

Effects of COVID-19 Pandemic on the Diagnosis of Melanoma and Keratinocyte Carcinomas: a Systematic Review and Meta-analysis

Pablo DÍAZ-CALVILLO^{1,2}, Daniel MUÑOZ-BARBA^{1,2}, Clara UREÑA-PANIEGO^{1,2}, Lara Valeska MAUL³, Sara CERMINARA³, Lisa KOSTNER³, Antonio MARTÍNEZ LÓPEZ^{1,2,*} and Salvador ARIAS-SANTIAGO^{1,2,4}

¹Department of Dermatology, Virgen de las Nieves University Hospital, ²Instituto de Investigación Biosanitaria ibs.GRANADA, Granada, Spain, ³Department of Dermatology, University Hospital of Basel, Basel, Switzerland, ⁴Department of Dermatology, University of Granada, Granada, Spain

Since December 2019, the COVID-19 pandemic has profoundly affected healthcare. The real effects of the COVID-19 pandemic on skin cancer are still unclear, more than 3 years later. This study aims to summarise the pandemic's impact on skin cancer diagnosis and outcome. A systematic review and meta-analysis was conducted, selecting studies comparing skin cancer diagnosis and prognosis post-pandemic with pre-pandemic data. A total of 27 papers were reviewed including 102,263 melanomas and 271,483 keratinocyte carcinomas. During the initial pandemic months (January–July 2020), melanoma surgeries dropped by 29.7% and keratinocyte carcinomas surgeries by 50.8%. Early pandemic tumours exhibited greater thickness and stage. In a long-term period beyond the initial months, melanoma surgeries decreased by 9.3%, keratinocyte carcinomas by 16.6%. No significant differences were observed in the Breslow thickness of melanomas after the start of the pandemic (mean difference 0.06, 95% confidence interval -0.46, 0.58). Melanomas operated on post-pandemic onset had an increased risk of ulceration (odds ratio 1.35, 95% confidence interval 1.22–1.50). Keratinocyte carcinomas showed increased thickness and worsened stage post-pandemic. However, studies included were mostly retrospective and cross-sectional, reporting diverse data. This review indicates that the pandemic likely caused delays in skin cancer diagnosis and treatment, potentially impacting patient outcomes.

Key words: melanoma; squamous cell carcinoma; basal cell carcinoma; COVID-19.

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Corr: Antonio Martínez-López, Avenida de Madrid 15, ES-18014, Granada, Spain. E-mail: antoniomartinezlopez@aol.com

In December 2019, severe acute respiratory syndrome coronavirus type-2 (SARS-CoV-2) emerged in Wuhan, China. This virus has spread globally and has produced over 770 million COVID-19 cases and 6.9 million deaths worldwide (1). In the most affected countries, governments imposed general confinements and COVID-19 forced lifestyle changes (2). These measures also affected healthcare systems, necessitating adaptations to maintain patient care, with a noticeable neglect

SIGNIFICANCE

The COVID-19 pandemic has disrupted global healthcare since December 2019, with uncertain long-term effects on skin cancer. Our study reviewing 27 research papers and over 373,000 skin cancer cases found that from January to June 2020, melanoma surgeries decreased by 29.7%, and keratinocyte carcinomas surgeries by 50.8%. Tumours operated on during the pandemic's early months had increased thickness and stage. Even beyond this phase, melanoma surgeries remained down by 9.3%, and keratinocyte carcinomas by 16.6%. The study suggests that the pandemic likely led to delays in skin cancer diagnosis and treatment, potentially affecting patient outcomes.

of other diseases like skin cancer (3). Moreover, patients stopped consulting, primarily due to fear of infection (4).

Skin cancers are the most frequent tumours in humans, with an increasing incidence (5). Delays in diagnosis mean worse tumour stages, causing poorer survival rates and the need for more complex procedures, such as surgical flaps or grafts and adjuvant therapies (6, 7).

The true impact of the COVID-19 pandemic on skin cancer, over 3 years after its onset, remains unclear. Knowing these data could help to develop strategies to maintain early diagnosis in future confinements, potentially involving initiatives like tele dermatology, improved triaging, or educational campaigns.

The aim of this study is to summarise the COVID-19 pandemic's impact on skin cancer diagnosis and outcome.

METHODS

Design

A systematic review and meta-analysis were performed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist (8) (Table SII). The study protocol was registered on PROSPERO (www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42022369656).

Data sources and search strategy

Data were obtained from the following databases: MEDLINE, Embase, Scopus, Web of Science, and Cochrane Library.

We used the following search terms: (melanoma OR squamous cell carcinoma OR basal cell carcinoma) AND COVID-19, using the filters: "Humans" and "Adults".

For full search strategy for each database, see Appendix S1.

As our search strategy used index, some pertinent articles might not be included due to the indexing delay. To mitigate this, we supplemented the searches with manual screening. In addition, a supplementary search was carried out to lessen the possibility of publication bias by manually searching the reference lists of the articles that were selected for the review.

Inclusion and exclusion criteria

Inclusion: original article of clinical trial, cohort study, case-control study, or cross-sectional study, assessing changes in skin cancer diagnosis and prognosis after the pandemic and comparing with the pre-pandemic period, published in peer-reviewed journals and written in English or Spanish.

Exclusion: reviews, guidelines, protocols, letters, conference abstracts, unpublished studies, case reports, and case series.

The selection of articles was carried out by PDC, DMB, and CUP. Discrepancies were resolved by consensus among all authors.

Documentary quality

To assess risk of bias, we used the National Institutes of Health quality assessment tool (9). This contains 14 questions and, for each article, 1 point was assigned for each present item (if not applicable, not scored), categorised as good (>9 criteria), fair (5–9), or poor (<5) (Table S1).

Data extraction

Duplicate records were refined using EndNote X9 (Clarivate Analytics, London, UK). The articles were classified according to the variables: first author, year of publication, country, design, quality of the study, number of participants, skin cancer type studied, and the periods focused on for outcomes. We then stratified the data according to skin cancer type. For melanoma studies, we collected: pre-pandemic study period, pandemic study period, number of days in each period, number of tumours, age, sex, Breslow thickness, mitotic index, T-value (from the TNM), and staging according to the American Joint Committee on Cancer, eighth edition (10). In articles studying keratinocyte carcinomas (KC) we collected: pre-pandemic study period, pandemic study period, number of days in each period, type of tumour studied, number of tumours, age, sex, invasion depth, and T-value (10). Data of interest that were not included in the articles were calculated based on the data reported in each paper.

Studies were stratified according to whether they assessed the short-term effects of the pandemic (focusing on the months of first confinements: March–July 2020) or the long-term ones (beyond the months of first confinements or assessing the period of confinement in addition to later periods). From the studies that compared various periods before the pandemic, we obtained the average for the different variables. The studies were ordered according to the number of days studied.

Statistical analysis

Meta-analyses were performed if 3 or more articles had available data. Thus, the long-term effect of the COVID-19 pandemic on Breslow thickness and ulceration were estimated. In studies involving several pandemic periods, the data were combined into a single period. We used weighted data from the studies, which were then presented in forest plots along with their 95% confidence intervals. The heterogeneity among the studies was evaluated using the Cochrane Q statistic and I^2 measure. We observed high heterogeneity for Breslow thickness and used a random effects model to calculate the outcome. In contrast, we detected low heterogeneity for ulceration and used a fixed effects model to calculate the odds ratio. To assess publication bias we used funnel plots (Figs S1–S2). Sensitivity analyses were performed by excluding studies with a high risk of bias to assess significantly changes in the heterogeneity. The data analysis was conducted using Review Manager version 5.4 (Cochrane Collaboration, 2020).

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RESULTS

We identified 1,032 papers across databases (**Fig. 1**). After removing duplicate entries, 740 papers remained. Following screening, 658 were excluded: 328 were unrelated to skin cancer, 91 lacked a pre-pandemic control group, 231 were not original articles from clinical trial, cohort, case-control, or cross-sectional studies, 6 were not in English or Spanish, and 2 were inaccessible. Another 55 were excluded because they did not investigate changes in diagnosis or prognosis after the pandemic. Ultimately, 27 papers were included (**Table I**; 11–37).

Concerning study design, 16 cross-sectional studies, 10 cohort studies, and 1 case-control study were included. Using the National Institutes of Health quality assessment tool, 5 studies had “poor” quality and 22 “fair” quality. The majority of studies ($n=23$) were conducted in Europe, with Italy contributing the most ($n=7$). Four studies were from North America and 1 was from Australia. In total, 373,746 tumours were included: 102,263 melanomas and 271,483 KC. Fifteen studies focused on melanoma, 4 on KC, and 8 included both types. Concerning outcomes, 8 studies focused on short-term outcomes, 16 on long-term outcomes, and 3 on both. Six studies included more than 2 study periods (20, 23, 27, 29, 31). Four studies had different durations for the pre-pandemic and pandemic groups (15, 17, 18, 20). The pandemic time of study varied from 28 days (34) to 731 days (12), and the pre-pandemic period from 28 days (34) to 1,141 days (15).

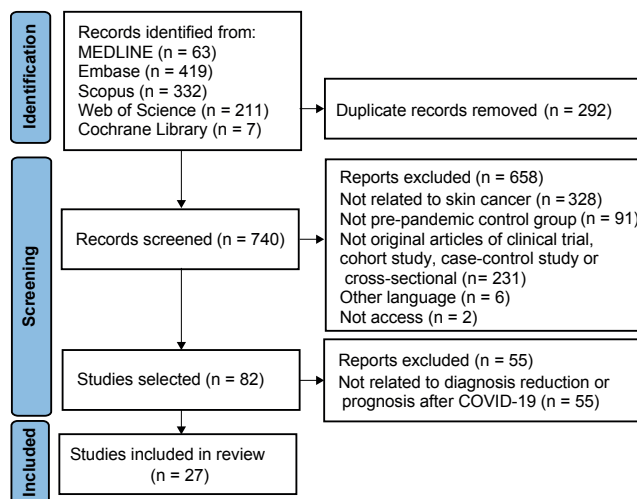


Fig. 1. Flow diagram of studies included in the review.

Short-term effects of COVID-19 on melanoma

Ten studies assessed the short-term effects of the pandemic on melanoma (**Table II**; 17, 20, 25, 26, 29–31, 34, 36), encompassing 17,962 melanomas. Considering the 7 papers that studied the same number of days before and after the pandemic (25, 26, 29–31, 34, 36), 4,411 melanomas were treated before and 3,100 after the pandemic, a reduction of 29.7%.

All 3 studies assessing Breslow thickness reported an increase after the pandemic (17, 20, 34). Two studies evaluated ulceration, revealing an increase in the percentage of ulcerated melanomas after the pandemic (34, 36).

Sangers et al. (20) and Tejera-Vaquero et al. (36) assessed the effects on TNM. In both studies T1 melanomas decreased, while T2, T3, and T4 melanomas increased. *In situ* melanomas were only assessed by Tejera-Vaquero et al. (36), observing a reduction after the pandemic.

Long-term effects of COVID-19 pandemic on melanoma

The long-term effects of COVID-19 pandemic on melanoma were studied in 18 papers (**Table III**; 11–20, 24, 26–28, 32, 34, 35, 37), involving 95,974 melanomas. Among studies that include the same number of days in periods studied before and after the pandemic (11–14, 16, 17, 19, 24, 26–28, 30, 32, 34, 35, 37), 40,305 patients underwent surgery before the pandemic and 36,541 afterwards, a decrease of 9.3%. The number of interventions declined in all of these studies, except for 3 of them (14, 35, 37). In the study with the longest time period studied

(12), the drop was from 163 to 138, while the study with the shortest time period studied (35) had a higher number of melanomas operated on after the pandemic, from 22 to 25.

Nine studies evaluated the effects of the pandemic on Breslow thickness (11, 12, 14, 15, 19, 20, 24, 27, 34, 35). In most, Breslow thickness worsened, notably in Martínez-López et al. (19) (1.08 to 2.65) and Jeremic et al. (15) (1.80 to 3.00). Seretis et al. (35), Hurley et al. (14), and in the first post-confinement period of Sangers et al. (20), reported lower Breslow thickness after the pandemic. A meta-analysis of 6 studies found no significant differences between pre-pandemic and pandemic periods, with a mean difference of 0.06 (95% CI, –0.46, 0.58) (**Fig. 2**). Sensitivity analyses demonstrated that excluding studies with a high risk of bias reduced heterogeneity, suggesting that study quality may influence observed heterogeneity. However, excluding studies with small sample sizes did not significantly impact heterogeneity.

Regarding ulceration, 8 studies assessed it (11, 12, 14, 15, 17, 19, 24, 34). All showed an increase in ulcerated melanomas, particularly in Martínez-López et al. (19) (11.7 to 22.6) and Jeremic et al. (15) (33.7 to 44.2), but with the exception of Kostner et al. (17) (21.2 to 20.6). Meta-analysis revealed a higher risk of ulceration in pandemic melanomas, with an odds ratio of 1.35 (95% CI 1.22–1.50) (**Fig. 3**). Sensitivity analyses did not show significant affectation of the heterogeneity.

Six studies evaluated T-value (12, 13, 18, 20, 24, 35). The percentage of *in situ* and T1 melanomas decreased after the pandemic, except for *in situ* melanomas in Jere-

Table I. Study characteristics

Study number	First author	Year of publication	Country	Study design	Quality	Participants	Tumour studied	Outcomes focused
1	Troesch (11)	2023	Switzerland, Germany, Austria, Italy	Cross-sectional	Fair	7865	Melanoma	Long term
2	Abed (12)	2022	Romania	Cohort	Fair	301	Melanoma	Long term
3	Davis (13)	2022	United States	Cohort	Fair	688	Melanoma	Long term
4	Hurley (14)	2022	Ireland	Cross-sectional	Fair	589	Melanoma	Long term
5	Jeremic (15)	2022	Serbia	Cross-sectional	Fair	393	Melanoma	Long term
6	Kleeman (16)	2022	Germany	Cross-sectional	Fair	242,985	Melanoma, KC	Long term
7	Kostner (17)	2022	Switzerland	Cohort	Fair	NR	Melanoma	Short term
8	Lamm (18)	2022	United States	Cross-sectional	Fair	112	Melanoma	Long term
9	Martínez-López (19)	2022	Spain	Cohort	Fair	130	Melanoma	Long term
10	Sangers (20)	2022	Netherlands	Cohort	Fair	89,266	Melanoma, KC	Short term, long term
11	Shahid (21)	2022	United Kingdom	Cross-sectional	Fair	174	KC	Long term
12	Silvia (22)	2022	Italy	Cross-sectional	Fair	214	KC	Long term
13	Slotman (23)	2022	Netherlands	Cross-sectional	Fair	49,040	KC	Short term
14	Ungureanu (24)	2022	Romania	Cohort	Fair	616	Melanoma	Long term
15	Anichini (25)	2021	Italy	Cross-sectional	Poor	5,542	Melanoma	Short term
16	Asai (26)	2021	Canada	Cohort	Fair	6,185	Melanoma, KC	Short term, long term
17	Berry (27)	2021	Australia	Cross-sectional	Poor	NR	Melanoma	Long term
18	Cocuz (28)	2021	Romania	Cross-sectional	Fair	246	Melanoma, KC	Long term
19	Ferrara (29)	2021	Italy	Cross-sectional	Poor	4,158	Melanoma, KC	Short term
20	Filoni (30)	2021	Italy	Cohort	Poor	130	Melanoma	Short term
21	Gualdi (31)	2021	Italy	Cohort	Fair	532	Melanoma	Short term
22	Güven (32)	2021	Turkey	Cross-sectional	Fair	25	Melanoma	Long term
23	Hamel (33)	2021	United States	Cross-sectional	Poor	594	KC	Short term
24	Hoellwerth (34)	2021	Austria	Cross-sectional	Fair	1,365	Melanoma	Short term, long term
25	Seretis (35)	2021	Greece	Cross-sectional	Fair	131	Melanoma, KC	Long term
26	Tejera-Vaquero (36)	2021	Spain	Cohort	Fair	1,758	Melanoma, KC	Short term
27	Valenti (37)	2021	Italy	Case-control	Fair	1,146	Melanoma, KC	Long term

KC: keratinocyte carcinoma.

Table II. Short-term effects of COVID-19 pandemic on melanoma

First author	Hoellwerth (34)			Asai (26)		Ferrara (29)		Sangers (20)		
	Pre-pandemic	Pandemic		Pre-pandemic	Pandemic	Pre-pandemic	Pandemic	Pre-pandemic	Pandemic	
Study period	Pre-pandemic	Pandemic		Pre-pandemic	Pandemic	Pre-pandemic	Pandemic	Pre-pandemic	Pandemic	
Dates of study period	16/03/2018–13/04/2018	16/03/2019–13/04/2019	16/03/2020–13/04/2020	11/03/2019–21/04/2019	09/03/2020–19/04/2020	11/03/2019–19/05/2019 + 12/03/2018–20/05/2018	09/03/2020–17/05/2020	01/01/2019–11/03/2020	12/03/2020–31/05/2020	
Number of days in the study period	28	28	28	41	41	69	69	436	80	
Number of melanomas	32	43	18	323	96	181	92	9,377	1037	
Age, years, mean (SD)	60 ^a	63 ^a	62 ^a	64.54 (15.91)	65.44 (15.12)	NR	NR	62.8 (15.0)	61.5 (16.0)	
Sex, % males/% females	56.3/43.7	41.9/58.1	55.6/44.4	52.9/46.1	59.4/40.6	NR	NR	50.2/49.8	47.7/52.3	
Breslow index, mm, mean (SD)	0.69*	0.58*	0.76*	NR	NR	NR	NR	1.5 (0.02)	1.66 (0.067)	
Ulceration, %	0.00	6.98	18.00	NR	NR	NR	NR	NR	NR	
Mitotic index, mean (SD)	NR	NR	NR	NR	NR	NR	NR	NR	NR	
Tis, %	NR	NR	NR	NR	NR	NR	NR	NR	NR	
T1, %	NR	NR	NR	NR	NR	NR	NR	58.6	52.3	
T2, %	NR	NR	NR	NR	NR	NR	NR	17.8	18.9	
T3, %	NR	NR	NR	NR	NR	NR	NR	11.0	13.2	
T4, %	NR	NR	NR	NR	NR	NR	NR	7.3	9.1	
Stage 0, %	NR	NR	NR	NR	NR	NR	NR	NR	NR	
Stage I, %	NR	NR	NR	NR	NR	NR	NR	NR	NR	
Stage II, %	NR	NR	NR	NR	NR	NR	NR	NR	NR	
Stage III, %	NR	NR	NR	NR	NR	NR	NR	NR	NR	
Stage IV, %	NR	NR	NR	NR	NR	NR	NR	NR	NR	
First author	Filoni (31)		Anichini (25)		Tejera-Vaquerizo (36)		Gualdi (31)	Kostner (17)		
Study period	Pre-pandemic	Pandemic	Pre-pandemic	Pandemic	Pre-pandemic	Pandemic	Pre-pandemic	Pandemic	Pre-pandemic	
Dates of study period	23/02/2019–21/05/2019	23/02/2020–21/05/2020	01/02/2019–30/04/2019	01/02/2020–30/04/2020	14/03/2019–13/06/2019	14/03/2020–13/06/2020	01/05/2017–31/07/2017 + 01/05/2018–31/07/2018 + 01/05/2019–31/07/2019	01/05/2020–31/07/2020	01/02/2019–15/03/2020	16/03/2020–22/06/2020
Number of days in the study period	87	88	89	90	91	91	93	93	409	98
Number of melanomas	66	64	3,156	2,386	352	207	295	237	NR	NR
Age, years, mean (SD)	NR	NR	NR	NR	64.0 (16.4)	62.9 (16.7)	NR	NR	NR	NR
Sex, % males/% females	NR	NR	NR	NR	44.3/55.7	57.5/42.5	NR	NR	NR	NR
Breslow index, mm, mean (SD)	NR	NR	NR	NR	NR	NR	NR	NR	1.2 (0.6–2.6)	1.4 (0.7–3.0)
Ulceration, %	NR	NR	NR	NR	13.9	20	NR	NR	NR	NR
Mitotic index, mean (SD)	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Tis, %	NR	NR	NR	NR	34.9	29.0	NR	NR	NR	NR
T1, %	NR	NR	NR	NR	31	26.6	NR	NR	NR	NR
T2, %	NR	NR	NR	NR	12.2	14.5	NR	NR	NR	NR
T3, %	NR	NR	NR	NR	11.6	11.6	NR	NR	NR	NR
T4, %	NR	NR	NR	NR	10.2	18.4	NR	NR	NR	NR
Stage 0, %	NR	NR	NR	NR	34.9	20.9	NR	NR	NR	NR
Stage I, %	NR	NR	NR	NR	39.7	36.7	NR	NR	NR	NR
Stage II, %	NR	NR	NR	NR	18.2	24.6	NR	NR	NR	NR
Stage III, %	NR	NR	NR	NR	5.7	8.2	NR	NR	NR	NR
Stage IV, %	NR	NR	NR	NR	1.7	1.4	NR	NR	NR	NR

SD: standard deviation; NR: not reported; ^amedian (range).

mic et al. (15), and T1 in Seretis et al. (35), Guven et al. (32), and the fourth period of Sangers et al. (20) (which corresponds to the second period of confinement in the Netherlands). T2, T3, and T4 tumours increased in all cases, except for Sangers et al. (20). Regarding tumour staging, the percentage of advanced tumours (stage III and IV) increased. In Hurley et al. (14), the percentage of metastatic melanomas decreased after the pandemic and in Sangers et al. (20) the data varied according to the period studied after the pandemic.

Short-term effects of COVID-19 pandemic on keratinocyte carcinomas

A total of 96,313 tumours were analysed in 6 studies (Table IV; 20, 23, 26, 29, 33, 36). Six studies focused on squamous cell carcinoma (SCC), 2 focus on SCC and basal cell carcinoma (BCC) and 2 studies do not specify the tumour type. Among studies considering the same

number of days before and after the pandemic (23, 26, 29, 33, 36), 39,407 tumours underwent surgery before and 19,389 afterwards, indicating a 50.8% reduction.

The invasion depth was only assessed in SCC in Sangers et al. (20). Sangers et al. (20) and Tejera-Vaquerizo et al. (36) considered the T-value, observing a decrease in the percentage of T1 tumours and an increase in the percentage of T2, T3, and T4 tumours after the pandemic.

Long-term effects of COVID-19 pandemic on keratinocyte carcinomas

A total of 247,263 tumours were analysed in 7 studies (Table V; 16, 20–22, 28, 35, 37). Five studies focused on SCC, 1 focused on SCC and BCC and 3 do not specify the tumour type. Among studies considering an equal number of days before and after the pandemic (16, 21–23, 28, 35, 37), 99,570 tumours underwent sur-

Table III. Long-term effects of COVID-19 on melanoma

First author	Seretis (35)		Berry (27)		Lamm (18)		Hurley (14)	
Study period	Pre-pandemic	Pandemic	Pre-pandemic	Pandemic	Pre-pandemic	Pandemic	Pre-pandemic	Pandemic
Dates of study period	20/05/2019–20/09/2019	20/05/2020–20/09/2020	01/04/2017–31/08/2017, 01/04/2018–31/08/2018, 01/04/2019–31/08/2019	01/04/2020–31/08/2020	01/05/2019–30/04/2020	01/05/2020–30/09/2021	01/03/2019–31/12/2019	01/03/2020–31/12/2020
Number of days in the study period	123	123	153	153	366	153	306	306
Number of melanomas	22	25	NR	NR, 48% less than pre-pandemic period	51	61	277	312
Age, years, mean (SD)	66.23 (13.97)	63.64 (18.19)	NR	NR	61.3 (2.09)	63.0 (1.98)	68.5 (25–96) ^a	63.1 (24–91) ^a
Sex, % males/ % females	81.8/18.2	44.0/56.0	NR	NR	62.7/37.3	52.5/47.5	49.5/50.5	46.8/53.2
Breslow index, mm, mean (SD)	6.88 (2.10) ^b	1.31 (0.59) ^c	2.06	2.70	NR	NR	3.11 (3.65)	2.60 (3.16)
Ulceration, %	NR	NR	NR	NR	NR	NR	22.7	29.9
Mitotic index, mean (SD)	NR	NR	NR	NR	NR	NR	1.60 (3.95)	2.29 (4.98)
Tis, %	37.5 ^d	1.1 ^e	18.3	7.5	9.8	4.9	NR	NR
T1, %	12.5 ^d	55.6 ^e	NR	NR	43.1	26.2	NR	NR
T2, %	0.0 ^d	22.2 ^e	NR	NR	29.4	34.4	NR	NR
T3, %	0.0 ^d	11.1 ^e	NR	NR	9.8	19.7	NR	NR
T4, %	50.0 ^d	0.0 ^e	NR	NR	7.8	14.8	NR	NR
Stage 0, %	NR	NR	NR	NR	9.8	3.2	NR	NR
Stage I, %	NR	NR	NR	NR	41.2	27.9	NR	NR
Stage II, %	NR	NR	NR	NR	15.7	8.2	NR	NR
Stage III, %	NR	NR	NR	NR	2	11.5	NR	NR
Stage IV, %	NR	NR	NR	NR	3.8	0.0	5.78	3.21
First author	Cocuz (28)		Kleeman (16)		Jeremic (15)		Kostner (18)	
Study period	Pre-pandemic	Pandemic	Pre-pandemic	Pandemic	Pre-pandemic	Pandemic	Pre-pandemic	Pandemic
Dates of study period	01/04/2019–29/02/2020	01/04/2020–28/02/2021	18/03/2019–17/03/2020	18/03/2020–17/03/2021	01/01/2017–14/03/2020	15/03/2020–31/03/2022	01/02/2019–16/03/2020	17/03/2020–30/04/2021
Number of days in the study period	335	334	366	365	1169	381	410	410
Number of melanomas	40	10	31,910	29,822	339	54	655	585
Age, years, mean (SD)	NR	NR	NR	NR	64.5 (15.8)	65.7 (15.3)	63.9 (15.3)	64.2 (15.2)
Sex, % males/ % females	NR	NR	NR	NR	55.8/44.2	55.6/44.4	60.6/39.4	58.8/41.2
Breslow index, mm, mean (SD)	2.06	2.70	NR	NR	1.80 (0.65–4.30) ^a	3.00 (1.50–5.30) ^a	2.23 (3.14)	2.23 (3.26)
Ulceration, %	NR	NR	NR	NR	33.7	44.2	21.2	20.6
Mitotic index, mean (SD)	NR	NR	NR	NR	2 (0–5) ^a	5 (1–12) ^a	NR	NR
Tis, %	NR	NR	9.80	7.94	NR	NR	NR	NR
T1, %	NR	NR	NR	NR	NR	NR	NR	NR
T2, %	NR	NR	NR	NR	NR	NR	NR	NR
T3, %	NR	NR	NR	NR	NR	NR	NR	NR
T4, %	NR	NR	NR	NR	NR	NR	NR	NR
Stage 0, %	NR	NR	NR	NR	16.8	20.4	NR	NR
Stage I, %	NR	NR	NR	NR	30.4	14.8	54.7	58.2
Stage II, %	NR	NR	NR	NR	15.0	11.1	22.0	18.8
Stage III, %	NR	NR	NR	NR	15.0	24.1	17.4	20.4
Stage IV, %	NR	NR	NR	NR	22.7	29.6	5.8	2.6
First author	Sangers (20)		Valenti (37)		Davis (13)		Asai (26)	
Study period	Pre-pandemic	Pandemic (post-first lockdown)	Pre-pandemic	Pandemic	Pre-pandemic	Pandemic	Pre-pandemic	Pandemic
Dates of study period	01/01/2019–11/03/2020	01/06/2020–13/10/2020	18/05/2019–18/11/2019	18/05/2020–18/11/2020	01/08/2019–31/03/2020	01/05/2020–31/12/2020	7/01/2019–29/09/2019	6/01/2020–27/09/2020
Number of days in the study period	436	135	184	184	244	245	265	265
Number of melanomas	9,377	3,532	224	237	375	313	1,399	804
Age, years, mean (SD)	62.8 (15.0)	63.1 (15.0)	64.3	65.4	65.7	67	NR	NR
Sex, % males/ % females	50.2/49.8	48.9/51.1	NR	NR	NR	NR	NR	NR
Breslow index, mm, mean (SD)	1.50 (0.02)	1.48 (0.03)	NR	NR	NR	NR	NR	NR
Ulceration, %	NR	NR	NR	NR	NR	NR	NR	NR
Mitotic index, mean (SD)	NR	NR	NR	NR	NR	NR	NR	NR
Tis, %	NR	NR	NR	NR	17.9	15.3	NR	NR
T1, %	58.6	58.1	NR	NR	55.8	42.8	NR	NR
T2, %	17.8	18.0	NR	NR	16.5	16.3	NR	NR
T3, %	11.0	11.4	NR	NR	7.2	9.6	NR	NR
T4, %	7.3	5.9	NR	NR	0.3	1.6	NR	NR
Stage 0, %	NR	NR	NR	NR	NR	NR	NR	NR
Stage I, %	NR	NR	NR	NR	NR	NR	NR	NR
Stage II, %	NR	NR	NR	NR	NR	NR	NR	NR
Stage III, %	NR	NR	NR	NR	NR	NR	NR	NR
Stage IV, %	NR	NR	NR	NR	NR	NR	NR	NR

Table III. Continued.

First author	Guven (32)		Martínez-López (19)		Ungureanu (24)	
Study period	Prepandemic	Pandemic	Pre-pandemic	Pandemic	Pre-pandemic	Pandemic
Dates of study period	01/03/2019–31/12/2019	01/03/2020–31/12/2020	15/03/2019–14/03/2020	15/03/2020–14/03/2021	01/03/2019–29/02/2020	01/03/2020–28/02/2021
Number of days in the study period	306	306	366	365	366	365
Number of melanomas	15	10	77	53	341	275
Age, years, mean (SD)	NR	NR	63.31 (1.88)	65.02 (2.27)	59	63
Sex, % males/ % females	NR	NR	44.2/55.8	43.4/56.6	48.1/51.9	50.2/49.8
Breslow index, mm, mean (SD)	NR	NR	1.08 (0.28)	2.65 (0.34)	1.37 (0.5–3.5) ^a	2.20 (0.70–5.11) ^a
Ulceration, %	NR	NR	11.7	22.6	32.8	40.7
Mitotic index, mean (SD)	NR	NR	1.40 (0.56)	3.58 (0.69)	3 (1–7) ^a	4 (1–10) ^a
Tis, %	NR	NR	NR	NR	17.3	14.2
T1, %	NR	NR	NR	NR	32.8	25.9
T2, %	NR	NR	NR	NR	13.5	12.8
T3, %	NR	NR	NR	NR	17.6	15.2
T4, %	NR	NR	NR	NR	18.4	30.2
Stage 0, %	NR	NR	39.0	17.0	NR	NR
Stage I, %	6.7	10.0	37.7	37.7	NR	NR
Stage II, %	26.7	10.0	11.7	22.6	NR	NR
Stage III, %	33.3	40.0	10.4	20.8	NR	NR
Stage IV, %	33.3	40.0	1.3	1.9	NR	NR

First author	Hoellwerth (35)			Troesch (11)		Aabed (12)			
Study period	Pre-pandemic	Pre-pandemic	Pandemic	Pandemic (second lockdown)	Pandemic (post-second lockdown)	Pre-pandemic	Pandemic	Pre-pandemic	Pandemic
Dates of study period	2018	2019	2020	14/10/2020–27/04/2021	28/04/2021–22/07/2021	01/09/2018–16/03/2020 ^f	17/03/2020 ^f –31/08/2021	01/01/2018–31/12/2019	01/01/2020–31/12/2022
Number of days in the study period	365	365	366	225	146	563	549	730	731
Number of melanomas	428	505	432	4,049	2,439	4,340	3,525	163	138
Age, years, mean (SD)	61	60	63	64.2 (15.0)	63.5 (15.0)	62.3 (16.2)	63.4 (15.6)	58.1 (16.3)	58.8 (15.9)
Sex, % males/ % females	53.3/46.7	51.5/48.5	54.0/46.0	50.6/49.4	46.4/53.6	53.0/47.0	53.0/47.0	53.4/46.6	50.7/49.3
Breslow index, mm, mean (SD)	0.65	0.6	0.7	1.51 (0.04)	1.59 (0.05)	1.02 (1.91)	1.25 (2.51)	1.1 (0.4)	1.8 (0.5)
Ulceration, %	4.91	4.36	8.33	NR	NR	10.0	13.0	17.2	24.6
Mitotic index, mean (SD)	NR	NR	NR	NR	NR	NR	NR	NR	NR
Tis, %	NR	NR	NR	NR	NR	NR	NR	3.7	2.2
T1, %	NR	NR	NR	59.0	58.2	NR	NR	19.0	9.4
T2, %	NR	NR	NR	16.0	18.7	NR	NR	30.1	20.3
T3, %	NR	NR	NR	10.3	9.2	NR	NR	44.2	56.5
T4, %	NR	NR	NR	7.6	8.0	NR	NR	3.1	11.6
Stage 0, %	NR	NR	NR	NR	NR	38.0	35.0	3.7	2.2
Stage I, %	NR	NR	NR	NR	NR	34.0	33.0	12.3	6.5
Stage II, %	NR	NR	NR	NR	NR	13.0	13.0	25.8	11.6
Stage III, %	NR	NR	NR	NR	NR	8.0	10.0	55.2	68.1
Stage IV, %	NR	NR	NR	NR	NR	6.0	8.0	3.1	11.6

SD: standard deviation; NR: not reported; ^amedian (range); ^b5 patients analysed; ^c8 patients analysed; ^d8 patients analysed; ^e9 patients analysed; ^fdifferent dates for the end of the pre-pandemic period, and therefore the start of the pandemic period, depending on the first confirmed case in each country included in the study.

gery before and 83,036 after the pandemic, indicating a 16.6% reduction.

Shahid et al. (21) reported an increase in median invasion depth after the pandemic. Conversely, in Sangers et al. (20), all post-pandemic values across different periods were lower compared with the median invasion depth in pre-pandemic SCC. Kleemann et al. (16) noted a decrease

in the percentage of in situ KC, from 3.8% to 3.4%. No other study assessed changes in in situ tumours. T-value was evaluated in 3 studies, with Shahid et al. (21) and Seretis et al. (35) reporting a decrease in T1 SCC and an increase in T2, T3, or T4 tumours after the pandemic. However, in Sangers et al. (20) values were very similar pre-pandemic and in different pandemic periods. Valenti

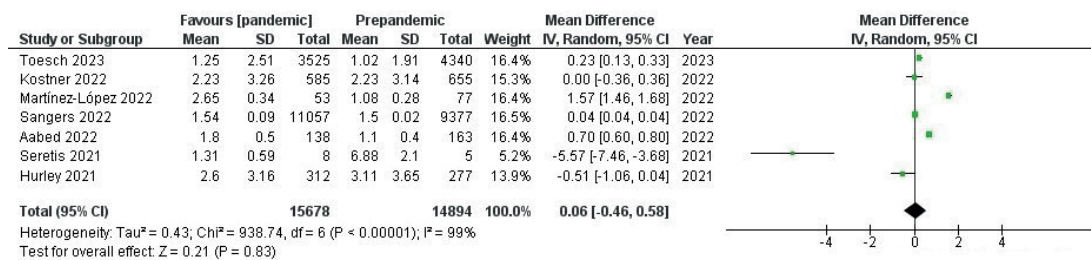


Fig. 2. Forest plot of Breslow thickness differences in papers studying long-term changes in melanoma.

Study or Subgroup	Pandemic		Prepandemic		Weight	Odds Ratio		Year
	Events	Total	Events	Total		M-H, Fixed, 95% CI	Year	
Toesch 2023	458	3525	434	4340	55.3%	1.34	[1.17, 1.55]	2023
Aabed 2022	34	138	28	163	3.2%	1.58	[0.90, 2.76]	2022
Jeremic 2022	24	54	114	339	2.8%	1.58	[0.88, 2.83]	2022
Kostner 2022	139	655	120	585	16.3%	1.04	[0.79, 1.37]	2022
Martínez-López 2022	12	53	9	77	0.9%	2.21	[0.86, 5.70]	2022
Ungureanu 2022	112	275	112	341	9.7%	1.40	[1.01, 1.95]	2022
Hoellwerth 2021	36	432	43	933	4.1%	1.88	[1.19, 2.98]	2021
Hurley 2021	93	312	63	277	7.7%	1.44	[1.00, 2.09]	2021
Total (95% CI)		5444		7055	100.0%	1.35	[1.22, 1.50]	
Total events	908		923					
Heterogeneity: $\chi^2 = 7.18$, $df = 7$ ($P = 0.41$); $I^2 = 3\%$								
Test for overall effect: $Z = 5.71$ ($P < 0.00001$)								

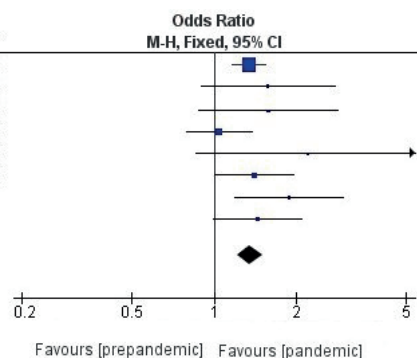


Fig. 3. Forest plot of ulceration in papers studying long-term changes in melanoma.

et al. (37) was the only one to assess the high-risk status of SCC, observing an increase from 1.1% to 5.0% after the pandemic.

DISCUSSION

In the short term, skin tumour diagnoses notably decreased, especially during widespread lockdowns (38). KC showed more significant reductions than melanomas, likely because healthcare centres prioritised melanoma treatment (39).

Hospital saturation during peak pandemic periods, primarily focused on COVID-19 care, diverted resources from conditions like skin cancer (3). Conversely, patients' fear of consultation was proposed as a determinant in delayed skin cancer diagnosis. In Tejera-Vaquero et al. (36), focusing on the months of general confinement in Spain, fear of SARS-CoV-2 infection was reported as a predictor of SCC diameter in multivariate analysis. Two surveys on changes in melanoma treatment during the pandemic observed a low percentage of alterations, mostly by patient choice. Fear of SARS-CoV-2 and mental health problems, particularly anxiety disease, were reported as the main causes (4).

Other non-cutaneous tumours experienced a reduction in post-pandemic diagnoses, with even breast, colorectal, and prostate cancer screening programmes being affected. This has been linked to poorer prognostic data at diagnosis (40).

Following confinements, various studies reported an increase in skin tumour diagnoses compared with previous years (23, 34). Patients who did not consult during confinement delayed their consultation until after the confinement. However, in the long term, we have observed a decrease in the number of skin tumours diagnosed. A more significant reduction was seen in KC (16.6%), compared with melanomas (9.3%).

During the first pandemic months, we observed poorer invasion depth and staging data. Following recommendations to prioritise surgeries for tumours with poorer prognosis, those with better prognosis were possibly delayed until hospital saturation allowed for interventions. Consequently, there was a relative increase in

tumours with higher invasion depth and worse stage. As reported by Tejera-Vaquero et al. (36), although the same number of SCC larger than 4 cm were operated on during the 3 months of confinement in Spain as in the 3 months before, these tumours accounted for a higher proportion of the total number of tumours operated on during confinement.

In the long term, we continue to observe worse prognostic data. Tumours with delayed diagnoses during confinement and those with treatment delayed in favour of tumours with a worse prognosis had a longer evolution time. Studies reported a median delay of 21 days from presentation to diagnosis for melanoma and 57 days for SCC (12, 21).

Time of tumour progression is a well-known factor associated with worse prognostic outcomes (41). A delay in melanoma diagnosis is associated with reduced survival rates and an increased demand for more intricate and less cost-effective procedures, including selective sentinel lymph node biopsy, positron emission tomography, or systemic treatment (12, 19, 42). Similarly, KC with an extended evolution time may need more complex surgical techniques with higher complication rates, such as flaps or skin grafts, or even other treatments like adjuvant radiotherapy or systemic therapies, although the impact on survival may not be as pronounced (7).

In papers studying both the short- and long-term effects of the pandemic, Hoellwerth et al. (34) found a 50% reduction in melanoma surgeries during the pandemic in an Austrian hospital and, in the long term, higher Breslow thickness and more ulcerated melanomas. Sangers et al. (20), conversely, noted more aggressive melanomas and SCC during the initial Dutch confinement, but no significant long-term pandemic impact, suggesting that slower-growing tumours' diagnoses were delayed, but not fast-growing ones. Two nationwide lockdowns were implemented in the Netherlands in 2020 and 2021 and routine care was downscaled. Furthermore, our meta-analysis showed no significant Breslow thickness worsening post-pandemic, unlike ulceration, possibly due to data heterogeneity across selected papers. As Martínez-López et al. (19) observed, ulceration correlates with higher Breslow thickness (43).

Table IV. Short term effects of COVID-19 pandemic on keratinocyte carcinomas [AQ4]

First author	Asai (26)		Hamel (34)		Ferrara (29)			
Study period	Pre-pandemic	Pandemic	Pre-pandemic		Pandemic	Pre-pandemic	Pandemic	
Dates of study period	11/03/2019–21/04/2019	09/03/2020–19/04/2020	11/01/2020–10/03/2020		11/03/2020–09/05/2020	11/03/2019–19/05/2019, 12/03/2018–20/05/2018	09/03/2020–17/05/2020	
Number of days in the study period	41	41	59		59	69	69	
Tumour studied	Not specified		SCC	BCC	SCC	BCC	Not specified	
Number of tumours	4,731	1,035	185	181	149	79	1,689	508
Age, years, mean (SD)	71.4 (13.6)	68.9 (13.0)	NR	NR	NR	NR	NR	NR
Sex, % males/ % females	54.75/45.25	60.58/39.42	NR	NR	NR	NR	NR	NR
Breslow index, mm, mean (SD)	NR	NR	NR	NR	NR	NR	NR	NR
Tis, %	NR	NR	NR	NR	NR	NR	NR	NR
T1, %	NR	NR	NR	NR	NR	NR	NR	NR
T2, %	NR	NR	NR	NR	NR	NR	NR	NR
T3, %	NR	NR	NR	NR	NR	NR	NR	NR
T4, %	NR	NR	NR	NR	NR	NR	NR	NR

First author	Sangers (20)		Tejera-Vaquerizo (36)		Slotman (23)			
Study period	Pre-pandemic	Pandemic	Pre-pandemic	Pandemic	Pre-pandemic	Pandemic		
Dates of study period	1/01/2019–11/03/2020	12/03/2020–31/05/2020	14/03/2019–13/06/2019	14/03/2020–13/06/2020	01/03/2017–31/05/2017, 01/03/2018–31/05/2018, 01/03/2019–31/05/2019	01/03/2020–31/05/2020		
Number of days in the study period	436	80	91	91	92	92		
Tumour studied	SCC		SCC		SCC	BCC	SCC	BCC
Number of tumours	31,654	4,175	770	429	6,017	25,834	4,272	12,917
Age, years, mean (SD)	76.8 (10.5)	76.4 (10.2)	79.8 (10.9)	79.0 (11.3)	NR	NR	NR	NR
Sex, % males/ % females	57.5/42.5	58.6/41.4	67.53/32.47	63.64/36.36	NR	NR	NR	NR
Breslow index, mm, mean (SD)	3.09 (2.05)	3.19 (2.03)	NR	NR	NR	NR	NR	NR
Tis, %	NR	NR	NR	NR	NR	NR	NR	NR
T1, %	74.1	73.4	70.1	54.5	NR	NR	NR	NR
T2, %	5.6	5.7	11.9	14.2	NR	NR	NR	NR
T3, %	7.3	8.6	16.7	29.6	NR	NR	NR	NR
T4, %	0.0	0.0	1.3	1.6	NR	NR	NR	NR

SD: standard deviation; NR: Not reported; SCC: squamous cell carcinoma; BCC: basal cell carcinoma.

Regarding countries' strategies, lockdowns and restrictions led to a significant reduction in medical activities, including skin cancer screenings (44). Studies from Canada and Italy reported 70% and 50% reduction in melanoma diagnoses during strict lockdown, respectively, emphasizing the correlation between delayed diagnosis and poor prognosis (26, 29). However, other studies from Italy and the Netherlands showed prompt management of severe cases, maintaining continuity in healthcare services (20, 25, 30). Collateral damage from containment measures underscores the need for adaptable healthcare delivery. Therefore, screening and management of skin cancer should persist with appropriate precautions during future pandemics. Notably, teleconsultation became widespread during the pandemic, proving useful in keeping patients in consultation and avoiding unnecessary travel. However, there is a risk of under-diagnosis, as total body examinations may be lost. Furthermore, providing health promotion and prevention information through tele dermatology is challenging. The impact of teleconsultation on skin cancer prognosis during the pandemic remains unclear and warrants assessment in future research (45).

Strengths

The study contributes significantly to the literature by addressing a timely and relevant topic, investigating the impact of the COVID-19 pandemic on melanoma and KC outcomes. It is the first systematic review to ana-

lyse the impact of COVID-19 pandemic on skin cancer beyond melanoma, using real-world data and adding a meta-analysis. Overall, the study fills a gap in our understanding of the impact of the COVID-19 pandemic on skin cancer and provides useful insights for healthcare professionals and policymakers.

Limitations

The COVID-19 pandemic is an ongoing situation and there may not yet be sufficient long-term data available to fully assess its impact on skin cancer outcomes. The studies included in our review were conducted mainly in Europe and North America, limiting generalisations, as no studies from Asia, South America, or Africa were included. Moreover, the varied implementation of pandemic measures across regions hinders comparisons across studies.

Most of the studies we included are retrospective and with a cross-sectional design, impacting their level of evidence. Additionally, none of the studies reached the "good" category in our quality assessment. Experimental studies to determine the real effects of the pandemic on skin cancer would not be possible, and skin cancer outcomes can be influenced by various factors, making it challenging to separate the effects of the pandemic from other variables, such as patient age, tumour stage, and comorbidities. Heterogeneity in variables and in study periods limits comparability across studies. Furthermore, combining BCC and SCC in the analysis might

Table V. Long-term effects of COVID-19 pandemic on keratinocyte carcinomas

First author	Shahid (21)		Silvia (22)		Seretis (35)		Valenti (38)		
Study period	Pre-pandemic	Pandemic	Pre-pandemic	Pandemic	Pre-pandemic	Pandemic	Pre-pandemic	Pandemic	
Dates of study period	01/10/2019–31/10/2019	01/10/2020–31/10/2020	01/12/2019–31/01/2020	01/12/2020–31/01/2021	20/05/2019–20/09/2019	20/05/2020–20/09/2020	18/05/2019–18/11/2019	18/05/2020–18/11/2020	
Number of days in the study period	31	31	62	62	123	123	184	184	
Tumour studied	SCC		Not specified		SCC		SCC		
Number of tumours	74	199	121	93	29	55	461	224	
Age, years, mean (SD)	81.4 (9.3)	81.0 (9.5)	NR	NR	77.21 (11.58)	77.82 (10.40)	64.3	65.4	
Sex, % males/ % females	58.73/41.27	72.73/27.27	NR	NR	72.41/27.59	72.73/27.27	51.79/48.21	56.96/43.03	
Breslow index, mm, mean (SD)	NR	NR			NR	NR	NR	NR	
Tis, %	NR	NR			NR	NR	NR	NR	
T1, %	45.9	31.3			55.2	52.7	NR	NR	
T2, %	52.7	61.5			31.0	34.5	NR	NR	
T3, %	1.4	6.3			10.3	12.7	NR	NR	
T4, %	0.0	1.0			3.4	0.0	NR	NR	
First author	Cocuz (28)								
Study period	Pre-pandemic				Pandemic				
Dates of study period	01/04/2019–29/02/2020				01/04/2020–28/02/2021				
Number of days in the study period	335	81	31	334	28	6			
Tumour studied	SCC	BCC	Basosquamous carcinoma	SCC	BCC	Basosquamous carcinoma			
Number of tumours	39			11					
Age, years, mean (SD)	NR	NR	NR	NR	NR	NR			
Sex, % males/ % females	NR	NR	NR	NR	NR	NR			
Breslow index, mm, mean (SD)	NR			NR					
Tis, %	NR			NR					
T1, %	NR			NR					
T2, %	NR			NR					
T3, %	NR			NR					
T4, %	NR			NR					
First author	Kleeman (16)			Sangers (20)					
Study period	Pre-pandemic		Pandemic		Pre-pandemic		Pandemic (post-first lockdown)	Pandemic (second lockdown)	Pandemic (post-second lockdown)
Dates of study period	18/03/2019–17/03/2020		18/03/2020–17/03/2021		01/01/2019–17/03/2020	01/06/2020–13/10/2020	14/10/2020–27/04/2021	28/04/2021–22/07/2021	28/04/2021–22/07/2021
Number of days in the study period	366		365		436	135	225	146	146
Tumour studied	Not specified		Not specified		SCC	SCC	SCC	SCC	SCC
Number of tumours	98734		82519		31654	11541	14930	6532	6532
Age, years, mean (SD)	NR		NR		76.8 (10.5)	77.2 (10.2)	77.2 (10.3)	77.2 (10.0)	77.2 (10.0)
Sex, % males/ % females	58.4/41.2, 53.8/46.2 ^a		58.9/41.1, 55.3/44.7 ^a		57.5/42.5	56.4/43.6	58.2/41.8	56.8/43.2	56.8/43.2
Breslow index, mm, mean (SD)	NR		NR		NR	NR	NR	NR	NR
Tis, %	3.8		3.4		NR	NR	NR	NR	NR
T1, %	NR		NR		74.1	73.0	74.0	73.4	73.4
T2, %	NR		NR		5.6	5.6	6.2	6.2	6.2
T3, %	NR		NR		7.3	6.9	6.8	6.1	6.1
T4, %	NR		NR		0.0	0.0	0.1	0.0	0.0

SD: standard deviation; NR: not reported; SCC: squamous cell carcinoma; BCC: basal cell carcinoma; ^asex reported for invasive tumours and non-invasive tumours.

introduce limitations. BCC typically exhibits a slower growth rate, rarely metastasizes and may not have been significantly impacted by the pandemic. Finally, we acknowledge that many studies in the literature were excluded from our review, particularly letters to the editor, which may limit the assessment of methodology and quality of evidence.

In conclusion, our review indicates that the COVID-19 pandemic has had a significant impact on skin cancer outcomes. Despite limitations in the reviewed studies, they provide valuable insights into the effects of the pandemic on skin cancer. The results suggest that the pandemic may have led to delays in skin cancer diagnosis and treatment, which may ultimately affect patient outcomes. However, further research is needed to fully understand the long-term effects of the pandemic on skin cancer outcomes and to identify strategies for mitigating its impact.

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Data sharing is not applicable to this article as no datasets were generated or analysed during the current study.

The authors have no conflicts of interest to declare.

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