Can the effects of the COVID-19 pandemic provide insights into the impact of melanoma underdiagnosis and delayed care?

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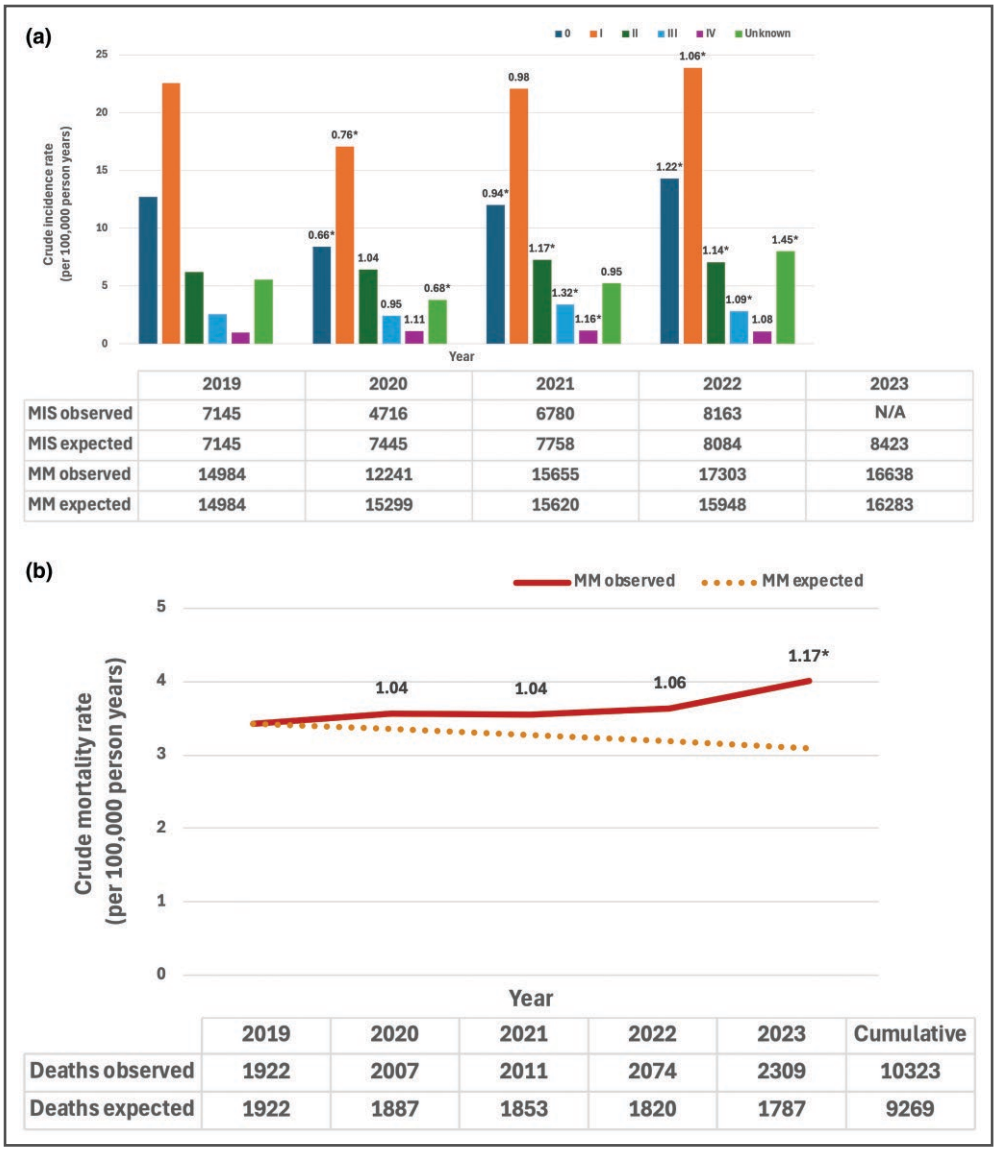
Dear Editor, We have shown that the previously rising incidence of melanoma *in situ* (MIS) and invasive (malignant) melanoma (MM) has been decelerating in England since the mid-2010s.[1] Mortality from MM has been declining in younger populations since the mid-2000s. Similar trends have been published in several other high-risk developed populations such as in the USA, Australia and several European countries.[2,3] More recent trends, variably influenced by the impact of the COVID-19 pandemic and health policy responses are yet to be fully elucidated. Data from the English Rapid Cancer Registration Dataset revealed 2485 (18%) fewer melanoma diagnoses in 2020 compared with 2019.[4] A meta-analysis of 25 studies including over 32 000 European patients found significant delays and reductions in diagnoses of *in situ* (stage 0) and stage I melanomas post-first lockdown compared with pre-COVID-19, along with increased stage III and ulcerated melanomas.[5] These findings suggest delayed presentations of melanoma and delayed care, which may result in poorer patient outcomes and higher healthcare burden.

Incidence and survival data from England, between 2019 and 2022 by stage, were extracted from the National Disease Registration Service (NDRS) 'Get Data Out' programme, with 2023 data not available by stage.[6] MIS [International Classification of Diseases (ICD)-10 code D03] and MM (ICD-10 code C43) overall incidence data were extracted from NDRS national statistics. Mortality data, between 2019 and 2023 in England, were extracted from the Office for National Statistics.[7] Data sources were openly available, requiring no ethical approval. Expected incidence of MIS and MM were extrapolated using the average annual percentage change (APC) trends derived by Joinpoint analysis of crude incidence rates from the previous two decades (+4.2% and +2.1%, respectively).[6] Expected mortality from MM was calculated in a similar way (APC –1.8%). χ^2 tests were used for statistical comparison of proportions. Confidence intervals (CIs) for incidence rate ratios were calculated using the exact Poisson method with significance assumed at $P<0.05$.

Crude incidence of both MM and MIS fell significantly in 2020 compared with 2019 ($IRR_{MIS}=0.66$, 95% CI 0.64–0.68; $IRR_{MM}=0.82$, 95% CI 0.80–0.84), subsequently increasing to higher than pre-pandemic levels even when accounting for pre-pandemic increasing trends (Figure 1a). MIS, stage I and II MM and melanoma of unknown stage diagnoses increased significantly in 2022 compared with pre-COVID-19 (2019 data). Incidence trend differences were not significant between genders. Mortality from MM consistently comprised 0.4% of all deaths in England between 2019 and 2023, annually. Previously declining crude mortality rates for MM shifted in 2020 and thereafter significantly increased in 2023 from 2019 ($IRR_{MM}=1.17$, 95% CI 1.10–1.24) (Figure 1b), without significant differences by gender. Over 1000 more deaths from MM were observed, compared with the number expected, in the period 2019–2023.

Limitations of this study include the short timeframe available for trend estimation. The use of crude rates renders comparison of these trends with other countries difficult. The APC from crude rates is higher than and should not be compared with age-standardized rates, and this difference reflects the ageing population of England. The 'Get Data Out' dataset by stage does not include MM in people < 25 years old or acral lentiginous melanomas, which account for < 2% MMs.

These findings contrast with the decelerating incidence trends and decreasing mortality for melanoma in England, between 2001 and 2019. The COVID-19 pandemic resulted in transient melanoma underdiagnosis in England in 2020 and delayed care, followed by increased mortality and incidence with a higher proportion of later-stage diagnoses for the following years. More years of follow-up data are needed to assess survival from MM. Close observation of trends over the next few years may identify melanoma incidence to rebound higher than expected owing to delayed MIS diagnoses presenting as MM, but this is not yet apparent. Diagnostic delays together with the higher burden of disease in older populations (for whom systemic anticancer therapies are less frequently used) are expected to add significant strains on healthcare systems. Thicker tumours presenting later quickly result in higher mortality.[8] These findings, albeit limited to 2019–2023 in England, show real increases in later-stage melanomas, thereby providing some reassurance to concerns on long-term



	2019	2020	2021	2022	2023
MIS observed	7145	4716	6780	8163	N/A
MIS expected	7145	7445	7758	8084	8423
MM observed	14984	12241	15655	17303	16638
MM expected	14984	15299	15620	15948	16283

	2019	2020	2021	2022	2023	Cumulative
Deaths observed	1922	2007	2011	2074	2309	10323
Deaths expected	1922	1887	1853	1820	1787	9269

Figure 1 (a) Crude incidence rate by stage for MIS (stage 0) and MM (stage I, II, III, IV or unknown) in England between 2019 and 2023. The number of observed and expected counts for MIS and MM per year are shown with expected counts calculated using the previous year's APC. IRRs between 2019 and following years are shown by stage. Data for 2023 by stage and for MIS were not available. (b) Crude mortality rates for MM between 2019 and 2023 in England. The number of observed and expected deaths from MM per year is shown below. IRRs between 2019 and following years are shown.APC, annual percentage change; IRRs, incidence rate ratios; MIS, melanoma *in situ*; MM, invasive (malignant) melanoma. Asterisks (*) denote statistical significance at $P < 0.05$.

overdiagnosis.[9] The risks of delayed presentation and treatment of melanoma highlight the importance of early detection and the need to emphasize primary prevention strategies. Future preparedness strategies may alleviate the impact of a pandemic on melanoma outcomes by ensuring accessibility and continuation of standard cancer services where feasible.

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Data availability: This study uses data that have been provided by patients and collected by the NHS as part of their care and

support. The data are collated, maintained and quality assured by the National Disease Registration Service, which is part of NHS England.

Ethics statement: This study was exempt from Institutional Review Board approval.

Patient consent: Not applicable.

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Co-primary endpoints PASI 90 and IGA 0/1 at Week 16 were met.**Secondary endpoints. †N= mNRI, missing data were imputed with mNRI (patients with missing data following treatment discontinuation due to lack of efficacy or a TRAE were counted as non-responders; multiple imputation methodology was used for other missing data). ‡43.9% (n=189/431), and 43.4% (n=116/267) of biologic-naïve and TNFi-IR PsA patients achieved the primary endpoint of ACR 50 at Week 16 in BE OPTIMAL and BE COMPLETE, respectively (vs 10.0% [n=28/281] and 6.8% [n=9/133] placebo, p<0.0001); 54.5% (n=235/431) and 51.7% (n=138/267) maintained it at Week 52 (NRI).[4–6]

ACR 50, ≥50% response in the American College of Rheumatology criteria; **AS**, ankylosing spondylitis; **CRP**, C-reactive protein; **DMARD**, disease-modifying antirheumatic drug; **HS**, hidradenitis suppurativa; **IGA**, Investigator's Global Assessment; **(m)NRI**, (modified) non-responder imputation; **MRI**, magnetic resonance imaging; **nr-axSpA**, non-radiographic axial spondyloarthritis; **NSAID**, non-steroidal anti-inflammatory drug; **PASI 75/90/100**, ≥75/90/100% improvement from baseline in Psoriasis Area and Severity Index; **PsA**, psoriatic arthritis; **PsD**, psoriatic disease; **PsO**, psoriasis; **TNFi-IR**, tumour necrosis factor-α inhibitor – inadequate responder; **TRAE**, treatment-related adverse event.

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