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Scottish Referral Guidelines for Suspected Cancer Update – Evidence Review (Skin)

The purpose of this document is to synthesise and critique evidence and insight related to referral guidelines for suspected skin cancer. Key themes have been determined from the literature. For each key theme e.g. individual symptoms, the papers are summarised separately with some high-level synthesis to provide steer on how this may impact referral guidelines. At the end of the document, a table comparing NICE NG12 and SRG guidelines can be found for reference.

This document includes evidence on the following topics:

- Individual symptoms.
- Primary care investigations relevant to skin cancer.
- Safety netting those with signs and symptoms of skin cancer.
- Risk stratification.
- Other topics where the evidence base is emerging.

Background

The main types of skin cancer are cutaneous squamous cell carcinoma (cSCC), basal cell carcinoma (BCC), and melanoma; there are also a number of much rarer skin cancer types)[i]. BCC is the most common type of skin cancer (around 75% of all skin cancers diagnosed). They develop from basal cells, found in the deepest part of the outer layer of the skin (the epidermis). It is rare for basal cell skin cancer to metastasise. SCC is faster growing than basal cell cancers, but also unlikely to metastasise. Around 23% of skin cancers are SCCs. They begin in cells called keratinocytes, which are found in the epidermis. Melanoma skin cancer is when abnormal cells in the skin start to grow and divide in an uncontrolled way and typically starts in skin cells called melanocytes[i].

In Scotland, incidence is captured differently for the three main types: all registered cases for melanoma and cSCC, first per person per annum for BCC. Many statistics are only available for melanoma skin cancer. BCC survival is generally very high while cSCC survival is comparable to low-risk melanoma.

[i] Types | Skin cancer | Cancer Research UK [Internet]. www.cancerresearchuk.org. Available from: https://www.cancerresearchuk.org/about-cancer/skin-cancer/types

Melanoma skin cancer is the 5th most common cancer in Scotland, accounting for 4% of all new cancer cases (data from 2018, 2019 and 2021). Scotland stage at diagnosis data is not publicly available for melanoma skin cancer. In Wales (2019) among melanoma skin cancer cases with a recorded stage, 66% were diagnosed at stage 1, 21% at stage 2, 10% at stage 3 and 4% at stage 4[ii].

Later stage at diagnosis is associated with more limited treatment options and therefore worse survival. Scotland survival by stage data is not publicly available for melanoma skin cancer. In England (2018), around 100% of those diagnosed at stage 1 survived their disease for 1 year or more, compared to 58% diagnosed at stage 4ii.

Being diagnosed via emergency presentation is associated with later stage at diagnosis. Scotland routes to diagnosis data is not publicly available for melanoma skin cancer. In Northern Ireland (2012-2016), among 1,762 cancer cases with a known route to diagnosis, 2% were diagnosed via emergency presentation[ii].

It is generally believed that melanoma occurs as a result of complex interaction between environmental, genetic and individual host factors. Important risk factors for melanoma include the number of common/atypical nevi, skin phenotype, family history of melanoma, actinic damage, history of sunburns, and excessive exposure to ultraviolet (UV) radiation, particularly in childhood and adolescence. The incidence of cutaneous malignant melanoma, which is mostly attributable (86%) to UV radiation exposure, has been steadily increasing over the past four decades in predominantly fair-skinned populations[iii].

Melanoma skin cancer was the fifth most common cancer site for the White ethnic group but was not in the 20 most common cancers for the Asian, Black or Mixed/Multiple ethnic groups between 2013 – 2017 in England. Age-standardised incidence rates in non-white minority ethnic groups were significantly lower than in the White ethnic group[iv]. Despite a lower incidence, ethnic minority groups are more likely to present with late-stage melanomas that are deeper and have higher incidences of regionally advanced or distant disease[v]. This is thought to be due to skin cancer being harder to diagnose in people with darker skin tones, where it is often misdiagnosed[vi,vii]. High incidence of skin

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[ii] Cancer Research UK. Early Diagnosis [Internet]. crukcancerintelligence.shinyapps.io. 2022. Available from: https://crukcancerintelligence.shinyapps.io/EarlyDiagnosis/
[iii] Memon, A. et al. Changing epidemiology and age-specific incidence of cutaneous malignant melanoma in England: An analysis of the national cancer registration data by age, gender and anatomical site, 1981–2018. The Lancet Regional Health - Europe 2, 100024 (2021).
[iv] Delon, C. et al. Differences in cancer incidence by broad ethnic group in England, 2013-2017. Br J Cancer 126, 1765–1773 (2022).
[v] Shao, K. & Feng, H. Racial and Ethnic Healthcare Disparities in Skin Cancer in the United States: A Review of Existing Inequities, Contributing Factors, and Potential Solutions. *J Clin Aesthet Dermatol* **15**, 16 (2022).
[vi] Avilés-Izquierdo, J. A. *et al.* Who detects melanoma? Impact of detection patterns on characteristics and prognosis of patients with melanoma. *J Am Acad Dermatol* **75**, 967–974 (2016).
[vii] Gupta, A. K., Bharadwaj, M. & Mehrotra, R. Skin Cancer Concerns in People of Color: Risk Factors and Prevention. *Asian Pac J Cancer Prev* **17**, 5257 (2016).

cancer is associated with increased age, in males and increased deprivation, and diagnosed cancers are more likely to be of an advanced stage[viii,ix].

The majority (80%) of melanomas noticed by dermatologists are incidental findings[vi]. Alongside this, UK dermatology services receive more urgent referrals for suspected cancer (USCR) than any other specialty and referral rates have rapidly increased with conversion[x] rates generally decreasing. Since 2009, there was a steady decline in the conversion rate of skin cancer referrals, from 8.3% to 6.5% in 2019/2020 in England[xi]. Earlier diagnosis and prompt recognition and referral, supported by referral guidelines is important to reducing late stage diagnoses.

Search Strategy

Search terms: PubMed search for combinations of the following terms: skin, cancer, PPV, risk, prevalence, symptomatic, presentation, primary care, each symptom (e.g. lesion), investigation (and specifics e.g. dermascope, dermoscopy, teledermatology), recognition, referral, stage, routine, routes to diagnosis, comorbidity.

Date: 2015 – present. In the table summaries, the only papers included from pre-2015 are those that are relevant for explaining differences in Scottish Referral Guidelines (SRG) and NICE NG12 guidelines. These have been gathered from NICE NG12 Evidence Review document.

Peer-reviewed literature

Note: grey rows in the table represent studies that have already been summarised earlier in the document.
Note: throughout the evidence review, the cancer type is described as in the original study. Sub-types are specified if available.

Topic: Individual Symptoms
Summary:

[viii] Memon, A. *et al.* Changing epidemiology and age-specific incidence of cutaneous malignant melanoma in England: An analysis of the national cancer registration data by age, gender and anatomical site, 1981–2018. *The Lancet Regional Health - Europe* **2**, 100024 (2021).
[ix] Venables, Z. C. *et al.* Nationwide Incidence of Metastatic Cutaneous Squamous Cell Carcinoma in England. *JAMA Dermatol* **155**, 298–306 (2019).
[x] Defined as: the proportion of urgent suspected cancer referrals that result in a cancer diagnosis
[xi] CancerData NHS. Cancer Waiting Times (CWT) urgent suspected cancer referrals: referral, conversion and detection rates. https://www.cancerdata.nhs.uk/cwt_conversion_and_detection (2022).

The evidence base supports the inclusion of all the existing suspected skin cancer symptoms currently in the Scottish Referral Guidelines (SRG) for Suspected Cancer. Note - post-2015 there was more evidence on prevalence of symptoms at presentation in the skin cancer population rather than specific positive predictive values of symptoms in a primary care setting. Pre-2015, 3 papers were identified in the NG12 evidence review estimating PPVs for melanoma, SCC and BCC which are described further down in this summary.

- **Abnormal mole/skin lesion** is the most common symptom of skin cancer. In the majority of skin cancer patients, this occurred as the **only symptom**. For this reason, skin cancer is known as a cancer which has a **narrow symptom signature.**
- The overall quality of evidence for evaluation of skin cancer symptoms is high. Most studies used large national primary care cohorts, had rigorous methodology for analysis, and reported limitations comprehensively. Most research is primarily in an England context.
- Evidence post-2015 did not provide estimates of PPVs for skin cancer. Pre-2015, PPV estimates for abnormal lesions range from 0.8-2.3% for melanoma (Emery, 2010, Walter, 2012). Non-pigmented raised skin lesions presenting in a primary care setting were associated with a positive predictive value of 41% for squamous cell carcinoma (Rosendahl, 2012). The PPV of pigmented lesions for BCC were estimated between 0.6-1.8% (Emery, 2010, Walter, 2012), and non-pigmented lesions demonstrated a much higher PPV of 27% (Rosendahl, 2012).

GPs need to be able to distinguish 'normal' changes in skin lesions from 'abnormal' changes that may indicate skin cancer. For this reason, they use diagnostic aids to detect features indicating possible melanoma, such as checklists designed for use by non-dermatologists. The 'ABCDE' rule is an easy-to-remember system for doing this, which encompasses several clinical features of melanoma, including **A**symmetry, **B**order irregularity, **C**olour variation (both intralesional colour variation as well as a colour that is different from the patient's other nevi), **D**iameter greater than 6mm, and **E**volving (a new or changing lesion). Another tool, the weighted 7-point checklist (W7PCL) consists of 7 items (change in shape, size and/or colour, inflammation, crusting/bleeding, sensory change, diameter ≥ 7 mm). symptoms are divided into major (change in shape, size and/or colour) scoring 2 points each and minor (inflammation, crusting/bleeding, sensory change, diameter ≥ 7 mm) scoring 1 point. The W7PCL has been recommended for use by all primary care professionals in the assessment of pigmented skin lesions by NICE since 2005. There are some minor differences between the two checklists which are discussed in more detail below. ABCDE determines a size >6mm to be of concern, whereas the W7PCL recommends >7mm. Additionally, the W7PCL is more specific with symptoms the patient may experience, such as: inflammation, oozing and change in sensation. ABCDE checklist incorporates this in the following sentence: 'Evolutionary changes in colour, size, symmetry, surface characteristics, and symptoms.'

Rationale for some of the differences between the NG12 and SRG could not be ascertained from recent available evidence:

- NG12 recommends using a weighted 7-point checklist (W7PCL) to evaluate skin cancer symptoms while SRG recommends using the ABCDE rule. Referenced in the 2015 NICE NG12 evidence review, Walter et al. found that the weighted 7-point checklist performed well in a primary care setting: sensitivity 73.3%, specificity 57.1%, positive predictive value 24.1%, negative predictive value 92.0%, while maintaining high sensitivity of 91.7% for clinically significant lesions (melanoma) and moderate specificity of 53.4% for melanoma[xii].
- NG12 recommends referral if the patient scores 3 or more using the weighted 7PCL (minimum 2 symptom items), while SRG states 1 or more. The 2015 NICE NG12 evidence review states that for 1 or more symptoms reported the PPV is 2.7%, while a score of 3 or more with the weighted 7PCL has a PPV of 3.4%[xii].
- NG12 mentions a lesion diameter of 7mm or more, versus 6mm or more in SRG. The 2015 NICE NG12 evidence review included lesion-based analysis from Walter et al., which indicated that suspicious pigmented lesions larger than 7 mm in diameter had a PPV of 3.9%, supporting inclusion in the guidelines[xii].
- For altered sensation and oozing, SRG mentions that these symptoms should be "persistent", but this is not specified in NG12 or the NG12 evidence review.
- NG12 does not give specific guidelines about new or changing pigmented nail line or unexplained lesions in a nail, while this is outlined in SRG. These symptoms were not mentioned in the 2015 NICE NG12 evidence review.

Paper number	Study	Summary	Notes
1	Koo MM, Swann R, Mcphail S, Abel GA, Elliss-Brookes L, Rubin GP et al. Presenting symptoms of cancer and stage at diagnosis: evidence from a cross-sectional, population-based study. 2019.	This paper examines associations between common presenting symptoms of cancer and stage at diagnosis. There has been debate around whether symptoms present at an early enough stage for there to be the possibility for meaningful clinical intervention.	• Cross-sectional population-based study, using NCRAS data. • National Cancer Diagnosis Audit (NCDA) and National Cancer Registration and Analysis Service (NCRAS) data (2014), England only.

[xii] Walter, F. M. *et al.* Using the 7-point checklist as a diagnostic aid for pigmented skin lesions in general practice: a diagnostic validation study. *Br J Gen Pract* **63**, (2013).

	doi:10.1016/S1470-2045(19)30595-9.	This study indicated that of the 20 symptoms evaluated, **abnormal mole** presented in 584 cases (n=7997) of which, in 564 cases it was the only symptom. It was consistently associated with a narrow cancer site signature and lower odds (1%) of stage IV disease (melanoma).	• Sample size: 7,997, aged 25 or older. • **Limitation:** recording of symptoms and extraction of information from primary care records might be incomplete or biased. • Did not report positive predictive values (PPV) • Melanoma only, not reference to other skin cancers.
2	Zakkak N, Barclay ME, Swann R, McPhail S, Rubin G, Abel GA et al. The presenting symptom signatures of incident cancer: evidence from the English 2018 National Cancer Diagnosis Audit. *OPEN Epidemiology British Journal of Cancer* 2024; 130: 297–307.	This paper examined (1) the frequency of presenting symptoms by cancer site and (2) the frequency of cancer site by presenting symptom. • Skin cancer (melanoma) was found to be a cancer which was dominated by a frequent **single presenting symptom** (71% with abnormal mole/lesion). • Among skin cancer patients, **abnormal mole/lesion** was the most common symptom (83%, along with 6% non-specific symptom, 1% lump/mass/lymph node, 3% ulceration, 1% respiratory). It has a narrow symptom range so likely to have meaningfully high predictive	• Retrospective national population-based cohort study. • Sample size: 55,122 patients; 2,790 skin (melanoma) cancer patients. • Aged 25 or older. • NCDA 2018 data, England only • **Limitations:** ○ Case-only analysis so cannot make inferences about PPV. Surveys for GPs

		values, although empirical documentation of the symptom signature of melanoma is limited.	regarding presenting symptoms were filled out retrospectively and therefore, could be prone to bias. ○ Melanoma only, not reference to other skin cancers.
3	Avilés-Izquierdo JA, Molina-López I, Rodrígues-Lomba E, Marquez-Road, I, Suarez-Ferandez R, Lazaro-Ochaita P. Who detects melanoma? Impact of detection patterns on characteristics and prognosis of patients with melanoma. *Journal of American Academy of Dermatology* 2016; 75(5): 967-974.	This paper examined (1) the routes to melanoma detection and (2) impact of detection patterns on the characteristics and prognosis of melanoma. This study found that: • Most melanomas are self-detected (53%). • Among these patients, 32% consulted because of **bleeding (unspecified location), itching/pain (unspecified location), or increase in size of lesion**. • There were more melanomas **self-detected among women** than among men. • Self-detected melanomas more likely to have histologic ulceration, developed more metastases, and were responsible for more melanoma-related deaths during follow-up than patients with melanomas that were detected by dermatologists.	• Retrospective observational study. • Sample: 783 patients with cutaneous melanoma who had a histological diagnosis between 1996 and 2012, Madrid, Spain. • **Limitations:** ○ Data from Spain so may not be representative of UK health system.

		• Men had significantly more melanomas on non–easily visible locations than women did. • Among melanomas noticed by dermatologists, 80% were **incidental findings**.	

Topic: Investigation findings
Summary: For a GP to refer a patient to the suspected skin cancer pathway, patients will have presented with an abnormal mole or lesion, which will be visually inspected by the GP. Dermoscopy is defined as the use of dermatoscopes to take photos of abnormal skin lesions. 'Teledermatology' refers to the use of static digital images to triage, diagnose, monitor or assess skin conditions without the patient being physically present, enabling rapid fast-track diagnosis of skin conditions. Available evidence suggests that both dermoscopy and teledermatology may aid in the triage of suspicious skin lesions in primary care leading to timelier diagnosis, improved outcomes and a reduction in unnecessary biopsies and referrals. • Paper 4 reported dermoscopy performed by **trained** specialists is more sensitive and specific in classifying skin lesions than clinical examination with the naked eye alone. However, when used by untrained or less experienced clinicians, accuracy can be no better than visual inspection alone[vii], and there is a danger of increased excisions, over-referral or false reassurance. • NG12 recommends urgent suspected cancer referral of patients if dermoscopy examination shows signs of melanoma. Evidence included in the 2015 NICE NG12 evidence review (Rosendahl et al.) found that it improves the diagnostic accuracy for non-melanocytic lesions[xiii]. It takes time to train clinicians to use dermoscopy, and training dropout rates have been shown to be high. Further research found that training in dermoscopy was not considered a priority for many GPs either due to other more pressing concerns within their practices or the perceived complexity of dermoscopy. Dermoscopy also faces other barriers such as equipment costs[xiv]. • SRG does not mention use of dermoscopy.

[xiii] Rosendahl, C., Tschandl, P., Cameron, A. & Kittler, H. Diagnostic accuracy of dermatoscopy for melanocytic and nonmelanocytic pigmented lesions. *J Am Acad Dermatol* **64**, 1068–1073 (2011).
[xiv] Fee, J. A., McGrady, F. P. & Hart, N. D. Dermoscopy use in primary care: a qualitative study with general practitioners. *BMC Primary Care* **23**, 1–10 (2022).

Teledermatology has the potential to improve cancer services by reducing waiting times and ensuring only those deemed at higher risk for referral are triaged into secondary care. This is reflected in the literature, along with some evidence of cost-effectiveness but more research is needed to establish the best way of providing teledermatology services.			
Paper number	Study	Summary	Notes

4	Jones OT, Jurascheck LC, van Melle MA, Hickman S, Burrows NP et al. Dermoscopy for melanoma detection and triage in primary care: a systematic review. *BMJ Open* 2019; 9(8): e027529.	This study conducted a systematic review on use of dermoscopy to triage suspicious skin lesions in primary care settings, and challenges for implementation.
		
		It found that dermoscopy, with appropriate training, was associated with **improved diagnostic accuracy** for melanoma and benign lesions and reduced unnecessary excisions and referrals (this was not clearly defined in the paper).
			• Systematic review.
			• Ninety-five articles underwent full-text review and 23 met the inclusion criteria. These 23 articles reported data relating to 49769 lesions and 3708 primary care practices (PCPs).
			• Studies were from MEDLINE, Cochrane Central, EMBASE, Cumulative Index to Nursing and Allied Health Literature, and SCOPUS bibliographic databases from 1 January 1990 to 31 December 2017.
			• **Limitations:**
			  ○ Included studies were of varying quality.
			  ○ Due to the heterogeneity of the included papers, did not undertake any meta-analysis.

5	Dinnes J, Deeks JJ, Chuchu N, di Ruffano LF,	This study aimed to determine the diagnostic accuracy of dermoscopy alone, or when added to visual	• Systematic review

	Matin RN, Thomson DR et al. Dermoscopy, with and without visual inspection, for diagnosing melanoma in adults. *Cochrane Database of Systematic Reviews* 2018; 12.	inspection of a skin lesion, for the detection of cutaneous invasive melanoma and atypical intraepidermal melanocytic variants in adults. Studies were separated according to whether the diagnosis was recorded face-to-face (in-person), or based on remote (image-based), assessment.
		
		Meta-analysis found dermoscopy to **be more accurate** than visual inspection alone with a relative diagnostic odds ratio (RDOR) of 4.7 for in-person evaluations of dermoscopy versus visual inspection alone; and RDOR of 5.6 for image-based evaluation of dermoscopy versus image-based visual inspection alone.
			• Included 104 publications reporting on 103 study cohorts with 42,788 lesions (including 5700 cases), providing 354 datasets for dermoscopy.
			• MEDLINE references that showed good agreement (89% with a kappa of 0.77), between screeners.
			• **Limitations:**
			  ○ Stringent application of review inclusion criteria meant that some studies included in previous reviews were excluded.
			  ○ Poor reporting of primary studies, in particular limiting assessment of methodological quality, and limiting both the assessment of studies by prior testing of participants and by observer expertise in dermoscopy.

Sub-topic: Teledermatology			

6	Chuchu N, Dinnes J, Takwoingi Y, Matin RN, Bayliss SE, Davenport C et al. Teledermatology for diagnosing skin cancer in adults. *Cochrane Database Systematic Review* 2018; 12(12): CD013193.	The study aimed to determine the diagnostic accuracy of teledermatology for the detection of any skin cancer (melanoma, BCC or cutaneous SCC) in adults, and to compare its accuracy with that of in-person diagnosis. The study suggests that: • Less than 7% of malignant skin lesions were missed by teledermatology. • Teledermatology is likely to **aid decision-making** in primary care to decide which skin lesions need to be seen by a skin specialist. • Using magnified images, in addition to photographs of the lesion, **improves accuracy** (average sensitivity was 94.9% (95% confidence interval (CI) 90.1% to 97.4%) and specificity (84.3% (95% CI 48.5% to 96.8%)) (from four studies). • Referral accuracy data comparing teledermatology against a face-to-face reference standard suggested **good agreement** (sensitivities of over 90%).	• Systematic review • Included 22 studies, 16 studies comparing teledermatology diagnoses to the final lesion diagnoses (diagnostic accuracy) for 4057 lesions and 879 malignant cases. • **Limitations:** ○ Studies were generally small and heterogeneous and methodological quality was difficult to judge due to poor reporting.
7	Ali OME, Wright B, Goodhead C, Hampton PJ. Patient-Led Skin Cancer Teledermatology without Dermoscopy during the Covid pandemic: Important lessons for the	This study aimed to assess the role of a mobile phone application in remote skin cancer assessment at two centres for urgent (melanoma & squamous cell carcinoma) and non-urgent skin cancer referrals, investigating the feasibility of using patient-taken images without dermoscopy for remote diagnosis.	• Retrospective feasibility study. • Two cohorts during the COVID-19 pandemic from centres in the North Bristol NHS Trust. Included urgent skin cancer referrals (melanoma & SCC) and non-urgent skin cancer referrals.

	development of future patient-facing teledermatology & AI-assisted self-diagnosis. *Clinical and Experimental Dermatology* 2024; llae126	• Remote consultations **reduced face-to-face appointments** by 90% and urgent referrals by 63% for BCC.
		• Diagnostic concordance (consultant vs histological diagnosis) rates of 72% and 83% were observed for BCC (n=107) and urgent skin cancers (n=704), respectively.
		
		This data would indicate **improved diagnostic concordance** using the mobile phone teledermatology application compared to un-assisted GP detection of malignant skin cancer (sensitivity 66.7% (95% confidence interval (CI), 50.3–79.8) for lesions and 63.6% (95% CI, 46.7–77.8)) for individuals affected with malignancy.[20]
			April – August 2020, N = 1385 of which 704 (51%) of patients completed remote consultations.
			• Limitations:
			  ○ Patient-led imaging only with no comparison to patient-facing dermoscopy.
			  ○ Lack of data collected about usability by patients or clinicians.

8	Livingstone J, Solomon J. An assessment of the cost-effectiveness, safety of referral and patient satisfaction of a general practice teledermatology service. *London Journal of Primary Care*, 2015; 7(2): 31-35.	This study aimed to determine: (1) whether teledermatology in a single general practice is cost-effective, (2) whether the correct types of cases are being referred, and (3) if patients are satisfied with the service.
		
		• Teledermatology saved £12,460 over the 3-year period compared to standard of care.
		• Patients were followed for up to 51 months and **no lesions were found to be malignant** in those that had a negative diagnosis.
			• Retrospective analysis of 6500 patient records over three years.
			• Sample size, n=248 adult patients (aged 18+)
			• **Limitations:**
			  ○ Single general practice in suburban Greater London.
			  ○ Survey completion was low (n=129) and may not have been fully

		• 97% of patients rated themselves as **satisfied/very satisfied** and 93% found the procedure comfortable/very comfortable. • The median wait for the photos to be taken was 7 days, and 1-2 weeks for results.	representative of the whole cohort. ○ Cost calculations did not include the time taken to train staff to take and forward the photographs.
9	Elliot LG, Sharma M. Teledermatology 2-week-wait skin cancer referrals during COVID-19 pandemic: a service evaluation. *Clinical and Experimental Dermatology,* 2022; 47(2): 458-459.	This study aimed to evaluate the effectiveness and appropriateness of teledermatology services for skin cancer referrals. It found that: • Of the 120 suspected diagnoses made by GP/ACP/ANP, 76 (63.3%) were referred as either malignant melanoma (MM), squamous cell carcinoma (SCC) or other malignant (OM). • Dermatologist assessment identified 16 of the 120 total referrals (13%) as suspected MM/SCC/OM. This study supported the need for training and support for GPs, ACPs and ANPs in dermatology diagnostic skills for skin cancer assessment.	• Single centre service evaluation in England. • Evaluated over a 2-week period in 2021 (n=120). • **Limitations:** ○ No referrals with dermoscopic images. ○ Unclear if practitioners had adequate assessment skills for skin cancer detection. ○ Only 1 centre evaluated. ○ No comparison to the current standard of care which would give more meaningful results. ○ Correspondence piece so not a full paper, lacking detailed methods, results and discussion.

10	Jones K, Lennon E, McCathie K, Millar A, Isles C, McFadyen, Shearer H. Teledermatology to reduce face-to-face appointments in general practice during the COVID-19 pandemic: a quality improvement project. *BMJ Open Quality* 2022; 11:e001789.	This study aimed to increase the weekly percentage of remote dermatological consultations to greater than 80% and to reduce the weekly percentage of dermatological face-to-face consultations to less than 50%. It found that: • Over 80% of dermatological consultations in primary care can be dealt with remotely if patients provide high-quality supporting images. • In the absence of high-quality images, it might not be possible to reduce dermatological face-to-face consultations below 50% in primary care. • It is likely that patient education to provide better quality images is needed to allow reduction in face-to-face consultations below 50% in primary care.	• Quality improvement study • 253 dermatological consultations were analysed: 170 of these were telephone consultations with 308 supporting images. • Data were collected weekly by reviewing Egton Medical Information Systems (EMIS) and Docman records. • **Limitations:** ○ Small patient sample approached for feedback (less than 1%; 27 of 3836 patients).

Inequalities			
Summary: Patients in rural areas may need further safety netting as melanoma-specific mortality was found to be significantly lower in individuals residing in small towns than in large urban areas.			
Paper number	**Study**	**Summary**	**Notes**

11	Murchie P, Adam R, Khor WL, Raja EA, Iversen L, Brewster DH et al. Impact of rurality on processes and outcomes in melanoma care: results from a whole-Scotland melanoma cohort in primary and secondary care. *Br J Gen Pract*. 2018; 68(673): e566-575.	This study aimed to investigate the impact of rurality on setting of melanoma excision and mortality in a whole-nation cohort.
		
		It found that:
		• Odds of primary care excision increased with **increasing rurality/remoteness**. Compared with those in urban areas, those in the most remote rural locations had almost twice the odds of melanoma excision in primary care (adjusted odds ratio [aOR] 1.92; 95% confidence interval [CI] = 1.33 to 2.77).
		• No significant association was found between urban or rural residency and all-cause mortality.
		• **Melanoma-specific mortality was significantly lower** in individuals residing in small towns than in large urban areas (adjusted hazards ratio [HR] 0.53; 95% CI = 0.33 to 0.87) with no trend towards poorer survival with increasing rurality.
			• Data-linkage population-based cohort study.
			• All patients diagnosed with cutaneous melanoma in Scotland between 1 January 2005 and 3 December 2013 (n=9519).
			• Data from the Scottish Cancer Registry and National Records of Scotland.
			• Limitations:
			  ○ Only studied patients from a single health board (Grampian) in Northeast Scotland.
			  ○ Numbers in some categories were small.
			• Analysis accounted for clustering by health board, but not at GP level or by the clinician performing the excisions, where outcomes might be more strongly correlated.

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Topic: Safety Netting			
Summary: • Paper 12 reported people who have been investigated along an urgent pathway for skin cancer are at greater risk of being diagnosed with skin cancers in the years 1-5 following referral, which could provide opportunities for earlier recognition of this higher risk group. • Skin cancer is more likely to be misdiagnosed in black patients compared to white patients. Late-stage diagnosis of skin cancer in this cohort could be influenced by delays in the patient, primary care or diagnostic interval (See **'Background'**).			
Paper number	**Study**	**Summary**	**Notes**

12	Scott SE, Gildea C, Nicholson BD, Evans RE, Waller J, Smith D et al. Future cancer risk after urgent suspected cancer referral in England when cancer is not found: a national cohort study. *Lancet Oncology* 2023; 24(11): 1242-1251	This study aimed to investigate the risk of cancer occurrence within 1-5 years of finding no cancer following an urgent suspected cancer referral.
		
		The study found that:
		• Skin cancer demonstrated one of the largest numbers and **absolute rates of subsequent cancers** diagnosed after referral through the urgent suspected skin cancer pathway.
		• Skin cancer was not commonly diagnosed in the years 1-5 post-referral across any other referral pathways
		• The occurrence of subsequent cancer remained relatively stable over time but was highest in years 1–2 across all referral pathways (including skin cancer).
		• The absolute rate of subsequent cancers following skin cancer referral was **higher in males than females**, in those with White
			• National cohort study linking data from the Cancer Waiting Times dataset and the National Cancer Registry dataset between April 2013 and March 2014. England only.
			• Sample size: 1,367,680 urgent suspected cancer referrals, identifying 6,0188 (5·1%) with cancer diagnosis in years 1–5 (63, 112 total cancers) across the 8 main referral pathways.
			• **Limitations:**
			  ○ Reporting of urgent suspected cancer referrals is different in Scotland despite similar clinical context.
			  ○ Triage, cancer investigations, and

		ethnicity than other ethnicities, and in older adults than younger adults and children or adolescents. • Higher absolute cancer rates were also found in those with a **previous history of cancer** versus no previous history and previous urgent suspected cancer referral versus no referral. • Rate of subsequent cancers did not appear to differ by Index of Multiple Deprivation quintile.	screening programmes have changed since the cohort was referred in 2013–14. ○ Doesn't account for confounders other than age and gender, or survivorship bias and the competing risk of death from non-cancer causes.

Topic: Risk Stratification

Summary:

- There is evidence to show that older people and men are at an increased risk of skin cancer, with more lesions being detected on the trunk and upper limbs in these groups.
- Advanced stage melanoma at the point of diagnosis is also more likely in older people, men and those in more deprived areas, particularly older, white male patients in deprived areas.
- Paper 13 reported an estimated 3.1% increase in stage 1 and 2 melanomas may occur if socio-demographic inequalities in stage at diagnosis were eliminated.
- Defining high-risk populations using risk prediction models may help targeted screening and early detection approaches e.g. Williams self-assessed clinical risk estimation model (Paper 16). Models that can identify individuals at a higher risk of melanoma are not yet standard of care and are an emerging intervention.

Paper number	Study	Summary	Notes
13	Barclay ME, Abel GA, Greenberg DC, Rous B, Lyratzopoulos G. Socio-demographic variation in stage at diagnosis of	This study examined the association between stage at diagnosis for common cancers in England and socio-demographic variation. The following associations were found:	• Cross sectional study • Data from the English cancer registry in 2015 • N=202,001 • **Limitations:**

	breast, bladder, colon, endometrial, lung, melanoma, prostate, rectal, renal and ovarian cancer in England and its population impact. *Br J Cancer.* 2021; 124(7):1320-1329. doi:10.1038/s41416-021-01279-z	• **Increasing age** was strongly associated with increase in the odds of advanced stage melanoma at diagnosis. • **Men** were at higher risk of advanced stage at diagnosis for melanoma. • **Increasing deprivation** was associated with higher risk of advanced stage melanoma. It was noted that social factors may contribute to sex differences in stage at diagnosis for melanoma, such as differences between men and women in bodily awareness and help-seeking behaviour. An estimated 3.1% increase in stage 1 and 2 melanomas may occur if socio-demographic inequalities in stage at diagnosis were eliminated.	○ stage data missing for some patients; health-care related factors were not considered
14	Memon A, Bannister P, Rogers I, Sundin J, Al-Ayadhy B, James PW et al. Changing epidemiology and age-specific incidence of cutaneous malignant melanoma in England: An analysis of the national cancer registration data by age, gender and anatomical site, 1981-2018. *Lacet*	This study aimed to examine whether there have been changes in the epidemiology of melanoma in England during the past four decades. • Incidence of melanoma among young people in England has stabilised. • Incidence increased substantially in **older** population. • Steeper increase in incidence in **males**, which is consistent with their relatively greater sun exposure and poor sun-protective behaviour. • Increase in the **melanoma of the trunk and upper limb** is likely due to increasing trend in	• Retrospective population-based cohort study. • Office for National Statistics/Public Health England individual level data for patients diagnosed with melanoma in England 1981-2018 (cases, n=265,302). • **Limitations:** ○ Lack of information on precise sub-sites prevented further insights into the pattern and causative

	Regional Health Europe 2021; 100024.	intermittent high intensity recreational UV radiation exposure (e.g. sunbathing, holidaying in places with strong sunlight, indoor tanning).	impact of UV radiation exposure.

15	Venables ZC, Autier P, Nijsten et al. Nationwide Incidence of Metastatic Cutaneous Squamous Cell Carcinoma in England. *JAMA Dermatol.* 2018; 155(3): 298-306.	The study aimed to assess the national incidence of cutaneous SCC (cSCC) and metastatic SCC (mcSCC) in England from 2013 through 2015.
		
		The study found that:
		• Increased primary cSCC tumor count was observed in **older, white male patients in lower deprivation quintiles.**
		• Significant increases in the risk of metastasis were observed in patients who were **aged 80 to 89 years who were immunosuppressed** (HR, 1.99; 95% CI, 1.64-2.42), and in **higher deprivation quintiles** (HR for highest quintile, 1.64; 95% CI, 1.35-2.00).
		• Primary cSCC located on the **ear** (HR, 1.70; 95% CI, 1.42-2.03) and **lip** (HR, 1.85; 95% CI, 1.29-2.63) were at highest risk of metastasis.
			• Retrospective, population-based cohort study.
			• Data for this cohort of patients with cSCC and mcSCC in England were provided by the NCRAS (January 1, 2013, through December 31, 2015).
			• Patients with nodal or distant mcSCC from 2013 to 2015 were identified from the group of 93 890 patients diagnosed with a cSCC during the study period.
			• **Limitations:**
			  ○ Limited to 3 years
			  ○ Did not identify patients with multiple cSCC in 2013 through 2015.
			  ○ The estimation of mcSCC occurrences may be underestimated as there is no *ICD-10* code is specific to mcSCC.

16	Usher-Smith JA, Kassianos AP, Emery JD, Abel GA, Teoh Z, et al. Identifying people at	Defining high-risk populations using risk prediction models may help targeted screening and early detection approaches. Models that can identify individuals at a higher risk of melanoma are not yet	• Multi-site feasibility study. • Data provided by NCRAS 2023-2015 (n=93,890).

	higher risk of melanoma across the UK: a primary-care-based electronic survey. *British Journal of Dermatology* 2017; 176(4): 939-948.	standard of care and are an emerging intervention. The Williams self-assessed clinical risk estimation model is an example of such a model, selected from a systematic review of literature[xv] as the only model validated outside of the development population.
		
		This study aimed to assess the feasibility of identifying people at higher risk of melanoma using the Williams self-assessed clinical risk estimation model in U.K. primary care.
		
		The results found that:
		• Mean melanoma risk score was 17.15 ± 8·51.
		• There were **small regional differences** – risk is lower in England compared to Scotland (P = 0.001) and Wales (P < 0.001).
		• After **weighting to the age and sex distribution**, different potential cut-offs would allow between 4% and 20% of the population to be identified as higher risk, and those groups would contain 30% and 60%, respectively of those likely to develop melanoma.
		• Collecting data on the melanoma risk profile of the general population in U.K. primary care is both **feasible and acceptable** for patients in a general practice setting.
			• Participants were recruited from general practices in Eastern England (n = 10), Northeast Scotland (n = 6) and North Wales (n = 6) between February 2014 and March 2015.
			• **Limitations:**
			  ○ Limited to 3 years
			  ○ Did not identify patients with multiple SCC.
			  ○ Immunosuppression is likely to have been underestimated owing to reliance on hospital diagnosis and coding.

[xv] Usher-Smith, J. A., Emery, J., Kassianos, A. P. & Walter, F. M. Risk prediction models for melanoma: A systematic review. *Cancer Epidemiology Biomarkers and Prevention* **23**, 1450–1463 (2014).

17	Lyman M, Mills JO, Shipman AR. A dermatological questionnaire for general practitioners in England with a focus on melanoma; misdiagnosis in black patients compared to white patients. *Journal of the European Academy of Dermatology and Venereology* 2016; 31(4): 625-628.	The aim of this study was to obtain data on the diagnosis rate of melanoma in the primary care setting, with particular attention to white vs. black skin types. The questionnaire results show a clear **increased misdiagnosis** of melanoma in black patients in primary care vs. white. Of the two black skin melanoma pictures, 177/287 (62%) and 90/287 (31%) responses were incorrectly identified, compared to 37/287 (13%) and 19/287 (7%) in the white skin melanoma pictures.	• Observational survey. • Online questionnaire sent to 2975 GP practices in England and 287 responses were received. • **Limitations:** ○ The questionnaire contained 20 high-quality picture questions of differing common skin conditions. 4/20 questions were melanomas, two on white and two on black skin.

Emerging Topics

Many non-invasive tests and diagnostic technologies have been developed to aid skin cancer diagnosis, including high frequency ultrasonography, optical coherence tomography, reflectance confocal microscopy, and computer-assisted diagnosis. They have been evaluated in several recent Cochrane reviews, all of which found a paucity of evidence for their accuracy in either primary or specialist care settings[xvi].

More recently, there has been an emergence of artificial intelligence-enabled applications for the detection of cancerous skin lesions. There is accumulating evidence that artificial intelligence and machine learning (AI/ML) can assist clinicians to make better clinical decisions, or even replace human judgement in some instances. Studies have shown that AI/ML algorithms can perform on par with or better than consultant dermatologists, and that AI/ML algorithms can assist clinicians in the diagnosis of skin cancers in primary care[xvii]. It could be

[xvi] Jones, O. T., Ranmuthu, C. K. I., Hall, P. N., Funston, G. & Walter, F. M. Recognising Skin Cancer in Primary Care. Adv Ther 37, 603 (2020).
[xvii] Jones, O. T. *et al.* Artificial intelligence and machine learning algorithms for early detection of skin cancer in community and primary care settings: a systematic review. *Lancet Digit Health* **4**, e466–e476 (2022).

applied to teledermatology services to help reduce referral rates while maintaining patient safety, but more evidence is needed to support widespread implementation[xviii].

Comparison of Scottish Referral Guidelines and NG12 Guidelines for suspected skin cancers	
NICE NG12 (Last updated 2015)	SRG
Malignant melanoma of the skin: 1.7.1 Refer people using a suspected cancer pathway referral for melanoma if they have a suspicious pigmented skin lesion with a weighted 7-point checklist score of 3 or more. [2015] Weighted 7-point checklist Major features of the lesions (scoring 2 points each): • change in size • irregular shape • irregular colour. Minor features of the lesions (scoring 1 point each): • largest diameter 7 mm or more • inflammation • oozing • change in sensation. 1.7.2 Refer people using a suspected cancer pathway referral if dermoscopy suggests melanoma of the skin. [2015]	Lesions on any part of the body which have one or more of the following features: • Change in colour, size or shape in an existing mole • Moles with **A**symmetry, **B**order irregularity, **C**olour irregularity, **D**iameter increasing or >6mm • New growing nodule with or without pigment • Persistent (more than four weeks) ulceration, bleeding or oozing • Persistent (more than four weeks) surrounding inflammation or altered sensation • New or changing pigmented line in a nail or unexplained lesion in a nail • Slow growing, non-healing or keratinising lesions with induration (thickened base) • Any melanoma or invasive SCC or a high risk BCC diagnosed from biopsy • Any unexplained skin lesion in an immuno-suppressed patient • BCC invading potentially dangerous areas, for example peri-ocular, auditory meatus or any major vessel or nerve

[xviii] Marsden, H. *et al.* Accuracy of an artificial intelligence as a medical device as part of a UK-based skin cancer teledermatology service. *Front Med (Lausanne)* **11**, (2024).

1.7.3 Consider a suspected cancer pathway referral for melanoma in people with a pigmented or non-pigmented skin lesion that suggests nodular melanoma. [2015] **Squamous cell carcinoma** 1.7.4 Consider a suspected cancer pathway referral for people with a skin lesion that raises the suspicion of squamous cell carcinoma. [2015] **Basal cell carcinoma** 1.7.5 Consider routine referral for people if they have a skin lesion that raises the suspicion of a basal cell carcinoma. (Typical features of basal cell carcinoma include: an ulcer with a raised rolled edge; prominent fine blood vessels around a lesion; or a nodule on the skin [particularly pearly or waxy nodules].) [2015] 1.7.6 Only consider a suspected cancer pathway referral for people with a skin lesion that raises the suspicion of a basal cell carcinoma if there is particular concern that a delay may have a significant impact, because of factors such as lesion site or size. [2015] 1.7.7 Follow NICE's guidance on improving outcomes for people with skin tumours including melanoma for advice on who should excise suspected basal cell carcinomas. [2015]	**Good practice points** • Lesions which are suspicious for melanoma should not be removed in primary care. All excised skin specimens should be sent for pathological examination • Lesions suspicious of basal cell carcinomas (BCC) may not require urgent referral, except those invading potentially dangerous areas • Referrals should be accompanied by an accurate description of the lesion (including size, pain and tenderness) and photos if possible, subject to clinical governance arrangements, to permit appropriate triage