The use of teledermatology for the diagnosis of skin cancer in adults

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Abstract

Background

Early accurate detection of all skin cancer types is essential to guide appropriate management and to improve morbidity and survival. Melanoma and squamous cell carcinoma (SCC) are high risk skin cancers which have the potential to metastasise and ultimately lead to death, whereas basal cell carcinoma (BCC) is usually localised with potential to infiltrate and damage surrounding tissue. Anxiety around missing early curable cases needs to be balanced against inappropriate referral and unnecessary excision of benign lesions. Teledermatology provides a way for generalist clinicians to access the opinion of a specialist dermatologist for skin lesions that they consider to be suspicious without referring the patients concerned through the normal referral pathway. Teledermatology consultations can be ‘store-and-forward’ with electronic digital images of a lesion sent to a dermatologist for review at a later time, or can be live and interactive consultations using video conferencing to connect the patient, referrer and dermatologist in real time.

Objectives

To determine the diagnostic accuracy of teledermatology for the detection of any skin cancer (melanoma, BCC or cSCC) in

adults, and to compare its accuracy with that of in-person diagnosis.

Search methods

We undertook a comprehensive search of the following databases from inception up to August 2016: Cochrane Central Register of Controlled Trials; MEDLINE; EMBASE; CINAHL; CPCI; Zetoc; Science Citation Index; US National Institutes of Health Ongoing Trials Register; NIHR Clinical Research Network Portfolio Database; and the World Health Organization International Clinical Trials Registry Platform. We studied reference lists and published systematic review articles.

Selection criteria

Studies evaluating skin cancer diagnosis for teledermatology alone, or in comparison with face-to-face diagnosis by a specialist clinician, compared with a reference standard of histological confirmation or clinical follow-up and expert opinion. Studies evaluating the referral accuracy of teledermatology compared with a reference standard of face-to-face diagnosis by a specialist clinician were also included.

Data collection and analysis

Two review authors independently extracted all data using a standardised data extraction and quality assessment form (based on QUADAS-2). We contacted authors of included studies where information related to the target condition of any skin cancer was missing. Data permitting, we estimated summary sensitivities and specificities using the bivariate hierarchical model. Due to scarcity of data, no covariate investigations were undertaken for this review. For illustrative purposes, estimates of sensitivity and specificity were plotted on coupled forest plots for diagnostic threshold and target condition under consideration.

Main results

Twenty-two studies were included reporting diagnostic accuracy data for 4057 lesions and 879 malignant cases (16 studies) and referral accuracy data for reported data for 1449 lesions and 270 ‘positive’ cases as determined by the reference standard face-to-face decision (six studies). Methodological quality was variable with poor reporting hindering assessment. The overall risk of bias was rated as high or unclear for participant selection, reference standard and participant flow and timing in at least half of all studies; the majority were considered at low risk of bias for the index test. The applicability of study findings were of high or unclear concern for the majority of studies in all domains assessed due to the recruitment of study participants from secondary care settings or specialist clinics rather than from the primary or community-based settings in which teledermatology is more likely to be used and due to the acquisition of lesion images by dermatologists or in specialist imaging units rather than by primary care clinicians.

Seven studies provided data for the primary target condition of any skin cancer (1588 lesions and 638 malignancies). For the correct diagnosis of lesions as malignant using photographic images, summary sensitivity was 94.9% (95% CI 90.1 to 97.4%) and summary specificity 84.3% (95% CI 48.5 to 96.8%) (from four studies). Individual study estimates using dermoscopic images or a combination of photographic and dermoscopic images generally suggested similarly high sensitivities with highly variable specificities. Limited comparative data suggested similar diagnostic accuracy between teledermatology assessment and in-person diagnosis by a dermatologist; however, data were too scarce to draw firm conclusions. For the detection of invasive melanoma or atypical intraepidermal melanocytic variants both sensitivities and specificities were more variable. Sensitivities ranged from 59% (95% CI 42% to 74%) to 100% (95% CI 54% to 100%) and specificities from 30% (95% CI 22% to 40%) to 100% (95% CI 93% to 100%), with reported diagnostic thresholds including the correct diagnosis of melanoma, classification of lesions as ‘atypical’ or ‘typical as well as the decision to refer or to excise a lesion.

Referral accuracy data comparing teledermatology against a face-to-face reference standard suggested good agreement for lesions considered to require some positive action by face to face assessment (sensitivities of over 90%). For lesions considered of less concern when assessed face-to-face (e.g. for those not recommended for excision or referral), agreement was more variable with teledermatology specificities ranging from 57% (95% CI 39 to 73%) to 100% (95% CI 86% to 100%), suggesting that remote assessment is more likely recommend excision, referral or follow-up compared to in-person decisions.

Authors' conclusions

Studies were generally small and heterogeneous and methodological quality was difficult to judge due to poor reporting. Bearing in mind concerns regarding the applicability of study participants and of lesion image acquisition in specialist settings, our results suggest that teledermatology can correctly identify the majority of malignant lesions. Using a more widely defined threshold to identify ‘possibly’ malignant cases or lesions that should be considered for excision is likely to appropriately triage those lesions requiring face-to-face assessment by a specialist. Despite the increasing use of teledermatology on an international level, the evidence base to support its ability to accurately diagnose lesions and to triage lesions from primary to secondary care is lacking and further prospective and pragmatic evaluation is needed.

Plain language summary

What is the diagnostic accuracy of teledermatology for the diagnosis of skin cancer in adults?

Why is improving the diagnosis of skin cancer important?

There are different types of skin cancer. Melanoma is one of the most dangerous forms and it is important to identify it early so that it can be removed. If it is not recognised when first brought to the attention of doctors (also known as a false negative test result) treatment can be delayed resulting in the melanoma spreading to other organs in the body and possibly causing

early death. Cutaneous squamous cell carcinoma (cSCC) and basal cell carcinoma (BCC) are usually localised skin cancers, although cSCC can spread to other parts of the body and BCC can cause disfigurement if not recognised early. Calling something a skin cancer when it is not really a skin cancer (a false positive result) may result in unnecessary surgery and other investigations that can cause stress and worry to the patient. Making the correct diagnosis is important. Mistaking one skin cancer for another can lead to the wrong treatment being used or lead to a delay in effective treatment.

What is the aim of the review?

The aim of this Cochrane review was to find out whether teledermatology is accurate enough to identify which people with skin lesions need to be referred to see a specialist dermatologist and who can be safely reassured that their lesion is not malignant. Researchers in Cochrane included 22 studies to answer this question.

What was studied in the review?

Teledermatology means sending pictures of skin lesions or rashes to a specialist for advice on diagnosis or management. It is a way for primary care clinicians (GPs) to get an opinion from a specialist dermatologist without having to refer patients through the normal referral pathway. Teledermatology can involve sending photographs or magnified images of a skin lesion taken with a special camera (dermatoscope) to a skin specialist to look at or it might involve immediate discussion about a skin lesion between a GP and a skin specialist using video conferencing.

What are the main results of the review?

The review included 22 studies, 16 studies comparing teledermatology diagnoses to the final lesion diagnoses (diagnostic accuracy) 4057 lesions and 879 malignant cases and five studies comparing teledermatology decisions to the decisions that would be made with the patient present (referral accuracy) for 1449 lesions and 270 ‘positive’ cases.

The studies were very different from each other in terms of the types of individuals with suspicious skin cancer lesions included and the type of teledermatology used. A single reliable estimate of the accuracy of teledermatology could not be made. For the correct diagnosis of a lesion to be a skin cancer, data suggested that less than 7% of malignant skin lesions were missed by teledermatology. Study results were too variable to tell us how many people would be referred unnecessarily for a specialist dermatology appointment following a teledermatology consultation. Without access to teledermatology services however, most of the lesions included in these studies would likely be referred to a dermatologist.

How reliable are the results of the studies of this review?

In the included studies, the final diagnosis of skin cancer was made by lesion biopsy and the absence of skin cancer was confirmed by biopsy or by follow up over time to make sure the skin lesion remained negative for melanoma. This is likely to have been a reliable method for deciding whether patients really had skin cancer. In a few studies, a diagnosis of no skin cancer was made by a skin specialist rather than biopsy. This is less likely to have been a reliable method for deciding whether patients really had skin cancer. Poor reporting of what was done in the study made it difficult for us to say how reliable the study results are. Selecting some patients from specialist clinics instead of primary care along with different ways of doing teledermatology were common problems.

Who do the results of this review apply to?

Studies were conducted in: Europe (n=14; 64%), North America (n=4; 18%), South America (n=2; 9%) or Oceania (n=2; 9%). The average age of people who were studied was 52 years; however, the majority of studies included at least some people under the age of 16 years. The percentage of people with skin cancer ranged between 2% and 88% with an average of 30%, which is much higher than would be observed in a primary care setting in the UK.

What are the implications of this review?

Teledermatology is likely to be a good way of helping GPs to decide which skin lesions need to be seen by a skin specialist. Our review suggests that using magnified images in addition to photographs of the lesion improves accuracy. More research is needed to establish the best way of providing teledermatology services.

How up-to-date is this review?

The review authors searched for and used studies published up to August 2016.

*In these studies, biopsy, clinical follow up, or specialist clinician diagnosis were the reference standards.

Background

This review is one of a series of Cochrane Diagnostic Test Accuracy (DTA) reviews on the diagnosis and staging of melanoma and keratinocyte skin cancers conducted for the National Institute for Health Research (NIHR) Cochrane Systematic Reviews Programme. For the purposes of these reviews, diagnostic accuracy is assessed by the sensitivity and specificity of a test. Appendix 1 shows the content and structure of the programme and Appendix 2 provides a glossary of terms used and a table of acronyms used is provided in Appendix 3.

Target condition being diagnosed

There are three main forms of skin cancer. Melanoma is the most widely known amongst the general population, yet the commonest skin cancers in Caucasian populations are those arising from keratinocytes: basal cell carcinoma (BCC) and cutaneous squamous cell carcinoma (cSCC) (Gordon 2013; Madan 2010). In 2003, the World Health Organization estimated that between two and three million ‘non-melanoma’ skin cancers (of which BCC and cSCC are estimated to account for around 80% and 16% of cases respectively) and 132,000 melanoma skin cancers occur

globally each year (WHO 2003).

In this diagnostic test accuracy review there are three target conditions of interest (a) melanoma, (b) basal cell carcinoma, and (c) cutaneous squamous cell carcinoma.

Melanoma

Melanoma arises from uncontrolled proliferation of melanocytes - the epidermal cells that produce pigment or melanin. Cutaneous melanoma refers to any skin lesion with malignant melanocytes present in the dermis, primarily including superficial spreading, nodular, acral lentiginous, and lentigo maligna melanoma variants (see Figure 1). Melanoma *in situ* refers to abnormal melanocytes that are contained within the epidermis and have not yet invaded the dermis, but are at risk of progression to melanoma if left untreated. Lentigo maligna, a subtype of melanoma *in situ* in chronically sun-damaged skin, denotes another form of proliferation of abnormal melanocytes. All forms of melanoma *in situ* can progress to invasive melanoma if growth breaches the dermoepidermal junction during a vertical growth phase , however malignant transformation is both lower and slower for lentigo maligna than for other forms of melanoma *in situ* (Kasprzak 2015). Melanoma *in situ* and lentigo maligna are both atypical intraepidermal melanocytic variants. Melanoma is one of the most dangerous forms of skin cancer, with the potential to metastasise to other parts of the body via the lymphatic system and blood stream. It accounts for only a small percentage of skin cancer cases but is responsible for up to 75% of skin cancer deaths (Boring 1994; Cancer Research UK 2017).

The incidence of melanoma rose to over 200,000 newly diagnosed cases worldwide in 2012 (Erdmann 2013; Ferlay 2015), with an estimated 55,000 deaths (Ferlay 2015). The highest incidence is observed in Australia with 11,405 new cases of melanoma of the skin (ACIM 2014) and in New Zealand with 2,341 registered cases (HPA and MelNet NZ 2014) in 2010. For 2014 in the USA, the predicted incidence was 73,870 per annum and the predicted number of deaths 9,940 (Siegel 2015). The highest rates in Europe are seen in north-western Europe and the Scandinavian countries, with highest incidence reported in Switzerland of 25.8 per 100,000 in 2012. Rates in the UK have trebled from 4.6 and 6.0 per 100,000 in men and women, respectively in England in 1990, to 18.6 and 19.6 per 100,000 in 2012 (EUCAN 2012). In the UK, melanoma has one of the fastest rising incidence rates of any cancer, and has had the biggest projected increase in incidence between 2007 and 2030 (Mistry 2011). In the decade leading up to 2013, age standardised incidence increased by 46%, with 14,500 new cases in 2013 and 2,459 deaths in 2014 (Cancer Research UK 2017). Rates are higher in women than in men; however, the rate of incidence in men is increasing faster than in women (Arnold 2014).The rising incidence in melanoma is thought to be primarily related to an increase in recreational sun exposure and tanning bed use and an increasingly ageing population with higher lifetime recreational ultraviolet (UV) exposure, in conjunction with possible earlier detection (Linos 2009; Belbasis 2016). Putative risk factors, including eye and hair colour, skin type and density of freckles, history of melanoma, sunburn, and presence of particular lesion types, are reviewed in detail elsewhere (Belbasis 2016).

A database of over 40,000 US patients from 1998 onwards which assisted the development of the 8th American Joint Committee on Cancer (AJCC) Staging System indicated a five-year survival of 97% to 99% for stage I melanoma, dropping to between 32% and 93% in stage III disease depending on tumour thickness, the presence of ulceration and number of involved nodes (Gershenwald 2017). While these are substantial increases relative to survival in 1975 (Cho 2014), increasing incidence between 1975 and 2010 means that mortality rates have remained static during the same period. This observation coupled with increasing incidence of localised disease, suggests that improved survival rates may be due to earlier detection and heightened vigilance (Cho 2014). Targeted therapies for stage IV melanoma have improved survival expectation and immunotherapies are evolving such that long term survival benefit is being documented (e.g. using BRAF-inhibitors (Chapman 2012; Villanueva 2010) and MEK inhibitors (Larkin 2014; Dummer 2014), and immunomodulation (Chapman 2011; Hamid 2013; Hodi 2010).

Basal cell carcinoma

BCC can arise from multiple stem cell populations, including from the bulge and interfollicular epidermis (Grachtchouk 2011). BCC growth is usually localised, but it can infiltrate and damage surrounding tissue, sometimes causing considerable destruction and disfigurement, particularly when located on the face (Figure 1). The four main subtypes of BCC are superficial, nodular, morphoeic or infiltrative, and pigmented. They typically present as slow-growing asymptomatic papules, plaques, or nodules which may bleed or form ulcers that do not heal (Firnhaber 2012). People with a BCC often present themselves to healthcare professionals with a non-healing lesion rather than specific symptoms such as pain. Many lesions are diagnosed incidentally (Gordon 2013).

BCCs most commonly occur on sun-exposed areas of the head and neck (McCormack 1997), and are more common in men and in people over the age of 40. A rising incidence of BCC in younger people has been attributed to increased recreational sun exposure (Bath-Hextall 2007; Gordon 2013; Musah 2013). Other risk factors include Fitzpatrick skin types I and II (Fitzpatrick 1975; Lear 1997; Maia 1995); previous skin cancer history; immunosuppression; arsenic exposure; and genetic predisposition, such as in basal cell naevus (Gorlin) syndrome (Gorlin 2004; Zak-Prelich 2004). Annual incidence is increasing worldwide; Europe has experienced an average increase of 5.5% per year over the last four decades, the USA 2% per year, while estimates for the UK show incidence appears to be increasing more steeply at a rate of an additional 6 / 100,000 persons per year (Lomas 2012). The rising incidence has been explained by an ageing population, changes in the distribution of known risk factors, particularly ultraviolet radiation, and improved detection due to the increased awareness amongst both practitioners and the general population (Verkouteren 2017). Hoorens 2016 points to evidence for a gradual increase in the size of BCCs over time, with delays in diagnosis ranging from 19 to 25 months.

According to National Institute for Health and Care Excellence (NICE) guidance (NICE 2010), low risk BCCs are nodular lesions occuring in patients older than 24 years old who are not immunosuppressed and do not have Gorlin syndrome. Furthermore, low risk lesions are usually located below the clavicle; small (< 1 cm) with well-defined margins; not recurrent following incomplete excision; and not in awkward or highly visible locations (NICE 2010). Superficial BCCs are also typically low risk and may be amenable to medical treatments such as photodynamic therapy or topical chemotherapy (Kelleners-Smeets 2017). Assigning BCCs as low or high risk influences the management options (Batra 2002; Randle 1996).

Advanced locally destructive BCC can be found on the H-area of the face (Lear 2014) and can arise from long-standing untreated lesions or from a recurrence of aggressive basal cell carcinoma after primary treatment (Lear 2012). Very rarely, BCC metastasises to regional and distant sites resulting in death, especially cases of large neglected lesions in those who are immunosuppressed or those with Gorlin syndrome (McCusker 2014). Rates of metastasis are reported at 0.0028% to 0.55% (Lo 1991), with very poor survival rates. It is recognised that basosquamous carcinoma (more like a high risk SCC in behaviour and not considered a true BCC) is likely to have accounted for many cases of apparent metastases of BCC hence the spuriously high reported incidence in some studies of up to 0.55% which is not seen in clinical practice (Garcia 2009).

Squamous cell carcinoma of the skin

Primary cSCC arises from the keratinocytes of the outermost layer (epidermis) of the skin. People with cSCC often present with an ulcer or firm (indurated) papule, plaque, or nodule (Firnhaber 2012; Griffin 2016) often with an adherent crust and poorly defined margins (Madan 2010). cSCC can arise in the absence of a precursor lesion or it can develop from pre-existing actinic keratosis or Bowens disease (squamous cell carcinoma *in situ*) with an estimated annual risk of progression being <1% to 20% for newly arising lesions (Alam 2001) and 5% for pre-existing lesions (Kao 1986). It remains locally invasive for a variable length of time, but has the potential to spread to the regional lymph nodes or via the bloodstream to distant sites, especially in immunosuppressed individuals (Lansbury 2010). High risk lesions are those arising on the lip or ear, recurrent cSCC, lesions arising on non-exposed sites, scars or chronic ulcers, tumours more than 20mm in diameter and depth of invasion more than 4mm and poor differentiation on pathological examination (Motley 2009). Perineural nerve invasion of at least > 0.1 mm in diameter is a further documented risk factor for high risk cSCC (Carter 2013).

Chronic ultraviolet light exposure through recreation or occupation is strongly linked to cSCC occurrence (Alam 2001). It is particularly common in people with fair skin and in less common genetic disorders of pigmentation, such as albinism, xeroderma pigmentosum, and recessive dystrophic epidermolysis bullosa (RDEB) (Alam 2001). Other recognised risk factors include immunosuppression; chronic wounds; arsenic or radiation exposure; certain drug treatments, such as voriconazole and BRAF inhibitors; and previous skin cancer history (Baldursson 1993; Chowdri 1996; Dabski 1986; Fasching 1989; Lister 1997; Maloney 1996; O'Gorman 2014). In solid organ transplant recipients, cSCC is the most common form of skin cancer, with estimates of the risk of developing cSCC 65 to 253 times that of the general population (Hartevelt 1990; Jensen 1999; Lansbury 2010). Overall, local and metastatic recurrence of cSCC at five years is estimated at 8% and 5% respectively (Rowe 1992). The five-year survival rate of metastatic cSCC of the head and neck is around 60% (Moeckelmann 2018).

Treatment

For primary melanoma, the mainstay of definitive treatment is wide local excision of the lesion, to remove both the tumour and any malignant cells that might have spread beyond the visible margins of the surrounding skin (Sladden 2009; Marsden 2010; NICE 2015a; Garbe 2016; SIGN 2017). Recommended surgical margins vary according to tumour thickness (Garbe 2016) and stage of disease at presentation (NICE 2015a).

Treatment options for BCC and cSCC include surgery, other destructive techniques such as cryotherapy or electrodesiccation and topical chemotherapy. A Cochrane systematic review of 27 randomised controlled trials (RCTs) of interventions for BCC found very little good quality evidence for any of the interventions used (Bath-Hextall 2007a). Complete surgical excision of primary BCC has a reported five-year recurrence rate of <2% (Griffiths 2005; Walker 2006), leading to significantly fewer recurrences than treatment with radiotherapy (Bath-Hextall 2007a). After apparent clear histopathological margins (serial vertical sections) after standard excision biopsy with 4mm surgical peripheral margins taken there is a 5-year reported recurrence rate of around 4% (Drucker 2017). Mohs micrographic surgery, whereby horizontal sections of the tumour are microscopically examined intraoperatively, and re-excision is undertaken until the margins are tumour-free, can be considered for high risk lesions such as on the centre of the face where standard wider excision margins might lead to incomplete excision or considerable functional impairment (Bath-Hextall 2007a; Motley 2009; Lansbury 2010; Stratigos 2015). Bath-Hextall and colleagues (Bath-Hextall 2007a) found a single trial comparing MMS with a 3mm surgical margin excision in BCC (Smeets 2004); the update of this study showed non-significantly lower recurrence at 10 years with Mohs micrographic surgery (4.4% compared to 12.2% after surgical excision, P = 0.10) (van Loo 2014).

The main treatments for high risk BCC include standard surgical excision, Mohs micrographic surgery, and radiotherapy. For low risk or superficial subtypes of BCC, or for those with small and or multiple BCCs at low risk sites (Marsden 2010), destructive techniques other than excisional surgery may be used (e.g. electrodesiccation and curettage or cryotherapy (Alam 2001; Bath-Hextall 2007a)). Alternatively, non-surgical ('non-destructive') treatments may be considered (Bath-Hextall 2007a; Kim 2014; Drew 2017), including topical chemotherapy such as imiquimod (Williams 2017), 5-fluorouracil (5-FU) (Arits 2013), ingenol mebutate (Nart 2015) and photodynamic therapy

(PDT) (Roozeboom 2016). Bath-Hextall 2007aNon-surgical treatments are most frequently used for superficial forms of BCC, with one head to head trial suggesting topical imiquimod is superior to PDT and 5-FU (Jansen 2018). Although non-surgical approaches are increasingly used, they do not allow histological confirmation of tumour clearance, and their efficacy is dependent on accurate characterisation of the histological subtype and depth of tumour such that a baseline diagnostic biopsy can be helpful. The 2007 systematic review of BCC interventions found limited evidence from very small RCTs for these approaches (Bath-Hextall 2007a), which have only partially been filled by subsequent studies (Bath-Hextall 2014; Kim 2014; Roozeboom 2012). Most BCC trials have compared interventions within the same treatment class, and few have compared medical versus surgical treatments (Kim 2014).

Vismodegib, a first-in-class Hedgehog signalling pathway inhibitor is now available for the treatment of metastatic or locally advanced BCC based on the pivotal study ERIVANCE BCC (Sekulic 2012). It is licensed for use in these patients where surgery or radiotherapy is inappropriate, e.g. for treating locally advanced periocular and orbital BCCs with orbital salvage of patients who otherwise would have required exenteration (Wong 2017). However, NICE has recently recommended against the use of vismodegib based on cost effectiveness and uncertainty of evidence (NICE 2017).

A systematic review of interventions for primary cSCC found only one RCT eligible for inclusion (Lansbury 2010). Current practice therefore relies on evidence from observational studies, as reviewed in Lansbury 2013, for example. Surgical excision with predetermined margins is usually the first-line treatment (Motley 2009; Stratigos 2015). Estimates of recurrence after MMS, surgical excision, or radiotherapy, which are likely to have been evaluated in higher risk populations, have shown pooled recurrence rates of 3%, 5.4% and 6.4%, respectively with overlapping confidence intervals; the review authors advised caution when comparing results across treatments (Lansbury 2013).

Index test(s)

Teledermatology is a term used to describe the delivery of dermatological care through information and communication technology (Bashshur 2015). It uses imaging modalities to provide specialist dermatology services either to other healthcare professionals (such as general practitioners), or to patients directly (Ndegwa 2010). It is considered a valuable tool in the diagnosis and management of skin disease, because of the visual nature of skin lesions / rashes (Warshaw 2011). Teledermatology allows an increased information flow between primary care physicians and dermatologists, which could lead to a reduction in waiting times and limit unnecessary referrals (Ndegwa 2010; Warshaw 2010b; Bashshur 2015). In rural areas, where access to speciality services can have significant and potentially off-putting travel and time implications for the patient, teledermatology has the potential to widen access to specialist opinion.

Teledermatology consultations can be conducted in two main ways, store-and-forward or ‘asynchronous’, and live interactive or ‘synchronous’ (Ndegwa 2010). With the store-and-forward approach, clinicians and patients are separated by both time and space, as electronic digital images are taken and then transmitted to a dermatologist for review at a later unspecified time (Warshaw 2011). The pictures can be digital photographic (or ‘macroscopic’) images, or can be magnified dermoscopic images taken using a dermatoscope. Images are often accompanied by a summary of the patient history and demographic information as part of a consultation package (Ndegwa 2010). Furthermore, recent developments in smartphone technology have also introduced a new platform for transferring lesion images from one setting to another (Chuchu 2018). The store-and-forward approach is advantageous as it requires less sophisticated technology and lower-cost equipment (Warshaw 2011); however, it does not allow the specialist to take a direct history, request additional views, or communicate in detail the purpose of management to the patient or referrer (Ndegwa 2010).

Live interactive teledermatology uses video-conferencing and image transmission to connect the patient, referrer and dermatologist in real time (Ndegwa 2010). The dermatologist and patient can interact verbally in a similar manner to a traditional clinic-based encounter, but more extensive telecommunications infrastructure and time are needed (Ndegwa 2010).

Clinical Pathway

The diagnosis of melanoma can take place in primary, secondary, and tertiary care settings by both generalist and specialist healthcare providers. In the UK, people with concerns about a new or changing skin lesion will usually present first to their general practitioner (GP) or, less commonly, directly to a specialist in secondary care, which could include a dermatologist, plastic surgeon, other specialist surgeon (such as an ear, nose, and throat (ENT) specialist or maxillofacial surgeon), or ophthalmologist (Figure 2). Current UK guidelines recommend that all suspicious pigmented lesions presenting in primary care should be assessed by taking a clinical history and visual inspection guided by the revised seven-point checklist (MacKie 1990). Those with suspected melanoma or cSCC should be referred for appropriate specialist assessment within two weeks (Chao 2013; Marsden 2010; NICE 2015a). Evidence is emerging, however, to suggest that excision of melanoma by GPs is not associated with increased risk compared with outcomes in secondary care (Murchie 2017). In the UK, low risk BCC are usually recommended for routine referral, with urgent referral for those in whom a delay could have a significant impact on outcomes, for example due to large lesion size or critical site (NICE 2015b). Appropriately qualified generalist care providers increasingly undertake management of low risk BCC in the UK such as by excision of low risk lesions (NICE 2010). Similar guidance is in place in Australia (CCAAC Network 2008).

Teledermatology consultations can aid more appropriate triage of lesions, providing reassurance for benign lesions and referral via urgent or non-urgent routes to secondary care (e.g., for suspected basal cell carcinoma. The distinction between setting and examiner qualifications and experience is important, as specialist clinicians might work in primary care settings

(for example, in the UK, GPs with a special interest in dermatology and skin surgery who have undergone appropriate training), and generalists might practice in secondary care settings (for example, GPs working alongside dermatologists in secondary care, or plastic surgeons who do not specialise in skin cancer). The level of skill and experience in skin cancer diagnosis will vary for both generalist and specialist care providers and will also impact on test accuracy.

For referred lesions, the specialist clinician will use history-taking, visual inspection of the lesion (in comparison with other lesions on the skin) usually in conjunction with dermoscopic examination, and palpation of the lesion and associated regional nodal basins to inform a clinical decision. If melanoma is suspected, then urgent 2mm excision biopsy is recommended (Lederman 1985; Lees 1991); for cSCC predetermined surgical margin excision or a diagnostic biopsy may be considered. BCC and pre-malignant lesions potentially eligible for nonsurgical treatment may undergo a diagnostic biopsy before initiation of therapy. Equivocal melanocytic lesions for which a definitive clinical diagnosis cannot be reached may undergo surveillance to identify any lesion changes that would indicate excision biopsy or reassurance and discharge for those that remain stable over a period of time.

Prior test(s)

Although smartphone applications and community- or high street pharmacy-based teledermatology services (for example the Boots 'Mole Scanning Service' www.boots.com/health-pharmacy-advice/skin-services/mole-scanning-service) can increasingly be accessed directly by people who have concerns about a skin lesion (Kjome 2016), the diagnosis of skin cancer is still based on history-taking and clinical examination by a suitably qualified clinician. In the UK, this is typically undertaken at two decision points – first in primary care where the GP makes a decision to refer or not to refer, and then a second time by a dermatologist or other secondary care clinician where a decision is made to biopsy or excise or not.

Visual inspection of the skin is undertaken iteratively, using both implicit pattern recognition (non-analytical reasoning) and more explicit 'rules' based on conscious analytical reasoning (Norman 2009), the balance of which will vary according to experience and familiarity with the diagnostic question. Various attempts have been made to formalise the "mental rules" involved in analytical pattern recognition for melanoma (Sober 1979; Friedman 1985; MacKie 1985; MacKie 1990; Thomas 1998; Grob 1998); however, visual inspection for keratinocyte skin cancers relies primarily on pattern recognition. Accuracy has been shown to vary according to the expertise of the clinician. Primary care physicians have been reported to miss over half of BCCs (Offidani 2002) and to misdiagnose one third of BCCs (Gerbert 2000). In contrast, an Australian study found that trained dermatologists were able to detect 98% of BCCs, but with a specificity of only 45% (Green 1988).

A range of technologies have emerged to aid diagnosis to reduce the number of diagnostic biopsies or inappropriate surgical procedures. Dermoscopy using a hand-held microscope has become the most widely used tool used by clinicians to improve diagnostic accuracy of pigmented lesions, in particular for melanoma (Dinnes 2018b); it is less well established for the diagnosis of BCC or cSCC. Dermoscopy (also referred to as dermatoscopy or epiluminescence microscopy or ELM) uses a hand-held microscope and incident light (with or without oil immersion) to reveal subsurface images of the skin at increased magnification of x 10 to x 100 (Kittler 2001). Used alongside clinical examination, dermoscopy has been shown in some studies to increase the sensitivity of clinical diagnosis of melanoma from around 60% to as much as 90% (Kittler 1999; Carli 2002; Bono 2006; Stanganelli 2000) with much smaller effects in others (Benelli 1999; Bono 2002). The accuracy of dermoscopy depends on the experience of the examiner (Kittler 2001), with accuracy when used by untrained or less experienced examiners potentially no better than clinical inspection alone (Binder 1997; Kittler 2002).

The diagnostic accuracy, and comparative accuracy, of visual inspection and dermoscopy have been evaluated in a further three reviews in this series (Dinnes 2018a; Dinnes 2018b; Dinnes 2018c).

Role of index test(s)

The use of teledermatology by primary care or by other generalist clinicians has the potential to ensure that people with suspicious lesions are appropriately referred for examination by a specialist clinician, and people with non-suspicious lesions are appropriately reassured and managed in primary care. If an accurate triage is made, the proportion of people who are referred unnecessarily will be minimised and those lesions requiring urgent referral and treatment correctly identified. By creating an environment where there is facilitated access to more specialist services, selective dermatology referral could ultimately reduce costs while enabling a faster, more reliable and more efficient service (Piccolo 2002). Increased information flow between primary care physicians and dermatologists also has the potential effect of increasing knowledge and reducing isolated decision-making (Bashshur 2015).

When diagnosing potentially life-threatening conditions such as melanoma, the consequences of falsely reassuring a person that they do not have skin cancer can be potentially fatal, as the delay to diagnosis means that the window for successful early treatment may be missed. To minimise these false-negative diagnoses, a good diagnostic test for melanoma demonstrates high sensitivity and high negative predictive value (NPV), i.e., very few of those with a negative test result will actually have a melanoma. Giving falsely positive test results (meaning the test has poor specificity and a high false-positive rate) resulting in the removal of lesions that turn out to be benign, is arguably less of an error than missing a potentially fatal melanoma, but does have implications for patient welfare and costs. False-positive diagnoses not only cause unnecessary scarring from the biopsy or excision procedure, but also increase patient anxiety whilst they await the definite histology results and increase healthcare costs as the number needed to remove to yield one melanoma diagnosis increases.

Delay in diagnosis of a BCC as a result of a false-negative test is not as serious as for melanoma because BCCs are usually slow-growing and unlikely to metastasise. However, delayed diagnosis can result in a larger and more complex excision with consequent greater morbidity. Very sensitive diagnostic tests for BCC however may compromise on lower specificity leading

to a higher false-positive rate, and an enormous burden of skin surgery, such that a balance between sensitivity and specificity is needed. The situation for cSCC is more similar to melanoma in that the consequences of falsely reassuring a person that they do not have skin cancer can be serious and potentially fatal. Thus, a good diagnostic test for cSCC should demonstrate high sensitivity and a corresponding high negative predictive value. In summary, a test that can reduce false positive clinical diagnoses without missing true cases of disease has patient and resource benefits. False-positive clinical diagnoses not only cause unnecessary morbidity from the biopsy, but could lead to initiation of inappropriate therapies and also increase patient anxiety.

Alternative test(s)

Teledermatology provides an alternative means for primary care clinicians (and therefore patients) to access specialist opinion compared to the standard referral process from primary to secondary care. Although the general public can also seek advice on skin lesions, they may be concerned about doing so via smartphone applications or from services provided within community or “high street” pharmacies. These are not considered direct alternatives to teledermatology services.

A number of other tests that may have a role in diagnosis of skin cancer have been reviewed as part of our series of systematic reviews, including visual inspection and dermoscopy (Dinnes 2018a; Dinnes 2018b; Dinnes 2018c), smartphone applications (Chuchu 2018). reflectance confocal microscopy (RCM) (Dinnes 2018d; Dinnes 2018e), optical coherence tomography (OCT) (Ferrante di Ruffano 2018a), and computer-aided diagnosis (CAD) techniques applied to various types of images including those generated by dermoscopy, diffuse reflectance spectrophotometry (DRS) and electrical impedance spectroscopy (EIS) (Ferrante di Ruffano 2018b), and high frequency ultrasound (Dinnes 2018f). Evidence permitting, the accuracy of available tests will be compared in an overview review, exploiting within-study comparisons of tests and allowing the analysis and comparison of commonly used diagnostic strategies where tests may be used singly or in combination.

Rationale

Our series of reviews of diagnostic tests used to assist clinical diagnosis of melanoma aims to identify the most accurate approaches to diagnosis and provide clinical and policy decision-makers with the highest possible standard of evidence on which to base decisions. With increasing rates of skin cancer and the push towards the use of dermoscopy and other high resolution image analysis in primary care, the anxiety around missing early cases needs to be balanced against the risk of over referrals, to avoid sending too many people with benign lesions for a specialist opinion. It is questionable whether all skin cancers picked up by sophisticated techniques, even in specialist settings, help to reduce morbidity and mortality, or whether newer technologies run the risk of increasing false-positive diagnoses. It is also possible that use of some technologies, e.g., widespread use of dermoscopy in primary care with no training, could actually result in harm by missing melanomas if they are used as replacement technologies for traditional history-taking and clinical examination of the entire skin. Many branches of medicine have noted the danger of such "gizmo idolatry" amongst doctors (Leff 2008).

Although teledermatology is increasingly used, the accuracy of different approaches to providing teledermatology services (e.g. store-and-forward versus live-link modalities, and use of clinical versus dermoscopic images) has yet to be fully established. A review by Warshaw 2011 suggested that both store-and-forward and live-link teledermatology had acceptable diagnostic accuracy and concordance when compared with clinical face-to-face diagnosis; however, clinic-based dermatology had superior diagnostic accuracy (i.e. in comparison to store-and-forward teledermatology consultations). As with any technology requiring significant investment, a full understanding of the benefits including patient acceptability and cost-effectiveness in comparison to usual practice should be obtained before such an approach can be recommended; establishing the accuracy of diagnosis and referral accuracy is one of the key components. Given the rapidly changing evidence base in skin cancer diagnosis, there is a need for an up-to-date analysis of the accuracy of teledermatology for skin cancer diagnosis.

This review follows a generic protocol which covers the full series of Cochrane DTA reviews for the diagnosis of melanoma (Dinnes 2015a); aspects of this review which relate to the diagnosis of BCC and cSCC follow the generic protocol that was written to cover the reviews in the series for the diagnosis of keratinocyte skin cancers (Dinnes 2015b). The Background and Methods sections of this review therefore use some text that was originally published in the protocols (Dinnes 2015a; Dinnes 2015b) and text that overlaps some of our other reviews (Dinnes 2018a; Dinnes 2018b; Chuchu 2018).

Objectives

To determine the diagnostic accuracy of teledermatology for the detection of any skin cancer (melanoma, BCC or cSCC) in adults, and to compare its accuracy with that of in-person diagnosis.

Accuracy was estimated separately according to the type of teledermatology images used:

i. Photographic images

ii. Dermoscopic images

iii. Photographic and dermoscopic images

Secondary objectives

1) To determine the diagnostic accuracy of teledermatology for the detection of invasive melanoma or atypical intraepidermal melanocytic variants in adults, and to compare its accuracy with that of in-person diagnosis.

2) To determine the diagnostic accuracy of teledermatology for the detection of invasive melanoma only, in adults, and to

compare its accuracy with that of in-person diagnosis.

3) To determine the diagnostic accuracy of teledermatology for the detection of BCC in adults, and to compare its accuracy with that of in-person diagnosis.

4) To determine the diagnostic accuracy of teledermatology for the detection of cSCC in adults, and to compare its accuracy with that of in-person diagnosis.

5) To determine the referral accuracy of teledermatology, i.e. to compare diagnostic decision making based on teledermatology images with that of an in-person consultation.

Investigation of sources of heterogeneity

We set out to address a range of potential sources of heterogeneity for investigation across our series of reviews, as outlined in our generic protocols (Dinnes 2015a; Dinnes 2015b) and described in Appendix 4; however, our ability to investigate these was necessarily limited by the available data on each individual test reviewed.

Methods

Criteria for considering studies for this review

Types of studies

We included test accuracy studies that allow comparison of the result of the index test with that of a reference standard, including the following:

- studies where all participants receive a single index test and a reference standard;
- studies where all participants receive more than one index test(s) and reference standard;
- studies where participants are allocated (by any method) to receive different index tests or combinations of index tests and all receive a reference standard (between-person comparative studies (BPC));
- studies that recruit series' of participants unselected by true disease status;
- diagnostic case-control studies that separately recruit diseased and non-diseased groups (see Rutjes 2005); however, we did not include studies that compared results for malignant lesions to those for healthy skin (i.e. with no lesion present).
- both prospective and retrospective studies; and
- studies where previously acquired clinical or dermoscopic images were retrieved and prospectively interpreted for study purposes.

We excluded studies from which we could not extract 2x2 contingency data or if they included less than five cases of either melanoma, BCC or cSCC or less than five benign lesions. For studies of referral accuracy where a lesion's final diagnosis may not be reported, at least 5 ‘positive’ cases as identified by the expert diagnosis reference standard were required. The size threshold of five is arbitrary. However such small studies are unlikely to add precision to estimate of accuracy.

Participants

We included studies in adults with lesions suspicious for skin cancer or adults at high risk of developing skin cancer. We excluded studies that recruited only participants with malignant or benign final diagnoses.

We excluded studies conducted in children, or which clearly reported inclusion of more than 50% of participants aged 16 and under.

Index tests

Studies evaluating teledermatology alone, or teledermatology in comparison with face-to-face diagnosis were included.

The following index tests were eligible for inclusion:

1. Store-and-forward teledermatology
2. Real-time 'live link' teledermatology

Data for face-to-face clinical diagnosis against a histological reference standard was also included where reported, to allow a direct comparison with teledermatology to be made.

Although primary care clinicians can in practice be specialists in skin cancer, we considered primary care physicians as generalist practitioners and dermatologists as specialists. Within each group, we extracted any reporting of special interest or accreditation in skin cancer.

Target conditions

The primary target condition was defined as the detection of any skin cancer, primarily cutaneous melanoma, BCC or cSCC.

Four additional definitions of the target condition were considered in secondary analyses, namely the detection of:

1. invasive cutaneous melanoma alone
2. invasive cutaneous melanoma or atypical intraepidermal melanocytic variants (including melanoma *in situ*, lentigo maligna)
3. BCC and
4. cSCC.

We also considered referral accuracy, comparing decision making from teledermatology compared with the face-to-face decisions for the same lesions. These decisions could include the decision to excise a lesion, follow-up a lesion or refer a

lesion for face-to-face assessment.

Reference standards

Teledermatology can be assessed in terms of a) diagnostic accuracy in comparison to the final lesion diagnosis and b) referral accuracy in comparison to a face-to-face expert management decision.

To establish diagnostic accuracy, the ideal reference standard is histopathological diagnosis in all eligible lesions. A qualified pathologist or dermatopathologist should perform histopathology. Ideally, reporting should be standardised detailing a minimum dataset to include the histopathological features of melanoma to determine the American Joint Committee on Cancer (AJCC) Staging System (e.g. Slater 2014). We did not apply this minimum dataset requirement as a necessary inclusion criterion, but extracted any pertinent information.

Partial verification (applying the reference test only to a subset of those undergoing the index test) was of concern given that lesion excision or biopsy are unlikely to be carried out for all benign-appearing lesions within a representative population sample. Therefore to reflect what happens in reality, we accepted clinical follow-up of benign-appearing lesions as an eligible reference standard, whilst recognising the risk of differential verification bias (as misclassification rates of histopathology and follow-up will differ). Additional eligible reference standards included cancer registry follow-up and 'expert opinion' with no histology or clinical follow-up.

All of the above were considered eligible reference standards for establishing lesion final diagnoses (diagnostic accuracy) with the following caveats:

- all study participants with a final diagnosis of the target disorder must have a histological diagnosis, either subsequent to the application of the index test or after a period of clinical follow-up, and
- at least 50% of all participants with benign lesions must have either a histological diagnosis or clinical follow-up to confirm benignity.

To establish referral accuracy of teledermatology (i.e. the ability of the remote observer to approximate an in-person diagnosis), the action recommended by the remote observer was compared with an in-person ‘expert opinion’ reference standard (i.e. the diagnosis or management recommendation of an appropriately qualified clinician made face-to-face with the study participant).

Search methods for identification of studies

Electronic searches

The Information Specialist (SB) carried out a comprehensive search for published and unpublished studies. A single large literature search was conducted to cover all topics in the programme grant (see Appendix 1 for a summary of reviews included in the programme grant). This allowed for the screening of search results for potentially relevant papers for all reviews at the same time. A search combining disease-related terms with terms related to the test names, using both text words and subject headings was formulated. The search strategy was designed to capture studies evaluating tests for the diagnosis or staging of skin cancer. As the majority of records were related to the searches for tests for staging of disease, a filter using terms related to cancer staging and to accuracy indices was applied to the staging test search, to try to eliminate irrelevant studies, for example, those using imaging tests to assess treatment effectiveness. A sample of 300 records that would be missed by applying this filter was screened and the filter adjusted to include potentially relevant studies. When piloted on MEDLINE, inclusion of the filter for the staging tests reduced the overall numbers by around 6000. The final search strategy (Appendix 5), incorporating the filter, was subsequently applied to all bibliographic databases as listed below. The final search result was cross-checked against the list of studies included in five identified reviews (Bashshur 2015; Ndegwa 2010; Warshaw 2011; Whited 2006; Whited 2016). Our search identified all but one of the studies, and this study is not indexed on MEDLINE. The Information Specialist devised the search strategy, with input from the Trials Search Co-ordinator from the CSG (Cochrane Skin Group).

We searched the following bibliographic databases to 29 August 2016 for relevant published studies:

- MEDLINE via OVID (from 1946);
- MEDLINE In-Process & Other Non-Indexed Citations via OVID; and
- EMBASE via OVID (from 1980).

We searched the following bibliographic databases to 30 August 2016 for relevant published studies:

- the Cochrane Central Register of Controlled Trials (CENTRAL) Issue 7, 2016, in the Cochrane Library;
- the Cochrane Database of Systematic Reviews (CDSR) Issue 8, 2016 in the Cochrane Library;
- Cochrane Database of Abstracts of Reviews of Effects (DARE) Issue 2, 2015;
- CRD HTA (Health Technology Assessment) database Issue 3, 2016;
- CINAHL (Cumulative Index to Nursing and Allied Health Literature via EBSCO from 1960).

We searched the following databases for relevant unpublished studies:

- CPCI (Conference Proceedings Citation Index) via Web of Science™ (from 1990);
- Zetoc (from 1993)
- SCI Science Citation Index Expanded™ via Web of Science™ (from 1900, using the "Proceedings and Meetings Abstracts" Limit function).

We searched the following trials registers:

- The US National Institutes of Health Ongoing Trials Register (www.clinicaltrials.gov);
- NIHR Clinical Research Network Portfolio Database (http://www.nihr.ac.uk/research-and-impact/nihr-clinical-research-network-portfolio/);
- The World Health Organization International Clinical Trials Registry Platform (apps.who.int/trialsearch/).

We aimed to identify all relevant studies regardless of language or publication status (published, unpublished, in press, or in progress). No date limits were applied.

Searching other resources

We have included information about potentially relevant ongoing studies in the Characteristics of ongoing studies tables. We have screened relevant systematic reviews identified by the searches for their included primary studies, and included any missed by our searches. We have checked the reference lists of all included papers, and subject experts within the author team have reviewed the final list of included studies. No citation searching has been conducted.

Data collection and analysis

Selection of studies

Titles and abstracts were screened by at least one author (JDi or NC), with any queries discussed and resolved by consensus. A pilot screen of 539 MEDLINE references showed good agreement (89% with a kappa of 0.77) between screeners. Primary test accuracy studies and test accuracy reviews (for scanning of reference lists) of any test used to investigate suspected melanoma, basal cell carcinoma (BCC), or cutaneous squamous cell carcinoma (cSCC) were included at initial screening. Inclusion criteria (Appendix 6) were applied independently by both a clinical reviewer (from one of a team of twelve clinician reviewers) and a methodologist reviewer (JDi or NC) to all full text articles, disagreements were resolved by consensus or by a third party (JDe, CD, HW, and RM). Authors of eligible studies were contacted when insufficient data were presented to allow for the construction of 2x2 contingency tables.

Data extraction and management

One clinical (as detailed above) and one methodological reviewer (JDi, NC or LFR) independently extracted data concerning details of the study design, participants, index test(s) or test combinations and criteria for index test positivity, reference standards, and data required to populate a 2x2 diagnostic contingency table for each index test using a piloted data extraction form. Data were extracted at all available index test thresholds. Disagreements were resolved by consensus or by a third party (JDe, CD, HW, and RM).

Authors of included studies were contacted where information related to the target condition (in particular to allow the differentiation of invasive cancers from '*in situ*' variants) or diagnostic threshold were missing. Authors of conference abstracts published from 2013 to 2015 were contacted to ask whether full data were available. If no full paper was identified, we marked conference abstracts as 'pending' and will revisit them in a future review update.

Dealing with multiple publications and companion papers

Where multiple reports of a primary study were identified, we maximised yield of information by collating all available data. Where there were inconsistencies in reporting or overlapping study populations, we contacted study authors for clarification in the first instance. If this contact with authors was unsuccessful, we used the most complete and up-to-date data source where possible.

Assessment of methodological quality

We assessed risk of bias and applicability of included studies using the QUADAS-2 checklist (Whiting 2011), tailored to the review topic (see Appendix 7). The modified QUADAS-2 tool was piloted on a small number of included full text articles. One clinical (as detailed above) and one methodological reviewer (JDi, NC or LFR) independently assessed quality for the remaining studies; any disagreement was resolved by consensus or by a third party where necessary (JDe, CD, HW, and RM).

Statistical analysis and data synthesis

Our unit of analysis was the lesion rather than the patient because (i) in skin cancer initial treatment is directed to the lesion rather than systemically (thus it is important to be able to correctly identify cancerous lesions for each person), and (ii) it is the most common way in which the primary studies reported data. Although there is a theoretical possibility of correlations of test errors when the same people contribute data for multiple lesions , most studies include very few people with multiple lesions and any potential impact on findings is likely to be very small, particularly in comparison with other concerns regarding risk of bias and applicability. For the diagnosis of melanoma, any BCCs or invasive cSCCs that were correctly identified by teledermatology but that were identified as melanomas in the 'disease negative' group were considered as true negative test results rather than as false positives, on the basis that excision of such lesions would be a positive outcome for the participants concerned. For the diagnosis of BCC however, any melanomas or cSCCs that were mistaken for BCCs were considered false positive results. This decision was taken on the basis that the clinical management of a lesion considered to be a BCC might be quite different to that for a melanoma or cSCC and could potentially lead to a negative outcome for the participants concerned, for example if a treatment other than excision was initiated.

For preliminary investigations of the data, estimates of sensitivity and specificity were plotted on coupled forest plots and in receiver operating characteristic (ROC) space for each index test, target condition and reference standard combination. When meta-analysis was possible and there were at least four studies, we used a bivariate model to obtain summary estimates of sensitivity and specificity (Chu 2006; Reitsma 2005). When there were less than four

studies and little or no heterogeneity was observed in ROC space, we pooled sensitivity and specificity using fixed effect logistic regression (Takwoingi 2017). Data for face-to-face diagnosis were included only if reported in comparison to teledermatology diagnosis. Using these direct (head-to-head) comparisons, a comparative meta-analysis to compare the accuracy of teledermatology with face-to-face diagnosis was not possible because there were few studies. However, we tabulated results from the studies and estimated differences in sensitivity and specificity. Since these comparative studies did not report the cross classified results of the two index tests in those with and without a particular form of skin cancer, we were unable to compute confidence intervals for the differences using methods that account for the paired nature of the data. Therefore, we assumed independence between the sensitivities and between the specificities of the two tests, and calculated 95% confidence intervals for the differences using the Newcombe-Wilson method without continuity correction (Newcombe 1998). Analyses were performed using Stata version 15 (Stata 2017).

Investigations of heterogeneity

We examined heterogeneity by visually inspecting forest plots of sensitivity and specificity, and summary ROC (SROC) plots. We were unable to perform meta-regression to investigate potential sources of heterogeneity due to insufficient numbers of studies.

Sensitivity analyses

Sensitivity analyses were not conducted due to limited data.

Assessment of reporting bias

Because of uncertainty about the determinants of publication bias for diagnostic accuracy studies and the inadequacy of tests for detecting funnel plot asymmetry (Deeks 2005), we did not perform tests to detect publication bias.

Results

Results of the search

A total of 34,347 unique references were identified and screened for inclusion. Of these, 1051 full text papers were reviewed for eligibility for any one of the suite of reviews of tests to assist in the diagnosis of melanoma or keratinocyte skin cancer; 203 publications were included in at least one review in our series and 848 publications were excluded (see Figure 3 PRISMA flow diagram of search and eligibility results).

Of the 125 studies tagged as potentially eligible for this review of teledermatology, 22 publications were included. Exclusions from the review were primarily due to: lack of test accuracy data to complete a 2x2 contingency table (31 studies), ineligible populations (38 studies) or target conditions (n = 19), not accuracy studies (n = 23) and inadequate sample size (less than five cases of skin cancer, less than five benign lesions, or for referral accuracy, less than five 'positive' cases identified by the expert diagnosis reference standard) (n = 7) or reference standards (11 studies). Of the 31 studies for which a 2x2 table could not be constructed, 11 reported only agreement between observers or between teledermatology and the reference standard and 14 had at least one piece of missing data. A list of the 103 studies with reasons for exclusion is provided in Characteristics of excluded studies, with a list of all studies excluded from the full series of reviews available as a separate pdf.

The corresponding authors of 12 studies were contacted and asked to supply further information to allow study inclusion or to clarify diagnostic thresholds or target condition definition. Responses were received from four authors allowing inclusion of all four studies to this review (Borve 2015; Mahendran 2005; Warshaw 2010; Wolf 2013). One of the four authors was not able to provide all of the information requested such that the data presented in the paper could only be partially included in this review (Warshaw 2010).

The 22 included study publications report on a total of 22 cohorts of lesions and provided 96 datasets (individual 2x2 contingency tables). Sixteen studies (73%) including 4057 lesions and 879 malignant cases reported data for the *diagnostic* accuracy of teledermatology (Arzberger 2016; Borve 2015; Bowns 2006; Congalton 2015; Coras 2003; Ferrara 2004; Grimaldi 2009; Jolliffe 2001a; Kroemer 2011; Massone 2014; Moreno Ramirez 2005; Piccolo 2000; Piccolo 2004; Silveira 2014; Warshaw 2010; Wolf 2013), five of which also reported data for the diagnostic accuracy of expert face-to-face clinical diagnosis (Coras 2003; Jolliffe 2001a; Kroemer 2011; Piccolo 2000; Warshaw 2010). Six studies (27%) including 1449 lesions reported data for the *referral* accuracy of teledermatology, i.e. teledermatology diagnosis or management action as the index test versus expert face-to-face diagnosis or management action as the reference standard (Jolliffe 2001b; Mahendran 2005; Manahan 2015; Oliveira 2002; Phillips 1998; Shapiro 2004); these studies included 270 'positive' cases as determined by the reference standard face-to-face decision. A cross-tabulation of studies by reported comparisons, target conditions and types of image used is provided in Table 1 and summary study details are presented in Appendix 8.

Studies were primarily prospective case series (n = 18; 82%), with two retrospective case series (9%) (Moreno Ramirez 2005; Piccolo 2004) and two case-control studies (9%) (Ferrara 2004; Wolf 2013), three of which retrospectively selected previously acquired images for prospective evaluation in the study (Piccolo 2004; Ferrara 2004; Wolf 2013). Studies were conducted in: Europe (n=14; 64%), including five studies from Austria (Arzberger 2016; Kroemer 2011; Massone 2014; Piccolo 2000; Piccolo 2004) and four from the UK (Bowns 2006; Jolliffe 2001a; Jolliffe 2001b; Mahendran 2005); North America (Warshaw 2010; Wolf 2013; Phillips 1998; Shapiro 2004) (n=4; 18%); or South America (Oliveira 2002 ; Shapiro 2004) (n=2; 9%); or in Australia (Manahan 2015) or New Zealand (Congalton 2015) (n=2; 9%). Eight (36.4%) studies included only pigmented (Coras 2003; Grimaldi 2009; Jolliffe 2001a; Moreno Ramirez 2005; Piccolo 2000; Wolf 2013) or melanocytic (Ferrara 2004; Piccolo 2004) lesions (Piccolo 2004 restricting to acral lesions only); the remainder

included any suspicious lesion.

Ten studies were based in primary care or community-based settings. In seven studies, lesion images were acquired in primary care (Borve 2015; Grimaldi 2009; Mahendran 2005; Massone 2014; Moreno Ramirez 2005;Oliveira 2002; Shapiro 2004), two studies were based in a community skin cancer screening outreach programme with image acquisition for 'remote' assessment by specialists in a secondary care setting (Silveira 2014) or using live transmission video-conferencing (Phillips 1998), and one recruited participants at high risk of melanoma who took images of their own lesions that they 'did not like the look of' using a smartphone (Manahan 2015). No studies were conducted in high street pharmacy type settings. Five of the ten studies reported the diagnostic accuracy of the teledermatology image-based assessment (Borve 2015; Grimaldi 2009; Massone 2014; Moreno Ramirez 2005; Silveira 2014), and five examined referral accuracy, comparing the teledermatology assessment against specialist in-person assessment (Mahendran 2005; Manahan 2015 ; Oliveira 2002 ; Phillips 1998; Shapiro 2004). Of these studies, nine were prospective in design and one was retrospective (Moreno Ramirez 2005).

In 12 studies, lesion images were acquired at a secondary care dermatology or pigmented lesion clinic (Arzberger 2016; Congalton 2015; Ferrara 2004; Jolliffe 2001a; Jolliffe 2001b; Kroemer 2011; Piccolo 2000; Piccolo 2004; Warshaw 2010 ; Wolf 2013;), from a private dermatology practice (Coras 2003) or in a medical imaging unit (Bowns 2006) at the time of the patient consultation, and remote image-based diagnoses were made by a second dermatologist. Of these studies, nine were prospective in design, two studies retrieved routinely collected lesion images for prospective 'teledermatology' examination (Piccolo 2004 ; Wolf 2013) and one did not clearly report how lesion images were acquired (Ferrara 2004). Six studies reported data only for the diagnostic accuracy of specialist image-based assessment (Arzberger 2016; Bowns 2006; Congalton 2015; Ferrara 2004; Piccolo 2004; Wolf 2013), five compared the diagnostic accuracy of image-based diagnosis to that of a dermatologist's face-to-face diagnosis (Coras 2003; Jolliffe 2001a; Kroemer 2011; Piccolo 2000; Warshaw 2010), and one examined referral accuracy, comparing specialist image-based assessment against specialist in-person assessment (Jolliffe 2001b).

Ten evaluations reported data using photographic images for teledermatology consultations (Jolliffe 2001a; Jolliffe 2001b; Kroemer 2011; Mahendran 2005; Moreno Ramirez 2005; Oliveira 2002; Shapiro 2004; Silveira 2014; Warshaw 2010; Wolf 2013), nine for a combination of clinical and dermoscopic images (Arzberger 2016; Borve 2015; Bowns 2006; Congalton 2015; Coras 2003; Grimaldi 2009; Manahan 2015 ; Massone 2014; Piccolo 2000), and three reported data for diagnosis using dermoscopic images only (Ferrara 2004; Kroemer 2011; Piccolo 2004). The final study (Phillips 1998) reported referral accuracy data for live link teledermatology using three cameras: a full-body camera, a lens for close-up views and a magnifying lens to allow magnified examination and examination with polarised light. The Warshaw 2010 paper also reported accuracy data for diagnosis using a combination of photographic and dermoscopic images, however we were unable to obtain underlying 2x2 data to allow the inclusion of this aspect of the study.

Images for store and forward teledermatology were obtained using a mobile phone camera alone (Kroemer 2011) or coupled with a dermatoscope (Borve 2015; Kroemer 2011; Manahan 2015); using still images from a video camera (Jolliffe 2001a; Jolliffe 2001b); using a combination of film and digital images (Ferrara 2004); or using a digital camera (n = 13) to acquire photographs (Mahendran 2005; Moreno Ramirez 2005; Oliveira 2002; Shapiro 2004; Silveira 2014; Warshaw 2010; Wolf 2013), dermoscopic images (Ferrara 2004; Piccolo 2004) or both (Arzberger 2016; Congalton 2015; Coras 2003; Grimaldi 2009; Massone 2014; Piccolo 2000). In Bowns 2006 photographic and dermoscopic images were acquired in a medical photography unit (equipment not described). Details of the digital cameras and mobile phones used are provided in Characteristics of included studies. Observers were provided with additional clinical information along with the digital image of the lesion in 18 studies (82%), three did not clearly report whether additional clinical information was provided (Arzberger 2016; Grimaldi 2009; Manahan 2015) and one did not provide any further patient related information (Wolf 2013). The remote observers were reported to be dermatologists in 19 (86%) studies, oncologists in one, a mixture of dermatologists and other health care professionals (e.g. oncologists, plastic surgeons) in two (9%).

In the five studies providing a direct comparison of teledermatology with in-person evaluation by a dermatologist (Coras 2003; Kroemer 2011; Jolliffe 2001a; Piccolo 2000; Warshaw 2010), diagnosis was based on visual inspection of the lesion with dermoscopy used for some (proportions not reported) (Coras 2003; Jolliffe 2001a; Kroemer 2011; Warshaw 2010) or for all lesions (Piccolo 2000). One study reported using tpattern analysis (Coras 2003), and the remaining three (50%) studies did not specify any algorithm used to aid diagnosis. The direct comparison of teledermatology with in-person evaluation by a general practitioner provided in Grimaldi 2009 was not included in this review as it is not directly relevant to teledermatology in this context.

For the 16 studies reporting diagnostic accuracy,11 (69%) used histology alone as the reference standard (Arzberger 2016; Congalton 2015; Coras 2003; Ferrara 2004; Jolliffe 2001a; Kroemer 2011; Piccolo 2000; Piccolo 2004; Silveira 2014; Warshaw 2010; Wolf 2013), three (19%) used both histology and expert opinion for some benign lesions (Borve 2015; Bowns 2006; Massone 2014) and two studies (12%) used histology and follow-up of clinically benign appearing lesions (Grimaldi 2009; Moreno Ramirez 2005). The median number of study participants was 76.5 (inter-quartile range (IQR) 48.5, 182.2) (reported in 10 studies), and median number of lesions was 116 (IQR 45, 240). The median prevalence of skin cancer was 30% (IQR 21% to 45%) and median percentage of male participants was 46% (IQR 35%, 47%) (reported in 9 studies). Where reported (8 studies), the median age was 52 years (IQR 43y, 65y) (reported in 8 studies). Four of the 16 diagnostic accuracy studies did not report the range in age of included participants (Bowns 2006; Coras 2003; Grimaldi 2009; Wolf 2013), four restricted inclusion to adults only (Borve 2015; Massone 2014; Silveira 2014; Warshaw 2010) and eight studies included participants under the age of 16 (Arzberger 2016; Congalton 2015; Ferrara 2004; Jolliffe 2001a; Kroemer 2011; Moreno Ramirez 2005; Piccolo 2002; Piccolo 2004); however data were not presented to allow

data to be extracted excluding children.

For the six studies reporting referral accuracy, the face-to-face reference standard diagnosis was made by the same dermatologist undertaking the teledermatology assessment in three studies, either within one to two weeks (Oliveira 2002; Mahendran 2005) or with a gap of several months between assessments (Jolliffe 2001b), by a dermatology trainee under the supervision of the tele-dermatologist (Manahan 2015), or a different dermatologist in two studies (Phillips 1998; Shapiro 2004). The median number of study participants was 50 (IQR 49, 72) (reported in all 6 studies), and median number of lesions was 107 (IQR 94, 253). The reported decisions of the face-to-face expert included diagnosis of malignancy (Oliveira 2002 ; Phillips 1998), decision to excise (Mahendran 2005 ; Phillips 1998 ; Shapiro 2004), or decision to see face-to-face (Jolliffe 2001b ; Manahan 2015); the median overall percentage of 'positive' expert diagnoses was 15% (IQR 10 to 41%). The median age of included participants was reported in only one study as 46.7 years (Phillips 1998); two studies reported age ranges of 8 to 94 years (Jolliffe 2001b) and 50 to 64 years (Manahan 2015) and four did not report the range in ages of included participants (Mahendran 2005 ; Oliveira 2002 ; Phillips 1998 ; Shapiro 2004). The percentage of male participants ranged from 15.7% (Phillips 1998) to 49% (Manahan 2015) (reported in three studies).

Methodological quality of included studies

The overall methodological quality of included studies is summarized in Figure 4 and Figure 5. At least half of studies were consider at high or unclear risk of bias for participant selection, reference standard and flow and timing domains while the majority were at low risk for the index test. The applicability of study findings were of high or unclear concern for the majority of studies in all domains assessed.

For participant selection, seven studies (32%) were assessed to be at low risk of bias (Borve 2015; Bowns 2006; Grimaldi 2009; Jolliffe 2001b; Mahendran 2005; Oliveira 2002; Warshaw 2010) and five (23%) studies were at high risk (Congalton 2015; Ferrara 2004; Moreno Ramirez 2005; Massone 2014; Wolf 2013). Four studies applied inappropriate participant exclusions (such as excluding poor quality images, or difficult to diagnose lesions) (Congalton 2015, Massone 2014, Moreno Ramirez 2005, Wolf 2013); and two studies used a case control type study design with separate selection of malignant cases and lesions with benign diagnosis (Ferrara 2004; Wolf 2013). Two thirds of studies (n = 14) were considered at high concern for applicability of participants, due to recruitment from secondary care or specialist clinics rather than from the primary setting in which teledermatology is more likely to be used (12/22; Arzberger 2016; Bowns 2006; Congalton 2015; Coras 2003; Jolliffe 2001a; Jolliffe 2001b; Kroemer 2011; Moreno Ramirez 2005; Piccolo 2000; Piccolo 2004; Warshaw 2010; Wolf 2013) and/or due to inclusion of multiple lesions per participant (6/22; Congalton 2015; Grimaldi 2009; Jolliffe 2001b; Kroemer 2011; Manahan 2015; Warshaw 2010). Two studies were rated as low concern for participant applicability (Oliveira 2002; Phillips 1998).

For the index test, all of the teledermatology assessments were judged at low risk of bias for the index test apart from Phillips 1998, in which it was unclear whether the teledermatology diagnoses were made blinded to the decision to the face-to-face clinician (reference standard). One study was judged of low concern for applicability of teledermatology (Massone 2014) and 12 (45%) studies were of high concern (Arzberger 2016; Bowns 2006; Congalton 2015; Coras 2003; Ferrara 2004; Jolliffe 2001a; Jolliffe 2001b; Kroemer 2011; Piccolo 2000; Piccolo 2004; Warshaw 2010; Wolf 2013), due to images acquired by dermatologists based in secondary care settings or from pigmented lesion clinic databases rather than images acquired in primary care. For the five studies reporting direct comparisons of teledermatology with face-to-face clinical diagnoses, two (40%) studies were at low risk of bias (Coras 2003; Warshaw 2010) and three (60%) were judged unclear, as the thresholds used were not clearly pre-specified (Jolliffe 2001a; Kroemer 2011; Piccolo 2000). For the comparison between tests, there was no blinding between store-and-forward teledermatology and face-to-face clinical diagnosis in Jolliffe 2001a; the remaining four comparative studies did not describe any blinding (Coras 2003; Kroemer 2011; Piccolo 2000; Warshaw 2010). One study (20%) was of low concern for applicability of the face-to face diagnosis (Coras 2003) and four of unclear concern of applicability as the thresholds used for diagnosis were not clearly reported to allow replication of methods (Jolliffe 2001a; Kroemer 2011; Piccolo 2000; Warshaw 2010).

For the reference standard domain 10 (45%) studies were at low risk of bias (Arzberger 2016; Congalton 2015; Coras 2003; Ferrara 2004; Jolliffe 2001a; Piccolo 2000; Piccolo 2004; Silveira 2014; Warshaw 2010; Wolf 2013) and twelve (55%) were rated as high risk either because they were referral accuracy studies using only expert face-to-face diagnosis as the reference standard (Jolliffe 2001b; Mahendran 2005; Manahan 2015; Oliveira 2002; Phillips 1998; Shapiro 2004) or because they were diagnostic accuracy studies that did not meet our criteria for an adequate reference standard (i.e. > 80% of lesion with histology and up to 20% with clinical follow-up; see Appendix 7) (Borve 2015; Bowns 2006; Grimaldi 2009; Kroemer 2011; Massone 2014; Moreno Ramirez 2005). Only two studies clearly reported blinding of the reference standard diagnosis to the teledermatology assessment (Phillips 1998; Shapiro 2004) and two did not implement any blinding (Oliveira 2002; Mahendran 2005); these were all referral accuracy studies. Six studies were of low concern for the applicability of the reference standard, including three of the sixteen diagnostic accuracy studies (Ferrara 2004; Piccolo 2004; Warshaw 2010) that clearly reported the level of experience of the histopathologist and three of the six referral accuracy studies that reported the expertise of the face-to-face reference standard diagnosis.

For flow and timing of participants, two referral accuracy studies were rated as low risk of bias (Jolliffe 2001b; Phillips 1998) and 17 studies (77%) were at high risk of bias; either because they did not use the same reference standard for all participants (Borve 2015; Bowns 2006; Grimaldi 2009; Massone 2014; Moreno Ramirez 2005) or they did not include all study participants in the final analysis (Arzberger 2016; Congalton 2015; Coras 2003; Jolliffe 2001a; Kroemer 2011; Mahendran 2005; Manahan 2015; Massone 2014; Moreno Ramirez 2005; Oliveira 2002; Shapiro 2004; Silveira 2014;

Warshaw 2010; Wolf 2013). For flow and timing of participants, 72% (n = 13) were high risk of bias either because they did not use the same reference standard for all participants or they did not include all study participants in the final analysis. Fourteen studies (64%) did not clearly report the interval between reference standard and index test.

Findings

Study results are summarised below according to target condition with results of meta-analyses in Table 2 with summary details in Appendix 8. Lack of data and between study variation in populations, approaches to teledermatology and target conditions considered, limited the pooled analyses that could be undertaken.

1.1 Target condition: detection of any skin cancer

The diagnostic accuracy of teledermatology assessment for the detection of the primary target condition of any skin cancer was reported in seven studies with a total of 1588 lesions and 638 cases of skin cancer. Forest plots of study data are provided in Figure 6 with results of meta-analysis in Figure 7.

Four studies compared diagnosis based on photographic images to histology (Figure 6). In three studies sensitivities for the correct diagnosis of malignancy ranged from 93% (95% CI 77% to 99%) to 100% (95% CI 75% to 100%) and specificities from 88% (95% CI 77% to 95%) to 96% (95% CI 82% to 100%) (Jolliffe 2001a; Kroemer 2011; Moreno Ramirez 2005). All three studies reported a cross-tabulation of lesion final diagnoses against the diagnosis on teledermatology such that data could be extracted for the detection of any malignancy, regardless of any misclassification of one skin cancer for another, e.g. a BCC diagnosed as a melanoma or vice versa. Similarly high sensitivity was observed in Silveira 2014 (96%, 95% CI 94% to 98%) but specificity was outlying at 25% (95% CI 14% to 39%); data here were presented for the detection of 'malignant' versus benign cases with no breakdown of individual lesion diagnoses given. The low specificity in Silveira 2014 result was likely due to the recruitment of participants with lesions deemed to be highly clinically suspicious after visual inspection of the lesion during a community screening programme; the prevalence of malignancy was 87.5% with only 52 benign cases in a sample of 416 lesions.

The pooled result across the four studies indicated summary sensitivity of 94.9% (95% CI 90.1 to 97.4%) and summary specificity 84.3% (95% CI 48.5 to 96.8%) based on 717 lesions and 452 cases of skin cancer (Table 2; Figure 7).

One study (Kroemer 2011) also reported diagnosis based on dermoscopic images only versus histology, sensitivity was lower than for assessment using photographic images (85%, 95% CI 71% to 94% versus 93%, 95% CI 82% to 99%) with similar specificities (Figure 6).

Three studies compared image-based diagnosis based on both clinical and dermoscopic images to histology for 928 lesions and 215 cases of skin cancer (Figure 6). Each study used a slightly different threshold to decide test positivity: the correct classification of lesions as malignant versus benign (Massone 2014), lesions considered malignant or possibly malignant (Borve 2015), or lesion recommended for excision (Arzberger 2016). Sensitivities were 100% in all three studies. Specificities ranged from 25% (95% CI 5% to 57%) (Arzberger 2016) to 92% (95% CI 74% to 99%) (Massone 2014). The latter was a primary care based study for which accuracy data could only be estimated for a subgroup of 32 of the original 962 lesions (Massone 2014). Arzberger 2016 included participants at particularly high risk for melanoma, while Borve 2015 included large proportions of seborrhoeic keratosis (19%) and actinic keratosis (9%) in the disease negative group. These factors may have made differentiating a malignant case from a benign one more challenging.

No statistical pooling was undertaken for these studies due to variation in threshold and heterogeneity in specificities.

Two studies compared remote image-based assessment with in-person diagnosis by a dermatologist (Jolliffe 2001a; Kroemer 2011) for the detection of any skin cancer using the same diagnostic thresholds as for the teledermatology decision. Jolliffe 2001a reported 100% (95% CI 75% to 100%) sensitivity for both assessments, while Kroemer 2011 reported 100% (95% CI 92% to 100%) sensitivity for in-person diagnosis compared to 93% (95% CI 82% to 99%) for diagnosis using photographic images and 85% (95% CI 71% to 94%) for dermoscopic image based assessment (Table 3; Figure 6). Both studies reported only marginal differences in specificity between approaches.

1.2 Target condition: invasive melanoma or atypical intraepidermal melanocytic variants

The diagnostic accuracy of teledermatology assessment for the detection of invasive cutaneous melanoma or atypical intraepidermal variants was reported in nine studies for a total of 2510 lesions with 206 melanomas (Figure 8), only two of which also reported data for the detection of any skin cancer (Table 2).

In the four studies comparing diagnosis based on photographic images to histology (1834 lesions and 106 melanomas), sensitivities ranged from 59% (95% CI 42% to 74%) to 100% (95% CI 48% to 100%) and specificities from 30% (95% CI 22% to 40%) to 100% (95% CI 93% to 100%) (Kroemer 2011; Moreno Ramirez 2005; Warshaw 2010; Wolf 2013). In three studies, the data extracted were for the correct diagnosis of melanoma whereas in Wolf 2013, lesions were classified as 'atypical' or 'typical' as opposed to reporting the correct diagnosis of melanoma. The difference in the diagnostic decision recorded in Wolf 2013 is likely to account for the low specificity observed.

The relatively low sensitivity and specificity observed in Warshaw 2010 is difficult to explain but may be related to differences in population characteristics between studies. Two studies restricted inclusion to pigmented lesions considered clinically atypical by at least one dermatologist (Wolf 2013) or meeting explicit criteria that might suggest a higher risk for melanoma (Moreno Ramirez 2005), Wolf 2013 selecting specific lesion types and excluding those with an equivocal diagnosis. Kroemer 2011 included participants with any lesion type who were either self-referred or referred by a local doctor to general dermatology clinic. Warshaw 2010 also included any lesion type (pigmented or non-pigmented) from

participants who required or requested removal of one or more skin lesions (denoted 'high risk' by the study authors) or from patients who were referred by non-dermatology healthcare providers for specialist assessment (denoted as 'lower risk'); furthermore, lesions in 30 histopathologic categories with less than 25 lesions were excluded (n=171).

Two studies compared dermoscopic image-based diagnosis to histology (Ferrara 2004; Kroemer 2011), sensitivities were between 71% (95% CI 29% to 96%) and 100% (95% CI 48% to 100%) and specificities were 60% (95% CI 15% to 95%) to 97% (95% CI 91% to 99%). Ferrara 2004 reported sensitivity of 71% (95% CI 29% to 96%) and specificity 60% (95% CI 15% to 95%) for the correct differentiation of seven melanomas from five benign lesions. Kroemer 2011 reported very similar sensitivity and specificity for the correct diagnosis of melanoma using only dermoscopic images to their result using non-magnified photographic images: sensitivities with both approaches were 100% (95% CI 48% to 100%) while specificities were 98% (95% CI 96%, 100%) using photographic images compared to 97% (95% CI 91, 99%) for dermoscopic images. Data were not presented for diagnosis using both clinical and dermoscopic images; however, the study reports that "re-evaluation of both image types in (discordant cases) did not improve the diagnostic accuracy of teleconsultations" (Kroemer 2011).

Four studies compared teledermatology based on both clinical and dermoscopic images to histology in 664 lesions with 93 cases of melanoma or atypical intraepidermal melanocytic variants (Bowns 2006; Congalton 2015; Coras 2003; Grimaldi 2009). Summary estimates of sensitivity were 85.4% (95% CI 68.3% to 94.1%) and specificity 91.6% (95% CI 81.1% to 96.5%) (Table 2; Figure 9).

Across the 10 teledermatology datasets the number of melanomas missed ranged from 0 (two datasets, both from Kroemer 2011) to 17 (Warshaw 2010).

Three studies in this group compared teledermatology assessment of images to face-to-face diagnosis by a dermatologist (Coras 2003; Kroemer 2011; Warshaw 2010) (Table 3). In Warshaw 2010, the diagnostic accuracy of teledermatology diagnosis of melanoma using photographic images and patient history was considerably lower compared to an in-person dermatologist diagnosis (using visual inspection with or without the use of dermoscopy as determined by the individual clinician); data from the author showed that sensitivity was 15% lower for teledermatology assessment (95% CI -0.33 to 0.06) and specificity was 22% lower (95% CI -0.26 to -0.19) (Table 3). The accuracy of the expert face-to-face diagnosis was nevertheless relatively low, with sensitivity of 73% (95% CI 57 to 86%) and specificity 63% (95% CI 61 to 66%) (Figure 8). The two studies comparing teledermatology diagnosis using both macro and dermoscopic images demonstrated only marginal differences between the two approaches (Coras 2003; Kroemer 2011) (Table 3).

1.3 Target condition: invasive cutaneous melanoma

The diagnostic accuracy of teledermatology assessment for the detection of invasive melanoma was reported in Piccolo 2000 for 43 lesions selected for their 'diagnostic difficulty (11 cases of melanoma) and in Piccolo 2004 for the differentiation of acral melanoma (n=6) from benign acral lesions (n=71) (Figure 10). In Piccolo 2000, the sensitivity for store-and-forward teledermatology assessment was 82% (95% CI 48% to 98%) and specificity 100% (95% CI 89% to 100%) in comparison to in-person dermatologist assessment of the same lesions where sensitivity was 73% (95% CI 39% to 94%) and specificity 97% (95% CI 84% to 100%) (one invasive melanoma missed in the face-to-face encounter was identified using teledermatology). Similar teledermatology accuracy (based on a consensus' of 6 out of 11 observers) was obtained for acral lesions in Piccolo 2004 using only dermoscopic images: observed sensitivity was 83% (95% CI 36 to 100%) and specificity 96% (95% CI 88 to 99%).

1.4 Target condition: BCC

The diagnostic accuracy of teledermatology assessment for the detection BCC was reported in four studies (Figure 11 and Figure 12):

Three evaluations of photographic images for 301 lesions with 62 cases of BCC (Jolliffe 2001a; Kroemer 2011; Moreno Ramirez 2005), produced summary estimates of sensitivity of 93.5% (95% CI 84.0% to 97.6%) and specificity 95.8% (95% CI 92.4% to 97.7%) (Table 2 and Figure 10). A total of four BCCs were missed in two studies (Kroemer 2011; Moreno Ramirez 2005).

One study (Kroemer 2011) reported lower sensitivity using dermoscopic images (80%, 95% CI 61% to 92%) compared to photographic images (90%, 95% CI 73% to 98%), due to an additional two BCCs being mistaken for actinic keratosis. A further study (Bowns 2006) reporting data only for teledermatology using clinical and dermoscopic images also reported low sensitivity for BCC of 66% (95% CI 46% to 82%). Both studies reported specificities of 93% and over (Figure 11).

A comparison with expert face-to-face assessment was provided in two studies (Table 3). Kroemer 2011 reported higher sensitivity and specificity in the face-to-face assessments and Jolliffe 2001a reported almost identical sensitivity and specificity estimates from the two approaches.

1.5 Target condition: cSCC

Kroemer 2011 also reported accuracy for the detection of cSCC in 104 lesions with 10 cases of cSCC. Sensitivities of 90% (95% CI 55% to 100%) (1 cSCC missed) were achieved for diagnosis based on photographic images and for the face-to-face assessments, with sensitivity of 60% (4 cSCCs missed) for remote assessment based on dermoscopic images (95% CI 26% to 88%) (Figure 13). Specificities were over 98% for all three approaches to diagnosis.

1.6 Referral accuracy

Six studies gave information on diagnostic decision making by teledermatology consultants compared to expert face-to-face decisions (as the reference standard) (Figure 14).

Four studies reported data for store and forward teledermatology using photographic images, either for the diagnosis of malignancy (Oliveira 2002), for the decision to excise a lesion (Mahendran 2005; Shapiro 2004), for the decision to refer versus not refer (Jolliffe 2001b) or to excise or follow-up at a later date (Mahendran 2005). Jolliffe 2001b reported data both for teledermatology by a dermatologist and by a dermatology registrar. It was not possible to pool results across these studies due to heterogeneity in the teledermatology

Perfect or almost perfect agreement between teledermatology and face-to-face consultation was observed in two studies (sensitivities 100% and specificities 98% to 100%; Oliveira 2002; Shapiro 2004), while Mahendran 2005 also reported 100% sensitivity both for the decision to excise a lesion and the decision to excise or follow-up (Figure 14). In Jolliffe 2001b the sensitivity of teledermatology by the dermatologist was 69% (95% CI 61 to 77%), with 44 lesions recommended for face-to-face consultation 'missed' by the remote observer, compared to 92% for the registrar's teledermatology assessment (12 lesions 'missed').

Specificities were more variable with 69% (95% CI 55 to 81%) and 57% (95% CI 39 to 73%) reported in Mahendran 2005 for the decision to excise a lesion and the decision to excise or follow-up a lesion and 85% (95% CI 82 to 87%) and 67% (95% CI 63 to 70%) reported in Jolliffe 2001b for the dermatologist and dermatology registrar for the decision to refer a lesion. The number of lesions recommended for some action by the teledermatogist that were not recommended for action by the ace-to-face exert in these studies ranged from 16 (Mahendran 2005) to 217 (Jolliffe 2001b).

Manahan 2015 reported the sensitivity and specificity of the teledermatogist's decision to recommend a lesion for face-to-face consultation based on macro and dermoscopic images compared to the same recommendation by the face-to-face dermatologist (301 lesions; 35 recommended for face-to-face consultation): the resulting sensitivity was 91% (95% CI 77 to 98%) with 3 lesions 'missed' and specificity was 89% (95% CI 85 to 93%) with 28 lesions recommended for a face-to-face visit that were not selected by the in-person dermatologist.

Finally, Phillips 1998 reported data for the accuracy of live link teledermatology using video conferencing compared to a dermatologist's face-to-face decision (as the reference standard) for 107 lesions. Data were reported at three different thresholds: for the correct diagnosis of a skin cancer (melanoma BCC or cSCC), for the classification of a lesion as definitely or probably malignant, and for the decision to biopsy a lesion. Sensitivities were 67% (95% CI 22 to 96%), 60% (95% CI 15 to 95%) and 82% (95% CI 48 to 98%) respectively, and specificities were 96% (95% CI 90 to 99%) for both the correct diagnosis of a skin cancer and lesions definitely or probably malignant and 86% (95% CI 78 to 93%).

Investigations of heterogeneity

We were unable to undertake planned formal investigations of heterogeneity due to insufficient number of studies.

Discussion

Although in some countries teledermatology services may provide recommendations to allow skin cancer management (including biopsy or excision) in a primary care setting, in the UK teledermatology consultations for the most part ensure that people with potentially malignant skin lesions are appropriately referred from a generalist (usually primary care) setting for specialist assessment and treatment. The primary objective of this review was therefore to assess the accuracy of teledermatology for the detection of any skin cancer in adults, comparing its accuracy with that of an in-person specialist diagnosis.

Summary of main results

We included 22 studies: 16 considering the diagnostic accuracy of image-based teledermatology (five in comparison to an in-person assessment), and six examining the referral accuracy of teledermatology assessment. Key results are presented in the Summary of findings table 1. The overall risk of bias was rated as high or unclear for participant selection, reference standard and participant flow and timing in at least half of all studies; the majority were considered at low risk of bias for the index test. The applicability of study findings were of high or unclear concern for the majority of studies in all domains assessed due to the recruitment of study participants from secondary care settings or specialist clinics rather than from the primary or community-based settings in which teledermatology is more likely to be used and due to the acquisition of lesion images by dermatologists or in specialist imaging units rather than by primary care clinicians.

Seven studies addressed our primary objective of the detection of any skin cancer. For the correct diagnosis of lesions as malignant, summary sensitivity from four studies using photographic images was 94.9% (95% CI 90.1, 97.4%) and summary specificity 84.3% (95% CI 48.5, 96.8%). Individual study estimates using dermoscopic images or a combination of photographic and dermoscopic images generally suggested similarly high sensitivities with highly variable specificities. Limited comparative data suggested similar diagnostic accuracy between teledermatology assessment and in-person diagnosis by a dermatologist however data were too scarce to draw firm conclusions.

For the detection of invasive melanoma or atypical intraepidermal melanocytic variants both sensitivities and specificities were very variable, with reported diagnostic thresholds including the correct diagnosis of melanoma, classification of lesions as 'atypical' or 'typical as well as the decision to refer or to excise a lesion. For teledermatology using photographic images, sensitivities ranged from 59% (95% CI 42% to 74%) to 100% (95% CI 54% to 100%) and specificities from 30% (95% CI 22% to 40%) to 100% (95% CI 93% to 100%) in four studies. For teledermatology using both photographic and dermoscopic images summary estimates for another four studies were 85.4% (95% CI 68.3% to 94.1%) for sensitivity and 91.6% (95% CI 81.1% to 96.5%) for specificity. The number of melanomas missed ranged from 0 to 17.

Referral accuracy data comparing teledermatology against a face-to-face reference standard was based on a number of different diagnostic decisions including the diagnosis of malignancy, the decision to excise a lesion, the decision to refer versus not refer, or to excise or follow-up at a later date. Agreement was generally good for lesions considered to require some positive action by face to face assessment (sensitivities of over 90%). For lesions considered of less concern when assessed face-to-face (e.g. for those not recommended for excision or referral), agreement was more variable with teledermatology specificities ranging from 57% (95% CI 39, 73%) to 100% (95% CI 86%, 100%), suggesting that remote assessment is more likely recommend excision, referral or follow-up compared to in-person decisions.

Sources of heterogeneity

Across all studies, wide variations in sensitivity and specificity were observed for all definitions of the target condition. Studies were generally small with varying approaches to teledermatology assessment, including the use of clinical and or dermoscopic images, use of mobile phone cameras, digital cameras or video images, and varying thresholds for deciding test positivity. The definition of the target condition also varied such that data for the primary objective could only be extracted from 7 of the 16 studies assessing diagnostic accuracy, 9 studies reporting data only for the detection of individual skin cancers. . These factors somewhat limited our ability to pool results across studies and further, to draw conclusions regarding the accuracy of teledermatology. .

Observed limitations of primary studies

Overall, four key limitations of the studies were observed:

1) the spectrum (or case mix) of different lesion types varied across studies, with a relatively high prevalence of malignant lesions

Study participants were largely recruited from secondary care settings or from pigmented lesion clinic databases rather than from primary care or other limited prior testing settings and half of studies assessing diagnostic accuracy relied on a histological reference standard, i.e. all included participants underwent lesion excision. In others, accuracy data could be extracted for less than a quarter of lesions assessed at a virtual lesion clinic (Congalton 2015) or as part of a preventative medical screening programme (Massone 2014). Recruited participants are therefore more likely to have lesions with a higher index of suspicion of malignancy compared to those for whom a GP might have considered a teledermatology assessment in practice, thereby limiting the generalisability of study results. These 'spectrum effects' are an increasingly recognised concept for medical tests, often leading to lower sensitivity and higher specificity when applied in settings with participants with limited prior testing compared to participants further down the referral pathway (Usher-Smith 2016). The direction of effect is not consistent across tests and diseases however (Leeflang 2013), the mechanisms in action often being complex and sometimes difficult to identify.

2) study definitions of 'malignancy' varied and teledermatology results were often not provided according to lesion type

In four included studies, the reported definition of malignancy did not accord with our protocol defined definition, with studies including melanoma metastases, Bowens disease or '*in situ* cSCC', actinic keratosis, or severely dysplastic naevi as 'malignant'. In some cases, data were reported to allow reclassification of these lesions as disease negative for at least some of the reported thresholds for test positivity (Borve 2015; Massone 2014), however, for others (Bowns 2006; Congalton 2015), reclassification of these lesions as disease positive was not possible and these studies could only be included in our analyses for the detection of individual skin cancers (melanoma or BCC). Other studies had to be excluded from the review altogether due to varying definitions of 'malignant' (e.g. Borve 2013; Manahan 2015a; Tandjung 2015). The lack of teledermatology results according to lesion type further limited our ability to comment on the implications of missed malignancies; the failure to pick up a melanoma or cSCC potentially carrying more severe consequences in comparison to a missed BCC.

3) the definition of a positive teledermatology result varied and was not always relevant to decision making in practice

Of the 16 diagnostic accuracy studies, only three studies reported data for the decision to excise a lesion (one for any skin cancer and two for the detection of melanoma), and five reported data for teledermatologists' classification of lesions as malignant (or probably malignant). Nine of the sixteen studies focused on teledermatologists' ability to correctly diagnose lesions as melanomas (n=8) or as BCCs (n=4) which, although of interest, is not the primary factor driving teledermatology decisions in practice where the key judgement in most circumstances is whether or not a lesion should be referred for a face-to-face consultation.

4) insufficient comparisons were available for the diagnostic accuracy of teledermatology-based diagnosis and diagnosis based on a face-to-face dermatology clinic visit

Only five of the 16 studies assessing diagnostic accuracy included a comparison of teledermatology-based diagnosis with diagnosis based on in-person diagnosis by a dermatologist; two for the detection of any skin cancer (Jolliffe 2001a; Kroemer 2011) and three for the detection of melanoma (Jolliffe 2001a; Kroemer 2011; Piccolo 2000). We were therefore unable to adequately assess whether a teledermatology diagnosis of malignancy accurately reflects a diagnosis made in-person. The six studies of referral accuracy suggest that diagnosis of individual lesions using store-and-forward teledermatology could miss around 10% of lesions recommended for clinical action (e.g. surgical excision) during a face-to-face consultation (even up to 31% in one study) and is also likely to recommend an action is required for lesions that are considered of less or no concern when seen in-person. In practice, a face-to-face consultation also allows a total body skin examination which may lead to incidental skin cancers being picked up which could also be missed by the teldermatology referral of only one or two lesions (Hanson 2016).

Our systematic review of dermoscopy as an addition to visual inspection of a lesion for the diagnosis of melanoma found in-person dermoscopy (including 26 studies) to be substantially more accurate compared to diagnosis based on dermoscopic images (including 60 studies) (RDOR 4.65, 95% CI 2.43, 9.08.5; P<0.0001) (Dinnes 2018b). Despite a number of contributing factors, including differences in study populations, different algorithms to assist test interpretation and differences in observer experience, we concluded that remote test interpretation cannot approximate a physical, face-to-face patient to clinician interaction. In particular, total body skin examination is likely to have a significant impact on the decision to excise a lesion suspected to be melanoma (Grob 1998; Argenziano 2012; Aldridge 2013). Only two of the 22 included teledermatology studies mentioned the use of total body photography (Arzberger 2016; Phillips 1998). It is notable also, that across the 60 image-based evaluations in the review of dermoscopy, half (30/60) were blinded to all other patient information and only 17 (28%) provided observers with the photographic image of the same lesion to assist test interpretation (Dinnes 2018b). It is not inconceivable that an image-based assessment with full patient information provided in the context of a proper teledermatology consultation would provide a closer approximation of the diagnostic decision that would be made with the patient present.

Strengths and weaknesses of the review

The strengths of this review include an in-depth and comprehensive electronic literature search, systematic review methods including double extraction of papers by both clinicians and methodologists, and contact with authors to allow study inclusion or clarify data. A clear analysis structure was planned to allow test accuracy to be estimated according to varying definitions of the target condition and a detailed and replicable analysis of methodologic quality was undertaken.

The main concerns for the review are the lack of studies, small sample sizes, heterogeneity in teledermatology assessments, inadequate reporting of primary studies to allow quality to be fully judged and importantly, the lack of clinical applicability of the findings due to participant recruitment from, and image acquisition in, referral settings.

In comparison to other available systematic (Ndegwa 2010; Warshaw 2011) and non systematic (Bashshur 2015; Whited 2006; Whited 2016) reviews, our review provides a focus on the triaging or diagnosis of skin cancer as opposed to the evaluation of teledermatology for any dermatological disorder. The two most recently published reviews either found evidence generally in support of teledermatology (Bashshur 2015) or suggesting inferior accuracy compared to in-person assessments for pigmented lesions (Whited 2016). We, on the other hand, were unable to identify sufficient evidence to establish the diagnostic accuracy of teledermatology in comparison to a face-to-face clinical assessment. Our reviews of the diagnostic accuracy of visual inspection of suspicious skin lesions for the detection of melanoma (Dinnes 2018a) and of dermoscopy in comparison to visual inspection of a suspicious skin lesion (Dinnes 2018b) suggest that image-based assessment may not be equivalent to a face-to-face patient: clinician interaction. However, both reviews focused on the correct diagnosis of melanoma as opposed to any skin cancer, neither included studies that were specifically designed to evaluate teledermatology programmes and did not examine any effect on accuracy from potential improvements in image quality over time.

Our *a priori* decision to exclude studies with fewer than five malignant cases could be construed as a weakness of the review; however, of the seven studies excluded on this basis, five were also excluded due other reasons such as inability to construct a 2x2 contingency table or ineligible study populations and one used multiple images of only four lesions to examine the effect of the positioning of a lesion within an image on clinicians ability to detect it (Chen 2002). The final study which was excluded only on the basis of sample size reported the effect of adding dermoscopic images to an existing teledermatology consultation system for 63 lesions fulfilling the criteria for teleconsultation (Moreno-Ramirez 2006); all three malignant lesions were correctly picked up using both photographic images and with the addition of dermoscopic images (100% sensitivities) while specificities were 65% and 78% respectively.

We were also unsuccessful in our attempts to contact the authors of 8 of 12 studies which could have been eligible for inclusion in the review, especially those studies which reported only agreement between observers or agreement with final lesion diagnoses rather than a providing results in a 2x2 contingency table format. Furthermore, only partial data was provided to allow the inclusion of one study in the review (Warshaw 2010); the review would be considerably strengthened if data for teledermatology using dermoscopic images could have been included. Finally, the review was limited to the identification of skin cancer rather than assessing the potential additional benefits of teledermatology such as positive identification of benign lesions such as actinic keratosis (Janda 2015).

Ongoing technological advances are continually improving the quality, clarity and colour-rendition of digital images taken with cameras and mobile phones. The ability to zoom in on new larger image files potentially provides even more detailed information compared to observation of a lesion with the naked eye alone. Such advances could be of particular help in the triage of lesions with no distinguishing features (for example for the identification of amelanotic melanomas), the additional magnification potentially giving subtle clues to aid diagnosis. Although we have documented the equipment used to obtain images in the included studies we are unable to identify any clear effects from changes in technology.

Our review of the diagnostic accuracy of teledermatology was also unable to evaluate a number of other pertinent factors:

i. the archiving and auditable trail provided by a teledermatology consultation. With conventional face-to-face consultations, much of the interchange is verbal and unrecorded; for teleconsultation however, every aspect of the referral and diagnostic opinion are recorded such that it can be reviewed and audited at a later date.

ii. the possibility of ‘crowd-review’ of lesion images. In-person clinical assessment is often conducted by a single clinician, consultation with other qualified clinicians reserved for more difficult lesions or to support more junior clinicians. The nature of teledermatology diagnosis lends itself to lesion review by multiple clinicians and to have virtual multidisciplinary review of cases if necessary.

iii. changing the referral behaviour of primary care clinicians. The availability of a teledermatology service could result in a specialist opinion being sought for much earlier presentations of conditions than would normally be the case, which not only changes the spectrum of lesion types observed by teledermatologists, potentially impacting on their accuracy, but could ultimately result in over diagnosis and treatment. For example, some lesions identified and either excised or treated nonsurgically following a teleconsultation might have resolved spontaneously if monitored for longer in primary care, or if referred for a standard face-to-face consultation. The effect on referral behaviour is likely to be exacerbated where ease of access to a teledermatology service for a specialist opinion may be preferred by GP trainees to seeking the opinion of a more experienced GP.

iv. possible over-reliance by GPs and reassurance for patients on a benign diagnosis from a teledermatology consultation. As with all clinical consultations, a diagnostic opinion from a teledermatology consultation is limited to the quality of the clinical information provided and the circumstances at the time of consultation. If those circumstances change, for example if a pigmented lesion diagnosed as ‘benign’ evolves or changes its nature in some way, then that lesion should be reviewed. ‘Safety-netting’ such lesions is an important part of management and monitoring in primary care.

Applicability of findings to the review question

The data included in this review are unlikely to be generally applicable to the intended setting. The majority of studies recruited participants from secondary care or referral settings rather than from primary care settings where patients are far less likely to have skin cancer, and potentially suspicious lesions are likely to be earlier in their development and evolution. Lesion images were often acquired in secondary care rather than being acquired in primary care and transmitted for a specialist opinion using teledermatology. Considerable heterogeneity in approaches to teledermatology were also observed limiting generalisability.

Authors' conclusions

Implications for practice

Studies were generally small and heterogeneous and methodological quality was difficult to judge due to poor reporting. Bearing in mind concerns regarding the applicability of study participants and of lesion image acquisition in specialist settings, our results suggest that teledermatology can be relied upon to correctly identify the majority of malignant lesions. Using a more widely defined threshold to identify ‘possibly’ malignant cases or lesions that should be considered for excision is likely to appropriately triage those lesions requiring face-to-face assessment by a specialist.

Implications for research

Despite the increasing use of teledermatology on a national and international level, the evidence base to support its ability to accurately triage lesions from primary to secondary care is lacking and further prospective and pragmatic evaluation is needed. Consecutive series of participants with suspicious skin lesions judged to require a specialist opinion by GPs should be recruited (i.e. excluding those clearly judged to be malignant or benign) and referred for store-and-forward teledermatology in comparison to routine referral to a dermatologist. The reason for referral (e.g. exclusion of melanoma to avoid an urgent or ‘2 week wait’ referral, exclusion of cSCC or BCC, or exclusion of “any skin cancer”) should be clearly recorded. “State-of-the-art” digital photography should be used (potentially utilising mobile phone cameras) to allow the full benefit of current technology to be exploited, and compared with smartphone applications, and systematic follow-up of non-excised lesions implemented to avoid over-reliance on a histological reference standard. The level of training and experience of both the referring and specialist clinicians should be explicit to allow the generalisability of results to be judged. Any future research study needs to be clear about the diagnostic pathway followed by study participants, and should conform to the updated Standards for Reporting of Diagnostic Accuracy (STARD) guideline (Bossuyt 2015).

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Contributions of authors

JD was the contact person with the editorial base.
JD and NC co-ordinated contributions from the co-authors and wrote the final draft of the review.
JD, NC, OB and JM screened papers against eligibility criteria.

JD and NC obtained data on ongoing and unpublished studies.
JD, NC, OB and JM appraised the quality of papers.
JD, NC, OB and JM extracted data for the review and sought additional information about papers.
JD and NC entered data into RevMan.
JD, NC and YT analysed and interpreted data.
JD, JJD, NC, YT and CD worked on the methods sections.
JD, FW, RM, OB, JM, RNM and HCW drafted the clinical sections of the background and responded to the clinical comments of the referees.
JD, JJD, CD and YT responded to the methodology and statistics comments of the referees.
KG and OS were the consumer co-author and checked the review for readability and clarity, as well as ensuring outcomes are relevant to consumers.
JD is the guarantor of the update.

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Differences between protocol and review

Due to the small number of studies available, a single review has been produced that evaluates the accuracy of teledermatology in all skin cancers; this replaces the two reviews intended in the protocols to separately address cutaneous melanoma and keratinocyte cancers.

Primary objectives and primary target condition have been changed from detection of cutaneous invasive melanoma alone and detection of BCC or cSCC as per the two protocols, to the detection of any skin cancer, as the appropriate triage of any malignant skin lesion to specialist care is the key issue for teledermatology. The detection of the target condition of invasive melanoma alone has instead been included as a secondary objective.

Heterogeneity investigations and sensitivity analyses were limited by the data available.

We proposed to supplement the database searches by searching the annual meetings of appropriate organisations (e.g., British Association of Dermatologists Annual Meeting, American Academy of Dermatology Annual Meeting, European Academy of Dermatology and Venereology Meeting, Society for Melanoma Research Congress, World Congress of Dermatology, European Association of Dermato Oncology), however due to volume of evidence retrieved from database searches and time restrictions we were unable to do this.

For quality assessment, the QUADAS-2 tool was further tailored according to the review topic. In terms of analysis, restriction to analysis of per patient data was not performed due to lack of data.

Published notes

Characteristics of studies

Characteristics of included studies

Arzberger 2016

Patient Selection

A. Risk of Bias	
Patient Sampling	**Study design:** Case series **Data collection:** Prospective **Period of data collection:** May to Oct 2009 **Country:** Austria
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	Unclear risk

B. Concerns regarding applicability	
Patient characteristics and setting	**Inclusion criteria:** Study participants with at least one of the following factors associated with moderate-to-high risk of melanoma: (i) personal or first-degree relative history of melanoma; (ii) history of dysplastic naevi; (iii) > 5 atypical naevi; (iv) > 100 naevi; (v) lesion suspicious for melanoma were included in the study **Setting:** Specialist Clinic (Pigmented Skin Lesion Clinic Medical Univeristy of Graz) **Prior testing:** Not reported **Setting for prior testing:** Not reported **Exclusion criteria:** None reported **Sample size (patients):** No. eligible: 70; No. included: 20 **Sample size (lesions):** No. eligible:1922; No. included: 23 **Participant characteristics:** **Age (yrs):** Range: 11-81; **Gender:** Male: 35, Female 35 **Lesion characteristics:** None reported
Are the included patients and chosen study setting appropriate?	No
Did the study avoid including participants with multiple lesions?	Yes
Are there concerns that the included patients and setting do not match the review question?	High

Index Test

Index tests	**Teledermatology** **Acquisition and transmission of images:** After clinical examination patients had total body photography performed by a by an experienced dermatology nurse or dermatology resident (took on the role of a "melanographer"), images were taken using the MoleMap program , without regard of the decision made at the FtF examination. Without regard to the medical decision resulting from the F2F evaluation, the melanographer acquired body-sector photographs (Nikon D40 and D50 digital SLR, Nikon Corporation Tokyo, Japan) and photographs of selected skin lesions were those that were: "(i) highly suspicious; (ii) concerning; (iii) changing and/or different; (iv) > 3 mm; (v) itching, bleeding, inflamed; or (vi) suspicious for basal cell carcinoma (BCC) or squamous cell carcinoma". Selected lesions had a close-up macroscopic and a dermoscopic image taken. Images were then uploaded to a centralized server in New Zealand, which was accessible to the participating TDs. **Nature of images used:** clinical and dermoscopic **Any additional patient information provided:** total body images **Observer qualifications (remote diagnosis)**; Dermatologists (experts in dermoscopy) **Diagnosis based on:** Single observer Number: 4 **Method of diagnosis:** Four remote teledermoscopy experts evaluated the total body images and dermoscopic images, and gave a recommendation for each lesion **Management options(*diagnostic threshold*):** The recommendations for management included: “self-monitoring”, “short-term monitoring” and “excision”

Teledermatology

A. Risk of Bias	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
If a threshold was used, was it pre-specified?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk

B. Concerns regarding applicability	
Was the test applied and interpreted in a clinically applicable manner?	No
Were thresholds or criteria for diagnosis reported in sufficient detail to allow replication?	Unclear
Was the test interpretation carried out by an experienced examiner?	Yes
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	High

Face to face diagnosis

A. Risk of Bias

B. Concerns regarding applicability

Reference Standard

A. Risk of Bias	
Target condition and reference standard(s)	**Reference standard:** Histology **Details:** *Histology (excision)* Lesions were selected for excision after conventional F2F total body and dermoscopic examination of all lesions, performed by an individual dermatologists with expertise in the assessment of pigmented lesions. Histopathological examination of excised lesions was performed at the Dermatopathology Laboratory at the Medical University Graz, Graz, Austria - No. patient/lesions: 23 - Disease positive: 9 - Disease negative: 14 **Target condition (Final diagnoses)** - Melanoma (invasive): 8 - Melanoma (in situ): 1 - BCC: 2 - Other: 12 melanocytic nevi
Is the reference standards likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk

B. Concerns regarding applicability	
For studies comparing teledermatology/face to face clinical diagnosis to histology, was histology interpretation carried out by an experienced histopathologist or by a dermatopathologist?	Unclear
For studies comparing teledermatology to face to face diagnosis, was the clinical diagnosis carried out by an experienced observer?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Unclear

Flow and Timing

A. Risk of Bias	
Flow and timing	50 patients were excluded from the final analysis (48 patients were discharged with the recommendation to do monthly self-skin examination and 2 patients were followed up) 20 patients had their lesions excised (included in the final analysis) The interval between index test and reference standard is not clearly reported, however it appears to be simultaneously
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
If the reference standard includes clinical follow-up of borderline/benign appearing lesions, was there a minimum follow-up following application of index test(s) of at least: 3 months for melanoma or cSCC or 6 months for BCC?	
Could the patient flow have introduced bias?	High risk

Comparative

A. Risk of Bias
Comparative

B. Concerns regarding applicability

Notes

Notes	-

Borve 2015

Patient Selection

A. Risk of Bias	
Patient Sampling	**Study design:** Case series **Data collection:** Prospective **Period of data collection** Jan 2011-Dec 2012 **Country:** Sweden
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk

B. Concerns regarding applicability	
Patient characteristics and setting	**Inclusion criteria:** All patients over 18 years of age with one or more skin lesions of concern requiring referral to a dermatologist were eligible for inclusion in the study using the TDS referral system. **Setting:** Primary this is where patients were recruited, (20 primary healthcare centres (PHCs) in western Sweden); **Prior testing:** N/A **Setting for prior testing:** N/A **Exclusion criteria:** Excluded patients were those who did not fulfil the inclusion criteria, did not attend the face-to-face (FTF) visit(s), did not comply or if their skin lesions were located on a body part that could not be photographed. **Sample size (patients):** No. eligible: 902; No. included: 816 **Participant characteristics:** **Age (yrs):** mean = 54 years (range 18-93 years) **Gender:** Females n = 474 (61.3%)) **Lesion characteristics:** Not reported
Are the included patients and chosen study setting appropriate?	Yes
Did the study avoid including participants with multiple lesions?	Unclear
Are there concerns that the included patients and setting do not match the review question?	Unclear

Index Test

Index tests	**Teledermatology** **Acquisition and transmission of images:** For all eligible participants, GPs used the smartphone TDS referral system. The GP took one clinical and one dermoscopic image using an iPhone 4 with a FotoFinder Handyscope app, alongside this a standardised query form is filled out including all the relevant clinical information. This is then sent through a secure web-based TDS platform (Tele-Dermis) with a secure socket layer encryption. Simultaneously the participating dermatologists are sent an email that a new referral is ready for assessment. **Nature of images used:** clinical photographs and dermoscopic images **Any additional patient information provided:** clinical information **Diagnosis based on:** Single; number of examiners 4 **Observer qualifications (remote diagnosis):** Dermatologist and Dermatology resident (3 specialists in dermatology and one resident in dermatology) **Method of diagnosis:** The dermatologists logged onto the Tele-Dermis® platform to review the referrals on an17- or 19-inch liquid crystal display monitor. They chose from standardised triage responses including an assessment of the nature of the lesion (benign, malignant or unclear), one or more possible diagnoses, the priority given (high, within 2 weeks; medium, within 4 weeks or low, within 8–12 weeks), suggested management (none, medical therapy, destructive therapy or surgery) and, finally, a dermoscopic description.

Teledermatology

A. Risk of Bias	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
If a threshold was used, was it pre-specified?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk

B. Concerns regarding applicability	
Was the test applied and interpreted in a clinically applicable manner?	Yes
Were thresholds or criteria for diagnosis reported in sufficient detail to allow replication?	Unclear
Was the test interpretation carried out by an experienced examiner?	Yes
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear

Face to face diagnosis

A. Risk of Bias

B. Concerns regarding applicability

Reference Standard

A. Risk of Bias	
Target condition and reference standard(s)	**Histological plus expert diagnosis** **Histology: (n=551)** **Details:** All MMs and SCCs (keratoacanthomas were classified as SCCs) were confirmed histopathologically. The final diagnosis was confirmed histopathologically in 292 TDS referrals (36%) and 259 paper referrals (35%) **Expert diagnosis (face to face diagnosis at Dermatology clinic) (n=265)** **Method of diagnosis:** Dermatologists used dermoscopy to evaluate the study lesions and also carried out full body skin examination **Prior test data:** All relevant clinical information (FTF visits were not blinded to the results of the teledermoscopists) **Diagnostic threshold:** Not reported **Diagnosis based on:** Single **Number of examiners:** Not reported **Observer qualifications:** Dermatologists (Specialists in dermoscopy) **Experience in practice:** High **Experience with index test:** High # **Target condition (Final diagnoses)** **Malignant:** Malignant melanoma: 19 (2.3%); Melanoma in-situ: 16 (2.0%); Squamous cell carcinoma: 17 (2.1%); Squamous cell carcinoma in situ: 7 (0.9%); Basal cell carcinoma: 109 (13.4%); Actinic keratosis: 61 (7.5%); Other malignant: 0 **Benign:** Dysplastic nevi: 89 (10.9%); Benign naevus: 236 (28.9%); Seborrhoeic keratosis: 125 (15.3%); Other benign: 137 (16.8%)
Is the reference standards likely to correctly classify the target condition?	No
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk

B. Concerns regarding applicability	
For studies comparing teledermatology/face to face clinical diagnosis to histology, was histology interpretation carried out by an experienced histopathologist or by a dermatopathologist?	Unclear
For studies comparing teledermatology to face to face diagnosis, was the clinical diagnosis carried out by an experienced observer?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Unclear

Flow and Timing

A. Risk of Bias	
Flow and timing	1. Excluded participants: None reported 2. Time interval to reference test: All patients were called to attend a FTF visit at the corresponding department of Dermatology. A suspicion of MM or SCC was triaged within 2 weeks. After the triage process, all patients were managed according to standard protocols at the hospitals independently of the referral method.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	No
Were all patients included in the analysis?	Yes
If the reference standard includes clinical follow-up of borderline/benign appearing lesions, was there a minimum follow-up following application of index test(s) of at least: 3 months for melanoma or cSCC or 6 months for BCC?	Yes
Could the patient flow have introduced bias?	High risk

Comparative

A. Risk of Bias
Comparative

B. Concerns regarding applicability

Notes

Notes	-

Bowns 2006

Patient Selection

A. Risk of Bias	
Patient Sampling	**Study design:** Case series **Data collection:** Prospective **Period of data collection** Not reported **Country** UK
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk

B. Concerns regarding applicability	
Patient characteristics and setting	**Inclusion criteria:** Patients (with skin lesions) who were either referred to the 2-week wait or 'target' clinics, or those initially referred to the normal outpatient service but who were diverted by the consultant on the basis of the referral form. **Setting:** Specialist unit (skin cancer/pigmented lesions clinic): **Prior testing:** - Clinical and/or dermatoscopic suspicion (Not clearly described, but all referred with certain degree of concern based on referral to 2-week wait or urgency graded by consultant based on referral letter) **Setting for prior testing:** Primary **Exclusion criteria:** Not reported **Sample size (patients):** Not reported but < 256 as a number of patients were referred for > 1 lesion, all treated as independent **Sample size (lesions):** No. eligible: 267; No. included: 256 **Participant characteristics:** Not reported **Age (yrs):** Broken down by age band; 61% were aged over 55 **Gender:** Male: 46.9% **Lesion characteristics:** Not reported
Are the included patients and chosen study setting appropriate?	No
Did the study avoid including participants with multiple lesions?	Unclear
Are there concerns that the included patients and setting do not match the review question?	High

Index Test

Index tests	**Teledermatology** **Acquisition and transmission of images:** lesion images were taken at the Medical Photography Unit (equipment not described) before an outpatient appointment with a dermatologist using both normal photographic methods and a dermatoscope. **Nature of images used:** Clinical and Dermoscopic **Any additional patient information provided:** Initial referral forms or letter provided **Method of diagnosis**: An independent dermatologist assessed the photographs and gave their most likely diagnosis and level of confidence in the diagnosis. They also gave an opinion on whether the lesion was malignant and a recommendation on whether they would wish to see the patient. **Diagnosis based on:** Single observer **Number of examiners:** 3 consultants **Observer qualifications (remote diagnosis):** Dermatologist (experience not reported)

Teledermatology

A. Risk of Bias	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
If a threshold was used, was it pre-specified?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk

B. Concerns regarding applicability	
Was the test applied and interpreted in a clinically applicable manner?	No
Were thresholds or criteria for diagnosis reported in sufficient detail to allow replication?	Unclear
Was the test interpretation carried out by an experienced examiner?	Unclear
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	High

Face to face diagnosis

A. Risk of Bias

B. Concerns regarding applicability

Reference Standard

A. Risk of Bias	
Target condition and reference standard(s)	**Reference standard: Histological diagnosis plus other** **Details:** Histology was undertaken in 164 cases, including 78/85 malignant cases and 86/171 benign cases (50.3%) **Face to Face diagnosis/Expert opinion** - Details: final diagnoses for 92 lesions reached by FtF decision only (visual inspection +/-use of dermoscopy (not specified)), including 7/85 malignant ('mainly with diagnoses of BCC or Bowen's disease') and 85/171 benign cases Number of examiners: 7 consultant dermatologists **Experience in practice:** Not reported **Experience with index test:** Not reported **Target condition (Final diagnoses as per expert clinical diagnosis and histology)** -Malignant: Melanoma (invasive): 19 - Melanoma (in situ): 5; - BCC: 29; - cSCC: 16; - Other malignant: 1 Benign: Severe dysplasia: 3; - Sebhorrheic keratosis: 70; - Benign naevus: 64; - 'Benign' diagnoses: 9 Bowen's/in situ SCC; 15 solar keratosis; 25 other benign
Is the reference standards likely to correctly classify the target condition?	No
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk

B. Concerns regarding applicability	
For studies comparing teledermatology/face to face clinical diagnosis to histology, was histology interpretation carried out by an experienced histopathologist or by a dermatopathologist?	Unclear
For studies comparing teledermatology to face to face diagnosis, was the clinical diagnosis carried out by an experienced observer?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Unclear

Flow and Timing

A. Risk of Bias	
Flow and timing	1. Excluded participants: 11 excluded - Wrong lesion imaged (n=7), Histology already undertaken (n=3), Image file lost (n=3) 2. Time interval to reference test: Medical photographs were taken immediately prior to face to face consultation. Reference diagnosis was based on face to face with or without histology. Time to histology not reported
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	No
Were all patients included in the analysis?	Yes
If the reference standard includes clinical follow-up of borderline/benign appearing lesions, was there a minimum follow-up following application of index test(s) of at least: 3 months for melanoma or cSCC or 6 months for BCC?	
Could the patient flow have introduced bias?	High risk

Comparative

A. Risk of Bias
Comparative

B. Concerns regarding applicability

Notes

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Congalton 2015

Patient Selection

A. Risk of Bias	
Patient Sampling	**Study design:** Case series **Data collection:** Prospective **Period of data collection:** 1st April 2012 to 31st of March 2013 **Country:** New Zealand
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	No
Could the selection of patients have introduced bias?	High risk

B. Concerns regarding applicability	
Patient characteristics and setting	**Inclusion criteria:** All patients referred from primary care with skin lesions suspicious for melanoma triaged via a virtual lesion clinic (VLC) instead of being seen face-to-face at a hospital clinic. Referrals that indicated 1–6 lesions of concern were included. **Setting:** Secondary (general dermatology) and Private care **Prior testing:** Clinical and/or dermatoscopic suspicion **Setting for prior testing:** Primary **Exclusion criteria:** Difficult to diagnose lesions--location/site of lesion skin lesions on scalp and genitals were generally excluded, as were those where body site was not clearly identified in the referral. **Sample size (patients):** No. eligible: 345; No. included: 310 **Sample size (lesions):** No. included: 613 **Participant characteristics:** **Age (yrs):** Median: 58; Range: 15-92 **Gender:** Male: 142; Female 168 **Race/Ethnicity (%):** White: 242 (78%); Black or African American: 12 (4%); Hispanic or Latino: 3 (<1%); Asian: 16 (5%); Other: Maori - 16 (5%)Pacific islanders - 12 (3%); Missing: 12 (4%) **Lesion characteristics:** Not reported
Are the included patients and chosen study setting appropriate?	No
Did the study avoid including participants with multiple lesions?	No
Are there concerns that the included patients and setting do not match the review question?	High

Index Test

Index tests	**Teledermatology** **Acquisition and transmission of images:** Patients attended two imaging clinics run by a private teledermatology company (MoleMap NZ). Total body photography not offered. Macroscopic and dermoscopic images were captured using a Canon G6 camera or MoleCam; regional anatomic views captured using Nikon D3100. Information on the referred lesions such as whether the patient had noticed any changes in size, colour, bleeding and itching was recorded. Hair and eye colour, skin type, previous history of sun exposure and family/personal history of skin cancers were also captured. Files were archived using proprietary software (MoleMap NZ) and uploaded to a secure server via a virtual private network. **Nature of images used:** Clinical and dermoscopic images **Any additional patient information provided:** Patient details **Diagnosis based on:** Single observer **Number of examiners** 2 **Observer qualifications (remote diagnosis):** Dermatologist **Method of diagnosis**: Using the MoleMapDiagnose software, two experienced dermatologists reviewed patient details and images remotely, making a diagnosis and suggesting management. **Management options(*diagnostic threshold*):** options included: "(i) specialist assessment or excision of the lesion; (ii) re-imaging in 3-months' time to detect change (e.g., atypical naevus without criteria for immediate excision); (iii) discharge to care of general practitioner (GP) e.g., for cryotherapy or topical therapy; (iv) self-monitoring and (v) lesion of no concern."

Teledermatology

A. Risk of Bias	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
If a threshold was used, was it pre-specified?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk

B. Concerns regarding applicability	
Was the test applied and interpreted in a clinically applicable manner?	No
Were thresholds or criteria for diagnosis reported in sufficient detail to allow replication?	Unclear
Was the test interpretation carried out by an experienced examiner?	Yes
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	High

Face to face diagnosis

A. Risk of Bias	
Were the index test results interpreted without knowledge of the results of the reference standard?	
If a threshold was used, was it pre-specified?	
Could the conduct or interpretation of the index test have introduced bias?	

B. Concerns regarding applicability	
Was the test applied and interpreted in a clinically applicable manner?	
Were thresholds or criteria for diagnosis reported in sufficient detail to allow replication?	
Was the test interpretation carried out by an experienced examiner?	
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	

Reference Standard

A. Risk of Bias	
Target condition and reference standard(s)	**Reference standard - Histology alone;** 129 lesions were excised; 123 considered suspicious for malignancy on teledermatology. 5 considered benign and 1 'undiagnosable', **Target condition (Final diagnoses as per expert clinical diagnosis and histology)** - Melanoma (in situ and invasive, or not reported): 48 - Other malignant: NMSC=45 - 'Benign' diagnoses: 32
Is the reference standards likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk

B. Concerns regarding applicability	
For studies comparing teledermatology/face to face clinical diagnosis to histology, was histology interpretation carried out by an experienced histopathologist or by a dermatopathologist?	Unclear
For studies comparing teledermatology to face to face diagnosis, was the clinical diagnosis carried out by an experienced observer?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Unclear

Flow and Timing

A. Risk of Bias	
Flow and timing	1. Excluded participants: One patient was excluded from further analysis because he attended the VLC after the referred lesion had been excised;A further 484 lesions assessed a the virtual lesion clinic but with no final diagnoses reported cannot be included. 2. Time interval to reference test: Medical photographs were taken immediately prior to face to face consultation.
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
If the reference standard includes clinical follow-up of borderline/benign appearing lesions, was there a minimum follow-up following application of index test(s) of at least: 3 months for melanoma or cSCC or 6 months for BCC?	Unclear
Could the patient flow have introduced bias?	High risk

Comparative

A. Risk of Bias	
Comparative	
Was each index test result interpreted without knowledge of the results of other index tests or testing strategies?	
Was the interval between application of the index tests less than one month?	
Are there any concerns that the test comparison could have introduced bias?	

B. Concerns regarding applicability	
Were all tests applied and interpreted in a clinically applicable manner?	
Are there concerns that the test comparison differs from the review question?	

Notes

Notes	-

Coras 2003

Patient Selection

A. Risk of Bias	
Patient Sampling	**Study design:** Case series **Data collection:** Prospective **Period of data collection** 16 month period. Does not say the date **Country** Germany
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	Unclear risk

B. Concerns regarding applicability	
Patient characteristics and setting	**Inclusion criteria:** Pigmented skin lesions undergoing excision due to diagnosis of melanoma or atypical nevus, to rule out melanoma or at the patient's request **Setting:** Secondary (general dermatology) (teledermatoscopy diagnosis); Private care- Face to face diagnosis **Prior testing:** Not reported **Setting for prior testing:** Not reported **Exclusion criteria:** None reported **Sample size (patients):** Not reported **Sample size (lesions):** No. eligible: 90; No. included: 45 **Participant characteristics:** None reported **Lesion characteristics:** None reported
Are the included patients and chosen study setting appropriate?	No
Did the study avoid including participants with multiple lesions?	Unclear
Are there concerns that the included patients and setting do not match the review question?	High

Index Test

Index tests	**In person assessment** (for those comparing FtF vs histology) **Method of diagnosis:** Participating dermatologists with experience in dermatoscopy established a clinical diagnosis based on pattern analysis after personal consultation with the patient in their private practice clinics. **Prior test data:** Not reported **Diagnostic threshold:** Not reported **Diagnosis based on:** Single **Number of examiners**: 3 **Observer qualifications:** Dermatologist (experts with great experience in dermoscopy) **Experience in practice:** High **Experience with index test:** High # **Teledermatology** **Acquisition and transmission of images:** Each of the participating dermatologists acquired digital images after face to face consultation using the same technical equipment (Dermogenius ultra - hand-held CCD camera with pixel size 512x512), and sent them via an email attachment with corresponding patient data and medical history. **Nature of images used:** Clinical photographs and dermoscopic images **Any additional patient information provided:** Clinical examination and/or case notes **Observer qualifications (remote diagnosis):** Physician experienced in dermatoscopy **Diagnosis based on:** Single observer **Method of diagnosis:** A physician evaluated the images and made a diagnosis based on the images and history of the patient **Other detail:** The participating dermatologists used the same technical equipment for the acquisition of digital images.

Teledermatology

A. Risk of Bias	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
If a threshold was used, was it pre-specified?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk

B. Concerns regarding applicability	
Was the test applied and interpreted in a clinically applicable manner?	No
Were thresholds or criteria for diagnosis reported in sufficient detail to allow replication?	Unclear
Was the test interpretation carried out by an experienced examiner?	Yes
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	High

Face to face diagnosis

A. Risk of Bias	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
If a threshold was used, was it pre-specified?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk

B. Concerns regarding applicability	
Was the test applied and interpreted in a clinically applicable manner?	Yes
Were thresholds or criteria for diagnosis reported in sufficient detail to allow replication?	Yes
Was the test interpretation carried out by an experienced examiner?	Yes
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern

Reference Standard

A. Risk of Bias	
Target condition and reference standard(s)	**Reference standard:** Histology **Details:** The histological diagnosis of majority of cases was performed at the Department of Dermatology Regensburg **Target condition (Final diagnoses)** - Melanoma (in situ and invasive, or not reported): 16 - 'Benign' diagnoses: 29
Is the reference standards likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk

B. Concerns regarding applicability	
For studies comparing teledermatology/face to face clinical diagnosis to histology, was histology interpretation carried out by an experienced histopathologist or by a dermatopathologist?	Unclear
For studies comparing teledermatology to face to face diagnosis, was the clinical diagnosis carried out by an experienced observer?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Unclear

Flow and Timing

A. Risk of Bias	
Flow and timing	1. Excluded participants: They reported that many images were of poor quality (10) and that only 45 biopsies were done 50 patients who did not have histology excluded 2. Time interval to reference test:Unclear 3. Time interval between index test(s): most likely days (email transmission of images for remote assessment).
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
If the reference standard includes clinical follow-up of borderline/benign appearing lesions, was there a minimum follow-up following application of index test(s) of at least: 3 months for melanoma or cSCC or 6 months for BCC?	
Could the patient flow have introduced bias?	High risk

Comparative

A. Risk of Bias	
Comparative	Each of the participating dermatologists who conducted a face to face clinical diagnosis acquired digital images of the lesion, and send them via an email attachment with corresponding patient data and medical history.
Was each index test result interpreted without knowledge of the results of other index tests or testing strategies?	Unclear
Was the interval between application of the index tests less than one month?	Unclear
Are there any concerns that the test comparison could have introduced bias?	Unclear risk

B. Concerns regarding applicability	
Were all tests applied and interpreted in a clinically applicable manner?	Yes
Are there concerns that the test comparison differs from the review question?	Low concern

Notes

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Ferrara 2004

Patient Selection

A. Risk of Bias	
Patient Sampling	**Study design:** Case control **Data collection:** Retrospective image selection / Prospective interpretation **Period of data collection** Not reported **Country** Not reported; likely Italy
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	No
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	High risk

B. Concerns regarding applicability	
Patient characteristics and setting	**Inclusion criteria:** Pigmented melanocytic lesions with dermoscopic images (a single image per case) and accompanying histological material were retrieved; approach to lesion selection was not described. **Setting:** Unspecified **Prior testing:** Clinical and/or dermatoscopic suspicion **Setting for prior testing:** Not reported **Exclusion criteria:** None reported **Sample size (patients):** Not reported **Sample size (lesions):** No. included: 12 **Participant characteristics:** 10 males and two females, aged 14–79 years (median 41). **Lesion characteristics:** Seven lesions had been removed from the trunk, four from the limbs and one from the face. The lesions ranged in size from 4 mm to 14 mm in diameter (median 6 mm).
Are the included patients and chosen study setting appropriate?	Unclear
Did the study avoid including participants with multiple lesions?	Unclear
Are there concerns that the included patients and setting do not match the review question?	Unclear

Index Test

Index tests	**Teledermatology** **Acquisition and transmission of images:** Dermoscopic images were either acquired on film (Dermaphot) and then digitized (n=8) or were acquired directly from a digital camera (n=4); (MoleMax or Videocap) photographic images were also available in 9/12 cases. **Nature of images used:** - dermoscopic images **Any additional patient information provided:** Clinical examination and/or case notes **Observer qualifications (remote diagnosis):** Dermatologist **Diagnosis based on:** Single observer Number of examiners: 3 **Method of diagnosis:** Stored images were viewed on a standard-resolution colour monitor by 3 remote consultants in a single session; the teledermoscopy diagnosis (melanoma or other lesion type) was recorded by a single consultant (GA), followed by a teledermatopathology diagnosis (by LC based on histological image). The original histological diagnosis from the consultation file was then presented (by GF, apparently along with the original clinical diagnosis). “Dermoscopic–pathological remarks” were made (by HPS) and finally a consensus diagnosis was reached by two consultants (LC and HPS); the latter was taken as the ‘gold standard’ for the study

Teledermatology

A. Risk of Bias	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
If a threshold was used, was it pre-specified?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk

B. Concerns regarding applicability	
Was the test applied and interpreted in a clinically applicable manner?	No
Were thresholds or criteria for diagnosis reported in sufficient detail to allow replication?	Unclear
Was the test interpretation carried out by an experienced examiner?	Yes
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	High

Face to face diagnosis

A. Risk of Bias

B. Concerns regarding applicability

Reference Standard

A. Risk of Bias	
Target condition and reference standard(s)	**Reference standard** Histological diagnosis alone **Details:** Twelve cases with dermoscopic images (a single image per case) and accompanying histological material were retrieved from consultation files. The conventional histopathology diagnosis was regarded as the gold standard: a consensus diagnosis between two consultants was requested in order to minimize any influence of the previous dermatopathology diagnosis **Target condition (Final diagnoses)** - Melanoma (in situ and invasive, or not reported): 7 - Invasive melanoma-4, Melanoma in-situ-3, 'Benign' diagnoses: 5, Junctional nevus 1; Reed naevus 1; Blue naevus 1; Actinic lentigo 1; Spitz naevus 1
Is the reference standards likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk

B. Concerns regarding applicability	
For studies comparing teledermatology/face to face clinical diagnosis to histology, was histology interpretation carried out by an experienced histopathologist or by a dermatopathologist?	Yes
For studies comparing teledermatology to face to face diagnosis, was the clinical diagnosis carried out by an experienced observer?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern

Flow and Timing

A. Risk of Bias	
Flow and timing	1. Excluded participants: Not reported 2. Time interval to reference test: images taken at time of FtF consultation; interval to excision NR 3. Time interval between index test(s): Not reported
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
If the reference standard includes clinical follow-up of borderline/benign appearing lesions, was there a minimum follow-up following application of index test(s) of at least: 3 months for melanoma or cSCC or 6 months for BCC?	
Could the patient flow have introduced bias?	Unclear risk

Comparative

A. Risk of Bias
Comparative

B. Concerns regarding applicability

Notes

Notes	-

Grimaldi 2009

Patient Selection

A. Risk of Bias	
Patient Sampling	**Study design:** Case series **Data collection:** Prospective **Period of data collection:** Oct 2005 - Mar 2006 **Country** Italy
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk

B. Concerns regarding applicability	
Patient characteristics and setting	**Inclusion criteria:** Cutaneous pigmented lesions with digital images forwarded by primary care physicians to a referral centre for confirmation of diagnosis. **Setting:** Primary (Lesions selected for referral by GPs; accuracy of GP diagnosis assessed); - Secondary (general dermatology); Telediagnosis by expert observer also assessed **Prior testing:** Not reported **Setting for prior testing:** Not reported **Exclusion criteria:** Lesions whose removal had been explicitly demanded by the patients for aesthetic reasons, as well as those irritated or subjected to trauma **Sample size (patients):** No. included: 197 **Sample size (lesions):** No. included: 235 **Participant characteristics:** Not reported **Lesion characteristics:** Not reported
Are the included patients and chosen study setting appropriate?	Yes
Did the study avoid including participants with multiple lesions?	No
Are there concerns that the included patients and setting do not match the review question?	High

Index Test

Index tests	**In person face to face clinical assessment by GP** not included in this review **Teledermatology** **Acquisition and transmission of images:** Images acquired by PCPs using Konica Minolta Dimage Z10 digital cameras (zoom 0, automatic setting, macro off, flash off) coupled with 3Gen 37 mm dermoscopes (with annular white LED lamp). All PCPs involved in the programme were asked not to start any therapy, but to send the images acquired to the reference centre first. All photographed lesions were uploaded from the peripheral units to the central research unit for telediagnosis with only a two-step judgment (before and after dermoscopy) formulated by the sending physician. **Nature of images used:** Clinical photographs; Dermoscopic images **Any additional patient information provided:** Unclear **Observer qualifications (remote diagnosis)**;Dermatologist; Plastic surgeons Number of observers: unclear **Experience in practice:** High experience or 'Expert' **Experience with index test:** Not described **Method of diagnosis:** Unclear but telediagnosis may also have followed ABCD, study states "after second appraisal of the images received made by the reference unit) the appropriate guidelines for every case, established in relation to the formulated and controlled diagnosis...When the diagnosed lesion was considered as 'needing control' by the medical staff of the reference centre, the patient was included in a periodic observation programme, according to which images of the lesions were recorded and compared at set intervals, according to a protocol If the cutaneous lesion was judged as 'needing surgery' the therapeutic programme (radical removal, sentinel lymph node biopsy, reconstructive surgery, other therapies) was carried out at the Plastic Surgery Unit of the University of Siena in all cases, after verification of the digital images and checks on the patient"

Teledermatology

A. Risk of Bias	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
If a threshold was used, was it pre-specified?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk

B. Concerns regarding applicability	
Was the test applied and interpreted in a clinically applicable manner?	Yes
Were thresholds or criteria for diagnosis reported in sufficient detail to allow replication?	Unclear
Was the test interpretation carried out by an experienced examiner?	Yes
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear

Face to face diagnosis

A. Risk of Bias	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
If a threshold was used, was it pre-specified?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk

B. Concerns regarding applicability	
Was the test applied and interpreted in a clinically applicable manner?	Yes
Were thresholds or criteria for diagnosis reported in sufficient detail to allow replication?	Yes
Was the test interpretation carried out by an experienced examiner?	Yes
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern

Reference Standard

A. Risk of Bias	
Target condition and reference standard(s)	**Reference standard:** Histological diagnosis plus follow up **Details:** Two hundred and nineteen benign lesions were investigated by dermoscopic follow up (after 2, 4 and 6 months) in the peripheral centres, and in all cases the diagnosis was confirmed (no clinical change) by telediagnosis from the main centre. These cases were subsequently controlled at regular 6 month follow-up checks. Sixteen lesions were labelled as 'to be removed' at the final check. *Histology (not further described)* No. patients/lesions: 16; Disease positive: 5; Disease negative: 11 *Clinical FU plus histology of suspicious lesions* Length of FU: 6 months - No. patients: 219; Disease positive: 0; Disease negative: 208 **Target condition (Final diagnoses)** - Melanoma (in situ and invasive, or not reported): 5 - Other: 230 benign
Is the reference standards likely to correctly classify the target condition?	No
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk

B. Concerns regarding applicability	
For studies comparing teledermatology/face to face clinical diagnosis to histology, was histology interpretation carried out by an experienced histopathologist or by a dermatopathologist?	Unclear
For studies comparing teledermatology to face to face diagnosis, was the clinical diagnosis carried out by an experienced observer?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Unclear

Flow and Timing

A. Risk of Bias	
Flow and timing	1. Excluded participants: Not reported 2. Time interval to reference test: Not reported 3. Time interval between index test(s): All the digital images from the peripheral centres (235 lesions) were forwarded to the reference centre in real time
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	No
Were all patients included in the analysis?	Yes
If the reference standard includes clinical follow-up of borderline/benign appearing lesions, was there a minimum follow-up following application of index test(s) of at least: 3 months for melanoma or cSCC or 6 months for BCC?	Yes
Could the patient flow have introduced bias?	High risk

Comparative

A. Risk of Bias	
Comparative	
Was each index test result interpreted without knowledge of the results of other index tests or testing strategies?	No
Was the interval between application of the index tests less than one month?	Yes
Are there any concerns that the test comparison could have introduced bias?	High risk

B. Concerns regarding applicability	
Were all tests applied and interpreted in a clinically applicable manner?	Yes
Are there concerns that the test comparison differs from the review question?	Low concern

Notes

Notes	-

Jolliffe 2001a

Patient Selection

A. Risk of Bias	
Patient Sampling	**Study design:** Case series **Data collection:** Prospective **Period of data collection** Not reported **Country** UK
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	Unclear risk

B. Concerns regarding applicability	
Patient characteristics and setting	**Inclusion criteria:** Patients referred by their GP for dermatological assessment of a pigmented lesion at the Pigmented Lesion Clinic **Setting:** Specialist unit (skin cancer/pigmented lesions clinic) **Prior testing:** not explicitly mention but most likely clinical examination **Setting for prior testing:** Primary **Sample size (patients):** No. eligible: 138; No. included: 138 **Sample size (lesions):** No. eligible: 144 No. included: 144-clinical diagnosis 140-telederm **Participant characteristics:** **Age (yrs):** - Range: 15-94 years **Gender:** - Male: 48 (34%) ; Female 90 (66%) **Lesion characteristics:** Not reported
Are the included patients and chosen study setting appropriate?	No
Did the study avoid including participants with multiple lesions?	Yes
Are there concerns that the included patients and setting do not match the review question?	High

Index Test

Index tests	**In person face to face clinical assessment** **Method of diagnosis:** At the Pigmented Lesion Clinic a clinical diagnosis (+/- the use of dermoscopy) based upon information in the referral letter and examination findings was made and recorded by the examining doctor **Prior test data:** Clinical examination and/or case notes **Diagnostic threshold:** Not reported **Diagnosis based on:** Single Number of examiners: 1 **Observer qualifications:** Dermatologist **Experience in practice:** Unclear **Experience with index test:** Unclear # **Teledermatology** **Acquisition and transmission of images:** The examining doctor using a single chip video camera, obtained an image of the pigmented lesion. The image was then archived using proprietary software and images were transmitted through a Fast Screen Machine2 video overlay card and viewed on a 15 inch monitor. **Nature of images used:** Clinical **Any additional patient information provided:** Clinical examination and/or case notes **Observer qualifications (remote diagnosis)**;Dermatologist **Diagnosis based on:** Single observer Number of observers:1 **Method of diagnosis:** The anonymous video images and the general practitioner's referral letter were then viewed several months later by the same doctor who performed the in-person assessment and a diagnosis made. **Management options:** Not reported

Teledermatology

A. Risk of Bias	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
If a threshold was used, was it pre-specified?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk

B. Concerns regarding applicability	
Was the test applied and interpreted in a clinically applicable manner?	No
Were thresholds or criteria for diagnosis reported in sufficient detail to allow replication?	Unclear
Was the test interpretation carried out by an experienced examiner?	Unclear
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	High

Face to face diagnosis

A. Risk of Bias	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
If a threshold was used, was it pre-specified?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk

B. Concerns regarding applicability	
Was the test applied and interpreted in a clinically applicable manner?	Yes
Were thresholds or criteria for diagnosis reported in sufficient detail to allow replication?	Unclear
Was the test interpretation carried out by an experienced examiner?	Yes
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear

Reference Standard

A. Risk of Bias	
Target condition and reference standard(s)	**Reference standard:** Histological diagnosis alone Lesions had been excised either to confirm or refute clinical suspicion of malignancy or atypia. No patient had a lesion removed on account of the study **Target condition (Final diagnoses)** **Malignant** - Melanoma (in situ and invasive, or not reported): 2; Lentigo maligna: 2; BCC: 9 **Benign diagnoses** Atypical naevus: 5; Benign melanocytic naevus: 89; Seborrhoeic keratosis: 9; Solar lentigo: 7; Blue naevus: 4; Freckle: 2; Spitz naevus: 2; Dermoid cyst: 2; Pyogenic granuloma: 2; Congenital naevus: 1; Naevus sebaceous: 1; Dermatofibroma: 1; Haemangioma: 1; Abscess: 1; Nodular hidradenoma: 1; Noncaseating granuloma: 1; Apocrine hidrocystoma: 1; Angiokeratoma circumscriptum: 1
Is the reference standards likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk

B. Concerns regarding applicability	
For studies comparing teledermatology/face to face clinical diagnosis to histology, was histology interpretation carried out by an experienced histopathologist or by a dermatopathologist?	Unclear
For studies comparing teledermatology to face to face diagnosis, was the clinical diagnosis carried out by an experienced observer?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Unclear

Flow and Timing

A. Risk of Bias	
Flow and timing	1. Excluded participants: In four cases it was impossible to make a diagnosis from the image, due to poor image quality. 2. Time interval to reference test: Not reported 3. Time interval between index test(s): The same doctor viewed the images several months after examining the patient in clinic
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
If the reference standard includes clinical follow-up of borderline/benign appearing lesions, was there a minimum follow-up following application of index test(s) of at least: 3 months for melanoma or cSCC or 6 months for BCC?	
Could the patient flow have introduced bias?	High risk

Comparative

A. Risk of Bias	
Comparative	The anonymous video images and the general practitioner's referral letter were then viewed several months later by the same doctor and a diagnosis made.the same doctor who performed the clinical examination viewed the images. The doctor's potential memory of a lesion may therefore be perceived to be a source of bias. In reality over 800 pigmented lesions had been seen by this doctor between the in-person and video examinations, making memory of a specific lesion less likely.
Was each index test result interpreted without knowledge of the results of other index tests or testing strategies?	Unclear
Was the interval between application of the index tests less than one month?	No
Are there any concerns that the test comparison could have introduced bias?	High risk

B. Concerns regarding applicability	
Were all tests applied and interpreted in a clinically applicable manner?	No
Are there concerns that the test comparison differs from the review question?	High

Notes

Notes	-

Jolliffe 2001b

Patient Selection

A. Risk of Bias	
Patient Sampling	**Study design:** Case series **Data collection:** Prospective **Period of data collection:** Not reported **Country:** UK
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk

B. Concerns regarding applicability	
Patient characteristics and setting	**Inclusion criteria:** All patients referred to the dermatology departments of the Royal Free Hospital or the Whittington Hospital during the study period by their GPs for assessment of a pigmented lesion **Setting:** Specialist unit (skin cancer/pigmented lesions clinic) **Prior testing:** GP referral for dermatological assessment at a Pigmented Lesion Clinic **Setting for prior testing:** Primary **Exclusion criteria:** None reported **Sample size (patients):** No. included: 611 **Sample size (lesions):** No. included: 819 **Participant characteristics:** **Age (yrs):** Range: 8 to 94 years **Gender:** Male: 196 (24%); Female 90 (66%) **Lesion characteristics:** Not reported
Are the included patients and chosen study setting appropriate?	No
Did the study avoid including participants with multiple lesions?	No
Are there concerns that the included patients and setting do not match the review question?	High

Index Test

Index tests	**Teledermatology** **Acquisition and transmission of images:** lesion images were taken by the examining doctor using a single-chip video camera; images were viewed on a 15-inch monitor and stored as JPEG files with minimum compression; overhead artificial illumination was used throughout and the best image used if a series were taken. **Nature of images used:** Clinical **Any additional patient information provided:** Clinical examination and/or case notes **Observer qualifications (remote diagnosis)**;Dermatologist **Diagnosis based on:** Single observer Number of observers: 3 **Method of diagnosis:** images were viewed several months later alongside GP referral information independently by all three doctors. **Management options:** The clinician made a decision whether a lesion warranted a referral or not on the basis of the image and referral information.

Teledermatology

A. Risk of Bias	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
If a threshold was used, was it pre-specified?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk

B. Concerns regarding applicability	
Was the test applied and interpreted in a clinically applicable manner?	No
Were thresholds or criteria for diagnosis reported in sufficient detail to allow replication?	Unclear
Was the test interpretation carried out by an experienced examiner?	Yes
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	High

Face to face diagnosis

A. Risk of Bias

B. Concerns regarding applicability

Reference Standard

A. Risk of Bias	
Target condition and reference standard(s)	**Reference standard:** Expert diagnosis (face to face diagnosis at Dermatology clinic) **Details:** Participants were seen in clinic by a registrar or one of two consultant dermatologists. Following history taking and clinical examination, a treatment plan was formed (reassure, review with photograph or biopsy lesion) and clinical diagnosis recorded. Clinical diagnoses were then grouped into lesions `not to be missed' (i.e. reference standard positive) including “malignant melanoma, basal cell carcinoma (BCC), atypical naevus, keratoacanthoma and pyogenic granuloma (owing to the potential clinical confusion with amelanotic melanoma)” and benign lesions (i.e. reference standard negative), including benign melanocytic naevus, seborrhoeic keratosis, congenital naevus, dermatofibroma, solar lentigo and actinic keratosis. **Target condition (Final diagnoses as per expert clinical diagnosis)** **Disease positive:** Melanoma (invasive): 9; BCC: 19; Lentigo maligna 1 **Disease negative:** Sebhorrheic keratosis:152; Benign melanocytic naevus 361; Postinflammatory hyperpigmentation 2; Blue naevus 2; Atypical naevus 112; Nail infection 2; Congenital naevus 27; Haematoma 2; Dermatofibroma 25; Eczema 2; Solar lentigo 23; Keratoacanthoma 1; Foreign body 1; Angioma 18; Abscess 1; Actinic keratosis 13; Spitz naevus 1; Fibroepithelial polyp 11; Dermoid cyst 1; Viral wart 10; Apocrine hidradenoma 1; Chloasma 1; Comedone 5; Cutaneous horn 1; Dermatosis papulosis nigrans 4; Congenital arteriovenous malformation 1; Naevus sebaceus 4; Psoriasis 1; Scar/fibrosis 3; Spider naevus 1; Pyogenic granuloma 2
Is the reference standards likely to correctly classify the target condition?	No
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk

B. Concerns regarding applicability	
For studies comparing teledermatology/face to face clinical diagnosis to histology, was histology interpretation carried out by an experienced histopathologist or by a dermatopathologist?	Yes
For studies comparing teledermatology to face to face diagnosis, was the clinical diagnosis carried out by an experienced observer?	Yes
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern

Flow and Timing

A. Risk of Bias	
Flow and timing	Patients had the FtF consultation first before having their lesions images. The images were then viewed several months later in conjunction with the GP's referral information by all three doctors independently.
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
If the reference standard includes clinical follow-up of borderline/benign appearing lesions, was there a minimum follow-up following application of index test(s) of at least: 3 months for melanoma or cSCC or 6 months for BCC?	
Could the patient flow have introduced bias?	Low risk

Comparative

A. Risk of Bias
Comparative

B. Concerns regarding applicability

Notes

Notes	-

Kroemer 2011

Patient Selection

A. Risk of Bias	
Patient Sampling	**Study design:** Not reported **Data collection:** Prospective **Period of data collection:** Reports "a 3 month period" - no dates mentioned **Country:** Austria
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Unclear risk

B. Concerns regarding applicability	
Patient characteristics and setting	**Inclusion criteria:** Patients self-referred or referred by a local doctor for evaluation of a skin tumour.men or women with benign and/or malignant skin tumours of melanocytic or nonmelanocytic origin. **Setting:** Secondary (general dermatology) Medical U of Graz, Austria. Dept of Derm **Prior testing:** Clinical suspicion of malignancy without dermatoscopic suspicion; Patient request for evaluation/excision physician or self referral **Setting for prior testing:** Primary; all patients were self referred or referred by a local doctor **Exclusion criteria:** None reported **Sample size (patients):** No. eligible: 88; No. included: 80 of 88 **Sample size (lesions):** No. eligible: 113 lesions; No. included: They report 104 of 113 tumours of 80 of 88 patients were tele-evaluated. If you add all in table 1, you get more than 113 (there were up to 3 (total 322) clinical and 3 dermoscopic (total 278) images). **Participant characteristics:** **Age (yrs):** Mean: missing; Median: 69; - Range: 3-93 **Gender:** Male: 41/88 available. Not stated who withdrew; Female 47/88 were available. Not clear who remained **Race/Ethnicity (%):** Missing: not stated, but they are Austrian **Lesion characteristics** Not reported
Are the included patients and chosen study setting appropriate?	No
Did the study avoid including participants with multiple lesions?	No
Are there concerns that the included patients and setting do not match the review question?	High

Index Test

Index tests	**In person face to face clinical assessment** **Method of diagnosis:** Not clear from paper how in-person assessment was conducted but most likely visual inspection of the skin (+/- use of dermoscopy) no algorithm described **Prior test data:** unclear **Diagnostic threshold:** unclear **Diagnosis based on:** single Number of examiners: unclear **Observer qualifications:** not reported **Experience in practice:** not reported **Experience with index test:** not reported # **Teledermatology** **Acquisition and transmission of images:** Lesions were selected during the outpatient visit and up to three clinical (autofocus mode) and dermoscopic images (macro mode) images were obtained by the clinician using a mobile phone with a built in mega-pixel camera (for clinical photos) (Nokia N73 with a built-in 3.2-megapixel camera; Nokia, Helsinki, Finland) with the addition of a pocket dermoscopy device attached to the camera lens for dermoscopic images (DermLite II PRO HR; 3Gen LLC, Dana Point, CA, U.S.A.). Images were stored in JPEG format and saved on a computer USB port. Clinical and dermoscopic datasets of each lesion together with relevant clinical information (age, sex, tumour onset, location and patient history) were separately transmitted via a virtual private network for online consultation **Nature of images used:** Clinical photographs and Dermoscopic images **Any additional patient information provided:** Clinical examination and/or case notes relevant clinical information **Observer qualifications (remote diagnosis)**; Dermatologist (board certified with clinical expertise in teledermatology and dermoscopy) **Diagnosis based on:** Single observer; n = 1 **Method of diagnosis:** A board-certified dermatologist (H.P.S.) with clinical expertise in teledermatology and dermoscopy reviewed each set of clinical and dermoscopic images separately. The lesions were grouped into four diagnostic categories (benign melanocytic, benign nonmelanocytic, malignant melanocytic and malignant non-melanocytic skin tumours). The teleconsultant based on this then recorded one primary and one differential diagnosis

Teledermatology

A. Risk of Bias	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
If a threshold was used, was it pre-specified?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk

B. Concerns regarding applicability	
Was the test applied and interpreted in a clinically applicable manner?	No
Were thresholds or criteria for diagnosis reported in sufficient detail to allow replication?	Yes
Was the test interpretation carried out by an experienced examiner?	Yes
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	High

Face to face diagnosis

A. Risk of Bias	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
If a threshold was used, was it pre-specified?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk

B. Concerns regarding applicability	
Was the test applied and interpreted in a clinically applicable manner?	Yes
Were thresholds or criteria for diagnosis reported in sufficient detail to allow replication?	Unclear
Was the test interpretation carried out by an experienced examiner?	Yes
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear

Reference Standard

A. Risk of Bias	
Target condition and reference standard(s)	**Reference standard:** Histological diagnosis and Expert diagnosis **Details:** Histopathology was used as the gold standard in 78/104 (75%), including for 32/58 benign lesions (55%) . According to ethical principles and to the standards of routine practice, the clinical and dermoscopic face-to-face (FTF) diagnoses were considered adequate in those patients with clinically and dermoscopically benign and nonsuspicious lesions (i.e. 44% of benign group), and no biopsy procedure was performed. **Target condition (Final diagnoses)** **Malignant** - Melanoma (invasive): 2, Melanoma (in situ): 1, BCC: 30, cSCC:10, Lentigo maligna: 3 **Benign** - Sebhorrhoeic keratosis: 6, Actinic keratosis: 17, Bowen's disease 1, Benign naevus:15, Other: Soft tissue tumour 4, angioma 4 , solar lentigo 3, virus induced tumour 1, trichilemmoma 0, and other 7
Is the reference standards likely to correctly classify the target condition?	No
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk

B. Concerns regarding applicability	
For studies comparing teledermatology/face to face clinical diagnosis to histology, was histology interpretation carried out by an experienced histopathologist or by a dermatopathologist?	Unclear
For studies comparing teledermatology to face to face diagnosis, was the clinical diagnosis carried out by an experienced observer?	Unclear
Are there concerns that the target condition as defined by the reference standard does not match the question?	Unclear

Flow and Timing

A. Risk of Bias	
Flow and timing	1. Excluded participants: 3 patients declined participation. In 33% of cases, no history could be obtained. 2 clinical and 18 dermoscopic pictures were inadequate, so 104 tumours from 80 patients were included 2. Time interval to reference test: It does not state 3. Time interval between index test(s): It says there was a month delay between clinical and dermoscopic telederm picture evaluation
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
If the reference standard includes clinical follow-up of borderline/benign appearing lesions, was there a minimum follow-up following application of index test(s) of at least: 3 months for melanoma or cSCC or 6 months for BCC?	
Could the patient flow have introduced bias?	High risk

Comparative

A. Risk of Bias	
Comparative	There was a month delay between face to face assessment and clinical and dermoscopic telederm evaluation
Was each index test result interpreted without knowledge of the results of other index tests or testing strategies?	Unclear
Was the interval between application of the index tests less than one month?	Yes
Are there any concerns that the test comparison could have introduced bias?	Unclear risk

B. Concerns regarding applicability	
Were all tests applied and interpreted in a clinically applicable manner?	No
Are there concerns that the test comparison differs from the review question?	High

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Mahendran 2005

Patient Selection

A. Risk of Bias	
Patient Sampling	**Study design:** Case series **Data collection:** Prospective **Period of data collection:** no dates, but over 18 months **Country:** UK
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk

B. Concerns regarding applicability	
Patient characteristics and setting	**Inclusion criteria:** Patients with a suspicious skin lesion seen by their local GP, had to have a lesion worthy of dermatologist assessment, had to be willing to have photographic images taken of the lesion, had to be willing to see a dermatologist outpatient **Setting:** Primary this is where patients were recruited; Secondary (general dermatology) This is where the final diagnosis was made **Prior testing:** Clinical suspicion of malignancy without dermatoscopic suspicion **Setting for prior testing:** Primary **Exclusion criteria:** 15% Poor quality index test image **Sample size (patients):** No. included: unclear **Sample size (lesions):** No. included: 106 **Participant characteristics:** None reported **Lesion characteristics** Not reported
Are the included patients and chosen study setting appropriate?	Yes
Did the study avoid including participants with multiple lesions?	Unclear
Are there concerns that the included patients and setting do not match the review question?	Unclear

Index Test

Index tests	**Teledermatology** **Acquisition and transmission of images:** GPs took images of suspicious skin lesions using a digital camera (Nikon Coolpix 950 digital camera (1200 x 1600 pixel resolution), the photograph together with all the relevant history and details about the skin lesion were sent via email to the dermatology department **Nature of images used:** Clinical photographs **Any additional patient information provided:** Past history; dermographics, site of lesion **Observer qualifications (remote diagnosis)**; Dermatologist (Consultant dermatologists) **Diagnosis based on:** Single observer (diagnosis made by one of 2 consultants) **Method of diagnosis:** The remote observer gave a diagnosis or differential diagnosis plus a hypothetical management plan where possible. **Management options:** Management options included reassuring the patient, minor operation, no action but further review appointment required

Teledermatology

A. Risk of Bias	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
If a threshold was used, was it pre-specified?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk

B. Concerns regarding applicability	
Was the test applied and interpreted in a clinically applicable manner?	Yes
Were thresholds or criteria for diagnosis reported in sufficient detail to allow replication?	Unclear
Was the test interpretation carried out by an experienced examiner?	Yes
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear

Face to face diagnosis

A. Risk of Bias

B. Concerns regarding applicability

Reference Standard

A. Risk of Bias	
Target condition and reference standard(s)	**Reference standard: Expert diagnosis (face to face diagnosis at Dermatology clinic)** **Details:** All of the patients were subsequently seen in the dermatology outpatient clinic by one of the same two consultants within 2 weeks and the clinical diagnosis and actual management plan were recorded; lesions also seen FTF by a trainee dermatologist (specialist registrar year 3) 'blinded' to the consultants' reports but the 2x2 data appear to be for the consultant FTF assessment **Target condition (Final diagnoses)** **Malignant** - Melanoma (invasive): 4, BCC: 37, cSCC 4 **Benign diagnoses** - AK 10, Bowen's 7, SC 4; Lentigo maligna 1; - atypical dysplastic nevi 6; Sebhorrheic keratosis: 27; Benign naevus: 20; Other: dermatofibroma 11; Inflammatory dermatoses 8; Haemangioma 3; Scar 3; Viral wart 3; Cellular naevus 2; Chondrodermatitis nodularis helices 2; Congenital naevus 2; Dilated pore of Winer 2; Lesion resolved 2; Squamous papilloma 2; Blue naevus 1; Halo naevus 1; Lichenoid keratosis 1; Myxoid cyst 1; Pressure sore 1; Pyogenic granuloma 1; Sebaceous gland hyperplasia 1
Is the reference standards likely to correctly classify the target condition?	No
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk

B. Concerns regarding applicability	
For studies comparing teledermatology/face to face clinical diagnosis to histology, was histology interpretation carried out by an experienced histopathologist or by a dermatopathologist?	Yes
For studies comparing teledermatology to face to face diagnosis, was the clinical diagnosis carried out by an experienced observer?	Yes
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern

Flow and Timing

A. Risk of Bias	
Flow and timing	1. Excluded participants: 57 'excluded' as could not be managed by TD and no FtF decision given; either insufficient quality for assessment (n=24) or need to see in clinic to make a decision 2. Time interval to reference test: within 2 weeks 3. Time interval between index test(s): not stated
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
If the reference standard includes clinical follow-up of borderline/benign appearing lesions, was there a minimum follow-up following application of index test(s) of at least: 3 months for melanoma or cSCC or 6 months for BCC?	Yes
Could the patient flow have introduced bias?	High risk

Comparative

A. Risk of Bias
Comparative

B. Concerns regarding applicability

Notes

Notes	-

Manahan 2015

Patient Selection

A. Risk of Bias	
Patient Sampling	**Study design:** Case series **Data collection:** Prospective **Period of data collection:** NR **Country:** Australia
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Unclear risk

B. Concerns regarding applicability	
Patient characteristics and setting	**Inclusion criteria:** Participants aged 50–64 years at high risk of melanoma (fair skin type, previous skin excisions, personal or family history) recruited via the 'QSkin' study (500/43,794 participants were mailed an invitation to participate; plus volunteers who requested participation (n=59) after learning about the study via university websites or in the local news. Only those with a suitable smartphone could participate. Participants instructed to submit "photos of moles or spots that they 'did not like the look of'", and were given instructions about how to select lesions based on asymmetry and colour. **Setting:** Community **Prior testing:** None **Setting for prior testing:** N/A **Exclusion criteria:** No smartphone **Sample size (patients):** 500 (invited) plus 58 volunteers; Of the 230 who completed the questionnaire, the first 58 who expressed interest and had a suitable smartphone were enrolled. 50 attended for FtF skin examination, 1 of whom was later excluded **Sample size (lesions):** 341 lesions included; 309 with a primary teledermatology diagnosis **Participant characteristics:** **Age (yrs):** 50 to 64 yrs; **Gender**: 49% male; Other: 31% with first-degree family member with melanoma and 90% self-reported a fair skin type **Lesion characteristics:** Back 106 (34%); Chest/abdomen 57 (18%); Legs 56 (18%); Arms 46 (15%); head/neck 44 (14%)
Are the included patients and chosen study setting appropriate?	Unclear
Did the study avoid including participants with multiple lesions?	No
Are there concerns that the included patients and setting do not match the review question?	High

Index Test

Index tests	**Teledermatology** **Acquisition and transmission of images:** Study primarily aimed to evaluate skin self-examination (SSE) (participants randomised to receive 10-step guide to SSE) and mobile teledermatology. All participants used Handyscope FotoFinder dermoscope smartphone attachment (FotoFinder Systems GmbH, Bad Birnbach, Germany) and Handyscope app, to obtain and send magnified lesion image along with a second clinical (macro) image to verify the anatomical site of each skin lesion. **Nature of images used:** Clinical and dermoscopic **Any additional patient information provided:** **Diagnosis based on:** Single observer **Number of examiners:** n=1 **Observer qualifications (remote diagnosis):** Board certified dermatologist, experienced in teledermatology **Method of diagnosis:** Unclear; method of viewing images not reported. Dermatologist indicated whether the photograph was suitable to provide a diagnosis before making management recommendation. **Management options:** primary diagnosis, with up to two differential diagnoses (cannot extract 2x2), and whether clinical skin examination (FtF) was required (Action).

Teledermatology

A. Risk of Bias	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
If a threshold was used, was it pre-specified?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk

B. Concerns regarding applicability	
Was the test applied and interpreted in a clinically applicable manner?	Unclear
Were thresholds or criteria for diagnosis reported in sufficient detail to allow replication?	Unclear
Was the test interpretation carried out by an experienced examiner?	Yes
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear

Face to face diagnosis

A. Risk of Bias

B. Concerns regarding applicability

Reference Standard

A. Risk of Bias	
Target condition and reference standard(s)	**Reference standard:** Face-to-face expert diagnosis (referral accuracy) **Details:** Clinical skin examination performed by a dermatology registrar under supervision of the dermatologist who undertook the telediagnosis.The same management options were recommended in the FtF consultation **Target condition (Clinical diagnoses FtF)** **Malignant:** BCC 13; SCC/IEC 1 **Benign**: Atypical naevus 4; benign naevus 165; solar lentigo 22; Sebhorrheic keratosis 81. Non-pigmented: actinic keratosis 34; dermatofibroma 2; other 18 **Recommendation to see FtF (ref standard):** 35
Is the reference standards likely to correctly classify the target condition?	No
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk

B. Concerns regarding applicability	
For studies comparing teledermatology/face to face clinical diagnosis to histology, was histology interpretation carried out by an experienced histopathologist or by a dermatopathologist?	
For studies comparing teledermatology to face to face diagnosis, was the clinical diagnosis carried out by an experienced observer?	Unclear
Are there concerns that the target condition as defined by the reference standard does not match the question?	Unclear

Flow and Timing

A. Risk of Bias	
Flow and timing	**Excluded participants:** 8 /58 participants did not attend for FtF examination; 1/58 outwith age restriction; 32/341 lesions did not appear to have a primary teledermatology diagnosis **Time interval to reference test:** not reported **Time interval between index test(s): N/A**
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
If the reference standard includes clinical follow-up of borderline/benign appearing lesions, was there a minimum follow-up following application of index test(s) of at least: 3 months for melanoma or cSCC or 6 months for BCC?	
Could the patient flow have introduced bias?	High risk

Comparative

A. Risk of Bias
Comparative

B. Concerns regarding applicability

Notes

Notes	-

Massone 2014

Patient Selection

A. Risk of Bias	
Patient Sampling	**Study design:** Case series **Data collection:** Prospective **Period of data collection:** February 2008 to February 2010 **Country:** Austria
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Unclear
Did the study avoid inappropriate exclusions?	No
Could the selection of patients have introduced bias?	High risk

B. Concerns regarding applicability	
Patient characteristics and setting	**Inclusion criteria:** Patients undergoing health screening for a health insurance company at three preventive health care centres in Austria selected by general practitioners (GP) for second-opinion teleconsulting as part of a preventative medical screening programme **Setting:** Private care **Prior testing:** Clinical and/or dermatoscopic suspicion **Setting for prior testing:** Private care **Exclusion criteria:** Poor quality index test image **Sample size (patients):** No. eligible: 112; No. included: 30 **Sample size (lesions):** No. eligible: 121; No. included: 32 **Participant characteristics:** **Age (yrs):** Mean: 47; Median: 47; Range: 18-84 **Gender:** Male: not reported for the number of patients for which data is presented only given the overall number from eligible patients 642 (93%) Female not reported for the number of patients for which data is presented only given the overall number from eligible patients 48 (7%) **Lesion characteristics:** not reported
Are the included patients and chosen study setting appropriate?	Unclear
Did the study avoid including participants with multiple lesions?	Yes
Are there concerns that the included patients and setting do not match the review question?	Unclear

Index Test

Index tests	**Teledermatology** **Acquisition and transmission of images:** GPs screened patients and if they noted a suspicious skin lesion then they acquired dermoscopic and if needed photographic images of the same skin lesion. photographic images were taken using a digital camera, with the addition of a polarised light contact dermatoscope for the dermoscopic images (Canon Powershot digital camera (Canon Inc., Tokyo, Japan) and DermLite Photo; 3Gen LLC, San Juan Capistrano, CA, USA) adjusted from MoleMax System (Derma Medical Systems, Vienna, Austria)). Images correlated by only age, sex and location of the lesion were transmitted via a virtual private network for teleconsultation. No personal patients' data were transmitted. **Nature of images used:** Clinical photographs and dermoscopic images **Any additional patient information provided:** age, sex and location of the lesion **Diagnosis based on:** Single observer **Number of examiners:** 2 **Observer qualifications (remote diagnosis):** Dermatologist (with high experience of dermoscopy) **Method of diagnosis:** One of two dermatologists reviewed the images within 48hrs. They first reviewed the quality of images on a 3-point scale, ranging from excellent (1) to low quality (3). Secondly they assessed the lesion and grouped them into one of four groups (1) benign melanocytic, (2) malignant melanocytic, (3) benign non-melanocytic and (4) malignant non-melanocytic lesions and defined them according to WHO guidelines. **Management options:** They also recorded management of the patient as follows "(i) no further treatment or follow-up in 3, 6 or 12 months interval in case of benign skin lesions, (ii) referral to a local dermatologist for FTF examination in case of suspicious skin lesions and (iii) excision in case of suspected malignancy."

Teledermatology

A. Risk of Bias	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
If a threshold was used, was it pre-specified?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk

B. Concerns regarding applicability	
Was the test applied and interpreted in a clinically applicable manner?	Yes
Were thresholds or criteria for diagnosis reported in sufficient detail to allow replication?	Yes
Was the test interpretation carried out by an experienced examiner?	Yes
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Low concern

Face to face diagnosis

A. Risk of Bias

B. Concerns regarding applicability

Reference Standard

A. Risk of Bias	
Target condition and reference standard(s)	**Reference standard:** Histological diagnosis plus Face to Face diagnosis/Expert opinion **Details:** Patients visiting the health care centres were coming from different towns of Austria therefore no institutions were specifically recommended but the patients were free to select a dermatologist of their choice for further assessment. No feedback was requested, it was possible to collect follow up data only for the patients referred to the Department or that responded to a phone call or a letter. Of these cases only 19 had histology and 13 had a face to face expert assessment. *Histology (not further described)* - No. patients/lesions: 19; Disease positive: 7; Disease negative: 12 *Expert opinion* - No. patients: 13; Disease positive: 0; Disease negative: 13 **Target condition (Final diagnoses)** **Malignant** Melanoma: 2, BCC: 5 **Benign** Dysplastic nevi: 11, Sebhorrheic keratosis: 4, Other: Angioma=2 Porokeratosis=1 Actinic keratosis=1
Is the reference standards likely to correctly classify the target condition?	No
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk

B. Concerns regarding applicability	
For studies comparing teledermatology/face to face clinical diagnosis to histology, was histology interpretation carried out by an experienced histopathologist or by a dermatopathologist?	Unclear
For studies comparing teledermatology to face to face diagnosis, was the clinical diagnosis carried out by an experienced observer?	Unclear
Are there concerns that the target condition as defined by the reference standard does not match the question?	Unclear

Flow and Timing

A. Risk of Bias	
Flow and timing	1. Excluded participants: it was possible to collect follow up data only for the patients referred to the Department or that responded to a phone call or a letter. A total of 112 patients were eligible as attending the department of dermatology but of these 82 patients were lost to follow up 2. Time interval to reference test: not reported 3. Time interval between index test(s): not reported
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	No
Were all patients included in the analysis?	No
If the reference standard includes clinical follow-up of borderline/benign appearing lesions, was there a minimum follow-up following application of index test(s) of at least: 3 months for melanoma or cSCC or 6 months for BCC?	
Could the patient flow have introduced bias?	High risk

Comparative

A. Risk of Bias
Comparative

B. Concerns regarding applicability

Notes

Notes	-

Moreno Ramirez 2005

Patient Selection

A. Risk of Bias	
Patient Sampling	**Study design:** Case series **Data collection:** Retrospective **Period of data collection:** between January and April 2004 **Country:** Spain
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	Unclear risk

B. Concerns regarding applicability	
Patient characteristics and setting	**Inclusion criteria:** Patients with pigmented, circumscribed lesions fulfilling at least one of the following criteria: a changing lesion ('ABCD changes'), recent lesion (less than three-year history), multiple lesions (more than 20 melanocytic naevi counted by the GP), symptomatic lesion (pain, itching, bleeding),or concerned about moles. **Setting:** Specialist unit (skin cancer/pigmented lesions clinic) **Prior testing:** Most likely clinical examination (the reasons for teleconsultation were listed as concern about moles; recent pigmented lesion; changing lesions; symptoms; multiple lesions) **Setting for prior testing:** Unspecified **Exclusion criteria:** Not reported **Sample size (patients):** No. eligible: 219; No. included: 57 patients included in the final analysis **Participant characteristics:** **Age (yrs):** Mean: 43 years; Range: 2-84years **Gender:** Male: 77 (35%); Female 142 (65%) **Lesion characteristics:** not reported
Are the included patients and chosen study setting appropriate?	No
Did the study avoid including participants with multiple lesions?	Unclear
Are there concerns that the included patients and setting do not match the review question?	High

Index Test

Index tests	**Teledermatology** **Acquisition and transmission of images:** Two digital pictures were taken by the GP using a digital camera at a resolution of 1600x1200 pixels (Coolpix 4300, Nikon). A panoramic view of the lesion area and a close up of the lesion were taken. Images were inserted into a word document with relevant clinical information. This was transmitted via the intranet to an email account at the pigmented lesion clinic (PLC). **Nature of images used:** Clinical photographs **Any additional patient information provided:** Clinical examination and/or case notes **Diagnosis based on:** Unclear how many remote observers Number of examiners: not reported **Observer qualifications (remote diagnosis):** Dermatologist **Method of diagnosis:** At the teleconsultation, observers classified the lesions as being either "benign melanocytic naevus, multiple melanocytic naevi (>20 naevi as seen on teleconsultation), atypical naevus,7 congenital naevus, blue naevus, solar lentigo, lentigo maligna, melanoma, special melanocytic lesion (genital naevus, acral naevus, recurrent naevus), seborrhoeic keratoses, basal cell carcinoma (BCC), dermatofibroma, vascular lesion, non-pigmented lesion, or a 'difficult to diagnose' lesion". After evaluation of the pictures and clinical information, a report was returned to the GP at the primary-care centre, with suggestions regarding the diagnosis and management of the case **Management options:** The management options were limited to 'referral' or 'non-referral' of the patient to the face-to-face clinic. Patients who had readily identifiable benign lesions such as benign melanocytic naevus, solar lentigo, seborrhoeic keratoses, dermatofibroma, vascular lesions and non-pigmented lesions were not referred to the PLC. All other remaining categories were routinely referred to the PLC for face to face assessment.

Teledermatology

A. Risk of Bias	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
If a threshold was used, was it pre-specified?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk

B. Concerns regarding applicability	
Was the test applied and interpreted in a clinically applicable manner?	Yes
Were thresholds or criteria for diagnosis reported in sufficient detail to allow replication?	Unclear
Was the test interpretation carried out by an experienced examiner?	Yes
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear

Face to face diagnosis

A. Risk of Bias

B. Concerns regarding applicability

Reference Standard

A. Risk of Bias	
Target condition and reference standard(s)	**Reference standard:** Histological diagnosis plus face to face diagnosis/Expert opinion **Details**: At the PLC, physical and dermoscopic examinations were carried out, as well as excisional biopsy in suspicious or malignant cases, and follow-up of patients with risk factors for melanoma (16/25 benign underwent histology) **Target condition (Final diagnoses)** - Melanoma (in situ): 1, BCC: 23, Lentigo maligna 3 - dysplastic nevi 16, common nevi 8 Blue nevi 4
Is the reference standards likely to correctly classify the target condition?	No
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk

B. Concerns regarding applicability	
For studies comparing teledermatology/face to face clinical diagnosis to histology, was histology interpretation carried out by an experienced histopathologist or by a dermatopathologist?	Unclear
For studies comparing teledermatology to face to face diagnosis, was the clinical diagnosis carried out by an experienced observer?	Unclear
Are there concerns that the target condition as defined by the reference standard does not match the question?	Unclear

Flow and Timing

A. Risk of Bias	
Flow and timing	1. Excluded participants: difficult to diagnosis cases excluded 2. Time interval to reference test: unclear--only mention "Teleconsultation reports were sent to the GP in a mean time of 44 h (range 2–96 h). Patients referred to the face-to-face clinic were seen within the following two weeks (mean¼8 days, range 5–14). Dermatologistsat the PLC spent an average of 2.3 h per week in evaluating the teleconsultations received." 3. Time interval between index test(s): N/A
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	No
Were all patients included in the analysis?	No
If the reference standard includes clinical follow-up of borderline/benign appearing lesions, was there a minimum follow-up following application of index test(s) of at least: 3 months for melanoma or cSCC or 6 months for BCC?	
Could the patient flow have introduced bias?	High risk

Comparative

A. Risk of Bias
Comparative

B. Concerns regarding applicability

Notes

Notes	-

Oliveira 2002

Patient Selection

A. Risk of Bias	
Patient Sampling	**Study design:** Case series **Data collection:** Unclear but appears prospective **Period of data collection:** NR **Country:** Brazil
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk

B. Concerns regarding applicability	
Patient characteristics and setting	**Inclusion criteria:** Participants with suspect dermatological identified by an assistant nurse who had undergone training to identify potentially malignant skin lesions. Only those who attended for face-to-face assessment were included. **Setting:** Primary care; Centro de Saúde Escola Geraldo de Paula Souza (primary care public health service) **Prior testing:** None **Setting for prior testing:** N/A **Exclusion criteria:** None reported **Sample size (patients):** 103 eligible; 90 included **Sample size (lesions):** 90 **Participant characteristics:** NR **Lesion characteristics:** NR
Are the included patients and chosen study setting appropriate?	Yes
Did the study avoid including participants with multiple lesions?	Yes
Are there concerns that the included patients and setting do not match the review question?	Low concern

Index Test

Index tests	**Teledermatology** **Acquisition and transmission of images:** Lesions photographed in primary care by an assistant nurse using a Kodak DC265 Zoom digital camera. 2 hr training in the use of the camera was provided and included instruction on the installation of the camera's software and transferring the images to the PC. Images were sent by nurse with an electronic case report form and included her diagnostic impression whether the lesion was non-malignant or malignant **Nature of images used:** Clinical **Any additional patient information provided:** Patient record **Diagnosis based on:** Single observer **Number of examiners:** 1 **Observer qualifications (remote diagnosis):** Dermatologist from the Department of Dermatology of the Faculty of Medicine of the University of São Paulo **Method of diagnosis:** Not clearly described. All cases were assessed remotely by a dermatologist prior to the in-person evaluation **Management options:** Malignant or benign; malignant diagnosis indicated biopsy needed

Teledermatology

A. Risk of Bias	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
If a threshold was used, was it pre-specified?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk

B. Concerns regarding applicability	
Was the test applied and interpreted in a clinically applicable manner?	Yes
Were thresholds or criteria for diagnosis reported in sufficient detail to allow replication?	Unclear
Was the test interpretation carried out by an experienced examiner?	Unclear
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear

Face to face diagnosis

A. Risk of Bias

B. Concerns regarding applicability

Reference Standard

A. Risk of Bias	
Target condition and reference standard(s)	**Reference standard:** Expert diagnosis (referral accuracy) **Details:** Within a week the same dermatologist saw the patient in-person. Patients were referred for biopsy when skin cancer was the suspected diagnosis. The in person assessments by the dermatologist (and the biopsy results in a few cases) were used as reference. **Target condition (FtF diagnoses)** **Malignant** **Benign**
Is the reference standards likely to correctly classify the target condition?	No
Were the reference standard results interpreted without knowledge of the results of the index tests?	No
Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk

B. Concerns regarding applicability	
For studies comparing teledermatology/face to face clinical diagnosis to histology, was histology interpretation carried out by an experienced histopathologist or by a dermatopathologist?	
For studies comparing teledermatology to face to face diagnosis, was the clinical diagnosis carried out by an experienced observer?	Unclear
Are there concerns that the target condition as defined by the reference standard does not match the question?	Unclear

Flow and Timing

A. Risk of Bias	
Flow and timing	**Excluded participants:** 2 lesions without a tele-dx **Time interval to reference test:** 1 week from photographs being taken **Time interval between index test(s): N/A**
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
If the reference standard includes clinical follow-up of borderline/benign appearing lesions, was there a minimum follow-up following application of index test(s) of at least: 3 months for melanoma or cSCC or 6 months for BCC?	
Could the patient flow have introduced bias?	High risk

Comparative

A. Risk of Bias
Comparative

B. Concerns regarding applicability

Notes

Notes	-

Phillips 1998

Patient Selection

A. Risk of Bias	
Patient Sampling	**Study design:** Case series **Data collection:** Not reported but appears prospective **Period of data collection:** 1996 **Country:** US
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Unclear risk

B. Concerns regarding applicability	
Patient characteristics and setting	**Inclusion criteria:** Participants attending four skin cancer screenings at community hospitals in rural eastern North Carolina. **Setting:** Community **Prior testing:** None **Setting for prior testing:** N/A **Exclusion criteria:** None reported **Sample size (patients):** 51 **Sample size (lesions):** 107 **Participant characteristics:** **Age (yrs):** 46.7y; Male: 8 (15.7%) **Lesion characteristics:**
Are the included patients and chosen study setting appropriate?	Yes
Did the study avoid including participants with multiple lesions?	Yes
Are there concerns that the included patients and setting do not match the review question?	Low concern

Index Test

Index tests	**Teledermatology** **Acquisition and transmission of images:** All sites were on a 1/2 T-1 link (786 kbs). All sites had three cameras available, each of which was used in evaluating the patients: a full-body camera, a lens for viewing the lesions close up, and a magnifying lens that allowed even closer views as well as examination with polarized light (CLI CODEC (Panasonic 3-chip or Canon 1-chip)). All monitors offered 620 lines of resolution. It is not clear who operated the cameras during the teleconsultations. The in-person evaluation was conducted first so that if a complete skin examination was performed, representative lesions were selected by the on-site physician for evaluation by the remote physician. **Nature of images used:** Live link **Any additional patient information provided:** Physicians could communicate directly with the patient **Diagnosis based on:** Single observer **Number of examiners:** 2; each examiner was the on-site physician at two screenings and the "remote physician" at two screenings. **Observer qualifications (remote diagnosis):** Dermatologist **Method of diagnosis:** **Management options:** Most likely diagnosis for a given lesion; the degree of concern that a specific lesion was malignant; and recommendation as to whether to do a biopsy of the lesion.

Teledermatology

A. Risk of Bias	
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear
If a threshold was used, was it pre-specified?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk

B. Concerns regarding applicability	
Was the test applied and interpreted in a clinically applicable manner?	Unclear
Were thresholds or criteria for diagnosis reported in sufficient detail to allow replication?	Unclear
Was the test interpretation carried out by an experienced examiner?	Unclear
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear

Face to face diagnosis

A. Risk of Bias

B. Concerns regarding applicability

Reference Standard

A. Risk of Bias	
Target condition and reference standard(s)	**Reference standard: Expert diagnosis (referral accuracy)** **Details:** All patients were first evaluated by the on-site physician. Patients were given a choice of having a total body examination, only the sun-exposed skin, or a specific lesion(s) evaluated by the on-site physician. This physician recorded specific lesions on an image of the human body and the most likely diagnosis for a given lesion; the degree of concern that a specific lesion was malignant; and recommendation as to whether to do a biopsy of the lesion. If a complete skin examination was performed, representative lesions were selected by the on-site physician for evaluation by the remote physician. The patient was subsequently seen by the remote dermatologist, and the same data were recorded. **Target condition (FtF diagnoses)** **Malignant:** BCC 2; SCC 3; lentigo maligna 1 **Benign:** SK 27; BN 32; AK 14; lentigo 10; Other 30
Is the reference standards likely to correctly classify the target condition?	No
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk

B. Concerns regarding applicability	
For studies comparing teledermatology/face to face clinical diagnosis to histology, was histology interpretation carried out by an experienced histopathologist or by a dermatopathologist?	
For studies comparing teledermatology to face to face diagnosis, was the clinical diagnosis carried out by an experienced observer?	Unclear
Are there concerns that the target condition as defined by the reference standard does not match the question?	Unclear

Flow and Timing

A. Risk of Bias	
Flow and timing	**Excluded participants:** None described **Time interval to reference test:** Consecutive **Time interval between index test(s): N/A**
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
If the reference standard includes clinical follow-up of borderline/benign appearing lesions, was there a minimum follow-up following application of index test(s) of at least: 3 months for melanoma or cSCC or 6 months for BCC?	
Could the patient flow have introduced bias?	Low risk

Comparative

A. Risk of Bias
Comparative

B. Concerns regarding applicability

Notes

Notes	-

Piccolo 2000

Patient Selection

A. Risk of Bias	
Patient Sampling	**Study design:** Case series **Data collection:** Prospective **Period of data collection:** states 3 months but no specific dates given **Country:** Austria (Graz)
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	Unclear risk

B. Concerns regarding applicability	
Patient characteristics and setting	**Inclusion criteria:** Patients with pigmented skin lesions selected because of their diagnostic difficulty and subsequently excised for a histopathological evaluation. **Setting:** Unspecified described as a multicentre study **Prior testing:** lesions included in the study were selected because of their diagnostic difficulty does not specify what prior tests were done **Setting for prior testing:** Unspecified **Exclusion criteria:** Poor quality index test image (all images scoring 4 were excluded from the study) **Sample size (patients):** No. included: 40 patients **Sample size (lesions):** No. included: 43 **Participant characteristics:** **Age (yrs):** Median 39.5 years, (range 3–91 years) **Gender:** Male: 21 (53%); Female 19 (47%) **Lesion characteristics** **Lesion site:** Face 2; Head 1, Neck 1, Trunk 8, Arms 3, Legs 7, Back 20, Buttocks 1
Are the included patients and chosen study setting appropriate?	No
Did the study avoid including participants with multiple lesions?	Yes
Are there concerns that the included patients and setting do not match the review question?	High

Index Test

Index tests	**In person face to face clinical assessment** **Method of diagnosis:** All lesions were examined with a dermatoscope during the face to face clinical diagnosis. Diagnosis was made by a expert dermatologist based on clinical features and dermoscopic findings. No specific algorithm (e.g. the Stolz index) was used for dermoscopic diagnosis. **Prior test data:** Unclear **Diagnostic threshold:** Not reported **Diagnosis based on:** Single Number of examiners: 1 **Observer qualifications:** Dermatologist (an expert in the diagnosis of pigmented skin lesions) **Experience in practice:** High **Experience with index test:** High **Teledermatology** **Acquisition and transmission of images:** Each image was acquired following the in-person consultation with the digital camera at a fixed 10-fold magnification. Two different lenses were used to capture clinical and dermoscopic images (DCS 460,Kodak, Rochester, NY, USA), which used a Nikon body (N90, Nikon, Tokyo, Japan); original image size 2036x3060 pixels in RGB colour mode (32 bit/pixel), then compressed to 511x768 pixels (24 bit/pixel). These were stored on a prototype teledermatology workstation and distributed to remote centres via email together with basic patient data (initials, age, sex and site of the lesion). **Nature of images used:** Clinical photographs and dermoscopic images **Any additional patient information provided:** patient data (initials, age, sex and site of the lesion). **Diagnosis based on:** Single observer Number of examiners 11 **Observer qualifications (remote diagnosis):** Dermatologists (6), residents in dermatology (2), Internist (1), GP (1), Oncologist (1) **Experience in practice:** Not described **Experience with index test:** Mixed experience (low and high experience combined) **Method of diagnosis:** Not reported

Teledermatology

A. Risk of Bias	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
If a threshold was used, was it pre-specified?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk

B. Concerns regarding applicability	
Was the test applied and interpreted in a clinically applicable manner?	No
Were thresholds or criteria for diagnosis reported in sufficient detail to allow replication?	Unclear
Was the test interpretation carried out by an experienced examiner?	Yes
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	High

Face to face diagnosis

A. Risk of Bias	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
If a threshold was used, was it pre-specified?	Unclear
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk

B. Concerns regarding applicability	
Was the test applied and interpreted in a clinically applicable manner?	Yes
Were thresholds or criteria for diagnosis reported in sufficient detail to allow replication?	Unclear
Was the test interpretation carried out by an experienced examiner?	Yes
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear

Reference Standard

A. Risk of Bias	
Target condition and reference standard(s)	**Reference standard:** Histological diagnosis alone **Details:**All lesions were excised for a histopathological evaluation **Target condition (Final diagnoses)** - Melanoma (in situ and invasive, or not reported): 11, BCC: 3 - Sebhorrheic keratosis: 2, Benign naevus: Melanocytic naevus 23, 'Benign' diagnoses: Angiokeratoma 1, lentigines 3
Is the reference standards likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk

B. Concerns regarding applicability	
For studies comparing teledermatology/face to face clinical diagnosis to histology, was histology interpretation carried out by an experienced histopathologist or by a dermatopathologist?	Unclear
For studies comparing teledermatology to face to face diagnosis, was the clinical diagnosis carried out by an experienced observer?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Unclear

Flow and Timing

A. Risk of Bias	
Flow and timing	1. Excluded participants: Not reported 2. Time interval to reference test: Not reported 3. Time interval between index test(s): Not reported
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
If the reference standard includes clinical follow-up of borderline/benign appearing lesions, was there a minimum follow-up following application of index test(s) of at least: 3 months for melanoma or cSCC or 6 months for BCC?	
Could the patient flow have introduced bias?	Unclear risk

Comparative

A. Risk of Bias	
Comparative	Remote observers received images via email
Was each index test result interpreted without knowledge of the results of other index tests or testing strategies?	Yes
Was the interval between application of the index tests less than one month?	Unclear
Are there any concerns that the test comparison could have introduced bias?	Unclear risk

B. Concerns regarding applicability	
Were all tests applied and interpreted in a clinically applicable manner?	No
Are there concerns that the test comparison differs from the review question?	High

Notes

Notes	-

Piccolo 2004

Patient Selection

A. Risk of Bias	
Patient Sampling	**Study design:** Case series **Data collection:** Retrospective image selection / Prospective interpretation **Period of data collection:** Not reported **Country:** Multicentre study participating centres were in Italy, Japan, Austria and Slovenia Images used were from University of Graz Austria and University of L'Aquila Italy
Was a consecutive or random sample of patients enrolled?	Unclear
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Unclear risk

B. Concerns regarding applicability	
Patient characteristics and setting	**Inclusion criteria:** Patients with melanocytic acral lesions (71 common melanocytic naevi and 6 melanomas) from 73 patients at the Department of Dermatology University of Graz and Department of Dermatology, University ofL'Aquila **Setting:** Secondary **Prior testing:** Selected for excision (no further detail) **Setting for prior testing:** Unspecified **Exclusion criteria:** None reported **Sample size (patients):** No. included: 73 **Sample size (lesions):** No. included: 77 **Participant characteristics:** **Age (yrs):** Mean: 28 years; range: 4 to 77 years **Gender:** Male: 34; Female 39 **Lesion characteristics** **Lesion site:** 67 lesions located on the lower extremities (58 on the plantar surface, 4 on the external part of the foot, 3 on the toe, and 2 on the dorsal aspect of the foot) and 10 on the upper extremities (8 on the palm and 2 on the finger).
Are the included patients and chosen study setting appropriate?	No
Did the study avoid including participants with multiple lesions?	Yes
Are there concerns that the included patients and setting do not match the review question?	High

Index Test

Index tests	**Teledermatology** **Acquisition and transmission of images:** Dermoscopic images of 48 melanocytic acral lesions were acquired at the Department of Dermatology, University of Graz, using the MoleMax II System at 30x magnification. Dermoscopic photographs acquired with Heine Dermaphot equipment at 10x magnification were retrieved from the database of the Department of Dermatology, University of L'Aquila images. All images in the study were compressed (to facilitate email transmission) at the Department of Dermatology,University of L'Aquila.The images selected represented all the acral lesions included in the databases of the two dermatology departments. photographic images were not included. The dermoscopic images, together with the essential clinical data (age and sex of patient and site of the lesion), were transmitted individually by email to 11 colleagues in eight remote centres. **Nature of images used:** Dermoscopic images **Any additional patient information provided:** Case notes **Diagnosis based on:** Single observer Number of examiners 11 dermatologists **Observer qualifications (remote diagnosis):** Dermatologist (varying experience from high to low dependant on numbers of years of specialization in pigmented skin lesions) **Method of diagnosis:** Images were analysed the images on a PC monitor by each observer, first to diagnose acral melanoma or atypical lesions, and second to categorize the lesions according to the Saida classification. An acral naevus was considered to be atypical when at least 6 of the 11 observers made this diagnosis. **Management options**: Observers also made a management recommendation of digital dermoscopy follow-up or surgical excision

Teledermatology

A. Risk of Bias	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
If a threshold was used, was it pre-specified?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk

B. Concerns regarding applicability	
Was the test applied and interpreted in a clinically applicable manner?	No
Were thresholds or criteria for diagnosis reported in sufficient detail to allow replication?	Yes
Was the test interpretation carried out by an experienced examiner?	Yes
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	High

Face to face diagnosis

A. Risk of Bias

B. Concerns regarding applicability

Reference Standard

A. Risk of Bias	
Target condition and reference standard(s)	**Reference standard:** Histological diagnosis alone **Details:** All lesions had been surgically excised and histopathologically diagnosed by two dermatopathologists. **Target condition (Final diagnoses)** - Melanoma: 6 acral melanomas - Benign naevus: 71 acral melanocytic naevi
Is the reference standards likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk

B. Concerns regarding applicability	
For studies comparing teledermatology/face to face clinical diagnosis to histology, was histology interpretation carried out by an experienced histopathologist or by a dermatopathologist?	Yes
For studies comparing teledermatology to face to face diagnosis, was the clinical diagnosis carried out by an experienced observer?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern

Flow and Timing

A. Risk of Bias	
Flow and timing	1. Excluded participants: none reported 2. Time interval to reference test: not reported 3. Time interval between index test(s): N/A
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	Yes
If the reference standard includes clinical follow-up of borderline/benign appearing lesions, was there a minimum follow-up following application of index test(s) of at least: 3 months for melanoma or cSCC or 6 months for BCC?	
Could the patient flow have introduced bias?	Unclear risk

Comparative

A. Risk of Bias
Comparative

B. Concerns regarding applicability

Notes

Notes	-

Shapiro 2004

Patient Selection

A. Risk of Bias	
Patient Sampling	**Study design:** Case series **Data collection:** Prospective **Period of data collection:** July 10 1998, and August 4, 2000 **Country:** US
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	Unclear risk

B. Concerns regarding applicability	
Patient characteristics and setting	**Inclusion criteria:** PCP referred only those patients with skin growths that posed a true diagnostic challenge **Setting:** Primary, recruitment of study participants from PCP (Estimated 50% of PCP patients have dermatologic lesions that are encountered during routine evaluation and 3% present exclusively for dermatologic reasons) - Private (face to face consultation with the local dermatologist in private practice) - Secondary care (images sent from PCP to academic dermatologist for SAF dermatological consultation) **Prior testing:** A network community PCP recruited patients whom he judged to require dermatologic consultation for evaluation of a cutaneous growth **Setting for prior testing:** Primary **Exclusion criteria:** Patients who underwent previous evaluation by a dermatologist were excluded from the study **Sample size (patients):** No. eligible: 61; No. included: 49 **Sample size (lesions):** not reported **Participant characteristics:** not reported **Lesion characteristics** not reported
Are the included patients and chosen study setting appropriate?	Yes
Did the study avoid including participants with multiple lesions?	Unclear
Are there concerns that the included patients and setting do not match the review question?	Unclear

Index Test

Index tests	**Teledermatology** **Acquisition and transmission of images:** Images were acquired by the primary care physician (PCP) using an Olympus D-600L digital camera. The first image captured the head and upper trunk. This was followed by an image of the affected body part.The image and a clinical history were downloaded to a personal computer using a serial port interface and accompanying software.The image transmission was performed via e-mail using HUPNet, a private encrypted University of Pennsylvania Health System area network **Nature of images used:** Clinical photographs **Any additional patient information provided:** clinical history **Observer qualifications (remote diagnosis):** Dermatologist (n=1); (academic dermatologist with over 20 years experience in clinical dermatology) **Diagnosis based on:** Single observer Number of observers:1 **Method of diagnosis:** The images were reviewed by the PCP immediately before they were sent to a board certified academic dermatologist for teledermatologic consultation.After assessing the case, the teledermatologist notified the PCP of the diagnosis or differential diagnosis and indicate on a standard data collection sheet whether a sampling biopsy was necessary. The reason for recommending biopsy was specified as well. **Management options:** asked to choose a management plan from 15 entries including 3 biopsy plans (to rule out malignancy, to establish a diagnosis, or to remove a benign lesion for cosmetic purposes)

Teledermatology

A. Risk of Bias	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
If a threshold was used, was it pre-specified?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk

B. Concerns regarding applicability	
Was the test applied and interpreted in a clinically applicable manner?	Yes
Were thresholds or criteria for diagnosis reported in sufficient detail to allow replication?	Unclear
Was the test interpretation carried out by an experienced examiner?	Yes
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear

Face to face diagnosis

A. Risk of Bias

B. Concerns regarding applicability

Reference Standard

A. Risk of Bias	
Target condition and reference standard(s)	**Face to face diagnosis as reference standard** **Method of diagnosis:** The patients were simultaneously scheduled for an FTF visit with the local dermatologist (F.C.L.), who is in private practice, within 1 month. The FTF dermatologist completed a standardized consultation form notifying the PCP of his decision regarding the diagnosis, differential diagnosis, and whether a biopsy was indicated. A biopsy was performed at that visit by the FTF dermatologist if the FTF dermatologist or the SAF teledermatologist favoured biopsy of the lesion **Prior test data:** The telediagnosis triage decision was contained in a sealed envelope which was opened by the FTF dermatologist after making his decision. Biopsy was then carried out by the FTF dermatologists if recommended by either dermatologist. **Diagnostic threshold:** Not described **Diagnosis based on:** Single Number of examiners: One **Observer qualifications:** Dermatologist **Experience in practice:** over 20 years of experience in clinical dermatology **Experience with index test:** High **Target condition (for 26 lesions undergoing biopsy; 23 on dermatologist recommendation and 3 at patient request)** **Malignant:** 5 BCC, 4 cSCC **Benign:** 17 benign neoplasms **Assumed benign** (no biopsy): 23 (including one patient who refused biopsy)
Is the reference standards likely to correctly classify the target condition?	No
Were the reference standard results interpreted without knowledge of the results of the index tests?	Yes
Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk

B. Concerns regarding applicability	
For studies comparing teledermatology/face to face clinical diagnosis to histology, was histology interpretation carried out by an experienced histopathologist or by a dermatopathologist?	Yes
For studies comparing teledermatology to face to face diagnosis, was the clinical diagnosis carried out by an experienced observer?	Yes
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern

Flow and Timing

A. Risk of Bias	
Flow and timing	1. Excluded participants: 11 breached the study protocol and were not included in the analysis. Of the latter 11, 4 failed to present to the FTF dermatologist, 4 saw a different FTF dermatologist, 1 died of unrelated causes before seeing the FTF dermatologist, and 2 underwent evaluation of different lesions by the SAF teledermatologist and FTF dermatologist. 2. Time interval to reference test: The patients were simultaneously scheduled for an FTF visit with the local dermatologist (F.C.L.), who is in private practice, within 1 month. 3. Time interval between index test(s): N/A
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
If the reference standard includes clinical follow-up of borderline/benign appearing lesions, was there a minimum follow-up following application of index test(s) of at least: 3 months for melanoma or cSCC or 6 months for BCC?	
Could the patient flow have introduced bias?	High risk

Comparative

A. Risk of Bias
Comparative

B. Concerns regarding applicability

Notes

Notes	-

Silveira 2014

Patient Selection

A. Risk of Bias	
Patient Sampling	**Study design:**Case series **Data collection:** Prospective **Period of data collection** April 2010 and July 2011 **Country** Brazil
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Unclear
Could the selection of patients have introduced bias?	Unclear risk

B. Concerns regarding applicability	
Patient characteristics and setting	**Inclusion criteria:** Individuals with skin lesions that were determined to be suspicious after a direct visual inspection by a physician. All of the patients examined at the Mobile Prevention Unit were previously screened by a nurse from the local municipality who was trained at Barretos Cancer Hospital. **Setting:** Community Mobile Prevention Unit (MPU) **Prior testing:**Not described **Setting for prior testing:** Unspecified **Exclusion criteria:** none reported **Sample size (lesions):** No. included: 416 **Participant characteristics:** **Age (yrs):** Mean 63.5, (range 19 to 93 years) **Gender:** Not reported **Lesion characteristics:** Site:- Head and Neck 273 (75.0); Trunk 28 (7.6); Upper limbs 61 (16.7); Lower limbs 2 (0.5) Skin type scale;- 1-2 295 (81); 3-4 69 (19); 5-6 0 (0)
Are the included patients and chosen study setting appropriate?	Yes
Did the study avoid including participants with multiple lesions?	Unclear
Are there concerns that the included patients and setting do not match the review question?	Unclear

Index Test

Index tests	**Teledermatology** **Acquisition and transmission of images:** Community (patients were evaluated in the MPU, and their lesions were photographed by the MPU physician using a digital camera - Sony Cybershot DSC-5780 digital camera with 8.1-megapixel resolution) **Nature of images used:** Clinical photographs **Any additional patient information provided:** information such as age, skin complexion, location of the lesion, stage and pathology results were collected **Observer qualifications (remote diagnosis):** Oncologists at the Barretos Cancer Hospital (BCH); both the oncologists and the MPU physician have more than 10-years of experience in skin cancer screening Number of observers:2 **Diagnosis based on:** Single observer **Method of diagnosis:** All of the digital images were coded, stored and submitted at random to two oncologists at BCH, they were blinded to the MPU physician's diagnosis and pathology reports, and classified the images using the following options: 1) a malignant lesion, oncological treatment is indicated; 2) a benign lesion, no treatment required; 3) unknown; or 4) a low-quality image

Teledermatology

A. Risk of Bias	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
If a threshold was used, was it pre-specified?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk

B. Concerns regarding applicability	
Was the test applied and interpreted in a clinically applicable manner?	Yes
Were thresholds or criteria for diagnosis reported in sufficient detail to allow replication?	Unclear
Was the test interpretation carried out by an experienced examiner?	Yes
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear

Face to face diagnosis

A. Risk of Bias

B. Concerns regarding applicability

Reference Standard

A. Risk of Bias	
Target condition and reference standard(s)	**Reference standard:** Histological diagnosis **Details:** Lesions classified as possibly malignant at the mobile unit were excised or biopsied **Target condition (Final diagnoses)** - Melanoma: 5, BCC: 286, cSCC: 59, Malignant other:14 - Benign diagnosis: 52
Is the reference standards likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk

B. Concerns regarding applicability	
For studies comparing teledermatology/face to face clinical diagnosis to histology, was histology interpretation carried out by an experienced histopathologist or by a dermatopathologist?	Unclear
For studies comparing teledermatology to face to face diagnosis, was the clinical diagnosis carried out by an experienced observer?	Unclear
Are there concerns that the target condition as defined by the reference standard does not match the question?	Unclear

Flow and Timing

A. Risk of Bias	
Flow and timing	**Excluded participants**: 21 (4.6%) were excluded from the study because of poor quality photos, leaving 439 patients with pathological results. 23/439 (5.2%) were excluded because of incomplete data preventing the identification of the patient, **Interval between reference standard and index test**: appears consecutive “lesions were imaged, biopsied/removed and submitted for histopathological examination” 364 (87.5%) were confirmed to be malignant by the biopsy, 52 were diagnosed by expert opinion
Was there an appropriate interval between index test and reference standard?	Yes
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
If the reference standard includes clinical follow-up of borderline/benign appearing lesions, was there a minimum follow-up following application of index test(s) of at least: 3 months for melanoma or cSCC or 6 months for BCC?	
Could the patient flow have introduced bias?	High risk

Comparative

A. Risk of Bias
Comparative

B. Concerns regarding applicability

Notes

Notes	-

Warshaw 2010

Patient Selection

A. Risk of Bias	
Patient Sampling	**Study design:** Case series **Data collection:** Prospective **Period of data collection:** Nov 2002 to Aug 2005 **Country:** US
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	Yes
Did the study avoid inappropriate exclusions?	Yes
Could the selection of patients have introduced bias?	Low risk

B. Concerns regarding applicability	
Patient characteristics and setting	**Inclusion criteria:** Patients enrolled at the Department of Veteran Affairs dermatology clinic who required (or requested) removal of one or more skin neoplasms ('high-risk group') and participants who were referred to general dermatology clinic by non-dermatology healthcare providers for evaluation of a skin neoplasm (lower risk group). Biopsied lesions only were included. Warshaw 2009 and Warshaw 2009a included data for participants primary lesions only whereas Warshaw 2010 includes all biopsied lesions, pigmented or non-pigmented, from histopathologic lesion categories with >=25 lesions **Setting:** Secondary (general dermatology) **Prior testing:** Selected for excision (no further detail) **Setting for prior testing:** Secondary (general dermatology) **Exclusion criteria:** individuals requesting or referred for skin tag removal only or with papulosquamous or eczematous conditions (non-neoplastic), previous biopsy of the lesion, and inability to comprehend and give informed consent **Sample size (patients):** No. eligible: 2152; No. included: NR **Sample size (lesions):** No. eligible: 3021 enrolled; 1685 biopsied and eligible for inclusion; No. included: 1514 **Age:** Mean: Pigmented: 66 Non-pigmented: 71; Range: Pigmented: 23-94 Non-pigmented: 21-94 **Gender:** Male: Pigmented: 519 (95.8%) Non-pigmented: 712 (97.8%) **Race/Ethnicity** - White: Pigmented: 97.1% Non-pigmented: 98.9%; Black or African American: Pigmented: 1.3% Non-pigmented: 0.7%; Other: Pigmented: 1.5% Non-pigmented: 0.4% **High risk characterisitics** - History of melanoma: Pigmented: 34; 6.3% Non-pigmented: 16; 2.2% - History of non-melanoma skin cancer: Pigmented: 147; 27.1% Non-pigmented: 260; 35.7% **Lesion characteristics** - Clinical characteristics (appearance) - Non-pigmented (%): For index lesions only (n=1270): 728 (57.3%) - Other: Pigmented: 19.4% size change, 16.6% itching, 9.6% bleeding Non-pigmented: 32.1%% size change, 23.9% itching, 26.6% bleeding **Lesion site** - Head/Neck: Pigmented: 38.2% Non-pigmented: 70.1% - Trunk: Pigmented: 24.2% Non-pigmented: 13.9% - Upper limbs/shoulder: Pigmented: 31.2% Non-pigmented: 12.0% - Lower limbs/hip: Pigmented: 5.7% Non-pigmented: 3.0% - Buttock/groin: Pigmented: 0.7% Non-pigmented: 1.1%
Are the included patients and chosen study setting appropriate?	No
Did the study avoid including participants with multiple lesions?	No
Are there concerns that the included patients and setting do not match the review question?	High

Index Test

Index tests	**In person assessment** **Method of diagnosis:** Visual inspection +/- use of dermoscopy ("the clinical examination could include all options normally available in the clinical setting (eg, palpation, diascopy, dermatoscopy) **Prior test data:** Selected for excision (no further detail) **Diagnostic threshold:** Qualitative (Recorded primary diagnosis and up to two differential diagnoses, plus a choice of four basic management plans (remove/biopsy/destroy, observe/ reassure, antifungal treatment, antibiotic treatment, anti-inflammatory treatment) Primary diagnosis Clinicians had a choice of 17 common diagnoses for one primary and up to two differential diagnoses **Diagnosis based on:** Single observer **Number of examiners:** 11 staff dermatologists **Observer qualifications:** Dermatologist **Experience in practice:** Not described **Experience with index test:** Not described # **Teledermatology** **Acquisition and transmission of images:** The standard method used in most teledermatology settings at the onset of the study,15-20 and PLD images were obtained for each lesion following in-person consultation. Two macro images (distance and close-up; digital Nikon Coolpix 4500 with a Nikon SL-1 ring flash [Nikon, Melville, NY]) were obtained of each lesion. In addition, for lesions more than 2 mm in height, a macro angle (approximately 908 from the skin surface) was also taken. One PLD (digital Nikon Coolpix 4500 with a 3Gen DermLite lens attachment) was also obtained. (Dermoscopy images taken and accuracy reported but insufficient data obtained from authors to allow their inclusion in this review. Dermoscopy images unlikely to have influenced macro image interpretation as "for each participant, a sequence of two image ‘‘packages’’ was sent. The teledermatologist received a macro package (distance and close-up, with or without an angle image) alone or with a PLD image. **Nature of images used:** Clinical photographs **Any additional patient information provided:** Clinical examination and/or case notes (the standardized patient and lesion history collected by the research assistants) **Observer qualifications (remote diagnosis)**; Dermatologist (with > 5 years experience and recognised pigmented skin lesion expert) **Diagnosis based on:** Single observer Number of observers:3 **Method of diagnosis:** Using the same diagnostic and management categories as used by clinic dermatologists, the teledermatologists recorded one primary diagnosis, up to two differential diagnoses, and a management plan for each lesion.

Teledermatology

A. Risk of Bias	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
If a threshold was used, was it pre-specified?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk

B. Concerns regarding applicability	
Was the test applied and interpreted in a clinically applicable manner?	No
Were thresholds or criteria for diagnosis reported in sufficient detail to allow replication?	Unclear
Was the test interpretation carried out by an experienced examiner?	Yes
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	High

Face to face diagnosis

A. Risk of Bias	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
If a threshold was used, was it pre-specified?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk

B. Concerns regarding applicability	
Was the test applied and interpreted in a clinically applicable manner?	Yes
Were thresholds or criteria for diagnosis reported in sufficient detail to allow replication?	Unclear
Was the test interpretation carried out by an experienced examiner?	Yes
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Unclear

Reference Standard

A. Risk of Bias	
Target condition and reference standard(s)	**Histological reference standard.** A board-certified dermatopathologist who was not involved with any clinic assessments coded all histopathologic diagnoses based on the pathology report. **- No. patients/lesions**: 1514 **Target condition** **Malignant** Melanoma: 41, BCC: 410, cSCC: 240 **Benign** 'Benign' diagnoses: benign keratoses 223; dysplastic nevi 154; actinic kerastoses 145; benign nevi 138; cysts 73; benign appendageal tumours 35; lentigines 29; benign vascular neoplasms 26
Is the reference standards likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk

B. Concerns regarding applicability	
For studies comparing teledermatology/face to face clinical diagnosis to histology, was histology interpretation carried out by an experienced histopathologist or by a dermatopathologist?	Yes
For studies comparing teledermatology to face to face diagnosis, was the clinical diagnosis carried out by an experienced observer?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Low concern

Flow and Timing

A. Risk of Bias	
Flow and timing	**Excluded participants:** histopathologic categories with <25 lesions (n=171) **Time interval to reference test:** Patients (from the VA clinic) were scheduled for a research appointment before, but on the same day as, their dermatology clinic consult appointment. But timing to histology not reported Patients from the general dermatology clinic undergoing a biopsy for a skin neoplasm (because of physician recommendation or patient request) were also invited to participate. - likely that photographs taken on same day as excision but again not reported as such **Time interval between index test(s):** Immediate - photographs taken on day of FtF appointment
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
If the reference standard includes clinical follow-up of borderline/benign appearing lesions, was there a minimum follow-up following application of index test(s) of at least: 3 months for melanoma or cSCC or 6 months for BCC?	
Could the patient flow have introduced bias?	High risk

Comparative

A. Risk of Bias	
Comparative	
Was each index test result interpreted without knowledge of the results of other index tests or testing strategies?	Unclear
Was the interval between application of the index tests less than one month?	Unclear
Are there any concerns that the test comparison could have introduced bias?	Unclear risk

B. Concerns regarding applicability	
Were all tests applied and interpreted in a clinically applicable manner?	Yes
Are there concerns that the test comparison differs from the review question?	Low concern

Notes

Notes	-

Wolf 2013

Patient Selection

A. Risk of Bias	
Patient Sampling	**Study design:** Case control **Data collection:** Retrospective image selection / Prospective interpretation **Period of data collection** Not reported **Country** US
Was a consecutive or random sample of patients enrolled?	Yes
Was a case-control design avoided?	No
Did the study avoid inappropriate exclusions?	No
Could the selection of patients have introduced bias?	High risk

B. Concerns regarding applicability	
Patient characteristics and setting	**Inclusion criteria:** Patients with pigmented lesions that were considered atypical in clinical appearance by at least one dermatologist and for which a clear histologic diagnosis had been rendered by a board-certified dermatopathologist. Images selected from image database in following categories: categories: invasive melanoma, melanoma *in situ*, lentigo, benign nevus (including compound, junctional, and low-grade dysplastic nevi), dermatofibroma, seborrheic keratosis, and hemangioma. Sampling not described. **Setting:** - Unspecified **Prior testing:** - Selected for excision (no further detail) **Setting for prior testing:** - Unspecified **Exclusion criteria:** Study exclusion criteria: Poor quality index test image, Images that contained any identifiable features, such as facial features, tattoos, or labels with patient information, were excluded or cropped to remove the identifiable features or information. Lesions with equivocal diagnoses, such as “melanoma cannot be ruled out” or “atypical melanocytic proliferation,” were excluded, as were Spitz nevi, pigmented spindle cell nevus of Reed, other uncommon or equivocal lesions, and lesions with moderate or high-grade atypia. **Sample size (patients):** Not reported **Sample size (lesions):** 188 **Participant characteristics:** Not reported **Lesion characteristics:** Not reported
Are the included patients and chosen study setting appropriate?	No
Did the study avoid including participants with multiple lesions?	Unclear
Are there concerns that the included patients and setting do not match the review question?	High

Index Test

Index tests	**Teledermatology** **Acquisition and transmission of images:** The images of skin lesions were selected from a database of images that are captured routinely before skin lesion removal to allow clinicopathologic correlation in making medical management decisions. Only used close-up images of lesions and those that contained any identifiable features, such as facial features, tattoos, or labels with patient information, were excluded or cropped to remove the identifiable features or information. **Nature of images used:** photographic images **Any additional patient information provided:** No further information used **Method of diagnosis:** Application 4 which was run on a smartphone sent each image to a board-certified dermatologist for evaluation, and assessment that was returned to the user within 24 hours. The identity of the dermatologist was not given, and it was unclear whether all the images were read by the same dermatologist or by several different dermatologists. The output given was “atypical,” which was considered to be a positive test result, or “typical,” which was considered to be a negative test result. **Diagnosis based on:** Unlcear how many observers Number of examiners: Unclear **Observer qualifications (remote diagnosis):** Board certified dermatologist **Experience in practice:** Unclear **Experience with index test:** Unclear

Teledermatology

A. Risk of Bias	
Were the index test results interpreted without knowledge of the results of the reference standard?	Yes
If a threshold was used, was it pre-specified?	Yes
Could the conduct or interpretation of the index test have introduced bias?	Low risk

B. Concerns regarding applicability	
Was the test applied and interpreted in a clinically applicable manner?	No
Were thresholds or criteria for diagnosis reported in sufficient detail to allow replication?	Yes
Was the test interpretation carried out by an experienced examiner?	Yes
Are there concerns that the index test, its conduct, or interpretation differ from the review question?	High

Face to face diagnosis

A. Risk of Bias

B. Concerns regarding applicability

Reference Standard

A. Risk of Bias	
Target condition and reference standard(s)	**Reference standard** - Histological diagnosis alone **Details:** *Histology (not further described)* **Target condition (Final diagnoses)** Malignant - Melanoma (in situ and invasive): 60 Benign - 'Benign' diagnoses: 128
Is the reference standards likely to correctly classify the target condition?	Yes
Were the reference standard results interpreted without knowledge of the results of the index tests?	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	Low risk

B. Concerns regarding applicability	
For studies comparing teledermatology/face to face clinical diagnosis to histology, was histology interpretation carried out by an experienced histopathologist or by a dermatopathologist?	Unclear
For studies comparing teledermatology to face to face diagnosis, was the clinical diagnosis carried out by an experienced observer?	
Are there concerns that the target condition as defined by the reference standard does not match the question?	Unclear

Flow and Timing

A. Risk of Bias	
Flow and timing	1. **Excluded participants**: We reviewed a total of 390 images for possible inclusion in this study. We excluded 202 as being of poor image quality, containing identifiable patient information or features, or lacking sufficient clinical or histological information. 2. **Time interval to reference test**: N/A
Was there an appropriate interval between index test and reference standard?	Unclear
Did all patients receive the same reference standard?	Yes
Were all patients included in the analysis?	No
If the reference standard includes clinical follow-up of borderline/benign appearing lesions, was there a minimum follow-up following application of index test(s) of at least: 3 months for melanoma or cSCC or 6 months for BCC?	
Could the patient flow have introduced bias?	High risk

Comparative

A. Risk of Bias
Comparative

B. Concerns regarding applicability

Notes

Notes	-

Footnotes

ABCD(E) - asymmetry, border, colour, differential structures (enlargement); AK - actinic keratosis; AMN – atypical melanocytic naevi; BCC - basal cell carcinoma; BD – Bowen's disease; BN – benign naevi; BPC – between person comparison (of tests); CAD – computer assisted diagnosis; CCS – case control study; CD – compact disc; CM – cutaneous melanoma; CMM - cutaneous malignant melanoma; CS – case series; cSCC – cutaneous squamous cell carcinoma; DF – dermatofibroma; Dx – diagnosis; ELM – epiluminescence microscopy; FPs - false positives; FU – follow-up ; GP – general practitioner; H&E – haematoxylin and eosin stain; LPLK – lichen planus-like keratosis; LS – lentigo simplex; MM – malignant melanoma; MiS – melanoma in situ (or lentigo maligna); MN – melanocytic naevi; MSDSLA - multispectral digital skin lesion analysis device; N/A – not applicable; NC – non comparative; NMLs – non melanocytic lesions; NR – not reported; P – prospective; PCPs – primary care providers; PLC – pigmented lesion clinic; PSL – pigmented skin lesion; R –retrospective; RCM – reflectance confocal microscopy; RCT – randomised controlled trial; SCC - squamous cell carcinoma; SD – standard deviation; SDDI - short-term sequential digital dermoscopy imaging; SK – seborrhoeic keratosis; SN – Spitz nevi; SSM – superficial spreading melanoma; SVS – support vector system; VI – visual inspection; WPC – within person comparison (of tests)

Characteristics of excluded studies

Armstrong 2007

Reason for exclusion	EXCLUDE not a primary study

Baba 2005

Reason for exclusion	EXCLUDE on study population

Badertscher 2015

Reason for exclusion	~EXCLUDE on 2x2 data; for VI/Derm - only gives number of correct diagnoses (not broken down by TP/TN) and gives GP 'score' between T0 and T1 ~EXCLUDE on index test - not a teledermatology study

Barnard 2000

Reason for exclusion	EXCLUDE on target condition; *The primary target condition are not relevant to our reviews.*

Bashshur 2015

Reason for exclusion	EXCLUDE not a primary study *narrative review*

Bataille 2011

Reason for exclusion	EXCLUDE conference abstract

Bergmo 2000

Reason for exclusion	EXCLUDE not a primary study

Borve 2013

Reason for exclusion	EXCLUDE on target condition; *includes 1 melanoma metastases and 1 in situ SCC as D+ (these make up 5% of malignant group); author contacted (*Table 2 provides estimates of the diagnostic accuracy of the face-to-face dermatologist and the two teledermoscopists, however in order to include the results in our review we would need the underlying 2x2 contingency tables for these statistics. Is it at all possible for you to provide us with them for each observer, particularly in regard to the 'Primary diagnosis' and the 'Benign vs malignant')

Boyce 2011

Reason for exclusion	EXCLUDE on study population *No breakdown given- just 7 suspicious lesions.* EXCLUDE on reference standard; *No data given but only 7 referred on for formal assessment. Definitely <50% histology rate*

Braun 2000

Reason for exclusion	EXCLUDE on 2x2 data ~EXCLUDE but contact authors. can get sensitivity from table II but specificity unclear - appears to give n/% of correct identification of each lesion type rather than FPs Table II describes accuracy - is this % correct per lesion type? Do you have data on numbers misclassified as melanoma, or other malignancy, i.e. FPs? Is there overlap with later publications, e.g. Coras 2003?

Brown 2000

Reason for exclusion	EXCLUDE not a primary study

Burgiss 1997

Reason for exclusion	EXCLUDE on reference standard reports actions on tele-diagnosis (primarily for cost purposes) and does not give final diagnoses (histo) or FtF diagnosis for all lesions

Chen 2002

Reason for exclusion	EXCLUDE on sample size *Study was based on individual patient images (<5 cases). Only 4 lesions in total used in study (nBCC x 1, SK x1, KA x1, AK x1).*

D'Elia 2007

Reason for exclusion	EXCLUDE on study population *Not focused on suspected skin cancer* EXCLUDE on 2x2 data; *looks at agreement between diagnoses only*

Di Stefani 2007

Reason for exclusion	EXCLUDE on sample size; *<5 malignant: of 7 excised: one melanoma (melanoma in situ associated with a nevus), one pigmented BCC, and five melanocytic nevi. Both tele-dx recommended the 2 malignancies for excision but no further breakdown of agreement/disagreement given* EXCLUDE on 2x2 data 7 'D+' according to FtF decision to excise but only reports kappa values for agreement with tele-dx

Du Moulin 2003

Reason for exclusion	EXCLUDE on study population EXCLUDE on target condition

Edison 2008

Reason for exclusion	EXCLUDE on study population

Eminovic 2009

Reason for exclusion	EXCLUDE not a primary study EXCLUDE on study population EXCLUDE on target condition

Fabbrocini 2008

Reason for exclusion	EXCLUDE on 2x2 data; *there isn't sufficient data provided for each index test to populate 2x2 table* EXCLUDE but contact authors*: As we can only include DTA studies - Do you have a cross tabulation of each clinician's diagnosis (e.g. at threshold of >=3 on 7 point checklist) against the histological diagnosis and/or a cross tabulation of the remote diagnosis against the Face to Face diagnoses?*

Ferrandiz 2007

Reason for exclusion	EXCLUDE on study population; *all have a strong clinical diagnosis of NMSC or fast growing tumour, the purpose of the test is primarily to inform treatment plans* EXCLUDE on 2x2 data; *a) 4 of the original 134 appear to have missing histology and b) don't know what the additional clinical cases of each lesion were classed as on histology e.g. the 14 extra BCCs and 5 KAs*

Ferrandiz 2012

Reason for exclusion	EXCLUDE on target condition *on included CM*

Gilmour 1998

Reason for exclusion	EXCLUDE on study population EXCLUDE on target condition

Granlund 2003

Reason for exclusion	EXCLUDE on study population

Griffiths 2010

Reason for exclusion	EXCLUDE on reference standard

Harrison 1998

Reason for exclusion	EXCLUDE on target condition - no breakdown of final diagnoses (histo) or of recommendations from FtF consultation EXCLUDE on sample size - can't tell how many D+ for either reference standard EXCLUDE on 2x2 data - no underlying data provided; *diagnostic 'accuracy' of teleconsultation reported as 71% for 210 patients compared to 49% for the referring general practitioners (49%). Also states that "telemedicine was able to detect malignancies in 94% of cases compared with only 70% detected by general practitioners.*

Heffner 2009

Reason for exclusion	EXCLUDE on target condition

Hicks 2003

Reason for exclusion	EXCLUDE not a primary study

High 2000

Reason for exclusion	EXCLUDE on study population - not all suspected of skin cancer 'dermatologic conditions' including dermatitis, acne, verruca, etc. EXCLUDE on 2x2 data - reports agreement only; no breakdown of diagnoses/management decisions EXCLUDE on reference standard; Table of final diagnoses appears to be based on FtF diagnoses with histology obtained for 69/106 (65%), so is ineligible for a tele-dx vs histo comparison (diagnostic acuracy) and is not tele-dx vs FtF (referral accuracy) either

Hue 2016

Reason for exclusion	EXCLUDE on reference standard - final diagnoses/FtF decisions given only for 17 recommended for rapid referral on tele-dx; no data for remaining 395 with non-urgent derm referral/annual FU recommendation/discharge. EXCLUDE on sample size - for Tele-dx vs Histo, only 5 excised incl 1 melanoma EXCLUDE on 2x2 - no data for tele-dx vs FtF

Hwang 2014

Reason for exclusion	EXCLUDE on study population

Ishioka 2009

Reason for exclusion	EXCLUDE on target condition *No breakdown of disease positive 'malignant' provided*

Kahn 2013

Reason for exclusion	EXCLUDE on target condition

Knol 2006

Reason for exclusion	EXCLUDE on study population

Krupinski 1999

Reason for exclusion	EXCLUDE on 2x2 data; *reports only diagnostic concordance/agreement*

Lamel 2012

Reason for exclusion	EXCLUDE on 2x2 data *reports only summary concordance in diagnosis and management decisions between decisions based on mobile phone image and in person; insufficient detail to work out referral accuracy.* EXCLUDE but contact authors: *Study presents data on diagnostic and management concordance between in person and remote (via mobile phone app) diagnoses, are any diagnostic accuracy data available, e.g. observers diagnosis of malignant lesion when assessed remotely versus FtF diagnosis of malignancy?*

Lamminen 2000

Reason for exclusion	EXCLUDE not a primary study

Lesher 1998

Reason for exclusion	EXCLUDE on study population - incl people with 'skin problems' (incl wide range of diagnoses) EXCLUDE on sample size - could extract referral accuracy (tele-dx vs FtF) but only 4 lesions with malignant diagnosis on FtF (4 BCCs).

Lewis 1999

Reason for exclusion	EXCLUDE on 2x2 data; *Study appears to meet all eligibility criteria but disease prevalence not given alongside sensitivity/specificity.* EXCLUDE but contact authors: *authors contacted* (Sensitivity and specificity of remote diagnosis in comparison to FtF diagnosis are provided but we would need number D+ in order to complete 2x2 table)

Loane 1998

Reason for exclusion	EXCLUDE on study population

Loane 1998a

Reason for exclusion	EXCLUDE not a primary study

Loane 2000

Reason for exclusion	EXCLUDE on study population *not focused on potentially malignant skin lesions; cannot derive any comparative data for detection of 'tumours'*

Loane 2001

Reason for exclusion	EXCLUDE not a primary study

Loane 2001a

Reason for exclusion	EXCLUDE on study population

Lowitt 1998

Reason for exclusion	EXCLUDE on study population

Lyon 1997

Reason for exclusion	EXCLUDE on 2x2 data: *for operative referrals, only histo diagnosis given with overall no. of disagreements by FtF and tele-dx; no clear breakdown of index test results to derive 2x2* EXCLUDE on study population; *not all suspected of skin cancer*

Martinez-Garcia 2007

Reason for exclusion	EXCLUDE on 2x2 data *Not test accuracy* EXCLUDE on reference standard - no reference standard reported; describes only tele-dx

Massone 2007

Reason for exclusion	EXCLUDE on reference standard - does not meet our criteria for for diagnostic accuracy ref standard (only 12/25 (48%) of benign group with histo, including 1 AK as benign instead of malignant); and data not presented to allow extraction of referral accuracy (tele-dx vs FtF) [incls 955 lesions and reports tele-dx recommendations for all 955; 121 were recommended for excision or for FtF consult but FU data only available for 32 of these (19 with histo dx and 13 with FtF diagnosis)] EXCLUDE on 2x2 data - data not clearly presented to allow extraction of referral accuracy (tele-dx vs FtF alone); can only extract tele-dx vs FtF diagnosis of malignany if we assume that all 7 malignant lesions were diagnosed as such by FtF - from table 2 we only know that all 7 were excised presumably following FtF consult.

May 2008

Reason for exclusion	EXCLUDE on 2x2 data: *no data for a 2x2 table* EXCLUDE on index test - *effect on consultant priority of GP referral with photograph vs referral with no accompanying photograph*

McGraw 2009

Reason for exclusion	EXCLUDE on study population

McManus 2008

Reason for exclusion	EXCLUDE on study population

Moreno-Ramirez 2006

Reason for exclusion	EXCLUDE on sample size - comparison is Tele-dx vs final diagnosis (58/61 were biopsied); only 1 melanoma and 2 BCC

Moreno-Ramirez 2007

Reason for exclusion	EXCLUDE on reference standard: does not meet either criteria for eligible reference standard. *Table 1 crosstabs the telediagnosis (refer/not refer) against a gold standard which appears to be a combination of the face to face diagnosis (for those with clinically and dermoscopically benign and nonsuspicious lesions, and with a diagnostic confidence level of 3 after the face to face diagnosis) and histology (those with higher concern at FtF evaluation were excised).*

Moreno-Ramirez 2009

Reason for exclusion	EXCLUDE on study population EXCLUDE on reference standard

Ndegwa 2010

Reason for exclusion	EXCLUDE not a primary study *Technology report*

Nordal 2001

Reason for exclusion	EXCLUDE on study population EXCLUDE on target condition

Oakley 1997

Reason for exclusion	EXCLUDE on study population EXCLUDE on target condition

Oakley 2006

Reason for exclusion	EXCLUDE on 2x2 data; insufficient data presented. EXCLUDE but contact authors: *We are looking to compare telederm dx with FtF diagnosis within a diagnostic accuracy framework (i.e. in a 2x2 contingency table) but in order to include your paper we would need information on the misdiagnoses. Using the FtF diagnosis as the gold standard, we can use the data in Table 2 to derive the 'sensitivity' of the tele-Dx agreement for diagnosis of melanoma, BCC and SCC (%agreement), but we would need to know the % of tele-dx reports that 'misdiagnosed' the other lesion types as malignant in order to derive 'specificity'. Would you be at all able to supply this data?* *We could use the data in Table 6 to cross-tabulate the management decisions between the two approaches, if we collapse the tele-Dx cat3 and cat4 groups together. However the % agreement for the teledermatology classification adds to greater than 100.*

Oztas 2004

Reason for exclusion	EXCLUDE on study population EXCLUDE on target condition

Pak 1999

Reason for exclusion	EXCLUDE not a primary study *review of service*

Pak 2002

Reason for exclusion	EXCLUDE conference abstract *no full text paper found*

Pak 2003a

Reason for exclusion	EXCLUDE on study population

Pak 2003b

Reason for exclusion	EXCLUDE on study population

Pak 2007

Reason for exclusion	EXCLUDE on reference standard *reference standard not clear*

Pak 2009

Reason for exclusion	EXCLUDE not a primary study

Patro 2015

Reason for exclusion	EXCLUDE on target condition

Perednia 1998

Reason for exclusion	EXCLUDE on study population; *not all suspected of skin cancer* EXCLUDE on index test; *not an evaluation of accuracy of teledermatology but of effect of access to telemedicine on GP confidence and referral decisions*

Phillips 1997

Reason for exclusion	EXCLUDE on sample size - 68 lesions; FtF diagnosis of 4 skin cancers (tele- and FtF diagnoses concordant for 1 melanoma and 2 BCC; FtF dx of 1 additional SCC in 1 further patient); no final diagnoses (Histo) recorded EXCLUDE on 2x2 data – presents agreement between observers only EXCLUDE on study population – not all suspected of skin cancer

Piccolo 1999

Reason for exclusion	EXCLUDE on 2x2 data - Reports data for tele-dx, FtF and Histo; breakdown of discordant results between Tele-dx vs FtF and Tele-dx vs Histo is given but only gives number (%) concordant; does not give number TP and TN to allow 2x2 to be estimated for either comparison

Piccolo 2002

Reason for exclusion	EXCLUDE not a primary study; review article

Rashid 2003

Reason for exclusion	EXCLUDE on study population

Ribas 2010

Reason for exclusion	EXCLUDE on study population

Romero 2010

Reason for exclusion	EXCLUDE on study population

Romero 2014

Reason for exclusion	EXCLUDE on study population

Seidenari 2004

Reason for exclusion	EXCLUDE on 2x2 data; *No data to populate 2x2 table just ROC curve values given.* EXCLUDE but contact authors; *TABLE 5 provides AUC values for each diagnosis for both formats and observers; requested data in 2x2 format, e.g. for melanoma 'certain' against final diagnosis and for melanoma 'certain or fairly certain' against final diagnosis?*

Senel 2013

Reason for exclusion	EXCLUDE on 2x2 data *no accuracy data available For teledermatology it looks like they have only given us the % of correct diagnoses (Table 6) per dermatologist for but give no breakdown by disease positive/negative so can't work out 2x2 data.*

Shin 2014

Reason for exclusion	EXCLUDE on target condition

Tait 1999

Reason for exclusion	EXCLUDE on study population - not all suspected of skin cancer 'people with visible skin lesion or lesions' (wide range in diagnoses recorded)

Tan 2010

Reason for exclusion	EXCLUDE on reference standard. No reference standard described EXCLUDE on 2x2 data. *Not test accuracy; reports agreement between 5 dermatologists' tele*-diagnosis*, not against histology or FtF diagnosis*

Tan 2010a

Reason for exclusion	EXCLUDE on 2x2 data. *Study appears to meet eligibility criteria however,although sensitivity and specificity values are provided in Table 4 per Dermatologist it is not possible to work back to the underlying 2x2 (final diagnoses by histopath not given and FtF diagnoses for the same 491 lesions differ in Table 1 according to Dermatolgost A and Dermatologist B)*

Tandjung 2015

Reason for exclusion	EXCLUDE on target condition *'Malignant' includes: AK, Bowen's, dysplastic nevus, lentigo maligna, SCC, BCC, MM, keratoacanthoma* EXCLUDE on index test *GPs sent images for teledermatology opinion; then free to send for biopsy or not; results shown are only for those that were biopsied, according to Teledermatology advice*

Taylor 2001

Reason for exclusion	EXCLUDE on study population. *Not all suspected of skin cancer; wide variety of conditions included* EXCLUDE on 2x2 data. *Reports % agreement only*

Tucker 2005

Reason for exclusion	EXCLUDE on target condition. No breakdown of either final diagnoses or tele-dx EXCLUDE on 2x2 data. Reports agreement only EXCLUDE on study population - not all suspected of skin cancer

van der Heijden 2013

Reason for exclusion	EXCLUDE on 2x2 data - only reports Kappa values for histology vs FtF and histology vs Tele-dx (for each of 4 teledermatologists) but no underlying data given.

Vano-Galvan 2011

Reason for exclusion	EXCLUDE on study population *not specific to skin cancer,* popl includes infectious disease and inflammatory disease EXCLUDE on 2x2 data. *Only gives % agreement between tele-dx and FtF (gold standard)*

Warshaw 2009

Reason for exclusion	EXCLUDE on 2x2 data. *Only reports accuracy.* EXCLUDE duplicate or related publication; *author contacted in regard to 2010 paper* EXCLUDE but contact author. Study presents diagnostic accuracy of teledermatology and clinic diagnosis in comparison to histopathology; in order to include in our review, data would need to be presented as a 2x2 contingency table, either per type of malignancy e.g. tele-dx classification of melanoma vs not melanoma against histological diagnosis of melanoma/not melanoma, or with malignant diagnoses grouped together, ie tele-dx of malignancy vs not malignant against same histological breakdown. Ideally we would like this data for the clinic diagnosis and for each method of tele-diagnosis. Is it at all possible to provide this information? Same would go for the study of non-pigmented lesions (also Warshaw 2009), and if possible for the 2010 paper reporting the subgroup of lesions >=25mm (Warshaw 2010). **Author provided some data for detection of melanoma only and for use of macro images only for 2010 paper (pigmented and non-pigmented lesion combined)

Warshaw 2009a

Reason for exclusion	EXCLUDE on 2x2 data. *Only reports accuracy.* EXCLUDE duplicate or related publication; *author contacted in regard to 2010 paper* EXCLUDE but contact author. *See* Warshaw 2010

Warshaw 2010a

Reason for exclusion	EXCLUDE on 2x2 data; *Not test accuracy - inter-observer agreement for sub-sample of* Warshaw 2009 */* Warshaw 2010 *trial*

Warshaw 2015

Reason for exclusion	EXCLUDE on 2x2 data; *only gives agreement between Teledermatology diagnosis and Face to Face diagnosis*

Watson 2010

Reason for exclusion	EXCLUDE on target condition

Weingast 2013

Reason for exclusion	EXCLUDE on study population

Weinstock 2002

Reason for exclusion	EXCLUDE not a primary study

Weinstock 2009

Reason for exclusion	EXCLUDE not a primary study

Whited 1999

Reason for exclusion	EXCLUDE on 2x2 data. *only gives % agreement between tele-dx and FtF and % correct diagnoses of Tele-dx vs histo*

Whited 2002

Reason for exclusion	EXCLUDE not a primary study

Whited 2003

Reason for exclusion	EXCLUDE not a primary study

Whited 2004

Reason for exclusion	EXCLUDE not a primary study

Whited 2006

Reason for exclusion	EXCLUDE not a primary study; *review article*

Whited 2010

Reason for exclusion	EXCLUDE not a primary study

Whited 2016

Reason for exclusion	EXCLUDE not a primary study

Williams 2001

Reason for exclusion	EXCLUDE not a primary study

Williams 2007

Reason for exclusion	EXCLUDE not a primary study

Wootton 2000

Reason for exclusion	EXCLUDE on study population EXCLUDE on target condition

Zelickson 1997

Reason for exclusion	EXCLUDE on study population

Footnotes

ABCD(E) - asymmetry, border, colour, differential structures (enlargement); AK - actinic keratosis; AMN – atypical melanocytic naevi; AUC - area under curve; BCC - basal cell carcinoma; BD – Bowen's disease; BN – benign naevi; CM – cutaneous melanoma; CMM - cutaneous malignant melanoma; CSCC – cutaneous squamous cell carcinoma; Derm – dermoscopy; DF – dermatofibroma; Dx – diagnosis; ELM – epiluminescence microscopy; FNs- false negatives; FPs - false positives; FtF - face-to-face; FU – follow-up ; GP – general practitioner; H&E – haematoxylin and eosin stain; Histo - histology; LPLK – lichen planus-like keratosis; LS – lentigo simplex; MM – malignant melanoma; MiS – melanoma in situ (or lentigo maligna); MN – melanocytic naevi; N/A – not applicable; NMLs – non melanocytic lesions; NR – not reported; PCPs – primary care providers; PLC – pigmented lesion clinic; PSL – pigmented skin lesion; ROC - receiver operating characteristic; SCC - squamous cell carcinoma; SK – seborrhoeic keratosis; SN – Spitz nevi; SSM – superficial spreading melanoma; tele-Dx - teledermatology diagnosis; VI – visual inspection.

Characteristics of studies awaiting classification

Footnotes

Characteristics of ongoing studies

Footnotes

Summary of results tables

1 Summary of findings table

Question:	**What is the diagnostic accuracy of teledermatology for the detection of skin cancer in adults?**
Population:	Adults with lesions suspicious for skin cancer
Index test:	Teledermatology (TD) using photographic and/or dermoscopic images

Question:	**What is the diagnostic accuracy of teledermatology for the detection of skin cancer in adults?**		
Comparator test:	Face-to-face diagnosis using visual inspection and/or dermoscopy		
Target condition:	Any skin cancer, including invasive melanoma and atypical intraepidermal melanocytic variants, basal cell carcinoma (BCC), cutaneous squamous cell carcinoma (cSCC), or any other skin cancer		
Reference standard:	Histology with or without long term follow-up (diagnostic accuracy); Expert face-to-face diagnosis (for referral accuracy)		
Action:	If accurate, positive results ensure the malignant lesions are not missed but are appropriately referred for specialist assessment or are treated appropriately in a non-referred setting, and those with negative results can be safely reassured and discharged.		
Quantity of evidence	**Number of studies**	**Total lesions**	**Total cases**
Diagnostic accuracy	16	4057	879
Referral accuracy	6	1449	270
Limitations			
Risk of bias:	Low risk for participant selection in 7 studies; high risk (5) from case control design (2) or inappropriate exclusion criteria (4). Low risk for teledermatology assessments (22). Low risk for comparison with face-to-face diagnosis (2/5); unclear (3). Low risk for reference standard (10/22); high risk from use of expert diagnosis alone - referral accuracy (6) or inadequate reference standard (6). High risk for participant flow (17) due to differential verification (5), and exclusions following recruitment (14); timing of tests was not mentioned in 14 studies.		
Applicability of evidence to question:	High concern (14/22) for applicability of participants due to recruitment from secondary care or specialist clinics (12) or inclusion of multiple lesions per participant (6). High concern for applicability of teledermatology assessments (12/22) due to images acquired by dermatologists secondary care settings or in medical imaging units rather than images acquired in primary care. Low concern for reference standard (6/22); unclear concern due to lack of information concerning the expertise of the histopathologist (13) or expert face-to-face diagnosis (3).		
FINDINGS:			
Seven studies reported diagnostic accuracy data for the primary target condition of any skin cancer; 9 studies for the detection of invasive melanoma or atypical intraepidermal melanocytic variants; 2 studies for invasive melanoma alone; and four studies for BCC alone. Six studies reported only referral accuracy data (teledermatology decisions versus face-to-face decisions). The findings presented are based on results for the primary target condition of any skin cancer and for the detection of invasive melanoma or atypical intraepidermal melanocytic variants.			
Diagnostic accuracy data	**Number of datasets**	**Total lesions**	**Total malignant**
Test: TD using photographic images for any skin cancer	4	717	452
	Three studies reported a cross-tabulation of lesion final diagnoses against the diagnosis on teledermatology such that data could be extracted for the detection of any malignancy, regardless of any misclassification of one skin cancer for another, e.g. a BCC diagnosed as a melanoma or vice versa; and one study presented data for the detection of 'malignant' versus benign cases with no breakdown of individual lesion diagnoses given. Summary sensitivity was 94.9% (95% CI 90.1 to 97.4%) and summary specificity 84.3% (95% CI 48.5, 96.8%). Two studies providing a direct comparison between teledermatology assessment and in-person diagnosis by a dermatologist the data suggested similar accuracy between approaches; however, data were too scarce to draw firm conclusions.		
Test: TD using clinical and dermoscopic images for any skin cancer	3	928	215
	Sensitivities were 100% in all three studies. Specificities ranged from 25% (95% CI 5% to 57%) to 92% (95% CI 74% to 99%). Studies used varying thresholds to decide test positivity and included highly selected populations. No statistical pooling was undertaken.		
Test: TD using photographic images for invasive melanoma or atypical intraepidermal melanocytic variants	4	1834	106
	Sensitivities ranged from 59% (95% CI 42% to 74%) to 100% (95% CI 54% to 100%) and specificities from 30% (95% CI 22% to 40%) to 100% (95% CI 93% to 100%). Diagnostic thresholds were correct diagnosis of melanoma (n=3) or classification as 'atypical' or 'typical'. Populations also varied, some including only atypical or higher risk pigmented lesions and excluding equivocal lesions and others including both pigmented and non-pigmented lesions who were either self-referred or were deemed to require lesion excision. The number of melanomas missed ranged from 0 to 17.		

Question:	What is the diagnostic accuracy of teledermatology for the detection of skin cancer in adults?		
Test: TD using photographic and dermoscopic images for invasive melanoma or atypical intraepidermal melanocytic variants	4	664	93
	Summary estimates were 85.4% (95% CI 68.3% to 94.1%) for sensitivity and 91.6% (95% CI 81.1% to 96.5%) for specificity. Sensitivities were lower for the correct diagnosis of melanoma (71% to 81%) compared to the decision to refer or to excise a lesion (96% to 100%). The number of melanomas missed ranged from 0 to 7.		
All data (referral accuracy)	**6**	**1449**	**270**
	TD diagnoses were reported based on photographic images alone (n=4), photographic and dermoscopic images (1) and using live link TD (1). Diagnostic decisions on TD varied, including the diagnosis of malignancy, the decision to excise a lesion, the decision to refer versus not refer, or to excise or follow-up at a later date. For store and forward TD sensitivities were generally above 90% indicating good agreement between remote image-based decisions with the face to face reference standard for lesions considered to require some positive action by face to face assessment. Specificities were more variable ranging from 57% (95% CI 39 to 73%) to 100% (95% CI 86% to 100%) suggesting that remote assessment is more likely recommend excision, referral or follow-up for lesions considered of less concern when assessed face-to-face.		

Footnotes

BCC - basal cell carcinoma; CI - confidence interval; cSCC - cutaneous squamous cell carcinoma; TD - teledermatology

Additional tables

1 Cross tabulation of included studies against target condition assessed, by type of images used for teledermatology

Studies of diagnostic accuracy - Teldermatology vs Histology					FtF diagnosis[2] vs Histology	Teldermatology vs expert FtF
Study	**Any skin cancer**	**Melanoma[1]**	**BCC**	**cSCC**		**Action**
Arzberger 2016	Photo/Derm (excise or not)					
Borve 2015	Photo/Derm (dx as malignant/ possibly malignant)					
Bowns 2006		Photo/Derm (dx as MM/MiS)	Photo/Derm (dx as BCC)			
Congalton 2015		Photo/Derm (excise or not)				
Coras 2003		Photo/Derm* (dx as MM/MiS)			dx as MM	
Ferrara 2004		Derm only (dx as MM/MiS)				
Grimaldi 2009		Photo/Derm* (excise or not)			[GP dx as suspicious for malignancy; data not included]	
Jolliffe 2001a	Photo only* (dx as any SC)	<5 MM	Photo only* (dx as BCC)		dx as any SC dx as BCC	
Kroemer 2011	Photo only* Derm only* (dx as malignant)	Photo only* Derm only* (dx as MM/MiS)	Photo only* Derm only* (dx as BCC)	Photo only* Derm only* (dx as cSCC)	dx as malignant dx as MM/MiS dx as BCC dx as cSCC	
Massone 2014	Photo/Derm (dx as malignant)					
Moreno Ramirez 2005	Photol only (dx as malignant)	Photo only (dx as MM/MiS)	Photo only (dx as BCC)			

Studies of diagnostic accuracy - Teldermatology vs Histology					FtF diagnosis[2] vs Histology	Teldermatology vs expert FtF
Study	Any skin cancer	Melanoma[1]	BCC	cSCC		Action
Piccolo 2000		Photo/Derm* (dx as MM)			dx as MM	
Piccolo 2004		Derm only (dx as MM)				
Silveira 2014	Photo only (dx as malignant)					
Warshaw 2010		Photo only* (dx as MM/MiS)			dx of MM/MiS	
Wolf 2013		Photo only (dx as atypical)				
Studies of referral accuracy - Teledermatology versus expert face-to-face decision						
Jolliffe 2001b						Clin only (refer or not)
Mahendran 2005						Clin only (excise or not)
Manahan 2015						Clin/Derm (see FtF)
Oliveira 2002						Clin only (dx as malignant)
Phillips 1998						Live link (dx as any SC; def/prob malignant/ excise or not)
Shapiro 2004						Clin only (excise or not)

Footnotes

BCC - basal cell carcinoma; cSCC - cutaneous squamous cell carcinoma; Derm - dermoscopic images; dx - diagnosis; FtF - face-to-face; FU - follow-up; MiS - melanoma in situ (atypical intraepidermal melanocytic variants); MM - invasive melanoma; Photo - photographic images; Rx - treat or treatment; SC - skin cancer; TD - teledermatology

1 all include melanoma in situ as disease positive apart from Piccolo 2000 and Piccolo 2004 which report detection of invasive melanoma only

2 face to face diagnosis by an expert/dermatologist unless otherwise stated

*Includes a direct comparison with expert face-to-face diagnosis versus Histology

2 Summary estimates of sensitivity and specificity for teledermatology

Index test*, target condition	Studies	Cases/Number of participants	Summary sensitivity (95% CI) %	Summary specificity (95% CI) %
Teledermatology photographic image, Any	4	452 / 717	94.9 (90.1 to 97.4)	84.3 (48.5 to 96.8)
Teledermatology photographic/dermoscopic image, MM+MiS	4	93 / 664	85.4 (68.3 to 94.1)	91.6 (81.1 to 96.5)
Teledermatology photographic image vs histology, BCC	3	62 /301	93.5 (84.0 to 97.6)	95.8 (92.4 to 97.7)

Footnotes

Any - any skin cancer; BCC - basal cell carcinoma; CI - confidence interval; MM+MiS = Invasive melanoma and atypical intraepidermal melanocytic variants

*Reference standard was histology for all comparisons

3 Direct comparisons of teledermatology with face-to-face diagnosis of melanoma and other types of skin cancer

Study	Sensitivity (true positives/cases) %		Difference (95% CI)	Specificity (true negatives/non cases) %		Difference (95% CI)
Any skin cancer						
	Teledermatology photographic image	*Expert face-to-face*		*Teledermatology photographic image*	*Expert face-to-face*	
Jolliffe 2001a	100 (13/13)	100 (13/13)	0.00 (-2.28, 2.28)	92.9 (118/127)	94.7 (124/131)	-1.74 (-8.18, 4.49)
Kroemer 2011	93 (43/46)	100 (46/46)	-0.06 (-0.17, 0.02)	88 (51/58)	90 (52/58)	-0.02 (-0.14, 0.10)
	Teledermatology dermoscopic image	*Expert face-to-face*		*Teledermatology dermoscopic image*	*Expert face-to-face*	
Kroemer 2011	85 (39/46)	100 (46/46)	-0.15 (-0.28, -0.04)	91 (53/58)	90 (52/58)	0.02 (-0.13, 0.09)
Invasive melanoma or atypical intraepidermal melanocytic variants						
	Teledermatology *photographic*+dermoscopic image	Expert face-to-face		Teledermatology *photographic*+dermoscopic image	Expert face-to-face	
Coras 2003	81 (13/16)	88 (14/16)	-0.06 (-0.32, 0.20)	93 (27/29)	93 (27/29)	0.00 (-0.16, 0.16)
	Teledermatology dermoscopic image	Expert face-to-face		Teledermatology dermoscopic image	Expert face-to-face	
Kroemer 2011	100 (5/5)	100 (5/5)	0.00 (-0.43, 0.43)	98 (97/99)	99 (98/99)	-0.01 (-0.06, 0.04)
Warshaw 2010	59 (24/41)	73 (30/41)	-0.15 (-0.33, 0.06)	41 (604/1473)	63 (930/1473)	-0.22 (-0.26, -0.19)*
Invasive melanoma						
	Teledermatology photographic/dermoscopic image	*Expert face-to-face*		*Teledermatology photographic/dermoscopic image*	*Expert face-to-face*	
Piccolo 2000	81.8 (9/11)	72.7 (8/11)	9.10 (-25.2, 41.2)	100 (32/32)	96.9 (31/32)	3.13 (-7.90, 15.7)
Basal cell carcinoma						
	Teledermatology photographic image	*Expert face-to-face*		*Teledermatology photographic image*	*Expert face-to-face*	
Jolliffe 2001a	100 (9/9)	100 (9/9)	0.00 (-29.9, 29.9)	97.0 (127/131)	97.8 (132/135)	-0.83 (-5.60, 3.68)

Footnotes

CI - confidence interval;

* denotes statistically significant difference

References to studies

Included studies

Arzberger 2016

* Arzberger E, Curiel-Lewandrowski C, Blum A, Chubisov D, Oakley A, Rademaker M, et al. Teledermoscopy in High-risk Melanoma Patients: A Comparative Study of Face-to-face and Teledermatology Visits. Acta Dermato-Venereologica 2016;96(6):779-83. [Other: ER4:25012365; PubMed: 26776245]

Borve 2015

Borve A, Dahlen Gyllencreutz J, Terstappen K, Johansson Backman E, Aldenbratt A, Danielsson M, et al. Smartphone teledermoscopy referrals: a novel process for improved triage of skin cancer patients. Acta Dermato-Venereologica 2015; 95(2):180-90. [PubMed: 24923283]

Bowns 2006

* Bowns IR, Collins K, Walters SJ, McDonagh AJ. Telemedicine in dermatology: a randomised controlled trial. Health Technology Assessment (Winchester, England) 2006;10(43):iii-iv, ix-xi, 1-39. [Other: ER4:15465874; PubMed: 17049140]

Congalton 2015

* Congalton AT, Oakley AM, Rademaker M, Bramley D, Martin RC. Successful melanoma triage by a virtual lesion clinic (teledermatoscopy). Journal of the European Academy of Dermatology & Venereology 2015;29(12):2423-8. [Other: ER4:25012348; PubMed: 26370585]

Coras 2003

* Coras B, Glaessl A, Kinateder J, Klovekorn W, Braun R, Lepski U, et al. Teledermatoscopy in daily routine--results of the first 100 cases. Current Problems in Dermatology 2003;32:207-12. [Other: ER4:18375040; PubMed: 12472014]

Ferrara 2004

Ferrara G, Argenziano G, Cerroni L, Cusano F, Di Blasi A, Urso C, et al. A pilot study of a combined dermoscopic–pathological approach to the telediagnosis of melanocytic skin neoplasms. Journal of Telemedicine and Telecare 2004;10(1):34–8. [PubMed: 15006214]

Grimaldi 2009

* Grimaldi L, Silvestri A, Brandi C, Nisi G, Brafa A, Calabro M, et al. Digital epiluminescence dermoscopy for pigmented cutaneous lesions, primary care physicians, and telediagnosis: a useful tool? Journal of Plastic, Reconstructive & Aesthetic Surgery: JPRAS 2009;62(8):1054-8. [Other: ER4:15465940; PubMed: 18547883]

Jolliffe 2001a

* Jolliffe VM, Harris DW, Whittaker SJ. Can we safely diagnose pigmented lesions from stored video images? A diagnostic comparison between clinical examination and stored video images of pigmented lesions removed for histology. Clinical & Experimental Dermatology 2001;26(1):84-7. [Other: ER4:15465970; PubMed: 11260186]

Jolliffe 2001b

Jolliffe VM, Harris DW, Morris R, Wallace P, Whittaker SJ. Can we use video images to triage pigmented lesions? British Journal of Dermatology 2001;145(6):904-10. [PubMed: 11899143]

Kroemer 2011

* Kroemer S, Fruhauf J, Campbell TM, Massone C, Schwantzer G, Soyer HP, et al. Mobile teledermatology for skin tumour screening: diagnostic accuracy of clinical and dermoscopic image tele-evaluation using cellular phones. British Journal of Dermatology 2011;164(5):973-9. [Other: ER4:15465982; PubMed: 21219286]

Mahendran 2005

* Mahendran R, Goodfield MJ, Sheehan-Dare RA. An evaluation of the role of a store-and-forward teledermatology system in skin cancer diagnosis and management. Clinical & Experimental Dermatology 2005;30(3):209-14. [Other: ER4:15465998; PubMed: 15807671]

Manahan 2015

Manahan MN, Soyer HP, Loescher LJ, Horsham C, Vagenas D, Whiteman DC, et al. A pilot trial of mobile, patient-performed teledermoscopy. British Journal of Dermatology 2015;172(4):1072-80.

Massone 2014

* Massone C, Maak D, Hofmann-Wellenhof R, Soyer HP, Fruhauf J. Teledermatology for skin cancer prevention: an experience on 690 Austrian patients. Journal of the European Academy of Dermatology & Venereology 2014; 28(8):1103-8. [Other: ER4:17941088; PubMed: 24372877]

Moreno Ramirez 2005

* Moreno Ramirez D, Ferrandiz L, Bernal AP, Duran RC, Martin JJ, Camacho F. Teledermatology as a filtering system in pigmented lesion clinics. Journal of Telemedicine & Telecare 2005;11(6):298-303. [Other: ER4:15466016; PubMed: 16168166]

Oliveira 2002

Oliveira MR, Wen CL, Neto CF, Silveira PS, Rivitti EA, Bohm GM. Web site for training nonmedical health-care workers to identify potentially malignant skin lesions and for teledermatology. Telemedicine Journal and E-health 2002;8(3):323-32.

Phillips 1998

Phillips CM, Burke WA, Allen MH, Stone D, Wilson JL. Reliability of telemedicine in evaluating skin tumors. Telemedicine Journal 1998;4(1):5-9.

Piccolo 2000

* Piccolo D, Smolle J, Argenziano G, Wolf IH, Braun R, Cerroni L, et al. Teledermoscopy--results of a multicentre study on 43 pigmented skin lesions. Journal of Telemedicine & Telecare 2000;6(3):132-7. [Other: ER4:15466059; PubMed: 10912329]

Piccolo 2004

* Piccolo D, Soyer HP, Chimenti S,Argenziano G, Bartenjev I, Hofmann-Wellenhof R, et al. Diagnosis and categorization of acral melanocytic lesions using teledermoscopy. Journal of Telemedicine & Telecare 2004; 10(6):346-50. [Other: ER4:15466061; PubMed: 15603633]

Shapiro 2004

* Shapiro M, James WD, Kessler R, Lazorik FC, Katz KA, Tam J, et al. Comparison of skin biopsy triage decisions in 49 patients with pigmented lesions and skin neoplasms: store-and-forward teledermatology vs face-to-face dermatology. Archives of Dermatology 2004;140(5):525-8. [Other: ER4:15466120; PubMed: 15148095]

Silveira 2014

Silveira CE, Silva TB, Fregnani JH, da Costa Vieira RA, Haikel RL, Syrjänen K, et al. Digital photography in skin cancer screening by mobile units in remote areas of Brazil. BMC Dermatology 2014;14:19. [PubMed: 25539949]

Warshaw 2010

Warshaw EM, Gravely AA, Nelson DB. Accuracy of teledermatology/teledermoscopy and clinic-based dermatology for specific categories of skin neoplasms. Journal of the American Academy of Dermatology 2010;63(2):348-52.

Wolf 2013

Wolf JA, Moreau JF, Akilov O, Patton T, English JC 3rd, Ho J, et al. Diagnostic inaccuracy of smartphone applications for melanoma detection. JAMA Dermatol 2013;149(4):422-6. [PubMed: 23325302]

Excluded studies

Armstrong 2007

Armstrong AW, Dorer DJ, Lugn NE, Kvedar JC. Economic evaluation of interactive teledermatology compared with conventional care. Telemedicine Journal and E-health 2007;3(2):91-9. [DOI: 10.1089/tmj.2006.0035]

Baba 2005

Baba M, Seckin D, Kapdagli S. A comparison of teledermatology using store-and-forward methodology alone, and in combination with Web camera videoconferencing. Journal of Telemedicine and Telecare 2005;11(7):354-60. [DOI: 10.1258/135763305774472097]

Badertscher 2015

Badertscher N, Tandjung R, Senn O, Kofmehl R, Held U, Rosemann T, et al. A multifaceted intervention: no increase in general practitioners' competence to diagnose skin cancer (minSKIN) - randomized controlled trial. Journal of the European Academy of Dermatology & Venereology 2015;29(8):1493-9.

Barnard 2000

Barnard CM, Goldyne ME. Evaluation of an asynchronous teleconsultation system for diagnosis of skin cancer and other skin diseases. Telemedicine Journal and E-health 2000;6(4):379-84.

Bashshur 2015

Bashshur RL, Shannon GW, Tejasvi T, Kvedar JC, Gates M. The Empirical Foundations of Teledermatology: A Review of the Research Evidence. Telemedicine Journal and E-Health 2015;21(12):953-79.

Bataille 2011

Bataille V, Hargest E, Brown V, Blackwell V, Dawe S, Cooper A, et al. A teledermatology pilot study in Hertfordshire: Triage of 2-week-wait referrals. British Journal of Dermatology 2011;165(Suppl 1):137-8.

Bergmo 2000

Bergmo TS. A cost-minimization analysis of a realtime teledermatology service in northern Norway. Journal of Telemedicine and Telecare 2000;6(5):273-7.

Borve 2013

Borve A, Terstappen K, Sandberg C, Paoli J. Mobile teledermoscopy-there's an app for that! Dermatology Practical &

Conceptual 2013;3(2):41-8.

Boyce 2011

Boyce Z, Gilmore S, Xu C, Soyer HP. The remote assessment of melanocytic skin lesions: A viable alternative to face-to-face consultation. Dermatology 2011;223(3):244-50.

Braun 2000

Braun RP, Meier M, Pelloni F, Ramelet AA, Schilling M, Tapernoux B, et al. Teledermatoscopy in Switzerland: a preliminary evaluation. Journal of the American Academy of Dermatology 2000;42(5 Pt 1):770-5.

Brown 2000

Brown N. Exploration of diagnostic techniques for malignant melanoma: an integrative review. Clinical Excellence for Nurse Practitioners 2000;4(5):263-71.

Burgiss 1997

Burgiss SG, Julius CE, Watson HW, Haynes BK, Buonocore E, Smith GT. Telemedicine for dermatology care in rural patients. Telemedicine Journal and E-health 1997;3(3):227-33. [DOI: 10.1089/tmj.1.1997.3.227]

Chen 2002

Chen K, Lim A, Shumack S. Teledermatology: influence of zoning and education on a clinician's ability to observe peripheral lesions. Australasian Journal of Dermatology 2002;43(3):171-4.

D'Elia 2007

D'Elia PB, Harzheim E, Fisher PD, Ramos MC, Bordin R. Agreement between dermatological diagnoses made by direct observation and digital images [Concordancia entre diagnosticos dermatologicos feitos presencialmente e por imagens digitais]. Anais Brasileiros de Dermatologia 2007;82(6):521-7.

Di Stefani 2007

Di Stefani A, Zalaudek I, Argenziano G, Chimenti S, Soyer HP. Feasibility of a two-step teledermatologic approach for the management of patients with multiple pigmented skin lesions. Dermatologic Surgery 2007;33(6):686-92.

Du Moulin 2003

Du Moulin MF, Bullens-Goessens YI, Henquet CJ, Brunenberg DE, de Bruyn-Geraerds DP, Winkens RA, et al. The reliability of diagnosis using store-and-forward teledermatology. Journal of Telemedicine and Telecare 2003;9(5):249-52.

Edison 2008

Edison KE, Ward DS, Dyer JA, Lane W, Chance L, Hicks LL. Diagnosis, diagnostic confidence, and management concordance in live-interactive and store-and-forward teledermatology compared to in-person examination. Telemedicine Journal and E-Health 2008;14(9):889-95. [DOI: 10.1089/tmj.2008.0001]

Eminovic 2009

Eminovic N, de Keizer NF, Wyatt JC, ter Riet G, Peek N, van Weert HC, et al. Teledermatologic consultation and reduction in referrals to dermatologists: a cluster randomized controlled trial. Archives Dermatology 2009;145(5):558-64.

Fabbrocini 2008

Fabbrocini G, Balato A, Rescigno O, Mariano M, Scalvenzi M, Brunetti B. Telediagnosis and face-to-face diagnosis reliability for melanocytic and non-melanocytic 'pink' lesions. Journal of the European Academy of Dermatology & Venereology 2008; 22(2):229-34.

Ferrandiz 2007

Ferrandiz L, Moreno RD, Nieto-Garcia A, Carrasco R, Moreno-Alvarez P, Galdeano R, et al. Teledermatology-based presurgical management for nonmelanoma skin cancer: a pilot study. Dermatologic Surgery 2007;33(9):1092-8.

Ferrandiz 2012

Ferrandiz L, Ruiz-de-Casas A, Martin-Gutierrez FJ, Peral-Rubio F, Mendez-Abad C, Rios-Martin JJ, et al. Effect of teledermatology on the prognosis of patients with cutaneous melanoma. Archives of Dermatology 2012;148(9):1025-8.

Gilmour 1998

Gilmour E, Campbell SM, Loane MA, Esmail A, Griffiths CE, Roland MO, et al. Comparison of teleconsultations and face-to-face consultations: preliminary results of a United Kingdom multicentre teledermatology study. British Journal of Dermatology 1998;139(1):81-7.

Granlund 2003

Granlund H, Thoden CJ, Carlson C, Harno K. Realtime teleconsultations versus face-to-face consultations in dermatology: immediate and six-month outcome. Journal of Telemedicine and Telecare 2003;9(4):204-9.

Griffiths 2010

Griffiths WA. Improving melanoma diagnosis in primary care--a tele-dermatoscopy project. Journal of Telemedicine and

Telecare 2010;16(4):185-6.

Harrison 1998

Harrison PV, Kirby B, Dickinson Y, Schofield R. Teledermatology--high technology or not? Journal of Telemedicine and Telecare 1998;4(Suppl 1):31-2.

Heffner 2009

Heffner VA, Lyon VB, Brousseau DC, Holland KE, Yen K. Store-and-forward teledermatology versus in-person visits: A comparison in pediatric teledermatology clinic. Journal of the American Academy of Dermatology 2009;60(6):956-61.

Hicks 2003

Hicks LL, Boles KE, Hudson S, Kling B, Tracy J, Mitchell J, et al. Patient satisfaction with teledermatology services. Journal of Telemedicine and Telecare 2003;9(1):42-5.

High 2000

High WA, Houston MS, Calobrisi SD, Drage LA, McEvoy MT. Assessment of the accuracy of low-cost store-and-forward teledermatology consultation. Journal of the American Academy of Dermatology 2000;42(5):776-83.

Hue 2016

Hue L, Makhloufi S, Sall N'Diaye P, Blanchet-Bardon C, Sulimovic L, Pomykala F, et al. Real-time mobile teledermoscopy for skin cancer screening targeting an agricultural population: an experiment on 289 patients in France. Journal of the European Academy of Dermatology & Venereology 2016;30(1):20-4.

Hwang 2014

Hwang JS, Lappan CM, Sperling LC, Meyerle JH. Utilization of Telemedicine in the U.S. Military in a Deployed Setting. Military Medicine 2014;179(11):1347-53.

Ishioka 2009

Ishioka P, Tenorio JM, Lopes PR, Yamada S, Michalany NS, Amaral MB, et al. A comparative study of teledermatoscopy and face-to-face examination of pigmented skin lesions. Journal of Telemedicine and Telecare 2009;15(5):221-5.

Kahn 2013

Kahn E, Sossong S, Goh A, Carpenter D, Goldstein S. Evaluation of skin cancer in Northern California Kaiser Permanente's store-and-forward teledermatology referral program. Telemedicine Journal and E-health 2013;19(10):780-5.

Knol 2006

Knol A, van den Akker TW, Damstra RJ, de Haan J. Teledermatology reduces the number of patient referrals to a dermatologist. Journal of Telemedicine and Telecare 2006;12(2):75-8.

Krupinski 1999

Krupinski EA, LeSueur B, Ellsworth L, Levine N, Hansen R, Silvis N, et al. Diagnostic accuracy and image quality using a digital camera for teledermatology. Telemedicine Journal 1999;5(3):257-63.

Lamel 2012

Lamel SA, Haldeman KM, Ely H, Kovarik CL, Pak H, Armstrong AW. Application of mobile teledermatology for skin cancer screening. Journal of the American Academy of Dermatology 2012;67(4):576-81.

Lamminen 2000

Lamminen H, Tuomi ML, Lamminen J, Uusitalo H. A feasibility study of realtime teledermatology in Finland. Journal of Telemedicine and Telecare 2000;6(2):102-7.

Lesher 1998

Lesher JL Jr, Davis LS, Gourdin FW, English D, Thompson WO. Telemedicine evaluation of cutaneous diseases: A blinded comparative study. Journal of the American Academy of Dermatology 1998;38(1):27-31.

Lewis 1999

Lewis K, Gilmour E, Harrison PV, Patefield S, Dickinson Y, Manning D, et al. Digital teledermatology for skin tumours: a preliminary assessment using a receiver operating characteristics (ROC) analysis. Journal of Telemedicine and Telecare 1999;5(Suppl 1):S57-8.

Loane 1998

Loane MA, Bloomer SE, Corbett R, Eedy DJ, Gore HE, Mathews C, et al. Patient satisfaction with realtime teledermatology in Northern Ireland. Journal of Telemedicine and Telecare 1998;4(1):36-40.

Loane 1998a

Loane MA, Corbett R, Bloomer SE, Eedy DJ, Gore HE, Mathews C, et al. Diagnostic accuracy and clinical management by realtime teledermatology. Results from the Northern Ireland arms of the UK Multicentre Teledermatology Trial. Journal of Telemedicine and Telecare 1998;4(2):95-100.

Loane 2000

Loane MA, Bloomer SE, Corbett R, Eedy DJ, Hicks N, Lotery HE, et al. A comparison of real-time and store-and-forward teledermatology: a cost-benefit study. British Journal of Dermatology 2000;143(6):1241-7.

Loane 2001

Loane MA, Bloomer SE, Corbett R, Eedy DJ, Evans C, Hicks N, et al. A randomized controlled trial assessing the health economics of realtime teledermatology compared with conventional care: an urban versus rural perspective. Journal of Telemedicine and Telecare 2001;7(2):108-18.

Loane 2001a

Loane MA, Oakley A, Rademaker M, Bradford N, Fleischl P, Kerr P, et al. A cost-minimization analysis of the societal costs of realtime teledermatology compared with conventional care: results from a randomized controlled trial in New Zealand. Journal of Telemedicine and Telecare 2001;7(4):233-8.

Lowitt 1998

Lowitt MH, Kessler II, Kauffman C, Hooper FJ, Siegel E, Burnett JW. Teledermatology and in-person examinations: A comparison of patient and physician perceptions and diagnostic agreement. Archives of Dermatology 1998;134(4):471-6.

Lyon 1997

Lyon CC, Harrison PV. A portable digital imaging system in dermatology: Diagnostic and educational applications. Journal of Telemedicine and Telecare 1997;3(1_suppl):81-3.

Martinez-Garcia 2007

Martinez-Garcia S, del Boz-Gonzalez J, Martin-Gonzalez T, Samaniego-Gonzalez E, Crespo-Erchiga V. Teledermatology. Review of 917 teleconsults. Actas Dermo-Sifiliograficas 2007;98(5):318-24.

Massone 2007

Massone C, Hofmann-Wellenhof R, Ahlgrimm-Siess V, Gabler G, Ebner C, Soyer HP. Melanoma screening with cellular phones. PLoS ONE (Electronic Resource) 2007;2(5):e483.

May 2008

May C, Giles L, Gupta G. Prospective observational comparative study assessing the role of store and forward teledermatology triage in skin cancer. Clinical and Experimental Dermatology 2008;33(6):736-9.

McGraw 2009

McGraw TA, Norton SA. Military aeromedical evacuations from central and southwest Asia for ill-defined dermatologic diseases. Archives of Dermatology 2009;145(2):165-70.

McManus 2008

McManus J, Salinas J, Morton M, Lappan C, Poropatich R. Teleconsultation program for deployed soldiers and healthcare professionals in remote and austere environments. Prehospital & Disaster Medicine 2008;23(3):210-6.

Moreno-Ramirez 2006

Moreno Ramirez D, Ferrandiz L, Galdeano R, Camacho FM. Teledermatoscopy as a triage system for pigmented lesions: a pilot study. Clinical and Experimental Dermatology 2006;31(1):13-8.

Moreno-Ramirez 2007

Moreno Ramirez D, Ferrandiz L, Nieto-Garcia A, Carrasco R, Moreno-Alvarez P, Galdeano R, et al. Store-and-forward teledermatology in skin cancer triage: experience and evaluation of 2009 teleconsultations. Archives of Dermatology 2007; 143(4):479-84.

Moreno-Ramirez 2009

Moreno Ramirez D, Ferrandiz L, Ruiz-de-Casas A, Nieto-Garcia A, Moreno-Alvarez P, Galdeano R, et al. Economic evaluation of a store-and-forward teledermatology system for skin cancer patients. Journal of Telemedicine and Telecare 2009;15(1):40-5.

Ndegwa 2010

Ndegwa S, Prichett-Pejic W, McGill S, Murphy G, Severn M. Teledermatology services: rapid review of diagnostic, clinical management, and economic outcomes. Ottawa: Canadian Agency for Drugs and Technologies in Health (CADTH), 2010.

Nordal 2001

Nordal EJ, Moseng D, Kvammen B, Løchen ML. A comparative study of teleconsultations versus face-to-face consultations. Journal of Telemedicine and Telecare 2001;7(5):257-65.

Oakley 1997

Oakley AM, Astwood DR, Loane M, Duffill MB, Rademaker M, Wootton R. Diagnostic accuracy of teledermatology: results of a preliminary study in New Zealand. New Zealand Medical Journal 1997;110(1038):51-3.

Oakley 2006

Oakley AM, Reeves F, Bennett J, Holmes SH, Wickham H. Diagnostic value of written referral and/or images for skin lesions. Journal of Telemedicine and Telecare 2006;12(3):151-8.

Oztas 2004

Oztas MO, Calikoglu E, Baz K, Birol A, Onder M, Calikoglu T, et al. Reliability of Web-based teledermatology consultations. Journal of Telemedicine and Telecare 2004;10(1):25-8.

Pak 1999

Pak HS, Welch M, Poropatich R. Web-based teledermatology consult system: preliminary results from the first 100 cases. Studies in Health Technology and Informatics 1999;64:179-84.

Pak 2002

Pak HS. Teledermoscopy: a specific application of teledermotology. SKINmed 2002;1(1):18-9.

Pak 2003a

Pak HS, Harden D, Cruess D, Welch ML, Poropatich R. Teledermatology: an intraobserver diagnostic correlation study, part I. Cutis 2003;71(5):399-403.

Pak 2003b

Pak HS, Harden D, Cruess D, Welch ML, Poropatich R. Teledermatology: an intraobserver diagnostic correlation study, Part II. Cutis 2003;71(6):476-80.

Pak 2007

Pak H, Triplett CA, Lindquist JH, Grambow SC, Whited JD. Store-and-forward teledermatology results in similar clinical outcomes to conventional clinic-based care. Journal of Telemedicine and Telecare 2007;13(1):26-30.

Pak 2009

Pak HS, Datta SK, Triplett CA, Lindquist JH, Grambow SC, Whited JD. Cost minimization analysis of a store-and-forward teledermatology consult system. Telemedicine Journal and E-health 2009;15(2):160-5.

Patro 2015

Patro B, Tripathy J, De D, Sinha S, Singh A, Kanwar AJ. Diagnostic agreement between a primary care physician and a teledermatologist for common dermatological conditions in North India. Indian Dermatology Online Journal 2015;6(1):21-6.

Perednia 1998

Perednia DA, Wallace J, Morrisey M, Bartlett M, Marchionda L, Gibson A, et al. The effect of a teledermatology program on rural referral patterns to dermatologists and the management of skin disease. Studies in health technology and informatics 1998;52(Pt 1):290-3.

Phillips 1997

Phillips CM, Burke WA, Shechter A, Stone D, Balch D, Gustke S. Reliability of dermatology teleconsultations with the use of teleconferencing technology. Journal of the American Academy of Dermatology 1997;37(3):398-402.

Piccolo 1999

Piccolo D, Smolle J, Wolf IH, Peris K, Hofmann-Wellenhof R, Dell'Eva G, et al. Face-to-face diagnosis vs telediagnosis of pigmented skin tumors: a teledermoscopic study. Archives of Dermatology 1999;135(12):1467-71.

Piccolo 2002

Piccolo D, Peris K, Chimenti S, Argenziano G, Soyer HP. Jumping into the future using teledermoscopy. SKINmed 2002; 1(1):20-4.

Rashid 2003

Rashid E, Ishtiaq O, Gilani S, Zafar A. Comparison of store and forward method of teledermatology with face-to-face consultation. Journal of Ayub Medical College, Abbottabad 2003;15(2):34-6.

Ribas 2010

Ribas J, da Graça Souza Cunha M, Schettini AP, Barros da Rocha Ribas C. Concordância entre diagnósticos dermatológicos obtidos por consulta presencial e por análise de imagens digitais. Anais Brasileiros de Dermatologia 2010; 85(4):441-7.

Romero 2010

Romero G, Sanchez P, Garcia M, Cortina P, Vera E, Garrido JA. Randomized controlled trial comparing store-and-forward teledermatology alone and in combination with web-camera videoconferencing. Clinical and Experimental Dermatology 2010; 35(3):311-7.

Romero 2014

Romero Aguilera G, Cortina de la Calle P, Vera Iglesias E, Sánchez Caminero P, García Arpa M, Garrido Martín JA. Interobserver reliability of store-and-forward teledermatology in a clinical practice setting. Actas Dermo-Sifiliográficas (English Edition) 2014;105(6):605-13.

Seidenari 2004

Seidenari S, Pellacani G, Righi E, Di Nardo A. Is JPEG compression of videomicroscopic images compatible with telediagnosis? Comparison between diagnostic performance and pattern recognition on uncompressed TIFF images and JPEG compressed ones. Telemedicine Journal and E-health 2004;10(3):294-303.

Senel 2013

Senel E, Baba M, Durdu M. The contribution of teledermatoscopy to the diagnosis and management of non-melanocytic skin tumours. Journal of Telemedicine and Telecare 2013;19(1):60-3.

Shin 2014

Shin H, Kim DH, Ryu HH, Yoon SY, Jo SJ. Teledermatology consultation using a smartphone multimedia messaging service for common skin diseases in the Korean army: a clinical evaluation of its diagnostic accuracy. Journal of Telemedicine and Telecare 2014;20(2):70-4.

Tait 1999

Tait CP, Clay CD. Pilot study of store and forward teledermatology services in Perth, Western Australia. Australasian Journal of Dermatology 1999;40(4):190-3.

Tan 2010

Tan E, Oakley A, Soyer HP, Haskett M, Marghoob A, Jameson M, et al. Interobserver variability of teledermoscopy: an international study. British Journal of Dermatology 2010;163(6):1276-81.

Tan 2010a

Tan E, Yung A, Jameson M, Oakley A, Rademaker M. Successful triage of patients referred to a skin lesion clinic using teledermoscopy (IMAGE IT trial). British Journal of Dermatology 2010;162(4):803-11.

Tandjung 2015

Tandjung R, Badertscher N, Kleiner N, Wensing M, Rosemann T, Braun RP, et al. Feasibility and diagnostic accuracy of teledermatology in Swiss primary care: process analysis of a randomized controlled trial. Journal of Evaluation in Clinical Practice 2015;21(2):326-31.

Taylor 2001

Taylor P, Goldsmith P, Murray K, Harris D, Barkley A. Evaluating a telemedicine system to assist in the management of dermatology referrals. British Journal of Dermatology 2001;144(2):328-33.

Tucker 2005

Tucker WF, Lewis FM. Digital imaging: a diagnostic screening tool? International Journal of Dermatology 2005;44(6):479-81.

van der Heijden 2013

van der Heijden JP, Thijssing L, Witkamp L, Spuls PI, de Keizer NF. Accuracy and reliability of teledermatoscopy with images taken by general practitioners during everyday practice. Journal of Telemedicine and Telecare 2013;19(6):320-5.

Vano-Galvan 2011

Vano-Galvan S, Hidalgo A, Aguayo-Leiva I, Gil-Mosquera M, Rios-Buceta L, Plana MN, et al. (Store-and-forward teledermatology: assessment of validity in a series of 2000 observations). Actas Dermo-Sifiliograficas 2011;102(4):277-83.

Warshaw 2009

Warshaw EM, Lederle FA, Grill JP, Gravely AA, Bangerter AK, Fortier LA, et al. Accuracy of teledermatology for pigmented neoplasms. Journal of the American Academy of Dermatology 2009;61(5):753-65.

Warshaw 2009a

Warshaw EM, Lederle FA, Grill JP, Gravely AA, Bangerter AK, Fortier LA, et al. Accuracy of teledermatology for nonpigmented neoplasms. Journal of the American Academy of Dermatology 2009;60(4):579-88.

Warshaw 2010a

Warshaw EM, Gravely AA, Bohjanen KA, Chen K, Lee PK, Rabinovitz HS, et al. Interobserver accuracy of store and forward teledermatology for skin neoplasms. Journal of the American Academy of Dermatology 2010;62(3):513-6.

Warshaw 2015

Warshaw EM, Gravely AA, Nelson DB. Reliability of store and forward teledermatology for skin neoplasms. Journal of the American Academy of Dermatology 2015;72(3):426-35.

Watson 2010

Watson AJ, Bergman H, Williams CM, Kvedar JC. A randomized trial to evaluate the efficacy of online follow-up visits in the

management of acne. Archives of Dermatology 2010;146(4):406-11.

Weingast 2013

Weingast J, Scheibböck C, Wurm EM, Ranharter E, Porkert S, Dreiseitl S, et al. A prospective study of mobile phones for dermatology in a clinical setting. Journal of Telemedicine and Telecare 2013;19(4):213-8.

Weinstock 2002

Weinstock MA, Nguyen FQ, Risica PM. Patient and referring provider satisfaction with teledermatology. Journal of the American Academy of Dermatology 2002;47(1):68-72.

Weinstock 2009

Weinstock MA. Evaluation of in-person dermatology versus teledermatology. Journal of the American Academy of Dermatology 2009;61(5):902-3.

Whited 1999

Whited JD, Hall RP, Simel DL, Foy ME, Stechuchak KM, Drugge RJ, et al. Reliability and accuracy of dermatologists' clinic-based and digital image consultations. Journal of the American Academy of Dermatology 1999;41(5):693-702.

Whited 2002

Whited JD, Hall RP, Foy ME, Marbrey LE, Grambow SC, Dudley TK, et al. Teledermatology's impact on time to intervention among referrals to a dermatology consult service. Telemedicine Journal and E-health 2002;8(3):313-21.

Whited 2003

Whited JD, Datta S, Hall RP, Foy ME, Marbrey LE, Grambow SC, et al. An economic analysis of a store and forward teledermatology consult system. Telemedicine Journal and E-health 2003;9(4):351-60.

Whited 2004

Whited JD, Hall RP, Foy ME, Marbrey LE, Grambow SC, Dudley TK, et al. Patient and clinician satisfaction with a store-and-forward teledermatology consult system. Telemedicine Journal and E-health 2004;10(4):422-31.

Whited 2006

Whited JD. Teledermatology research review. International Journal of Dermatology 2006;45(3):220-9.

Whited 2010

Whited JD. Economic analysis of telemedicine and the teledermatology paradigm. Telemedicine Journal and E-health 2010; 16(2):223-8.

Whited 2016

Whited JD. Diagnosis and management of pigmented skin lesions using teledermatology. Current Dermatology Reports 2016;5(2):90-5.

Williams 2001

Williams T, May C, Esmail A, Ellis N, Griffiths C, Stewart E, et al. Patient satisfaction with store-and-forward teledermatology. Journal of Telemedicine and Telecare 2001;7(Suppl 1):45-6.

Williams 2007

Williams CM, Qureshi A, Geller A, Kvedar J. Skin cancer education program via teledermatology: Is it effective? Journal of the American Academy of Dermatology 2007;56(2):AB100.

Wootton 2000

Wootton R, Bloomer SE, Corbett R, Eedy DJ, Hicks N, Lotery HE, et al. Multicentre randomised control trial comparing real time teledermatology with conventional outpatient dermatological care: societal cost-benefit analysis. BMJ 2000; 320(7244):1252-6.

Zelickson 1997

Zelickson BD, Homan L. Teledermatology in the nursing home. Archives of Dermatology 1997;133(2):171-4.

Studies awaiting classification

Ongoing studies

Other references

Additional references

ACIM 2014

Australian Cancer Database. Melanoma of the skin for Australia (ICD10 C43).. In: Australian Cancer Incidence and Mortality (ACIM) Books (http://www.aihw.gov.au/acim-books/). Australian Institute of Health and Welfare, 2011.

Alam 2001

Alam M, Ratner D. Cutaneous squamous-cell carcinoma (Review). New England Journal of Medicine 2001;344(13):975-83. [PubMed: 11274625]

Aldridge 2013

Aldridge RB, Naysmith L, Ooi ET, Murray CS, Rees JL. The importance of a full clinical examination: assessment of index lesions referred to a skin cancer clinic without a total body skin examination would miss one in three melanomas. Acta Dermato-Venereologica 2013;93(6):689-92. [PubMed: 23695107]

Argenziano 2012

Argenziano G, Zalaudek I, Hofmann-Wellenhof R, Bakos RM, Bergman W, Blum A, et al. Total body skin examination for skin cancer screening in patients with focused symptoms. Journal of the American Academy of Dermatology 2012; 66(2):212-19. [PubMed: 21757257]

Arits 2013

Arits AH, Mosterd K, Essers BA, Spoorenberg E, Sommer A, De Rooij MJ, et al. Photodynamic therapy versus topical imiquimod versus topical fluorouracil for treatment of superficial basal-cell carcinoma: a single blind, non-inferiority, randomised controlled trial. Lancet Oncology 2013;14(7):647-54. [DOI: 10.1016/S1470-2045(13)70143-8]

Arnold 2014

Arnold M, Holterhues C, Hollestein LM, Coebergh JW, Nijsten T, Pukkala E, et al. Trends in incidence and predictions of cutaneous melanoma across Europe up to 2015. Journal of the European Academy of Dermatology & Venereology 2014; 28(9):1170-8. [PubMed: 23962170]

Baldursson 1993

Baldursson B, Sigurgeirsson B, Lindelof B. Leg ulcers and squamous cell carcinoma. An epidemiological study and a review of the literature. Acta Dermato-Venereologica 1993;73(3):171-4. [PubMed: 8105611]

Bath-Hextall 2007

Bath-Hextall F, Leonardi-Bee J, Smith C, Meal A, Hubbard R. Trends in incidence of skin basal cell carcinoma. Additional evidence from a UK primary care database study. International Journal of Cancer 2007;121(9):2105-8. [PubMed: 17640064]

Bath-Hextall 2007a

Bath-Hextall FJ, Perkins W, Bong J, Williams HC. Interventions for basal cell carcinoma of the skin. Cochrane Database of Systematic Reviews 2007, Issue 1. Art. No.: CD003412 DOI: 10.1002/14651858.CD003412.pub2.

Bath-Hextall 2014

Bath-Hextall F, Ozolins M, Armstrong SJ, Colver GB, Perkins W, Miller PS, et al. Surgical excision versus imiquimod 5% cream for nodular and superficial basal-cell carcinoma (SINS): a multicentre, non-inferiority, randomised controlled trial. Lancet Oncology 2014;15(1):96-105. [PubMed: 24332516]

Batra 2002

Batra RS, Kelley LC. A risk scale for predicting extensive subclinical spread of nonmelanoma skin cancer. Dermatologic Surgery 2002;28(2):107-12; discussion 112. [PubMed: 11860418]

Belbasis 2016

Belbasis L, Stefanaki I, Stratigos AJ, Evangelou E. Non-genetic risk factorsfor cutaneous melanoma and keratinocyte skin cancers: An umbrella review of meta-analyses.. Journal of Dermatological Science 2016;84(3):330-339.

Benelli 1999

Benelli C, Roscetti E, Pozzo VD, Gasparini G, Cavicchini S. The dermoscopic versus the clinical diagnosis of melanoma. European Journal of Dermatology 1999;9(6):470-6. [PubMed: 10491506]

Binder 1997

Binder M, Schwarz M, Steiner A, Kittler H, Muellner M, Wolff K, et al. Epiluminescence microscopy of small pigmented skin lesions: short-term formal training improves the diagnostic performance of dermatologists. Journal of the American Academy of Dermatology 1997;36(2 Pt 1):197-202. [PubMed: 9039168]

Bono 2002

Bono A, Bartoli C, Cascinelli N, Lualdi M, Maurichi A, Moglia D, et al. Melanoma detection. A prospective study comparing diagnosis with the naked eye, dermatoscopy and telespectrophotometry. Dermatology 2002;205(4):362-6. [PubMed: 12444332]

Bono 2006

Bono A, Tolomio E, Trincone S, Bartoli C, Tomatis S, Carbone A, et al. Micro-melanoma detection: a clinical study on 206 consecutive cases of pigmented skin lesions with a diameter < or = 3 mm. British Journal of Dermatology 2006;155(3):570-3.

Boring 1994

Boring CC, Squires TS, Tong T, Montgomery S. Cancer statistics, 1994. CA: a Cancer Journal for Clinicians 1994; 44(1):7-26. [PubMed: 8281473]

Bossuyt 2015

Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig L, et al. STARD 2015: an updated list of essential items for reporting diagnostic accuracy studies. BMJ 2015;351:h5527. [DOI: 10.1136/bmj.h5527; PubMed: 26511519]

Cancer Research UK 2017

Cancer Research UK. Skin cancer statistics. www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/skin-cancer#heading-One (accessed prior to 19 July 2017).

Carli 2002

Carli P, De Giorgi V, Argenziano G, Palli D, Giannotti B. Pre-operative diagnosis of pigmented skin lesions: in vivo dermoscopy performs better than dermoscopy on photographic images. Journal of the European Academy of Dermatology & Venereology 2002;16(4):339-46.

Carter 2013

Carter JB, Johnson MM, Chua TL, Karia PS, Schmults CD. Outcomes of primary cutaneous squamous cell carcinoma with perineural invasion: an 11-year cohort study. JAMA Dermatology 2013;149(1):35-41. [DOI: 10.1001/jamadermatol.2013.746; PubMed: 23324754]

CCAAC Network 2008

Cancer Council Australia & Australian Cancer Network. Basal Cell Carcinoma, Squamous Cell Carcinoma (and related lesions) - a guide to clinical management in Australia. www.cancer.org.au/content/pdf/HealthProfessionals/ClinicalGuidelines/Basal_cell_carcinoma_Squamous_cell_carcinoma_Guic Final_with_Corrigendums.pdf (accessed 19 May 2015).

Chao 2013

Chao D, London Cancer North and East. London Cancer, Guidelines for Cutaneous Malignant Melanoma Management August 2014. www.londoncancer.org/media/76373/london-cancer-melanoma-guidelines-2013-v1.0.pdf (accessed 25 February 2015).

Chapman 2011

Chapman PB, Hauschild A, Robert C, Haanen JB, Ascierto P, Larkin J, et al. Improved survival with vemurafenib in melanoma with BRAF V600E mutation. New England Journal of Medicine 2011;364(26):2507-16. [PubMed: 21639808]

Chapman 2012

Chapman PB, Hauschild A, Robert C, Larkin J, Haanen JB, Ribas A, et al. Updated overall survival (OS) results for BRIM-3, a phase III randomized, open-label, multicenter trial comparing BRAF inhibitor vemurafenib (vem) with dacarbazine (DTIC) in previously untreated patients with BRAFV600E-mutated melanoma. Journal of Clinical Oncology 2012;30(15 Suppl 1):8502. [EMBASE: 71004853]

Cho 2014

Cho H, Mariotto AB, Schwartz LM, Luo J, Woloshin S. When do changes in cancer survival mean progress? The insight from population incidence and mortality. Journal of the National Cancer Institute. Monographs 2014;2014(49):187-97. [PubMed: 25417232]

Chowdri 1996

Chowdri NA, Darzi MA. Postburn scar carcinomas in Kashmiris. Burns 1996;22(6):477-82. [PubMed: 8884010]

Chu 2006

Chu H, Cole SR. Bivariate meta-analysis for sensitivity and specificity with sparse data: a generalized linear mixed model approach (comment). Journal of Clinical Epidemiology 2006;59(12):1331-2. [PubMed: 17098577]

Chuchu 2018

Chuchu N, Takwoingi Y, Dinnes J, Matin RN, Bassett O, Moreau J, et al. Smartphone applications for triaging adults with skin lesions that are suspicious for melanoma. Cochrane Database of Systematic Reviews (in press).

Dabski 1986

Dabski K, Stoll HL Jr, Milgrom H. Squamous cell carcinoma complicating late chronic discoid lupus erythematosus. Journal of Surgical Oncology 1986;32(4):233-7. [PubMed: 3736067]

Deeks 2005

Deeks JJ, Macaskill P, Irwig L. The performance of tests of publication bias and other sample size effects in systematic reviews of diagnostic test accuracy was assessed. Journal of Clinical Epidemiology 2005;58(9):882-93. [PubMed: 16085191]

Dinnes 2018a

Dinnes J, Deeks JJ, Grainge MJ, Chuchu N, Ferrante di Ruffano L, Matin RN, et al. Visual inspection for the diagnosis of cutaneous melanoma in adults. Cochrane Database of Systematic Reviews (in press).

Dinnes 2018b

Dinnes J, Deeks JJ, Grainge MJ, Chuchu N, Ferrante di Ruffano L, Matin RN, et al. Dermoscopy, with and without visual inspection, for the diagnosis of cutaneous melanoma in adults. Cochrane Database of Systematic Reviews (in press).

Dinnes 2018c

Dinnes J, Deeks JJ, Chuchu N, Matin RN, Thompson D, Wong KY, et al. Visual examination and dermoscopy, alone or in combination, for the diagnosis of keratinocyte skin cancers in adults. Cochrane Database of Systematic Reviews (in press).

Dinnes 2018d

Dinnes J, Deeks JJ, Saleh D, Chuchu N, Bayliss SE, Takwoingi Y, et al. Reflectance confocal microscopy for the diagnosis of cutaneous melanoma in adults. Cochrane Database of Systematic Reviews (in press).

Dinnes 2018e

Dinnes J, Deeks JJ, Saleh D, Chuchu N, Bayliss SE, Takwoingi Y, et al. Reflectance confocal microscopy for the diagnosis of keratinocyte skin cancers in adults. Cochrane Database of Systematic Reviews (in press).

Dinnes 2018f

Dinnes J, Bamber J, Chuchu N, Bayliss SE, Takwoingi Y, Davenport C, et al. High frequency ultrasound for the diagnosis of skin cancer in adults. Cochrane Database of Systematic Reviews (in press).

Drew 2017

Drew BA, Karia PS, Mora AN, Liang CA, Schmults CD. Treatment patterns, outcomes, and patient satisfaction of primary epidermally limited nonmelanoma skin cancer. Dermatologic Surgery 2017;43(12):1423-30. [DOI: 10.1097/DSS.0000000000001225; PubMed: 28661992]

Drucker 2017

Drucker A, Adam GP, Langberg V, Gazula A, Smith B,Moustafa F, Weinstock MA, Trikalinos TA. Treatments for Basal Cell and Squamous Cell Carcinoma of the Skin. Comparative Effectiveness Reviews, No. 199.. Rockville (MD): Agency for Healthcare Research and Quality (US), 2017.

Dummer 2014

Dummer R, Arenberger P, Ascierto PA, De Groot JW, Hallmeyer S, Lotem M, et al. 1130TiP-NEMO: a phase 3 trial of binimetinib (MEK162) versus dacarbazine in patients with advanced NRAS-mutant melanoma who are untreated or have progressed after any number of immunotherapy regimens. Annals of Oncology 2014;25(suppl_4):iv392. [PubMed: 28171154]

Erdmann 2013

Erdmann F, Lortet-Tieulent J, Schuz J, Zeeb H, Greinert R, Breitbart EW, et al. International trends in the incidence of malignant melanoma 1953-2008--are recent generations at higher or lower risk? International Journal of Cancer 2013; 132(2):385-400. [PubMed: 22532371]

EUCAN 2012

EUCAN, International Agency for Research on Cancer. Malignant melanoma of skin: Estimated incidence, mortality & prevalence for both sexes, 2012. eco.iarc.fr/eucan/Cancer.aspx?Cancer=20 (accessed 29 July 2015).

Fasching 1989

Fasching MC, Meland NB, Woods JE, Wolff BG. Recurrent squamous-cell carcinoma arising in pilonidal sinus tract--multiple flap reconstructions. Report of a case.. Diseases of the Colon & Rectum 1989;32(2):153-8. [PubMed: 2914529]

Ferlay 2015

Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012. International Journal of Cancer 2015;136(5):E359-86. [PubMed: 25220842]

Ferrante di Ruffano 2018a

Ferrante di Ruffano L, Dinnes J, Deeks JJ, Chuchu N, Bayliss SE, Davenport C, et al. Optical coherence tomography for the diagnosis of skin cancer in adults. Cochrane Database of Systematic Reviews (in press).

Ferrante di Ruffano 2018b

Ferrante di Ruffano L, Takwoingi Y, Dinnes J, Chuchu N, Bayliss SE, Davenport C, et al. Computer assisted diagnosis techniques (dermoscopy and spectroscopy-based) for the diagnosis of skin cancer in adults. Cochrane Database of Systematic Reviews (in press).

Firnhaber 2012

Firnhaber JM. Diagnosis and treatment of basal cell and squamous cell carcinoma. American Family Physician 2012;

86(2):161-168.

Fitzpatrick 1975

Fitzpatrick TB. Soleil et peau. Journal de Médecine Esthétique 1975;2:33-4.

Friedman 1985

Friedman RJ, Rigel DS, Kopf AW. Early detection of malignant melanoma: the role of physician examination and self-examination of the skin. CA: a Cancer Journal for Clinicians 1985;35(3):130-51. [PubMed: 3921200]

Garbe 2016

Garbe C, Peris K, Hauschild A, Saiag P, Middleton M, Bastholt L, et al. Diagnosis and treatment of melanoma. European consensus-based interdisciplinary guideline - Update 2016. European Journal of Cancer 2016;63:201-17. [PubMed: 27367293]

Garcia 2009

Garcia C, Poletti E, Crowson AN. Basosquamous carcinoma. Journal of the American Academy of Dermatology 2009; 60(1):137-43. [PubMed: 19103364]

Gerbert 2000

Gerbert B, Bronstone A, Maurer T, Hofmann R, Berger T. Decision support software to help primary care physicians triage skin cancer: a pilot study. Archives of Dermatology 2000;136(2):187-92. [PubMed: 10677094]

Gershenwald 2017

Gershenwald JE, Scolyer RA, Hess KR, Sondak VK, Long GV, Ross MI, et al. Melanoma staging: Evidence-based changes in the American Joint Committee on Cancer eighth edition cancer staging manual. CA: A Cancer Journal for Clinicians 2017; 67(6):472-492. [DOI: 10.3322/caac.21409]

Gordon 2013

Gordon R. Skin cancer: an overview of epidemiology and risk factors. Seminars in Oncology Nursing 2013;29(3):160-9. [PubMed: 23958214]

Gorlin 2004

Gorlin RJ. Nevoid basal cell carcinoma (Gorlin) syndrome. Genetics in Medicine 2004;6(6):530-9. [PubMed: 15545751]

Grachtchouk 2011

Grachtchouk M, Pero J, Yang SH, Ermilov AN, Michael LE, Wang A, et al. Basal cell carcinomas in mice arise from hair follicle stem cells and multiple epithelial progenitor populations. Journal of Clinical Investigation 2011;121(5):1768-81. [PubMed: 21519145]

Green 1988

Green A, Leslie D, Weedon D. Diagnosis of skin cancer in the general population: clinical accuracy in the Nambour survey. Medical Journal of Australia 1988;148(9):447-50. [PubMed: 3283506]

Griffin 2016

Griffin LL, Ali FR, Lear JT. Non-melanoma skin cancer. Clinical Medicine 2016;16(1):62-5. [PubMed: 26833519]

Griffiths 2005

Griffiths RW, Suvarna SK, Stone J. Do basal cell carcinomas recur after complete conventional surgical excision? British Journal of Plastic Surgery 2005;58(6):795-805. [PubMed: 16086990]

Grob 1998

Grob JJ, Bonerandi JJ. The 'ugly duckling' sign: identification of the common characteristics of nevi in an individual as a basis for melanoma screening. Archives of Dermatology 1998;134(1):103-4. [PubMed: 9449921]

Hamid 2013

Hamid O, Sosman JA, Lawrence DP, Sullivan RJ, Ibrahim N, Kluger HM, et al. Clinical activity, safety, and biomarkers of MPDL3280A, an engineered PD-L1 antibody in patients with locally advanced or metastatic melanoma (mM). Journal of Clinical Oncology 2013;31(15 Suppl 1):Abstract 9010. [EMBASE: 71099860]

Hanson 2016

Hanson JL, Kingsley-Loso JL, Grey KR, Raju SI, Parks PR, Bershow AL, Warshaw EM. Incidental melanomas detected in veterans referred to dermatology. Journal of the American Academy of Dermatology 2016;74(3):462-9. [PubMed: 26612677]

Hartevelt 1990

Hartevelt MM, Bavinck JN, Kootte AM, Vermeer BJ, Vandenbroucke JP. Incidence of skin cancer after renal transplantation in The Netherlands. Transplantation 1990;49(3):506-9. [PubMed: 2316011]

Hodi 2010

Hodi FS, O'Day SJ, McDermott DF, Weber RW, Sosman JA, Haanen JB, et al. Improved survival with ipilimumab in patients with metastatic melanoma. New England Journal of Medicine 2010;363(8):711-23. [PubMed: 20525992]

Hoorens 2016

Hoorens I, Vossaert K, Pil L, Boone B, De Schepper S, Ongenae K, et al. Total-body examination vs lesion-directed skin cancer screening. JAMA Dermatology 2016;152(1):27-34. [PubMed: 26466155]

HPA and MelNet NZ 2014

Health Promotion Agency and the Melanoma Network of New Zealand (MelNet). New Zealand Skin Cancer Primary Prevention and Early Detection Strategy 2014 to 2017. www.sunsmart.org.nz//sites/default/files/documents/NZ%20Skin%20Cancer%20PrimaryPrevention%20and%20EarlyDetection (accessed 29 May 2018).

Janda 2015

Janda M. Teledermatology: its use in the detection and management of actinic keratosis. Current Problems in Dermatology 2015;46:101-7. [PubMed: 25561213]

Jansen 2018

Jansen MHE, Mosterd K, Arits AHMM, Roozeboom MH, Sommer A, Essers BAB, et al. Five-year results of a randomized controlled trial comparing effectiveness of photodynamic therapy, topical imiquimod, and topical 5-fluorouracil in patients with superficial basal cell carcinoma. Journal of Investigative Dermatology 2018;138(3):527-33. [DOI: 10.1016/j.jid.2017.09.033; PubMed: 29045820]

Jensen 1999

Jensen P, Hansen S, Moller B, Leivestad T, Pfeffer P, Geiran O, et al. Skin cancer in kidney and heart transplant recipients and different long-term immunosuppressive therapy regimens. Journal of the American Academy of Dermatology 1999;40(2 Pt 1):177-86. [PubMed: 10025742]

Kao 1986

Kao GF. Carcinoma arising in Bowen's disease. Archives of Dermatology 1986;122(10):1124-6. [PubMed: 3767398]

Kasprzak 2015

Kasprzak JM, Xu YG. Diagnosis and management of lentigo maligna: a review. Drugs in Context 2015;4:212281. [PubMed: 26082796]

Kelleners-Smeets 2017

Kelleners-Smeets NW, Mosterd K, Nelemans PJ. Treatment of low-risk basal cell carcinoma. Journal of Investigative Dermatology 2017;137(3):539-40. [PubMed: 28235442]

Kim 2014

Kim DD, Tang JY, Ioannidis JP. Network geometry shows evidence sequestration for medical vs. surgical practices: treatments for basal cell carcinoma. Journal of Clinical Epidemiology 2014;67(4):391-400. [PubMed: 24491794]

Kittler 1999

Kittler H, Seltenheim M, Dawid M, Pehamberger H, Wolff K, Binder M. Morphologic changes of pigmented skin lesions: a useful extension of the ABCD rule for dermatoscopy. Journal of the American Academy of Dermatology 1999;40(4):558-62. [PubMed: 10188673]

Kittler 2001

Kittler H, Binder M. Risks and benefits of sequential imaging of melanocytic skin lesions in patients with multiple atypical nevi. Archives of Dermatology 2001;137(12):1590-5. [PubMed: 11735709]

Kittler 2002

Kittler H, Pehamberger H, Wolff K, Binder M. Diagnostic accuracy of dermoscopy (Review). Lancet Oncology 2002; 3(3):159-65. [PubMed: 11902502]

Kjome 2016

Kjome RLS, Wright DJ, Bjaaen AB, Garstad KW, Valeur M. Dermatological cancer screening: Evaluation of a new communitypharmacy service. Research in Social & Administrative Pharmacy : RSAP 2017;13(6):1214-7. [DOI: 10.1016/j.sapharm.2016.12.001; PubMed: 27964893]

Lansbury 2010

Lansbury L, Leonardi-Bee J, Perkins W, Goodacre T, Tweed JA, Bath-Hextall FJ. Interventions for non-metastatic squamous cell carcinoma of the skin. Cochrane Database of Systematic Reviews 2010, Issue 4. Art. No.: CD007869 DOI: 10.1002/14651858.CD007869.pub2.

Lansbury 2013

Lansbury L, Bath-Hextall F, Perkins W, Stanton W, Leonardi-Bee J. Interventions for non-metastatic squamous cell

carcinoma of the skin: systematic review and pooled analysis of observational studies. BMJ 2013;347:f6153. [PubMed: 24191270]

Larkin 2014

Larkin J, Ascierto PA, Dréno B, Atkinson V, Liszkay G, Maio M, et al. Combined Vemurafenib and Cobimetinib in BRAF-Mutated Melanoma. New England Journal of Medicine 2014;371(20):1867-76. [PubMed: 25265494]

Lear 1997

Lear JT, Tan BB, Smith AG, Bowers W, Jones PW, Heagerty AH, et al. Risk factors for basal cell carcinoma in the UK: case-control study in 806 patients. Journal of the Royal Society of Medicine 1997;90(7):371-4. [PubMed: 9290417]

Lear 2012

Lear JT. Oral hedgehog-pathway inhibitors for basal-cell carcinoma. New England Journal of Medicine 2012;366(23):2225-6. [PubMed: 22670909]

Lear 2014

Lear JT, Corner C, Dziewulski P, Fife K, Ross GL, Varma S, et al. Challenges and new horizons in the management of advanced basal cell carcinoma: a UK perspective. British Journal of Cancer 2014;111(8):1476-81. [DOI: 10.1038/bjc.2014.270; PubMed: 25211660]

Lederman 1985

Lederman JS, Sober AJ. Does biopsy type influence survival in clinical stage I cutaneous melanoma? Journal of the American Academy of Dermatology 1985;13(6):983-7. [PubMed: 4078105]

Leeflang 2013

Leeflang MM, Rutjes AW, Reitsma JB, Hooft L, Bossuyt PM. Variation of a test's sensitivity and specificity with disease prevalence. CMAJ 2013;185(11):E537-44. [PubMed: 23798453]

Lees 1991

Lees VC, Briggs JC. Effect of initial biopsy procedure on prognosis in stage I invasive cutaneous malignant melanoma: review of 1086 patients. British Journal of Surgery 1991;78(9):1108-10. [PubMed: 1933198]

Leff 2008

Leff B, Finucane TE. Gizmo idolatry. JAMA 2008;299(15):1830-2. [PubMed: 18413879]

Linos 2009

Linos E, Swetter SM, Cockburn MG, Colditz GA, Clarke CA. Increasing burden of melanoma in the United States. Journal of Investigative Dermatology 2009;129(7):1666-74. [PubMed: 19131946]

Lister 1997

Lister RK, Black MM, Calonje E, Burnand KG. Squamous cell carcinoma arising in chronic lymphoedema. British Journal of Dermatology 1997;136(3):384-7. [PubMed: 9115922]

Lo 1991

Lo JS, Snow SN, Reizner GT, Mohs FE, Larson PO, Hruza GJ. Metastatic basal cell carcinoma: report of twelve cases with a review of the literature. Journal of the American Academy of Dermatology 1991;24(5 Pt 1):715-9. [PubMed: 1869642]

Lomas 2012

Lomas A, Leonardi-Bee J, Bath-Hextall F. A systematic review of worldwide incidence of nonmelanoma skin cancer. British Journal of Dermatology 2012;166(5):1069-80. [PubMed: 22251204]

MacKie 1985

MacKie RM, English J, Aitchison TC, Fitzsimons CP, Wilson P. The number and distribution of benign pigmented moles (melanocytic naevi) in a healthy British population. British Journal of Dermatology 1985;113(2):167-74. [PubMed: 4027184]

MacKie 1990

MacKie RM. Clinical recognition of early invasive malignant melanoma. BMJ 1990;301(6759):1005-6. [PubMed: 2249043]

Madan 2010

Madan V, Lear JT, Szeimies RM. Non-melanoma skin cancer. Lancet 2010;375(9715):673-85. [PubMed: 20171403]

Maia 1995

Maia M, Proenca NG, de Moraes JC. Risk factors for basal cell carcinoma: a case-control study. Revista de Saude Publica 1995;29(1):27-37. [PubMed: 8525311]

Maloney 1996

Maloney ME. Arsenic in Dermatology. Dermatologic Surgery 1996;22(3):301-4. [PubMed: 8599743]

Marsden 2010

Marsden JR, Newton-Bishop JA, Burrows L, Cook M, Corrie PG, Cox NH, et al. BAD Guidelines: Revised UK guidelines for the management of cutaneous melanoma 2010. British Journal of Dermatology 2010;163(2):238-56. [PubMed: 20608932]

McCormack 1997

McCormack CJ, Kelly JW, Dorevitch AP. Differences in age and body site distribution of the histological subtypes of basal cell carcinoma. A possible indicator of differing causes. Archives of Dermatology 1997;133(5):593-6. [PubMed: 9158412]

McCusker 2014

McCusker M, Basset-Seguin N, Dummer R, Lewis K, Schadendorf D, Sekulic A, et al. Metastatic basal cell carcinoma: Prognosis dependent on anatomic site and spread of disease. European Journal of Cancer 2014;50(4):774-83. [PubMed: 24412051]

Mistry 2011

Mistry M, Parkin DM, Ahmad AS, Sasieni P. Cancer incidence in the United Kingdom: projections to the year 2030. British Journal of Cancer 2011;105(11):1795-803. [PubMed: 22033277]

Moeckelmann 2018

Moeckelmann N, Ebrahimi A, Dirven R, Liu J, Low TH, Gupta R, et al. Analysis and comparison of the 8th edition American Joint Committee on Cancer (AJCC) nodal staging system in cutaneous and oral squamous cell cancer of the head and neck. Annals of Surgical Oncology 2018;25(6):1730-6. [DOI: 10.1245/s10434-018-6340-x; PubMed: 29352431]

Motley 2009

Motley RJ, Preston PW, Lawrence CM. Multi-professional Guidelines for the Management of the Patient with Primary Cutaneous Squamous Cell Carcinoma. www.bsds.org.uk/uploads/pdfs/SCCguide2009.pdf (accessed 15/11/2017).

Murchie 2017

Murchie P, Amalraj Raja E, Brewster DH, Iversen L, Lee AJ. Is initial excision of cutaneous melanoma by General Practitioners (GPs) dangerous? Comparing patient outcomes following excision of melanoma by GPs or in hospital using national datasets and meta-analysis. European Journal of Cancer 2017;86:373-84. [PubMed: 29100192]

Musah 2013

Musah A, Gibson JE, Leonardi-Bee J, Cave MR, Ander EL, Bath-Hextall F. Regional variations of basal cell carcinoma incidence in the U.K. using The Health Improvement Network database (2004-10). British Journal of Dermatology 2013; 169(5):1093-9. [PubMed: 23701520]

Nart 2015

Nart IF, Armayones SG, Medina FV, Orti MB, Orpinell XB. Basal cell carcinoma treated with ingenol mebutate. Journal of the American Academy of Dermatology 2015;5(Suppl 1):AB180.

Newcombe 1998

Newcombe RG. Interval estimation for the difference between independent proportions: comparison of eleven methods. Statistics in Medicine 1998;17(8):873-890.

NICE 2010

National Institute of Clinical Excellence. NICE Guidance on Cancer Services. Improving Outcomes for People with Skin Tumours including Melanoma (update): The Management of Low-risk Basal Cell Carcinomas in the Community.. www.nice.org.uk/guidance/csg8/resources/improving-outcomes-for-people-with-skin-tumours-including-melanoma-2010-partial-update-773380189 (accessed 27 November 2017).

NICE 2015a

National Collaborating Centre for Cancer. Melanoma: assessment and management. www.nice.org.uk/guidance/ng14 (accessed prior to 20 February 2018).

NICE 2015b

National Institute for Health and Clinical Excellence. Suspected cancer: recognition and referral. www.nice.org.uk/guidance/ng12 (accessed prior to 20 February 2018).

NICE 2017

NICE. Vismodegib for treating basal cell carcinoma. www.nice.org.uk/guidance/ta489 (accessed prior to 28 March 2018).

Norman 2009

Norman G, Barraclough K, Dolovich L, Price D. Iterative diagnosis. BMJ 2009;339:b3490. [DOI: 10.1136/bmj.b3490]

O'Gorman 2014

O'Gorman SM, Murphy GM. Photosensitizing medications and photocarcinogenesis. Photodermatology, Photoimmunology & Photomedicine 2014;30(1):8-14. [PubMed: 24393207]

Offidani 2002

Offidani A, Simonetti O, Bernardini ML, Alpagut A, Cellini A, Bossi G. General practitioners' accuracy in diagnosing skin cancers. Dermatology 2002;205(2):127-30. [PubMed: 12218226]

Randle 1996

Randle HW. Basal cell carcinoma. Identification and treatment of the high-risk patient. Dermatologic Surgery 1996; 22(3):255-61. [PubMed: 8599737]

Reitsma 2005

Reitsma JB, Glas AS, Rutjes AW, Scholten RJ, Bossuyt PM, Zwinderman AH. Bivariate analysis of sensitivity and specificity produces informative summary measures in diagnostic reviews (Review). Journal of Clinical Epidemiology 2005; 58(10):982-90. [PubMed: 16168343]

Roozeboom 2012

Roozeboom MH, Arits AH, Nelemans PJ, Kelleners-Smeets NW. Overall treatment success after treatment of primary superficial basal cell carcinoma: a systematic review and meta-analysis of randomized and nonrandomized trials. British Journal of Dermatology 2012;167(4):733-56. [PubMed: 22612571]

Roozeboom 2016

Roozeboom MH, Arits AH, Mosterd K, Sommer A, Essers BA, de Rooij MJ, et al. Three-year follow-up results of photodynamic therapy vs. Imiquimod vs. fluorouracil for treatment of superficial basal cell carcinoma: A single-blind, noninferiority, randomized controlled trial. Journal of Investigative Dermatology 2016;136(8):1568-74. [PubMed: 27113429]

Rowe 1992

Rowe DE, Carroll RJ, Day CL Jr. Prognostic factors for local recurrence, metastasis, and survival rates in squamous cell carcinoma of the skin, ear, and lip. Implications for treatment modality selection. Journal of the American Academy of Dermatology 1992;26(6):976-90. [PubMed: 1607418]

Rutjes 2005

Rutjes AW, Reitsma JB, Vandenbroucke JP, Glas AS, Bossuyt PM. Case-control and two-gate designs in diagnostic accuracy studies (Review). Clinical Chemistry 2005;51(8):1335-41. [PubMed: 15961549]

Sekulic 2012

Sekulic A, Migden MR, Oro AE, Dirix L, Lewis KD, Hainsworth JD, et al. Efficacy and safety of vismodegib in advanced basal-cell carcinoma. New England Journal of Medicine 2012;366(23):2171-9. [PubMed: 22670903]

Siegel 2015

Siegel R, Miller K, Jemal A. Cancer statistics, 2015. CA: a Cancer Journal for Clinicians 2014;65(1):5-29. [PubMed: 25559415]

SIGN 2017

Scottish Intercollegiate Guidelines Network. Cutaneous Melanoma. www.sign.ac.uk/sign-146-melanoma.html (accessed prior to 19 July 2017).

Sladden 2009

Sladden MJ, Balch C, Barzilai DA, Berg D, Freiman A, Handiside T, et al. Surgical excision margins for primary cutaneous melanoma. Cochrane Database of Systematic Reviews 2009, Issue 10. Art. No.: CD004835 DOI: 10.1002/14651858.CD004835.pub2.

Slater 2014

Slater D, Walsh M. Standards and datasets for reporting cancers: Dataset for the histological reporting of primary cutaneous malignant melanoma and regional lymph nodes, May 2014. www.rcpath.org/Resources/RCPath/Migrated%20Resources/Documents/G/G125_DatasetMaligMelanoma_May14.pdf (accessed 29 July 2015).

Smeets 2004

Smeets NW, Krekels GA, Ostertag JU, Essers BA, Dirksen CD, Nieman FH, et al. Surgical excision vs Mohs' micrographic surgery for basal-cell carcinoma of the face: randomised controlled trial. Lancet 2004;364(9447):1766-72. [PubMed: 15541449]

Sober 1979

Sober AJ, Fitzpatrick TB, Mihm MC, Wise TG, Pearson BJ, Clark WH, et al. Early recognition of cutaneous melanoma. JAMA 1979;242(25):2795-9. [PubMed: 501893]

Stanganelli 2000

Stanganelli I, Serafini M, Bucch L. A cancer-registry-assisted evaluation of the accuracy of digital epiluminescence microscopy associated with clinical examination of pigmented skin lesions. Dermatology 2000;200(1):11-6. [PubMed:

10681607]

Stata 2017

Stata [Computer program]. Version 15. College Station, TX, USA: StataCorp, 2017.Available at www.stata.com.

Stratigos 2015

Stratigos A, Garbe C, Lebbe C, Malvehy J, del Marmol V, Pehamberger H, et al. Diagnosis and treatment of invasive squamous cell carcinoma of the skin: European consensus-based interdisciplinary guideline. European Journal of Cancer 2015;51(14):1989-2007. [PubMed: 26219687]

Takwoingi 2017

Takwoingi Y, Guo B, Riley RD, Deeks JJ. Performance of methods for meta-analysis of diagnostic test accuracy with few studies or sparse data. Statistical Methods in Medical Research 2017;26(4):1896-911. [DOI: 10.1177/0962280215592269]

Thomas 1998

Thomas L, Tranchand P, Berard F, Secchi T, Colin C, Moulin G. Semiological value of ABCDE criteria in the diagnosis of cutaneous pigmented tumors. Dermatology 1998;197(1):11-7. [PubMed: 9693179]

Usher-Smith 2016

Usher-Smith JA, Sharp SJ, Griffin SJ. The spectrum effect in tests for risk prediction, screening, and diagnosis. BMJ 2016; 353:i3139. [DOI: 10.1136/bmj.i3139]

van Loo 2014

van Loo E, Mosterd K, Krekels GA, Roozeboom MH, Ostertag JU, Dirksen CD, et al. Surgical excision versus Mohs' micrographic surgery for basal cell carcinoma of the face: A randomised clinical trial with 10 year follow-up. European Journal of Cancer 2014;50(17):3011-20. [PubMed: 25262378]

Verkouteren 2017

Verkouteren JAC, Ramdas KHR, Wakkee M, Nijsten T. Epidemiology of basal cell carcinoma: scholarly review. British Journal of Dermatology 2017;177(2):359-372. [DOI: 10.1111/bjd.15321]

Villanueva 2010

Villanueva J, Vultur A, Lee JT, Somasundaram R, Fukunaga-Kalabis M, Cipolla AK, et al. Acquired resistance to BRAF inhibitors mediated by a RAF kinase switch in melanoma can be overcome by cotargeting MEK and IGF-1R/PI3K. Cancer Cell 2010;18(6):683-95. [PubMed: 21156289]

Walker 2006

Walker P, Hill D. Surgical treatment of basal cell carcinomas using standard postoperative histological assessment. Australasian Journal of Dermatology 2006;47(1):1-12. [PubMed: 16405477]

Warshaw 2011

Warshaw EM, Hillman YJ, Greer NL, Hagel EM, MacDonald R, Rutks IR, et al. Teledermatology for diagnosis and management of skin conditions: A systematic review. J Am Acad Dermatol 2011;64(4):759-72. [PubMed: 21036419]

Whiting 2011

Whiting PF, Rutjes AW, Westwood ME, Mallett S, Deeks JJ, Reitsma JB, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Annals of Internal Medicine 2011;155(8):529-36. [PubMed: 22007046]

WHO 2003

World Health Organisation. INTERSUN: The Global UV Project. A guide and compendium. www.who.int/uv/publications/en/Intersunguide.pdf 2003 (accessed 20 May 2015).

Williams 2017

Williams HC, Bath-Hextall F, Ozolins M, Armstrong SJ, Colver GB, Perkins W, et al. Surgery versus 5% imiquimod for nodular and superficial basal cell carcinoma: 5-year results of the SINS randomized controlled trial. Journal of Investigative Dermatology 2017;137(3):614-619. [PubMed: 27932240]

Wong 2017

Wong KY, Fife K, Lear JT, Price RD, Durrani AJ. Vismodegib for locally advanced periocular and orbital basal cell carcinoma: A review of 15 consecutive cases. Plastic and Reconstructive Surgery Global Open 2017;5(7):e1424. [PubMed: 28831360]

Zak-Prelich 2004

Zak-Prelich M, Narbutt J, Sysa-Jedrzejowska A. Environmental risk factors predisposing to the development of basal cell carcinoma. Dermatologic Surgery 2004;30(2 Pt 2):248–52. [PubMed: 14871217]

Other published versions of this review

Dinnes 2015a

Dinnes J, Matin RN, Moreau JF, Patel L, Chan SA, Wong KY, et al. Tests to assist in the diagnosis of cutaneous melanoma in adults: a generic protocol. Cochrane Database of Systematic Reviews 2015, Issue 10. Art. No.: CD011902 DOI: 10.1002/14651858.CD011902.

Dinnes 2015b

Dinnes J, Wong KY, Gulati A, Chuchu N, Leonardi-Bee J, Bayliss SE, et al. Tests to assist in the diagnosis of keratinocyte skin cancers in adults: a generic protocol. Cochrane Database of Systematic Reviews 2015, Issue 10. Art. No.: CD011901 DOI: 10.1002/14651858.CD011901.

Classification pending references

Data and analyses

Data tables by test

Test	Studies	Participants
1 Teledermatology - photographic image vs Histology (Any)	4	717
2 Teledermatology - dermoscopic image vs Histology (Any)	1	104
3 Teledermatology - photographic+dermoscopic image vs Histology (Any)	3	871
4 Expert Face to face (VI+Dermoscopy) vs Histology (Any)	2	248
5 Teledermatology - photographic image vs Histology (MM+MiS)	4	1834
6 Teledermatology - dermoscopic image vs Histology (MM+MiS)	2	116
7 Teledermatology photographic+dermoscopic image vs Histology (MM+MiS)	4	664
8 GP Face to face (Visual inspection only) vs Histology (MM+MiS)	1	235
9 GP Face to face (VI+Dermoscopy) vs Histology (MM+MiS)	1	235
10 Expert face to face (VI+Dermoscopy) (MM+MiS)	3	1663
11 Teledermatology - photographic+dermoscopic image vs Histology (MM)	1	43
12 Expert face to face (VI+Dermoscopy) vs Histology (MM)	1	43
13 Teledermatology - dermoscopic image vs Histology (Acral MM)	1	77
14 Teledermatology - photographic image vs Histology (BCC)	3	301
15 Teledermatology - dermoscopic image vs Histology (BCC)	1	104
16 Teledermatology - photographic+dermoscopic image vs Histology (BCC)	1	256
17 Expert face to face (VI+Dermoscopy) vs Histology (BCC)	2	248
18 Teledermatology - photographic image vs Histology (cSCC)	1	104
19 Teledermatology - dermoscopic image vs Histology (cSCC)	1	104
20 Expert face to face (VI+Dermoscopy) vs Histology (cSCC)	1	104
21 Teledermatology - photographic image vs face to face clinical diagnosis (Immediate action)	3	951
22 Teledermatology - photographic image vs face to face clinical diagnosis (Dx of malignancy)	1	90
23 Teledermatology - photographic image vs face to face clinical diagnosis (Immediate action or FU)	1	106
24 Teledermatology - photographic image vs face to face clinical diagnosis (Immediate action; Registrar data)	1	796
25 Teledermatology - photographic/dermoscopic image vs face to face clinical diagnosis (Immediate action)	1	301
26 Teledermatology - live link vs face to face clinical diagnosis (diagnosis of any skin cancer)	1	107
27 Teledermatology - live link vs face to face clinical diagnosis (definitely/probably malignant)	1	107
28 Teledermatology - live link vs face to face clinical diagnosis (biopsy decision)	1	107

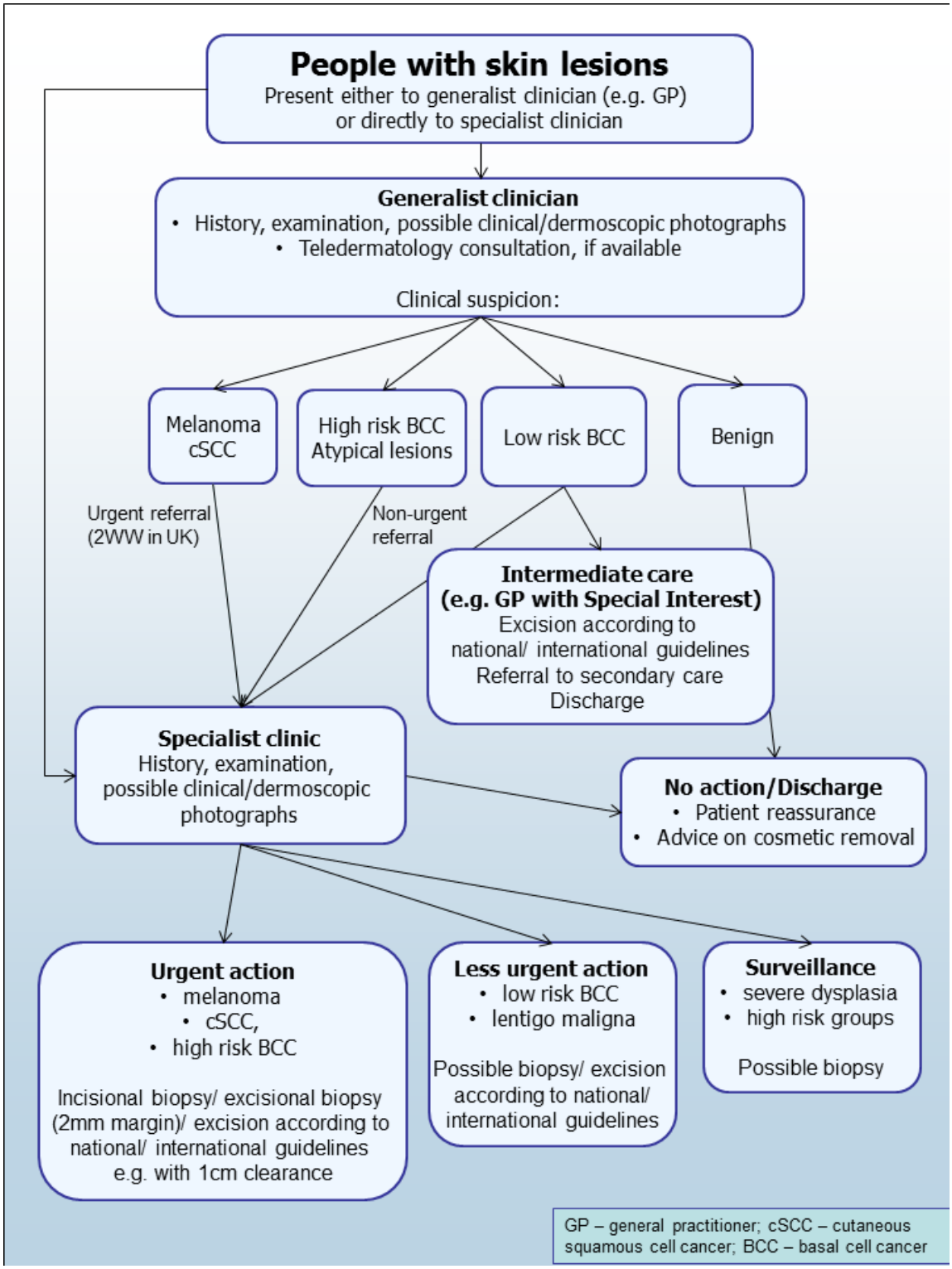
Figures

Figure 1

Caption

Sample photograph of superficial spreading melanoma(left), BCC (centre) and SCC (right)

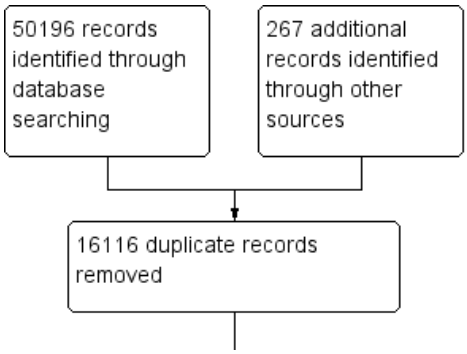
Figure 2

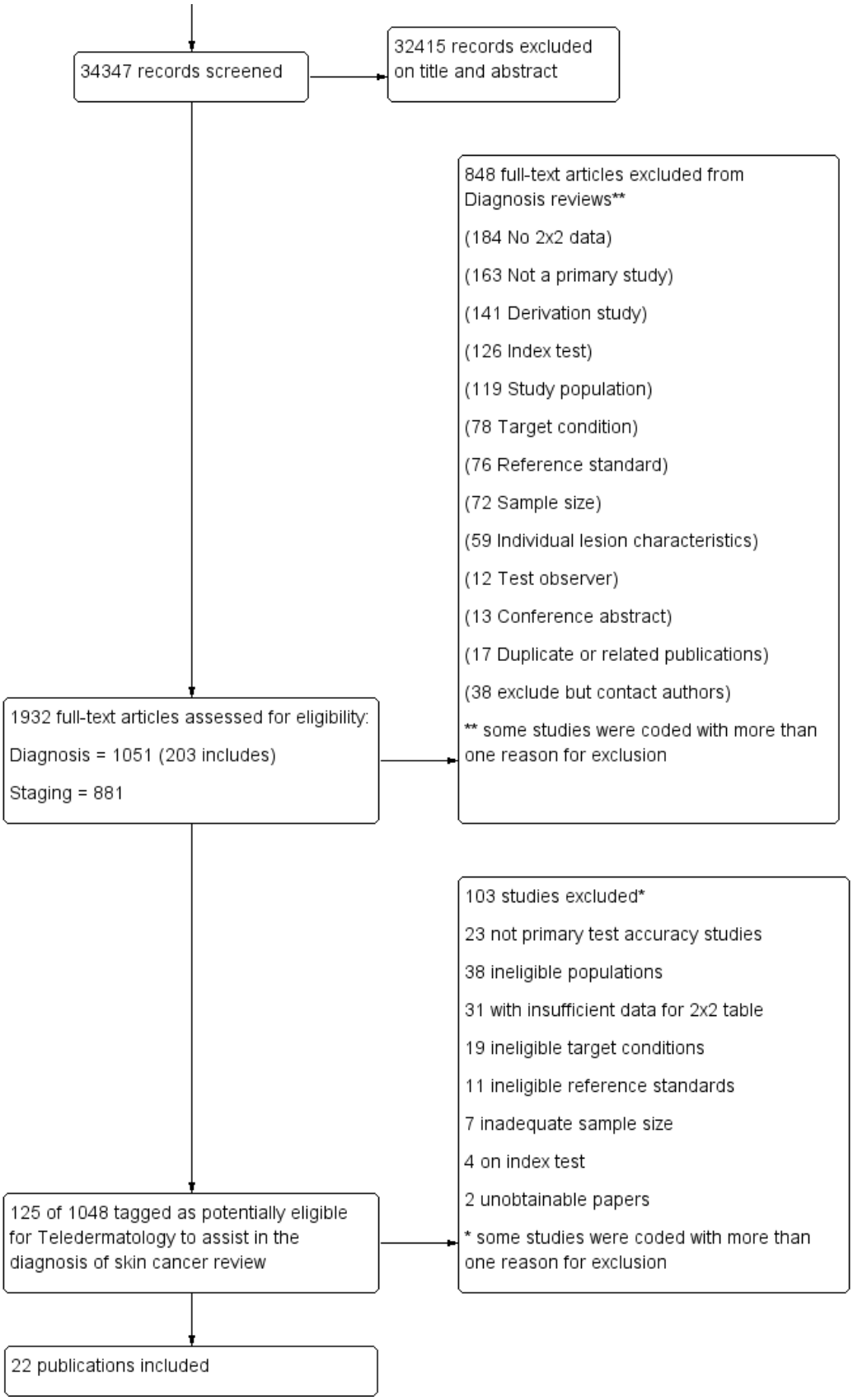


Caption

Current clinical pathway for people with skin lesions

Figure 3

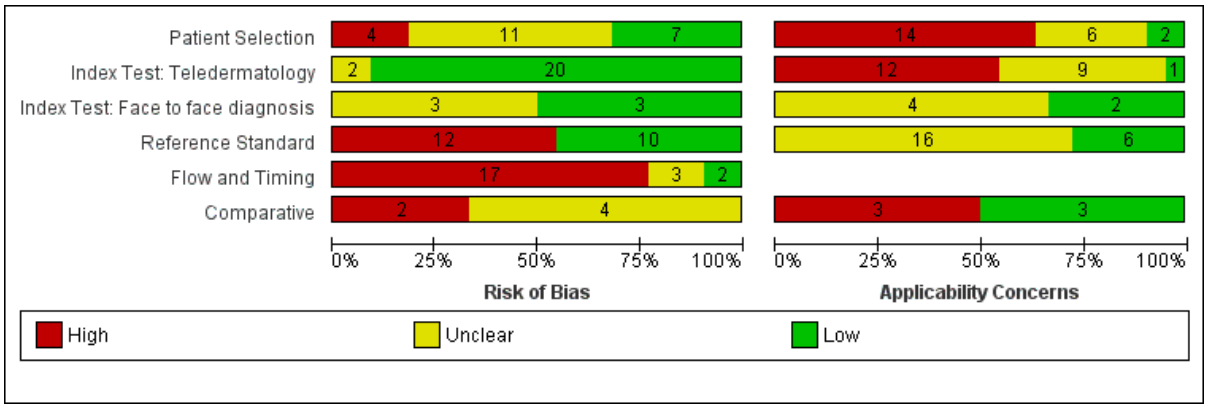




Caption

PRISMA flow diagram.

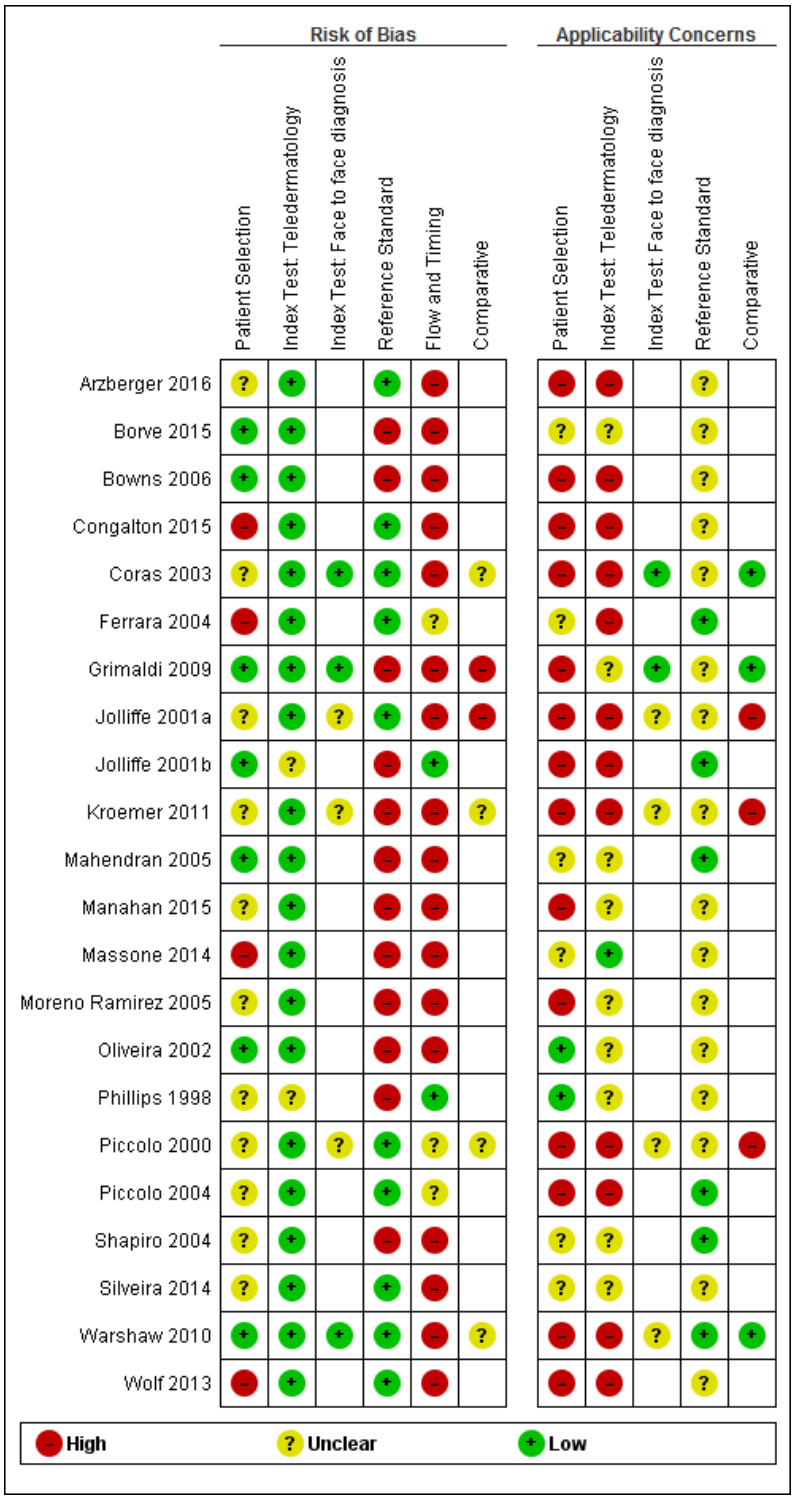
Figure 4



Caption

Risk of bias and applicability concerns graph: review authors' judgements about each domain presented as percentages across included studies

Figure 5



Caption

Risk of bias and applicability concerns summary: review authors' judgements about each domain for each included study

Figure 6 (Analysis 1)

Teledermatology - photographic image vs Histology (Any)

Study	TP	FP	FN	TN	Image aquisition	Device	Sensitivity (95% CI)	Specificity (95% CI)
Silveira 2014	350	39	14	13	Community	Digital camera	0.96 [0.94, 0.98]	0.25 [0.14, 0.39]
Moreno Ramirez 2005	27	1	2	27	Primary care	Digital camera	0.93 [0.77, 0.99]	0.96 [0.82, 1.00]
Kroemer 2011	43	7	3	51	Secondary care	Mobile phone camera	0.93 [0.82, 0.99]	0.88 [0.77, 0.95]
Jolliffe 2001a	13	9	0	118	Secondary care	Video images	1.00 [0.75, 1.00]	0.93 [0.87, 0.97]

Teledermatology - dermoscopic image vs Histology (Any)

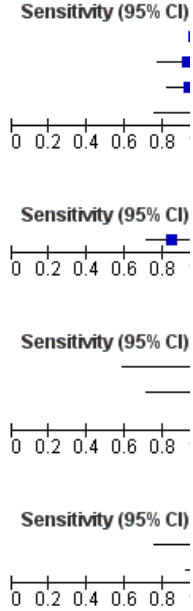
Study	TP	FP	FN	TN	Image aquisition	Device	Sensitivity (95% CI)	Specificity (95% CI)
Kroemer 2011	39	5	7	53	Secondary care	Mobile phone camera & dermoscope	0.85 [0.71, 0.94]	0.91 [0.81, 0.97]

Teledermatology - photographic+dermoscopic image vs Histology (Any)

Study	TP	FP	FN	TN	Image aquisition	Device	Sensitivity (95% CI)	Specificity (95% CI)
Massone 2014	7	2	0	23	Primary care	Digital camera & dermoscope	1.00 [0.59, 1.00]	0.92 [0.74, 0.99]
Arzberger 2016	11	9	0	3	Secondary care	Digital camera & dermoscope	1.00 [0.72, 1.00]	0.25 [0.05, 0.57]
Borve 2015	168	302	0	346	Secondary care	Mobile phone camera & dermoscope	1.00 [0.98, 1.00]	0.53 [0.49, 0.57]

Expert Face to face (VI+Dermoscopy) vs Histology (Any)

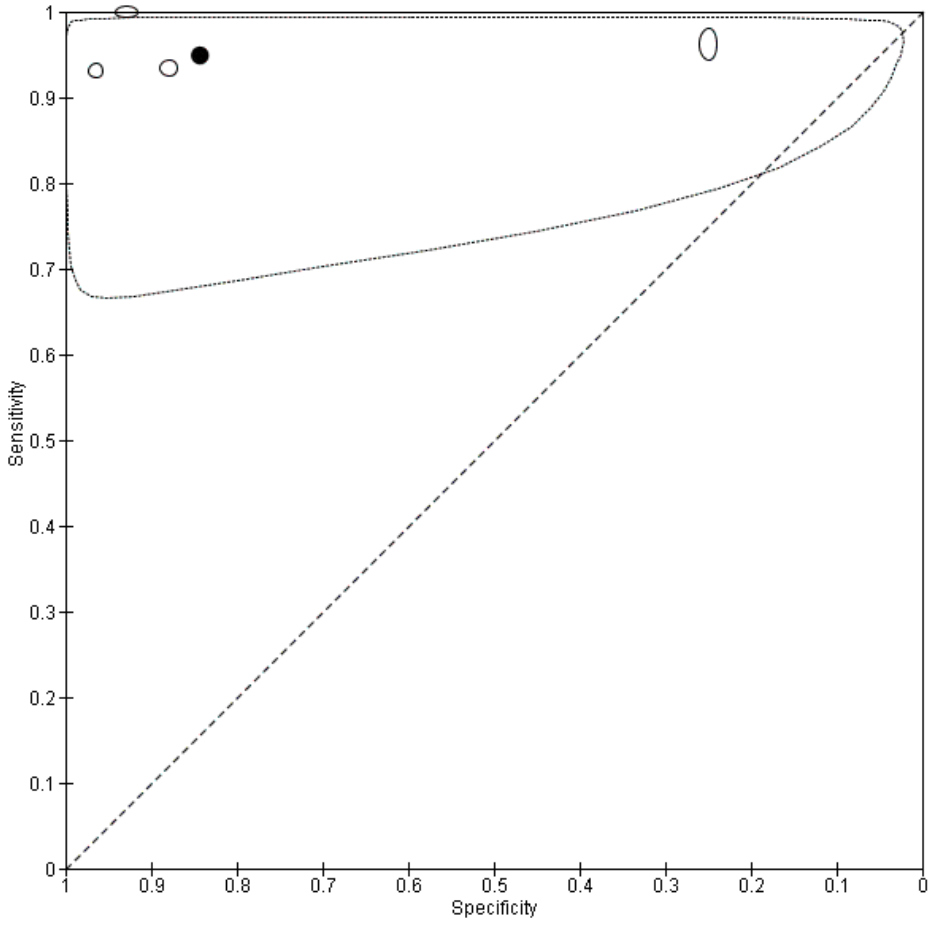
Study	TP	FP	FN	TN	Image aquisition	Device	Sensitivity (95% CI)	Specificity (95% CI)
Jolliffe 2001a	13	7	0	124	N/A	N/A	1.00 [0.75, 1.00]	0.95 [0.89, 0.98]
Kroemer 2011	46	6	0	52	N/A	N/A	1.00 [0.92, 1.00]	0.90 [0.79, 0.96]



Caption

Forest plot of tests for the detection of any skin cancer (Any)

Figure 7 (Analysis 2)



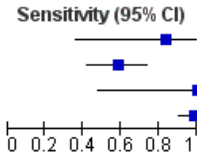
Caption

Summary ROC Plot of Teledermatology using photographic images vs histology for the detection of any skin cancer (Any).

Figure 8 (Analysis 3)

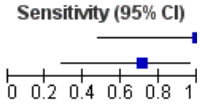
Teledermatology - photographic image vs Histology (MM+MiS)

Study	TP	FP	FN	TN	Image aquisition	Device	Sensitivity (95% CI)	Specificity (95% CI)
Moreno Ramirez 2005	5	0	1	51	Primary care	Digital camera	0.83 [0.36, 1.00]	1.00 [0.93, 1.00]
Warshaw 2010	24	869	17	604	Secondary care	Digital camera & dermoscope	0.59 [0.42, 0.74]	0.41 [0.38, 0.44]
Kroemer 2011	5	2	0	97	Secondary care	Mobile phone camera	1.00 [0.48, 1.00]	0.98 [0.93, 1.00]
Wolf 2013	53	73	1	32	Secondary care	Not reported	0.98 [0.90, 1.00]	0.30 [0.22, 0.40]



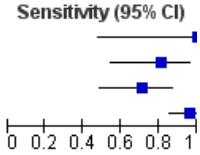
Teledermatology - dermoscopic image vs Histology (MM+MiS)

Study	TP	FP	FN	TN	Image aquisition	Device	Sensitivity (95% CI)	Specificity (95% CI)
Kroemer 2011	5	3	0	96	Secondary care	Mobile phone camera & dermoscope	1.00 [0.48, 1.00]	0.97 [0.91, 0.99]
Ferrara 2004	5	2	2	3	Unclear	Digital camera & dermoscope	0.71 [0.29, 0.96]	0.60 [0.15, 0.95]



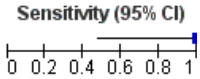
Teledermatology photographic+dermoscopic image vs Histology (MM+MiS)

Study	TP	FP	FN	TN	Image aquisition	Device	Sensitivity (95% CI)	Specificity (95% CI)
Grimaldi 2009	5	11	0	219	Primary care	Digital camera & dermoscope	1.00 [0.48, 1.00]	0.95 [0.92, 0.98]
Coras 2003	13	2	3	27	Private care	Digital camera & dermoscope	0.81 [0.54, 0.96]	0.93 [0.77, 0.99]
Bowns 2006	17	11	7	221	Secondary care	Digital camera & dermoscope	0.71 [0.49, 0.87]	0.95 [0.92, 0.98]
Congalton 2015	46	23	2	57	Secondary care	Digital camera & dermoscope	0.96 [0.86, 0.99]	0.71 [0.60, 0.81]



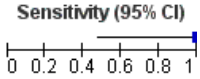
GP Face to face (Visual inspection only) vs Histology (MM+MiS)

Study	TP	FP	FN	TN	Image aquisition	Device	Sensitivity (95% CI)	Specificity (95% CI)
Grimaldi 2009	5	63	0	167	N/A	N/A	1.00 [0.48, 1.00]	0.73 [0.66, 0.78]



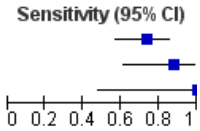
GP Face to face (VI+Dermoscopy) vs Histology (MM+MiS)

Study	TP	FP	FN	TN	Image aquisition	Device	Sensitivity (95% CI)	Specificity (95% CI)
Grimaldi 2009	5	24	0	206	N/A	N/A	1.00 [0.48, 1.00]	0.90 [0.85, 0.93]



Expert face to face (VI+Dermoscopy) (MM+MiS)

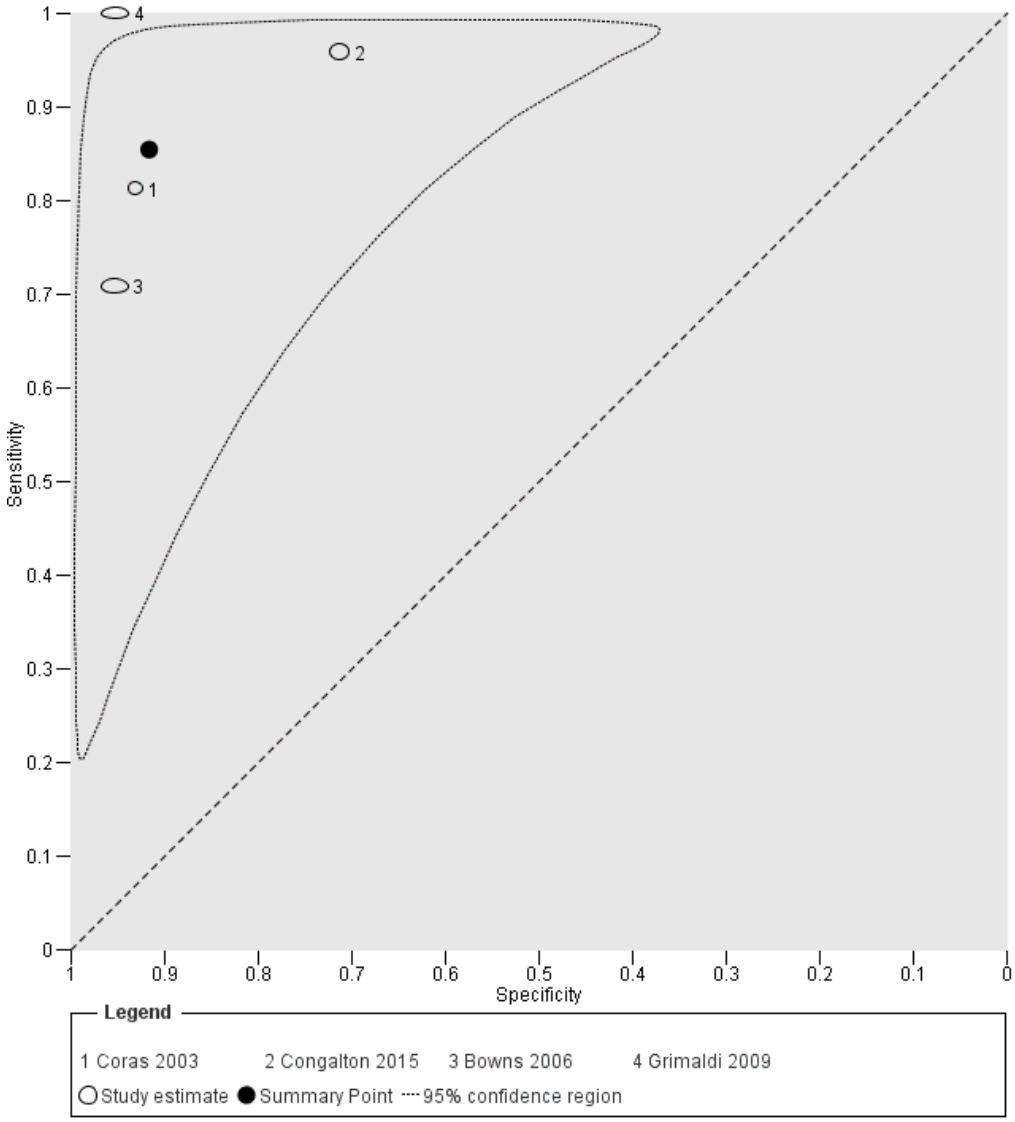
Study	TP	FP	FN	TN	Image aquisition	Device	Sensitivity (95% CI)	Specificity (95% CI)
Warshaw 2010	30	543	11	930	N/A	N/A	0.73 [0.57, 0.86]	0.63 [0.61, 0.66]
Coras 2003	14	2	2	27	N/A	N/A	0.88 [0.62, 0.98]	0.93 [0.77, 0.99]
Kroemer 2011	5	1	0	98	N/A	N/A	1.00 [0.48, 1.00]	0.99 [0.95, 1.00]



Caption

Forest plot of tests for the detection of invasive melanoma or atypical intraepidermal melanocytic variants (MM+MiS)

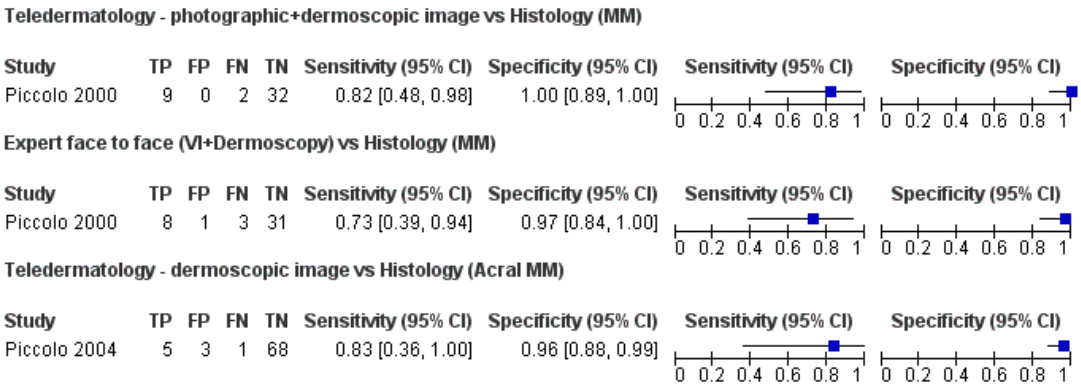
Figure 9 (Analysis 4)



Caption

Summary ROC Plot of Teledermatology using clinical and dermoscopic images for the detection of invasive melanoma or atypical intraepidermal melanocytic variants (MM+MiS).

Figure 10 (Analysis 5)



Caption

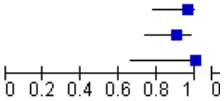
Forest plot of tests for the detection of invasive melanoma

Figure 11 (Analysis 6)

Teledermatology - photographic image vs Histology (BCC)

Study	TP	FP	FN	TN	Image aquisition	Device	Sensitivity (95% CI)	Specificity (95% CI)
Moreno Ramirez 2005	22	1	1	33	Primary care	Digital camera	0.96 [0.78, 1.00]	0.97 [0.85, 1.00]
Kroemer 2011	27	5	3	69	Secondary care	Mobile phone camera	0.90 [0.73, 0.98]	0.93 [0.85, 0.98]
Jolliffe 2001a	9	4	0	127	Secondary care	Video images	1.00 [0.66, 1.00]	0.97 [0.92, 0.99]

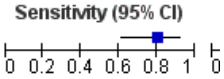
Sensitivity (95% CI)



Teledermatology - dermoscopic image vs Histology (BCC)

Study	TP	FP	FN	TN	Image aquisition	Device	Sensitivity (95% CI)	Specificity (95% CI)
Kroemer 2011	24	5	6	69	Secondary care	Mobile phone camera & dermoscope	0.80 [0.61, 0.92]	0.93 [0.85, 0.98]

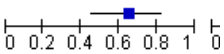
Sensitivity (95% CI)



Teledermatology - photographic+dermoscopic image vs Histology (BCC)

Study	TP	FP	FN	TN	Image aquisition	Device	Sensitivity (95% CI)	Specificity (95% CI)
Bowns 2006	19	9	10	218	Secondary care	Digital camera & dermoscope	0.66 [0.46, 0.82]	0.96 [0.93, 0.98]

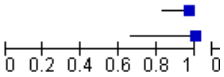
Sensitivity (95% CI)



Expert face to face (VI+Dermoscopy) vs Histology (BCC)

Study	TP	FP	FN	TN	Image aquisition	Device	Sensitivity (95% CI)	Specificity (95% CI)
Kroemer 2011	29	4	1	70	N/A	N/A	0.97 [0.83, 1.00]	0.95 [0.87, 0.99]
Jolliffe 2001a	9	3	0	132	N/A	N/A	1.00 [0.66, 1.00]	0.98 [0.94, 1.00]

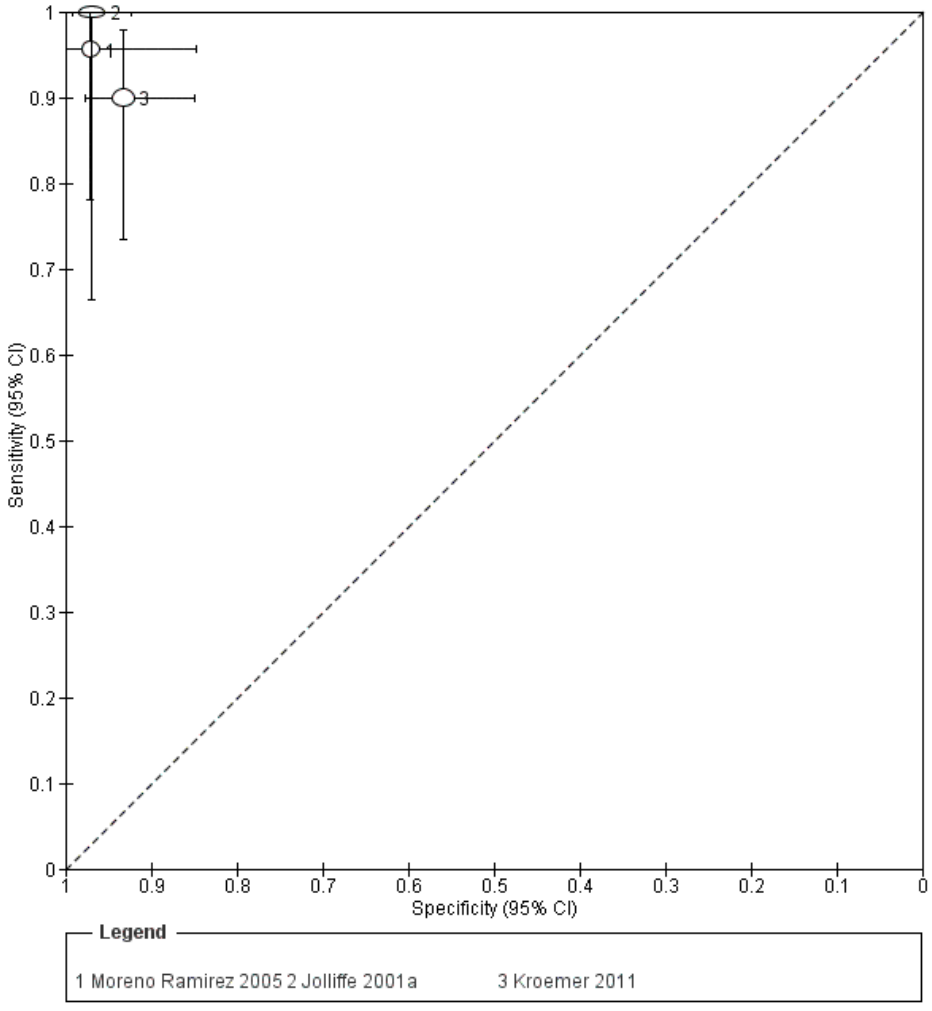
Sensitivity (95% CI)



Caption

Forest plot of tests for the detection of BCC

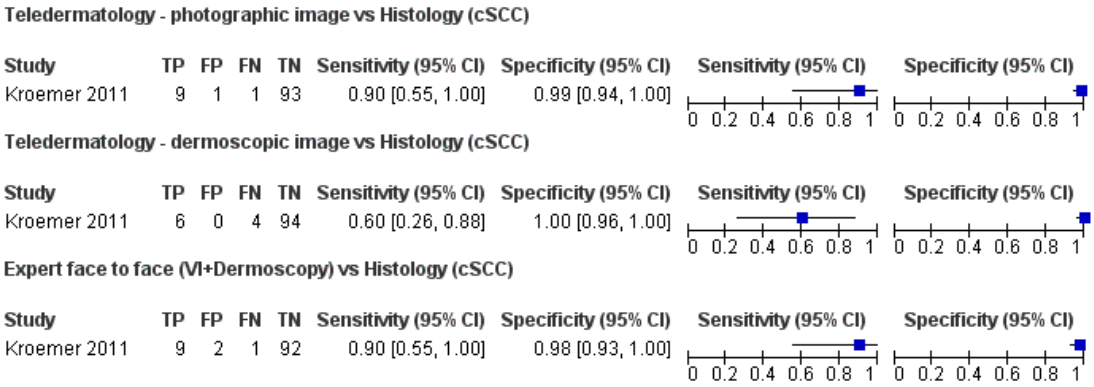
Figure 12 (Analysis 11)



Caption

ROC Plot Teledermatology using photographic images alone vs histology for the detection of BCC

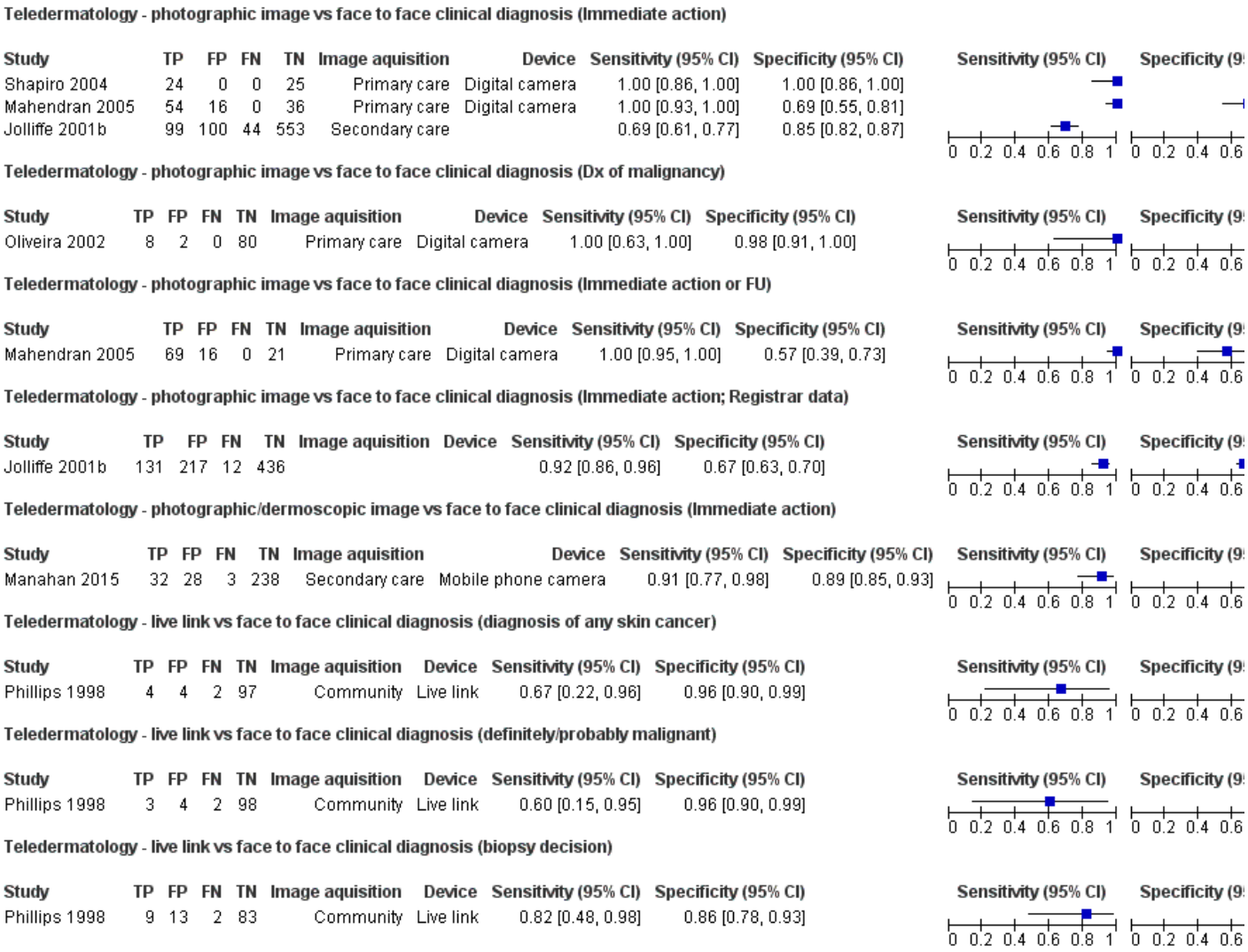
Figure 13 (Analysis 7)



Caption

Forest plot of tests for the detection of cSCC.

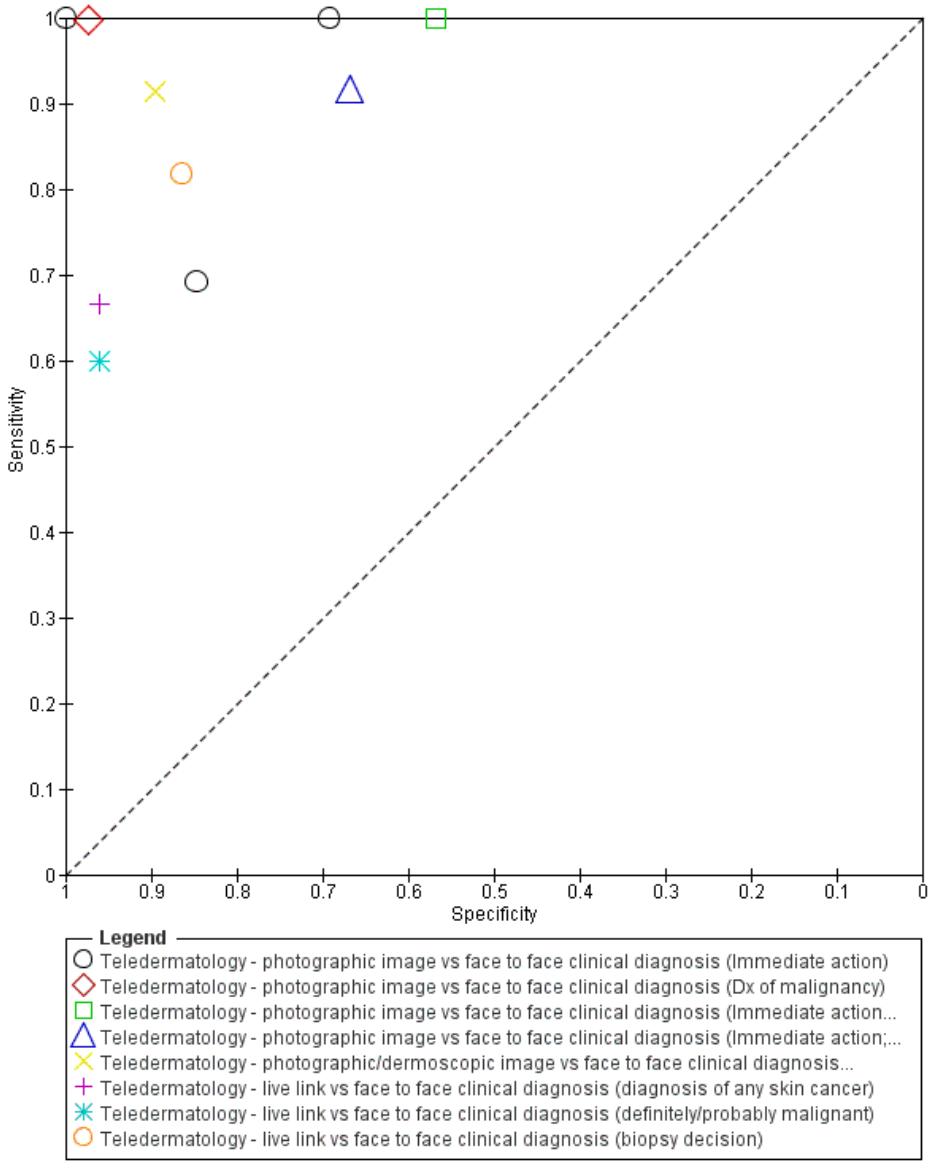
Figure 14 (Analysis 9)



Caption

Forest plot of tests for referral accuracy (expert in-person diagnosis as reference standard)

Figure 15 (Analysis 9)



Caption

ROC Plot of Teledermatology diagnosis or decision versus face-to-face expert diagnosis (reference standard) at any threshold for action

Sources of support

Internal sources

- No sources of support provided

External sources

- NIHR Systematic Review Programme, UK
- The National Institute for Health Research (NIHR), UK
  The NIHR, UK, is the largest single funder of the Cochrane Skin Group

Feedback

Appendices

1 Current content and structure of the Programme Grant

List of reviews	Estimated number of studies
Diagnosis of melanoma	
1. Visual inspection versus visual inspection plus dermoscopy	120
2. Teledermatology	12
3. Mobile phone applications	2
4. Computer-aided diagnosis: dermoscopy based and spectroscopy based techniques	37
5. Reflectance confocal microscopy	19
6. High frequency ultrasound	3
7. Overview: comparing the accuracy of tests for which sufficient evidence was identified either alone or in combination	–
Diagnosis of keratinocyte skin cancer (basal cell carcinoma and cutaneous squamous cell carcinoma)	
8. Visual inspection ± dermoscopy	22
9. Computer aided diagnosis: dermoscopy based and spectroscopy based techniques	3
10. Optical coherence tomography	6
11. Reflectance confocal microscopy	9
12. High frequency ultrasound	1
13. Exfoliative cytology	5
14. Overview: comparing the accuracy of tests for which sufficient evidence was identified either alone or in combination	–
Staging of melanoma	
15. Ultrasound	25 to 30
16. Computer tomography	5 to 10
17. Positron emission tomography or positron emission tomography-computer tomography	20 to 25
18. Magnetic resonance imaging	5
19. Sentinel lymph node biopsy ± high frequency ultrasound	70
20. Overview: comparing the accuracy of tests for which sufficient evidence was identified either alone or in combination	–
Staging of cutaneous squamous cell carcinoma	
21. Imaging tests review	10 to 15
22. Sentinel lymph node biopsy ± high frequency ultrasound	15 to 20

2 Glossary of terms

Term	Definition
Atypical intraepidermal melanocytic variant	Unusual area of darker pigmentation contained within the epidermis that may progress to an invasive melanoma; includes melanoma *in situ* and lentigo maligna
Atypical naevi	Unusual looking but noncancerous mole or area of darker pigmentation of the skin
BRAF V600 mutation	BRAF is a human gene that makes a protein called B-Raf which is involved in the control of cell growth. BRAF mutations (damaged DNA) occur in around 40% of melanomas, which can then be treated with particular drugs.
BRAF inhibitors	Therapeutic agents which inhibit the serine-threonine protein kinase BRAF mutated metastatic melanoma.
Breslow thickness	A scale for measuring the thickness of melanomas by the pathologist using a microscope, measured in mm from the top layer of skin to the bottom of the tumour.
Congenital naevi	A type of mole found on infants at birth

Term	Definition
Dermoscopy	Whereby a handheld microscope is used to allow more detailed, magnified, examination of the skin compared to examination by the naked eye alone
False negative	An individual who is truly positive for a disease, but whom a diagnostic test classifies them as disease-free.
False positive	An individual who is truly disease-free, but whom a diagnostic test classifies them as having the disease.
Histopathology/Histology	The study of tissue, usually obtained by biopsy or excision, for example under a microscope.
Incidence	The number of new cases of a disease in a given time period.
Index test	A diagnostic test under evaluation in a primary study
Lentigo maligna	Unusual area of darker pigmentation contained within the epidermis which includes malignant cells but with no invasive growth. May progress to an invasive melanoma
Lymph node	Lymph nodes filter the lymphatic fluid (clear fluid containing white blood cells) that travels around the body to help fight disease; they are located throughout the body often in clusters (nodal basins).
Melanocytic naevus	An area of skin with darker pigmentation (or melanocytes) also referred to as ‘moles’
Meta-analysis	A form of statistical analysis used to synthesise results from a collection of individual studies.
Metastases/metastatic disease	Spread of cancer away from the primary site to somewhere else through the bloodstream or the lymphatic system.
Micrometastases	Micrometastases are metastases so small that they can only be seen under a microscope.
Mitotic rate	Microscopic evaluation of number of cells actively dividing in a tumour.
Morbidity	Detrimental effects on health.
Mortality	Either (1) the condition of being subject to death; or (2) the death rate, which reflects the number of deaths per unit of population in relation to any specific region, age group, disease, treatment or other classification, usually expressed as deaths per 100, 1000, 10,000 or 100,000 people.
Multidisciplinary team	A team with members from different healthcare professions and specialties (e.g. urology, oncology, pathology, radiology, and nursing). Cancer care in the National Health Service (NHS) uses this system to ensure that all relevant health professionals are engaged to discuss the best possible care for that patient.
Prevalence	The proportion of a population found to have a condition.
Prognostic factors/indicators	Specific characteristics of a cancer or the person who has it which might affect the patient’s prognosis.
Receiver operating characteristic (ROC) plot	A plot of the sensitivity and 1 minus the specificity of a test at the different possible thresholds for test positivity; represents the diagnostic capability of a test with a range of binary test results
Receiver operating characteristic (ROC) analysis	The analysis of a ROC plot of a test to select an optimal threshold for test positivity
Recurrence	Recurrence is when new cancer cells are detected following treatment. This can occur either at the site of the original tumour or at other sites in the body.
Reference Standard	A test or combination of tests used to establish the final or ‘true’ diagnosis of a patient in an evaluation of a diagnostic test
Reflectance confocal microscopy (RCM)	A microscopic technique using infrared light (either in a handheld device or a static unit) that can create images of the deeper layers of the skin
Sensitivity	In this context the term is used to mean the proportion of individuals with a disease who have that disease correctly identified by the study test
Specificity	The proportion of individuals without the disease of interest (in this case with benign skin lesions) who have that absence of disease correctly identified by the study test
Staging	Clinical description of the size and spread of a patient’s tumour, fitting into internationally agreed categories.

Term	Definition
Subclinical (disease)	Disease that is usually asymptomatic and not easily observable, e.g. by clinical or physical examination.
Systemic treatment	Treatment, usually given by mouth or by injection, that reaches and affects cancer cells throughout the body rather than targeting one specific area.

3 Content of algorithms used to assist melanoma diagnosis by visual inspection alone

ABCD (Friedman 1985; Rigel 1993; Pehamberger 1993) **ABCDE (Carli 1994; Cristofolini 1994; Thomas 1998; Benelli 1999; Benelli 2001; Abbasi 2004)** **BCD (McGovern 1992)**	**Seven-point checklist (MacKie 1985; MacKie 1990; Keefe 1990)**	**Seven-point checklist (revised) (MacKie 1990; Healsmith 1994)**
A – asymmetry • variable centripetal growth of melanocytes (Friedman 1985) • “geometrical asymmetry in two axes of the tumour” (Thomas 1998; Benelli 1999; Benelli 2001) • “one half does not match the other half” (McGovern 1992); not separately scored in study “because we believed that asymmetry and border irregularity were linked” B - irregular borders • irregular shape with notching or scalloping of border (Friedman 1985) • “edges are ragged, notched, or blurred (McGovern 1992) • “irregular and notched” (Cristofolini 1994) • “unsharp or ill-defined or angular” (Thomas 1998) • “ragged or indented” (Benelli 1999, Benelli 2001) C - colour • variable pigmentation, multiple colours; various of hues of brown, also black, blue, red and white (Friedman 1985) • “pigmentation is not uniform; shades of tan, brown and black are present with dashes of red, white, or blue” (McGovern 1992) • “mottled-haphazard display” (Cristofolini 1994) • “presence of at least two different colours within the lesion (with the exception of the usual symmetrical darkening of the lesion in its center)” (Thomas 1998; Benelli 2001) • “multiple colours” (Abbasi 2004) D - diameter equal or superior to 6mm • all studies agree E - evolution • “changes in pigmentation” (Cristofolini 1994) • “enlargement of the surface (and not in height) of the lesion; anamnestic criterion based on the patient’s description of the	• sensory change, (greater awareness of the lesion or mild itch); • diameter of >=1 cm; • growth of the lesion; • an irregular edge; • irregular pigment with different shades of brown and black in the lesion; • inflammation • crusting, oozing, or bleeding. Presence of 3 or more suggestive of melanoma	MacKie 1990, Mackie 1991, and Healsmith 1994 describe the revised criteria as: Major signs • Change in size • Change in shape • Change in colour Minor signs • Inflammation • Crusting or bleeding • Sensory change • Diameter >=7 mm “a patient with a pigmented lesion with any one of the major signs should be considered for referral and that the presence of any of the minor signs should be a further stimulus to referral.” (MacKie 1990)

natural history of the lesion" (Thomas 1998) • "elevation, enlargement or change in the color of the lesion" (Benelli 1999; Benelli 2001) • "evolving (with respect to size, shape, shades of colour, surface features, or symptoms)" (Abbasi 2004) McGovern 1992 describes 7 characteristics as: "increasing size, variegation, inflammation, irregular outline, greater than 1cm diameter, itch, bleeding" These are expanded on in MacKie 1990, who describes the original (1985) criteria as: • sensory change, often described as a greater awareness of the lesion but also as a mild itch; • diameter of 1 cm or greater; • growth of the lesion; • an irregular edge; • irregular pigment with different shades of brown and black in the lesion; • inflammation (a reddish tinge within the lesion); and • crusting, oozing, or bleeding. • >=3 criteria should prompt referral (MacKie 1990)		

4 Proposed sources of heterogeneity

i. Population characteristics

- general versus higher risk populations
- patient population: Primary /secondary / specialist unit
- lesion suspicion: general suspicion/atypical/equivocal/NR
- lesion type: any pigmented; melanocytic
- inclusion of multiple lesions per participant
- ethnicity

ii. Index test characteristics

- the nature of and definition of criteria for test positivity
- observer experience with the index test
- approaches to lesion preparation (e.g., the use of oil or antiseptic gel for dermoscopy)

iii. Reference standard characteristics

- reference standard used
- whether histology-reporting meets pathology-reporting guidelines
- use of excisional versus diagnostic biopsy
- whether two independent dermatopathologists reviewed histological diagnosis

iv. Study quality

- consecutive or random sample of participants recruited
- index test interpreted blinded to the reference standard result
- index test interpreted blinded to the result of any other index test
- presence of partial or differential verification bias (whereby only a sample of those subject to the index test are verified by the reference test or by the same reference test with selection dependent on the index test result)
- use of an adequate reference standard
- overall risk of bias

5 Final search strategies

Melanoma search strategies to August 2016

Database: Ovid MEDLINE(R) 1946 to August week 3 2016

Search strategy:

1 exp melanoma/

2 exp skin cancer/

3 exp basal cell carcinoma/

4 basalioma$1.ti,ab.

5 ((basal cell or skin) adj2 (cancer$1 or carcinoma$1 or mass or masses or tumour$1 or tumor$1 or neoplasm$1 or adenoma$1 or epithelioma$1 or lesion$1 or malignan$ or nodule$1)).ti,ab.

6 (pigmented adj2 (lesion$1 or mole$ or nevus or nevi or naevus or naevi or skin)).ti,ab.

7 (melanom$1 or nonmelanoma$1 or non-melanoma$1 or melanocyt$ or non-melanocyt$ or nonmelanocyt$ or keratinocyt$).ti,ab.

8 nmsc.ti,ab.

9 (squamous cell adj2 (cancer$1 or carcinoma$1 or mass or masses or tumor$1 or tumour$1 or neoplasm$1 or adenoma$1 or epithelioma$1 or epithelial or lesion$1 or malignan$ or nodule$1) adj2 (skin or epiderm$ or cutaneous)).ti,ab.

10 (BCC or CSCC or NMSC).ti,ab.

11 keratinocy$.ti,ab.

12 Keratinocytes/

13 or/1-12

14 dermoscop$.ti,ab.

15 dermatoscop$.ti,ab.

16 photomicrograph$.ti,ab.

17 exp epiluminescence microscopy/

18 (epiluminescence adj2 microscop$).ti,ab.

19 (confocal adj2 microscop$).ti,ab.

20 (incident light adj2 microscop$).ti,ab.

21 (surface adj2 microscop$).ti,ab.

22 (visual adj (inspect$ or examin$)).ti,ab.

23 ((clinical or physical) adj examin$).ti,ab.

24 3 point.ti,ab.

25 three point.ti,ab.

26 pattern analys$.ti,ab.

27 ABCD$.ti,ab.

28 menzies.ti,ab.

29 7 point.ti,ab.

30 seven point.ti,ab.

31 (digital adj2 (dermoscop$ or dermatoscop$)).ti,ab.

32 artificial intelligence.ti,ab.

33 AI.ti,ab.

34 computer assisted.ti,ab.

35 computer aided.ti,ab.

36 neural network$.ti,ab.

37 exp diagnosis, computer-assisted/

38 MoleMax.ti,ab.

39 image process$.ti,ab.

40 automatic classif$.ti,ab.

41 image analysis.ti,ab.

42 SIAscop$.ti,ab.

43 Aura.ti,ab.

44 (optical adj2 scan$).ti,ab.

45 MelaFind.ti,ab.

46 SIMSYS.ti,ab.

47 MoleMate.ti,ab.

48 SolarScan.ti,ab.

49 VivaScope.ti,ab.

50 (high adj3 ultraso$).ti,ab.

51 (canine adj2 detect$).ti,ab.

52 ((mobile or cell or cellular or smart) adj ((phone$1 adj2 app$1) or application$1)).ti,ab.

53 smartphone$.ti,ab.

54 (DermoScan or SkinVision or DermLink or SpotCheck).ti,ab.

55 Mole Detective.ti,ab.

56 Spot Check.ti,ab.

57 (mole$1 adj2 map$).ti,ab.

58 (total adj2 body).ti,ab.

59 exfoliative cytolog$.ti,ab.

60 digital analys$.ti,ab.

61 (image$1 adj3 software).ti,ab.

62 (teledermatolog$ or tele-dermatolog$ or telederm or tele-derm or teledermoscop$ or tele-dermoscop$ or teledermatoscop$ or tele-dermatoscop$).ti,ab.

63 (optical coherence adj (technolog$ or tomog$)).ti,ab.

64 (computer adj2 diagnos$).ti,ab.

65 exp sentinel lymph node biopsy/

66 (sentinel adj2 node).ti,ab.

67 nevisense.mp. or HFUS.ti,ab.

68 electrical impedance spectroscopy.ti,ab.

69 history taking.ti,ab.

70 patient history.ti,ab.

71 (naked eye adj (exam$ or assess$)).ti,ab.

72 (skin adj exam$).ti,ab.

73 physical examination/

74 ugly duckling.mp. or UD.ti,ab.

75 ((physician$ or clinical or physical) adj (exam$ or triage or recog$)).ti,ab.

76 ABCDE.mp. or VOC.ti,ab.

77 clinical accuracy.ti,ab.

78 Family Practice/ or Physicians, Family/ or clinical competence/

79 (confocal adj2 microscop$).ti,ab.

80 diagnostic algorithm$1.ti,ab.

81 checklist$.ti,ab.

82 virtual imag$1.ti,ab.

83 volatile organic compound$1.ti,ab.

84 dog$1.ti,ab.

85 gene expression analy$.ti,ab.

86 reflex transmission imag$.ti,ab.

87 thermal imaging.ti,ab.

88 elastography.ti,ab.

89 or/14-88

90 (CT or PET).ti,ab.

91 PET-CT.ti,ab.

92 (FDG or F18 or Fluorodeoxyglucose or radiopharmaceutical$).ti,ab.

93 exp Deoxyglucose/

94 deoxy-glucose.ti,ab.

95 deoxyglucose.ti,ab.

96 CATSCAN.ti,ab.

97 exp Tomography, Emission-Computed/

98 exp Tomography, X-ray computed/

99 positron emission tomograph$.ti,ab.

100 exp magnetic resonance imaging/

101 (MRI or fMRI or NMRI or scintigraph$).ti,ab.

102 exp echography/

103 Doppler echography.ti,ab.

104 sonograph$.ti,ab.

105 ultraso$.ti,ab.

106 doppler.ti,ab.

107 magnetic resonance imag$.ti,ab.

108 or/90-107

109 (stage$ or staging or metasta$ or recurrence or sensitivity or specificity or false negative$ or thickness$).ti,ab.

110 "Sensitivity and Specificity"/

111 exp cancer staging/

112 or/109-111

113 108 and 112

114 89 or 113

115 13 and 114

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations 29 August 2016

Search strategy:

1 basalioma$1.ti,ab.

2 ((basal cell or skin) adj2 (cancer$1 or carcinoma$1 or mass or masses or tumour$1 or tumor$1 or neoplasm$1 or adenoma$1 or epithelioma$1 or lesion$1 or malignan$ or nodule$1)).ti,ab.

3 (pigmented adj2 (lesion$1 or mole$ or nevus or nevi or naevus or naevi or skin)).ti,ab.

4 (melanom$1 or nonmelanoma$1 or non-melanoma$1 or melanocyt$ or non-melanocyt$ or nonmelanocyt$ or keratinocyt$).ti,ab.

5 nmsc.ti,ab.

6 (squamous cell adj2 (cancer$1 or carcinoma$1 or mass or masses or tumor$1 or tumour$1 or neoplasm$1 or adenoma$1 or epithelioma$1 or epithelial or lesion$1 or malignan$ or nodule$1) adj2 (skin or epiderm$ or cutaneous)).ti,ab.

7 (BCC or CSCC or NMSC).ti,ab.

8 keratinocy$.ti,ab.

9 or/1-8

10 dermoscop$.ti,ab.

11 dermatoscop$.ti,ab.

12 photomicrograph$.ti,ab.

13 (epiluminescence adj2 microscop$).ti,ab.

14 (confocal adj2 microscop$).ti,ab.

15 (incident light adj2 microscop$).ti,ab.

16 (surface adj2 microscop$).ti,ab.

17 (visual adj (inspect$ or examin$)).ti,ab.

18 ((clinical or physical) adj examin$).ti,ab.

19 3 point.ti,ab.

20 three point.ti,ab.

21 pattern analys$.ti,ab.

22 ABCD$.ti,ab.

23 menzies.ti,ab.

24 7 point.ti,ab.

25 seven point.ti,ab.

26 (digital adj2 (dermoscop$ or dermatoscop$)).ti,ab.

27 artificial intelligence.ti,ab.

28 AI.ti,ab.

29 computer assisted.ti,ab.

30 computer aided.ti,ab.

31 neural network$.ti,ab.

32 MoleMax.ti,ab.

33 image process$.ti,ab.

34 automatic classif$.ti,ab.

35 image analysis.ti,ab.

36 SIAscop$.ti,ab.

37 Aura.ti,ab.

38 (optical adj2 scan$).ti,ab.

39 MelaFind.ti,ab.

40 SIMSYS.ti,ab.

41 MoleMate.ti,ab.

42 SolarScan.ti,ab.

43 VivaScope.ti,ab.

44 (high adj3 ultraso$).ti,ab.

45 (canine adj2 detect$).ti,ab.

46 ((mobile or cell or cellular or smart) adj ((phone$1 adj2 app$1) or application$1)).ti,ab.

47 smartphone$.ti,ab.

48 (DermoScan or SkinVision or DermLink or SpotCheck).ti,ab.

49 Mole Detective.ti,ab.

50 Spot Check.ti,ab.

51 (mole$1 adj2 map$).ti,ab.

52 (total adj2 body).ti,ab.

53 exfoliative cytolog$.ti,ab.

54 digital analys$.ti,ab.

55 (image$1 adj3 software).ti,ab.

56 (teledermatolog$ or tele-dermatolog$ or telederm or tele-derm or teledermoscop$ or tele-dermoscop$ or teledermatoscop$ or tele-dermatoscop$).ti,ab.

57 (optical coherence adj (technolog$ or tomog$)).ti,ab.

58 (computer adj2 diagnos$).ti,ab.

59 (sentinel adj2 node).ti,ab.

60 nevisense.mp. or HFUS.ti,ab.

61 electrical impedance spectroscopy.ti,ab.

62 history taking.ti,ab.

63 patient history.ti,ab.

64 (naked eye adj (exam$ or assess$)).ti,ab.

65 (skin adj exam$).ti,ab.

66 ugly duckling.mp. or UD.ti,ab.

67 ((physician$ or clinical or physical) adj (exam$ or triage or recog$)).ti,ab.

68 ABCDE.mp. or VOC.ti,ab.

69 clinical accuracy.ti,ab.

70 (Family adj (Practice or Physicians)).ti,ab.

71 (confocal adj2 microscop$).ti,ab.

72 clinical competence.ti,ab.

73 diagnostic algorithm$1.ti,ab.

74 checklist$.ti,ab.

75 virtual imag$1.ti,ab.

76 volatile organic compound$1.ti,ab.

77 dog$1.ti,ab.

78 gene expression analy$.ti,ab.

79 reflex transmission imag$.ti,ab.

80 thermal imaging.ti,ab.

81 elastography.ti,ab.

82 or/10-81

83 (CT or PET).ti,ab.

84 PET-CT.ti,ab.

85 (FDG or F18 or Fluorodeoxyglucose or radiopharmaceutical$).ti,ab.

86 deoxy-glucose.ti,ab.

87 deoxyglucose.ti,ab.

88 CATSCAN.ti,ab.

89 positron emission tomograph$.ti,ab.

90 (MRI or fMRI or NMRI or scintigraph$).ti,ab.

91 Doppler echography.ti,ab.

92 sonograph$.ti,ab.

93 ultraso$.ti,ab.

94 doppler.ti,ab.

95 magnetic resonance imag$.ti,ab.

96 or/83-95

97 (stage$ or staging or metasta$ or recurrence or sensitivity or specificity or false negative$ or thickness$).ti,ab.

98 96 and 97

99 82 or 98

100 9 and 99

Database: Embase 1974 to 29 August 2016

Search strategy:

1 *melanoma/

2 *skin cancer/

3 *basal cell carcinoma/

4 basalioma$.ti,ab.

5 ((basal cell or skin) adj2 (cancer$1 or carcinoma$1 or mass or masses or tumour$1 or tumor$1 or neoplasm$ or adenoma$ or epithelioma$ or lesion$ or malignan$ or nodule$)).ti,ab.

6 (pigmented adj2 (lesion$1 or mole$ or nevus or nevi or naevus or naevi or skin)).ti,ab.

7 (melanom$1 or nonmelanoma$1 or non-melanoma$1 or melanocyt$ or non-melanocyt$ or nonmelanocyt$ or keratinocyt$).ti,ab.

8 nmsc.ti,ab.

9 (squamous cell adj2 (cancer$1 or carcinoma$1 or mass or tumor$1 or tumour$1 or neoplasm$1 or adenoma$1 or epithelioma$1 or epithelial or lesion$1 or malignan$ or nodule$1) adj2 (skin or epiderm$ or cutaneous)).ti,ab.

10 (BCC or cscc).mp. or NMSC.ti,ab.
11 keratinocyte.ti,ab.
12 keratinocy$.ti,ab.
13 or/1-12
14 dermoscop$.ti,ab.
15 dermatoscop$.ti,ab.
16 photomicrograph$.ti,ab.
17 *epiluminescence microscopy/
18 (epiluminescence adj2 microscop$).ti,ab.
19 (confocal adj2 microscop$).ti,ab.
20 (incident light adj2 microscop$).ti,ab.
21 (surface adj2 microscop$).ti,ab.
22 (visual adj (inspect$ or examin$)).ti,ab.
23 ((clinical or physical) adj examin$).ti,ab.
24 3 point.ti,ab.
25 three point.ti,ab.
26 pattern analys$.ti,ab.
27 ABCD$.ti,ab.
28 menzies.ti,ab.
29 7 point.ti,ab.
30 seven point.ti,ab.
31 (digital adj2 (dermoscop$ or dermatoscop$)).ti,ab.
32 artificial intelligence.ti,ab.
33 AI.ti,ab.
34 computer assisted.ti,ab.
35 computer aided.ti,ab.
36 neural network$.ti,ab.
37 MoleMax.ti,ab.
38 exp diagnosis, computer-assisted/
39 image process$.ti,ab.
40 automatic classif$.ti,ab.
41 image analysis.ti,ab.
42 SIAscop$.ti,ab.
43 (optical adj2 scan$).ti,ab.
44 Aura.ti,ab.
45 MelaFind.ti,ab.
46 SIMSYS.ti,ab.
47 MoleMate.ti,ab.
48 SolarScan.ti,ab.
49 VivaScope.ti,ab.
50 confocal microscop$.ti,ab.
51 (high adj3 ultraso$).ti,ab.
52 (canine adj2 detect$).ti,ab.
53 ((mobile or cell$ or cellular or smart) adj ((phone$1 adj2 app$1) or application$1)).ti,ab.
54 smartphone$.ti,ab.
55 (DermoScan or SkinVision or DermLink or SpotCheck).ti,ab.

56 Spot Check.ti,ab.

57 Mole Detective.ti,ab.

58 (mole$1 adj2 map$).ti,ab.

59 (total adj2 body).ti,ab.

60 exfoliative cytolog$.ti,ab.

61 digital analys$.ti,ab.

62 (image$1 adj3 software).ti,ab.

63 (optical coherence adj (technolog$ or tomog$)).ti,ab.

64 (teledermatolog$ or tele-dermatolog$ or telederm or tele-derm or teledermoscop$ or tele-dermoscop$ or teledermatoscop$).mp. or tele-dermatoscop$.ti,ab.

65 (computer adj2 diagnos$).ti,ab.

66 *sentinel lymph node biopsy/

67 (sentinel adj2 node).ti,ab.

68 nevisense.ti,ab.

69 HFUS.ti,ab.

70 electrical impedance spectroscopy.ti,ab.

71 history taking.ti,ab.

72 patient history.ti,ab.

73 (naked eye adj (exam$ or assess$)).ti,ab.

74 (skin adj exam$).ti,ab.

75 *physical examination/

76 ugly duckling.ti,ab.

77 UD sign$.ti,ab.

78 ((physician$ or clinical or physical) adj (exam$ or recog$ or triage)).ti,ab.

79 ABCDE.ti,ab.

80 clinical accuracy.ti,ab.

81 *general practice/

82 (confocal adj2 microscop$).ti,ab.

83 clinical competence/

84 diagnostic algorithm$.ti,ab.

85 checklist$1.ti,ab.

86 virtual image$1.ti,ab.

87 volatile organic compound$1.ti,ab.

88 VOC.ti,ab.

89 dog$1.ti,ab.

90 gene expression analys$.ti,ab.

91 reflex transmission imaging.ti,ab.

92 thermal imaging.ti,ab.

93 elastography.ti,ab.

94 dog$1.ti,ab.

95 gene expression analys$.ti,ab.

96 reflex transmission imaging.ti,ab.

97 thermal imaging.ti,ab.

98 elastography.ti,ab.

99 or/14-93

100 PET-CT.ti,ab.

101 (CT or PET).ti,ab.

102 (FDG or F18 or Fluorodeoxyglucose or radiopharmaceutical$).ti,ab.

103 exp Deoxyglucose/

104 CATSCAN.ti,ab.

105 deoxyglucose.ti,ab.

106 deoxy-glucose.ti,ab.

107 *positron emission tomography/

108 *computer assisted tomography/

109 positron emission tomograph$.ti,ab.

110 *nuclear magnetic resonance imaging/

111 (MRI or fMRI or NMRI or scintigraph$).ti,ab.

112 *echography/

113 Doppler.ti,ab.

114 sonograph$.ti,ab.

115 ultraso$.ti,ab.

116 magnetic resonance imag$.ti,ab.

117 or/100-116

118 (stage$ or staging or metasta$ or recurrence or sensitivity or specificity or false negative$ or thickness$).ti,ab.

119 "Sensitivity and Specificity"/

120 *cancer staging/

121 or/118-120

122 117 and 121

123 99 or 122

124 13 and 123

Database: Cochrane Library (Wiley) 2016 searched 30 August 2016 CDSR Issue 8 of 12 2016 CENTRAL Issue 7 of 12 2016 HTA Issue 3 of 4 July 2016 DARE Issue 3 of 4 2015

Search strategy:

#1 melanoma* or nonmelanoma* or non-melanoma* or melanocyt* or non-melanocyt* or nonmelanocyt* or keratinocyte*

#2 MeSH descriptor: [Melanoma] explode all trees

#3 "skin cancer*"

#4 MeSH descriptor: [Skin Neoplasms] explode all trees

#5 skin near/2 (cancer* or carcinoma* or mass or masses or tumour* or tumor* or neoplasm* or adenoma* or epithelioma* or lesion* or malignan* or nodule*)

#6 nmsc

#7 "squamous cell" near/2 (cancer* or carcinoma* or mass or masses or tumour* or tumor* or neoplasm* or adenoma* or epithelioma* or lesion* or malignan* or nodule*) near/2 (skin or epiderm* or cutaneous)

#8 "basal cell" near/2 (cancer* or carcinoma* or mass or masses or tumour* or tumor* or neoplasm* or adenoma* or epithelioma* or lesion* or malignan* or nodule*)

#9 pigmented near/2 (lesion* or nevus or mole* or naevi or naevus or nevi or skin)

#10 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9

#11 dermoscop*

#12 dermatoscop*

#13 Photomicrograph*

#14 MeSH descriptor: [Dermoscopy] explode all trees

#15 confocal near/2 microscop*

#16 epiluminescence near/2 microscop*

#17 incident next light near/2 microscop*

#18 surface near/2 microscop*

#19 "visual inspect*"

#20 "visual exam*"
#21 (clinical or physical) next (exam*)
#22 "3 point"
#23 "three point"
#24 "pattern analys*"
#25 ABDC
#26 menzies
#27 "7 point"
#28 "seven point"
#29 digital near/2 (dermoscop* or dermatoscop*)
#30 "artificial intelligence"
#31 "AI"
#32 "computer assisted"
#33 "computer aided"
#34 AI
#35 "neural network*"
#36 MoleMax
#37 "computer diagnosis"
#38 "image process*"
#39 "automatic classif*"
#40 SIAscope
#41 "image analysis"
#42 "optical near/2 scan*"
#43 Aura
#44 MelaFind
#45 SIMSYS
#46 MoleMate
#47 SolarScan
#48 Vivascope
#49 "confocal microscopy"
#50 high near/3 ultraso*
#51 canine near/2 detect*
#52 Mole* near/2 map*
#53 total near/2 body
#54 mobile* or smart near/2 phone*
#55 cell next phone*
#56 smartphone*
#57 "mitotic index"
#58 DermoScan or SkinVision or DermLink or SpotCheck
#59 "Mole Detective"
#60 "Spot Check"
#61 mole* near/2 map*
#62 total near/2 body
#63 "exfoliative cytolog*"
#64 "digital analys*"
#65 image near/3 software
#66 teledermatolog* or tele-dermatolog* or telederm or tele-derm or teledermoscop* or tele-dermoscop* or teledermatoscop*

or tele-dermatolog*

#67 "optical coherence" next (technolog* or tomog*)

#68 computer near/2 diagnos*

#69 sentinel near/2 node*

#70 #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48 or #49 or #50 or #51 or #52 or #53 or #54 or #55 or #56 or #57 or #58 or #59 or #60 or #61 or #62 or #63 or #64 or #65 or #66 or #67 or #68 or #69

#71 ultraso*

#72 sonograph*

#73 MeSH descriptor: [Ultrasonography] explode all trees

#74 Doppler

#75 CT or PET or PET-CT

#76 "CAT SCAN" or "CATSCAN"

#77 MeSH descriptor: [Positron-Emission Tomography] explode all trees

#78 MeSH descriptor: [Tomography, X-Ray Computed] explode all trees

#79 MRI

#80 MeSH descriptor: [Magnetic Resonance Imaging] explode all trees

#81 MRI or fMRI or NMRI or scintigraph*

#82 "magnetic resonance imag*"

#83 MeSH descriptor: [Deoxyglucose] explode all trees

#84 deoxyglucose or deoxy-glucose

#85 "positron emission tomograph*"

#86 #71 or #72 or #73 or #74 or #75 or #76 or #77 or #78 or #79 or #80 or #81 or #82 or #83 or #84 or #85

#87 stage* or staging or metasta* or recurrence or sensitivity or specificity or "false negative*" or thickness*

#88 MeSH descriptor: [Neoplasm Staging] explode all trees

#89 #87 or #88

#90 #89 and #86

#91 #70 or #90

#92 #10 and #91

#93 BCC or CSCC or NMCS

#94 keratinocy*

#95 #93 or #94

#96 #10 or #95

#97 nevisense

#98 HFUS

#99 "electrical impedance spectroscopy"

#100 "history taking"

#101 "patient history"

#102 naked next eye near/1 (exam* or assess*)

#103 skin next exam*

#104 "ugly duckling" or (UD sign*)

#105 MeSH descriptor: [Physical Examination] explode all trees

#106 (physician* or clinical or physical) near/1 (exam* or recog* or triage*)

#107 ABCDE

#108 "clinical accuracy"

#109 MeSH descriptor: [General Practice] explode all trees

#110 confocal near microscop*

#111 "diagnostic algorithm*"

#112 MeSH descriptor: [Clinical Competence] explode all trees

#113 checklist*

#114 "virtual image*"

#115 "volatile organic compound*"

#116 dog or dogs

#117 VOC

#118 "gene expression analys*"

#119 "reflex transmission imaging"

#120 "thermal imaging"

#121 elastography

#122 #97 or #98 or #99 or #100 or #101 or #102 or #103 or #104 or #105 or #106 or #107 or #108 or #109 or #110 or #111 or #112 or #113 or #114 or #115 or #116 or #117 or #118 or #119 or #120 or #121

#123 #70 or #122

#124 #96 and #123

#125 #96 and #90

#126 #125 or #124

#127 #10 and #126

Database : CINAHL Plus (EBSCO) 1937 to 30 August 2016

Search strategy:

S1 (MH "Melanoma") OR (MH "Nevi and Melanomas+")

S2 (MH "Skin Neoplasms+")

S3 (MH "Carcinoma, Basal Cell+")

S4 basalioma*

S5 (basal cell) N2 (cancer* or carcinoma* or mass or masses or tumor* or tumour* or neoplasm* or adenoma* or epithelioma* or lesion* or malignan* or nodule*)

S6 (pigmented) N2 (lesion* or mole* or nevus or nevi or naevus or naevi or skin)

S7 melanom* or nonmelanoma* or non-melanoma* or melanocyt* or non-melanocyt* or nonmelanocyt*

S8 nmsc

S9 TX BCC or cscc or NMSC

S10 (MH "Keratinocytes")

S11 keratinocyt*

S12 S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11

S13 dermoscop* or dermatoscop* or photomicrograph* or (3 point) or (three point) or ABCD* or menzies or (7 point) or (seven point) or AI or Molemax or SIASCOP* or Aura or MelaFind or SIMSYS or MoleMate or SolarScan or smartphone* or DermoScan or SkinVision or DermLink or SpotCheck

S14 (epiluminescence or confocal or incident or surface) N2 (microscop*)

S15 visual N1 (inspect* or examin*)

S16 (clinical or physical) N1 (examin*)

S17 pattern analys*

S18 (digital) N2 (dermoscop* or dermatoscop*)

S19 (artificial intelligence)

S20 (computer) N2 (assisted or aided)

S21 (neural network*)

S22 (MH "Diagnosis, Computer Assisted+")

S23 (image process*)

S24 (automatic classif*)

S25 (image analysis)

S26 SIAScop*

S27 (optical) N2 (scan*)

S28 (high) N3 (ultraso*)

S29 elastography

S30 (mobile or cell or cellular or smart) N2 (phone*) N2 (app or application*)

S31 (mole*) N2 (map*)

S32 total N2 body

S33 exfoliative cytolog*

S34 digital analys*

S35 image N3 software

S36 teledermatolog* or tele-dermatolog* or telederm or tele-derm or teledermoscop* or tele-dermoscop* or teledermatoscop* or tele-dermatoscop* teledermatolog* or tele-dermatolog* or telederm or tele-derm or teledermoscop*

S37 (optical coherence) N1 (technolog* or tomog*)

S38 computer N2 diagnos*

S39 sentinel N2 node

S40 (MH "Sentinel Lymph Node Biopsy")

S41 nevisense or HFUS or checklist* or VOC or dog*

S42 electrical impedance spectroscopy

S43 history taking

S44 "Patient history"

S45 naked eye

S46 skin exam*

S47 physical exam*

S48 ugly duckling

S49 UD sign*

S50 (physician* or clinical or physical) N1 (exam*)

S51 clinical accuracy

S52 general practice

S53 (physician* or clinical or physical) N1 (recog* or triage)

S54 confocal microscop*

S55 clinical competence

S56 diagnostic algorithm*

S57 checklist*

S58 virtual image*

S59 volatile organic compound*

S60 gene expression analys*

S61 reflex transmission imag*

S62 thermal imaging

S63 S13 or S14 or S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48 OR S49 OR S50 OR S51 OR S52 OR S53 OR S54 OR S55 OR S56 OR S57 OR S58 OR S59 OR S60 OR S61 OR S62

S64 CT or PET

S65 PET-CT

S66 FDG or F18 or Fluorodeoxyglucose or radiopharmaceutical*

S67 (MH "Deoxyglucose+")

S68 deoxy-glucose or deoxyglucose

S69 CATSCAN

S70 CAT-SCAN

S71 (MH "Deoxyglucose+")

S72 (MH "Tomography, Emission-Computed+")

S73 (MH "Tomography, X-Ray Computed")

S74 positron emission tomograph*

S75 (MH "Magnetic Resonance Imaging+")

S76 MRI or fMRI or NMRI or scintigraph*

S77 echography

S78 doppler

S79 sonograph*

S80 ultraso*

S81 magnetic resonance imag*

S82 S64 OR S65 OR S66 OR S67 OR S68 OR S69 OR S70 OR S71 OR S72 OR S73 OR S74 OR S75 OR S76 OR S77 OR S78 OR S79 OR S80 OR S81

S83 stage* or staging or metasta* or recurrence or sensitivity or specificity or (false negative*) or thickness

S84 (MH "Neoplasm Staging")

S85 S83 OR S84

S86 S82 AND S85

S87 S63 OR S86

S88 S12 AND S87

Database: Science Citation Index SCI Expanded (Web of Science) 1900 to 30 August 2016

Conference Proceedings Citation Index (Web of Science) 1900 to 1 September 2016

Search strategy:

#1 (melanom* or nonmelanom* or non-melanoma* or melanocyt* or non-melanocyt* or nonmelanocyt* or keratinocyt*)

#2 (basalioma*)

#3 ((skin) near/2 (cancer* or carcinoma or mass or masses or tumour* or tumor* or neoplasm* or adenoma* or epithelioma* or lesion* or malignan* or nodule*))

#4 ((basal) near/2 (cancer* or carcinoma* or mass or masses or tumour* or tumor* or neoplasm* or adenoma* or epithelioma* or lesion* or malignan* or nodule*))

#5 ((pigmented) near/2 (lesion* or mole* or nevus or nevi or naevus or naevi or skin))

#6 (nmsc or BCC or NMSC or keratinocy*)

#7 ((squamous cell (cancer* or carcinoma* or mass or masses or tumour* or tumor* or neoplasm* or adenoma* or epithelioma* or lesion* or malignan* or nodule*))

#8 (skin or epiderm* or cutaneous)

#9 #8 AND #7

#10 #9 OR #6 OR #5 OR #4 OR #3 OR #2 OR #1

#11 ((dermoscop* or dermatoscop* or photomicrograph* or epiluminescence or confocal or "incident light" or "surface microscop*" or "visual inspect*" or "physical exam*" or 3 point or three point or pattern analy* or ABCDE or menzies or 7 point or seven point or dermoscop* or dermatoscop* or AI or artificial or computer aided or computer assisted or neural network* or Molemax or image process* or automatic classif* or image analysis or siascope or optical scan* or Aura or melafind or simsys or molemate or solarscan or vivascope or confocal microscop* or high ultraso* or canine detect* or cellphone* or mobile* or phone* or smartphone or dermoscan or skinvision or dermlink or spotcheck or spot check or mole detective or mole map* or total body or exfoliative psychology or digital or image software or optical coherence or teledermatology or telederm* or teledermoscop* or teledermatoscop* or computer diagnos* or sentinel))

#12 ((nevisense or HFUS or impedance spectroscopy or history taking or patient history or naked eye or skin exam* or physical exam* or ugly duckling or UD sign* or physician* exam* or physical exam* or ABCDE or clinical accuracy or general practice or confocal microscop* or clinical competence or diagnostic algorithm* or checklist* or virtual image* or volatile organic or VOC or dog* or gene expression or reflex transmission or thermal imag* or elastography))

#13 #11 or #12

#14 ((PET or CT or FDG or deoxyglucose or deoxy-glucose or fluorodeoxy* or radiopharma* or CATSCAN or positron emission or computer assisted or nuclear magnetic or MRI or FMRI or NMRI or scintigraph* or echograph* or Doppler or

sonograph* or ultraso* or magnetic reson*))

#15 ((stage* or staging or metast* or recurrence or sensitivity or specificity or false negative* or thickness*))

#16 #14 AND #15

#17 #16 OR #13

#18 #10 AND #17

Refined by: DOCUMENT TYPES: (MEETING ABSTRACT OR PROCEEDINGS PAPER)

6 Full text inclusion criteria

Criterion	Inclusion	Exclusion

Study design	<u>For diagnostic and staging reviews</u>
	• Any study for which a 2×2 contingency table can be extracted, e.g.
	  ◦ diagnostic case control studies
	  ◦ 'cross-sectional' test accuracy study with retrospective or prospective data collection
	  ◦ studies where estimation of test accuracy was not the primary objective but test results for both index and reference standard were available
	  ◦ RCTs of tests or testing strategies where participants were randomised between index tests and all undergo a reference standard (i.e. accuracy RCTs)
		• < 5 melanoma cases (diagnosis reviews)
		• < 10 participants (staging reviews)
		• Studies developing new criteria for diagnosis unless a separate 'test set' of images were used to evaluate the criteria (mainly digital dermoscopy)
		• Studies using 'normal' skin as controls
		• Letters, editorials, comment papers, narrative reviews
		• Insufficient data to construct a 2×2 table

Target condition	• Melanoma
	• Keratinocyte skin cancer (or non-melanoma skin cancer)
	  ◦ BCC or epithelioma
	  ◦ cSCC
		• Studies exclusively conducted in children
		• Studies of non-cutaneous melanoma or SCC

Population	<u>For diagnostic reviews</u> • Adults with a skin lesion suspicious for melanoma, BCC, or cSCC (other terms include pigmented skin lesion/nevi, melanocytic, keratinocyte, etc.) • Adults at high risk of developing melanoma skin cancer, BCC, or cSCC <u>For staging reviews</u> • Adults with a diagnosis of melanoma or cSCC undergoing tests for staging of lymph nodes or distant metastases or both	• People suspected of other forms of skin cancer • Studies conducted exclusively in children

Criterion	Inclusion	Exclusion
Index tests	<u>For diagnosis</u> • Visual inspection/clinical examination • Dermoscopy/dermatoscopy • Teledermoscpoy • Smartphone/mobile phone applications • Digital dermoscopy/artificial intelligence • Confocal microscopy • Ocular coherence tomography • Exfoliative cytology • High frequency ultrasound • Canine odour detection • DNA expression analysis/gene chip analysis • Other <u>For staging</u> • CT • PET • PET-CT • MRI • Ultrasound +/fine needle aspiration cytology FNAC • SLNB +/high frequency ultrasound • Other Any test combination and in any order Any test positivity threshold Any variation in testing procedure (e.g. radioisotope used)	• Sentinel lymph biopsy for therapeutic rather than staging purposes • Tests to determine melanoma thickness • Tests to determine surgical margins/lesion borders • Tests to improve histopathology diagnose • LND
Reference standard	<u>For diagnostic studies</u> • Histopathology of the excised lesion • Clinical follow-up of non-excised/benign appearing lesions with later histopathology if suspicious • Expert diagnosis (studies should not be included if expert diagnosis is the sole reference standard) <u>For studies of imaging tests for staging</u> • Histopathology (via LND or SLMB) • Clinical/radiological follow-up • A combination of the above <u>For studies of SLNB accuracy for staging</u> • LND of both SLN+ and SLn participants to identify all diseased nodes • LND of SLN+ participants and follow-up of SLN participants to identify a subsequent nodal recurrence in a *previously investigated* nodal basin	<u>For diagnostic studies</u> • Exclude if any disease positive participants have diagnosis unconfirmed by histology • Exclude if > 50% of disease negative participants have diagnosis confirmed by expert opinion with no histology or follow-up • Exclude studies of referral accuracy, i.e. comparing referral decision with expert diagnosis, unless evaluations of teledermatology or mobile phone applications
BCC: basal cell carcinoma; cSCC: cutaneous squamous cell carcinoma; CT: computed tomography; FNAC: fine needle aspiration cytology; LND: lymph node dissection; MRI: magnetic resonance imaging; PET: positron emission tomography; PET-CT: positron emission tomography computed tomography; RCT: randomised controlled trial; SCC: squamous cell carcinoma; SLN+: positive sentinel lymph node; SLn: negative sentinel lymph node; SLNB: sentinel lymph node biopsy.		

7 Quality assessment (based on QUADAS-2)

The QUADAS-2 checklist (Whiting 2011) was tailored to the review topic as follows below.

Participant selection domain (1)

Selective recruitment of study participants can be a key influence on test accuracy. In general terms, all participants eligible to undergo a test should be included in a study, allowing for the intended use of that test within the context of the study. We considered studies that separately sampled malignant and benign lesions to have used a case-control design; and those that supplemented a series of suspicious lesions with additional malignant or benign lesions to be at unclear risk of bias

In terms of exclusions, we considered studies that excluded particular lesion types (e.g. lentigo maligna), particular lesion sites, or that excluded lesions on the basis of image quality or lack of observer agreement (e.g. on histopathology) to be at high risk of bias.

In judging the applicability of patient populations to the review question, we considered restriction to particular lesion populations, such as melanocytic, nodular, high risk or restrictions by size or to lesions that had been excised to be of high concern for applicability. For teledermatology, lesions selected from referred populations rather than selected by GPs in a primary care setting were also judged to be high concern for applicability.

Given that diagnosis of skin cancer is primarily lesion-based, there is the potential for study participants with multiple lesions to contribute disproportionately to estimates of test accuracy, especially if they are at particular risk of having skin cancer. We considered studies that include a high number of lesions in relation to the number of participants in the study to be less representative than studies conducted in a more general population of participants (i.e., if the difference between the number of included lesions and number of included participants is greater than 5%).

Index test domain (2)

Given the potential for subjective differences in test interpretation for melanoma, the interpretation of the index test blinded to the result of the reference standard is a key means of reducing bias. For prospective studies and retrospective studies that used the original index test interpretation, the diagnosis will by nature be interpreted and recorded before the result of the reference standard is known; however, studies using previously acquired images could be particularly susceptible to information bias. For these studies to be at low risk of bias, we required a clear indication that observers were unaware of the reference standard diagnosis at time of test interpretation. An item was also added to assess the presence of blinding between interpretations of different algorithms, however this item was not included in the overall assessment of risk of bias.

Pre-specification of the index test threshold was considered present if the study clearly reported that the threshold used was not data driven, i.e., was not based on study results. Studies that did not clearly describe the threshold used but that required clinicians to record a diagnosis or management decision for a lesion were considered to be unclear on this criterion. Studies reporting accuracy for multiple numeric thresholds, where ROC analysis was used to select the threshold, or that reported accuracy for the presence of independently significant lesion characteristics with no separate test set of lesions were considered at high risk of bias.

In terms of applicability of the index test to the review question, we required images for teledermatology assessment to be acquired in primary by GPs or other primary care staff rather than by expert dermatologists or medical photographers in a specialist setting. We also required diagnosis to be made by a single observer as opposed to a consensus decision or average across multiple observers.

Despite the often subjective nature of test interpretation, it is also important for study authors to outline the particular lesion characteristics that were considered to be indicative for melanoma, for BCC or for cSCC, particularly where established algorithms or checklists were not used. Studies were considered of low concern if the threshold used was established in a prior study or sufficient threshold details were presented to allow replication.

Reference standard domain (3)

In an ideal study, consecutively recruited participants should all undergo incisional or excisional biopsy of the skin lesion regardless of level of clinical suspicion of melanoma. In reality, both partial and differential verification bias are likely. Partial verification bias may occur where histology is the only reference standard used, and only those participants with a certain degree of suspicion of malignancy based on the result of the index test undergo verification, the others either being excluded from the study or defined as being disease-negative without further assessment or follow-up, as discussed above.

Differential verification bias will be present where other reference standards are used in addition to histological verification of suspicious lesions. A typical example of verification bias in skin cancer occurs when investigators do not biopsy people with benign-appearing lesions but instead follow them up for a period of time to determine whether any malignancy subsequently develops (these would be false-negatives on the index test). We defined an 'adequate' reference standard as: all disease-positive individuals having a histological reference standard either at the time of application of the index test or after a period of clinical follow-up; and at least 80% of disease-negative participants have received a histological diagnosis, with up to 20% undergoing at least three months' follow-up of benign-appearing lesions.

A further challenge is the potential for incorporation bias, i.e., where the result of the index test is used to help determine the reference standard diagnosis. It is normal practice for the clinical diagnosis (usually by visual inspection or dermoscopy) to be included on pathology request forms and for the histopathologist to use this diagnosis to help with the pathology interpretation. Although inclusion of such clinical information on the histopathology request form is theoretically a form of incorporation bias, blinded interpretation of the histopathology reference standard is not normal practice, and enforcement of such conditions would significantly limit the generalisability of the study results. For studies comparing teledermatology against a histological reference standard, this item was therefore scored but did not contribute to the overall risk of bias. For studies comparing teledermatology against a face-to-face expert diagnosis, however this item was scored and did contribute to overall risk of bias.

In judging the applicability of the reference standard to our review question, scored studies as high concern around applicability if they used expert diagnosis (with no follow-up) as a reference standard in any patient, or did not report histology interpretation by a dermatopathologist.

Flow and timing domain (4)

In the ideal study, the acquisition of images for the teledermatology diagnosis and the reference standard diagnosis should be made consecutively or as near to each other in time as possible to avoid changes in lesion over time. We have defined a one-month period as an appropriate interval between application of the index test and the reference standard (either histological or face-to-face). For studies using clinical follow-up, a minimum three-month follow-up period has been defined

as at low risk of bias for detecting false-negatives. This interval was chosen based on a study showing that most false-negative melanomas will be diagnosed within three months of the initial negative index test although a small number will be diagnosed up to 12 months subsequently (Altamura 2008).

In assessing whether all patients were included in the analysis, we considered studies at high risk of bias if participants were excluded following recruitment.

Item	Response (delete as required)
PARTICIPANT SELECTION (1) - RISK OF BIAS	
1) Was a consecutive or random sample of participants or images enrolled?	**Yes** - if paper states consecutive or random **No** – if paper describes other method of sampling **Unclear** – if participant sampling not described
2) Was a case-control design avoided? [Note: A diagnostic case-control study separately recruits participants according to selected final diagnoses, e.g. those with melanoma, with BCC, with severe dysplasia and with mild dysplasia AND will usually deliberately sample certain numbers from each group such that the overall case mix of included participants and disease prevalence is not reflective of usual care.]	**Yes** - if case-control design clearly not used **No** – if study described as case-control or describes sampling specific numbers of participants with particular diagnoses **Unclear** – if not clearly described or you have any concerns that the authors have not selected a series of participants
3) Did the study avoid inappropriate exclusions, e.g. • 'difficult to diagnose' lesions not excluded • lesions not excluded on basis of disagreement between evaluators or histopathologists	**Yes** - if inappropriate exclusions were avoided **No** – if lesions were excluded that might affect test accuracy, e.g. 'difficult to diagnose' lesions, OR where disagreement between evaluators was observed **Unclear** – if not clearly reported but there is suspicion that difficult to diagnose lesions may have been excluded
Could the selection of participants have introduced bias? *If answers to all of questions 1) AND 2) AND 3) 'Yes' :* *If answers to any one of questions 1) OR 2) OR 3) 'No' :* *If answers to any one of questions 1) OR 2) OR 3) 'Unclear':*	*Risk is Low* *Risk is High* *Risk Unclear*
PARTICIPANT SELECTION (1) - CONCERNS REGARDING APPLICABILITY	
1) Are the included patients and chosen study setting appropriate to answer the review question, i.e. are the study results generalisable? This item is not asking whether exclusion of certain patient groups might bias the study's results (as in Risk of Bias above), but is asking whether the chosen study participants and setting are appropriate to answer our review question. Because we are looking to establish test accuracy in both primary presentation and referred participants, a study could be appropriate for one setting and not for the other, or it could be unclear as to whether the study can appropriately answer either question.	**Yes** – if patients included in the study appear to be generally representative of those who might present in a usual practice setting **No** if study participants were restricted to those in lesion subgroups, e.g. melanocytic only, or small lesions only, if only excised lesions were included, or lesions were selected from referred populations rather than selected by GPs in a primary care setting **Unclear –** if insufficient details are provided to determine the generalisability of study participants
2) Did the study **avoid including** participants with multiple lesions?	*Yes* – if the difference between the number of included lesions and number of included participants is less than 5% **No** – if the difference between the number of included lesions and number of included participants is greater than 5% **Unclear –** if it is not possible to assess

Item	Response (delete as required)
PARTICIPANT SELECTION (1) - RISK OF BIAS	
Is there concern that the included participants do not match the review question? *If the answer to question 1) and 2) 'Yes':* *If the answer to question 1) or 2) 'No':* *If the answer to question 1) or 2) 'Unclear':*	 ***Concern is Low*** ***Concern is High*** ***Concern is Unclear***
INDEX TEST (2) - RISK OF BIAS (to be completed per test evaluated)	
1) Was the index test or testing strategy result interpreted without knowledge of the results of the reference standard?	**Yes** - if index test described as interpreted without knowledge of the reference standard result or, for prospective studies, if index test is always conducted and interpreted prior to the reference standard **No** – if index test described as interpreted in knowledge of reference standard result **Unclear** – if index test blinding is not described
2) Was the diagnostic threshold at which the test was considered positive (i.e. melanoma, BCC or cSCC present) pre-specified?	**Yes -** if threshold was pre-specified (i.e. prior to analysing study results), ie results were not data driven **No -** if threshold was not pre-specified but was selected after analysis of results usually to maximise sensitivity and/or specificity, or multiple thresholds were tested **Unclear -** if not possible to tell whether or not diagnostic threshold was pre-specified
Could the conduct or interpretation of the index test have introduced bias? v FOR NC and BPC STUDIES *If answers to questions 1) and 2) 'Yes'* *If answers to either questions 1) or 2) 'No'* *If answers to either questions 1) or 2) 'Unclear'* v FOR WPC STUDIES *If answers to all questions 'Yes':* *If answers to any one question 'No' :* *If answers to any one of questions is 'Unclear':*	 ***Risk is Low*** ***Risk is High*** ***Risk is Unclear*** ***Risk is Low*** ***Risk is High*** ***Risk is Unclear***
INDEX TEST (2) - CONCERN ABOUT APPLICABILITY	
1) Was the test applied and interpreted in a clinically applicable manner?	**Yes** – in-person evaluation and single observer result present **No** - either image based and/or average or consensus result presented **Unclear** – if can't tell

Item	Response (delete as required)
PARTICIPANT SELECTION (1) - RISK OF BIAS	
2) Were thresholds or criteria for diagnosis reported in sufficient detail to allow replication? Study results can only be reproduced if the diagnostic threshold is described in sufficient detail. This item applies equally to studies using pattern recognition and those using checklists or algorithms to aid test interpretation	**Yes** – If the criteria for diagnosis of the target disorder were reported in sufficient detail to allow replication. If the study does not describe the threshold in detail BUT evaluates an established test/algorithm AND provides a citation to a previous study of the test in the Methods or Results, then respond Yes. **No** – if the criteria for diagnosis of the target disorder were not reported in sufficient detail to allow replication **Unclear** – If some but not sufficient information on criteria for diagnosis to allow replication were provided. If the study does not describe the threshold in detail BUT evaluates an established test/algorithm but with NO citation to a previous study of the test in the methods, then respond Unclear.
3) Was the test interpretation carried out by an experienced examiner?	**Yes** – if the test was interpreted by one or more speciality accredited dermatologists, or by examiners of any clinical background with special interest in dermatology and with any formal training in the use of the test **No** – if the test was not interpreted by an experienced examiner (see above) **Unclear** – if the experience of the examiner(s) was not reported in sufficient detail to judge OR if examiners described as 'Expert' with no further detail given **N/A** – if system-based diagnosis, i.e. no observer interpretation
Is there concern that the index test, its conduct, or interpretation differ from the review question? *If answers to questions 1),2) AND 3) 'Yes'* *If answers to questions 1),2) OR 3) 'No'* *If answers to questions 1),2) OR 3) 'Unclear'*	*Concern is Low* *Concern is High* *Concern is Unclear*
REFERENCE STANDARD (3) - RISK OF BIAS	

Item	Response (delete as required)
PARTICIPANT SELECTION (1) - RISK OF BIAS	
1) Is the reference standard likely to correctly classify the target condition? a) DISEASE POSITIVE - One or more of: -Histological confirmation of the target disorder following biopsy or lesion excision -Clinical follow up of benign appearing lesions following the application of the index test, leading to a histological diagnosis of the target disorder of interest: • at least 3 months for melanoma or cSCC • at least 6 months for BCC b) DISEASE NEGATIVE - One or more of: -Histological confirmation of absence of the target disorder following biopsy or lesion excision in at least 80% of disease negative participants -Clinical follow up of benign appearing lesions following the index test in up to 20% of disease negative participants of • at least 3 months for melanoma or cSCC • at least 6 months for BCC	**Yes** – if all disease positive participants underwent one of the listed reference standards **No** – If a final diagnosis for any disease positive participant was reached without histopathology **Unclear** – if the method of final diagnosis was not reported for any disease positive participant OR if the length of clinical follow-up used was not clear OR if a clinical follow-up reference standard was reported in combination with a participant-based analysis and it was not possible to determine whether the detection of a malignant lesion during follow-up is the same lesion that originally tested negative on the index test **Yes** – If at least 80% of benign diagnoses were reached by histology and up to 20% were reached by clinical follow up of for a minimum of 3 (or 6) months following the index test **No** – if more than 20% of benign diagnoses were reached by clinical follow up of a minimum of 3 (or 6) months following the index test OR if clinical follow-up period was less than 3 (or 6) months **Unclear** – if the method of final diagnosis was not reported for any participant with benign or disease negative diagnosis
2) Were the reference standard results interpreted without knowledge of the results of the index test? *Please score this item for all studies. Response to the item will not be incorporated into the overall risk of bias assessment for comparisons against a histological reference standard as histopathology interpretation is usually conducted with knowledge of the clinical diagnosis (from visual inspection and/or dermoscopy). Response to the item will be incorporated into the overall risk of bias assessment for comparisons against a face-to-face reference standard*	**For studies comparing teledermatology against a histological reference standard** **Yes** – if the histological reference standard diagnosis was reached blinded to the index test result **No** – if the histological reference standard diagnosis was reached with knowledge of the index test result **Unclear** – if blinded reference test interpretation was not clearly reported If the histopathologist is described as 'blinded' with no further detail as to whether the blinding applies to both index test or to clinical information (prior testing), we will assume that blinding is to the index test result only, unless further detail is provided **For studies comparing teledermatology against a face-to-face expert diagnosis** **Yes -** if the face-to-face reference standard diagnosis was described as interpreted without knowledge of the teledermatology diagnosis (e.g. the remote and face to face diagnosis was made by two different dermatologists) **No -** if the face-to-face reference standard diagnosis was made with knowledge of the teledermatology diagnosis or was made by the same dermatologist within a month of the remote image-based diagnosis **Unclear** – if it is not possible to tell whether knowledge of the teledermatology diagnosis could have influenced the reference standard diagnosis

Item	Response (delete as required)
PARTICIPANT SELECTION (1) - RISK OF BIAS	
Could the reference standard, its conduct, or its interpretation have introduced bias? For *comparisons against a histological reference standard*: *If answer to question 1) 'Yes'* *If answer to question 1) 'No':* *If answer to question 1) 'Unclear':* For *comparisons against a face-to-face reference standard*: *If answers to questions 1) AND 2 'Yes'* *If answers to questions 1) OR 2) 'No':* *If answers to questions 1) OR 2) 'Unclear':*	***Risk is Low*** ***Risk is High*** ***Risk is Unclear*** ***Risk is Low*** ***Risk is High*** ***Risk is Unclear***
REFERENCE STANDARD (3) - CONCERN ABOUT APPLICABILITY	
1) For studies comparing teledermatology/face-to-face clinical diagnosis to histology, was histology interpretation carried out by an experienced histopathologist or by a dermatopathologist?	**Yes –** if histology interpretation was reported to be carried out by an experienced histopathologist or dermatopathologist **No –** if histology interpretation was reported to be carried out by a less experienced histopathologist **Unclear** – if the experience/qualifications of the pathologist were not reported
2) For studies comparing teledermatology to face-to-face diagnosis, was the clinical diagnosis carried out by an experienced observer?	**Yes –** if face-to-face interpretation was reported to be carried out by an experienced dermatologist **No –** if face-to-face interpretation was reported to be carried out by a less experienced dermatologist **Unclear** – if the experience/qualifications of the face-to-face clinician were not reported
Is there concern that the target condition as defined by the reference standard does not match the review question? If answer to either questions 1) or 2), 'Yes': If answer to either questions 1) OR 2), 'No': If answer to either questions 1) OR 2), 'Unclear':	***Concern is Low*** ***Concern is High*** ***Concern is Unclear***
FLOW AND TIMING (4): RISK OF BIAS	
1) Was there an appropriate interval between index test and reference standard? *a)* For histopathological reference standard, was the interval between index test and reference standard <= 1month? *b)* If the reference standard includes clinical follow-up of borderline/benign appearing lesions, was there a minimum follow-up following application of index test(s) of at least: • 3 months for melanoma or cSCC • 6 months for BCC?	**Yes** – if study reports <=1 month between index and reference standard **No** – if study reports >1 month between index and reference standard **Unclear** – if study does not report interval between index and reference standard **Yes** – if study reports >=3 (or 6) months follow-up **No** – if study reports <3 (or 6) months follow-up **Unclear** – if study does not report length of clinical follow-up

Item	Response (delete as required)
PARTICIPANT SELECTION (1) - RISK OF BIAS	
2) Did all participants receive the same reference standard?	**Yes** – if all participants underwent the same reference standard **No** – if more than one reference standard was used **Unclear** – if not clearly reported
3) Were all participants included in the analysis?	**Yes** – if all participants were included in the analysis **No** – if some participants were excluded from the analysis **Unclear**– if not clearly reported
Could the participant flow have introduced bias? v **FOR NON COMPARATIVE and BPC STUDIES** *-If answers to questions 1)AND 2) AND 3) : 'Yes':* *-If answers to any one of questions 1) OR 2)OR 3) 'No' : If answers to any one of questions 1) OR 2)OR 3) 'Unclear' :*	*Risk is Low* *Risk is High* *Risk is Unclear*
Comparative domain: For (BPC) and/or within-person comparisons (WPC) of index tests or testing strategies (i.e. >1 index test applied per participant):	
Index tests	
1) was each index test result interpreted without knowledge of the results of other index tests or testing strategies?	**Yes -** if all index tests were described as interpreted without knowledge of the results of the others **No -** if the index tests were described as interpreted in the knowledge of the results of the others **Unclear** – if it is not possible to tell whether knowledge of other index tests could have influenced test interpretation **N/A** – if only one index test was evaluated **Not applicable**
2) Was the interval between application of index tests <= 1 month?	**Yes** – if study reports <=1 month between index tests **No** – if study reports >1 month between index tests **Unclear** – if study does not report interval between index tests
Clinical applicability of comparison 1) Were both tests applied and interpreted in a clinically applicable manner?	

8 Summary study details

Author & year Outcome	Study type Country Setting Patients (lesions)	Inclusion criteria	Store and forward teledermatology Image acquisition Image interpretation Diagnostic decision	Face to face diagnosis Method of diagnosis Diagnostic decision	Reference standard Final diagnoses Prevalence (Malignant)	Exclud particip final ar

Of 70 eligible patients only 20 were excised no information reported on the 50 patients who had expert diagnosis	Borve 2015 Any	BPC P-CS Primary and Secondary Sweden 772 (816)	Patients with one or more skin lesions of concern requiring referral to a dermatologist. (Accuracy was compared to a control group of an equal number of consecutive patients referred from other PHCs via the traditional paper-based referral system during the same period; data included in this review) Primary healthcare centres (PHCs) that regularly referred patients with skin lesions of concern were invited to participate.	Clinical and dermoscopic images acquired in primary care by GPs using smartphone digital camera and portable dermoscope using an iPhone 4 with a FotoFinder Handyscope app Remote dermatologists (n=4) reviewed images along with clinical information on an online platform and selected from standardised triage responses Decision recorded: • benign, malignant or unclear • malignancy as possible diagnosis • priority given (high, <2 weeks; medium, <4 weeks or low, 8–12 weeks), management (none, medical therapy, destructive therapy or surgery) • dermoscopic description.	Not evaluated	Histolo Expert Malign MM 19 cSCC Benign Dyspla 236 SK Other b *Actini 61 *cSCC 0.281

Histology plus Expert diagnosis MM 47; Mel Mets 1*; 40 BCC; 9 cSCC (incl in *situ*) Benign 32 0.403	One patient was excluded from further analysis because he attended the VLC after the referred lesion had been excised *one MM Mets incl as D+; cannot disaggregate *in situ* SCC; data excluded from our 'Any' skin cancer analysis	Coras 2003 MM	WPC-tests P-CS Secondary and Private Germany NR (46)	Pigmented skin lesions undergoing excision due to diagnosis of melanoma or atypical nevus, to rule out melanoma or at the patient's request	Clinical and dermoscopic images acquired at private clinic using digital camera coupled with dermoscope. A dermatologist (n=1) evaluated the images and made a diagnosis based on the images and history of the patient Decision recorded: • lesion diagnosis	Particip dermat (n=3) v experie dermat establi clinical based analysi person consult the pat private clinics.

Each GP (n=13) was asked to formulate a written first judgment of every lesion before digital acquisition using visual inspection alone and then following dermoscopy. The evaluation method followed the ABCD rule of dermoscopy according to Nachbar et al" Decision recorded: • benign vs suspicious for malignancy	Histology plus follow up (FU) (208 diagnosed as benign after 6 months FU) MM 5 Benign 230 0.021	not reported	Jolliffe 2001a ANY BCC	WPC-tests P-CS Specialist unit UK 138 (144)	Patients referred by their GP for dermatological assessment of a pigmented lesion at the Pigmented Lesion Clinic	Images PLC us chip vi The im archive proprie and im transm a Fast Machir overlay viewed clinical on a 15 monito qualific experti Decisic Clinica

Clinical and dermoscopic images acquired in primary care using a digital camera coupled with a dermoscope. Images were reviewed blinded to other information by dermatologist (n=2) within 48hrs (“No personal patients’ data were transmitted; patients were identified only by a progressive number”. Decision recorded: • correct diagnosis of malignancy • TD decisions for full sample included • Image quality • Lesion group: benign melanocytic or nonmelanocytic; malignant melanocytic or non-melanocytic • diagnosis • management decision - (i) no further treatment or follow-up in 3, 6 or 12 months interval (ii) referral to a local dermatologist for FTF examination (iii) excision in case of suspected malignancy. Not evaluated	Histology plus Expert clinical diagnosis Malignant: MM 2; BCC: 5 Dysplastic 11, SK 4, *AK 1, Other: 3 0.25	82/121 pts were lost to FU) i.e no histo diagnosis, including 4 considered to have melanoma and 8 with BCC *authors consider AK as D+; can be disaggregated and considered D-	Moreno Ramirez 2005 MM+MIS BCC ANY	NC R-CS Specialist unit Spain 57 patients included in the final analysis (NR)	Patients with pigmented, circumscribed lesions fulfilling at least one of the following criteria: a changing lesion (‘ABCD changes’), recent lesion (less than three-year history), multiple lesions (more than 20 melanocytic naevi counted by the GP), symptomatic lesion (pain, itching, bleeding), or patient concern about moles.	photog images primary a digita Images at PLC dermat alongsi informa Decisio • Lesi (incl BN, mela naev as s tele atyp lenti etc • Sug mar (‘ref ‘non the clini

Dermoscopic images acquired in secondary care using a dermoscopic digital camera. Images analysed along with information on age, sex and lesion site on a PC monitor by each dermatologist (n=11; 5 rated highly experienced in dermoscopy, 2 medium experience and 4 low level of experience.) Decision recorded: • acral melanoma vs atypical lesions (considered atypical when at least 6 of the 11 observers made this diagnosis.) • categorized according to the 'Saida' classification. • management recommendation (digital dermoscopy follow-up or surgical excision)		Histology Malignant: MM (Acral) 6 Acral melanocytic naevi 71 0.078	None reported	Silveira 2014 ANY	Non-comparative P-CS Community Brazil NR (416)	The pr include with sk that we determ suspici direct v inspect physici Comm Preven (MPU) screen people cervica cancer

Patients with pigmented lesions that were considered atypical in clinical appearance by at least one dermatologist and for which a clear histologic diagnosis had been rendered by a board-certified dermatopathologist(invasive melanoma, melanoma *in situ*, lentigo, benign nevus dermatofibroma, seborrheic keratosis, and hemangioma). Excluded equivocal diagnoses and specific lesion types.	photographic images acquired in routine secondary care prior to skin lesion removal). Four applications for smartphone devices were evaluated including one store and forward application (app 4) which can be run on a smartphone or from a website. Images sent to a board-certified dermatologist (n=NR) for evaluation within 24 hours. Decision recorded: • "atypical" (test positive) or "typical" (test negative) • Other options included "send another photograph" or "unable to categorize"		Histology Melanoma 44 Mel in-situ 16 Benign diagnosis 34 SK 20 lentigo 8 Hemangiona 2 Dermatofibroma 4 0.34	29 not evaluable excluded from analysis "send another photograph" or "unable to categorize," considered these images to be unevaluable in our analysis. (390 images for possible inclusion in this study. We excluded 202 as being of poor image quality, containing identifiable patient information or features, or lacking sufficient clinical or histological information.)	**Studies of referral accuracy (T**

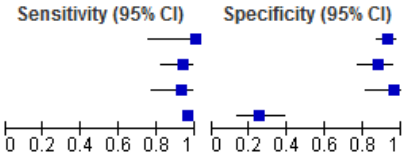
WPC-tests P-CS Primary and secondary UK 163 (163)	GPs recruited consecutive unselected patients with suspicious skin lesions whom they refer to the dermatology department in their normal practice	photographic images acquired in primary care by the GP using a digital camera (Nikon Coolpix 950 digital camera (1200 x 1600 pixel resolution). Images reviewed by one of two consultant dermatologists along with clinical information. Decision recorded: 1. diagnosis or differential diagnosis (2x2 cannot be extracted) 2. hypothetical management plan (reassurance; minor operation, no action but further review appointment required); 2x2 extracted for 2 thresholds • book for minor operation (immediate Action) vs not • book for minor operation or book further review appointment (immediate Action or FU) vs	Not evaluated as an index test	Expert clinical diagnosis (unclear but appears to be by the same TD consultants within 2 weeks) Consultant diagnoses (not histo confirmed) MM 4, BCC: 37, cSCC 4; AK 10, BD 7, SC 4; LM 1; Atypical 6; SK 27; BN 20; DF 11; Other: 36 Malignant: 27.6% Action required (FTF): 65.1%	57 (35%) excluded as no TD decision could be made; 24 (15%) poor quality images; 33 (20%) needed to be seen FTF.	Manah Action face or

Phillips 1998 Dx SC Malignant/probably malignant Excise	NC P-CS Community US 51 / 107	Participants attending four skin cancer screenings at community hospitals in rural eastern North Carolina. Patients were given a choice of having a total body examination, only the sun-exposed skin, or a specific lesion(s) evaluated by the on-site physician.	Live link teledermatology using: a full-body camera, a lens for viewing the lesions close up, and a magnifying lens that allowed even closer views as well as examination with polarized light. It is not clear who operated the cameras during the teleconsultations. If a complete patient skin examination was performed in-person, representative lesions were selected by the on-site physician for evaluation by the remote physician. Decision recorded: • Most likely diagnosis for a given lesion; • the degree of concern that a specific lesion was malignant; and • recommendation as to whether to do a biopsy of the lesion.	Not evaluated as an index test	All patients were first evaluated by the on-site physician who recorded specific lesions on an image of the human body and diagnosis/management decisions as per remote observer. Target condition (FtF diagnoses) Malignant: BCC 2; SCC 3; lentigo maligna 1 Benign: SK 27; BN 32; AK 14; lentigo 10; Other 30	None r

Graphs

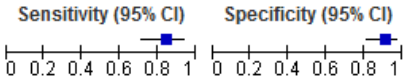
Teledermatology - photographic image vs Histology (Any)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Jolliffe 2001a	13	9	0	118	1.00 [0.75, 1.00]	0.93 [0.87, 0.97]
Kroemer 2011	43	7	3	51	0.93 [0.82, 0.99]	0.88 [0.77, 0.95]
Moreno Ramirez 2005	27	1	2	27	0.93 [0.77, 0.99]	0.96 [0.82, 1.00]
Silveira 2014	350	39	14	13	0.96 [0.94, 0.98]	0.25 [0.14, 0.39]



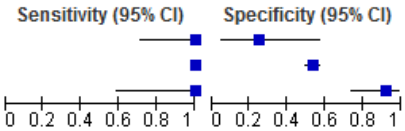
Teledermatology - dermoscopic image vs Histology (Any)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Kroemer 2011	39	5	7	53	0.85 [0.71, 0.94]	0.91 [0.81, 0.97]



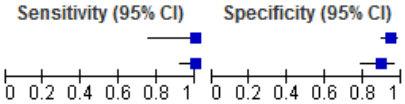
Teledermatology - photographic+dermoscopic image vs Histology (Any)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Arzberger 2016	11	9	0	3	1.00 [0.72, 1.00]	0.25 [0.05, 0.57]
Borve 2015	168	302	0	346	1.00 [0.98, 1.00]	0.53 [0.49, 0.57]
Massone 2014	7	2	0	23	1.00 [0.59, 1.00]	0.92 [0.74, 0.99]



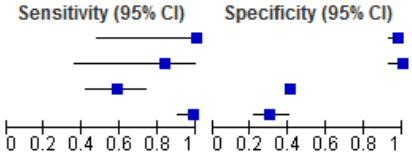
Expert Face to face (VI+Dermoscopy) vs Histology (Any)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Jolliffe 2001a	13	7	0	124	1.00 [0.75, 1.00]	0.95 [0.89, 0.98]
Kroemer 2011	46	6	0	52	1.00 [0.92, 1.00]	0.90 [0.79, 0.96]



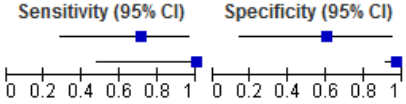
Teledermatology - photographic image vs Histology (MM+MiS)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Kroemer 2011	5	2	0	97	1.00 [0.48, 1.00]	0.98 [0.93, 1.00]
Moreno Ramirez 2005	5	0	1	51	0.83 [0.36, 1.00]	1.00 [0.93, 1.00]
Warshaw 2010	24	869	17	604	0.59 [0.42, 0.74]	0.41 [0.38, 0.44]
Wolf 2013	53	73	1	32	0.98 [0.90, 1.00]	0.30 [0.22, 0.40]



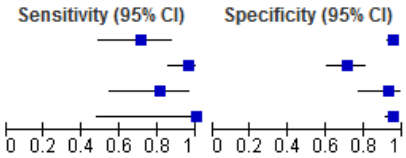
Teledermatology - dermoscopic image vs Histology (MM+MiS)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Ferrara 2004	5	2	2	3	0.71 [0.29, 0.96]	0.60 [0.15, 0.95]
Kroemer 2011	5	3	0	96	1.00 [0.48, 1.00]	0.97 [0.91, 0.99]



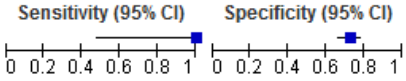
Teledermatology photographic+dermoscopic image vs Histology (MM+MiS)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Bowns 2006	17	11	7	221	0.71 [0.49, 0.87]	0.95 [0.92, 0.98]
Congalton 2015	46	23	2	57	0.96 [0.86, 0.99]	0.71 [0.60, 0.81]
Coras 2003	13	2	3	27	0.81 [0.54, 0.96]	0.93 [0.77, 0.99]
Grimaldi 2009	5	11	0	219	1.00 [0.48, 1.00]	0.95 [0.92, 0.98]



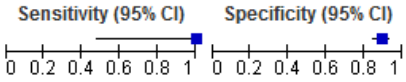
GP Face to face (Visual inspection only) vs Histology (MM+MiS)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Grimaldi 2009	5	63	0	167	1.00 [0.48, 1.00]	0.73 [0.66, 0.78]



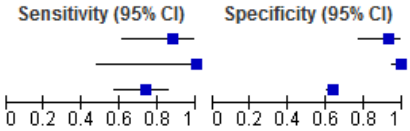
GP Face to face (VI+Dermoscopy) vs Histology (MM+MiS)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Grimaldi 2009	5	24	0	206	1.00 [0.48, 1.00]	0.90 [0.85, 0.93]



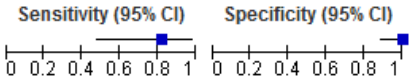
Expert face to face (VI+Dermoscopy) (MM+MiS)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Coras 2003	14	2	2	27	0.88 [0.62, 0.98]	0.93 [0.77, 0.99]
Kroemer 2011	5	1	0	98	1.00 [0.48, 1.00]	0.99 [0.95, 1.00]
Warshaw 2010	30	543	11	930	0.73 [0.57, 0.86]	0.63 [0.61, 0.66]



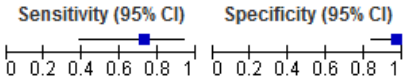
Teledermatology - photographic+dermoscopic image vs Histology (MM)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Piccolo 2000	9	0	2	32	0.82 [0.48, 0.98]	1.00 [0.89, 1.00]



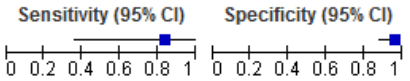
Expert face to face (VI+Dermoscopy) vs Histology (MM)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Piccolo 2000	8	1	3	31	0.73 [0.39, 0.94]	0.97 [0.84, 1.00]



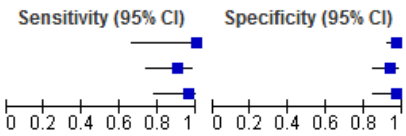
Teledermatology - dermoscopic image vs Histology (Acral MM)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Piccolo 2004	5	3	1	68	0.83 [0.36, 1.00]	0.96 [0.88, 0.99]



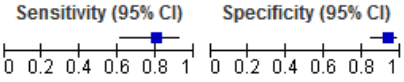
Teledermatology - photographic image vs Histology (BCC)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Jolliffe 2001a	9	4	0	127	1.00 [0.66, 1.00]	0.97 [0.92, 0.99]
Kroemer 2011	27	5	3	69	0.90 [0.73, 0.98]	0.93 [0.85, 0.98]
Moreno Ramirez 2005	22	1	1	33	0.96 [0.78, 1.00]	0.97 [0.85, 1.00]



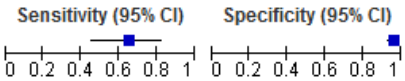
Teledermatology - dermoscopic image vs Histology (BCC)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Kroemer 2011	24	5	6	69	0.80 [0.61, 0.92]	0.93 [0.85, 0.98]



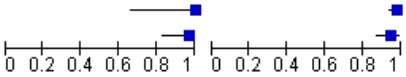
Teledermatology - photographic+dermoscopic image vs Histology (BCC)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Bowns 2006	19	9	10	218	0.66 [0.46, 0.82]	0.96 [0.93, 0.98]



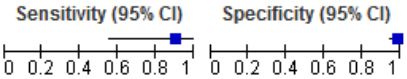
Expert face to face (VI+Dermoscopy) vs Histology (BCC)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Jolliffe 2001a	9	3	0	132	1.00 [0.66, 1.00]	0.98 [0.94, 1.00]
Kroemer 2011	29	4	1	70	0.97 [0.83, 1.00]	0.95 [0.87, 0.99]



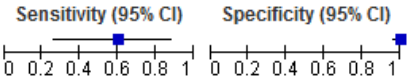
Teledermatology - photographic image vs Histology (cSCC)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Kroemer 2011	9	1	1	93	0.90 [0.55, 1.00]	0.99 [0.94, 1.00]



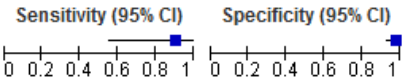
Teledermatology - dermoscopic image vs Histology (cSCC)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Kroemer 2011	6	0	4	94	0.60 [0.26, 0.88]	1.00 [0.96, 1.00]



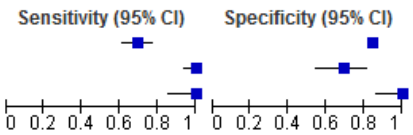
Expert face to face (VI+Dermoscopy) vs Histology (cSCC)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Kroemer 2011	9	2	1	92	0.90 [0.55, 1.00]	0.98 [0.93, 1.00]



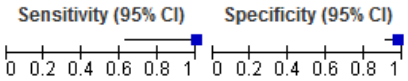
Teledermatology - photographic image vs face to face clinical diagnosis (Immediate action)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Jolliffe 2001b	99	100	44	553	0.69 [0.61, 0.77]	0.85 [0.82, 0.87]
Mahendran 2005	54	16	0	36	1.00 [0.93, 1.00]	0.69 [0.55, 0.81]
Shapiro 2004	24	0	0	25	1.00 [0.86, 1.00]	1.00 [0.86, 1.00]



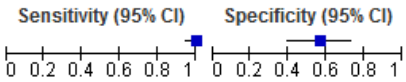
Teledermatology - photographic image vs face to face clinical diagnosis (Dx of malignancy)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Oliveira 2002	8	2	0	80	1.00 [0.63, 1.00]	0.98 [0.91, 1.00]



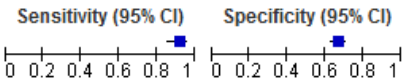
Teledermatology - photographic image vs face to face clinical diagnosis (Immediate action or FU)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Mahendran 2005	69	16	0	21	1.00 [0.95, 1.00]	0.57 [0.39, 0.73]



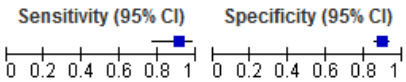
Teledermatology - photographic image vs face to face clinical diagnosis (Immediate action; Registrar data)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Jolliffe 2001b	131	217	12	436	0.92 [0.86, 0.96]	0.67 [0.63, 0.70]



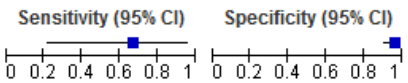
Teledermatology - photographic/dermoscopic image vs face to face clinical diagnosis (Immediate action)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Manahan 2015	32	28	3	238	0.91 [0.77, 0.98]	0.89 [0.85, 0.93]



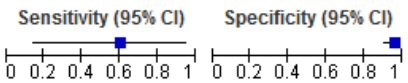
Teledermatology - live link vs face to face clinical diagnosis (diagnosis of any skin cancer)

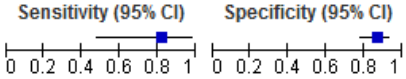
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Phillips 1998	4	4	2	97	0.67 [0.22, 0.96]	0.96 [0.90, 0.99]



Teledermatology - live link vs face to face clinical diagnosis (definitely/probably malignant)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Phillips 1998	3	4	2	98	0.60 [0.15, 0.95]	0.96 [0.90, 0.99]



Teledermatology - live link vs face to face clinical diagnosis (biopsy decision)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Phillips 1998	9	13	2	83	0.82 [0.48, 0.98]	0.86 [0.78, 0.93]