health Research, Policy and Practice. Dublin, Ireland. January 2015

	18Th Annual Scientific Meeting of the Association of University Departments of General Practice. Belfast, Northern Ireland. March 2015 European Congress of Epidemiology, Maastricht, Netherlands. June 2015 Society for Social Medicine Annual Conference. Dublin, Ireland. Sept 2015 Health Services Research Network Symposium. Nottingham, UK. July 2015
Cadogan SL, McHugh SM, Bradley CP, Browne JP, Cahill MR: **General practitioner views on the determinants of test ordering: a theory-based qualitative approach to the development of an intervention to improve immunoglobulin requests in primary care**. *Implementation Science* 2016, **11**(1):1-12.	*Oral presentation* World Congress of Primary Care. Rio, Brazil. November 2016 (upcoming) *Poster presentation* Society for Social Medicine Annual Conference. Dublin, Ireland. Sept 2015 Haematology Association of Ireland Annual Conference, Sligo, Ireland. October 2014 18Th Annual Scientific Meeting of the Association of University Departments of General Practice. Belfast, Northern Ireland. March 2015 Health Services Research Network Symposium. Nottingham, UK. July 2015
Cadogan SL, Browne JP, Bradley CP, Fitzgerald AP, Cahill MR: **Physician and practice level variation in primary care requesting patterns**	*Oral presentation* SPHeRE Health Research, Policy and Practice. Dublin, Ireland. January 2016

for laboratory tests. *Under review at British Journal of General Practice (August 2016).*	European Forum for Primary Care. Amsterdam, Netherlands. August 2015 Health Technology Assessment international (HTAi). Tokyo, Japan. May 2016
Cadogan SL, Browne JP, Bradley CP, Fitzgerald AP, Cahill MR: **Evaluation of guidelines combined with automated educational messages for the effective use of laboratory tests among Primary Care physicians: an interrupted time series.** *Submitted to the British Medical Journal Quality and Safety (September 2016).*	*Oral presentation* Health Technology Assessment international (HTAi). Tokyo, Japan. May 2016
Research title	**Other presentations**
Good Blood, Bad Blood, Good Blood, Bad Blood…..too much Blood?	*Doctoral Showcase Final* University College Cork, Cork, Ireland. June 2014
Overview of PhD research	*Lunchtime seminars* Department of Haematolgy, Cork University Hospital, Cork, Ireland. August 2014 Knowledge Translation Seminar, Ottawa Hospital Research Institute, Ottawa, Canada. Dec 2015

DECLARATION

I declare that this thesis has not been submitted for another degree at this or at any other University. The work, upon which this thesis is based, was carried out in collaboration with a team of researchers and supervisors who are duly acknowledged in the text of the thesis. The Library may lend or copy this thesis upon request.

Signed: _____ Date: _____

ACKNOWLEDGMENTS

I would like to thank my fantastic supervisory panel: Professor Mary Cahill, Professor John Browne and Professor Colin Bradley. The combination of your individual skills have undoubtedly made this a better thesis.

Prof Cahill – when I walked into the Department of Haematology to complete my BSc work experience back in 2009, I never could have imagined that I would be here seven years later submitting a PhD under your exceptional mentorship. I am so grateful for your continued support, guidance and encouragement over the past few years and have no doubt our research venture will continue for many more. Prof Browne – thank you for imparting on me, your incredible academic writing and critical appraisal skills. Because of your supervision, I am entering a career of health services research with more confidence in my academic writing ability. Prof Bradley – thank you for joining the supervisory panel and providing highly regarded primary care insight and qualitative expertise, as well as your much valued commentary throughout.

This research was funded by the Irish Health Research Board PhD Scholars Programme. I am forever grateful for my place on the programme. The programme provides scholars with exceptional resources, supporting the dissemination of research findings through publications and attendance at both national and international conferences, as well as funding training. I would like to thank the programme's administrative staff Carlos (RSCI) and Maureen (UCC) for their assistance throughout the PhD. I would also like to thank the '2012 cohort' of the programme, in particular, Jamie and Sarah – my 'UCC amigos'. From the dreaded 7am train journeys from Kent station, to the enjoyable dinner dates in Dublin, I am delighted to have found two new friends in this process. Thank you both for your support.

This PhD has given me the opportunity to see amazing parts of the world, including Nepal, Tokyo and Canada. The latter involved working with some of the most admirable implementation science experts in the field. I would like to thank everyone at the Ottawa Hospital Research Institute for making me feel so welcome during my five-week placement with them. In particular, Professor Jeremy Grimshaw for his excellent mentorship; Dr. Monica Taljaard for her statistical expertise; and Dr. Justin Presseau for sharing his knowledge of behaviour change techniques. But also, to the friends I made in the office – Larissa, Bev, Kelly and Daniel, thank you for all the memorable Canadian adventures while I was there.

This thesis involved the use of laboratory data, which was made possible by the staff at Cork University Hospital. I would like to thank the laboratory staff, in particular, Katherine Hooley, Therese Murphy, Grace Creedon, and Mary Ring for their much appreciated involvement and support. I would also like to thank Dr. Oonagh Gilligan for her expert advice in the design phase of the intervention material; Mr Aidan Kelleher for completing the data extraction; Dr. Mary Ryan and Ms Ciara McCarthy for facilitating clinical audits; and Mr Brendan O'Reilly for providing laboratory software training. This

research also utilised Primary Care Reimbursement Scheme data on GP list sizes – thank you to Dr. Howard Johnson for making this possible.

Despite the laboratory focus of this research, my home was the Department of Epidemiology and Public Health, UCC. I would like to thank my fantastic colleagues and friends in the department. In particular, thank you to Professor Ivan Perry for his much valued input and interest in this thesis; Ms Derlva Hogan for her exceptional and timely response to all departmental related queries; Dr. Sheena McHugh for her involvement with the qualitative component of this PhD (and for keeping Friday coffee morning alive) and; Dr. Tony Fitzgerald for his expert statistical advice on many occasions (usually when he should be gone home in the evenings). I would also like to thank Dr. Paul Beirne for always thinking of my career and providing me with the opportunity to participate in additional activities outside of my PhD, in particular, the Cochrane review and teaching. Thank you to all of my open plan colleagues, in particular, Aimée for the endless support and for sharing her thesis formatting skills (and her supply of rice cakes); Elsa and Caragh for their kind encouragement throughout; and Maureen for helping to organise the viva exam. Also, to the administrative staff, Vicky, Tara, Michelle and Ber – thank you for all your help over the years. Finally, a special thank you to Maura for proof reading the thesis and providing encouraging words when most needed, and not to mention the endless supply of coffee and chocolate (also when most needed).

This PhD process came with many ups and downs. I would like to thank those who experienced these the most – my housemates, friends and family. Thank you to my housemates Kieran and Liam for putting up with PhD life in the apartment. To my closest friends: Elaine, Erica, Lisa-Marie, Emma, Gill, Sarah, Amy, Katie, Dede, Siobhan and Aisling – thank you all for your encouragement and understanding throughout this process. In particular, for keeping me sane and smiling over the past four years (with many welcomed distractions from PhD life).

Finally, I would like to thank my amazing family. In particular, my parents, Jim and Myna for always believing in me – even when I doubted myself! I am incredibly lucky to have both of you in my corner. You have provided me with an upbringing beyond any child's expectation (and probably beyond any parent's expectation too). Thank you for everything – you are both truly amazing people.

THESIS ABSTRACT

Background

Laboratory testing plays a fundamental role in the screening, diagnoses and monitoring of many conditions. Given the increased pressures on the Irish health service, improving inefficiencies and reducing waste, while maintaining the quality of care is at the forefront of healthcare planning. Promoting optimal laboratory service utilisation could play a key role in reducing health expenditure, in particular by preventing the unnecessary use of costly downstream services that often arise as a result of testing.

Aims and objectives

The overall aim of this thesis was to design, implement and evaluate a behaviour change intervention for optimising serum immunoglobulin test use in primary care.

The thesis objectives were as follows:

1. To conduct a systematic review of the existing literature on the effectiveness of previous interventions targeting primary care test use.

2. Identify the barriers and enablers of improving test ordering for serum immunoglobulins among General Practitioners (GPs), using semi-structured interviews.

3. Identify the intervention components (behaviour change techniques and mode(s) of delivery) that could overcome the modifiable barriers and enhance the enablers.

4. Determine which GP and practice characteristics are associated with higher serum immunoglobulin test ordering patterns in the South of Ireland.

5. To implement and evaluate a behaviour change intervention targeting GP serum immunoglobulin test use in the Cork-Kerry region.

Structure and Methods

The published literature to date was synthesised in a systematic review (Chapter 3). This review was conducted in accordance with the Effective Practice and Organisation of Care (EPOC) guidelines and quality appraised using the Cochrane Collaboration risk of bias tool. A theory-based paper identifying the modifiable barriers and enablers to test ordering behaviour change and the selection of intervention components to overcome these is presented in Chapter 4. This involved using a combination of behaviour change models including the Theoretical Domains Framework (TDF), the behaviour change wheel constructs; capabilities, opportunities, motivations of behaviour (COM-B) and Behaviour Change Techniques (BCTs) to identify intervention functions best suited to targeting GP test ordering behaviour. The GP and practice characteristics associated with higher test ordering patterns are described in Chapter 5. These were identified by performing a multi-level analysis of all GP test orders in the studied region for a one-year time period, using routine laboratory data. The design of the intervention material and details on the implementation plans are provided in Chapter 6. Results of the effect of the intervention using nine-month follow up data are described in Chapter 7. This was performed using interrupted time-series with segmented Poisson regression models to assess the pre-and

post-intervention trend for serum immunoglobulin testing among GPs in the Cork-Kerry region of Ireland. Finally, a discussion of the key findings, strengths and limitations of the thesis and recommendations for future research are addressed (Chapter 8).

Key Findings

A number of different interventions were of variable efficacy at changing GP test ordering behaviour. However, generalisability across tests and methodological weakness were identified in these studies (Chapter 3). GP factors contributing to higher immunoglobulin test ordering in our sample included female gender and fewer years of clinical experience (Chapter 5). The lack of clear guidelines and knowledge on how to interpret the test results posed greatest problems for GPs. Four key intervention functions were identified for overcoming these modifiable barriers to effective test use; education, persuasion, enablement and environmental restructuring (Chapter 4). Following the introduction of a guideline and education-based strategy targeting the two key issues (by incorporating the four functions), test orders for serum immunoglobulins dropped significantly. A nine-month evaluation of the effectiveness of this intervention found a statistically significant 1.5% reduction in the fortnight-to-fortnight test ordering trend for serum immunoglobulins (Chapter 7).

Conclusions

This research provides an important overview of the behavioural factors influencing laboratory testing among GPs. The incorporation of behavioural theory, specifically the COM-B, TDF and BCT taxonomy, has supported the identification of factors such as

knowledge and the social and environmental context, which are key for understanding testing behaviours. Combining these context specific "mechanisms of change" with international evidence on what has previously worked, assisted in the development of an effective behaviour change intervention targeting serum immunoglobulin test use in primary care.

On the 25th of April 2015, I was extremely lucky.
Unfortunately, over 9,000 others were not. I dedicate this thesis to all those who lost their lives in the Gorkha Earthquake, Nepal.
RIP

1. INTRODUCTION

1.1 Introduction

One of the most consistent findings in health services research relates to gaps between ideal (as determined by scientific evidence) and actual care [1]. Laboratory testing is a fundamental diagnostic tool for supporting medical decisions [2]. It is essential for the screening, diagnosis and monitoring of disease, and thus indispensable in the practice of health care. However, demand for laboratory testing is increasing disproportionately to other medical activity, and the tests involved are becoming increasingly complex [3]. Moreover, evidence suggests that many tests are ordered unnecessarily [4, 5]. This thesis documents the GP ordering practice around the use of a frequently ordered complex test – serum immunoglobulin levels and immunoglobulin electrophoresis. It presents the evidence base, and outcome for the systematic design, implementation and evaluation of a behaviour change intervention focused on test ordering (using serum immunoglobulins as an exemplar) in primary care in the South of Ireland.

1.2 Research setting and data sources

This thesis utilises routine laboratory data on all GP serum immunoglobulin test orders in two adjacent counties in the South of Ireland, collectively known as the Cork-Kerry region. Approximately 500 GPs provide primary care services to over 665,000 people living in the region. All serum immunoglobulin test orders requested by these GPs are analysed in the same biochemistry laboratories in Cork University Hospital (CUH) and University Hospital Kerry (UHK). The laboratories share a laboratory information system (LIS) called APEX. Data relating to all test orders, including patient

information, test results, requesting GP data and practice surgery data are stored on the hospital's laboratory information technology (IT) system. For the purpose of this PhD, the routine data from both testing sites were extracted using Cognos Impromptu software and exported to Stata version 12 for statistical analysis. Other data sources utilised for this research included the Health Service Executive Primary Care Reimbursement Scheme (HSE-PCRS) claims data and Medical Council registration data. All data were merged using unique GP identifiers and patient hospital Medical Record Numbers (MRNs). Data sources, data cleaning and statistical analysis procedures are explained in detail in the methods sections of the papers and chapters throughout the thesis.

1.3 Overall aims and objectives

The overall aim of this thesis was to optimise serum immunoglobulin test use among GPs, through the design, implementation and evaluation of a behaviour change intervention and to develop a behaviour change example which could be applicable to other laboratory ordering in future.

In particular, the objectives were to:

1. Conduct a systematic review to synthesise the evidence to date on what interventions have been effective at improving test ordering behaviour in primary care.

2. Identify the barriers and enablers of improving test ordering for serum immunoglobulins among GPs (using semi-structured interviews).

3. Identify the intervention components (behaviour change techniques and mode(s) of delivery) that could overcome the modifiable barriers and enhance the enablers.

4. Determine which GP and practice characteristics are associated with high and low serum immunoglobulin test ordering patterns in the South of Ireland.

5. To implement and evaluate a behaviour change intervention targeting serum immunoglobulin use in the Cork-Kerry region.

1.4 Thesis outline

This thesis includes four papers addressing the specific objectives outlined in section 1.3.

Chapter two provides background information on the structure of the Irish healthcare system and laboratory testing in the context of General Practice in Ireland. It also provides the rationale for focusing on serum immunoglobulin tests, and why these tests are particularly problematic in primary care.

Chapter three. The first objective of this thesis was explored by conducting a systematic review to examine the existing literature regarding the effectiveness of behaviour change interventions targeting primary care testing patterns. The review was guided by the Effective Practice and Organisation of Care (EPOC) statement and potential biases were assessed using the Cochrane Collaboration's risk of bias tool [6].

This systematic review was published in Implementation Science and is presented in chapter three of this thesis.

Chapter four. Objectives two and three were addressed using a combination of theoretical, qualitative methods. The barriers and enablers for test ordering were explored through semi-structured interviews with sixteen GPs. These interviews were analysed using the Theoretical Domains Framework (TDF), which mapped the constructs; capabilities, opportunities, motivations of behaviour (COM-B). Finally, Behaviour Change Techniques (BCTs) were used to identify intervention functions best suited to targeting GP test ordering behaviour. This methods paper was published in Implementation Science and is presented in chapter four of this thesis.

Chapter five describes the potential GP and practice characteristics that need to be considered when studying GP serum immunoglobulin test ordering patterns (objective four). This paper involved the multilevel analysis of GP test orders for one year (2013), controlling for GP patient list size and composition.

Chapter six. Having identified the best-suited intervention strategy in papers one to three, chapter six presents the intervention study protocol. This chapter describes the study design, intervention materials, methodical considerations and statistical analysis plan followed to evaluate the laboratory based intervention.

Chapter seven presents the results of the nine-month post-intervention follow-up. This paper involved assessing the change in pre-and post-intervention test ordering patterns for serum immunoglobulins among GPs in the region, using routine laboratory data

from January 2012-July 2016. Data were analysed using an interrupted time series design with segmented Poisson regression models.

Chapter eight provides an overall discussion of the main findings, the strengths and limitations of this thesis and suggestions for future research.

2. BACKGROUND

2.1 Introduction

This chapter provides background information on the structure of the Irish healthcare system and the role of the laboratory and GPs in test ordering. It also describes the rationale behind selecting serum immunoglobulin tests, and why they are particularly problematic tests in primary care.

2.2 The Irish healthcare system

Ireland has a mixed health care system, financed both publically and privately. Public expenditure accounts for approximately 70-80% of total health care resources, and is mainly funded through general taxation [7]. Private expenditure includes both out-of-pocket payments and private health insurance contribution.

2.2.1 Context of General Practice in the Irish Health Service

In Ireland, GPs deliver primary care services. The majority of GPs are self-employed private practitioners providing services to the general population. A large proportion of general practitioners (but not all) provide free GP care to approximately two million people (44% of the population) through state contract arrangements [7]. The remainder of the population of Ireland generally pay for their GP visits on a per consultation basis. Individual patients who are eligible for free GP care are covered by the state-run General Medical Services (GMS) programme and hold either a Medical Card or a GP Visit Card. Medical Card holders must be below a certain income to qualify and, are eligible for free GP care, a range of medications and other products free of charge [7]. Medical Cards may also be granted on a discretionary basis for patients with

severe or chronic illness. The majority of those over 70 years of age will hold a Medical Card, subject to means testing. Specialist registration for GPs was introduced by the Medical Council in 2007. Under the terms of the Health Provision of General Practitioner Services Act 2012, it became mandatory for a GP to be on the specialist register of the Medical Council in order to obtain a GMS contract [8].

Certain people in Ireland who do not qualify for a medical card may apply to the HSE for a GP Visit Card, which allows them to visit their GP free of charge. Within the current Government Health Reform Programme, 'Future Health'12, priority is given to the introduction of free GP care for the entire population of Ireland on a phased basis [8]. The first phase of policy implementation involved the introduction of free GP care to children under the age of six in July 2015. This was extended to the over 70s in August 2015. Proposals exist to extend free GP care to the under 12's and the under 18's, with the gradual extension of free GP care to the population of Ireland. Within the provision of services, GPs have free access to laboratory testing. Extension of free GP service to patients has never been accompanied by a budget provision to deal with the probable associated increase in laboratory requests. The laboratory costs are borne in the hospital budgets and GPs (who are responsible for over 50% of the workload in most hospital laboratories) are usually unaware of costs, volume and workload increases in the laboratory medicine service.

2.3 Rationale behind study

Across Europe, delivering and financing health care in the primary care sector is quite differently organised [9]. There is evidence that the gatekeeping role of GPs increase the efficacy of the system and reduces costs [10]. A key priority for the health service

is to identify poor practices in relation to waste within the health service, specifically in laboratory service provision. The volume of test orders from GPs has risen significantly for many tests [11]. Laboratory tests must be appropriately ordered, reported promptly, correctly interpreted and inform future diagnosis and treatment of the patient [12]. However, evidence indicates the wasteful use of laboratory resources, with several studies reporting that between 25% and 40% of all test orders are unnecessary [13, 14]. For clinical biochemistry tests, such as immunoglobulins, this is expected to be higher, ranging from 26% to 98% of the total number of laboratory tests [15, 16]. However, the use of laboratory tests varies between countries, for example, being five times greater as a proportion of medical expenditure in the United States (US) compared with the United Kingdom (UK) or Ireland [17]. Further, many countries operate mixed public/private sector health economies with differing factors driving demand. As a result, any intervention attempting to influence laboratory demand must consider the context of the health-care system in which it is operating.

2.4 Laboratory use in Ireland

Laboratory testing is an integral part of the day-to-day practice of medicine, underlying around 70% of diagnoses and treatment decisions and 30% of GP encounters [18]. In Ireland, approximately 76 million tests are carried out annually [19]. These tests originate from various sources including accident and emergency, inpatient, outpatient and primary care, with 50% from the latter [19]. Laboratory services cost the Health Service Executive (HSE) approximately €469 million a year, representing 3-4% of the national health budget [19].

2.4.1 Cork University Hospital laboratory

The laboratory at Cork University Hospital (CUH) provides an Irish National Accreditation Board (INAB) accredited analytical and interpretative service on the management of patients with metabolic disturbances. In 2012, approximately 3.3 million tests were carried out on 606,953 blood samples received by the pathology laboratories at CUH [20]. Some key haematological laboratory tests performed in 2012 include, full blood counts (N=472,763), vitamin B12 (N=172,024), serum folate (N=171,370), and serum immunoglobulins (N=12,256). Approximately, 50% of these test orders came from primary care [20]. The CUH laboratories also provide backup services and analyses to South Infirmary Victoria University Hospital (SIVUH) Mallow General Hospital (MGH), Bantry General Hospital (BGH) and perform some analysis for University Hospital Kerry (UHK).

Haematology laboratory activity at CUH saw an increase in some specialised testing of 150% while high volume tests such as white cell counts increased by 3% in 2012 compared to figures for 2011 [20]. Test requests rise annually by 3-6% despite a similar level of morbidity in the population [20]. This suggests that some requests may be unnecessary, have a limited evidence base or be requested for non-medical reasons.

2.5 The complexity of laboratory testing

Determining the clinical relevance of tests is challenging for many reasons. Firstly, physicians order laboratory tests for a number reasons, and a given test has varying clinical relevance when used in different settings or for different reasons [21]. Secondly, laboratory tests are interpreted based on individual clinical scenarios, not as isolated or independent results and clinical details are frequently absent from the

request form [21]. Finally, diagnoses are based on both objective and subjective information and physicians presented with the same information may have differing interpretations of the importance or relevance of a test result [21].

Both clinicians and laboratory scientists recognise that clinical medicine is not a simple matter of matching signs and symptoms with the results of laboratory tests to generate a diagnosis and treatment plan. Most tests may be of more or less relevance to the individual patient depending on the physicians' interpretation of clinical history, review of systems, family history, signs and symptoms, physical examination, and the results of other tests or studies. For this reason, exploring the use of a test with specific requesting guidelines, requiring specialist clinical input for interpretation and management of significant abnormal results may be most useful and clinically important.

Often these specialist tests are 'low-volume' tests in the primary care setting. Research suggests that inappropriate testing is three times higher for 'low-volume' compared to 'high-volume' tests (32% vs 10%) [14]. 'Low-volume' can be defined as a test that is ordered at least ten times less frequently than the most commonly ordered tests [14]. Inappropriate testing may be more likely to occur with 'low-volume' tests due to a lack of familiarity with best treatment practices for the conditions under scrutiny [14].

As a result, this thesis explored serum immunoglobulin test ordering in primary care. Suspected inefficient test use in primary care was identified through local clinical laboratory auditing. In addition, borderline abnormal results were generating

significant numbers of referrals to haematology outpatients, some of which were unnecessary.

2.6 Serum immunoglobulin tests

For the purpose of this study, serum immunoglobulin test use among GPs in the South of Ireland was studied. Serum immunoglobulin tests should be ordered as part of the primary screen for suspected plasma cell dyscrasias (myeloma, lymphoma, chronic lymphatic leukaemia, heavy chain disease, and amyloidosis) [22]. Depending on the condition (e.g. myeloma), serum immunoglobulin tests may also be ordered periodically to monitor disease progression [22]. Low immunoglobulin levels define deficiencies of the humoral immune system (rare and mostly relevant in paediatric practice) while high immunoglobulin levels are observed in liver diseases, chronic inflammatory diseases, haematological disorders, infections (polyclonal gammopathy) and as monoclonal paraprotein in malignancies (myeloma and lymphoma) [23]. The interpretation of serum immunoglobulin test results often requires specialist input and can lead to other costly activities such as referral to secondary care.

2.6.1 Clinical impact of immunoglobulin test ordering patterns

In order to reduce waiting times for clinic appointments and provide increased service options, the haematology department at CUH commenced a virtual haematology clinic in 2009. The clinic is conducted through written correspondence with GPs following a review of laboratory data on the patient. In 2011, following an audit of this service, some problematic referral patterns were identified, particularly in relation to laboratory testing. That is high volumes of referrals which, following consultant

haematologist assessment, were predicted to be unlikely to add value clinically for specific haematology conditions. Analysis of the virtual clinic data showed that GPs were having difficulty identifying immunoglobulin results which were sinister from those that were likely to be transiently abnormal or those that simply require occasional monitoring.

Identifying this issue in the virtual clinic led to further consideration of the use of laboratory services, including the ordering of serum immunoglobulins. In 2013, GPs in the Cork-Kerry region ordered serum immunoglobulin tests for approximately 6,000 patients. From these requests, 1,052 patients were found to have a detectable paraprotein on serum protein electrophoresis. Paraproteins with an IgG level >10g/L or IgA level >5g/L, were deemed significantly high enough to warrant follow-up or referral to Haematology. In total, 2.4% (25/1,052 patients) exhibited paraprotein levels meeting these criteria. Three patient groups were identified among these 25 patients. The first comprised of three patients (0.29%) with concerning paraproteins indicating progression to myeloma, of which all were referred to and investigated by haematology. The second group were nine known myeloma patients that required monitoring (0.86%). The final group consisted of 13 monoclonal gammopathy of uncertain significance (MGUS) patients with stable paraproteins (1.24%), none with a significant health impact in 2013.

2.6.2 Unnecesssary serum immunoglobulin test use

The ‘necessity’ of laboratory tests can be viewed from several perspectives, in particular between primary and secondary care settings. However, from the perspective of making a positive diagnosis of a blood dyscrasia, immunoglobulin

testing can be overutilized or underutilized. Overutilization refers to tests that are ordered but not indicated, while underutilization refers to tests indicated but not ordered [14]. Overutilization can result in unnecessary blood draws and other follow up medical procedures [14]. It also increases the likelihood of false-positive results, which can lead to incorrect diagnoses, increased costs, and adverse outcomes due to unwarranted additional intervention. The pre-test probability of disease in general practice is relatively low, meaning false positive tests are common, even in tests with reasonable specificity. Specialist tests like serum immunoglobulins' are often difficult for GPs to interpret. The practical implication of this is that results which show the very common finding of a polyclonal gammopathy (benign reactive finding) are sometimes interpreted as myeloma or pre-myeloma and generate unnecessary referrals with attendant patient and GP anxiety. These scenarios along with false-positive results can lead to a cascade of further tests, so-called 'investigation momentum' [24].

Physicians typically judge the likelihood of a patient having a particular diagnosis by considering information from several sources and combining these separate assessments. However, the diagnostic implications of laboratory results are generally considered more consciously and formally based on their published performance data. The power of diagnostic tests is usually reported either as sensitivity and specificity, or their derived likelihood or diagnostic odds ratios, or as their positive predictive values (PPV) and negative predictive values (NPV) [25].

2.6.3 Role of serum immunoglobulins in diagnosis

The predictive value of serum immunoglobulin tests is limited when performed in settings in which the prevalence of myeloma is low, such as screening and for younger population, particularly females. Moreover, the PPV and NPV depend not only on its

sensitivity and specificity, but also on the likelihood of disease before the test is done (referred to as prior probability, prior likelihood, or prevalence of disease). A monoclonal spike (or paraprotein) on serum protein electrophoresis (SPEP) is a frequent finding in the general population and typically indicates an asymptomatic, pre-malignant condition called monoclonal gammopathy of undetermined significance (MGUS) [26]. MGUS occurs in around 3% of people older than 50 and is associated with a lifelong, low risk of progression to multiple myeloma or a related plasma cell dyscrasia. Patients with MGUS are divided into different categories based on low risk, intermediate risk, and high risk. If the serum monoclonal protein is <15 g/L, IgG type, and the free light chain ratio is normal, then the risk of eventual progression to multiple myeloma or related malignancy is low [27]. In this low-risk setting, a baseline bone marrow examination or skeletal survey is not routinely indicated if the clinical evaluation and laboratory values suggest MGUS [27]. Patients should be followed with SPEP six months after diagnosis and if stable can be followed every 2-3 years (or sooner if symptoms suggestive of disease progression arise) [27].

However, patients that fall in the intermediate and high risk MGUS category are managed differently. They usually have a serum monoclonal protein >15 g/L, IgA or IgM type, and/or an abnormal free light chain ratio. In this situation, a bone marrow biopsy should be carried out at baseline. These patients are followed with SPEP, complete blood count, serum calcium and creatinine levels six months after diagnosis and then yearly for life. Finally, those patients with smoldering (asymptomatic) multiple myeloma always receive a baseline bone marrow biopsy and mandatory skeletal survey [28].

Multiple myeloma is a cancer of the plasma cells in the bone marrow [29]. It is the second most common haematological cancer after lymphoma, with approximmately 200 patients diagnosed in Ireland each year. The cause of multiple myeloma is unknown and risk factors include age, radiation, agricultural exposures and familial risk. Prevalence is more common in those over 50 years, with higher male predominance. According to the Wilson and Jungner criteria, there should be a suitable and acceptable diagnostic test for the disease and good treatment options [30] Screening for multiple myeloma can be done by blood and urine protein electrophoresis, which is minimally invasive and relatively easy to perform. On detecting a monoclonal protein, a distinction between MGUS or Multiple myeloma should be made by further study, possibly including a bone marrow biopsy [31]. Myeloma is an incurable (though treatable) cancer. Because of this, if a GP suspects the diagnoisis for any reason or has clinical concerns, however unlikely, there can be significant utility in a negative test. Our study does not address this issue specifically.

2.7 PhD framework

This PhD set out to design, implement and evaluate a behaviour change intervention targeting problematic serum immunoglobulin testing in primary care. To do so, the stages of developing an intervention using the theory-based approaches outlined by French and colleagues were followed [32]. The authors developed a four-step framework for developing a theory-informed intervention (Table 2.1). The four steps represent: identifying the problem (who needs to do what, differently?); assessing the problem (using a theoretical framework, which barriers and enablers need to be addressed?); forming possible solutions (which intervention components could

overcome the modifiable barriers and enhance the enablers?); and evaluating the selected intervention (how can behaviour change be measured and understood?) [32].

Table 2.1 Steps for developing a theory-informed implementation intervention [32]

Step	Tasks
STEP 1: Who needs to do what, differently?	• Identify the evidence-practice gap • Specify the behaviour change needed to reduce the evidence-practice gap • Specify the health professional group whose behaviour needs changing
STEP 2: Using a theoretical framework, which barriers and enablers need to be addressed?	• From the literature, and experience of the development team, select which theory(ies), or theoretical framework(s), are likely to inform the pathways of change • Use the chosen theory(ies), or framework, to identify the pathway(s) of change and the possible barriers and enablers to that pathway • Use qualitative and/or quantitative methods to identify barriers and enablers to behaviour change
STEP 3: Which intervention components (behaviour change techniques and mode(s) of delivery) could overcome the modifiable barriers and enhance the enablers?	• Use the chosen theory or framework, to identify potential behaviour change techniques to overcome the barriers and enhance the enablers • Identify evidence to inform the selection of potential behaviour change techniques and modes of delivery • Identify what is likely to be feasible, locally relevant, and acceptable and combine identified components into an acceptable intervention that can be delivered

STEP 4: How can behaviour change be measured and understood?	• Identify mediators of change to investigate the proposed pathways of change • Select appropriate outcome measures • Determine feasibility of outcomes to be measured

Table 2.2 outlines the application of this framework to design, implement and evaluate a behaviour change intervention using serum immunoglobulin test requesting as a model, for use among GPs in the South of Ireland. It also provides a reference to the papers and chapters corresponding to the tasks fulfilled.

Table 2.2 The four steps of designing a theory-based intervention [32] applied to develop and evaluate an intervention targeting serum immunoglobulin testing in primary care in the South of Ireland

Steps	Tasks	Action taken	Papers	PhD Chapter
STEP 1: Who needs to do what, differently?	Identify the drivers of higher GP serum immunoglobulin test ordering patterns.	A cross-sectional study identifying the GP and practice characteristics associated with higher test ordering.	Determinants of testing	5
STEP 2: Using a theoretical framework, which barriers and enablers need to be addressed?	Using behaviour change theory, explore GP attitudes towards testing, and potential barriers and enablers for behaviour change.	Interviews carried out with GPs. Analysed and coded using theoretical domains framework, which were then mapped to the COM-B constructs to identify the best intervention strategy.	Theoretical design	4
STEP 3: Which intervention components (behaviour change techniques and mode(s) of delivery) could overcome the modifiable barriers and enhance the enablers?	Carry out a systematic review of the literature to identify previously effective interventions. Conduct GP interviews to identify feasible strategies.	A systematic review of previous interventions was completed, and results combined with findings of the interviews to ensure the intervention considers potential barriers and enablers in the context of Irish GP practice and structure.	Systematic review Theoretical design	3 4
STEP 4: How can behaviour change be measured and understood?	Assess the trend in the volume of serum immunoglobulin test orders before and after the intervention.	The effect of the intervention was evaluated using an interrupted time series, with segmented Poisson regression models.	Evaluation of Intervention	7

THE EFFECTIVENESS OF INTERVENTIONS TO IMPROVE LABORATORY REQUESTING PATTERNS AMONG PRIMARY CARE PHYSICIANS: A SYSTEMATIC REVIEW

SHARON L. CADOGAN

JOHN P. BROWNE

COLIN P. BRADLEY

MARY R. CAHILL

Published as: Cadogan SL, Browne JP, Bradley CP, Cahill MR: **The effectiveness of interventions to improve laboratory requesting patterns among primary care physicians: a systematic review**. *Implementation Science* 2015, **10**(1):167.

3.1 Abstract

Background: Laboratory testing is an integral part of day-to-day primary care practice, with approximately 30% of patient encounters resulting in a request. However, research suggests that a large proportion of requests do not benefit patient care and are avoidable. The aim of this systematic review was to comprehensively search the literature for studies evaluating the effectiveness of interventions to improve primary care physician use of laboratory tests.

Methods: A search of PubMed, Cochrane Library, Embase and SCOPUS (from inception to 09/02/14) was conducted. The following study designs were considered: systematic reviews, randomised controlled trials (RCTs), controlled clinical trials (CCTs), controlled before and after studies (CBAs) and interrupted time series analysis (ITSs). Studies were quality appraised using a modified version of the Effective Practice and Organisation of Care (EPOC) checklist. The population of interest were primary care physicians. Interventions were considered if they aimed to improve laboratory testing in primary care. The outcome of interest was the volume of laboratory tests.

Results: In total, 6,166 titles and abstracts were reviewed, followed by 87 full texts. Of these, 11 papers were eligible for inclusion in the systematic review. This included four RCTs, six CBAs and one ITS study. The types of interventions examined included education, feedback, guidelines, education with feedback, feedback with guidelines and changing order forms. The quality of included studies varied with seven studies deemed to have a low risk of bias, three with unclear risk of bias and one with a high risk of bias. All but one study found significant reductions in the volume of tests

following the intervention, with effect sizes ranging from 1.2% to 60%. Due to heterogeneity meta-analysis was not performed.

Conclusions: Interventions such as educational strategies, feedback, and changing test order forms may improve the efficient use of laboratory tests in primary care, however the level of evidence is quite low and the quality is poor. The reproducibility of findings from different laboratories is also difficult to ascertain from the literature. Some standardisation of both interventions and outcome measures is required to enable formal meta-analysis.

Key words: interventions, primary care, behaviour change, healthcare interventions, laboratory testing

3.2 Background

Laboratory testing is an integral part of day-to-day practice in medicine and supports approximately 70% of diagnoses and treatment decisions [18]. Further, among primary care physicians, an estimated 30% of patient visits result in a laboratory request [33]. Healthcare budgets worldwide are facing increasing pressure to reduce costs and remove inefficiencies, while maintaining quality and safety. Laboratory testing is a major component of healthcare budgets in absolute terms and demand for testing is increasing faster than medical activity [34]. In the National Health Service (NHS) in England, for example, an estimated £2.5 billion per annum is spent on laboratory services accounting for 3-4% of the UK national health budget [3, 35]. Despite this relatively small proportion of healthcare budget expenditure, laboratory testing often underpins more costly downstream care such as outpatient visits and radiology requests.

The unnecessary use of laboratory services has been highlighted by a meta-analysis of 108 studies involving 1.6 million results from 46 of the 50 most commonly ordered lab tests in medicine [14]. This found that, on average, 30% of all tests are likely to be unnecessary [14, 36]. With respect to primary care, US research has found that physicians order diagnostic laboratory tests for approximately 30% of patient visits [37]. Authors reported that test ordering factors including unnecessary test requests were responsible for 13% of testing process errors in primary care [38].

The overuse of laboratory services can stem from the physician, the patient and the broader policy context. For example, some studies have found that many physicians report uncertainty over when to order tests and how to interpret test results [33].

Reasons given for this include lack of knowledge about indications, costs, insurance restrictions and inconsistent names for the same test [37]. Meanwhile, patients have high expectations that blood tests are performed and have little understanding of the limitations of testing [36, 39]. Other factors include a lack of knowledge regarding the financial effect of laboratory testing on the health care system [40] and the increasing volume of laboratory tests available to physicians [3]. Furthermore, system level factors associated with laboratory testing patterns have been identified and include limitations of laboratory and/or surgery information technology systems [3, 41]. As a result, it has been recommended that the theoretical and contextual factors responsible for changing primary care physician behaviour should also be considered when designing interventions [42-45].

A number of approaches for reducing unnecessary test ordering in primary care have implemented. These comprise of interventions aimed at tackling both the overutilization and underutilization of tests through strategies such as including cost displays on electronic order forms, facilitating educational workshops and providing feedback to physicians on their test ordering patterns [46-48]. However, the effectiveness of these strategies vary, and, to date no systematic reviews have focused solely on studies evaluating test ordering behaviours of primary care physicians. Hence, the objective of this systematic review was to systematically and comprehensively search the literature for studies evaluating the effectiveness of interventions aimed at nudging primary care physicians' ordering practice further in a direction which will maximally impact patient care.

3.3 Methods

3.3.1 Primary objective

The main objective of this systematic review was to synthesise the available published literature on interventions focused on improving the appropriateness of laboratory requesting patterns from primary care.

3.3.2 Primary outcomes

The outcome of interest in this review was objectively measured provider performance (request rates or appropriateness of requests).

3.3.3 Types of studies

Systematic reviews, randomised controlled trials (RCTs), non-randomised controlled trials (NRCTs), controlled before-after studies (CBAs) and interrupted time series analysis (ITSs) were considered for this review.

3.3.4 Types of interventions

The review focused on interventions to change laboratory requesting patterns or improve laboratory requesting appropriateness.

3.3.5 Data sources

The following databases were searched for potentially eligible studies: PubMed (1966 to Feb 9th 2014) the Cochrane Library (1993 to Feb 9th 2014), Embase (1974 to Feb 9th 2014) and SCOPUS (1960 to Feb 9th 2014). Updated searches of the electronic databases were performed in November 2014 to ensure additional relevant papers were not published since.

3.3.6 Inclusion criteria

This review included interventions aimed at improving laboratory requesting patterns where objectively measured provider performance (requesting rates or appropriateness of requests) served as the dependent variable. Intervention studies were only considered if participants were primary care physicians, defined as any medically qualified physician providing primary health care and including general practitioners, family doctors, family physicians or family practitioners.

3.3.7 Search strategy

PubMed was searched for potentially eligible studies by combining relevant medical subject headings (MeSH terms) with subheadings and text words (e.g. “utilisation,” “laboratory test (s)”). Only citations on human subjects were included. Search terms and search findings are provided in Appendix 3. For completeness, searches were repeated without subheadings and the results of these two searches were combined. The same methods were used for searching the Cochrane Library, Embase (Elsevier) and Scopus databases. Electronic searches were supplemented by cross-checking the reference lists of all identified studies. Duplicate citations were identified and removed using EndNote citation manager.

3.3.8 Data collection and analysis

SLC carried out the electronic database searches. The search strategy for the review can be found in Appendix 3. Titles and abstracts of studies retrieved from the search strategy were reviewed independently by applying the appropriate inclusion/exclusion criteria. For each citation, two investigators (SLC and MRC) independently screened the titles and abstracts for potential relevance. The full-text article was obtained for all

potentially eligible studies. Any disagreements between SLC and MRC were resolved through discussion with a third reviewer (JPB).

Data were extracted from the included papers by a single reviewer (SLC). A second reviewer (JPB) checked data extraction sheets for errors. Information was extracted on study design, year of study, setting, participants, intervention characteristics and the reporting of results. A sample data extraction form can be found in Appendix 4. It was not deemed appropriate to conduct a meta-analysis due to the heterogeneity of interventions and outcomes across the included studies. Instead, the existing analyses reported in the articles reviewed were extracted and reported in a narrative format.

3.3.9 Quality assessment of included studies

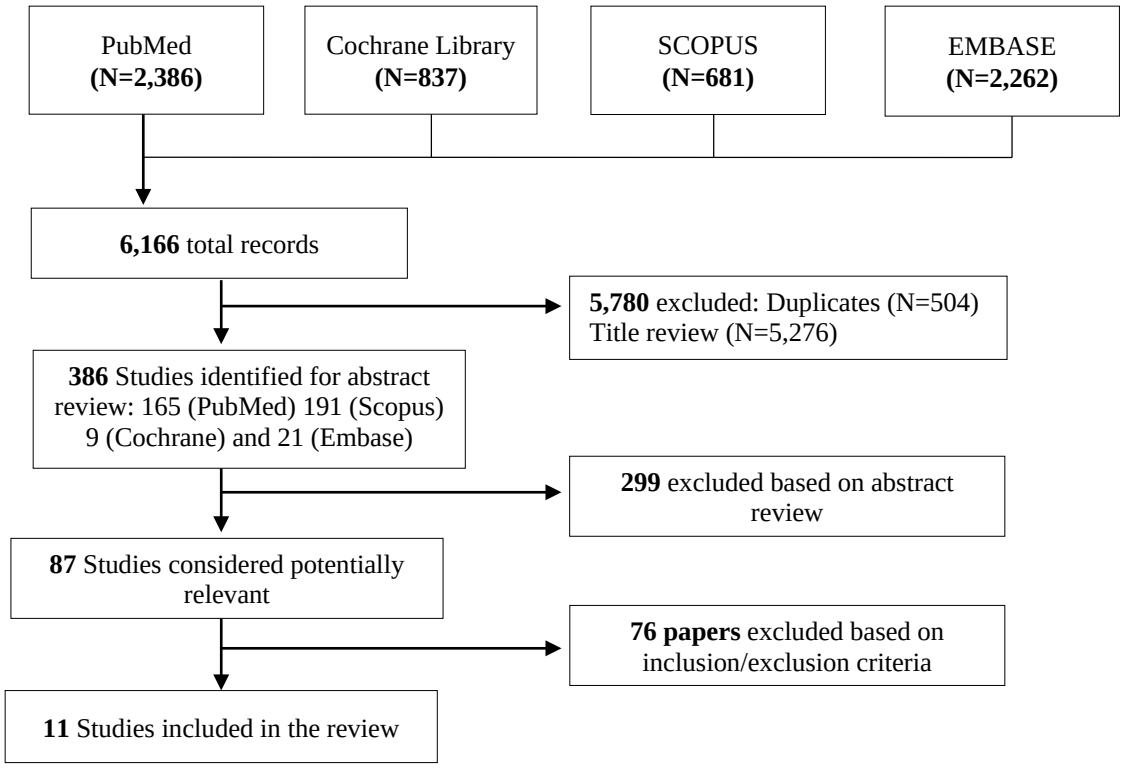
Included studies were independently assessed for quality and risk of bias by SLC and JPB, with any disagreements resolved by discussion. This was performed using a modified version of the Cochrane Effective Practice and Organisation of Care (EPOC) Data Collection Checklist and Quality Criteria for studies with a control group (RCTs, CCTs and CBAs) and for ITSs studies [6]. The tool is specifically designed for interventions aiming to improve practice, and provides a risk of bias assessment for each of the included study designs (RCT, CCT, CBA, and ITS). This comprises of nine quality standards for RCTs, CCTs and CBAs: generation of allocation sequence, concealment of allocation, baseline outcome measurements, baseline characteristics, incomplete outcome data, blinding of outcome assessor, and protection against contamination, selective outcome reporting and other risks of bias. For ITS study designs, the following three quality standards were also assessed: the independence of the intervention from other changes, the pre-specified shape of the intervention and if the intervention was unlikely to affect data collection [6].

3.4 Results

3.4.1 Search results

In total, 6,166 records of papers were identified from the search of the literature (Figure 3.1). 5,276 records were excluded based on a title review. A further 504 records were duplicates and also excluded. Of the 386 records remaining, 299 were excluded based on the abstract review. Full texts were obtained for the remaining 87 records, of which 11 papers met the inclusion criteria and were included in the review.

Figure 3.1 Flow diagram of the search strategy for the review



3.4.2 Risk of bias in included studies

Table 3.1 provides the details of quality assessment of the studies. Ten of the 11 studies were deemed to have a high risk of bias, while one study [49] was deemed to be of low risk. Randomisation and allocation concealment was adequately performed for the four included RCTs [48-51]. The most common reason for high risk of bias was the fact that participants (primary care physicians) in the intervention groups could not be

blinded. This introduces the risk of information bias as physicians may have altered their requesting behaviours based on knowledge of being assessed. Only one of the studies adequately blinded participants [49]. Also, a key limitation of the RCT by Thomas and colleagues [48] was the lack of power to detect interactions, and, hence, a much larger trial would be required to ensure that these interventions act independently. A key limitation of the included ITS study [46] was the physician-level design utilised with an absence of individual patient characteristics.

3.4.3 Characteristics of studies included in the review

Characteristics and the key findings of the included studies are presented in Table 3.2. Four of the studies were RCTs [48-51], six were before-after studies[47, 52-56] and one was an ITS [46] with a parallel control group. The included studies were conducted in the Netherlands [49, 50, 56], US [46], UK [48, 51], Italy [53], Israel [54, 55], Sweden [47] and New Zealand [52] with samples ranging in size from 44 to over 3,000 primary care physicians. The interventions covered by the review include education programmes [47, 49], laboratory profiles [53] clinical guidelines [50], guidelines and feedback combined [51], cost displays [46], the re-design of order forms [54-56] and the use of feedback and education strategies [48, 52].

3.4.3.1 Clinical guidelines and policy recommendations

In their RCT study, van Wijk et al. [50] found that decision support based on guidelines integrated with patient electronic records was more effective for changing blood test-ordering behaviour than decision support based on limited testing offered in modified request forms. Primary care physicians who had access to the guideline-based system had ordered 20% fewer tests per form than did primary care physicians who had access to the restricted system (mean ±SD 5.5 ±0.9 tests vs. 6.9 ± 1.6 tests,

respectively; P= 0.003, Mann-Whitney test) [50]. Similar findings were obtained in the adjusted multivariate regression analysis [50]. Controlling for practice characteristics and historic test ordering behaviour, 19% more tests were requested by primary care physicians with access to the restricted order form (RR:1.19; 95% CI: 1.10-1.29) [50]. The study also reported a difference in requesting patterns between the two groups for specific tests. For example, in the restricted group, 61.2% of order forms included an erythrocyte sedimentation rate test, compared with 44.1% in the guideline group ($p<0.001$) [50].

In a study using a CBA design and involving over 3,000 primary care physicians in New Zealand, Tomlin et al. [52] assessed the effect of three different marketing programmes promoting clinical guidelines. Each of these programmes involved written material advising of guideline recommendations. Individual laboratory-test use feedback data was distributed to each practice and professional development opportunities were provided. The study found that clear information marketed to primary care physicians improved the quality of laboratory test ordering [52]. Some key findings included a 42% reduction in erythrocyte sedimentation rate tests following the intervention (intervention physicians: -60%, comparison physicians: -18%, $p<0.01$) [52].

3.4.3.2 Feedback and reminders

Baker et al. [51] evaluated the use of feedback following guidelines in their RCT. Both groups received guidelines followed up with feedback about their use of selected tests. The first group of practices received feedback about their testing for thyroid function tests, rheumatoid factor and urine culture requests, while the second group received feedback about their serum lipids and viscosity requests. Hence, both groups were

intervention groups, but acted as control groups for the other group. The authors reported no change in laboratory requests quarterly feedback over a one-year time period for any of the five tests studied [51].

A multifaceted clustered RCT by Verstappen et al. [49] aimed to optimise primary care physicians' test ordering behaviour by means of practice-based strategies targeting tests for specific clinical problems. Thirteen groups of primary care physicians underwent the strategy for three clinical problems (arm A; cardiovascular topics, upper and lower abdominal complaints), while 13 other groups underwent the strategy for three other clinical problems (arm B; chronic obstructive pulmonary disease and asthma, general complaints, degenerative joint complaints). The strategy consisted of personalised graphical feedback, including a comparison of each physician's own data with those of colleagues; dissemination of national, evidence-based guidelines; and regular meetings on quality improvement in small groups [49]. Each of the arms of the trial acted as a control for each other. Physicians discussed personal feedback reports in small group meetings, related them to evidence-based clinical guidelines, and made plans for change. Authors reported a 12% reduction in the volume of total tests for arm A in the intervention group versus no change in the control arm ($p<0.001$) [49]. However, for arm B of the trial, no statistically significant changes were identified ($p=0.22$) [49].

In a third RCT by Thomas et al. [48], the use of feedback combined with educational reminder messages was assessed. The feedback intervention involved the use of a booklet containing graphical presentations of individual practice level ordering for the targeted tests. Each practice was compared to regional statistics over a three-year period. Educational reminders were developed in conjunction with the primary care

physicians and were included with test results. The study found that primary care practices receiving either or both feedback and reminders had significantly reduced laboratory test utilisation ($p<0.001$) [48]. The combined effect of the interventions resulted in a 22% reduction in total number of targeted tests ordered (OR = 0.78, 95% CI: 0.71-0.85) versus 13% for reminders alone (OR = 0.87, 95% CI: 0.81-0.94, p=<0.001) and 11% for feedback alone (OR= 0.89, 95% CI: 0.83-0.94, p=0.003) [48]. However, feedback led to greater reductions in the number of laboratory tests ordered compared with reminders, although the model-based analyses suggested similar effects (adjusted change relative to baseline performance in audit and feedback arm =12%; OR for reminders = 0.89, 95% CI 0.83 to 0.93, p=0.003) [48].

3.4.3.3 Education-based strategies

Baricchi et al. [53] evaluated the effect of seven pathology specific laboratory profiles for more effective test requesting, using a CBA study design. Training sessions were facilitated to educate the primary care physicians in the intervention group about these profiles and to discuss their presumed usefulness. Authors reported a 5% reduction in the volume of tests requested by the intervention group one year following the intervention compared with a 1% increase in the control group (p= <0.001) [53].

Also using a CBA study, Larsson et al. [47] assessed the effects of an education programme which involved a two-day lecture series at which each participant received a folder containing information relating to the guidelines for future reference. The authors reported significant changes ($p<0.05$) for nine of 14 tests [47]. They recommended that ordering rates for seven ratios should decrease, of which five did ($p<0.05$), and, that seven ratios should increase in volume, of which four did ($p<0.05$). None of the ratios significantly changed in the wrong direction [47].

3.4.3.4 Cost displays of pricing information

Using an ITS design, Horn et al. [46] evaluated the effect of implementing cost displays for laboratory tests in primary care. The authors reported a reduction (1%-2.6%) in the volume of tests ordered for five out of 27 different laboratory tests when the real-time display of cost information was provided electronically on patient record and results (estimated a reduction of between 0.4/1,000 visits per month to 5.6/1,000 visits per month, $p<0.001$) [46]. However, for higher cost tests a reduction in test requests was observed in only one of six such tests [46].

3.4.3.5 Changing order forms

Kahan et al. [54] evaluated a new version of a computerised order form for three target tests (vitamin B12, folic acid and ferritin) using a CBA study. Test requests for haemoglobin and iron were evaluated as controls. The authors reported a 31%-41% decrease in volume of requests for the three target tests at one-month follow-up, with a further decrease to 36%-53% two months after the intervention [54]. In comparison, the effect on test requests for controls tests ranged from -2%-3% [54]. A second CBA study in Israel by Shalev et al. [55] evaluated changing the format of the existing check-box laboratory order form that is embedded in a computerised medical record. This involved removing twenty-six tests from the form and adding two tests. They found that for deleted tests there was a 27% and 19.2% reduction one and two years after intervention respectively ($p<0.001$) [55]. For unchanged tests, the percentage changes were +18.4% in year one and -22.4% in year two. Meanwhile, a 60.7% (year one) and 90% (year two) increase in volume was found where tests were added to the order form ($p<0.001$) [55].

In a second CBA study, Zaat et al. [56] modified the request form so that it only had 15 tests listed and all other tests had to be hand written. The form also required more information about the reason for requesting the test. Primary care physicians in the intervention group received a copy of a booklet with descriptions of the essential characteristics of the 15 important tests on the new form. The authors reported an 18% reduction in the volume of laboratory test requested on a monthly basis for the intervention group [56]. In the comparison period the difference between groups was significant ($p<0.0001$) [56].

3.5 Discussion

This review aimed to identify and evaluate interventions for improving the use of laboratory tests among primary care physicians. Intervention strategies included: education, feedback, guidelines, cost displays, and changing the content of order forms. While included studies differed considerably in relation to the tests they assessed, the findings were consistently in the same direction, perhaps indicating some publication bias. All but one [51] of the included studies reported positive effects on laboratory testing patterns. However, a number of the studies included in this review have a high risk of bias and are lacking in certain areas of methodological quality.

Education based interventions appear to have promising effects on improving primary care physician laboratory testing patterns in this review [47, 49, 53]. This included evidence from a high-quality RCT [49]. Similar educational strategies have also been effective in changing other primary care behaviours including improving prescribing patterns for antibiotics [57], and referral for radiological assessments [58]. In particular, diagnoses or symptoms based education strategies involving a multi-

disciplinary approach proved effective [49, 53]. The sustainability of education-based strategies is often questioned in the literature. However, follow up of long term effects of the education programme implemented by Larsson et el. [47] found it can be achieved with regular re-enforcement [59].

Further, the literature suggests provider education is inexpensive and feasible for widespread delivery [60]. Larsson et al. [47] also reported direct laboratory cost savings of their education programme. Similarly, Verstappen et al. [61] evaluated the costs and cost reductions of their feedback and education based strategy [49]. However, as with many intervention studies, a lack of rigorous economic evaluation methods and poor clinical data is a key limitation of studies attempting to describe the economic value of their behaviour change strategies.

The feedback-based interventions in this review were multifaceted, and their effects were dependent on the particular combination of strategies used [48, 51, 52]. Feedback strategies have also shown positive results for other test ordering activities by primary care physicians such as electrocardiogram use [62, 63]. In particular, enhanced feedback combined with brief educational reminder messages had a positive effect on requesting patterns [48]. The broader literature also suggests that feedback interventions have improved success when combined with other education-based strategies, including outreach visits or educational reminders [64, 65]. In primary care, providing feedback may change attitudes towards current practice and subsequent clinical outcomes, by changing self-assessment, or by directing attention to a particular set of guidelines [66].

However, Baker et al. found that feedback was ineffective for changing primary care physician requesting behaviour when provided following guidelines [51]. The literature suggests that this may be explained by baseline performance, how often feedback is provided and how the feedback is provided [66, 67]. Moreover, individualised feedback in other areas of clinical performance has been shown to be more effective than general feedback, in particular when it is regular and repeated [68].

Implementation strategies for the delivery of education-based strategies may also be important, in particular, the dissemination of guidelines. Decision support based on limited testing offered in modified request forms was less effective compared to decision support based on guidelines integrated with patient electronic records for changing blood test-ordering behaviour [50]. However, the use of guidelines is often criticised with respect to the sustainability of change in the long-term [40].

Real-time display of cost information provided electronically on patient record and results showed a significant but small change in laboratory testing patterns [46]. However, this change was dependent on specifics of the test with insignificant changes for five out of six of the high-cost tests [46]. Little research exists on the effectiveness of cost displays for altering behaviour in the primary care, however, conflicting evidence exists among studies that have included physicians in hospital settings [69, 70]. In addition, diverse background health systems need to be considered when implementing a cost-display based strategy.

3.5.1 Implications for the implementation of interventions

Some multifaceted intervention strategies within the scope of this review have shown positive results although conflicting evidence exists in the wider literature on changing

healthcare professional behaviours [71, 72]. Grimshaw and colleagues highlight that few studies explain the rationale for the choice of a particular combination of interventions [72]. The authors conclude that if interventions are tailored to address local barriers to change then, multifaceted approaches may be more effective than individual interventions [72]. There is literature to support the belief that knowledge of pre-requesting variables contributes to the success of interventions in health professionals [73]. For example, some authors identified test decision points including primary care physicians' preference for risk [74] and perceived needs of the patient for reassurance [75]. Studies have also highlighted the importance of factors associated with wider health system performance [74].

Interestingly, in this review, none of the interventions appear to be designed based on the attitudes and behaviours responsible for laboratory testing patterns. The use of theory to understand such barriers has been recommended for the design of behaviour change interventions [42, 43]. In particular, Michie and colleagues have highlighted the importance of understanding the nature of the behaviour to be changed and the context [45]. The authors argue that designing interventions based on practitioner or researcher intuition rather than theory prevents an understanding of the behaviour change processes responsible for effective interventions [45]. To address this issue, they have developed a behaviour change theory, the 'capability, opportunity, motivation-behaviour (COM-B) system', which can be used as a taxonomy to map any identified barriers to the origin of the problem [44]. Hence, implementation strategies should also consider the theoretical and contextual factors responsible for changing primary care physician behaviour when designing interventions.

Similarly, the wider impacts of these interventions on the clinical outcome and the management of the patient need to be considered. There is a paucity of data on downstream effects of laboratory ordering. Few studies have attempted to link and quantify laboratory ordering with the subsequent ordering of radiology or out patients requests [76], and none have linked a reduction of laboratory orders with reduced follow-on requests. Further research on the proportion of laboratory requests, where the result (either normal or abnormal) leads to a quantifiable diagnosis, health gain or evidenced based health intervention - is required. Ultimately, the laboratory mission is to serve the patient and most studies to date have focused on the requester. Thus, while laboratory-based interventions to curtail inappropriate requests are valuable, they rarely have a patient focus. Aiming to reduce the volume of test requests may not be a satisfactory outcome of interest. The key drivers of demand management and improving the appropriateness of test requesting should include economic savings in the health service, but also, improved clinical outcomes for patients [3, 41]. In order to do so, a collaborative approach involving laboratories and clinicians may be most beneficial. For example, provision of interpretative comments on test reports is not only welcomed by users but has been suggested to influence requesting behaviour and, indeed, patient outcomes.

3.5.2 Limitations of this review

Firstly, the heterogeneity of the studies precludes a quantitative pooling of the results to produce any statistical inference; our study is thus essentially descriptive. Secondly, follow-up periods of the included studies varied, ranging from three months to two years. As a result, the findings may vary. Also, this review followed EPOC adapted guidelines when including study designs, and, included a mixture of RCTs, CBAs and

ITS study designs. The latter two study designs are weaker and more susceptible to bias due to their observational nature. Finally, not all included studies controlled for the same confounders, in particular, patient-level characteristics.

Another limitation of our review is that it is possible that additional studies with non-significant or negative effects were not published. This leads to publication bias which may have an impact on our findings. In particular, clinical laboratories may be carrying out routine audits of new strategies they have implemented, but may be not publishing less favourable negative results. Also, in many of the included studies, authors reported a suspicion of inappropriate testing as part of their motivation [46, 48-51, 53, 55, 56].

However, our study also has several strengths. Our literature search is exhaustive and provides a clears overview of the subject matter. The studies included are from practices within covering multiple geographic locations; thereby, the inferences of the review are generalizable to a large population.

3.6 Conclusion

Our review suggests that many different interventions may change primary care physician requesting patterns, in particular, multi-faceted interventions. However, due to the small number of studies and questionable validity and generalizability of findings of these studies, this review should encourage further better quality research in this area. While some of the included study designs are weak, the results are generally consistent in pointing to the need to intervene to improve test ordering behaviour. As a result, it is important that policy makers consider the benefits of providing the resources to further explore and implement some of these interventions

pending the conduct of better quality studies. The possibility of publication bias should be weighed when assessing interventions. However, due to the downstream expenditure resulting from laboratory testing, the cost and time associated with continuous quality improvement initiatives in laboratory medicine will be beneficial.

There is a paucity of theory-based interventions in relation to test ordering behaviours of physicians. Further research should concentrate on improving our understanding of when interventions such as education or guidelines are likely to be effective and how to improve them. In particular, current interventions have been limited to tackling only one or a very few elements of the behaviour change wheel. As a result, the determinants of success and failure remain unclear, and interventions may not be applicable to specific tests. Given the difficulties inherent in translating research into practice, it is reasonable to question whether the interventions we describe are generalizable or adaptable to other health care settings and conditions. Also, future studies that examine the effect of combined approaches, conducted by a multidisciplinary team are likely to be of interest. Hence, further research is needed to systematically examine the contextual and organisational factors likely to influence the behaviour change and implementation. In addition, research focused on the impact on patient care, further testing and diagnosis as a result of a change in laboratory ordering would assist with an appropriate policy for future laboratory services.

Table 3.1 Overview of the characteristics of the included intervention studies and the key findings

Reference	Setting	Design	Participants	Type	Intervention	Comparator	Follow-up	Effect of intervention
Horn et al. [46]	USA	ITS	215 primary care physicians (Five group practices)	Changing the order form	Cost displays within electronic health record at time of ordering (153 physicians)	Control group: no cost information (62 physicians)	12-month pre- and six-month post-intervention	Difference-in-difference approach. 1-2.6% reduction. 20% The cost displays resulted in a reduction of 0.4-5.6 laboratory orders per 1,000 visits per month ($p<0.001$).
Kahan et al. [54]	Israel	CBA	Not disclosed	Changing the order form	A new version of electronic order form	Older version of computerised order form	Six months pre- and four months post-intervention	31-41% reduction relative to the pre-intervention month, with 36-58% reduction the following month. -2-3% changes for control tests.
Shalev et al. [55]	Israel	CBA	865 primary care physicians	Changing the order form	Changing the number of tests on the order form (27 tests removed and two added – reducing the number of tests available using a check-box form from 51 to 26)	Standard form prior to intervention	12 months pre- and 24 months post-intervention	For deleted tests, there was a 27% and 19.2% reduction one and two years after the intervention, respectively.
Zaat et al. [74]	Netherlands	CBA	75 primary care physicians	Changing the order form	Volume of tests on order form reduced (hand written request if test not displayed) (47 physicians)	Standard form (28 physicians)	Five-months pre- (control) and 12 months post-intervention	18% reduction in the number of tests requested monthly in experimental group after the intervention compared to the control doctors.
Barrichi et al. [53]	Italy	CBA	44 primary care physicians	Education	Pathology-specific laboratory algorithms for seven common clinical scenarios were tested. Education was provided (eight	Current practice	12 months pre- and 12 months post-intervention (data on test requests for	5% reduction in the volume of tests requested by the intervention district one year following the intervention (retrospective audit) compared

					training sessions) to the physicians about the algorithms and their use (23 physicians).		randomly selected 30 days in each period)	with a 1% increase in the control district.
Larsson et al. [47]	Sweden	CBA	63 primary care physicians (19 practices)	Education	An education programme (two-day lecture series)	Current practice (Two practices)	Five months pre-intervention and four months post-intervention	Seven ratios were recommended to decrease in volume; five did at $p<0.05$. Seven were expected to increase in volume; four did at $p<0.05$.
Verstappen et al. [49]	Netherlands	RCT	174 primary care physicians (26 practices)	Education	A primary care physician based strategy focused on clinical problems and associated tests (85 physicians in arm A and 89 physicians in arm B)	Each group acted as a control for the other	Six-months pre- and six-months post-intervention	12% reduction in the volume of total tests in the intervention group versus no change in the control arm. 16% reduction of inappropriate tests for the intervention group.
van Wijk et al. [50]	Netherlands	RCT	60 primary care physicians (44 practices)	Guidelines	Guideline-based order form (29 physicians) versus restricted guideline based electronic order form (31 physicians)	Each group acted as a control for the other	Study period: 1st July 1994-30th June 1995	Decision support based on guidelines was more effective in changing blood test ordering than decision support based on initially displaying a limited number of tests. Primary care physicians who used BloodLink-Guideline requested 20% fewer tests on average than did practitioners who used BloodLink-Restricted (mean [±SD], 5.5 ± 0.9 tests vs. 6.9 ± 1.6 tests ($p=0.003$).

Baker et al. [51]	UK	RCT	96 primary care physicians (33 practices)	Guidelines Feedback	58 GPs (17 practices) guidelines followed by feedback about the numbers of thyroid function, rheumatoid factor test and urine cultures they ordered (quarterly for one year)	38 GPs (16 practices) received guidelines then feedback about lipid and plasma viscosity tests (each a control group for the other)	Baseline and one year post intervention	No effect. No change in volume of tests per 1,000 requested in either of the study groups for any of the tests
Thomas et al.[48]	UK	RCT	370 primary care physicians (85 practices)	Feedback Education	Quarterly feedback of requesting rates and reminder messages. Practices allocated to one of four groups: control (20 practices), enhanced feedback alone (22 practices), reminder messages alone (22 practices), or both enhanced feedback and reminder messages (21 practices)	Current practice	12 months pre- and post-intervention	11% reduction in requests for practices receiving enhanced feedback or reminder messages OR: 0.89, 95% CI: 0.83-0.93) compared with control group.
Tomlin et al. [52]	New Zealand	CBA	3,160, 3,140 & 3,335 primary care physicians	Guidelines Feedback Education	Three marketing programmes (guidelines, individual feedback & professional development)	Locum and other physicians not targeted by the programmes	Two years pre- and post-intervention	60% reduction in the number of ESR tests by the intervention group following the intervention versus an 18% reduction in comparison doctors after the intervention.

Table 3.2 Quality assessment of the included studies

Author	Intervention	Design	Independent of other changes	Knowledge of allocated intervention	Unlikely to affect data collection	Shape of effect pre-specified	Attrition bias	Selective reporting	Other risk of bias	Overall risk
Horn et al. [46]	Changing order form	ITS	**Low risk** The study had a control group	**High risk** Participants knew which intervention they were receiving	**Low risk** Sources and data collection methods same before and after intervention	**Low risk** Specified	**Unclear risk** Missing data unclear	**Low risk** Appropriate outcomes reported	**Low risk** No other potential bias	**High risk**

Author	Intervention	Design	Random sequence generation	Allocation concealment	Protection against contamination	Blinding	Attrition bias	Selective reporting	Similar at baseline	Overall risk
Shalev et al. [55]	Changing order form	CBA	**High risk** CBA study	**High risk** CBA study	**N/A** No control group	**High risk** No blinding	**Low risk** No missing data	**Low risk** Appropriate outcomes reported	**N/A** No control group	**High risk**
Kahan et al. [54]	Changing order form	CBA	**High risk** CBA study	**High risk** CBA study	**N/A** No control group	**High risk** No blinding	**Low risk** No missing data	**Low risk** Appropriate outcomes reported	**N/A** No control group	**High risk**
Zaat et al. [74]	Changing order form	CBA	**High risk** CBA study	**High risk** CBA study	**Unclear risk** No information in text	**High risk** Participants knew what they had been allocated to	**Low risk** No missing data	**Low risk** Appropriate outcomes reported	**Unclear risk** No information in text on baseline characteristics, baseline outcomes similar (Fig 1/2)	**High risk**

Baricchi et al. [77]	Education	CBA	**High risk** CBA study	**High risk** CBA study	**Unclear risk** No information in text	**High risk** Participants knew what they had been allocated to.	**Low risk** No missing data	**Low risk** Appropriate outcomes reported	**Unclear risk** No information in text	**High risk**
Larson et al. [47]	Education	CBA	**High risk** CBA study	**High risk** CBA study	**Unclear risk** No information in text	**High risk** Participants knew what they had been allocated to.	**Low risk** No missing data	**Low risk** Appropriate outcomes reported	**Unclear risk** No information in text	**High risk**
Verstappen et al. [49]	Education	RCT	**Low risk** Blocked randomization	**Low risk** Cluster trial, allocation after recruitment completed	**Low risk** Independent clinics	**Low risk** Controls were blinded, hence preventing the Hawthorne effect.	**Low risk** No missing data	**Low risk** Appropriate outcomes reported	**Low risk** Outcomes measured at baseline and baseline characteristics reported and similar	**Low risk**
van Wijk et al. [50]	Guidelines	RCT	**Low risk** "researcher not involved in the study…performed the randomisation using random-numbers table"	**Low risk** "each practice assigned by simple random allocation"	**Low risk** Separate practices	**High risk** All participants knew what they had been allocated to. Test ordering in controls may have been affected.	**Low risk** Missing data similar between groups and all participants accounted for	**Low risk** Appropriate outcomes reported	**Low risk** Similar baseline characteristics	**High risk**
Baker et al. [51]	Guidelines & Feedback	RCT	**Low risk** Random number table	**Low risk** Cluster trial, allocation after recruitment completed	**Low risk** primary care physicians work separately	**High risk** Participants knew what they had been allocated to. Test ordering in controls may have been affected.	**Low risk** No sites lost to follow-up	**Low risk** Appropriate outcomes reported	**High risk** Participants in group 2 had fewer patients' and GPs than group 1	**High risk**

Thomas et al.[48]	Feedback & Education	Cluster RCT	**Low risk** "cluster randomization...with a minimization procedure"	**Low risk** Cluster trial, allocation after recruitment completed.	**Low risk** Separate practices	**High risk** Participants knew what they had been allocated to. Test ordering in controls may have been affected.	**Low risk** No missing data	**Low risk** Appropriate outcomes reported	**Low risk** Similar baseline characteristics	**High risk**
Tomlin et al. [78]	Guidelines, Feedback & Education	CBA	**High risk** CBA study	**High risk** CBA study	**High risk** "Changes...might be explained by ….contamination of the comparison group"	**High risk** Participants knew what they had been allocated to. Test ordering in controls may have been affected.	**Low risk** No missing data	**Low risk** Appropriate outcomes reported	**High risk** Intervention group included GPs only while control group included locum GPs also.	**High risk**

GENERAL PRACTITIONER VIEWS ON THE DETERMINANTS OF TEST ORDERING: A THEORY-BASED QUALITATIVE APPROACH TO THE DEVELOPMENT OF AN INTERVENTION TO IMPROVE IMMUNOGLOBULIN REQUESTS IN PRIMARY CARE.

SHARON L CADOGAN

SHEENA M MCHUGH

COLIN P BRADLEY

JOHN P BROWNE

MARY R CAHILL

Published as: Cadogan SL, McHugh SM, Bradley CP, Browne JP, Cahill MR: **General practitioner views on the determinants of test ordering: a theory-based qualitative approach to the development of an intervention to improve immunoglobulin requests in primary care**. *Implementation Science* 2016, **11**(1):1-12.

4.1 Abstract

Background Research suggests that variation in laboratory requesting patterns may indicate unnecessary test use. Requesting patterns for serum immunoglobulins vary significantly between General Practitioners (GPs). This study aims to explore GP views on testing to identify the determinants of behaviour and recommend feasible intervention strategies for improving immunoglobulin test use in primary care.

Methods Qualitative semi-structured interviews were conducted with GPs requesting laboratory tests at Cork University Hospital or University Hospital Kerry in the South of Ireland. GPs were identified using a Health Service Executive laboratory list of GPs in the Cork-Kerry region. A random sample of GPs (stratified by GP requesting patterns) was generated from this list. GPs were purposively sampled based on the criteria of: location (urban/rural); length of time qualified and practice size (single-handed/group). Interviews were carried out between December 2014 and February 2015. Interviews were transcribed verbatim using NVivo 10 software and analysed using the framework analysis method. Emerging themes were mapped to the theoretical domains framework (TDF), which outlines 12 domains that can enable or inhibit behaviour change. The behaviour change wheel and behaviour change technique (BCT) taxonomy were then used to identify potential intervention strategies.

Results Sixteen GPs were interviewed, (ten males and six females). Findings suggest that intervention strategies should specifically target the key barriers to effective test ordering, while considering the context of primary care practice. Seven domains from the TDF were perceived to influence immunoglobulin test ordering behaviours, and

were identified as ‘mechanisms for change’ (knowledge, environmental context and resources, social/professional role and identity, beliefs about capabilities, beliefs about consequences, memory, attention and decision-making processes, and behavioural regulation). Using these TDF domains, seven BCTs emerged as feasible ‘intervention content’ for targeting GPs ordering behaviour. These included instructions on how to effectively request the test (how to perform behaviour), information on GPs’ use of the test (feedback on behaviour), information about patient consequences resulting from not doing the test (information about health consequences), laboratory/consultant based advice/education (credible source), altering the test ordering form (restructuring the physical environment), providing guidelines (prompts/cues) and adding interpretive comments to the results (adding objects to the environment). These BCTs aligned to four intervention functions: education, persuasion, environmental restructuring and enablement.

Conclusions This study has effectively applied behaviour change theory to identify feasible strategies for improving immunoglobulin test use in primary care using the TDF, ‘Behaviour Change Wheel’ and BCT taxonomy. The identified BCTs will form the basis of a theory-based intervention to improve the use of immunoglobulin tests among GPs. Future research will involve the development and evaluation of this intervention.

Keywords laboratory testing, primary care, interventions, Theoretical Domains Framework, behaviour change techniques, Behaviour Change Wheel

4.2 Background

Laboratory testing plays an increasingly important role in the diagnosis and monitoring of conditions managed by General Practitioners (GPs). An estimated 30% of all patient encounters result in a test order, and care planning has become increasingly dependent on the results of laboratory tests [79, 80]. This has led to greater scrutiny of the appropriateness of test ordering, with suggestions that as many as 70% of all tests may be unnecessary depending on the context of care [81-83]. Considerable variation in test ordering patterns by GPs has been identified, further supporting the likelihood that some ordered tests are unnecessary [84-86]. Further, in a recent US survey of over 1,700 participants, GPs reported uncertainty about ordering tests in 14.7% of diagnostic encounters and uncertainty in interpreting results in 8.3% of these encounters [33]. Healthcare services worldwide are under pressure to reduce their costs and a review commissioned by the UK Department of Health estimated that costs could be reduced by as much as 20% by improving utilisation of pathology services [87]. +

Inappropriate laboratory testing includes both over- and under-utilisation. Over-utilisation is wasteful, can increase the likelihood of false positives, poor treatment decisions and adverse outcomes due to unnecessary interventions [14]. Under-utilisation may result in morbidity resulting from delayed or missed diagnoses. Overuse and underuse of tests can both lead to longer hospital stays and contribute to legal liability. One large review of laboratory testing patterns found inappropriate testing was three times higher for low volume than high volume tests (32% vs 10%) [83]. ‘Low volume’ in this study implied a test that was ordered at least ten times less frequently than the most commonly ordered tests [83]. Inappropriate testing is more

likely to occur with low-volume tests which may be due to a lack of familiarity with best treatment practices for the conditions under scrutiny [14].

Our study explores the use of two related low-volume blood tests in primary care, serum immunoglobulins quantitation and immunoglobulin electrophoresis. These tests should be ordered as part of the primary screen for suspected plasma cell dyscrasias (myeloma, lymphoma, chronic lymphatic leukaemia, heavy chain disease, and amyloidosis). Immunoglobulins alone may also be requested as part of the diagnostic investigation of patients with recurrent documented infections [22].

Low serum immunoglobulin levels indicate a deficiency of the humoral immune system, while high immunoglobulin levels (with normal electrophoresis) are observed in liver diseases, infections and chronic inflammatory diseases. Raised levels with abnormal electrophoresis may indicate blood dyscrasia [23]. High levels of immunoglobulins are a feature of many clinical conditions in older patients but are only really diagnostically useful in specific haematological disorders such as myeloma and lymphoma. The clinical features of these conditions can be vague and non-specific and overlap with the symptoms of a wide range of other conditions. Thus, in older patients, immunoglobulin testing is probably best undertaken as a second-line investigation where there are other tests (such as a full blood count) which indicate the possibility of a blood dyscrasia. Knowing when to order immunoglobulins, therefore, can be challenging for GPs and may require a clinical judgement in the context of rather non-specific clinical features. Their interpretation is also difficult and often requires specialist input. Furthermore, once abnormal levels have been detected this can lead to other costly activities such as referral to secondary care that may ultimately

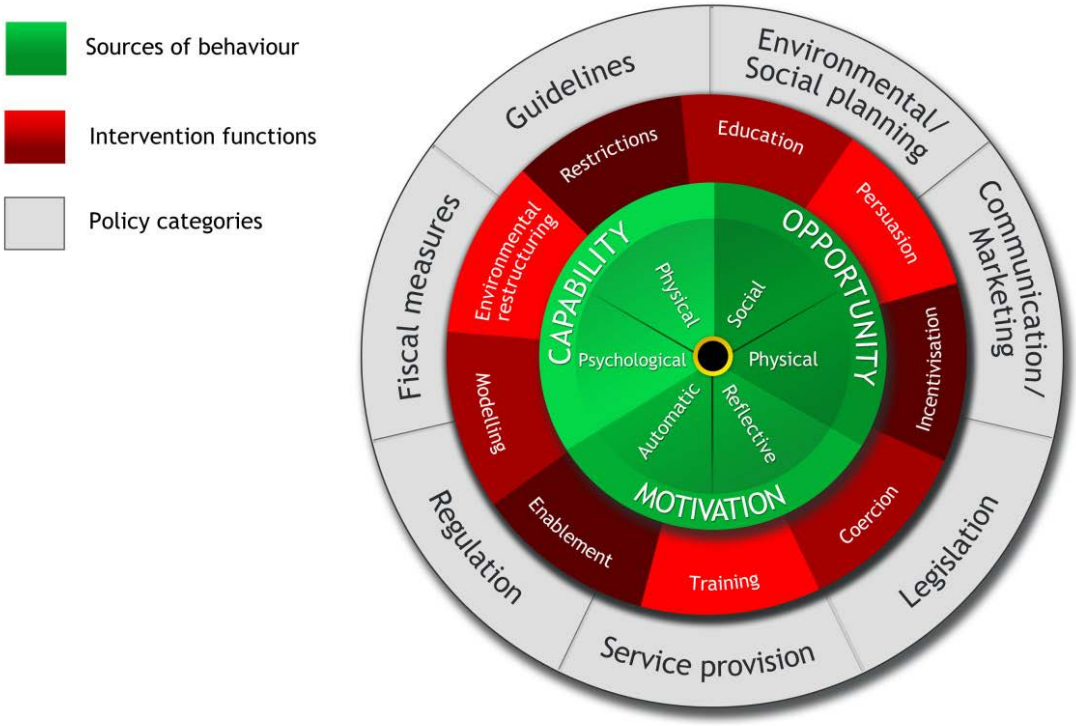
prove to have been futile. To date, no previous studies have studied GPs' serum immunoglobulin test ordering behaviour.

A recent systematic review identified a number of effective interventions for reducing inappropriate test ordering, defined as testing practices that do not lead to patient benefits [88]. Educational strategies [47, 49, 77], cost displays [89], changing order forms [54] and various methods of disseminating guidelines [48, 50] displayed positive effects. Ten out of 11 studies included in the review found significant reductions in the volume of tests following an intervention, with effect sizes ranging from 1.2 to 60% [88]. However, the positive effects of these interventions were often short-term, and none lasted longer than two years [88]. Implementation science experts have suggested that theory-based, targeted behaviour change techniques may maximise the potential long-term effects of such interventions [90]. In particular, there is a need to identify the key enablers and barriers to successful implementation of interventions in this area and to improve their design so that sustainability is ensured [91].

A growing body of literature supports the use of psychological theories in the development of behaviour change interventions [90, 92]. In particular, recent guidelines emphasise the need to report three aspects of behaviour change interventions [93]: the use of psychological theory to identify the factors which influence the target behaviour change (i.e., '*mechanism of action'*); the 'active ingredients' of behaviour change interventions (i.e., the intervention content); and, *how* this was delivered (i.e., who the intervention targeted, who delivered it, and in what format and setting). The theoretical domains framework (TDF) has been

identified as a useful tool for identifying the 'mechanism of action' and selecting behaviour change techniques (BCTs) to include in behavioural change interventions [44, 94]. The TDF is an elaboration of the six Capability, Opportunity and Motivation conditions of the 'Behaviour Change Wheel' (COM-B) [95] (see Figure 4.1). To date, a number of empirical studies have used the TDF to explore the implementation of BCTs with GPs including low back pain management [90] and medication prescribing [96].

Figure 4.1 The Behaviour Change Wheel



The aims of this study were to use the TDF and corresponding COM-B conditions to identify the enablers and barriers to altering immunoglobulin test ordering behaviour from the perspective of GPs, and to use this information to identify the corresponding BCTs and feasible intervention strategies to align requesting practice with possible health gain, for future evaluative research. The specific GP behaviours targeted in this

study were serum immunoglobulin test requests that were not correctly aligned with the presenting symptoms of patients or were unlikely to lead to patient benefit.

4.3 Methods

4.3.1 Study design

Qualitative semi-structured interviews were conducted with GPs in two adjacent counties in the Republic of Ireland.

4.3.2 Sampling and recruitment

All 587 practising GPs in the Cork-Kerry region were identified using a list provided by the Health Service Executive, the organisation that provides public healthcare in the Republic of Ireland. GPs were stratified by the volume of tests they had requested over the previous two years from the primary public hospitals in the region that provide the relevant laboratory services (Cork University Hospital and University Hospital Kerry). This involved categorising GPs into low (<10 tests/year), moderate (10-50 tests/year) and high (>50 tests/year) requesters for immunoglobulin tests. Within each category of requesting patterns, GPs were then purposively sampled based on the sampling criteria of: location (urban/rural); length of time qualified (<10 years, 10-20 years, >20 years); and practice size (single-handed/group). GPs were sent a written invitation letter and study information sheet, followed by a telephone call to determine if they were interested in participating. A ’ten plus three’ method, which has been previously recommended for theory-based interview studies, was used to determine our initial sample size target [97]. Ten GPs were interviewed and the material collected was analysed at this point. Three further GPs were then interviewed to check if any new insights were produced. If further interviews were deemed necessary, they would be conducted in blocks of three with a check for data saturation

at the end of each block. One additional block of three interviews was necessary to reach data saturation, giving a total of 16 interviews. Written informed consent was obtained from all participants prior to the interview.

4.3.3 Semi-structured interview process

Face-to-face semi-structured interviews were carried out in the primary care setting by one researcher (SLC) between December 2014 and February 2015. The interview topic guide was developed based on the second version of the TDF [98] and discussion among the authors and is summarised in Appendix 5. The topic guide and interview process were piloted by interviewing two GPs. Following this pilot, there were no changes to the topic guide, but refinements were made to the probes that were used to explore GP responses and to the interviewing style. These pilot interviews were facilitated in the same manner as the remaining interviews and are included in the final analysis with consent from the interviewees. Interviews were recorded and transcribed verbatim. NVivo 10 software was used to facilitate data analysis.

4.3.4 Data analysis

Stage one. Data analysis followed the Framework analysis approach [99]. Data familiarisation was carried out by re-reading the transcripts and listening back to interview recordings. Following open-coding, emergent themes were mapped onto the domains of the TDF and corresponding Capability, Opportunity, Motivation conditions. When themes were relevant to more than one domain, they were initially coded to both domains. All transcripts were coded by the researcher who conducted the interviews (SLC), and a subset of six interviews (including a sample of urban/rural, male/female and more/less experienced GPs) were independently coded and analysed by a second researcher (SMMH) as a method of verification of the initial analysis.

Coding and mapping by the independent researchers (SLC and SMMH) were compared. There were no major disagreements. Minor differences arose in relation to the mapping of codes to TDF domains, particularly when codes mapped to more than one domain. Any differences were resolved by consensus discussion; the researchers referred back to the original transcripts to reassess the context of the codes, and discussed the particular code in light of the breadth of data from other transcripts mapped to that TDF domain drawing on SLC's knowledge of all the interviews conducted and analysed.

Stage two. The BCT taxonomy, version 1 was then used to recommend potential 'intervention components', that is, strategies to improve laboratory testing in primary care [94, 100]. This taxonomy has been developed in order to standardise the content and reporting of intervention studies [94] and includes 93 BCTs grouped within 16 categories with detailed definitions of each [94]. This process involved mapping the BCTs to the TDF domains and corresponding capability, opportunity and motivation conditions of the 'behaviour change wheel' identified in stage 1 [100]. The full list of BCTs has previously been applied to the TDF by a group of behaviour change experts [44]. We used this list [44] along with a more recently published list (resulting from an expert mapping exercise) [101] as a reference tool for guiding our selection of BCTs. Our multidisciplinary research team reviewed the BCTs that had been mapped to key domains in order to reach consensus on the BCTs that should be selected for the intervention development. This selection process was guided by the interview data and focused on identifying barriers and facilitators that could feasibly be targeted based on the available intervention resources. For example, if time and perceived

workload were reported as major barriers to GP testing behaviours, BCTs that could be delivered more efficiently were to be prioritised.

4.3.5 Ethical approval

Ethical approval for the study was obtained from the Cork Research Ethics Committee (ref: ECM (ii) 07/01/14).

4.4 Results

4.4.1 Sample demographics

In total, sixteen GPs were interviewed, including ten males and six females. Table 4.1 provides details of the participants' characteristics categorised by location type (urban/rural).

Table 4.1 Characteristics of GPs interviewed based on urban/rural setting

GP characteristics	Urban (n=8)	Rural (n=8)	Total (N=16)
Gender			
Male	5	4	9
Female	3	4	7
Age Group			
30-40	2	2	4
40-50	4	2	6
50-60	0	2	2
>60	2	2	4
Training practice*			
Yes	5	5	10
No	3	3	6
Practice nurse^			
Yes	5	5	10
No	3	3	6
Practice type			
Solo GP	2	2	4
Group practice	6	6	12

*Training practice: a practice that facilitates trainee GPs on the Irish medical training scheme.
^ Practice nurse refers to whether the practice has a practice nurse employed.

4.4.2 Summary of findings from analysis at the level of theoretical domains

The analysis identified seven domains of the TDF that were relevant to 18 emerging themes (Table 4.2). These findings are described in greater detail below. The remaining domains that were not identified (intention, optimism, goals, emotion, social influences) are not discussed as not enough references to the relevant constructs were made.

Table 4.2 TDF domains identified and the corresponding key themes that evolved

TDF domains	Themes
Knowledge*	▪ Limited knowledge of when to use immunoglobulin tests effectively. ▪ GPs expressed difficulty with interpreting the results (particularly borderline abnormal results). ▪ Lack of knowledge of how to effectively manage patients when the result is abnormal (when to refer).
Environmental context and resources	▪ Lack of clear guidelines on when to use an immunoglobulin test in primary care. ▪ Need for instructions on when to refer patients with abnormal results.
Beliefs about consequences	▪ Excessive follow-up workload that comes with doing an Immunoglobulin test.
Beliefs about capabilities	▪ Feel they are poor at triaging patients for potential myeloma. ▪ GPs find interpreting immunoglobulin results difficult. ▪ Concern at what to do with an abnormal test result, in particular, borderline abnormal results.
Social/professional role	▪ Happy to do the tests for specialist monitoring purposes. ▪ Many GPs feel it's not a common test in primary care.
Memory, Attention and Decision Process	▪ A follow-up test performed on the basis of results of another test. ▪ Not a priority in primary care. ▪ Older patients with chronic back pain trigger the test for many. ▪ Small minority use them regularly for screening.
Behavioural regulation	▪ Education and guidelines mentioned the most. ▪ Electronic strategy highlighted as feasible/ systems-level strategy. ▪ Multidisciplinary approach.

*Knowledge and skills were merged due to overlapping constructs

The main domains from the TDF which emerged were: ‘knowledge’, ‘skill’, ‘environmental context and resources’, ‘social/professional role and identity’, ‘beliefs about capabilities’, ‘beliefs about consequences’, ‘memory, attention and decision-making processes’ and ‘behavioural regulation’.

4.4.2.1 Knowledge and skill

The domains ‘Knowledge’ and ‘Skill’ were merged as the constructs overlapped. That is, GPs primarily referred to ‘procedural’ knowledge and where competence or ability (skills) was mentioned, it was always linked to a lack of knowledge. Participants reported that knowledge was a key barrier when requesting immunoglobulins. In particular, GPs identified a number of different scenarios when they would request the test including “recurrent infections”, “respiratory problems” and “back pain”. The majority of GPs stated that they would be considering potential “myeloma” when they are requesting, however, a small minority of GPs identified other conditions including “rheumatoid arthritis” and “anaemia”. GPs reported that a need for greater guidance and training on when to use serum immunoglobulin tests would be beneficial.

> *“No, my natural feeling towards it would be I feel that I don't know enough about them. And I might be getting more value out of them if I knew more you know yeah”. (GP 6)*

> *“It’s confusing I mean it’s just a confusing area for us and when do we request them anyway?” (GP 2)*

The interpretation of immunoglobulin results was identified as a challenge by almost all GPs interviewed. In particular, they discussed difficulty interpreting borderline abnormal results and making treatment decisions for these cases.

"Well, it can be difficult to interpret. So often if there is a difficulty with them you basically have to ring the lab to confirm before you discuss with the patient because at that stage anyway you're talking about referring the patient on anyway". (GP 3)

"I find them very hard to interpret, and I end up ringing haematology about the interpretation". (GP 4)

4.4.2.2 Environmental context and resources

The majority of GPs mentioned a lack of clear guidelines on when to request an immunoglobulin test. GPs reported that they often phone the laboratory for advice in the absence of clear requesting and interpretative guidelines. GPs highlighted that this was time consuming, however, they commended the support of laboratory staff.

"I find the labs very good to be honest with you. They'll put you onto the consultant that's on duty at the time or if not they'll ring you back. So I've never had a problem with it". (GP 9)

Patient management post testing was also mentioned as a concern. In particular, a lack of information on the usefulness of the test for managing patients in primary care. For example, one GP used the test for screening patients but expressed that he did not know what to do with the result.

"…I suppose there are some issues like that I have to get advice from the haematologists where I'm you know at a loss where do we go from here. Do we just put it up on their record and leave it there as background information or do we proceed further with investigations". (GP 10)

4.4.2.3 Beliefs about capabilities

In general, the majority of GPs admitted a lack of confidence in their ability to use serum immunoglobulin tests, in particular, managing their patients who receive an abnormal result. Many reported that they often had to phone the laboratory and speak to the haematology registrar or consultant. Other stated that they often just referred these patients.

> *"I feel my ability to triage them is poor, and you don't want to be ringing the haem reg (haematology registrar) all of the time". (GP 13)*

> *"So, if I get an abnormal result, I'd either want to speak to a haem reg (haematology registrar) or refer on because I wouldn't be confident in managing an abnormal result". (GP 11)*

> *"If it's minor and it's fractional and the patient is well, I'm happy to do nothing. If it's significant and I'm just unsure, that's when I ring the reg (haematology registrar) or consultant". (GP 4)*

4.4.2.4 Beliefs about consequences

GPs stated the workload created by doing the tests was a deterrent, in particular having to liaise with the laboratory or haematology department.

> *"Exactly, because ironically in my experience doing immunoglobulins will lead to workload perhaps because I'm going to have to liaise with my hospital specialist colleagues' ah because to get their opinion on them actually". (GP 15)*

Also, a small number of GPs mentioned: "fear of litigation" and "fear of missing a myeloma" as other potential consequences leading to what they described as

potentially ineffective use of the test. Again, these consequences related back to their perceived lack of knowledge.

4.4.2.5 Social/professional role and identity

Some GPs reported that they request a large volume of immunoglobulins, often as a screening test. However, the majority of GPs referred to the test as a second or third line test, performed subsequent to previous tests. They stated that they considered immunoglobulins a rare test and one they would not perform regularly.

> *"We have a reg (registrar) and am we have two practice nurses and at the induction for the registrar there are certain blood tests we advise them not to perform regularly; this would be one of the ones we advise not to perform regularly". (GP 4)*

GPs highlighted that while they feel the test should be available in primary care, they often consider it a secondary care test and in few cases highlighted their gatekeeping role in using the test.

> *"You see GP's often wouldn't see them because if they are being monitored by haem (haematology). In fairness GP practices do them, but they probably do some with their forms to their nurse, but the GP won't see them. And often, if they come in with the form, it is the consultant's name of the form, and their results don't come back to us". (GP 13)*

Finally, younger female GPs (in their 30s) suggested that they may request fewer tests due to their patient demographics. They commented that the majority of their patients are younger females and children who are less likely to require the test.

> *"I see pretty much all women and children, and so I would have very little need. There is a very small number of older patients". (GP 13)*

> *"I think that because I am a young female GP I don't see a huge pile (volume) of older patients – so what I do is kiddies (children) and contraception and a lot of antenatal care and gynae (gynaecological) stuff". (GP 9)*

In particular, each of them highlighted that patients often grow with them (the GP) in terms of age, and suggested that more experienced male GPs may appropriately request more.

4.4.2.6 Memory, Attention and Decision Process

When asked about what prompts them to perform the test, GPs had many contrasting reasons, with many highlighting that they were unsure of when to do them. GPs discussed some key symptoms that would influence their decision-making process such a "chronic back pain", "persistent infections" or in some cases simply "age". These factors varied between GPs; however, almost all GPs mentioned myeloma as the potential endpoint diagnosis from doing the test.

> *"I use them primarily in situations where I think there might be something significant. So usually you tend to see it used in say recurrent infections or more particularly in patients who might potentially have multiple myeloma". (GP 5)*

Some GPs mentioned that they request the test to monitor patients with an existing diagnosis at the request of the consultant, where results of previous tests are available.

“Once they have been into the consultant and the consultant has said this is...just check it every 12 months, that's fine by me. I'll check it if its. I'll look at the results. I can very easily compare them to the last results on my computer and I can tell if it’s changing or if it's not changing”. (GP 2)

4.4.2.7 Behavioural regulation

GPs suggested potential strategies to help improve testing in primary care. GPs primarily requested education and guidelines on when to test, but also on how to interpret the results.

“I guess education is what we need really. You know what value it will be to us for our patient and for, obviously for information for helping the patient”. (GP 4)

“Yeah I suppose we need a one-page protocol so we know where we are going with this thing you know”. (GP 10)

In particular, they discussed the feasibility and receptiveness of educational based interventions in primary care. A key barrier according to the GPs was ensuring sustainable strategies are selected.

“Well I suppose the easy answer would be to say training or education or a booklet or a pamphlet but there's a great risk that if you produce a document like that it will be quickly glanced at, thrown in the bin, or what I would be doing, I would put it in a filling place, and I'd never look at it again. So you need to do something that is sustained and continuous actually I would say”. (GP 4)

"I think the education strategy has to be built in with reminders". (GP 2)

Two GPs discussed penalties, incentives, feedback and restrictive strategies. However, when discussed in detail, GPs concluded that the lack of knowledge would potentially hamper the effects of such strategies.

> *"Another thing of course would be either penalty or incentivisation whereby if and it's a sad thing to say but we respond to incentives. So if you over-prescribe, sorry over-request to a ridiculous degree you know four times the average then there should be some kind of a penalty. Or, if you're within certain ranges some kind of incentive. And, I think that would affect real change". (GP 12)*

> *"I think am the form…if you want a particular test that is out of the ordinary, I think that you should have to justify your reasons in the clinical details box for the test". (GP 9)*

Importantly, GPs stressed that a systems level approach needs to be followed, where possible at the laboratory level providing education or the use of an algorithm.

> *"I think it has to be at the systems level. Cause (because) I think a once-off workshop or once off piece of paper coming out to the practice won't make a difference here". (GP 14)*

> *"It has to be at the systems level. I think it has to be centrally delivered from the Department of Haematology". (GP 14)*

> *"Well I suppose if you had your algorithm so if you had like so complaints or five scenarios where so if the come in with this you should be ordering*

an S pep and you should be looking for such and such on the results. So if you did it that way". (GP 16)

"Yeah, maybe like a performer or an algorithm or some kind may be useful alright". (GP 12)

However, GPs mentioned that any strategy developed to improve the use of laboratory tests should be primary care responsive and consider the differing motivations of GPs versus specialist physicians. For example, many GPs stated that they perform laboratory tests to 'rule out' a diagnosis while, specialist physicians may be more likely to carry out tests to 'rule in' or confirm a diagnosis.

"You know because a lot of them, if they come back abnormal are very useful you know and this is one of the differences between general practice and hospital practice, the importance of normal blood tests. General practitioners generally do blood tests to out rule illnesses and hopefully getting normal results, whereas hospital practice would be much more inclined to do a blood test to confirm an abnormal result or to look for an abnormal result". (GP 6)

4.4.3 Application of BCT taxonomy and identification of potential intervention functions

Table 4.3 shows the final mapping of the BCTs to the identified TDF domains and COM-B components. Using previous work on mapping BCTs to the TDF, as outlined in the methods, the research team identified and selected seven BCTs with potential for inclusion in a future intervention involving GPs. This resulted in six of the 16 BCT groupings; 'shaping knowledge', 'feedback and monitoring', 'natural consequences', 'comparison of outcomes', 'antecedents' and 'associations'. Within these six

groupings, seven specific BCTs were found to be relevant (definitions of each of these can be found in Appendix 6). For example, the technique “Instructions on how to perform the behaviour” from the 93-item BCT taxonomy [94] was selected to target the GPs lack of knowledge on when to request the test, while another technique “prompts/cues” was used to target the feasibility of implementing an education based strategy. A full description of the selection and exclusion of BCTs can be found in Appendix 7.

Using these BCTs, four of the ten intervention functions were deemed potentially useful for developing an intervention targeting the GP population. Selected BCT functions included ‘education’, persuasion’, ‘environmental restructure’ and enablement’. Subsequently, potential intervention components were devised and include: providing guidelines on when to request the test, clearly communicating situations where testing is not beneficial for patient care education and giving advice (attached to results) on how to interpret results and manage patients with abnormal levels. These intervention strategies were also suggested by GPs during the interviews, and are likely to assist in the development of feasible and welcome interventions. Table 4.3 provides details of the mapping process for selecting the BCTs and intervention components. For example, for the domain ‘Knowledge’, the BCTs ‘information on how to perform the behaviour’ and ‘feedback on behaviour’ were selected. However, providing feedback on individual GP requesting patterns was deemed potentially inappropriate due to the lack of knowledge GPs expressed around when to request the test in the first instance.

Table 4.3 Suggested intervention content and mechanisms of action using the Behaviour Change Technique (BCT) taxonomy (v1); behaviour change wheel Capability Opportunity Motivation-Behaviour (COM-B) model; and Theoretical Domains Framework (TDF) [95]

Intervention component	**Mechanisms of action**		**Intervention content**		
	TDF[2]	**COM-B[1]**	**BCT group**	**BCTs**	**Functions**
Information and training about immunoglobulin use in primary care, i.e. provide guidelines on when to request and how to interpret results.	Kn MAD BR	C-(Psy.) C-(Phys.)	Shaping knowledge	Instructions on how to perform behaviour	Education
Provide feedback on individual GP feedback (volume of tests). NOTE: not a suitable strategy in this context	Kn	C-(Psy.)	Feedback and monitoring	Feedback on behaviour	Education Persuasion
Clearly communicate situations where immunoglobulin testing is not beneficial. (i.e. develop an algorithm of scenarios where tests should be performed, supported by consultant haematologists and GPs.	B Cap B Con	M-(Refl.)	Natural consequences Comparison of outcomes	Information about health consequences Credible source	Persuasion
Provide notes detailing consultant advice on the test results (ideally provided on the end of the test results).	Env **S**/P Id	O-(Phys.) O-(Soc.)	Antecedents Associations	Restructuring the physical environment Prompts/cues Adding objects to the environment	Environmental restructure Enablement

[1] COM-B components: C-(Psych), psychological capability; C-(Phys), physical capability; M-(Refl), reflective motivation; O-(Phys), physical opportunity; M-(Auto), automatic motivation. *Intervention functions in italics
[2]TDF domain abbreviations: Kn knowledge, MAD memory, attention and decision processes; BR behavioural regulation; Env environmental context and resources; B Cap, beliefs about capabilities; B Con, beliefs about consequences; S/P Id, social/professional role and identity

The final mapping of the relevant BCTs and corresponding intervention components to the COM-B and TDF models can be found in Table 4.4.

Table 4.4 Final mapping of relevant BCTs for the design of a strategy for improving immunoglobulin test use in primary care

				CAPABILITY			**OPPORTUNITY**		**MOTIVATION**	
				Psychological			Physical	Social	Reflective	
BCT group [94]	**BCT [102]**	**Functions**	**Support from interviews**	Kn*	MAD	BR	Env	S/P Id	B Con	B Cap
Feedback and monitoring	Feedback on behaviour	Education	GPs reported that they are not aware of how many tests they request, or if they request tests appropriately.	✓						
Shaping knowledge	Instructions on how to perform the behaviour	Education	GPs expressed a lack of knowledge about when to do the test and asked for standardised guidance or resources.	✓	✓	✓				
Associations	Prompts and cues	Enablement	GPs highlighted that a once off education strategy is not desirable. Instead, they suggested a reminder on test results.					✓		
Comparison of outcome	Credible source	Persuasion	GPs mentioned the importance of input from specialists with regard to patient management following an abnormal test result.						✓	
Antecedents	Restructuring the physical environment	Environmental restructure	GPs discussed current requesting procedure as a potential target (requesting more detail on order forms.				✓			
Antecedents	Adding objects to the environment	Environmental restructure	GPs discussed the lack of guidelines for interpreting test results and expressed interest interpretive comments on test results.				✓			
Natural consequences	Information about health consequences	Persuasion	GPs expressed concern over the consequences of not performing a test in terms of missing a myeloma diagnosis.							✓

***** TDF domain abbreviations: Kn knowledge, MAD memory, attention and decision processes; BR behavioural regulation; Env environmental context and resources; B Cap, beliefs about capabilities; B Con, beliefs about consequences; S/P Id, social/professional role and identity

4.5 Discussion

This study presents a systematic, theory-based approach to developing an intervention to improve test ordering in primary care. We found that serum immunoglobulin test ordering is influenced by many social and contextual factors. Using the BCT taxonomy, TDF and COM-B models, four potentially useful intervention functions on which to model future interventions have been identified. These are education, environmental restructuring, enablement and persuasion by specialists.

Evidence suggests that medical professionals respond differently than other healthcare professionals to interventions designed to change their behaviour [103] and that interventions are more likely to influence change if they target the factors underlying barriers to behaviour change [44]. The barriers to behaviour change also differ across healthcare professionals, and may result from differences in training, knowledge, work experience, personality, and other individual characteristics [104]. To our knowledge, this is the first study to identify these barriers in the primary care setting and develop potential strategies for improving test ordering using clearly delineated behaviour change theories. Two key barriers identified were a lack of knowledge on when to use immunoglobulin tests in primary care and how to interpret the results. Until these knowledge deficits are addressed, an audit and feedback approach to behaviour may be unsuccessful as the underlying drivers of inappropriate test ordering will not have been addressed. This is in line with the rejection of audit and feedback by the interviewees and the findings of previous studies [58, 105].

Interviewees emphasised that the passive provision of information alone is not sufficient to bring about behaviour change in primary care. The GPs interviewed

argued that highlighting a discrepancy between expected and actual test ordering rates may be perceived as judgmental of their professional capacity. In particular, they discussed their clinical motivation for performing tests and the context of primary care setting as key characteristics that should be considered [106].

Interviewees suggested that helping them to improve their knowledge through, for example, educational reminders or external support was likely to be successful. This support should come from specialists (‘a credible source’) and incorporate the dissemination of guidelines and feedback on how best to manage the patient. This is consistent with other studies on the value of education based specialist support strategies such as interactive educational sessions coupled with the use of local opinion leaders/physician champions and/or feedback reports [48, 49, 88]. The interviewed GPs also suggested that strategies should be designed at the laboratory level, such as changing the order forms or adding interpretive guidance to the results.

When designing specialist support services to guide test ordering, strategies should be responsive to the needs of both GPs and laboratory services. For example, while GP knowledge may be a barrier to behaviour change, strategies aimed at targeting testing behaviour also need to consider the motivation for testing in primary care, which may be to rule out a diagnosis rather than to rule in one. This may require educational messages to draw on a different knowledge base, for example, regarding the negative predictive value of the test rather than just information about the positive predictive value.

Our research suggests that specialist support should be provided from a credible source in an encouraging and non-judgemental manner. In the instance of immunoglobulins, haematologists are the best equipped to do so and therefore are well placed to assist the laboratory to formulate advice and comment on test interpretation. This support may best be provided in the form of interactive learning sessions with local opinion leaders and feedback reports generated at the laboratory level. Basic medical education could also incorporate information on immunoglobulin testing guidelines and interpretation.

4.5.1 Strengths and limitations

A key strength of this study is the systematic approach followed to identify key theoretical domains and select BCTs to support the development of an intervention in primary care. In doing so, we have followed existing recommendations on designing theory informed behaviour change interventions [90]. By making the relationship between the supporting theoretical framework and our intervention development explicit, it may be easier to identify how different elements of any subsequently designed intervention contribute to observed behaviour change. Also, in addition to identifying mediators of behaviour change to target using an intervention, the interviews have supplied valuable information about the clinical context in which the behaviours are currently performed. This information, along with the findings of our previous review [88], will inform decision-making around which intervention approaches should be employed in future research by our research group.

There are some limitations to this study. First, the findings reflect GPs' perceptions of influences on their clinical behaviours, but we do not have data on their actual

behaviour in specific cases. Finally, we have drawn on a particular set of psychological theories of behaviour change but there may be alternative theories or frameworks that might also be applicable to explain test ordering behaviour of primary care physicians.

4.6 Conclusion

This research provides an important overview of the behavioural factors influencing laboratory testing among GPs. The incorporation of behavioural theory, specifically the COM-B, TDF and BCT taxonomy, has supported the identification of factors such as knowledge and the social and environmental context, which are key for understanding testing behaviours. Selected BCTs provide the groundwork for developing a theory-based intervention to improve appropriate immunoglobulin testing in primary care. Future work will involve developing and evaluating an intervention using the selected BCTs.

PHYSICIAN AND PRACTICE LEVEL DETERMINANTS OF PRIMARY CARE TEST REQUESTS FOR SERUM IMMUNOGLOBULINS.

SHARON L. CADOGAN

JOHN P. BROWNE

COLIN P. BRADLEY

ANTHONY P. FITZGERALD

MARY R. CAHILL

Under review at Family Practice (August 2016)

5.1 Abstract

Background

Primary care test requests for serum immunoglobulins are rising rapidly, with concerns that many requests may be unnecessary. Evidence suggests certain types of General Practitioners (GPs) and practices are associated with higher test ordering.

Aims

To identify the physician and practice characteristics associated with immunoglobulin test ordering.

Design and setting

Retrospective, cross-sectional study using routine laboratory data on primary care serum immunoglobulin requests.

Methods

Data were linked with GP patient list size data. The primary outcome measure was the count of test requests per GP. Predictor variables were physician gender, years experience, practice region and type (number of GPs), GP patient list size and composition. Mixed-effects multilevel regression models were used to calculate incidence rate ratios (IRRs) with 95% confidence intervals (CI) for the associations between physician and practice characteristics and GP requesting. Sensitivity analysis was performed by limiting the model to the over 70 age category.

Results

In total, 5,990 immunoglobulin tests were ordered by 481 GPs in the South of Ireland during 2013. The number of tests ordered by individual GPs varied from one to 377. In the final fully adjusted Poisson regression analysis, physician factors were

associated with test ordering. Female gender (IRR: 1.81; 95% CI: 1.45-2.26) and less experience (IRR: 2.27; 95% CI: 1.47-3.51) were associated with higher requesting ($P<0.001$). None of the practice factors were associated with test ordering. Sensitivity analysis on the over 70 age category found similar results.

Conclusion

Education programmes about the nature and uses of immunoglobulins, targeted at female GPs and those with less experience, may be required.

5.2 Background

Laboratory testing is the single highest volume medical activity in healthcare and demand is rising year on year in many countries [11, 107, 108]. General Practitioners (GPs) initiate an estimated 50% of all requests [28], while approximately 30% of all primary care patient visits result in a laboratory test order [33]. Over the past 20 years, the number of new laboratory tests available to GPs has increased rapidly [33]. The volume of orders from GPs has also risen significantly for the most commonly ordered tests [11]. Given the increasing financial pressure on health systems, judicious laboratory testing is imperative. A better understanding of the determinants of GP test ordering is necessary, as evidence suggests that between 25% and 40% of all test orders are unnecessary [13, 14]. Differences in test ordering patterns of GPs has been linked to both physician and practice-level characteristics [109]. At the physician-level, higher test ordering has been reported in female GPs [110, 111] and GPs with less medical experience [112]. At the practice-level, both practice type and practice setting have been linked to GP test ordering patterns. Those in group practices have been shown to order significantly fewer tests than GPs in single handed or two-person practices [113]. Working in an urban practice has been positively linked to higher test ordering [111]. However, previous research has not considered the interaction of physician and practice factors in a multilevel model. Existing literature also does not account for individual GP patient list size or the composition of lists.

This study focuses on a low volume test, serum immunoglobulins, which poses a significant challenge to GPs [114]. These tests should be ordered as part of the primary screen for suspected plasma cell dyscrasias (myeloma, lymphoma, chronic lymphatic leukaemia, heavy chain disease, and amyloidosis) or when investigating for the very rare causes of immune deficiency [22]. Depending on the condition (e.g. myeloma),

serum immunoglobulin tests may also be ordered periodically to monitor disease progression [22]. In the UK, one of the largest increases in GP test use between 2005 and 2009 were for serum immunoglobulins with a relative increase of 73.4%, from 61 tests per GP in 2005 to 106 tests per GP in 2009) [11].

Immunoglobulins are particularly problematic in primary care [114]. High levels are a feature of many clinical conditions in older patients, but their greatest diagnostic value is in specific haematological disorders such as myeloma and lymphoma. Unfortunately, clinical features of these disorders can be vague and non-specific and overlap with the symptoms of a wide range of other conditions. Thus, in older patients, immunoglobulin testing is probably best undertaken as a second-line investigation where there are other tests (such as a full blood count) which indicate the possibility of a blood dyscrasia. Knowing when to order immunoglobulins can be challenging for GPs and may require a clinical judgement in the context of non-specific clinical features. Interpretation of test results is also difficult and often requires specialist input [114]. In particular, the rarity of the conditions that immunoglobulins are aimed at suggests that factors such as GP gender, medical experience and practice setting or number of GPs at a practice are all likely to be important drivers of using this test [114]. To date, no research has been carried out on physician and practice-level predictors of serum immunoglobulin testing.

The aim of this study was to identify the relationship between physician and practice characteristics and the volume of serum immunoglobulins requested among GPs in the South of Ireland, adjusting for the size and composition of GP public patient lists.

5.3 Methods

5.3.1 Study design and population

We conducted a cross-sectional study using one year (2013) of routine laboratory data to analyse the determinants of serum immunoglobulin test requests. The study was conducted in two adjacent counties (Cork and Kerry) in the South of Ireland which has a combined population of 664,534. All serum immunoglobulin analyses for these counties are processed at Cork University Hospital (CUH) and all GP test requests for the region are captured in our study.

5.3.2 Dependent variable

The dependent variable was the 2013 count of immunoglobulin test requests per GP.

5.3.3 Predictor variables

At the physician-level, we collected data on the following predictors of test ordering, the GPs' gender and their medical experience (years since graduation). The number of years since the GP graduated with their medical degree was used as a proxy for the GPs clinical experience as per previous research [112, 115, 116].

Practice-level predictors were practice setting (urban, rural) and the type of practice (single-handed, 2-4 GPs or >4 GPs). Rural is defined according to Irish census data as areas with no population centre above 1,500 people, with a population density below 150 per square km, and which are not part of an urban district [117]. The number of GPs practising at a given practice was used to describe the practice type as per previous research [113].

Information about the number of publically funded patients cared for by each GP was also included in the model (Appendix 8). This was used as a proxy for clinician workload and was used to make the request volumes of different GPs comparable. We also included the age and gender composition of publically funded patient lists in our model as the conditions associated with serum immunoglobulins are more common in older and male patients [118].

5.3.4 Data collection and cleaning

Immunoglobulin test order counts and data about GPs and their practices were extracted for 2013, using Cognos Impromptu software to interrogate the hospital's APEX laboratory system. The data fields requested were: request date, specimen number, test code, patient age, and gender, requesting GP, the location of test request, GP gender, surgery name, and address. The extracted data were exported from Cognos using Excel and imported into Stata v12 for analysis.

Data on GP list size and the gender and age composition of these lists were obtained from the Health Service Executive Primary Care Reimbursement Scheme (HSE-PSRC). In Ireland, patients under a certain income level are entitled to free health care through the General Medical Services (GMS) scheme. Those participating in this scheme are reimbursed by the HSE-PCRS for a range of services they provide to these patients. Information held in the HSE-PCRS database is retrievable at individual patient level using the GPs unique Medical Council record number. This number was used to merge HSE-PCRS data with the immunoglobulin laboratory data extracted at CUH. In 2013, 498 GPs were contracted to the GMS in the Cork-Kerry region and were registered to receive reimbursement for providing services to 265,000 eligible

GMS patients [119]. Of these patients, 54,988 were over the age of 70, representing approximately 97% of all the over 70s who live in Cork and Kerry [119].

Data on each GP's medical experience was obtained from the Medical Council, the statutory, regulatory and registration body for doctors in Ireland. Medical experience was defined as years since GPs qualified with their medical degree and was coded to "<10 years", "10-20 years" and ">20 years" as per previous research [112].

5.3.5 Data analysis

Mixed effects multilevel regression models were used to calculate incidence rate ratios (IRRs) with 95% confidence intervals (CI) for the associations between GP and practice characteristics and requesting patterns for serum immunoglobulins. Multilevel analyses were used to take into account the structure of the data: physicians were nested within practices. The model, therefore, consists of two levels: the physician level (level 1) and the practice level (level 2). The outcome (test requests) was modelled as a count variable with a conditional Poisson distribution [120]. Calculating variance estimates from random effects Poisson regressions rather than directly from the observed rates is a more statistically rigorous approach, which appropriately adjusts for lack of independence in requesting rates for GP in the same practice. Estimated regression coefficients were expressed as IRRs with 95% confidence intervals (CI).

To analyse the extent to which the final model was sensitive to the impact of not including non-GMS patients in the study a sub-analysis was performed by limiting the model to include the over 70s category only. Data were analysed using Stata v12.

5.4 Results

5.4.1 Sample characteristics

In total, 481 primary care physicians requested 5,990 serum immunoglobulins during 2013. This represents 96.6% of all GPs registered in the GMS scheme in the Cork-Kerry region in 2013. The remaining GPs may not have requested any immunoglobulins or were not active at the time. Table 5.1 provides the GP requesting patterns by physician and practice characteristics (both crude and adjusted for their standardised patient list sizes).

Table 5.1 GP requesting patterns (2013) by physician and practice characteristics (crude and adjusted for patient list sizes)

	Total GPs	**Total IG counts**	**Mean per GP[1](crude)**	**Standard deviation**	**Mean per 1,000 GMS patients[2]**
Totals	N=481	N=5,990	12.5	27.5	43.9
Physician level					
GP Gender					
Males	230	3,206	13.0	28.6	35.5
Females	251	2,784	12.1	26.6	*60.9*
Experience					
<10 years	68	519	7.6	9.2	*49.5*
10-20 years	125	1,108	9.1	10.1	36.9
>20 years	266	4,132	15.6	35.2	45.8
List size					
<500	299	3,649	8.9	19.9	44.0
500-1,000	166	1,875	31.7	50.4	43.7
>1,000	16	466	51.7	34.1	44.2
Practice level					
Location					
Urban	316	3,858	12.3	24.9	44.7
Rural	165	2,132	13.0	32.1	42.3
Practice type					
> 4 GPs	201	2,239	11.3	28.9	43.9
2-4 GPs	178	2,278	12.8	18.2	41.9
Single-handed	98	1,435	14.9	37.7	47.9

[1] Mean volume of immunoglobulin requests per GP per year

[2] Standardised for GP GMS list sizes and composition (patient age and gender adjusted) – GMS patients are public patients receiving free GP care

IG: immunoglobulins

5.4.2 Overview of GP requesting patterns

The crude mean count of test requests per GP for 2013 was 12.5 (SD: 25.5; range 1 to 377). The mean number of test orders was 43.9 per 1,000 public patients. Allowing for GP public list size had the greatest impact on requesting patterns by gender of the GP. Crude count data indicate female GPs requested fewer immunoglobulin tests (mean: 12.1) compared to male GPs (mean: 13.0). However, when we adjust for GP public patient list size and demographics, female GP test ordering rates are higher than males (60.9/1,000 patients versus 35.5/1,000 patients, respectively). Similarly, crude count data alone indicate the GPs with less than ten years' experience (mean: 7.6) order fewer tests than those with 10-20 years (mean: 9.1) or those with over 20 years' experience (mean: 15.6). GPs with less than ten years' experience had fewer patients, and when GMS list sizes and demographics were adjusted for, they had higher test ordering rates (49.5/1,000 patients). Figure 5.1 illustrates the total volume of requests per GP during 2013. In total, four GPs were outliers, requesting over 100 serum immunoglobulin tests per year.

Figure 5.1 Total serum immunoglobulin requests per GP in Cork-Kerry region, 2013

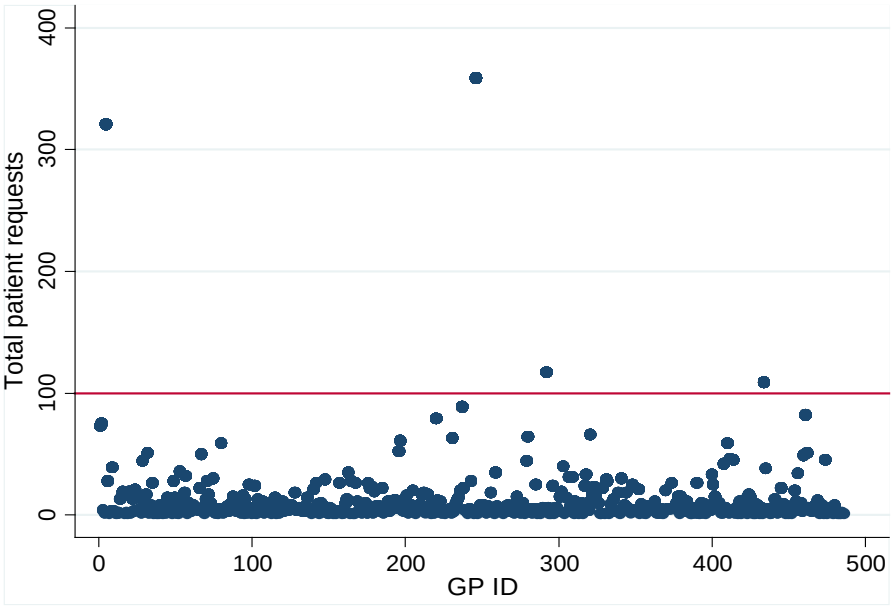


Figure 5.2 Distribution of GP immunoglobulion test ordering in the Cork-Kerry region, 2013

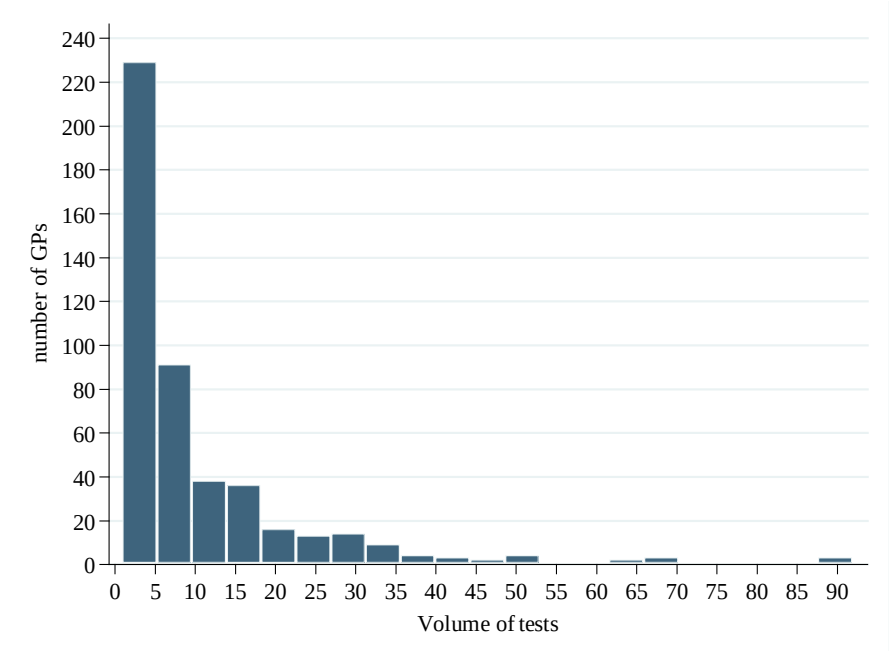


Figure 5.2 illustrates the distribution of GP test ordering among the sample, excluding the four outliers highlighted in figure 5.1. The obsesrved data are asymmetric (skewed right).

5.4.3 Requesting patterns by patient age and gender

In total, 30% (n=1,809) of immunoglobulin tests were requested for patients in the over 70 category, 25% (n=1,490) for patients in the 60-70 age category, 23% (n=1,377) for 45-60 age category, 16% (n=929) for 30-45 and 6% (n=385) for those in the under 30 age category. 61% (n=3,675) of test requests were for female patients.

5.4.4 Physician/practice characteristics and test ordering

Table 5.2 provides the results of the mixed-effects multilevel Poisson regression analysis. In model one (adjusted for GP gender and medical experience) all of the physician factors were associated with immunoglobulin requesting rates. Model two (adjusted for the physician factors plus practice location and practice type) also found

all of the physician factors to be associated with GP requesting rates for immunoglobulins. In particular, GP gender and medical experience were positively associated with immunoglobulin test ordering rates. Female GP requesting rates were 81% greater than male GPs (IRR: 1.81; 95% CI: 1.45-2.26, p<0.001). GPs with less than ten years' medical experience were also more likely to request immunoglobulin tests (IRR: 2.72; 95% CI: 1.47-3.51, p<0.001).

There were no statistically significant associations between the practice-level factors (location or practice type) and GP immunoglobulin test ordering rates.

Table 5.2 Physician and patient-level factors associated with GP immunoglobulin test ordering patterns, 2013

	MODEL 1 (physician only)			**MODEL 2 (physician + practice)**		
Variables*	**IRR[1]**	**(95% CI)**	**p-value[2]**	**IRR[1]**	**(95% CI)**	**p-value[2]**
Physician level						
GP gender			<0.001			<0.001
Female	1.80	(1.45-2.34)		1.81	(1.45-2.26)	
Male	1			1		
Experience			0.003			0.001
<10 years	2.12	(1.39-3.23)		2.27	(1.47-3.51)	
10-20 years	1.09	(0.86-1.39)		1.17	(0.80-1.42)	
>20 years	1			1		
Practice level						
Location						0.26
Rural				0.88	(0.70-1.10)	
Urban				1		
Practice type						0.52
>4 GPs				1.17	(0.88-1.56)	
2-4 GPs				1.07	(0.80-1.42)	
Single handed				1		

*Final fully adjusted model [1]Cluster grouping: primary care practices, Groups: 214 [2]p-values based on likelihood test ratio

5.4.5 Sensitivity analysis

Table 5.3 presents the results of the sensitivity analysis on the over 70 age category (fully adjusted model). Results were similar to that of the full model including all patient age groups. The strongest difference was among females, where the strength

of the association was greater in the subgroup analysis compared with the full dataset. Based on the fully adjusted model, female GPs requested over twice as many tests compared to males (IRR: 2.37; 95% CI: 1.76-3.18). Experience also remained strongly associated with test ordering among patients over 70. Those with less than ten years' experience were more than twice as likely to order a test compared to those with more than 20 years' experience (IRR: 2.55; 95% CI: 1.43-4.52).

Table 5.3 Physician and patient-level factors associated with GP Immunoglobulin test ordering patterns (70 age category), 2013

	MODEL 2 (physician + practice)		
Variables*	**IRR[1]**	**(95% CI)**	**p-value[2]**
Physician level			
GP gender			<0.001
Female	2.37	(1.76-3.18)	
Male	1		
Experience			<0.001
<10 years	2.55	(1.43-4.52)	
10-20 years	1.34	(0.97-1.86)	
>20 years	1		
Practice level			
Location			0.17
Rural	0.81	(0.60-1.10)	
Urban	1		
Practice type			0.18
>4 GPs	1.37	(0.93-2.00)	
2-4 GPs	1.07	(0.73-1.58)	
Single handed	1		

*Final fully adjusted model [1]Cluster grouping: primary care practices [2]p-values based on likelihood test ratio

5.5 Discussion

5.5.1 Summary of main findings

This study evaluated the relationship between certain physician and practice characteristics and the use of serum immunoglobulin tests over one year. The strongest predictors of test requests were physicians' gender and medical experience (years since graduating with a medical degree). No associations were found between practice-level factors and immunoglobulin test ordering rates.

5.5.2 Strengths and limitations

Unique strengths of this study are the inclusion of all GP requests for immunoglobulin tests in two large adjacent regions with a population in excess of 650,000, the use of patient list size and composition to allow for the fair comparison of different GPs and the use of multilevel modelling to separate GP and practice effects. An important limitation of our study is the use of HSE-PCRS data to characterise GP list size and composition. This data excludes private patients for which no accurate data is available in Ireland. Private patients account for approximately 66% of the average GPs list in Ireland [121]. However, a sensitivity analysis which included only patients over 70 years old, 97% of whom are covered by the GMS scheme, found the same physician factors to be associated with immunoglobulin test ordering rates. A further limitation is our exclusion of other predictor variables which may influence test requesting patterns such as the presence of an electronic ordering system in the practice [122].

5.5.3 Comparison with existing literature

Physicians' gender. This study showed that being a female GP was associated with higher serum immunoglobulin test ordering rates. This is consistent with previous studies examining the characteristics of GPs and test ordering behaviour [111, 123]. With the proportion of female physicians rising in most European countries [124], is important to investigate why females may be ordering more tests than their male counterparts. Previous research suggests that higher test ordering rates of female GPs may relate to differences in practice styles [125]. In Ireland, a recent national survey reported that female GPs see fewer patients on average per session than males [126]. The same report found less female GPs practice full-time, compared to males (70% versus 100% in the under 40 age group) and also retire at a younger age [126]. It is

possible that the experience of part-time GPs with certain low-volume tests falls below a critical threshold which leads them to excessive ordering.

Medical experience. GPs with less than ten years' experience were significantly higher requesters in this study. Previous research also found a statistically significant inverse association between years of experience and test ordering [112]. Further, in a previous qualitative study with GPs from this sample, it was suggested that younger GPs may be more likely to request serum immunoglobulins [114]. Potential reasons for this include a lack of confidence in their clinical judgement at this stage of their career and a fear of missing serious cancers such as myeloma [114].

Practice location and type. This study found no significant association between practice location (urban/rural), practice type (single-handed, 2-4, or 4 or more GPs) and GP test ordering patterns. This is in contrast with previous research reporting 18% fewer tests among GPs in group practices compared to those in single handed or two-person practices [113]. Working in an urban practice rather than a rural practice has also previously been linked to higher test ordering patterns [111]. It is possible that the practice level effects seen in previous studies were driven by physician level effects such as the gender and experience of GPs: these effects have been accounted for in our study. For example, it is possible that the excessive test ordering rates by urban practices was driven by the tendency for younger or less experienced GPs to work in these settings [126].

5.5.4 Implications for research and/or practice

Our research suggests that education programmes about the nature and uses of serum immunoglobulins, targeted at female GPs and those with less experience, may be

required. However, we recommend that further qualitative research is performed first to explore why female GPs and less experienced GPs order greater volumes of serum immunoglobulins. It must be emphasised that our study was not designed to detect inappropriate test ordering. It is possible that female GPs and those with less medical experience are behaving with an appropriate level of caution. The consequences of finding (or missing) pathology are very significant for the doctor and patient. Further study of the clinical utility of serum immunoglobulin test orders is required and currently ongoing in our study region.

5.6 Ethical approval

Ethical approval was granted by the clinical research ethics committee of the Cork University Teaching Hospitals (ref: ECM (ii) 07/01/14).

5.7 Acknowledgements

We would like to thank the laboratory staff at Cork University Hospital, in particular, Mr Aidan Kelleher for facilitating the data extraction and Mr Brendan O'Reilly for providing Cognos Impromptu software training for SLC.

USING SEGMENTED REGRESSION ANALYSIS OF INTERRUPTED TIME SERIES DATA TO ASSESS GUIDELINES COMBINED WITH EDUCATIONAL MESSAGES FOR IMPROVING THE USEOF SERUM, IMMUNOGLOBULIN TESTS IN PRIMARY CARE: STUDY PROTOCOL

SHARON L. CADOGAN

JOHN P. BROWNE

COLIN P. BRADLEY

MARY R. CAHILL

6.1 Abstract

Background

Implementation science experts recommend the use of tailored and theory-driven behaviour change interventions when targeting health care professionals. It has also been suggested that interventions designed with the involvement of those for whom it is intended, may be more effective. This study protocol describes the development of intervention material and details of the implementation plan for a strategy targeting the use of serum immunoglobulin tests in primary care.

Methods/Design

Segmented Poisson regression analysis of interrupted time series data (SRAITSD) will be performed to determine the impact of the intervention, both immediately (change in level) as well as over time (change in trend). The dataset will include routine laboratory data on all GP immunoglobulin requests between January 2012 and July 2016. Data will be arranged into fortnightly time segments (providing 96-time points pre- and 20 post-intervention) and analysed using Stata v12. The study results will be presented as incidence rate ratios (IRRs) with their corresponding 95% confidence intervals along with parameter coefficients and standard errors.

Discussion

This intervention strategy will respond to the specific needs of GPs identified using semi-structured interviews, which have been previously discussed in this thesis (Chapter 4). This will be combined with evidence from a systematic review of interventions that have previously worked (Chapter 1). Intervention components for this strategy were selected using a combination of behaviour change theories to

identify the ‘mechanisms for change’ and the intervention functions that are important for optimising immunoglobulin test ordering in primary care. This protocol describes how this information has been used to develop intervention material and devise an implementation plan. It also presents details of the proposed statistical analysis methods.

6.2 Background

Healthcare budgets face increasing pressure to reduce costs and remove inefficiencies while maintaining quality and safety. Laboratory testing plays an important role in healthcare expenditure [34]. An estimated €76 million is spent on laboratory services each year, accounting for 3-4% of the national health budget [20]. Despite this relatively small proportion of healthcare budget expenditure, laboratory testing often underpins more costly downstream care such as outpatient visits and radiology requests [127].

Many approaches for reducing unnecessary test ordering in primary care have been attempted [88], including changing order forms [54], cost displays [128] and various methods of disseminating guidelines [48, 50, 77]. We conducted a systematic review aimed at identifying and evaluating existing interventions for improving the use of laboratory tests among primary care physicians [88]. While included studies differed considerably in relation to the tests they assessed, some key findings were highlighted. Our review found that education-based interventions were successful at improving GP laboratory testing patterns [47, 49, 77], in particular, when used to deliver clinical guidelines [48]. Similar primary care activities have also shown positive effects of educational reminder-based interventions [58]. For example, the addition of educational messages to X-ray reports have been found to be effective for reducing radiography requests among primary care physicians [58], which also appeared to be sustainable in the long term [129].

Research suggests that interventions tailored to address identified barriers and enablers to change, were more effective when targeting healthcare professionals' behaviour

[91]. However, few studies explain how they choose a particular combination of interventions [72]. Intervention components for our study were identified using a combination of previously explained behaviour change theories to target the key barriers and enablers for changing immunoglobulin test ordering behaviour in primary care (Chapter 4). This protocol describes how this information has been used to develop and implement intervention material.

6.2.1 Aims and objectives

The aims of this study are to

1. Implement an education-based strategy among GPs in the South of Ireland.

2. Evaluate the effectiveness of this strategy using a quasi-experimental segmented regression of an interrupted time series design.

Specifically, the following research question will be addressed:

> Does the addition of automated interpretive educational messages to laboratory results, combined with a guideline algorithm alter GP use of immunoglobulin tests?

6.3 Methods

6.3.1 Study sample

The sample will include all GP requests for serum immunoglobulin tests in the Cork-Kerry region. Routine laboratory data will be extracted on all test orders between January 2012 and July 2016.

6.3.2 Ethical approval

Ethical approval for the study was obtained from the Cork Research Ethics Committee (ref: ECM (ii) 07/01/14) which can be found in Appendix 2.

6.3.3 Intervention development

The intervention strategy was designed based on the combined findings of our systematic review (Chapter 3) [88] and theoretical paper (Chapter 4) [114] previously discussed. The latter identified six BCTs and four corresponding intervention functions for designing an education-based strategy to improve immunoglobulin test use in primary care [95]. These intervention functions include education, enablement, persuasion and environmental restructuring. Definitions of each can be found in Table 6.1.

Table 6.1 Definitions of intervention functions [94] and selected intervention component

Function	Definition	Intervention component
Education	Increasing knowledge or understanding	• Provide guidelines on when to request the test and how to manage abnormal results using an algorithm design.
Persuasion	Using communication to induce positive or negative feelings or stimulate action	• Provide guidance on how to manage patients with abnormal immunoglobulin test results.
Environmental restructuring	Changing the physical or social context	• Provide automated interpretive comments to test reports.
Enablement	Increasing means/reducing barriers to increase capability or opportunity	• Provide details on how to interpret test results.

6.3.4 Description of the intervention content

The intervention consists of two components targeting test requesting behaviour issues raised by primary care physicians in our qualitative interviews (Chapter 4): a lack of knowledge about when to request the test, how to manage patients with abnormal results and uncertainty around how to interpret test results.

Algorithm guideline

The first component of the intervention targets the problem of when to request an immunoglobulin test and how to manage a patient with a raised (abnormal) immunoglobulin result. To do so, a one-page algorithm was designed based on current UK guidelines and can be found in Appendix 9 [29]. This provides information on when to request an immunoglobulin test, as well as the steps for managing patients who have raised immunoglobulins. The algorithm assists GP decision making on requesting further tests or when to refer a patient to see a consultant haematologist.

Interpretive messages

The second component of the intervention targets the issue of interpreting the test results. Educational messages providing interpretative comments will be added to the end of test results. In total, eight educational messages have been developed based on Myeloma guidelines and specialist input from consultant haematologists' and laboratory scientists [29]. Primary care test ordering motivations differ from that of secondary care specialists. To ensure GP responsiveness, the interpretive comments were reviewed and edited by a Professor of General Practice. These messages will provide guidance on how to interpret the test results, both in terms of possible diagnoses and future patient management decisions. The eight messages will be built into the laboratory IT system and added to test results electronically based on 'action

cues'. For example, "diffusely raised IgG" prompts the automated addition of the following interpretive message "Pattern of persistent infection or inflammation". A table outlining each of the educational messages and their corresponding 'action cues' can be found in Appendix 10.

Table 6.2 highlights how both components of the intervention align with the four intervention functions identified in the theoretical design paper.

Table 6.2 Details of the intervention component selected based on corresponding BCTs and functions

Strategy component	**Intervention content**	
	BCTs[1]	Functions[1]
The guideline algorithm		
Provides details on when to request and how to interpret results	Instructions on how to perform behaviour	Education
Clearly communicates situations where immunoglobulin testing is not beneficial (i.e. screening)	Information about health consequences	Persuasion
Designed by consultant haematologists using UK guidelines and revised by a primary care representative to ensure GP responsiveness	Credible source	Persuasion
Educational messages		
Provides interpretive comments detailing consultant advice on the test results	Restructuring the physical environment	Environmental restructure
Provides details on possible diagnoses	Prompts/cues	Enablement
Attached to the test results	Adding objects to the environment	Enablement

[1] Identified in theoretical paper previously described (Chapter 4)

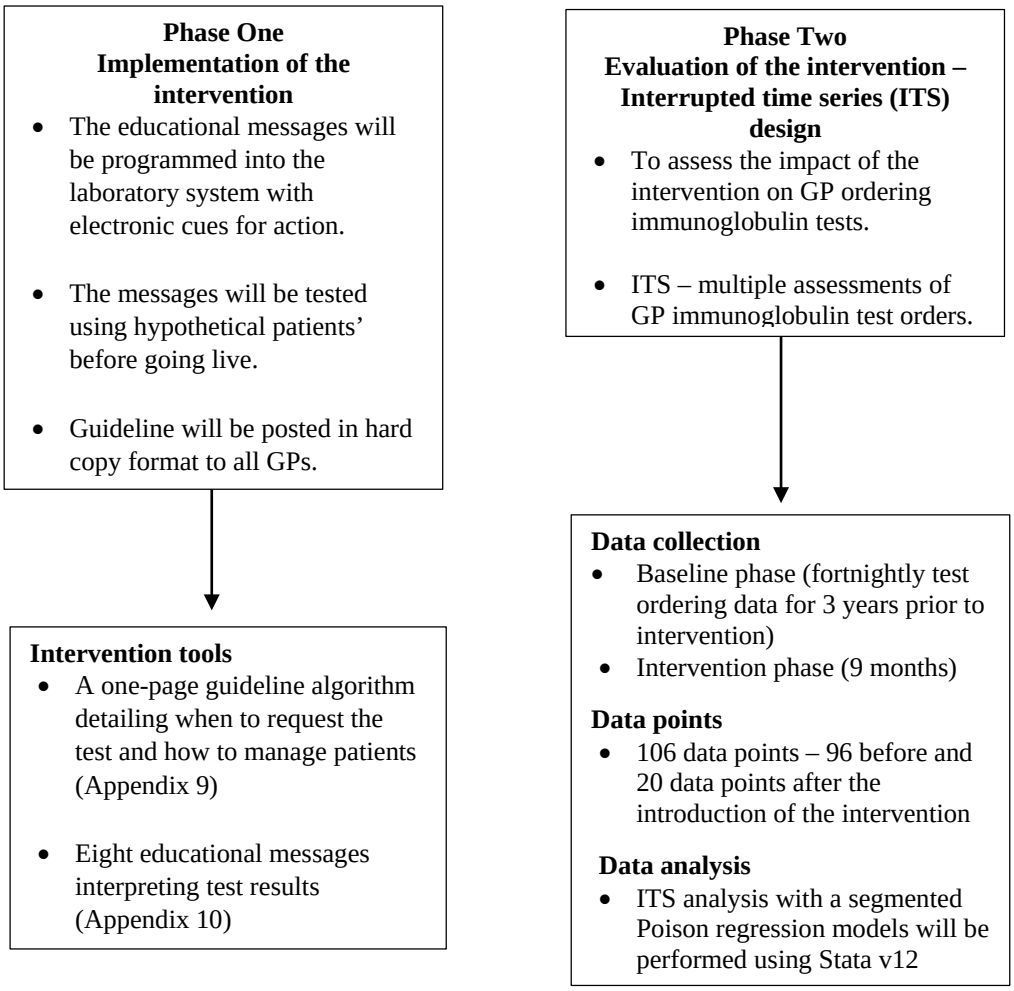
6.3.5 Implementation and evaluation plan

The intervention study will include a two-phase process (Figure 6.1). The first phase (implementation phase) will involve programming the interpretive educational

messages into the hospital's laboratory system, along with the corresponding 'action cues' for each message. These will be tested for errors using hypothetical patients for a number of weeks prior to the intervention going live. This phase will also involve sending a copy of guideline algorithm to all GPs in the region.

Once the intervention has been implemented, phase two will involve evaluating the effect on GP test ordering patterns after a nine-month time-period.

Figure 6.1 Two-phase process for implementing and evaluating the combined guideline and educational reminders intervention



6.3.6 Study design

The combined guidelines and educational messages intervention will be evaluated using a quasi-experimental ITS design. These designs include a range of non-randomised intervention studies, and are frequently used when it is not logistically feasible to conduct a randomised controlled trial (RCT). For example, medical informatics interventions are often difficult to randomise to individual healthcare providers. This is the case with our education messages strategy – the laboratory IT system does not facilitate the automated provision of educational messages to individual primary care practices.

A stepped-wedge trial is an alternative study design used in cases where individual level randomisation is not possible. In particular, it has been recommended as a potentially efficient and pragmatic alternative randomised study design for the evaluation of service delivery interventions where outcomes are based on routinely collected data [130]. However, they are time consuming with a long follow-up period required. Moreover, efficiency depends on the intra-cluster correlation and cluster size. Finally, it is unlikely that GP practices will be able to follow the randomisation schedule [131].

Research has found that quasi-experimental designs are strong alternatives to RCTs and stepped wedge designs [132]. Three quasi-experimental designs exist, which include latin squares, factorial and time series designs [133]. An interrupted time series design using segmented regression models was deemed most appropriate [132]. The additional time and resources required for the alternative study designs were not available whereas, the resource for a time series analysis was readily available. For

example, in latin square designs there are many experimental groups; each receives multiple treatments, in different sequences [133]. Similarly, in factorial designs there are many experimental groups; each gets a combination of treatments [132]. By contrast, in time series designs there is one group and one or more treatments; many observations over time [132]. In particular, this design can address secular trends including a change in the outcome over time, history such as a seasonal trend for times where requesting may be higher irrespective of the intervention; and random fluctuations with no discernible patterns [131].

Finally, access to high-quality routine laboratory data pertaining to all GP test orders along with the centralisation of laboratory services in the studied region, provides the necessary resources for implementing a region-wide strategy involving 100% of the target population. Our study design was developed in accordance with the quality criteria for ITS studies adapted by Ramsay and colleagues [131], which can be found in Appendix 11.

6.3.7 Sample size calculations

In ITS studies, sample size calculations are related to the estimation of the number of observations or time points at which data will be collected. A sufficient number of time points before and after the intervention is needed to conduct segmented regression analysis [131]. A general recommendation is for 12 data points before and 12 data points after the intervention [131], although this number is not based on estimates of power. There also need to be a sufficient number of observations (a minimum of 100 is desirable) at each fortnight segment to achieve an acceptable level of variability of the estimate at each time point [131]. Having at least 48 fortnightly

time-points pre-intervention permits an adequate evaluation of seasonal variation and other trends in the pre-intervention data [131]. Our ITS will include 96 data points before the introduction of the intervention (three years of data in two-week segments) and 20 data points after the introduction of the intervention (nine months of data in two-week segments).

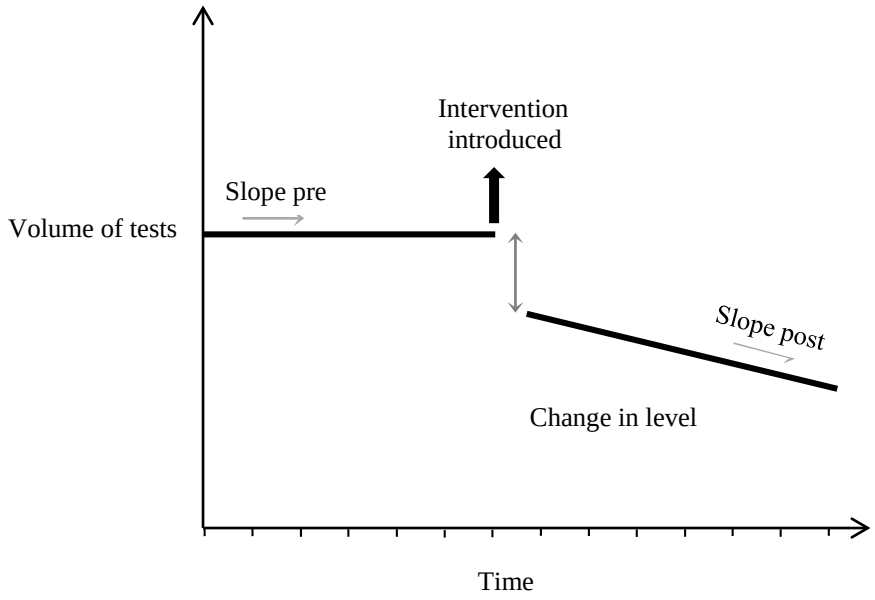
6.3.8 Data analysis plan

Segmented Poisson regression analysis of interrupted time series data (SRAITSD) will be used to determine the impact of the intervention (Figure 6.2), both immediately (change in level) as well as over time (change in trend). SRAITSD is an excellent analysis method for pragmatic studies because it minimises threats to internal validity while maximising external validity [131]. The analysis will be performed using Stata v12. The full segmented regression model will include the intercept (β_0), baseline trend (β_1), change in level (β_2) and the change in trend after the introduction of the intervention (β_3). The following model will be applied to estimate the effect of the intervention:

$$Y_t = \beta_0 + \beta_1 T + \beta_2 X_t + \beta_3 T X_t.$$

Where β_0 represents the baseline level at T=0, β_1 is interpreted as the change in outcome associated with a unit time increase (i.e. represents underlying pre-intervention trend), β_2 is the level change following the intervention and β_3 indicates the slope change following the intervention (using interaction term for time and intervention: TX_t.). The analysis will estimate the effect of the intervention while taking account of time trends, seasonal effects and autocorrelation among the observations. Results of the individual, full and most parsimonious models will be presented.

Figure 6.2: ITS study design with changes in level and trend (slope)



6.4 Potential limitations and methodological issues

Our proposed study has some potential limitations. The ITS design is susceptible to several potential threats to internal validity. However, we designed our methodology according to the ITS quality criteria recommended by Ramsay et al. [132] (Appendix 11) and the Strengthening the Reporting of Observational Studies in Epidemiology statement [134] (Appendix 12) to help overcome these threats.

The first potential limitation is changes in clinical practice independent of the introduction of the intervention may occur from the influence of other system changes or activities during the study period. For healthcare professionals and physicians, in particular, these include continuing professional development activities (e.g., participation in continued medical education (CME) activities such as didactic lectures, small-group workshops, and attendance at conferences). However, CUH is the only centre providing specialist haematological services for the region and other education strategies pertaining to serum immunoglobulin test use are unlikely.

A second limitation is many laboratory tests have a seasonal pattern due to the nature of the condition for which the test is requested. Seasonality can cause autocorrelation and overdispersion. We will assess the data for seasonality using Fourier terms (pairs of sine and cosine functions) [135]. Long-term patterns can be modelled more smoothly by fitting Fourier terms in the Poisson model. These are pairs of sine and cosine functions of time with an underlying period reflecting the full seasonal cycle (i.e. calendar year) and are particularly suited to capturing very regular seasonal patterns. A single sine/cosine pair will model seasonal variation in the outcome as a regular wave with a single peak and trough per calendar year (the position of the peak and trough are guided by the data). We will use extra sine/cosine pairs with shorter wavelengths which result in more flexible functions. Extreme values known as wild data points will also be dealt with by assessing the data plot for any outliers and follow recommended methods for handling such data [77].

6.5 Conclusion

This protocol has outlined the development of intervention material incorporating previously identified theoretical content (Chapter 4). The intervention will be rolled out in October 2015 in accordance with the described protocol. The effect of the intervention will be assessed using nine-months of post-intervention laboratory data following the methods described.

6.6 Acknowledgements

A special thank you to Dr Monica Taljaard and Professor Jeremy Grimshaw, Ottawa Hospital, Canada, for their expert advice on the study design. We would also like to

thank Dr Oonagh Gilligan for her expert opinion on revising the interpretive educational comments.

GUIDELINES COMBINED WITH EDUCATIONAL MESSAGES TO IMPROVE THE USE OF IMMUNOGLOBULIN TESTS IN PRIMARY CARE: AN INTERRUPTED TIME SERIES WITH SEGMENTED REGRESSION ANALYSIS

SHARON L. CADOGAN

JOHN P. BROWNE

COLIN P. BRADLEY

ANTHONY P. FITZGERALD

MARY R. CAHILL

Submitted to British Medical Journal, Quality and Safety (Sept 2016)

7.1 Abstract

Background Implementation science experts recommend that theory-based strategies, developed in collaboration with healthcare professionals, have a greater chance of success. In this study, the impact of a theory-based strategy for optimising the use of serum immunoglobulin testing in primary care is evaluated.

Methods We devised an intervention comprising of a combined guideline and educational messages based strategy, targeting previously identified general practitioner issues relevant to testing for serum immunoglobulins in the South of Ireland. The intervention was evaluated using an interrupted time series with segmented Poisson regression models using routine laboratory data from January 2012- July 2016. The data was organised into fortnightly segments (96-time points pre- and 20 post-intervention) and analysed using incidence rate ratios with their corresponding 95% confidence intervals along with parameter coefficients and standard errors.

Results In the full segmented regression model (including both change in level and change in slope pre- and post-intervention), the change in trend before and after the introduction of the intervention was statistically significant. The intervention was associated with a 1.5% percent reduction in the slope per fortnight (-1.51; 95% CI: -1.16, -1.86, $p<0.001$).

Conclusion Our tailored guideline combined with educational messages reduced serum immunoglobulin test ordering in primary care. Given the rarity of the conditions for which the test is utilised and the fact that we only have population (and not

individual patient level) data, further investigation is required to examine the clinical effects of this change in test ordering patterns.

7.1 Background

Healthcare budgets worldwide face increasing pressure to reduce costs and remove inefficiencies, while maintaining quality and safety. Laboratory testing is a major component of healthcare budgets, and demand for laboratory testing is increasing faster than other medical activity [34]. There are many reasons for this rise, including the availability of new tests [33] and clinical practice guidelines advising earlier screening to detect occult disease [5]. Given the increasing financial pressure on health systems, judicious laboratory testing is imperative. However, evidence suggests that many laboratory tests are ordered unnecessarily [4, 5]. As well as the cost implications, this can lead to harmful downstream effects such as further follow-up testing, specialist referrals and invasive diagnostic procedures [3, 14].

Serum immunoglobulins are a group of tests that pose particular challenges for primary care physicians. The test is primarily used to help with the diagnosis of haematological disorders such as myeloma and lymphoma. These disorders are rare, and their symptoms can be vague, non-specific and overlap with a wide range of other conditions [29]. Thus, immunoglobulin testing is probably best undertaken as a second-line investigation where there are other tests, such as a full blood count or radiological abnormalities, which indicate the possibility of a haematological disorder. Deciding when to request immunoglobulins can be challenging for primary care physicians and requires clinical judgement in the context of non-specific clinical features [114]. In the UK, one of the largest increases in primary care test use between 2005 and 2009 was for serum immunoglobulins with a relative increase of 73.4%, from 61 to 106 tests per physician per year [11]. There has been no contemporaneous increase in the incidence of blood dyscrasias that might explain this rise [118]. This

suggests that there is potential to improve the use serum immunoglobulin tests in primary care.

Our recent systematic review found that educational strategies, feedback and changing test order forms may improve the efficient use of laboratory tests in primary care [88]. In a related study, we used interviews with primary care physicians to explore different options for improving the use of serum immunoglobulins [114]. The interviewees expressed a lack of confidence in their ability to use the tests and were concerned about factors that could lead them to overuse the test in some circumstances (e.g. fear of litigation) and underuse them in others (e.g. the extra workload associated with liaising with haematology specialists). The study also found that interventions focused on education (increasing knowledge or understanding - what to do and why), enablement (increasing means/reducing barriers to increase capability or opportunity), persuasion (using communication to induce positive or negative feelings or stimulate action) and environmental restructuring (changing the physical or social context) were most likely to help the interviewees successfully change their ordering behaviours [88, 114].

Prior qualitative research by us was used to develop a theory-based intervention to improve the use of serum immunoglobulins by General Practitioners (GPs) [114]. Theory-based interventions utilise a combination of behaviour change models to select and design an intervention strategy [32]. The mechanisms for changing test ordering (barriers and enablers) were identified using the theoretical domains framework (TDF) and corresponding capability, opportunity and motivation conditions of the 'behaviour change wheel' known as the COM-B model [95]. Intervention content was then specified in terms of component behaviour change techniques (BCTs) [114].

These BCTs are based upon the four intervention functions identified in our qualitative research [95]. The intervention provides guidelines on when to request the test (education/enablement). It also clearly communicates situations where testing is beneficial for patient care (education) and how to manage patients with abnormal test results (enablement/persuasion). Finally, it provides details on how to interpret results (education/enablement) by attaching comments to test reports (environmental restructuring).

In this study, we use laboratory data and an interrupted time series (ITS) design to determine the impact of this intervention on serum immunoglobulin ordering rates.

7.2 Methods

7.2.1 Study sample and setting

Participants were all GPs located in the Cork-Kerry region of the Republic of Ireland. The region has a combined population of 664,534 and all serum immunoglobulin tests for the population are performed at one laboratory, located in Cork University Hospital (CUH).

7.2.2 Study design

The combined guideline and educational messages intervention was evaluated using a quasi-experimental ITS design and complies with the quality criteria for ITS studies adapted by Ramsay and colleagues (Appendix 11)[132].

7.2.3 Ethical approval

Ethical approval for the study was obtained from the Cork Research Ethics Committee (ref: ECM (ii) 07/01/14).

7.2.4 Description of the intervention

The first component of the intervention targets when to request an immunoglobulin test and how to further evaluate a patient with an abnormal finding. This involved creating a one-page guideline algorithm designed based on current UK guidelines, and can be found in Appendix 9 [29]. These guidelines provide information on when to request an immunoglobulin test, along with a patient evaluation plan following the test request.

The second element of the intervention assists with the interpretation of test results. Eight educational messages were developed by a multidisciplinary team of senior laboratory scientists and consultant haematologists based on myeloma guidelines [29] and reviewed by a Professor of General Practice to ensure they were appropriate for a GP audience (Appendix 10). The brief educational messages provide interpretative comments on test results and are added to the test reports sent to the requesting GP. These messages are activated using electronic 'action cues' which are defined as triggers or prompts for an action to be taken [136]. For example, "raised IgM with a normal electrophoresis" prompts the addition of the following interpretive message to the test results: "Patient has a slightly raised IgM. If anti-mitochondrial antibodies are negative, this may be consistent with recent infection, particularly viral. If anti-mitochondrial antibodies are positive, this may be consistent with primary biliary cirrhosis". Previously, GPs detected a "raised IgM with a normal electrophoresis" based on the provided reference ranges for abnormal levels (>2.9g/L). Now, the GP receives an interpretive comment added to the test result, which further explains the test result and possible cause or diagnosis. This information supports the GP with their

patient management plan. The eight ‘action cues’ and their corresponding educational messages can be found in Appendix 10.

7.2.5 Delivery of the intervention

The intervention strategy was introduced in October 2015. This involved sending a one-time hard copy of the guideline to all GPs practising in the Cork-Kerry region. GPs were identified using the HSE-GP list of GPs using the laboratory services at CUH. The laboratory-based educational messages were programmed into the laboratory system at CUH by the chief laboratory scientist. A three phase quality testing process (initial assessment, implementation plan and a review of effectiveness) was performed by the laboratory before the intervention was implemented using hypothetical patients. The messages were activated and embedded in electronic GP test reports each time the ‘action cue’ occurred.

7.2.6 Data collection

The count of immunoglobulin tests ordered by GPs in the Cork and Kerry region between January 2012 and July 2016 was compared before and after the introduction of the intervention. This routinely collected data was extracted from the hospital's laboratory system using Cognos Impromptu data extraction software and imported into Stata v12 for analysis.

7.2.7 ITS design

Total immunoglobulin requests were calculated at fortnightly time points. Time was rescaled so that the starting fortnightly segment is 1 (17/01/12), with time being measured backwards and forward from the date the intervention was introduced (20/10/16). This resulted in 96-time points pre- and 20-time points post-intervention.

A sufficient number of time points before and after the intervention is needed to conduct segmented regression analysis [131]. A general recommendation is for 12 data points before and 12 data points after the intervention [131], although this number is not based on estimates of power. There also needs to be a sufficient number of observations (a minimum of 100 is desirable) at each fortnight segment to achieve an acceptable level of variability of the estimate at each time point [131]. Having a greater number of time points pre-intervention (at least 48 fortnightly time-points) permits an adequate evaluation of seasonal variation and other trends in the pre-intervention data [131].

7.2.8 Statistical analysis

A segmented regression was used to examine the impact of the intervention, estimating the trend in the volume of immunoglobulin test orders before the intervention (January 2012-October 2015) and the changes in trend following the intervention (October 2015- July 2016). Segmented regression analysis of ITS data allow us to assess how much an intervention changes an outcome of interest, immediately (level change) and over time (trend change). When a separate control group is not available, analysis of the outcome of interest in the study group does not allow control for other events that may have influenced the outcome. However, the level and trend of the pre-intervention segment serve as the control for the post-intervention segment in single group time series, and still addresses important threats to internal validity and represent a methodologically acceptable design for measuring the impact of interventions. This technique that has previously been recommended for evaluating healthcare-based interventions [132, 137]. The three outcomes in the ITS analysis are the change in the count of test orders immediately after the intervention, the difference

between pre-intervention and post-intervention slopes (trend change), and the estimation of fortnightly average intervention effect after the intervention.

7.2.8.1 Regression analysis definitions

Four variables were included in the dataset. T: the time elapsed since the start of the observation period (17/01/12) expressed in fortnightly segments; X_t: a dummy variable indicating the pre-intervention period (coded 0) and post-intervention period (coded 1); TX_t: the time elapsed since the intervention and Y_t: the outcome at time *t.* The following segmented regression model was used for this analysis:

$$Y_t = \beta_0 + \beta_1 T + \beta_2 X_t + \beta_3 TX_t.$$

Where β_0 represents the baseline level at T=0, β_1 estimates the change in mean fortnightly test orders that occurs with each fortnight before the intervention (i.e. represents underlying pre-intervention trend), β_2 estimates the level change in the mean number of test orders immediately after the intervention, that is from the end of the preceding segment; and β_3 estimates the change in the trend (slope) in the mean fortnightly number of test orders after the intervention, compared to the trend before the intervention (using interaction term for time and intervention: TX_t). The sum of β_1 and β_3 is the post-intervention slope.

7.2.9 Checking for seasonality and wild data points

Many laboratory tests have a seasonal pattern due to the nature of the condition for which the test is requested. Seasonality can cause autocorrelation and overdispersion. We checked for seasonality using Fourier terms (pairs of sine and cosine functions) [135].

Long-term patterns can be modelled more smoothly by fitting Fourier terms in the Poisson model. These are pairs of sine and cosine functions of time with an underlying period reflecting the full seasonal cycle (i.e. calendar year) and are particularly suited to capturing very regular seasonal patterns. A single sine/cosine pair will model seasonal variation in the outcome as a regular wave with a single peak and trough per calendar year (the position of the peak and trough are guided by the data). We used harmonics (extra sine/cosine pairs with shorter wavelengths) which result in more flexible functions. Extreme values that did not seem to fit in the series, known as wild data points were dealt with by assessing the data plot for any outliers and follow recommended methods for handling such data [77].

7.3 Results

In total, 17,239 tests were requested in the pre-intervention period (January 2012-October 2015) and 3,627 tests in the post-intervention period (October 2016-July 2016). 568 fewer tests than expected (based on pre-intervention trend) were requested in the nine-month post-intervention period. The mean volume of requests per fortnight was 181 before the intervention and 172 after the intervention. Table 7.1 presents an overview of the patient demographics associated with test orders in the pre and post-intervention periods.

Table 7.1 Overview of serum immunoglobulin test orders pre and post intervention and characteristics of the patients' for which these tests were ordered

	Pre-intervention		Post-intervention	
	Total	**(%)**	**Total**	**(%)**
Test orders				
Total requests	17,239	(100)	3,627*	(100)
Mean count per fortnight	181		172	
Patient age category				
<30	1917	(11.1)	406	(11.2)
30-45	2630	(15.3)	569	(15.7)
45-60	4,046	(23.5)	823	(22.7)
60-70	3,613	(20.9)	752	(20.7)
>70	5,033	(29.2)	1,086	(29.9)
Patient gender				
Female	10,316	(60.0)	2,173	(59.9)
Male	6,894	(40.0)	1,454	(40.1)

*Based on the pre-intervention trend, the expected volume of tests in the post-intervention period was 4,195

7.3.1 The effect of the intervention

Table 7.2 provides details of the parameter estimates for the effects of the intervention on fortnightly GP requests for immunoglobulins. Table 7.3 contains the estimated differences in test ordering pre-and post-intervention with corresponding confidence intervals and p-values.

Table 7.2 Parameter estimates, standard errors and p-values from the full and most parsimonious segmented regression models predicting the fortnightly IGG counts before and after the intervention

Model[1]	**Coefficient**	**Std. error**	**P-value**
a) Model with level change			
Intercept β_0	5.1444	0.0155	<0.001
Baseline trend β_1	0.0015	0.0003	<0.001
Level change after intervention β_2	-0.1286	0.0241	<0.001
b) Model with trend change*			
Intercept β_0	5.1310	0.0152	<0.001
Baseline trend β_1	0.0019	0.0003	<0.001
Trend change after intervention β_3	-0.0152	0.0018	<0.001

c) Full segmented regression model[2]			
Intercept β_0	5.1353	0.0155	<0.001
Baseline trend β_1	0.0017	0.0003	<0.001
Level change after intervention β_2	0.0654	0.0362	0.07
Trend change after intervention β_3	-0.0191	0.0029	<0.001

[1] All models are adjusted for the four outliers occurring in December each year
[2] Adjusted for change in slope (trend change)
* Most parsimonious model: log-likelihood in model: 557.53

Table 7.3 Estimated change in immunoglobulin counts before and after the introduction of the guideline and education-based intervention

Model[1]	**Estimates (%)**	**95% CI**	**p-value**
a) Model with level change			
Trend	+0.15	0.10, 0.20	<0.001
Level change after intervention	-12.07	-7.82, -16.13	<0.001
b) Model with trend change*			
Trend before intervention	+0.19	0.14, 0.23	<0.001
Trend after intervention	-1.32	- 1.01, -1.65	<0.001
Absolute change in trend	-1.51	-1.16, -1.86	<0.001
c) Full segmented regression model[2]			
Level change	+6.75	-0.56, 14.60	0.07
Trend before intervention	+0.17	0.12, 0.23	<0.001
Trend after intervention	-1.87	1.35, 2.40	<0.001
Absolute change in trend	-1.70	1.18, 2.23	<0.001

[1] All models are adjusted for the four outliers occurring in December each year
[2] Adjusted for change in slope (trend change)
* Most parsimonious model

7.3.1.1 Model A: level change following the intervention

Model A (baseline trend and level change only) found an immediate drop in test ordering counts following the implementation of the guideline and education-based intervention (Figure 7.1).

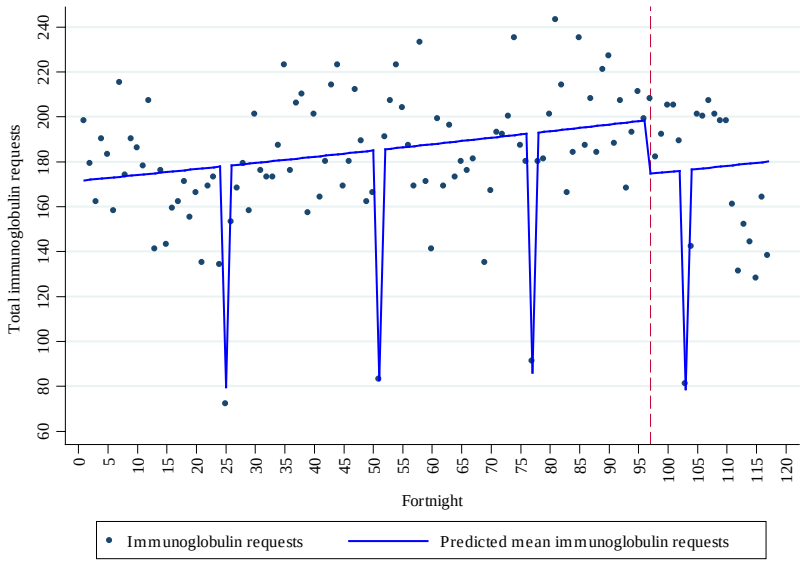


Figure 7.1 ITS model with a level change regression model (Model A).
Blue line: predicted slope based on the regression model allowing for a December effect. Red dashed line: the introduction of intervention. The time-points at fortnights 25, 52, 77 and 103 (dips in data) represent the same fortnightly time-period in December each year.

Before the introduction of the intervention, total test orders per fortnight were increasing at a rate of 0.15% (Table 7.3-A). In the first fortnight following the intervention, there was a 12.1% ($p<0.001$) drop in the count of test orders compared to the predicted trend (based on the pre-intervention time trend).

7.3.1.2 Model B: Change in trend following the intervention

In model B, the change in test ordering trend was modelled on its own (baseline trend and trend change only). There was a statistically significant reduction in the slope after the introduction of the intervention (Figure 7.2).

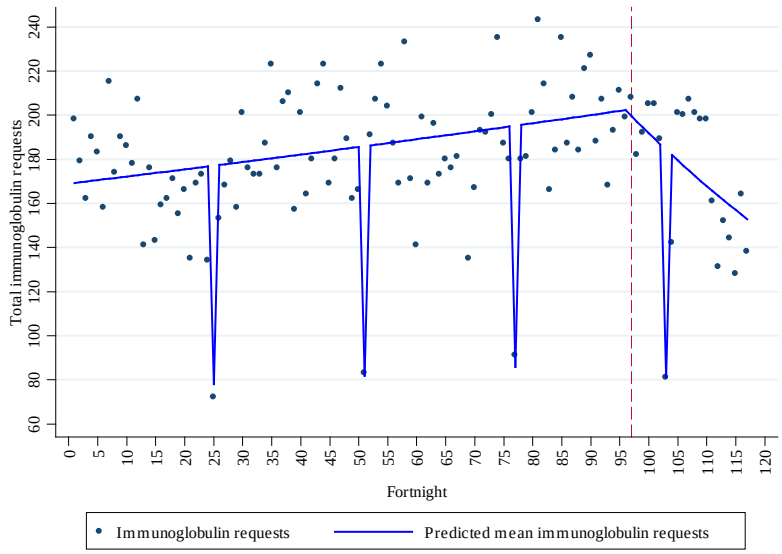


Figure 7.2 ITS model with a trend change regression model (Model B).
Blue line: predicted slope based on the regression model allowing for a December effect. Red dashed line: the introduction of intervention. The time-points at fortnights 25, 52, 77 and 103 (dips in data) represent the same fortnightly time-period in December each year.

Before the introduction of the intervention, test orders were increasing at a rate of 0.19% per fortnight ($p<0.001$). After the strategy had been implemented, test orders were falling at a rate of 1.3% per fortnight ($p<0.001$), with an absolute reduction of 1.5% in the slope pre- and post-intervention (Table 7.3-B).

7.3.1.3 Model C: The full segmented regression model

The fully adjusted segmented regression model (Figure 7.3) estimated both the level change and trend changes associated with the intervention, controlling for baseline level and trend.

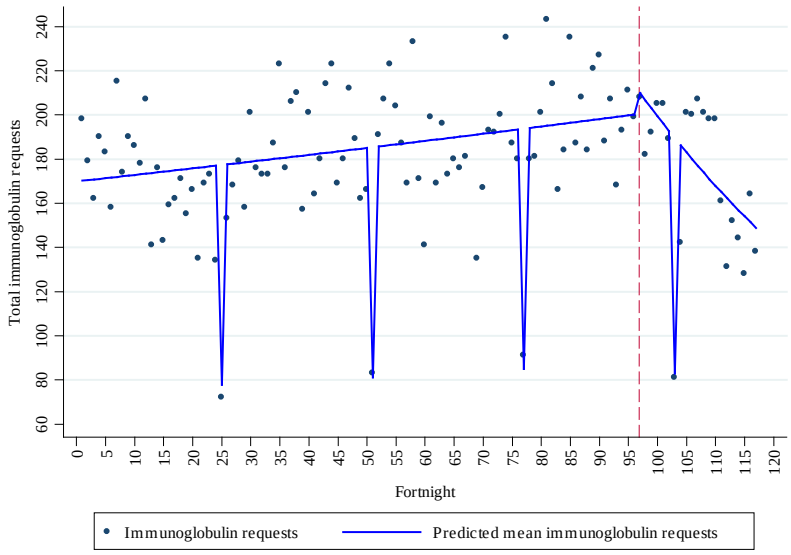


Figure 7.3 ITS model with a level change and trend change regression model (Model C).
Blue line: predicted slope based on the regression model allowing for a December effect. Red dashed line: the introduction of intervention. The time-points at fortnights 25, 52, 77 and 103 (dips in data) represent the same fortnightly time-period in December each year.

This model found that before the implementation of the combined guideline and educational messages strategy, test orders were increasing at a rate of 0.17% per fortnight ($p<0.001$). Post-intervention, test orders were falling at a rate of 1.9% per fortnight ($p<0.001$), with an absolute reduction of 1.7% in the slope pre- and post-intervention (Table 7.3-C). There was no statistically significant drop in the level of test orders immediately after the intervention ($p=0.07$).

7.3.1.4 The most parsimonious model

After stepwise elimination of non-significant terms in the fully adjusted model, the most parsimonious model was model B which contained the intercept, baseline trend and the significant trend change in the volume of test orders (Tables 7.2-B and 7.3-B).

7.3.2 Adjusting for seasonality and outliers

Figure 7.4 illustrates the effect of the guideline combined with educational messages strategy after adjusting for seasonality using a Fourier term. The association was largely unaffected by seasonality. Five outliers were evident in the data. At fortnight 68 (August 2015) an IT laboratory system failure was responsible for marked drop in requests. This time-point was dropped from the segmented regression model. Fortnights 25, 52, 77 and 103 all mark the same two-week period in December each year (2012-2016) with consistently low test orders. These time-points were controlled for in each of the segmented regression models (Table 7.2).

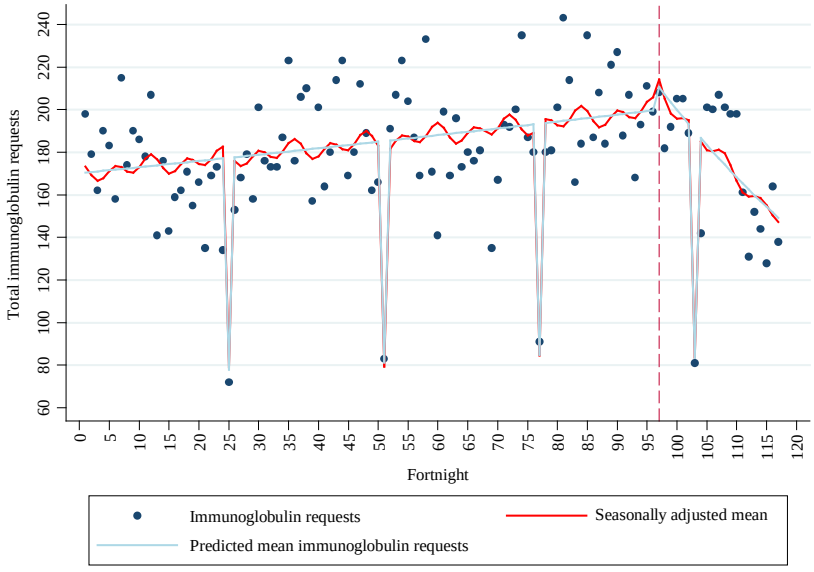


Figure 7.4 ITS model with a level change and trend change regression model (Model C adjusted for seasonality).
Solid red line: predicted trend based on seasonally adjusted regression model. Solid red line: predicted trend based on seasonally adjusted regression model allowing for a December effect. Faded blue line: de-seasonalised trend. Red dashed line: The introduction of intervention. The time-points at fortnights 25, 52, 77 and 103 (dips in data) represent the same fortnightly time-period in December each year.

7.4 Discussion

7.4.1 Summary of findings

To our knowledge, this is the first study to systematically design an intervention using a combination of theoretical approaches to improve test ordering in primary care. A nine-month evaluation of the effectiveness of this intervention found a statistically significant, sustained 1.5% fortnight-to-fortnight reduction in the volume of test orders for serum immunoglobulins.

7.4.3 Interpretation of the findings

This study set out to optimise laboratory ordering, using serum immunoglobulin tests as a case study. At the outset, there was a possibility of test ordering increasing, decreasing or remaining the same. We observed a reduction in test orders post-intervention. Therefore, a reasonable interpretation of our findings is that before the intervention, the level of test overuse was larger than the level of underuse, and our intervention, which deals with both problems, has led to a net reduction in test ordering. A possible explanation for this is the detailed interpretive comments provided on the test results. Prior, to the intervention, GPs expressed the need for specialist interpretation of test results, ideally accompanying the test result, as they do not always know or may be unable to recall all the possible reasons for particular findings [114]. Most abnormal results consist of benign elevations of immunoglobulins which do not have cancer (or pre-cancer correlates of the para-proteins). Thus, these messages may have shaped GP ordering behaviour by constantly reminding them of the benign nature of most abnormal serum immunoglobulin results. GPs also mentioned ‘fear of litigation’ and ’fear of missing a myeloma’ as other drivers of test ordering [114]. Providing clear guidelines and interpretive comments

on results may have increased confidence in GPs to request fewer tests. On the other hand, it is also probable that in a smaller group of patients, tests are now being ordered where they previously would not have been. For example, a small number of GPs expressed concern that they were unaware of certain clinical scenarios where immunoglobulin evaluation could be useful. The educational requesting algorithm should have increased awareness of these clinical scenarios [114]. However, it is important to note that regression to the mean is present. Hence, the most extreme requesters will always have the largest reduction regardless of whether you intervene or not. Exploring the phenomenon of regression to the mean and individual GP impact of the intervention is difficult, as this study was designed to look at the impact on ordering behaviours in all GPs as a group rather than on individuals.

This research provides an important insight into the behavioural factors influencing laboratory testing among GPs. The incorporation of behavioural theory, specifically the COM-B, TDF and BCT taxonomy, has supported the identification of factors such as knowledge and the social and environmental context, which are key for understanding testing behaviours. Prior to the intervention, a local audit on the clinical value of GP serum immunoglobulin test orders suggested probable overuse of the test in primary care. We have observed a reduction in test ordering in line with an expected improvement in appropriateness following the interventions. It is also reassuring that the demographic profile of patients before and after the intervention is very similar which suggests the test not being denied to any particular patient group to whom it was previously being provided. However, we still cannot say definitively that appropriateness has been improved. The most extreme requesters will always have the largest reduction regardless of whether you intervene or not. Further research, using

individual patient level data, is required – particularly to exclude the possibility that the intervention has led to tests being denied to patients who need them.

7.4.4 Strengths and limitations

A strength of this study was the systematic use of both qualitative and quantitative research methods, with explicit use of theory to create an intervention tailored to target barriers to changing clinicians behaviour [32]. A multidisciplinary team including biochemistry, haematology and primary care representatives, were involved in the development of the intervention. Finally, all immunoglobulin results requested by GPs in the two studied counties were analysed.

Segmented regression models have some limitations. The unit of analysis in the model was the fortnightly count of immunoglobulin tests, rather than each GP's individual test ordering counts per fortnight. Contrary to cross-sectional analysis methods, such as logistic regression, segmented regression analysis of time series data does not allow control for the patient or GP-level covariates. These would only confound the time series results, however, if they predicted the outcome and changed in relationship to the time of the intervention – this is unlikely to be the case. Finally, although the interpretive messages devised in this study were based on best practice guidelines [29], we have not measured the potential impact on the diagnosis of blood dyscrasias.

7.4.5 Conclusions and policy implications

Our findings suggest that GP test ordering can be improved by an intervention based on a guideline with educational messages. The use of a laboratory system to deliver interpretive comments on test results is a transferable strategy for all laboratories in Ireland, and internationally also as hospital pathology laboratories generally have

customisable systems with the capacity to readily alter the end user report. It is also likely that the behaviour change strategy used in this research is applicable to other specialised tests.

In total, 568 fewer tests than expected (based on pre-intervention trend) were requested in the nine-month post-intervention period. A cost comparison for reagent suppliers for the same time-period pre and post-intervention identified a reduction of €1,000 per month. We estimate that the reagent supply costs associated with serum immunoglobulin activity at CUH will decrease by €12,000 annually. While modest the financial benefits to the public health service in Ireland will be much larger if our intervention is applied to other settings and is found to work for other tests. This study was designed to target the key issues around GP serum immunoglobulin test ordering behaviour. At a policy level, the findings point to the possible benefits of laboratories becoming more actively engaged in GP education about test ordering. Any such engagement should seek to understand drivers of the GP behaviour first, and interventions should be jointly developed with GPs on the basis of sound behaviour change theory.

7.5 Acknowledgements

We would like to thank the laboratory staff at Cork University Hospital, in particular, Dr John O'Mullane, Ms Katherine Hooley, and Ms Grace Creedon (UHK). We would also like to thank Mr Aidan Kelleher for facilitating the data extraction and Mr Brendan O'Reilly for providing Cognos Impromptu software training for SLC, and Ms Mary Ring for providing comparative data from other tests.

8. OVERALL DISCUSSION

8.1 Introduction

This thesis has studied the design, implementation and evaluation of an intervention to optimise serum immunoglobulin test use in primary care. This chapter summarises the main findings of each of the papers included in the thesis. The main strengths and limitations are outlined. Some key health services research and policy implications are discussed. Areas for future research are proposed and a brief conclusion to the overall thesis is provided.

8.2 Summary of main findings

8.2.1 Effectiveness of previous interventions

The systematic review synthesised data on the effectiveness of previous interventions targeting laboratory testing behaviours among primary care physicians (Chapter 3). The review found that different interventions were of variable efficacy at changing primary care physician requesting patterns. Some interventions had no measurable effect. Even the most effective strategies (multi-faceted interventions and those involving educational strategies) show a modest effect. The number of relevant studies in this area is small and the validity and generalisability of some of the findings, questionable. Therefore, the review concluded that further high-quality research was needed in this area. In particular, there was a paucity of theory-based interventions in relation to doctors' test ordering behaviour. As a result, the determinants of success and failure remain unclear, and interventions may not be applicable to specific tests. This research systematically examined the contextual and organisational factors likely to influence the behaviour change and implementation.

8.2.2 Barriers and enablers for behaviour change

Building on the findings of the systematic review (Chapter 3), an intervention was designed using a combination of theoretical models (Chapter 4). This included identifying and addressing the barriers and enablers for changing immunoglobulin test ordering behaviour. Seven of domains from the TDF were identified as key barriers. These domains and their corresponding COM-B constructs aligned with seven BCTs, and four intervention functions were selected using the BCT framework: education, persuasion, enablement and environmental restructure. The incorporation of behavioural theory, specifically the COM-B, TDF and BCT taxonomy, has supported the identification of factors such as knowledge and the social and environmental context, which are key for understanding testing behaviours. Selected BCTs and intervention functions provided the groundwork for developing a theory-based intervention to improve appropriate immunoglobulin testing in primary care.

8.2.3 Determinants of higher test ordering

Using multilevel analysis of routine cross-sectional data for one year, the determinants (GP and practice characteristics) of higher test ordering for immunoglobulin tests were identified (Chapter 5). Adjusting for GP patient list size and composition, female gender and having fewer than ten years of clinical experience were found to be associated with higher test ordering patterns. This research suggests that education programmes about the nature and uses of serum immunoglobulins, targeted at female GPs and those with less experience, may be required. However, further qualitative research is required to explore why female GPs and less experienced GPs order greater volumes of serum immunoglobulins.

8.2.4 Implementation and evaluation of intervention

The combined guideline and educational messages intervention was designed based on the findings of the systematic review (Chapter 3), theoretical design paper (Chapter 4) along with considerations for the determinants of higher test ordering (Chapter 5). The four intervention functions identified in the theoretical study (Chapter 4) were used to develop the strategy material. The intervention provides guidelines on when to request the test (education/enablement). It also clearly communicates situations where testing is beneficial for patient care (education) and how to manage patients with abnormal test results (enablement/persuasion). Finally, it provides details on how to interpret results (education/enablement) by attaching comments to test reports (environmental restructuring). A nine-month evaluation of the effectiveness of this intervention found a statistically significant 1.5% fortnight-to-fortnight reduction in the test ordering trend for serum immunoglobulins (Chapter 6).

8.3 Strengths and limitations of thesis

This section provides a synopsis of the overall strengths and limitations of this thesis. The strengths and limitations of the four individual papers have been acknowledged and addressed in the previous chapters.

Given the increased pressures on the Irish health service, improving inefficiencies and reducing waste, while maintaining the quality of care is at the forefront of healthcare planning. Promoting optimal laboratory service utilisation could play a key role in reducing health expenditure, in particular by preventing the unnecessary use of costly downstream services that often arise as a result of testing. This study is the first to explore test use among GPs in Ireland. This work has been recognised as important by conference organisers and peers. The author has had many opportunities to present at

scientific conferences both nationally or internationally (listed at the beginning of this thesis) To date, two of the included papers have been published in peer-reviewed scientific journals (Appendix 13) a third is currently under review and the fourth has been submitted for review.

A key strength of this thesis is the clinical importance of studying serum immunoglobulin test ordering in primary care. In 2013, GPs in the study region requested 5,990 tests. Clinical audit of these orders identified 1,052 patients with a detectable paraprotein. 2.4% of these (25/1,052) had an abnormal paraprotein level which warranted follow-up or referral to specialist haematology services. Nine of these patients were existing myeloma patients attending haematology services, that were being monitored in primary care.

A further strength of this thesis lies in the four years of accurate and complete routine laboratory data used to explore test ordering patterns and to evaluate the impact of the intervention on test orders. The outcome of interest for both quantitative papers was an objective measure (volume of test orders). Data was available for 100% of the target population and the required demographic and practice level data were merged using unique identifiers, ensuring no room for error.

This thesis also has some limitations. As the data used in this thesis is cross-sectional, causal inference must be tentative. There are well-established criteria for causal inference which are extensively used in the interpretation of findings in epidemiological research. Another limitation of this research is the follow-up period after the intervention. The nine-month follow-up following the intervention is short, and although sufficient to demonstrate a positive result, longer follow-up is desirable.

In particular, given the low-volume nature of test ordering for serum immunoglobulins and the use of reinforcing educational messages, the effect of the intervention may increase with time as GPs become more familiar with the guidance of the interpretative comments.

The results of the thesis may be generalisable to other laboratory test ordering, but would have to be applied with caution, recognising the immunoglobulin specific issues that this work has identified.

8.4 Health services research and policy implications

This thesis has addressed a timely and relevant health services priority in Ireland – optimising the use of laboratory services. To our knowledge, this research is the first of its kind in Ireland to evaluate primary care test ordering practices, using serum immunoglobulins as an example. In 2008 the Royal College of Physicians of Ireland (RCPI) Faculty of Pathology undertook the development and implementation of a National Quality Assurance Programme aimed at minimising diagnostic error and ensuring timely, accurate and complete pathology diagnosis and reports. The National Quality Assurance Intelligence System (NQAIS) is now being used to centrally monitor the practices involved in analysing and interpreting patient samples. The programme identifies variations from best practice in laboratories and produces an overall national report. Ireland became the first country in the world to publicly report national metrics on the quality of its pathology system. This system for monitoring the quality of testing (pathology reporting) at hospital laboratories has been described as a breakthrough in managing the care of patients with breast, bowel and other cancers and diseases. However, this quality assurance programme does not assess the utility

of the laboratory tests ordered. International literature suggests that as much as 70% of test orders may not be necessary or benefit patient care [3].

The first step to ensuring that expensive and specialised laboratory blood tests are effectively used is to delineate ordering practice. Any attempts to improve patient outcomes by optimising laboratory testing will involve close collaboration between the laboratory and its GP users. Funded frameworks to promote research like that which we report, would be welcome and most likely cost effective. Evaluating the clinical impact of a test which is ordered and leads to an unnecessary referral to hospital services (or the effect of a test which was not ordered and leads to a delay in diagnosis) is difficult and requires intersectoral health services input and excellent clinical IT systems. The latter are currently lacking, while laboratory IT systems are relatively advanced and well embedded in accredited quality systems. This makes the analysis of laboratory activity as a gateway to improving quality for patients in general practice and the hospital an attractive place for research to commence.

The recent increased emphasis on financing health services research within the funding bodies in Ireland is welcome, and this work and that of others may mark an increased era of policy focuses on laboratory medicine in Ireland.

8.5 Future research recommendations

This thesis has identified some of the key drivers for higher immunoglobulin test ordering (Chapter 5) which include female gender and fewer years of clinical experience. Future studies are needed to explore why test ordering is higher among these specific GP groups. This research also identified a reduction in test order

volumes following the implementation of a behaviour change intervention tailored to target key barriers to change. Further investigation of the appropriateness of GPs' laboratory ordering patterns is required to investigate the impact of reduced test ordering following the implementation of our intervention. A simple measure of a number of tests ordered pre- and post-intervention only allows us to speculate on the impact of the intervention, and not the appropriateness of test orders. It is important that the clinical impact of reduced test ordering is studied to ensure patient care is not negatively impacted. This aspect of research is more difficult because of the less advanced clinical IT systems in the HSE. We also propose that other laboratory tests may benefit from analysis and intervention, including haematinic testing, thrombophilia testing and endocrine requests.

8.6 Conclusion

Considerable growth in laboratory workload generated by GP test orders has led to concerns about the appropriateness of this ordering, in particular of specialist tests such as immunoglobulins. This thesis explored the GP and practice characteristics associated with higher test ordering for immunoglobulins, along with the barriers and facilitators that need to be considered when designing a strategy to optimise test use in primary care. GP factors contributing to higher immunoglobulin test ordering include female gender and fewer years of clinical experience. Lack of clear guidelines and knowledge on how to interpret the test results posed greatest problems for GPs. Following the introduction of a guideline and education based strategy targeting these two key issues, test orders for serum immunoglobulins dropped significantly. This suggests that tests were being overused prior to the intervention. This was further supported by an audit (using one year of data) of the clinical impact of GP serum

immunoglobulin test orders on patients prior to the intervention, which indicated inefficiencies in test use. Once adequate time has elapsed to allow patient follow-up, there is a need to re-assess the clinical impact of test orders requested since the intervention was introduced.

9. REFERENCES

1. Grol R, Grimshaw J: **From best evidence to best practice: effective implementation of change in patients' care**. *The lancet* 2003, **362**(9391):1225-1230.

2. Horvath AR: **From Evidence to Best Practice in Laboratory Medicine**. *The Clinical Biochemist Reviews* 2013, **34**(2):47-60.

3. Fryer AA, Smellie WS: **Managing demand for laboratory tests: a laboratory toolkit**. *J Clin Pathol* 2013, **66**(1):62-72.

4. Moynihan R, Doust J, Henry D: **Preventing overdiagnosis: how to stop harming the healthy**. *Bmj* 2012(e3502).

5. McGregor MJ, Martin D: **Testing 1, 2, 3: Is overtesting undermining patient and system health?** *Canadian Family Physician* 2012, **58**(11):1191-1193.

6. **Effective Practice and Organisation of Care Review Group, Cochrane Data Collection Checklist** [https://epoc.cochrane.org/sites/epoc.cochrane.org/files/uploads/datacollectionchecklist.pdf]

7. Smith S: **Equity in Irish health care financing: measurement issues**. *Health Economics, Policy and Law* 2010, **5**(02):149-169.

8. Mc Govern E, Morris R: **Medical Workforce Planning: Future Demand for General Practitioners 2015-2025.** In. Dublin: Health Service Executive; 2015.

9. Thomson S, Foubister T, Mossialos E: **Financing health care in the European Union: challenges and policy responses**: World Health Organization; 2009.

10. Rosemann T, Wensing M, Rueter G, Szecsenyi J: **Referrals from general practice to consultants in Germany: If the GP is the initiator, patients' experiences are more positive**. *BMC health services research* 2006, **6**(1):5.

11. Busby J, Schroeder K, Woltersdorf W, Sterne JAC, Ben-Shlomo Y, Hay A, Hollingworth W: **Temporal growth and geographic variation in the use of laboratory tests by NHS general practices: using routine data to identify research priorities**. *The British Journal of General Practice* 2013, **63**(609):e256-e266.

12. Panteghini M: **The Future of Laboratory Medicine: Understanding the New Pressures**. *The Clinical Biochemist Reviews* 2004, **25**(4):207-215.

13. Gopal Rao G, Crook M, Tillyer ML: **Pathology tests: is the time for demand management ripe at last?** *Journal of Clinical Pathology* 2003, **56**(4):243-248.

14. Zhi M, Ding EL, Theisen-Toupal J, Whelan J, Arnaout R: **The landscape of inappropriate laboratory testing: a 15-year meta-analysis**. *PLoS One* 2013, **8**(11).

15. Van Walraven C, Naylor CD: **Do we know what inappropriate laboratory utilization is?: A systematic review of laboratory clinical audits**. *JAMA : the journal of the American Medical Association* 1998, **280**(6):550-558.

16. Wong ET, Lincoln TL: **Ready! fire!... aim!: An inquiry into laboratory test ordering**. *JAMA : the journal of the American Medical Association* 1983, **250**(18):2510-2513.

17. Smellie W: **Demand management and test request rationalization**. *Annals of clinical biochemistry* 2012, **49**(4):323-336.

18. Forsman RW: **Why is the laboratory an afterthought for managed care organizations?** *Clinical Chemistry* 1996, **42**(5):813-816.

19. Teamwork Management Services: **Implementing a new system of service delivery for Laboratory Medicine Services**. In.: Health Service Executive (HSE); 2007.

20. Pathology Cork Univeristy Hospital: **Management Review**. 2013.

21. Houben PHH, Winkens RAG, van der Weijden T, Vossen RCRM, Naus AJM, Grol RPTM: **Reasons for ordering laboratory tests and relationship with frequency of abnormal results**. *Scandinavian journal of primary health care* 2010, **28**(1):18-23.

22. Smellie WSA, Wilson D, McNulty CAM, Galloway MJ, Spickett GA, Finnigan DI, Bareford DA, Greig MA, Richards J: **Best practice in primary care pathology: review 1**. *Journal of Clinical Pathology* 2005, **58**(10):1016-1024.

23. Dispenzieri A, Gertz MA, Therneau TM, Kyle RA: **Retrospective cohort study of 148 patients with polyclonal gammopathy**. *Mayo Clin Proc* 2001, **76**(5):476-487.

24. Sah S, Elias P, Ariely D: **Investigation momentum: the relentless pursuit to resolve uncertainty**. *JAMA internal medicine* 2013, **173**(10):932-933.

25. Baldessarini RJ, Finklestein S, Arana GW: **The predictive power of diagnostic tests and the effect of prevalence of illness**. *Archives of General Psychiatry* 1983, **40**(5):569-573.

26. Gkotzamanidou M, Terpos E: **The role of immunoglobulins in monoclonal gammopathies.** *Biochemistry, Producion and Role in Immunity*:1.

27. Korde N, Kristinsson SY, Landgren O: **Monoclonal gammopathy of undetermined significance (MGUS) and smoldering multiple myeloma (SMM): novel biological insights and development of early treatment strategies**. *Blood* 2011:blood-2011-2001-270140.

28. Bird C: **Laboratory tests: guidance for general practitioners**. *BIOMEDICAL SCIENTIST* 2008, **52**(1):42.

29. Bird J, Behrens J, Westin J, Turesson I, Drayson M, Beetham R, D'Sa S, Soutar R, Waage A, Gulbrandsen N *et al*: **UK Myeloma Forum (UKMF) and Nordic Myeloma Study Group (NMSG): guidelines for the investigation of newly detected M-proteins and the management of monoclonal gammopathy of undetermined significance (MGUS)**. *Br J Haematol* 2009, **147**(1):22-42.

30. Wilson JMG, Jungner G: **Principles and practice of screening for disease**. *World Health Organization Public Health Paper* 1968(34).

31. Kumar SK, Mikhael JR, Buadi FK, Dingli D, Dispenzieri A, Fonseca R, Gertz MA, Greipp PR, Hayman SR, Kyle RA: **Management of newly diagnosed symptomatic multiple myeloma: updated Mayo Stratification of Myeloma and Risk-Adapted Therapy (mSMART) consensus guidelines**. In: *Mayo Clinic Proceedings: 2009*: Elsevier; 2009: 1095-1110.

32. French SD, Green SE, O'Connor DA, McKenzie JE, Francis JJ, Michie S, Buchbinder R, Schattner P, Spike N, Grimshaw JM: **Developing theory-informed behaviour change interventions to implement evidence into practice: a systematic approach using the Theoretical Domains Framework**. *Implement Sci* 2012, **7**(38):1748-5908.

33. Hickner J, Thompson PJ, Wilkinson T, Epner P, Shaheen M, Pollock AM, Lee J, Duke CC, Jackson BR, Taylor JR: **Primary care physicians' challenges in ordering clinical laboratory tests and interpreting results**. *The Journal of the American Board of Family Medicine* 2014, **27**(2):268-274.

34. Freedman DB: **Towards better test utilization–strategies to improve physician ordering and their impact on patient outcomes**. *The Journal of the International Federation of Clinical Chemistry and Laboratory Medicine*:15.

35. Beastall GH: **The modernisation of pathology and laboratory medicine in the UK: networking into the future**. *The Clinical Biochemist Reviews* 2008, **29**(1):3.

36. van Bokhoven MA, Pleunis-van Empel MC, Koch H, Grol RP, Dinant G-J, van der Weijden T: **Why do patients want to have their blood tested? A qualitative study of patient expectations in general practice**. *BMC family practice* 2006, **7**(1):75.

37. Colling CA, Volk LA, Jenter C, Dembowitz M, Bates DW, Simon SR: **Using a patient portal to communicate laboratory test results in community practices**. *Journal of General Internal Medicine* 2012, **27**:S543.

38. Hickner J, Graham D, Elder N, Brandt E, Emsermann C, Dovey S, Phillips R: **Testing process errors and their harms and consequences reported from family medicine practices: a study of the American Academy of Family Physicians National Research Network**. *Quality and Safety in Health Care* 2008, **17**(3):194-200.

39. Wong ET: **Cost-effective use of laboratory tests: A joint responsibility of clinicians and laboratorians**. *Clinics in Laboratory Medicine* 1985, **5**(4):665-672.

40. Solomon DH, Hashimoto H, Daltroy L, Liang MH: **Techniques to improve physicians' use of diagnostic tests: a new conceptual framework**. *JAMA : the journal of the American Medical Association* 1998, **280**(23):2020-2027.

41. Janssens PM: **Managing the demand for laboratory testing: options and opportunities**. *Clinica chimica acta* 2010, **411**(21):1596-1602.

42. Craig P, Dieppe P, Macintyre S, Michie S, Nazareth I, Petticrew M: **Developing and evaluating complex interventions: the new Medical Research Council guidance**. *Bmj* 2008, **29**(337).

43. Colquhoun HL, Brehaut JC, Sales A, Ivers N, Grimshaw J, Michie S, Carroll K, Chalifoux M, Eva KW: **A systematic review of the use of theory in randomized controlled trials of audit and feedback**. *Implement Sci* 2013, **8**(1):66.

44. Michie S, Johnston M, Francis J, Hardeman W, Eccles M: **From theory to intervention: mapping theoretically derived behavioural determinants to behaviour change techniques**. *Applied psychology* 2008, **57**(4):660-680.

45. Michie S, van Stralen MM, West R: **The behaviour change wheel: a new method for characterising and designing behaviour change interventions**. *Implementation Science* 2011, **6**(1):42.

46. Horn DM, Koplan KE, Senese MD, Orav EJ, Sequist TD: **The Impact of Cost Displays on Primary Care Physician Laboratory Test Ordering**. *Journal of General Internal Medicine* 2013:1-7.

47. Larsson A, Biom S, Wernroth ML, Hulten G, Tryding N: **Effects of an education programme to change clinical laboratory testing habits in primary care**. *Scandinavian journal of primary health care* 1999, **17**(4):238-243.

48. Thomas RE, Croal BL, Ramsay C, Eccles M, Grimshaw J: **Effect of enhanced feedback and brief educational reminder messages on**

laboratory test requesting in primary care: a cluster randomised trial. *Lancet* 2006, **367**(9527):1990-1996.

49. Verstappen WH, van der Weijden T, Sijbrandij J, Smeele I, Hermsen J, Grimshaw J, Grol RP: **Effect of a practice-based strategy on test ordering performance of primary care physicians: a randomized trial**. *JAMA : the journal of the American Medical Association* 2003, **289**(18):2407-2412.

50. van Wijk MA, van der Lei J, Mosseveld M, Bohnen AM, van Bemmel JH: **Assessment of decision support for blood test ordering in primary care. a randomized trial**. *Annals of internal medicine* 2001, **134**(4):274-281.

51. Baker R, Falconer Smith J, Lambert PC: **Randomised controlled trial of the effectiveness of feedback in improving test ordering in general practice**. *Scandinavian journal of primary health care* 2003, **21**(4):219-223.

52. Tomlin A, Dovey S, Gauld R, Tilyard M: **Better use of primary care laboratory services following interventions to 'market' clinical guidelines in New Zealand: a controlled before-and-after study**. *BMJ quality & safety* 2011, **20**(3):282-290.

53. Baricchi R, Zini M, Nibali MG, Vezzosi W, Insegnante V, Manfuso C, Polese A, Costoli V, Spelti A, Formisano D *et al*: **Using pathology-specific laboratory profiles in clinical pathology to reduce inappropriate test requesting: two completed audit cycles**. *BMC Health Serv Res* 2012, **12**:187.

54. Kahan NR, Waitman DA, Vardy DA: **Curtailing laboratory test ordering in a managed care setting through redesign of a computerized order form**. *The American journal of managed care* 2009, **15**(3):173-176.

55. Shalev V, Chodick G, Heymann AD: **Format change of a laboratory test order form affects physician behavior**. *International journal of medical informatics* 2009, **78**(10):639-644.

56. Zaat JO, van Eijk JT, Bonte HA: **Laboratory test form design influences test ordering by general practitioners in The Netherlands**. *Medical care* 1992, **30**(3):189-198.

57. Butler CC, Simpson SA, Dunstan F, Rollnick S, Cohen D, Gillespie D, Evans MR, Alam MF, Bekkers M-J, Evans J: **Effectiveness of multifaceted educational programme to reduce antibiotic dispensing in primary care: practice based randomised controlled trial**. *Bmj* 2012, **344**:d8173.

58. Eccles M, Steen N, Grimshaw J, Thomas L, McNamee P, Soutter J, Wilsdon J, Matowe L, Needham G, Gilbert F *et al*: **Effect of audit and feedback, and reminder messages on primary-care radiology referrals: a randomised trial**. *The Lancet* 2001, **357**(9266):1406-1409.

59. Mindemark M, Larsson A: **Long-term effects of an education programme on the optimal use of clinical chemistry testing in primary health care**. *Scandinavian journal of clinical and laboratory investigation* 2009, **69**(4):481-486.

60. Grimshaw JM, Thomas RE, MacLennan G, Fraser C, Ramsay CR, Vale L, Whitty P, Eccles MP, Matowe L, Shirran L *et al*: **Effectiveness and efficiency of guideline dissemination and implementation strategies**. *Health Technol Assess* 2004, **8**(6):1-72.

61. Verstappen WH, van Merode F, Grimshaw J, Dubois WI, Grol RP, van der Weijden T: **Comparing cost effects of two quality strategies to improve test ordering in primary care: a randomized trial**. *Int J Qual Health Care* 2004, **16**(5):391-398.

62. Winkens R, Pop P, Bugter-Maessen A, Grol R, Kester A, Beusmans G, Knottnerus J: **Randomised controlled trial of routine individual feedback to improve rationality and reduce numbers of test requests**. *The Lancet* 1995, **345**(8948):498-502.

63. Stafford RS: **Feedback intervention to reduce routine electrocardiogram use in primary care**. *Am Heart J* 2003, **145**(6):979-985.

64. O'Brien MA, Rogers S, Jamtvedt G, Oxman AD, Odgaard-Jensen J, Kristoffersen DT, Forsetlund L, Bainbridge D, Freemantle N, Davis DA *et al*: **Educational outreach visits: effects on professional practice and health care outcomes**. *Cochrane Database Syst Rev* 2007, **17**(4).

65. Forsetlund L, Bjorndal A, Rashidian A, Jamtvedt G, O'Brien MA, Wolf F, Davis D, Odgaard-Jensen J, Oxman AD: **Continuing education meetings and workshops: effects on professional practice and health care outcomes**. *Cochrane Database Syst Rev* 2009(2):CD003030.

66. Ivers N, Jamtvedt G, Flottorp S, Young JM, Odgaard-Jensen J, French SD, O'Brien MA, Johansen M, Grimshaw J, Oxman AD: **Audit and feedback: effects on professional practice and healthcare outcomes**. *Cochrane Database Syst Rev* 2012, **6**.

67. Ivers NM, Grimshaw JM, Jamtvedt G, Flottorp S, O'Brien MA, French SD, Young J, Odgaard-Jensen J: **Growing Literature, Stagnant Science? Systematic Review, Meta-Regression and Cumulative Analysis of Audit and Feedback Interventions in Health Care**. *J Gen Intern Med* 2014.

68. van Bokhoven MA, Koch H, Dinant GJ, Bindels PJ, Grol RP, van der Weijden T: **Exploring the black box of change in improving test-ordering routines**. *Fam Pract* 2008, **25**(3):139-145.

69. Feldman LS, Shihab HM, Thiemann D, Yeh HC, Ardolino M, Mandell S, Brotman DJ: **Impact of providing fee data on laboratory test ordering: a controlled clinical trial**. *JAMA internal medicine* 2013, **173**(10):903-908.

70. Bates DW, Kuperman GJ, Jha A, Teich JM, Orav EJ, Ma'luf N, Onderdonk A, Pugatch R, Wybenga D, Winkelman J *et al*: **Does the computerized display of charges affect inpatient ancillary test utilization?** *Archives of internal medicine* 1997, **157**(21):2501-2508.

71. Squires J, Sullivan K, Eccles M, Worswick J, Grimshaw J: **Are multifaceted interventions more effective than single-component interventions in changing health-care professionals behaviours? An overview of systematic reviews**. *Implementation Science* 2014, **9**(1):152.

72. Grimshaw J, Thomas R, MacLennan G, Fraser C, Ramsay C, Vale L, Whitty P, Eccles M, Matowe L, Shirran L *et al*: **Effectiveness and efficiency of guideline dissemination and implementation strategies**. *Health Technol Assess* 2004, **8**:1 - 72.

73. Solomon D, Hashimoto H, Daltroy L, Liang M: **Techniques to improve physicians use of diagnostic tests: a new conceptual framework**. *JAMA : the journal of the American Medical Association* 1998, **280**:2020 - 2027.

74. Zaat JO, van Eijk JT: **General practitioners' uncertainty, risk preference, and use of laboratory tests**. *Medical care* 1992, **30**(9):846-854.

75. van der Weijden T, van Bokhoven MA, Dinant GJ, van Hasselt CM, Grol RP: **Understanding laboratory testing in diagnostic uncertainty: a qualitative study in general practice**. *The British journal of general practice : the journal of the Royal College of General Practitioners* 2002, **52**(485):974-980.

76. Winkens RA, Grol RP, Beusmans GH, Kester AD, Knottnerus JA, Pop P: **Does a reduction in general practitioners' use of diagnostic tests lead to more hospital referrals?** *The British Journal of General Practice* 1995, **45**(395):289-292.

77. Baricchi R, Zini M, Nibali MG, Vezzosi W, Insegnante V, Manfuso C, Polese A, Costoli V, Spelti A, Formisano D *et al*: **Using pathology-specific laboratory profiles in clinical pathology to reduce inappropriate test requesting: two completed audit cycles**. *BMC Health Serv Res* 2012, **12**(187):1472-6963.

78. Tomlin A, Dovey S, Gauld R, Tilyard M: **Better use of primary care laboratory services following interventions to 'market' clinical guidelines in New Zealand: A controlled before-and-after study**. *BMJ Quality and Safety* 2011, **20**(3):282-290.

79. Wahner-Roedler DL, Chaliki SS, Bauer BA, Bundrick JB, Bergstrom LR, Lee MC, Cha SS, Elkin PL: **Who makes the diagnosis? The role of clinical skills and diagnostic test results**. *Journal of evaluation in clinical practice* 2007, **13**(3):321-325.

80. Hickner JM, Fernald DH, Harris DM, Poon EG, Elder NC, Mold JW: **Issues and initiatives in the testing process in primary care physician offices**. *Joint Commission Journal on Quality and Patient Safety* 2005, **31**(2):81-89.

81. Miyakis S, Karamanof G, Liontos M, Mountokalakis TD: **Factors contributing to inappropriate ordering of tests in an academic medical department and the effect of an educational feedback strategy**. *Postgraduate medical journal* 2006, **82**(974):823-829.

82. **Report of the second phase of the review of NHS pathology services in England**. In: *London: National Health Services.* Edited by Carter L; 2008.

83. Zhi M, Ding EL, Theisen-Toupal J, Whelan J, Arnaout R: **The landscape of inappropriate laboratory testing: a 15-year meta-analysis**. *PLoS One* 2013, **8**(11):e78962.

84. Mindemark M, Wernroth L, Larsson A: **Costly regional variations in primary health care test utilization in Sweden**. *Scandinavian journal of clinical and laboratory investigation* 2010, **70**(3):164-170.

85. Song Y, Skinner J, Bynum J, Sutherland J, Wennberg JE, Fisher ES: **Regional variations in diagnostic practices**. *N Engl J Med* 2010, **363**(1):45-53.

86. Verstappen WH, ter Riet G, Dubois WI, Winkens R, Grol RP, van der Weijden T: **Variation in test ordering behaviour of GPs: professional or context-related factors?** *Fam Pract* 2004, **21**(4):387-395.

87. Carter L: **Report of the second phase of the review of NHS pathology services in England**. *London: National Health Services* 2008.

88. Cadogan SL, Browne JP, Bradley CP, Cahill MR: **The effectiveness of interventions to improve laboratory requesting patterns among primary care physicians: a systematic review**. *Implementation Science* 2015, **10**(1):167.

89. Horn DM, Koplan KE, Senese MD, Orav EJ, Sequist TD: **The impact of cost displays on primary care physician laboratory test ordering**. *Journal of general internal medicine* 2014, **29**(5):708-714.

90. French SD, Green SE, O'Connor DA, McKenzie JE, Francis JJ, Michie S, Buchbinder R, Schattner P, Spike N, Grimshaw JM: **Developing theory-informed behaviour change interventions to implement evidence into practice: a systematic approach using the Theoretical Domains Framework**. *Implementation science : IS* 2012, **7**:38.

91. Baker R, Camosso-Stefinovic J, Gillies C, Shaw EJ, Cheater F, Flottorp S, Robertson N: **Tailored interventions to overcome identified barriers to change: effects on professional practice and health care outcomes**. *The Cochrane database of systematic reviews* 2010(3):CD005470-CD005470.

92. Francis JJ, Stockton C, Eccles MP, Johnston M, Cuthbertson BH, Grimshaw JM, Hyde C, Tinmouth A, Stanworth SJ: **Evidence-based selection of theories for designing behaviour change interventions: using methods based on theoretical construct domains to understand clinicians' blood transfusion behaviour**. *Br J Health Psychol* 2009, **14**(Pt 4):625-646.

93. Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, Altman DG, Barbour V, Macdonald H, Johnston M: **Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide**. *Bmj* 2014, **348**:g1687.

94. Michie S, Richardson M, Johnston M, Abraham C, Francis J, Hardeman W, Eccles MP, Cane J, Wood CE: **The behavior change technique taxonomy (v1) of 93 hierarchically clustered techniques: building an international consensus for the reporting of behavior change interventions**. *Annals of behavioral medicine : a publication of the Society of Behavioral Medicine* 2013, **46**(1):81-95.

95. Michie S, Atkins L, West R: **The behaviour change wheel: a guide to designing interventions**. 2015.

96. Duncan EM, Francis JJ, Johnston M, Davey P, Maxwell S, McKay GA, McLay J, Ross S, Ryan C, Webb DJ *et al*: **Learning curves, taking instructions, and patient safety: using a theoretical domains framework in an interview study to investigate prescribing errors among trainee doctors**. *Implement Sci* 2012, **7**(86):1748-5908.

97. Francis JJ, Johnston M, Robertson C, Glidewell L, Entwistle V, Eccles MP, Grimshaw JM: **What is an adequate sample size? Operationalising data saturation for theory-based interview studies**. *Psychology and Health* 2010, **25**(10):1229-1245.

98. Cane J, O'Connor D, Michie S: **Validation of the theoretical domains framework for use in behaviour change and implementation research**. *Implement Sci* 2012, **7**(1):37.

99. Gale NK, Heath G, Cameron E, Rashid S, Redwood S: **Using the framework method for the analysis of qualitative data in multi-disciplinary health research**. *BMC medical research methodology* 2013, **13**(1):117.

100. Michie S, van Stralen MM, West R: **The behaviour change wheel: A new method for characterising and designing behaviour change interventions**. *Implementation Science : IS* 2011, **6**:42-42.

101. Cane J, Richardson M, Johnston M, Ladha R, Michie S: **From lists of behaviour change techniques (BCTs) to structured hierarchies: comparison of two methods of developing a hierarchy of BCTs**. *Br J Health Psychol* 2015, **20**(1):130-150.

102. Michie S, Wood CE, Johnston M, Abraham C, Francis JJ, Hardeman W: **Behaviour change techniques: the development and evaluation of a taxonomic method for reporting and describing behaviour change interventions (a suite of five studies involving consensus methods, randomised controlled trials and analysis of qualitative data)**. *Health Technology Assessment* 2015.

103. Godin G, Bélanger-Gravel A, Eccles M, Grimshaw J: **Healthcare professionals' intentions and behaviours: A systematic review of studies based on social cognitive theories**. *Implementation Science* 2008, **3**(1):36.

104. Grol R, Wensing M, Eccles M, Davis D: **Improving patient care: the implementation of change in health care**: John Wiley & Sons; 2013.

105. Baker R, Falconer Smith J, Lambert PC: **Randomised controlled trial of the effectiveness of feedback in improving test ordering in general practice**. *Scandinavian journal of primary health care* 2003, **21**(4):219-223.

106. Ivers N, Jamtvedt G, Flottorp S, Young JM, Odgaard-Jensen J, French SD, O'Brien MA, Johansen M, Grimshaw J, Oxman AD: **Audit and feedback: effects on professional practice and healthcare outcomes**. *Cochrane Database Syst Rev* 2012, **6**:Cd000259.

107. Britt H, Miller GC, Henderson J, Bayram C, Valenti L, Harrison C, Charles J, Pan Y, Zhang C, Pollack A: **A decade of Australian general practice activity 2003-04 to 2012-13: General practice series no. 34**, vol. 34: Sydney University Press; 2013.

108. McGregor MJ, Martin D: **Testing 1, 2, 3 Is overtesting undermining patient and system health?** *Canadian Family Physician* 2012, **58**(11):1191-1193.

109. Whiting P, Toerien M, de Salis I, Sterne JA, Dieppe P, Egger M, Fahey T: **A review identifies and classifies reasons for ordering diagnostic tests**. *Journal of clinical epidemiology* 2007, **60**(10):981-989.

110. Ferrier BM, Woodward CA, Cohen M, Goldsmith CH: **Laboratory Tests: Which Physicians Order More?: How women's practices differ from men's**. *Canadian Family Physician* 1991, **37**:349-352.

111. Vinker S, Kvint I, Erez R, Elhayany A, Kahan E: **Effect of the characteristics of family physicians on their utilisation of laboratory tests**. *The British journal of general practice : the journal of the Royal College of General Practitioners* 2007, **57**(538):377-382.

112. Salloum S, Franssen E: **Laboratory investigations in general practice**. *Canadian Family Physician* 1993, **39**:1055.

113. Verstappen WH, ter Riet G, Dubois WI, Winkens R, Grol RP, van der Weijden T: **Variation in test ordering behaviour of GPs: professional or context-related factors?** *Family practice* 2004, **21**(4):387-395.

114. Cadogan SL, McHugh SM, Bradley CP, Browne JP, Cahill MR: **General practitioner views on the determinants of test ordering: a theory-based qualitative approach to the development of an intervention to improve immunoglobulin requests in primary care**. *Implementation Science* 2016, **11**(1):1-12.

115. Bugter-Maessen AM, Winkens RA, Grol RP, Knottnerus JA, Kester AD, Beusmans GH, Pop P: **Factors predicting differences among general practitioners in test ordering behaviour and in the response to feedback on test requests**. *Family practice* 1996, **13**(3):254-258.

116. Eisenberg JM, Nicklin D: **Use of diagnostic services by physicians in community practice**. *Medical care* 1981, **19**(3):297-309.

117. Brady Shipman M: **Irish Rural Structure and Gaeltacht Areas**. 2000.
118. Jagannath S, Richardson P, Munshi NC: **Multiple myeloma and other plasma cell dyscrasias**. *Cancer Management* 2011:1-20.

119. Burke P: **Primary Care Reimbursement Service; Statistical Analysis of Claims and Payments 2010.** . In.: Health Service Executive; 2010.

120. Cameron AC, Trivedi PK: **Regression analysis of count data**, vol. 53: Cambridge university press; 2013.

121. Murphy M, Brodie G, Byrne S, Bradley C: **An observational study of public and private general practitioner consultations in the Republic of Ireland**. *Irish Journal of Medical Science (1971-)* 2015, **184**(1):147-152.

122. Vardy DA, Simon T, Limoni Y, Kuperman O, Rabzon I, Cohen A, Cohen L, Shvartzman P: **The impact of structured laboratory routines in computerized medical records in a primary care service setting**. *Journal of medical systems* 2005, **29**(6):619-626.

123. KRISTIANSEN IS, Hjortdahl P: **The general practitioner and laboratory utilization: why does it vary?** *Family Practice* 1992, **9**(1):22-27.

124. Mayorova T, Stevens F, Scherpbier A, Velden Lvd, Zee Jvd: **Gender-related differences in general practice preferences: longitudinal evidence from the Netherlands 1982–2001**. *Health Policy* 2005, **72**(1):73-80.

125. Bensing JM, Van Den Brink-Muinen A, De Bakker DH: **Gender differences in practice style: a Dutch study of general practitioners**. *Medical care* 1993:219-229.

126. O'Dowd T, Ni Shúilleabháin A: **Structure of General Practice in Ireland 1982—2015**. 2016.

127. Misbah SA, Kokkinou V, Jeffery K, Oosterhuis W, Shine B, Schuh A, Theodoridis T: **The role of the physician in laboratory medicine: a European perspective**. *J Clin Pathol* 2013, **66**(5):432-437.

128. Horn DM, Koplan KE, Senese MD, Orav EJ, Sequist TD: **The impact of cost displays on primary care physician laboratory test ordering**. *J Gen Intern Med* 2014, **29**(5):708-714.

129. Ramsay CR, Eccles M, Grimshaw JM, Steen N: **Assessing the long-term effect of educational reminder messages on primary care radiology referrals**. *Clin Radiol* 2003, **58**(4):319-321.

130. Bachireddy C, Soule MC, Izenberg JM, Dvoryak S, Dumchev K, Altice FL: **Integration of health services improves multiple healthcare outcomes among HIV-infected people who inject drugs in Ukraine**. *Drug Alcohol Depend* 2014, **134**:106-114.

131. Wagner AK, Soumerai SB, Zhang F, Ross-Degnan D: **Segmented regression analysis of interrupted time series studies in medication use research**. *J Clin Pharm Ther* 2002, **27**(4):299-309.

132. Ramsay CR, Matowe L, Grilli R, Grimshaw JM, Thomas RE: **Interrupted time series designs in health technology assessment: lessons from two systematic reviews of behavior change strategies**. *Int J Technol Assess Health Care* 2003, **19**(4):613-623.

133. Campbell DT, Stanley JC: **Experimental and quasi-experimental designs for research**: Ravenio Books; 2015.

134. von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP: **Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies**. *Bmj* 2007, **335**(7624):806-808.

135. Bhaskaran K, Gasparrini A, Hajat S, Smeeth L, Armstrong B: **Time series regression studies in environmental epidemiology**. *International journal of epidemiology* 2013:dyt092.

136. Fogg BJ: **A behavior model for persuasive design**. In: *Proceedings of the 4th international Conference on Persuasive Technology: 2009*: ACM; 2009: 40.

137. Taljaard M, McKenzie JE, Ramsay CR, Grimshaw JM: **The use of segmented regression in analysing interrupted time series studies: an example in pre-hospital ambulance care**. *Implementation Science* 2014, **9**(1):1.

138. Melanson SEF: **Establishing benchmarks and metrics for utilization management**. *Clinica Chimica Acta* 2014, **427**:127-130.

139. Trisorio Liuzzi MP, Attolini E, Quaranta R, Paparella D, Cappabianca G, Di Serio F, Dell'Erba AS: **Laboratory request appropriateness in emergency: Impact on hospital organization**. *Clinical Chemistry and Laboratory Medicine* 2006, **44**(6):760-764.

140. Bastiaens GJ, Van Meer MP, Sim KL, Billingsley PF, James ER, Wiersma J, Van Grinsven T, Scholzen A, Bijker EM, Graumans W *et al*: **Safety and tolerability of PFSPZ challenge to volunteers taking chloroquine chemoprophylaxis (PFSPZ-CVAC) and protective efficacy of PFSPZ-CVAC against controlled human malaria infection**. *American Journal of Tropical Medicine and Hygiene* 2013, **1)**:69.

10. APPENDICES

Appendix 1 Details of additional publications, awards, training and teaching activities during the PhD

Additional non-thesis related publications published during the PhD

Beirne PV, Hennessy S, **Cadogan SL,** Shiely F, Fitzgerald T, MacLeod F. Needle size for vaccination procedures in children and adolescents. Cochrane Database of Systematic Reviews 2015, Issue 6. Art. No.: CD010720. DOI: 10.1002/14651858.CD010720.pub2

Cadogan SL, Keane E, Kearney PM. The effects of individual, family and environmental factors on physical activity levels in children: a cross-sectional study. BMC Pediatrics. 2014;14:107. doi:10.1186/1471-2431-14-107.

McNamee T, Hyland T, Harrington J, **Cadogan S**, Honari B, Perera K, Fitzgerald AP, Perry IJ, Cahill MR. Haematinic deficiency and macrocytosis in middle-aged and older adults. PloS one. 2013 Nov 7;8(11):e77743.

Committee membership

2013-2016 Member of the College of Medicine and Health Graduate Committee

International experience

2015 Five weeks were spent working with Professor Jeremy Grimshaw and a team of implementation science experts at Ottawa Hospital Research Institute, Ottawa, Canada.

Awards

2014 Finalist in UCC Doctoral Showcase, June 2014

2015 Co-author of paper awarded HSE Open Access Research Paper of the Year (primary care category)

2015 Awarded a place on the IEA 7th International Course on Epidemiological Methods in Pokhara, Nepal, April 2015 (event cancelled due to earthquake)

2015 Article accepted for publication in UCC Boolean Journal: Snippets of Doctoral Research, Nov 2015

2016 Awarded UCC Student Travel Bursary to present at HTAi Conference, Tokyo, Japan. May 2016.

Table 10.1 Details of training and workshops attended during PhD

Extra-credit modules, University College Cork		
Year	**Course**	**Facilitator**
2012	PG7016 Systematic reviews for the health sciences	Prof John Browne
2013	PG6003 Teaching and Learning	Dr Marian McCarthy

Other workshops attended while on the PhD scholars' programme		
Year	**Course/ workshop**	**Facilitator**
2013	Turbocharge your writing	Mr Hugh Kearns
2013	Seven secrets of highly successful PhD students	Mr Hugh Kearns
2014	NVIVO qualitative software training, Day 1 & 2	Mr Ben Meehan
2014	Grant preparation and writing workshop	Dr Kathleen Bennett
2014	Cochrane Systematic Review Training	Mr Martin Burton
2014	Publishing in a peer review journal	Dr Sara Scroter, BMJ
2014	Presentation Skills Irish Times Training	Irish Times representative
2014	Using Network analysis in policy analysis	Dr Niamh Humphries
2014	Multi-level modelling using Stata	Dr Gordon Lecke
2014	Present without PowerPoint	Dr Susan Steele
2015	The media and your research	Dr Sara Burke

Table 10.2 Teaching and supervision contributions to the Department of Epidemiology and Public Health

Year	**Course**	**Module**	**Role**
2012-2016	BSc Public Health	EH1004 Epidemiology 1	Teaching assistant
2012-2016	BSc Public Health	EH3000 Epidemiology 3	Teaching assistant
2012-2015	MPH (campus)	EH6052 Applied Research for Public Health	Guest lecturer
2013-2015	BSc Public Health	EH3012 Data Management for Public Health	Teaching assistant
2014-2016	BSc Public Health	EH1010 Introduction to Public Health	Student mentor
2014-2016	MPH (online)	EH6076 Applied Research for Public Health I (Online)	Teaching assistant Discussion board facilitator
2014	Graduate Entry Medicine	GM1020 Health and Disease in Society I	Guest lecturer
2015	BSc Public Health	EH4007 Research Project	Guest lecturer

Appendix 2 Copy of ethical approval letter from Cork Research Ethics Committee

UCC

Tel: + 353-21-490 1901
Fax: + 353-21-490 1919

Coláiste na hOllscoile Corcaigh, Éire
University College Cork, Ireland

COISTE EITICE UM THAIGHDE CLINICIÚIL
Clinical Research Ethics Committee

Lancaster Hall,
6 Little Hanover Street,
Cork,
Ireland.

Our ref: ECM 3 (ll) 07/01/14

16th December 2013

Dr Mary Cahill
Consultant Haematologist
Cork University Hospital
Wilton
Cork

Re: A mixed methods study exploring laboratory requesting and referrals to haematology out-patient services in the South of Ireland.

Dear Dr Cahill

The Chairman noted and filed the following:

- GP Information Leaflet Version 1.0 dated 9th December 2013
- Interview Guide Version 1.0 dated 9th Decembe 2013
- Data Collection Sheet Version 1.0 dated 9th December 2013.

Full approval is now granted to carry out the above study.

Yours sincerely

Professor Michael G Molloy
Chairman
Clinical Research Ethics Committee
of the Cork Teaching Hospitals

The Clinical Research Ethics Committee of the Cork Teaching Hospitals, UCC, is a recognised Ethics Committee under Regulation 7 of the European Communities (Clinical Trials on Medicinal Products for Human Use) Regulations 2004, and is authorised by the Department of Health and Children to carry out the ethical review of clinical trials of investigational medicinal products. The Committee is fully compliant with the Regulations as they relate to Ethics Committees and the conditions and principles of Good Clinical Practice.

Appendix 3 Search terms and search records for PubMed, Cochrane, Embase and Scopus databases

Table 10.3 Search terms and search records returned for the included databases

Search terms*	**Database**[+]			
	Scopus (Feb 09th 2014) LIMIT: humans	*EMBASE (Feb 09th 2014) LIMIT: humans & English language*	*Cochrane (1981-Feb 09th 2014) LIMIT: humans*	*PubMed (1981-Feb 09th 2014) LIMIT: humans*
	records returned	**records returned**	**records returned**	**records returned**
1. Laboratory test	355,218	193,805	7,536	92,822
2. Laboratory tests	355,218	59,254	7,536	77,746
3. Laboratory testing	109,218	52,719	7,531	37,044
4. Clinical laboratory tests	140,878	42,669	4,466	36,286
5. Laboratory requests	3,280	1,052	117	753
6. Laboratory orders	79,088	1,467	1,135	1,219
7. Clinical laboratory requests	1,476	785	65	429
8. Test orders	332,695	1,253	9,244	1,829
9. Laboratory use	1,105,378	103,694	7,952	566,999
10. Laboratory test utilization	4,928	1,842	76	1,731
11. Laboratory test requests	1,561	484	75	297
12. Lab requests	367	232	5	95
13. #1#2#3#4#5#6#7#8#9#10#11#12	904	310,976	20,635	568,963
14. Physician*	533,906	429,285	14895	379,721
15. Family physician	74,269	70,155	1942	55,359
16. Family physicians	74,269	59,685	1942	36,904
17. Family doctor	30,996	45,788	565	41,742
18. Family doctors	30,996	7694	565	45,361
19. Primary care physician	53,707	46,722	888	14,235
20. Primary care practice	80,473	72,714	559	46,756
21. Primary care physicians	53,707	50413	888	24,292
22. General practitioners	97,606	38,029	2,877	28,285
23. General practitioner	97,606	90,422	2,877	30,719
24. General practice	206,566	149,377	3607	114,625

25. Primary care doctors	14,931	6,299	28	30,123
26. Primary health care	178,733	177,459	3,447	137,689
27. Primary care provider	18,856	8,065	323	5,963
28. Primary care providers	18,856	14150	323	11,314
29. #14#15#16#17#18 #19#20#21#22#23 #24#25#26#27#28	18,768	700,614	29,622	570,365
30. intervention	733,111	386,906	80,333	282,989
31. Strategy	1,384,949	188,906	21706	159,097
32. Inappropriate	69,485	37,868	11339	32,513
33. Ordering performance	6,465	695	2681	491
34. Efficiency	1,384,080	103,505	6633	283,575
35. Volume, tests	174,045	18,932	9794	35,253
36. #30#31#32#33#34 #35	9,759	18,952	112,391	594,617
37. Trial	157,8224	1,082,279	305342	915,699
38. Article	1,889,975	8,184,301	79285	11,905,601
39. Audit	65,946	38,002	1098	27,870
40. Systematic review	133,162	116,281	19396	1,588,086
41. Before and after study	3,097,342	300,765	54656	990,275
42. #37#38#39#40#41	481,205	8,668,501	365251	11,976,838
43. #13#29#36#42 ^	**681**	**2,262**	**837**	**2,386**

[+] Updated searches performed on all databases November 2014

* Row 13: Search included laboratory test OR laboratory tests OR laboratory testing OR clinical laboratory tests OR laboratory requests OR laboratory orders OR clinical laboratory requests OR test orders OR laboratory use OR laboratory test utilisation OR laboratory test requests or lab requests (combination of search terms for laboratory testing from rows 1-12)

^ Full search: all search terms for laboratory test (row 13) AND all search terms for primary care physician (row 29) AND all search terms for intervention characteristics (row 36) AND all search terms for study designs (row 42)

Appendix 4 Example data extraction form for one of the studies included in the review

Table 10.4 Data extraction for one of the included studies in the systematic review

Paper: Thomas et al, 2006

Setting: Scotland, United Kingdom

Number of General Practitioners: 85 primary care practices (370 GPs)
Number receiving intervention:

- Feedback only: 22 practices
- Reminders only: 22 practices
- Both feedback and reminders: 21 practices
- Control group: 20 practices

Study design, duration and follow-up:
Cluster RCT, 2x2 factorial design.
Duration: 12 months (commenced in Feb 2002)
Data: 12-month pre-intervention and 12 month intervention period

Intervention:	**Control:**
Reminders group: Brief educational messages were added as reminders to the test result reports for nine laboratory tests sent to the requesting practice. The messages were activated by the laboratory system using cues and were presented at the same time as the test result. Feedback group: Feedback was quarterly, and consisted of a six-sided colour booklet presenting graphs of practice level data for each of the nine targeted tests and for each laboratory discipline as a whole. Every graph showed rates of test requesting over the previous three years (number per 10 000 patients per 6 months) for the practice compared with the regional rates. The booklets were posted to each family practitioner within each intervention group practice on four occasions (updated every three months from the start of the intervention period). Feedback and reminders group: The feedback was enhanced with the educational messages which were included alongside the graphs for each of the targeted tests.	Usual practice.

Outcome measures:

- The volume of laboratory tests ordered per practice were obtained for the 12 months before (pre-intervention) and during the 12 months of the intervention period.

Results:

	Pre-intervention	**Post- intervention**
- Control group:	1,071 (783-1,804)	1,226 (726-2,057)
- Feedback only:	1,233 (601-1,954)	1,079 (575-1,818)
- Reminders only:	1,329 (688-1,726)	1,317 (719-1,590)
- Both:	1,166 (492-1,749)	1,041 (362-1,515)

NOTE: Data are median (IQR) test requests per 10,000 patients per practice

- Practices that received either feedback or reminders were less likely than the control group to request the targeted tests in total (enhanced feedback OR: 0.87, 95%CI 0.81-0.94; p= 0.0004; reminder messages OR: 0.89, 95%CI: 0.83-0.93; p=0.003).

- Practices that received the combined (feedback and reminders group) were also significantly less likely than the control practices to request the target tests (OR: 0.78, 95%CI: 0.71-0.85).

- The effect varied across the target tests, although the general pattern was that of a reduction in test volumes.

- The enhanced feedback strategy reduced test ordering for all nine tests, which reached statistical significance (P<0.05) for four tests. (antibody screen, FSH, TSH and vitamin B12).

- The brief educational reminders messages showed a reduction in test requests for eight of the nine target tests, of which three reached statistical significance (carcino-embryonic antigen, TSH and vitamin B12)

Losses to follow-up: no losses to follow-up

Appendix 5 Topic Guide for GP interviews based on the Theoretical Domains Framework

Table 10.5 Topic Guide for interviews based on Theoretical Domains Framework

TDF Domains	TDF Definitions (Constructs)	Prompt questions
Knowledge	An awareness of the existence of something. (Knowledge including knowledge of condition/scientific rationale. Procedural knowledge. Knowledge of task environment.)	• Are you familiar with any guidelines for requesting immunoglobulins? • Are you comfortable interpreting results of immunoglobulin tests? • Knowledge their own and other GP requesting patterns (procedure knowledge) • Knowledge about problems associated with requesting (knowledge of task environment)
Skills	An ability or proficiency acquired through practice. (Skills Skills development Competence Ability Interpersonal skills Practice Skill assessment)	• Do you know how to do it/able to use tools?
Social professional role and identity	A coherent set of behaviours and displayed personal qualities of an individual in a social or work setting. (Professional identity Professional role Social identity Professional boundaries Professional confidence Group identity Leadership Organisational commitment)	• When would you request an immunoglobulin test? • Do you think immunoglobulins are important/appropriate part of your role?

Beliefs about capabilities	Acceptance of the truth, reality, or validity about an ability, talent, or facility that a person can put to constructive use. (Self-confidence Perceived competence Self-efficacy Perceived behavioural control Beliefs Self-esteem Empowerment Professional confidence)	• How confident would do you feel about requesting immunoglobulin tests? • Any difficulties in interpreting results or deciding when to test?
Beliefs about consequences	Acceptance of the truth, reality, or validity about outcomes of behaviour in a given situation. (Beliefs Outcome expectancies Characteristics of outcome expectancies Anticipated regret Consequences)	• How do you deal with an abnormal result?
Intention	A conscious decision to perform a behaviour or resolve to act in a certain way. Mental representations of outcomes or end state that an individual wants to achieve. (Stability of intentions Stages of change model Trans-theoretical Model and stages of change Implementation intention)	• Why do you do these tests?
Goals	Goals (distal/proximal) Goal priority Goal/Target setting Goals (autonomous/controlled) Action planning	

Memory, attention and decision processes	The ability to retain information, focus selectively on aspects of the environment and choose between two or more alternatives. (Memory Attention Attention control Decision making Cognitive overload/tiredness)	• Is it something you do routinely?
Environmental context and resources	Any circumstance of a person's situation or environment that discourages or encourages the development of skills and abilities, independence, social competence, and adaptive behaviour. (Environmental stressors Resources/material resources Organisational culture/climate Salient events/critical incidents Person x environment interaction Barriers and facilitators)	• Do resources influence whether you perform the test (e.g. any guidelines you follow)? • Are there clear guidelines available? • Are there clear communication channels (laboratories/ consultants etc.)? • Adequate communication telephone/written correspondence with Consultants prior to referral • Useful interaction with consultants where necessary
Social influences	Those interpersonal processes that can cause individuals to change their thoughts, feelings, or behaviours. (Social pressure Social norms Group conformity Social comparisons Group norms Social support Power Intergroup conflict Alienation Group identity Modeling)	• Do you seek opinions of colleagues in decision making / interpreting test results? • Why might there be variation in requesting patterns between GPs

Emotion	A complex reaction pattern, involving experiential, behavioural, and psychological elements, by which an individual attempts to deal with a personally significant matter or event. (Fear Anxiety Affect Stress Depression Positive/negative effect Burn-out)	• If appropriate…indirectly probe for any significant reasons such a fear of missing something or fear of litigation as motivators for testing.
Behavioral regulation	Anything aimed at managing or changing objectively observed or measured actions. (Self-monitoring Breaking habit Action planning)	• Are there any guidelines you follow?

Appendix 6 Behaviour Change Technique (BCT) groups and corresponding BCTs and definitions

Table 10.6 Behaviour Change Technique (BCT) groups, corresponding BCTs and definitions

BCT grouping [94]	Relevant BCT and definition [102]
1) Goals and planning	**N/A**
2) Feedback and monitoring	**Feedback on behaviour:** - Monitor and provide informative or evaluative feedback on performance of the behaviour
3) Social support	**N/A**
4) Shaping knowledge	I**nstructions on how to perform the behaviour** - Advise or agree on how to perform the behaviour (includes 'skills training')
5) Comparison of behaviour	**N/A**
6) Associations	P**rompts and cues** - Introduce and define environmental or social stimulus with the purpose of prompting or cueing the behaviour. The prompt or cue would normally occur at time/place of performance
7) Repetition and substitution	**N/A**
8) Comparison of outcomes	**Credible source** - Present verbal or visual communication from a credible source in favour of or against the behaviour
9) Reward and threat	**N/A**
10) Antecedents	**Restructuring the physical environment** - Change, or advise to change the physical environment in order to facilitate performance of the wanted behaviour or create barriers to the unwanted behaviour (other than prompts/cues, rewards/punishments) **Adding objects to the environment** - Add objects to the environment to facilitate performance of the behaviour
11) Identity	**N/A**
12) Scheduled consequences	**N/A**
13) Self-belief	**N/A**
14) Natural consequences	**Information about health consequences** - Provide information (e.g. written, verbal, visual) about health consequences of performing the behaviour
15) Regulation	**N/A**
16) Covert learning	**N/A**

Appendix 7 Mapping of behaviour change techniques (BCTs) to key domains for inclusion in the intervention

Table 10.7 Mapping of behaviour change techniques (BCTs) to key domains for inclusion in an intervention targeting immunoglobulin testing behaviour of General Practitioners

TDF Domain	BCTs identified using Cane et al. [101]*	BCTs identified using Michie et al. [44]*	Selected and excluded BCTS
Knowledge	1. Feedback on behaviour 2. Biofeedback 3. *Antecedents* 4. *Health consequences*	5. *Instructions on how to perform behaviour*	Selected BCT: 3, 4, 5 BCT 3/5: Provide information and training about immunoglobulin use in primary care, i.e. provide guidelines on when to request and how to interpret results. BCT 4: Clearly communicate situations where immunoglobulin testing is not beneficial. (i.e. develop an algorithm of scenarios where tests should be performed). Non-selected BCTs: 1, 2 BCT 1: Individual GP feedback on requesting patterns, not within the scope of this project. BCT 2: Not relevant for the context of the study.
Memory, attn. & decision-making	none	1. Self-monitoring 2. Planning, implementation 3. *Prompts, triggers, cues*	Selected BCTs: 3 Mapped to behaviour regulation – see below for description) Non-selected BCTs: 1,2

			BCT 1: Not feasible for GPs to monitor behaviour in this instance. BCT 2: Not applicable for interventions in this setting.
Environmental context & resources	1. *Restructuring the physical environment* 2. Restructuring the social environment 3. Avoidance/changing exposure to cues for the behaviour 4. Discriminative (learned) cue 5. *Prompts/cues*	6. *Environmental changes (i.e. adding objects to facilitate behaviour)*	Selected BCTs: 1, 5, 6 BCTs 1, 5 6: Provide automated notes detailing consultant advice on the test results (ideally provided on the end of the test results) and with cues for activation. Non-selected BCTs: 2,3,4 BCT 2: Not possible in this context to restructure the social environment of GPs BCT 3: Not applicable for the target behaviour as the aim is to promote effective testing among GPs where provided cues to support decision making is useful rather avoiding exposure to such support/cues. BCT 4: Not within scope to offer any financial reward based on laboratory testing
Beliefs about capabilities	1. Focus on past success 2. Verbal persuasion to boost self-efficacy	3. Self-monitoring 4. Graded tasks, starting with easy tasks 5. Increasing skills: problem solving, decision-making, goal-setting 6. Coping skills 7. Rehearsal of relevant skills 8. *Social process of encouragement, pressure and support*	Selected BCTs: BCT 8 (mapped to professional role and identity – see description below) Non-selected BCTs: 1-7, 9-11 BCTs 1, 2, 6, 7, 9: Not feasible for this project due to variation in requesting patterns. For

		9. Feedback 10. Self-talk 11. Motivational interviewing	example, GPs would require individually tailored verbal persuasion. BCT 3: Immunoglobulin tests often require advice from consultants'/ lab scientists and the GP self-monitoring would not be feasible for this project. BCTs 4, 5: Not feasible due to the likely lengthy time-period and administration required to implement successfully. BCTs 10, 11: Not applicable for immunoglobulin testing behaviour change.
Beliefs about consequences	1. Vicarious reinforcement 2. Covert sensitisation 3. Covert conditioning 4. Emotional consequences 5. Threat 6. Pros and cons 7. Comparative imagining of future outcomes	8. Self-monitoring 9. *Persuasive communication (credible source)* 10. *Information regarding behaviour/outcome* 11. Feedback	Selected BCT: 9, 10 BCTs 9, 10: Clearly communicate situations where immunoglobulin testing is not beneficial (i.e. develop an algorithm of scenarios where tests should be performed, supported by consultant haematologists and GPs. Non-selected BCTs: 1-8, 11 BCTs 1-7: Not applicable for immunoglobulin testing behaviours. BCT 8: Immunoglobulin tests often require advice from consultants'/ lab scientists and the GP self-monitoring would not be feasible for this project.

			BCT 11: Not feasible for this project due to variation in requesting patterns. For example, GPs would require individually tailored verbal persuasion.
Professional role and identity	No BCTs are linked to this domain	1. *Social process of encouragement, pressure and support*	Selected BCTs: 1 BCT 1: Deliver a strategy developed by specialists and laboratory scientists' in conjunction with GPs to provide the necessary, feasible support/ guidelines on immunoglobulin testing procedures in primary care.
Behavioural regulation	1. Self-monitoring of behaviour	2. *Goal/target specified behaviour or outcome* 3. Contract 4. Planning, implementation *5. Prompts, triggers, cues* 6. Use of imagery	Selected BCTs: 2, 5 BCT 2, 5: Provide automated notes detailing consultant advice on the test results (ideally provided on the end of the test results) and with cues for activation. Non- selected BCTs: 1, 3, 4, 6 BCT 1: Immunoglobulin tests often require advice from consultants'/ lab scientists and the GP self-monitoring would not be feasible in this project. BCT 3: Contractual strategies not applicable for this laboratory testing behaviour change. BCT 4, 6: Not applicable for this context of this project.

*Selected BCTs are in italics

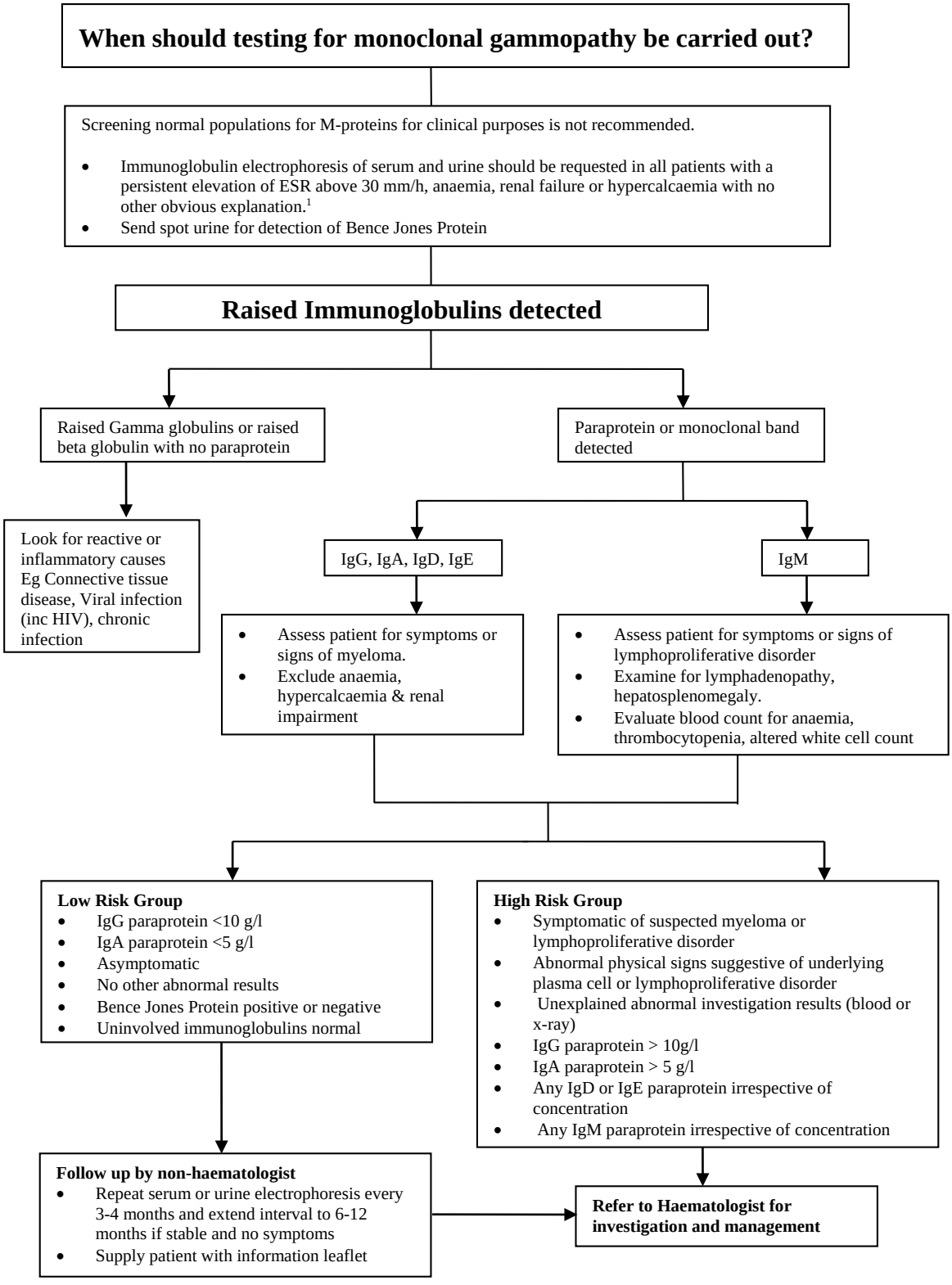
Appendix 8 Public patient list size demographics, 2013

Table 10.8 GP mean patient list size (HSE-PCRS), 2013 (crude and standardised for patient gender and age category)

	All	Males						Females					
	Mean [1]	**<30**	**30-45**	**45-60**	**60-70**	**>70**	**Total[2]**	**<30**	**30-45**	**45-60**	**60-70**	**>70**	**Total[3]**
Gender (GP)													
Males	271.14	38.89	71.91	49.77	45.72	126.5	**71.70**	46.16	87.49	48.55	44.77	133.8	**77.67**
Females	144.51	18.61	44.49	28.08	25.26	53.55	**36.81**	30.53	67.17	35.41	30.78	87.42	**52.01**
Experience													
<10years	62.76	20.86	28.16	16.71	16.44	57.83	**31.07**	28.00	52.33	25.00	31.33	61.35	**44.03**
10-20 years	176.76	17.15	55.03	35.36	31.44	77.98	**50.206**	32.72	71.96	31.53	29.63	80.37	**51.20**
>20 years	273.36	35.88	67.27	46.55	42.75	111.2	**64.53**	41.16	82.83	48.09	43.14	138.1	**74.43**
Location													
Urban	213.04	32.86	63.19	42.94	36.73	95.74	**57.54**	38.39	79.60	41.19	38.24	114.6	**65.27**
Rural	205.88	25.79	58.54	40.13	40.17	93.30	**59.64**	35.67	72.42	43.97	37.83	110.6	**65.21**
County													
Cork	204.43	29.29	59.04	40.24	35.44	89.82	**55.15**	36.21	75.28	40.44	35.65	109.9	**63.42**
Kerry	231.66	35.14	68.69	48.35	47.90	124.4	**69.24**	42.96	84.95	47.63	46.44	126.3	**71.89**
Practice type													
> 4 GPs	241.36	631.7	57.14	37.19	34.62	95.45	**54.72**	36.07	67.09	21.00	36.09	109.9	**62.26**
2-4 GPs	224.71	32.31	65.11	44.12	40.59	88.83	**58.51**	42.94	87.17	39.23	38.04	104.7	**66.47**
Single-handed	185.85	28.00	62.00	45.28	39.39	112.3	**63.20**	29.52	76.21	43.94	41.76	141.4	**69.54**

[1] Mean number of patients per GP by characteristic, 2013 (Overall mean=210.6 GMS patients)
[2] Mean number of male patients per GP by characteristic, 2013
[3] Mean number of female patients per GP by characteristic

Appendix 9 Copy of the MGUS guidelines algorithm sent to the GPs



Bird J, Behrens J, Westin J, Turesson I, Drayson M, Beetham R, D'Sa S, Soutar R, Waage A, Gulbrandsen N et al: UK Myeloma Forum (UKMF) and Nordic Myeloma Study Group (NMSG): guidelines for the investigation of newly detected M-proteins and the management of monoclonal gammopathy of undetermined significance (MGUS). Br J Haematol 2009, 147(1):22-42.

Appendix 10 Details of the eight educational interpretive comments attached to test reports

Table 10.9 Targeted laboratory tests, educational interpretive comments, and cues for adding interpretive messages to results report

Test	Action Cue	Brief educational message provided with result
ELE	Raised alpha-1 and alpha-2 globulins	Pattern may be consistent with low-grade inflammation.
IgG	Diffusely raised IgG	Pattern of persistent infection or inflammation.
IgG, IgA	Diffusely raised IgG and IgA	Polyclonally raised IgG and IgA - Pattern of persistent infection or inflammation.
IgA, IgG, IgM	IgA deficiency (IgA must be <0.1g/l with a normal IgG and IgM with a normal pattern)	Normal electrophoretic pattern but very low total IgA concentration – would be consistent with IgA deficiency. This is seen in approx. 1/500 of the population and often without clinical consequence.
IgM	Raised IgM with a normal electrophoresis	Patient has a slightly raised IgM. If Anti-Mitochondrial antibodies are negative, this may be consistent with recent infection, particularly viral. If Anti-Mitochondrial antibodies are positive this may be consistent with primary biliary cirrhosis.
IgA, ELE	Raised IgA with a normal electrophoresis	Normal Electrophoresis pattern with a slightly raised IgA – may be consistent with mucosal inflammation, autoimmune illnesses or liver disease.
IgM	Low IgM in an older patient (>70yrs) with normal electrophoresis	Slightly low IgM – this may be an incidental finding, particularly in older patients, but it may also be an indicator of some secondary immune suppression.
Interpretative comment for when a paraprotein is present		
PARA	If a faint band is present	Serum shows a small paraprotein with normal background gamma. This pattern could be an incidental finding in a patient of this age or may be seen secondary to recent infection. However, urine must be checked for Bence Jones protein and suggest recheck serum in 3-4 months to assess any progression. If you do have strong clinical indications e.g. hypercalcaemia, renal impairment, anaemia, bone pain, etc. suggest investigate further.

* IgG: Immunoglobulin G, IgA: Immunoglobulin A, IgM: Immunoglobulin M, ELE: serum protein electrophoresis and PARA: paraprotein

Appendix 11 Quality criteria followed in the design of the intervention

Table 10.10 Quality Criteria guidelines for Interrupted Time Series study designs[1]

Criteria	Comment
1. Intervention occurred independently of other changes over time DONE The intervention occurred independently of other changes over time NOT CLEAR Not specified (will be treated as NOT DONE if information cannot be obtained from the authors) NOT DONE Reported that intervention was not independent of other changes in time	DONE
2. Intervention was unlikely to affect data collection DONE Reported that intervention itself was unlikely to affect data collection (for example, sources and methods of data collection were the same before and after the intervention NOT CLEAR Not specified (treated as NOT DONE if information cannot be obtained from the authors) NOT DONE Intervention itself was likely to affect data collection (for example, any change in source or method of data collection reported)	DONE – data collection methods the same before and after intervention
3. The primary outcome was assessed blindly or was measured objectively DONE Stated explicitly that primary outcome variables were assessed blindly or outcome variables are objective e.g., length of hospital stay, drug levels assessed by a standardised test NOT CLEAR Not specified (treated as NOT DONE if information cannot be obtained from the authors) NOT DONE Outcomes were not assessed blindly	DONE – objective outcome
4. The primary outcome was reliable or was measured objectively DONE Two or more raters with agreement ≥90% or kappa ≥0.8 or outcome assessment is objective, e.g., length of hospital stay, drug levels assessed by a standardised test NOT CLEAR Reliability not reported for outcome measures obtained by chart extraction or collected by an Individual (will be treated as NOT DONE if information cannot be obtained from the authors) NOT DONE Two or more raters with agreement	DONE-objective outcome
5. The composition of the data set at each time point covered at least 80% of the total number of participants in the study DONE Data set covers 80–100% of total number of participants or episodes of care in the study	DONE – complete data set anticipated

NOT CLEAR Not specified (will be treated as NOT DONE if information cannot be obtained from the authors) NOT DONE Data set covers less than 80% of the total number of participants or episodes of care in the study	
6. The shape of the intervention effect was pre-specified DONE A rational explanation for the shape of intervention effect was given by the author(s) NOT CLEAR Not specified NOT DONE Any of the conditions above are not met	DONE
7. A rationale for the number and spacing of data points was described DONE Rationale for the number of points stated (e.g., monthly data for 12 months post-intervention was used because the anticipated effect was expected to decay) or sample size calculation performed NOT CLEAR Not specified NOT DONE Any of the conditions above are not met	DONE – methods section
8. The study was analysed appropriately using time series techniques DONE ARIMA models were used or time series regression models were used to analyse the data and serial correlation was adjusted/tested for NOT CLEAR Not specified NOT DONE Any of the conditions above are not met ITS, interrupted time series; ARIMA, autoregressive integrated moving average	

[1] **Source:** Ramsay CR, Matowe L, Grilli R, Grimshaw JM, Thomas RE: **Interrupted time series designs in health technology assessment: lessons from two systematic reviews of behaviour change strategies**. *Int J Technol Assess Health Care* 2003, **19**(4):613-623.

Appendix 12 Methodological and reporting recommendations for interrupted time series studies

Table 10.11 Methodological and reporting recommendations for interrupted time series studies

Item	Item no	Recommendation
Title and abstract	1	Indicate the study design (interrupted time series) in the title or abstract
Introduction		
Background/rationale	2	Provide background regarding the intervention and setting under investigation to support the study rationale and methods
Objectives	3	(a) State specific objectives and any pre-specified hypotheses (b) Distinguish between primary and secondary objectives
Methods		
Intervention	4	Define the intervention time point(s) used in the analysis
Participants	5	(a) List eligibility criteria and methods of selection (b) Define subgroups (c) Consider including a comparison group not exposed to the intervention as a secondary group of participants
Data sources and measurement	6	(a) List data source(s) (b) Comment on data completeness, validity, and changes in data coverage over time
Variables	7	(a) Define all variables • Outcome variable(s) • Descriptive and stratifying variable(s) (b) Comment on change in variable coding over time (c) Consider including details of variable coding in supplemental material, for example, appendix or research Web site

Statistical methods	8	(a) Report all statistical methods • Study time intervals, for example, monthly, quarterly • Regression model, for example, ARIMA, linear, segmented i) For ARIMA models, indicate the intervention function, for example, point, ramp, or step ii) Indicate the appropriateness of linear model(s) when applied • Number of pre-intervention, Post-intervention, and between intervention data points (b) Define the study period and number of pre-intervention data points used in forecasting (c) Indicate how autocorrelation, non-stationarity, and seasonality were tested and handled (d) Consider a lag period if intervention effects are gradual or delayed (e) Define and distinguish between primary and secondary or sensitivity analyses (f) Consider use of comparison outcome(s) and/or population(s) not exposed to the intervention(s) as secondary analyses (g) Report statistical software used for analysis
Results		
Participants	9	(a) Report the number of individuals and/or observations in each group analysed (b) Consider use of a flow diagram (c) Describe characteristics and indicate missing data
Outcome data	10	(a) Report the number of outcomes examined over the study period (b) Report the average, minimum, and maximum number of outcomes across time intervals (c) Report on data variability (d) Comment on outliers and ceiling or floor effects where relevant
Main results	11	(a) Present results using a graphical display with intervention time point(s) clearly defined (b) Consider including forecasted results graphically

		(c) Report absolute and/or relative change(s) and their significance, for example, clinical or policy and statistical
Other analyses	12	Report additional results (secondary and sensitivity analyses) in the article, appendix, or research Web site
Discussion		
Key results	13	Summarise key results with reference to study objectives
Context	14	(a) Provide context related to possible confounding • Discuss relevant co-interventions that occurred during the study period •Comment on the stability of participant characteristics over time •Comment on the stability of outcome coding over time (b) Discuss results of comparison analyses or provide a rationale if no comparison group was considered
Limitations	15	(a) Discuss limitations of the study (b) Comment on data variability and appropriateness of the number of data points (c) Comment on ceiling or floor effects and outliers where relevant (d) Discuss direction and magnitude of any potential bias
Interpretation	16	Provide overall interpretation of results considering objectives, limitations, results from similar studies, and other relevant evidence
Other information		
Funding	17	List funding source(s) and role of funders
References	18	Reference methodological articles that support statistical methods used

Source: Adapted from the Strengthening the Reporting of Observational Studies in Epidemiology statement [134]

Appendix 13 PDF versions of the two papers published in Implementation Science