Exploring melanoma shifts: a two-decade analysis in New Zealand

Daniel Wen, Jack S Pullman, Avinash Sharma, Bert van der Werf, Richard C W Martin

ABSTRACT

AIMS: New Zealand melanoma incidence rates are amongst the highest in the world. The study aims to provide information on the incidence of cutaneous melanoma in New Zealand from 2000 to 2022.

METHODS: De-identified data were extracted from the New Zealand Cancer Registry using the ICD-10 code for malignant melanoma (C34) and melanoma *in situ* (MIS) (D03) from 2000 to 2022. Statistical analysis was performed to calculate melanoma incidence rates.

RESULTS: Invasive melanoma (IM) incidence rates demonstrated an increasing trend from 2000 to 2008 (+1.10 per 100,000 person-years per year), followed by an inflection point at 2008 and then a decreasing trend from 2008 to 2022 (-0.28 per 100,000 person-years per year), which was not statistically different from zero/no change. MIS incidence increased from 30.3 to 72.1 per 100,000 person-years between 2000 and 2022.

CONCLUSIONS: The incidence of IM in New Zealand has plateaued in the last decade and was associated with an increase in MIS incidence over the same period. While this trend is encouraging, further research is required to investigate whether there is an actual decline in IM incidence.

World-wide cutaneous melanoma incidence has been increasing over time, with 324,635 new cases diagnosed in 2020.[1] New Zealand melanoma incidence rates are among the highest in the world and, in New Zealand, melanoma is the third most common cancer among both females and males. It ranks only behind breast and colorectal cancers in females, and prostate and colorectal cancers in males.[2]

The historical increase in invasive melanoma (IM) incidence rates has recently been slowing, and was expected to peak—and even reduce—by 2016.[3] This effect has been attributed to the maturity of mass prevention campaigns and the corresponding change in behaviour towards skin protection.[4]

Increase in melanoma thickness at presentation is associated with poorer prognosis.[5] Previous New Zealand data have shown an increase over time in the thickness of melanoma at presentation.[6,7] This differs from studies in the United States that show a decrease in Breslow thickness over time, possibly reflecting earlier detection.[8]

While the management of melanoma is an ever-evolving field, understanding of the latest trends in incidence are important to guide national and regional decision making. We examined melanoma incidence in previous studies covering the 1995–1999 and 2000–2004 periods.[6,7]

The study aims to provide the most recent information on the incidence of cutaneous melanoma in New Zealand by analysing data from the New Zealand Cancer Registry (NZCR) from 2000 to 2022.

Methods

Data collection

De-identified data were obtained from the NZCR by way of a systematic computerised search of the ICD-10 code for malignant melanoma (C34) from 2000 to 2022. Statutory notification of cancer in New Zealand has been present since 1994. The information obtained included: gender, age at diagnosis, year of diagnosis, district health board (DHB) of domicile and Breslow thickness. Ethnicity and mortality data were not recorded for this study and the authors intend to perform a separate analysis based on these parameters in a future analysis. Melanoma T-Stage was calculated using the American Joint Committee on Cancer (AJCC) 8th Edition staging system.[9] A second computerised search of the ICD-10 code for melanoma *in situ* (MIS) (D03) was performed to give overall incidence comparison data.

Inclusion criteria were all melanoma registrations from 2000 to 2022 according to ICD-10 code. Only one registration per person was included to avoid cases of metastatic melanoma. The New Zealand Census is performed every 5 years and has accounted for 97.4–98.0% of the population across

the three most recent censuses. New Zealand census data was retrieved from Stats NZ and population data from the 2006, 2013 and 2018 censuses was used in the statistical analysis.[10–12]

Statistical methods

All calculations were done using the statistical package R, version 4.1.1.[13] Age-standardised incidence rates for IM and MIS were calculated with standardisation to the US2000 standard population and confidence intervals [CI] were calculated with the Tiwari method using the R package dsrTest.[14] The overall trends for IM and MIS incidence were analysed using Joinpoint trend analysis software version 5.01.[15] The population data used for these calculations include the 2006, 2013 and 2018 census data with use of linear interpolation for the years between censuses.

A mixed-effect logistic regression model was used to: estimate the absolute IM and T-stage incidence rate for every 5-year age band; investigate the association between IM and MIS incidence; and examine the interactions of other variables such as domicile DHB. The best-fitted model between alternative models was identified using the minimum Akaike information criterion (AIC) value and the significance of variables was analysed using the Type II Wald Chi-squared test.[16] For all analyses, the assumptions of homogeneity of variances and normality of residuals were checked using the R package DHARMa.[17]

The median Breslow thickness per year was estimated by back transformation of data fitted on the logarithmic scale with a linear mixed-effect model. The logarithmically transformed values of the Breslow thickness were used to meet the analysis's assumptions: homogeneity of variances and normality of residuals. The same analysis was performed for Breslow thickness for each 5-year age band.

Results

There were 52,933 registered cases of IM between 2000 and 2022. All cases were included for analysis; however, 3,909 cases did not include a Breslow depth and therefore were excluded from Breslow thickness analyses but otherwise were included in all other analyses. Of these IM patients, 28,351 (53.6%) were male. The median age at diagnosis for females was 63.0 years (range 1–104 years), and 67.0 years (range 10–103 years) for males. Over the same period, 58,948 cases of MIS were registered.

Age-standardised incidence rate for IM and MIS

IM incidence rates demonstrated an increasing trend from 2000 to 2008 (+1.10 per 100,000 person-years per year), followed by an inflection point at 2008 and then a decreasing trend from 2008 to 2022 (-0.28 per 100,000 person-years per year), which was not statistically different from zero/no change. Over the study period there was a statistically significant increase in MIS incidence rates. MIS incidence increased from 30.3 per 100,000 person-years (95% CI 28.6–32.2 per 100,00 person-years) in 2000 to 72.1 per 100,000 person-years (95% CI 70.0–74.3 per 100,00 person-years) in 2022. Further details are available in Figure 1 and 2.

Gender

There was a significant difference in incidence rates between males and females (Figure 3). Trends show a similar incidence below the age of 60, with females having a slightly higher incidence between ages 25–50. After the age of 60, males had a significantly higher incidence than females ($p<0.01$).

Breslow thickness

The statistical model suggested that median Breslow thickness was reducing over the last 8–10 years of the study period (Figure 4). Across the entire study period, the median Breslow thickness was greater for males (0.80mm) than females (0.70mm).

T-stage

With increasing age, there was a greater incidence across all T-stage melanomas; however, beyond the age of 80 there appears to be a plateau in T1 and T2 incidence and an increasing proportion of higher T-stage melanomas (T3 and T4) with a greater increase in incidence for the higher stages (Figure 5). Age was a significant variable ($p<0.001$) for all T-stages except for T1 melanoma, and gender was a significant variable ($p<0.001$) for all T-stages.

DHB of domicile

There was a significant difference in age-standardised incidence of IM at different DHBs ($p<0.001$). When comparing DHB incidences averaged across the entire study period, Taranaki DHB had the greatest IM incidence rate at 77.5 per 100,000 person-years, whereas Counties Manukau DHB had the lowest melanoma incidence rate at

Figure 1: Joinpoint model displaying US2000 age-standardised incidence rate per 100,000 person-years between 2000 and 2022.

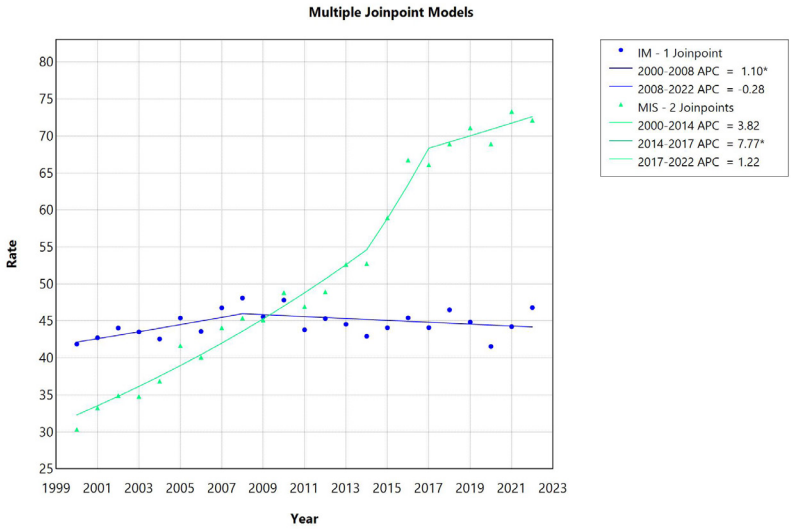


Figure 2: US2000 age-standardised incidence rate per 100,000 person-years between 2000 and 2022, separated by T-stage.

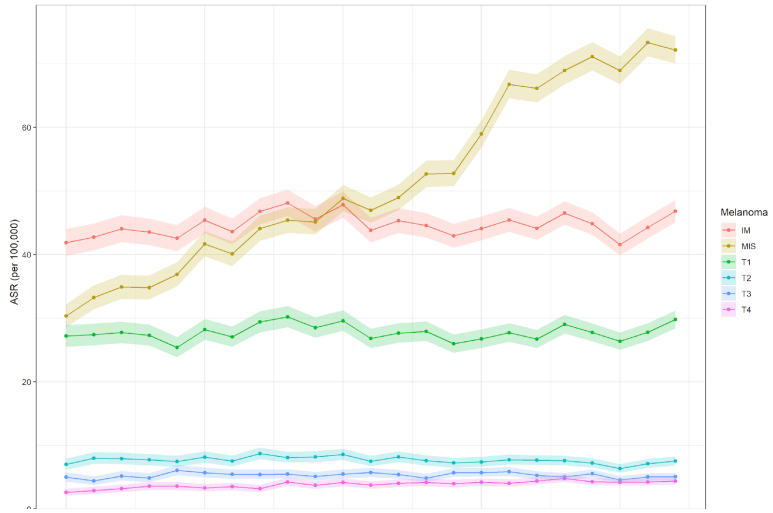


Figure 3: Combined IM and MIS incidence rate per 100,000 person-years for each age group among males and females between 2000 and 2022, with 95% CI.

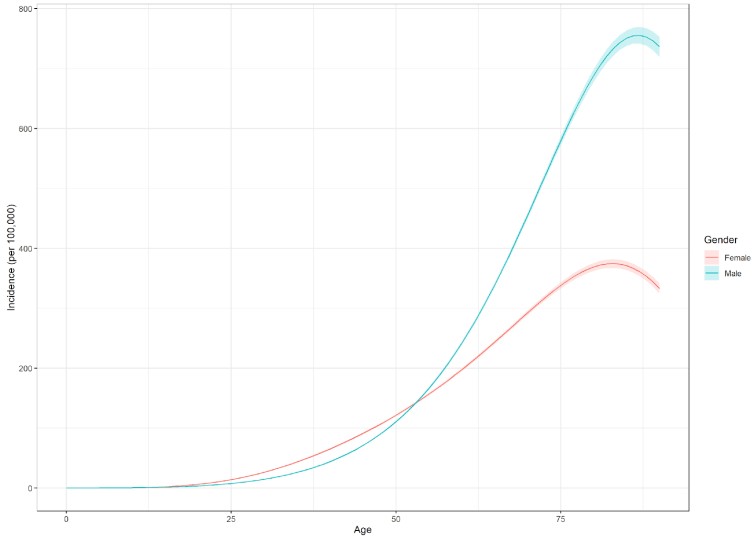


Figure 4: Median Breslow thickness between 2000 and 2022, with 95% CI.

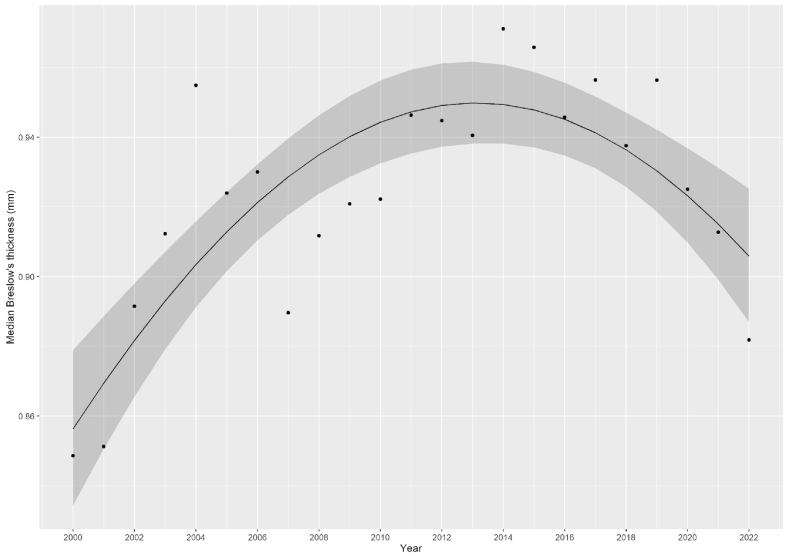


Figure 5: T-stage specific incidence rate per 100,000 person-years for each age group between 2000 and 2022, with 95% CI.

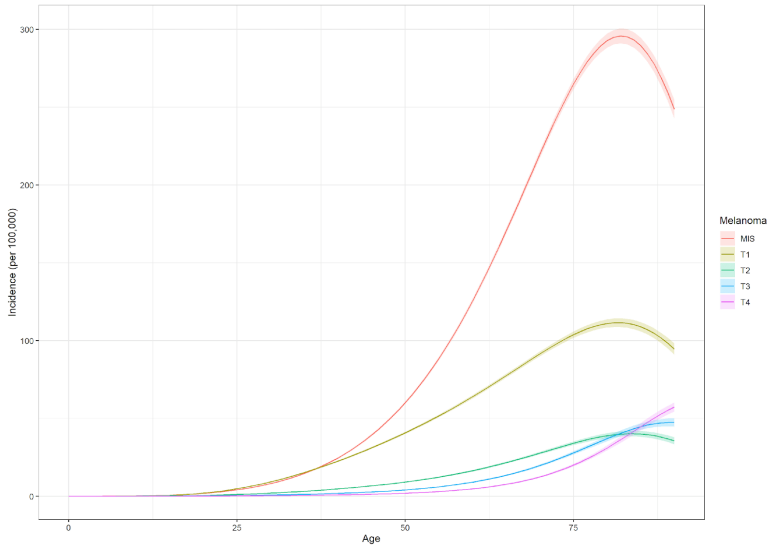
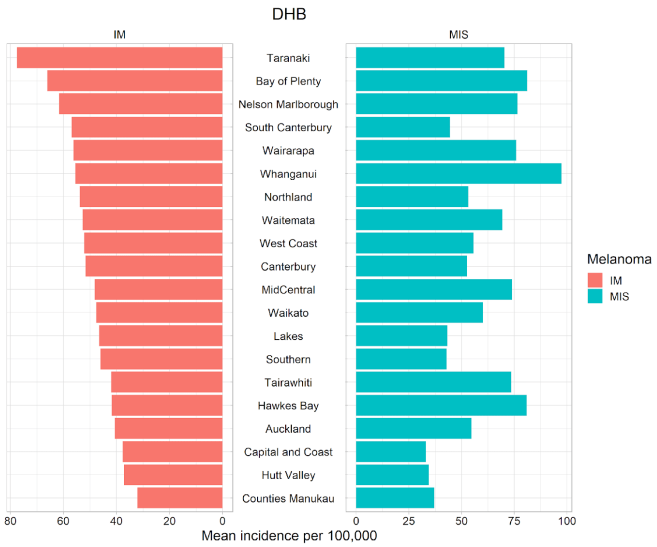


Figure 6: Mean incidence rate per 100,000 person-years by DHB region.



32.1 per 100,000 person-years (Figure 6). Across all DHBs, there was no association identified between MIS and IM incidence.

Discussion

This study looked at overall incidence rates of IM and MIS for the entire New Zealand population, with data taken from a national database. Mandatory reporting of cancer diagnosis to this database has been in place since 1994, and the authors believe it to be the most accurate way of obtaining data from the whole country.

The results of this study suggested a plateau or non-statistically significant decrease in the incidence of IM from 2008 onwards according to the Joinpoint analysis. This is a shift compared to data from the twentieth century, which showed exponential increases in melanoma incidence, and previous studies from the early 2000s, which had shown a plateau.[7,18]

The study also showed the incidence rates of MIS are increasing with time, which has been seen as a trend in previous literature.[19] However, care must be taken when interpreting MIS data due to the possibility of over-diagnosis of dysplastic naevi, with high rates of inter-observer variability between pathologists due to overlapping morphological features noted.[20]

Both the plateau in IM incidence and corresponding increase in MIS incidence may be due to the improved public awareness and early detection of pigmented lesions. Furthermore, there may be a contribution from the maturity of prevention campaigns and the corresponding change in behaviour towards skin protection. There has also been a push by local organisations advocating the increased use of dermatoscopy as part of routine skin assessment in primary care, although the nation-wide prevalence of this practice has not been measured. Interestingly, the plateau in IM incidence was predicted by algorithms performed by Whiteman et al.[3] They hypothesised a plateau phase in the early 2000s, where we were both seeing the positive effects of education campaigns in the younger population, but also an increasingly larger older population with a higher incidence of melanoma, therefore no overall change in incidence rates. Once the younger population ages, people who have been exposed to education campaigns from birth will make up a larger proportion of the overall population, and a decrease in the overall melanoma incidence would be observed. Other countries that have high incidences of melanoma (Australia, Denmark, Norway and the Netherlands) have yet to see a decrease in incidence.[21–23] The evolution in ethnic composition of New Zealand over time may be a confounding factor to the plateau in IM incidence. From the 2013 to 2018 census, the proportion of the New Zealand population that identified as European has decreased from 66.7% to 62.3% with a corresponding increase in mostly the Asian ethnic groups, in whom there is a notably lower melanoma incidence rate.[11,12] Further investigation on the specific incidence for each ethnicity is required.

The International Agency for Research on Cancer Global Cancer Observatory database (GLOBOCAN) reported a combined Australian and New Zealand age-standardised melanoma incidence of 35.8 per 100,000 person-years in 2020, which is different to our reported rate of 41.5 per 100,000 person-years for the 2020 year.[1] This discrepancy arises from a difference in data sources. GLOBOCAN calculated the 2020 incidence rates based on pre-2012 historical data projected and applied to the 2020 population,[24] whereas our calculations are derived from up-to-date 2023 New Zealand Ministry of Health data. Similarly, a recent publication describing the global burden of cutaneous melanoma in 2020, and further projecting melanoma incidence rates to the year 2040, has been based on this GLOBOCAN data,[25] and its accuracy may be limited. Caution must be taken when interpreting these large, worldwide database reports as accurate information for every country may not be available at the time of publication.

Males had a higher incidence of IM than females for the overall study period. When broken down by age band, there was a trend towards females having a higher incidence in the 25–50-year age groups, but a large divergence favouring males at a later age. This has been demonstrated previously,[6,7,26] and possible reasons for this are higher rates of intermittent sun exposure in younger females due to sun-tanning practices but a higher chronic life-time exposure to sun in males due to an increase in occupational sun exposure.[26] The reasons for differences seen between sexes is likely multifactorial, with immunological, endocrine, genetic and behavioural factors all playing a part.[27]

Median Breslow thickness at presentation appeared to be showing signs of decrease in the final 8–10 years of the study period. This is a trend that has been observed in other developed

countries and differs from previous data that showed increases in Breslow thickness over time in New Zealand.[7,28] As Breslow thickness is closely related to prognosis[5] it is encouraging to see this trend. T-stage based on AJCC 8th Edition provides a more detailed clinically significant indication of stage at presentation compared with Breslow thickness alone. While overall IM incidence appears to have a downward trend from 2008 onwards, there was not a statistically significant downward trend for any particular T-stage throughout the study period. Increasing age at presentation saw higher incidences of IM across all T-stages, with one exception. After the age of 80, there was a plateau and decrease in the incidence of T1 melanomas and a plateau in T2 melanomas. For the same age group, we saw increases in T3 and T4 melanomas with increasing age, reflecting a later presentation with more advanced melanomas for this group.

Historically, some regions of New Zealand have been reported to have incidence figures as high as 77.7 per 100,000 person years; the results of this study again confirm wide variation in IM incidence between regions.[29] Similar to 2000–2004, Taranaki DHB recorded the highest incidence (77.5 per 100,000 person-years), with Bay of Plenty (66.1 per 100,000 person-years) and Nelson Marlborough (61.6 per 100,000 person-years) second and third respectively. The differences in incidence between DHBs cannot be completely explained by sunshine hours, as some high sunshine areas such as Hawke's Bay had a low incidence of IM (41.7 per 100,000 person-years), and other DHBs that traditionally have fewer sunshine hours, such as Southern DHB, had a higher incidence (46.1 per 100,000 person-years). The underlying reason is likely to be multifactorial with contributions from confounding factors such as population ethnic composition, health literacy and ease of access to healthcare. The lowest incidence of IM was recorded in Counties Manukau DHB (32.1 per 100,000 person-years), likely due to the ethnic composition of the DHB catchment area.

We saw a low incidence of MIS in South Canterbury DHB (44.6 per 100,000 person-years), despite this region not having a similarly low figure for IM (56.8 per 100,000 person-years). Given that the results are derived from NZCR data, we consider this outlier recording to be likely due to incomplete reporting of MIS to the NZCR in this region. Alternatively, later diagnosis or lack of access to medical assessment may account for this.

Limitations

The ethnic composition of New Zealand has changed over time, with a relative increase in the proportion of the Asian population.[11,12] This may influence the incidence calculations by introduction of a larger proportion of the population that has a documented lower incidence rate and subsequent dilution of the at-risk group within the overall population. Further investigation on the specific incidence for each ethnicity is required. Furthermore, the COVID-19 pandemic spanned across the final 3 years of the study (2000–2022), which may have resulted in delayed presentations due to the hesitancy of patients to access healthcare during this period; to note, there was not an observed significant reduction in number of cases between 2000 and 2022. The authors' decision to limit registration to one per person avoids the risk of over-estimation due to cases of metastatic melanoma and recording residual melanoma at the primary site as a new melanoma; however, it also under-appreciates the burden of disease of patients in whom multiple primary melanoma develop during the study period. Unfortunately, the NZCR is limited in its ability to allow for specific data extraction to include the latter cases and this should be taken into account during the interpretation of the results of this study. The US2000 standard population was selected for statistical analysis purposes due to its similarity to New Zealand in being a developed nation and with the specific age population weightings; however, the authors acknowledge the differences in ethnic composition between these two populations, notably the lack of representation of the Indigenous Māori and Pacific populations.

Conclusion

The incidence of IM in New Zealand appears to have plateaued in the last decade and was associated with an increase in MIS incidence over the same period. We believe this is due to the maturity of prevention campaigns, increasing public awareness and increased GP and specialist use of dermatoscopy. While this trend is encouraging, further research is required to investigate whether there is a decline in IM incidence going forwards. The impact of changing incidence on melanoma-specific mortality and the influence of ethnicity are areas for future investigation.

COMPETING INTERESTS
We declare that all authors involved in the preparation and submission of this journal article have no commercial financial incentives related to the publication. We affirm that there are no competing interests that could compromise the integrity, objectivity or impartiality of the research and its reporting. We disclose no conflicts of interest that could potentially bias the findings or conclusions.
This study was registered and approved by the Waitematā District Health Board research ethics committee.

ACKNOWLEDGEMENTS
The authors would like to acknowledge the cooperation of the New Zealand Ministry of Health – Manatū Hauora in providing up-to-date data for melanoma registrations.

AUTHOR INFORMATION
Daniel Wen,* MBChB: Department of General Surgery, North Shore Hospital, Te Whatu Ora – Health New Zealand Waitematā, New Zealand.
Jack S Pullman,* BSc, MBChB, FRACS: Department of General Surgery, North Shore Hospital, Te Whatu Ora – Health New Zealand Waitematā, New Zealand.
Avinash Sharma, MBChB, MPH, FRACS, MD: Department of General Surgery, North Shore Hospital, Te Whatu Ora – Health New Zealand Waitematā, New Zealand.
Bert van der Werf, MSc: Department of Epidemiology and Biostatistics, School of Population Health, Faculty of Medical and Health Sciences, The University of Auckland, New Zealand.
Richard C W Martin, MBChB, FRACS, ChM: Department of General Surgery, North Shore Hospital, Te Whatu Ora – Health New Zealand Waitematā, New Zealand.
**Indicates joint first author*

CORRESPONDING AUTHOR
Dr Richard C W Martin: General Surgery Department, North Shore Hospital, Private Bag 93-503, Takapuna, Auckland, New Zealand, 0740.
E: Richard.Martin@waitematadhb.govt.nz

URL
https://nzmj.org.nz/journal/vol-137-no-1596/exploring-melanoma-shifts-a-two-decade-analysis-in-new-zealand

REFERENCES:
1. International Agency for Research on Cancer, World Health Organization, Global Cancer Observatory. Melanoma of skin [Internet]. [cited 2022 Jan 31]. Available from: https://gco.iarc.who.int/media/globocan/factsheets/cancers/16-melanoma-of-skin-fact-sheet.pdf
2. Ministry of Health – Manatū Hauora. Cancer: Historical summary 1948-2017 [Internet]. 2020 [cited 2022 Jan 31]. Available from: https://www.health.govt.nz/publication/cancer-historical-summary-1948-2017.
3. Whiteman DC, Green AC, Olsen CM. The Growing Burden of Invasive Melanoma: Projections of Incidence Rates and numbers of New Cases in Six Susceptible Populations through 2031. J Invest Dermatol. 2016;136(6):1161-1171. doi: 10.1016/j.jid.2016.01.035.
4. Makin JK, Warne CD, Dobbinson SJ, et al. Population and age-group trends in weekend sun protection and sunburn over two decades of the SunSmart programme in Melbourne, Australia. Br J Dermatol. 2013;168(1):154-161. doi: 10.1111/bjd.12082.
5. Sahin S, Rao B, Kopf AW, et al. Predicting ten-year survival of patients with primary cutaneous melanoma: corroboration of a prognostic model. Cancer. 1997;80(8):1426-1431.
6. Martin RC, Robinson E. Cutaneous melanoma in Caucasian New Zealanders: 1995-1999. ANZ J Surg. 2004;74(4):233-237. doi: 10.1111/j.1445-2197.2004.02945.x.
7. Liang JJ, Robinson E, Martin RC. Cutaneous melanoma in New Zealand: 2000-2004. ANZ J Surg. 2010;80(5):312-316. doi: 10.1111/j.1445-2197.2009.05199.x.
8. Shaikh WR, Dusza SW, Weinstock MA, et al. Melanoma Thickness and Survival Trends in the United States, 1989 to 2009. J Natl Cancer Inst. 2015;108(1):djv294. doi: 10.1093/jnci/djv294.
9. Gershenwald JE, Scolyer RA, Hess KR, et al. Melanoma of the Skin. Springer Publishing. 2017;8:563-585. doi:10.1007/978-3-319-40618-3_47.
10. Statistics New Zealand. A Report on the 2006 Post-enumeration Survey [Internet]. 2007 [cited 2022 Jan 31]. Available from: https://statsnz.contentdm.oclc.org/digital/api/collection/p20045coll20/id/385/download.
11. Statistics New Zealand. Post-enumeration survey: 2013 [Internet]. 2014 [cited 2022 Jan 31]. Available from: https://www.stats.govt.nz/information-releases/post-enumeration-survey-2013.
12. Statistics New Zealand. Post-enumeration survey: 2018 [Internet]. 2020 [cited 2022 Jan 31]. Available from: https://www.stats.govt.nz/information-releases/post-enumeration-survey-2018/.
13. R Core Team. The R Project for Statistical Computing [Internet]. 2021 [cited 2022 Jan 31]. Available from: https://www.R-project.org/.

14. Nelson M. dsrTest: Tests and Confidence Intervals on Directly Standardized Rates for Several Methods [Internet]. 2022 [cited 2022 Jan 31]. Available from: https://CRAN.R-project.org/package=dsrTest.
15. Kim HJ, Fay MP, Feuer EJ, Midthune DN. Permutation tests for joinpoint regression with applications to cancer rates. Stat Med. 2000;19(3):335-351. doi: 10.1002/(sici)1097-0258(20000215)19:3<335::aid-sim336>3.0.co;2-z.
16. Burnham KP, Anderson DR. Model Selection and Multimodel Inference: A Practical Information-Theoretic Approach. New York: Springer; 2002.
17. Hartig F. DHARMa: Residual diagnostics for hierarchical (multi-level/mixed) regression models [Internet]. 2022 [cited 2022 Jan 31]. Available from: https://cran.r-project.org/web/packages/DHARMa/vignettes/DHARMa.html.
18. Armstrong BK, Kricker A. Cutaneous melanoma. Cancer Surv. 1994;19-20:219-240.
19. Rice S, Zhou L, Martin R. Epidemiology of melanoma in situ in New Zealand: 2008-2012. N Z Med J. 2018;131(1482):73-79.
20. Stefanato CM. The "Dysplastic Nevus" Conundrum: A Look Back, a Peek Forward. Dermatopathology (Basel). 2018;5(2):53-57. doi: 10.1159/000487924.
21. Australian Government, Australian Institute of Health and Welfare. Cancer data in Australia [Internet]. 2022 [cited 2022 Jan 31]. Available from: https://www.aihw.gov.au/reports/cancer/cancer-data-in-australia/data?page=5.
22. Danckert B, Ferlay J, Engholm G. NORDCAN: Cancer incidence, mortality, prevalence and survival in the nordic countries, version 8.2 [Internet]. 2019 [cited 2022 Jan 31]. Available from: https://nordcan.iarc.fr/en/database.
23. Integraal Kankercentrum Nederland. NCR data & figures [Internet]. [cited 2022 Jan 31]. Available from: www.iknl.nl/en/ncr/ncr-data-figures.
24. International Agency for Research on Cancer, World Health Organization. Data and methods [Internet]. [cited 2022 Jul 1]. Available from: https://gco.iarc.fr/today/en/data-sources-methods.
25. Arnold M, Singh D, Laversanne M, et al. Global Burden of Cutaneous Melanoma in 2020 and Projections to 2040. JAMA Dermatol. 2022;158(5):495-503. doi: 10.1001/jamadermatol.2022.0160.
26. Cook MB, Dawsey SM, Freedman ND, et al. Sex disparities in cancer incidence by period and age. Cancer Epidemiol Biomarkers Prev. 2009;18(4):1174-1182. doi: 10.1158/1055-9965.EPI-08-1118.
27. Schwartz MR, Luo L, Berwick M. Sex Differences in Melanoma. Curr Epidemiol Rep. 2019;6(2):112-118. doi: 10.1007/s40471-019-00192-7.
28. Sneyd MJ, Cox B. Clinical and histologic factors associated with melanoma thickness in New Zealand Europeans, Maori, and Pacific peoples. Cancer. 2011;117(11):2489-2398. doi: 10.1002/cncr.25795.
29. Jones WO, Harman CR, Ng AK, Shaw JH. Incidence of malignant melanoma in Auckland, New Zealand: highest rates in the world. World J Surg. 1999;23(7):732-735. doi: 10.1007/pl00012378.