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Discussing the Integration of Traditional & Modern Approaches

World Epidemiology Conference
Interactive Session: Are traditional cohorts outdated?
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Cancer Council | THE UNIVERSITY OF SYDNEY

Disclosures

I am co-PI of an investigator-initiated trial of cervical screening, "Compass", run by the Australian Centre for Prevention of Cervical Cancer (ACPCC), which is a government-funded not-for-profit charity. The trial has received support from the Australian government and the ACPCC has received equipment and a funding contribution from Roche Molecular Diagnostics.

I am also co-PI on an implementation program *Elimination of Cervical Cancer in the Western Pacific (ECCWP)/ Elimination Partnership for Cervical Cancer in the Indo-Pacific (EPICC)* which has received support from the Australian government, the Minderoo Foundation and equipment donations from Cepheid Inc.

Discussing the integration of traditional and modern approaches

- What is a ‘traditional’ cohort study? Starting point:
  - Longitudinal follow-up of a defined group
  - Bespoke data collection (e.g. questionnaires, biomarkers, biometrics, imaging), at various follow-up points
- ‘Enhanced cohort’ – major value can be added by integrating cohort data with:
  - Linkage to routinely collected administrative or other research data is (e.g. electronic health records [EHRs], clinical registries
  - Biobanking activities
  - Aligned simulation modelling of longer term or whole-of-population outcomes
  - Cohort refresh/dynamic approaches.
- Both traditional and enhanced cohorts are intensive, expensive, and don’t fit with project-based funding models -> but the latter ultimately has ‘best bang for buck’.

Enhancing cohort data via linkage

- Any data asset has various quantifiable properties or ‘axes’.
- Linking to administrative or other research data can drastically increase the ‘depth of phenotyping’ of the cohort.

Shilo S, Rossman H & Segal E, Axes of a revolution: challenges and promises of big data in healthcare. *Nature Medicine* Volume 26, 29–38 (2020)

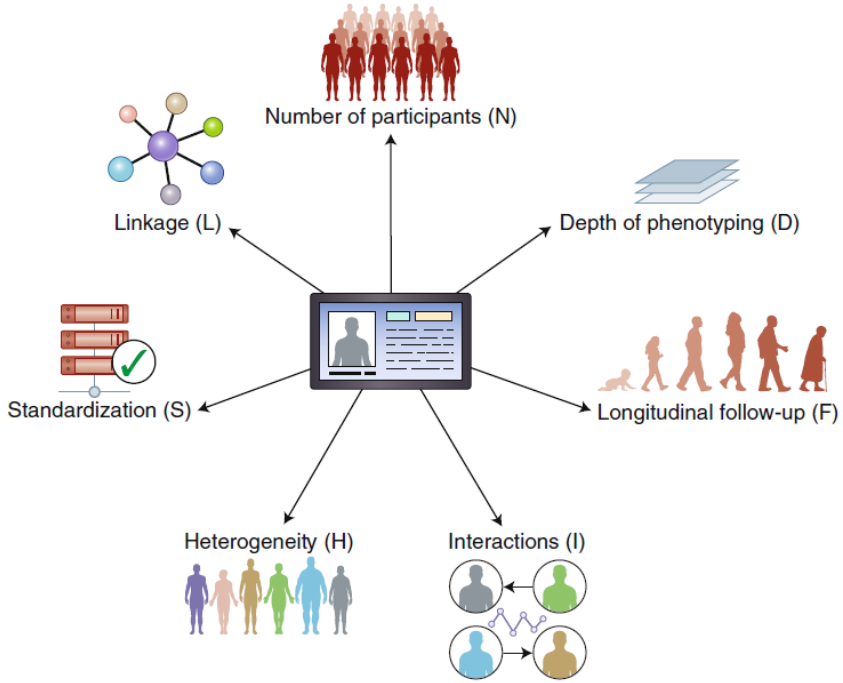
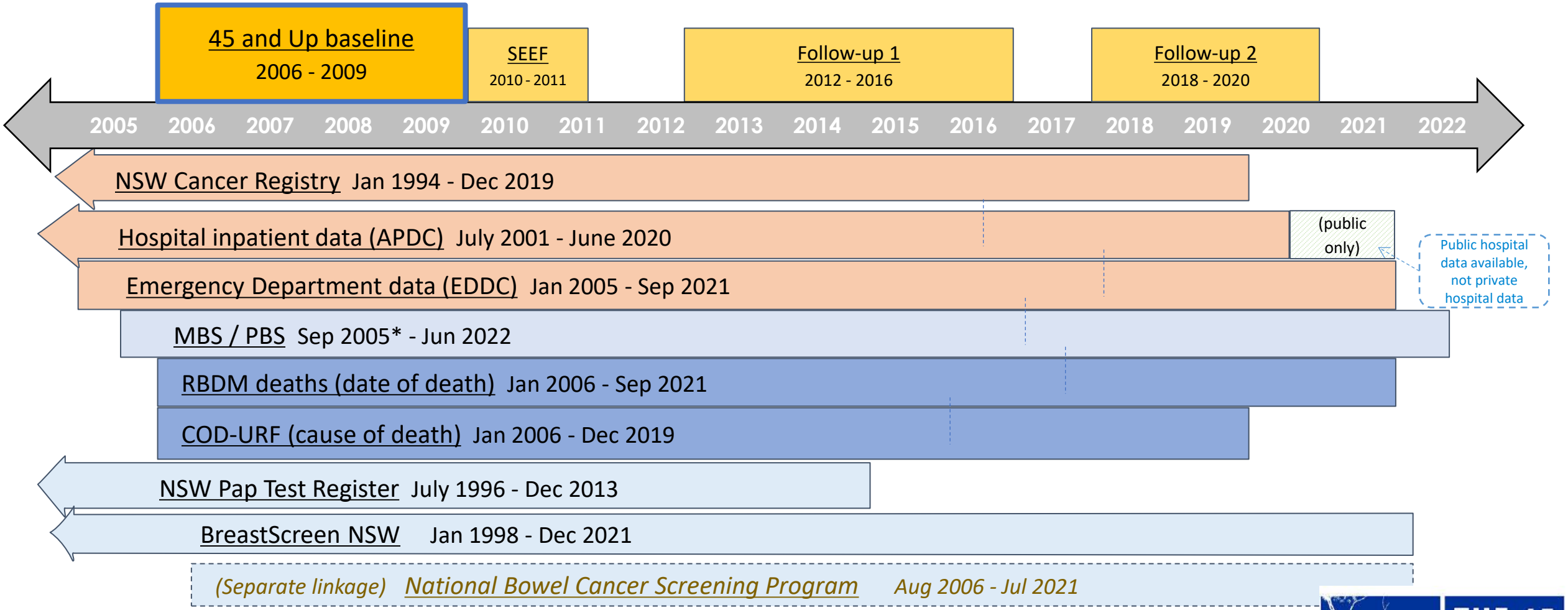


Fig. 1 | The different axes of health data. The complexity of large health datasets can be represented by distinct axes, each encompassing a quantifiable property of the data.

Example ‘Enhanced Cohort’ - The 45 and Up Study

260,000+ participants, the largest ongoing study of healthy ageing in the Southern Hemisphere.



APDC: Admitted Patient Data Collection; COD-URF: Cause of death unit record file; EDDC: Emergency Department Data Collection; MBS: Medicare Benefits Schedule;
PBS: Pharmaceutical Benefits Scheme; RBDM: Registry of Births, Deaths and Marriages; SEEF: Social, Economic and Environmental factors study.
** MBS/PBS data available from June 2004 for the first 103,000 participants in the 45 and Up Study (recruited Jan 2006 - Mar 2008).*

Bleicher K et al., Cohort Profile Update: The 45 and Up Study. Int J Epi 2022

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THE 45 AND UP STUDY
Research to improve health and wellbeing

A case study:
45 and Up data analysis underpinning evaluation of interventions in lung cancer control

Marianne Weber Stephen Wade Pavla Vaneckova Preston Ngo Peter Sarich Michael Caruana Yue He

Weber MF, Ngo PJ, Banks E, Steinberg J, Goldsbury DE, Grogan P, Canfell K.
Capacity of the 45 and Up Study to mobilise evidence-based improvements in cancer control: lung cancer case study. *Public Health Res Pract*. 2022 Dec 13;32(4):3242232.

Local evidence on cancer risk according to smoking exposure

Estimates from 45 and Up

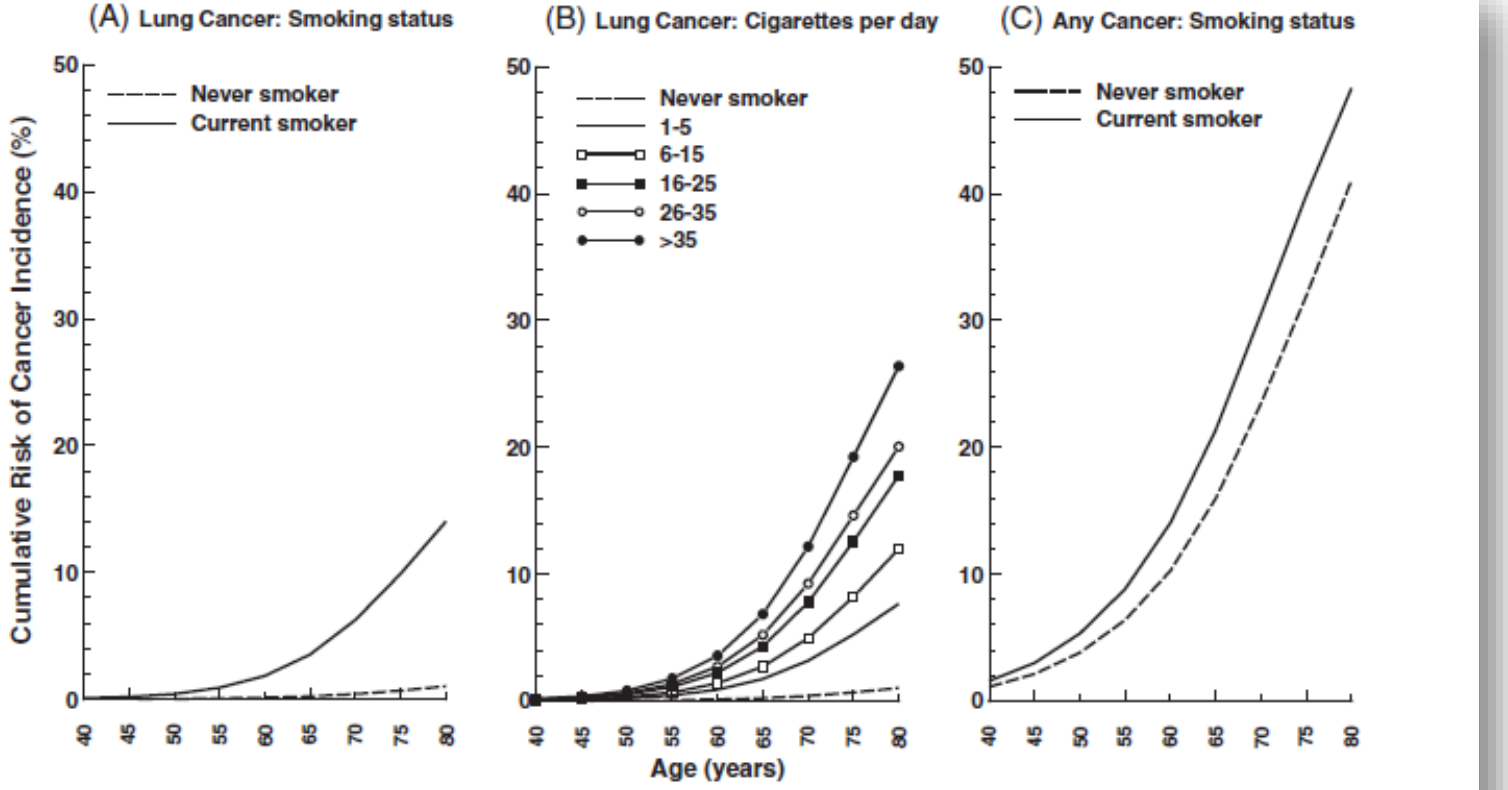

FIGURE 2 Cumulative risk of a cancer diagnosis to age 80 in the Australian population in 2010 for lung cancer among (A) current and never smokers and (B) by number of cigarettes smoked per day, and for (C) any cancer type among current and never smokers

Overall, current-smokers had increased risks of:

- **All cancers combined (HR=1.42, 95%CI:1.34-1.51)**
- **Lung cancer (HR= 7.66, 95%CI:14.65-21.29)**

vs. never-smokers.

Hazards increased with increasing smoking intensity; compared to never-smokers,

- **HR = 9 (95%CI:5-17) for 1-5 cigarettes/day**
- **39 (95%CI:26-58) for >35 cigarettes/day.**

Weber MF, Sarich PEA, Vaneckova P, Wade S, Egger S, Ngo P, Joshy G, Goldsbury DE, Yap S, Feletto E, Vassallo A, Laaksonen MA, Grogan P, O'Connell DL, Banks E, Canfell K. Cancer incidence and cancer death in relation to tobacco smoking in a population-based Australian cohort study. *Int J Cancer*. 2021 Sep 1;149(5):1076-1088.

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Forecasting future smoking prevalence

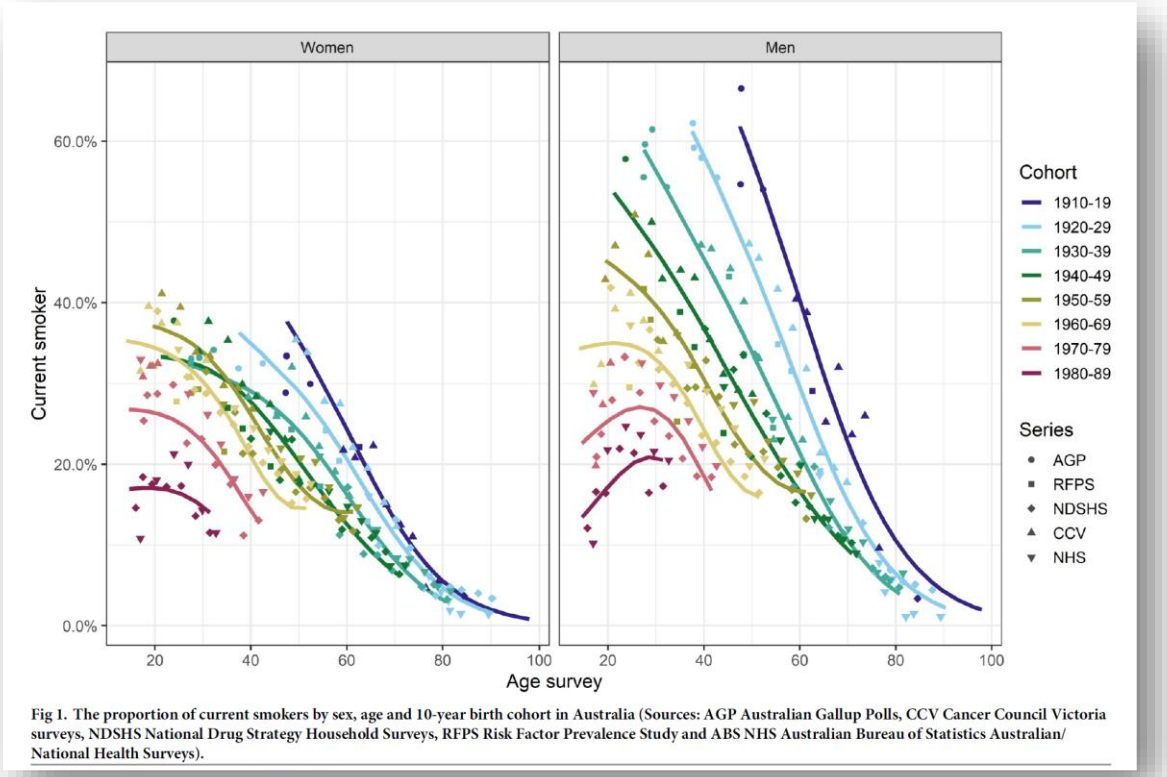


Fig 1. The proportion of current smokers by sex, age and 10-year birth cohort in Australia (Sources: AGP Australian Gallup Polls, CCV Cancer Council Victoria surveys, NDSHS National Drug Strategy Household Surveys, RFPS Risk Factor Prevalence Study and ABS NHS Australian Bureau of Statistics Australian/ National Health Surveys).

Vaneckova P, et al *PLoS One*. 2021 May 21;16(5):e0250824.

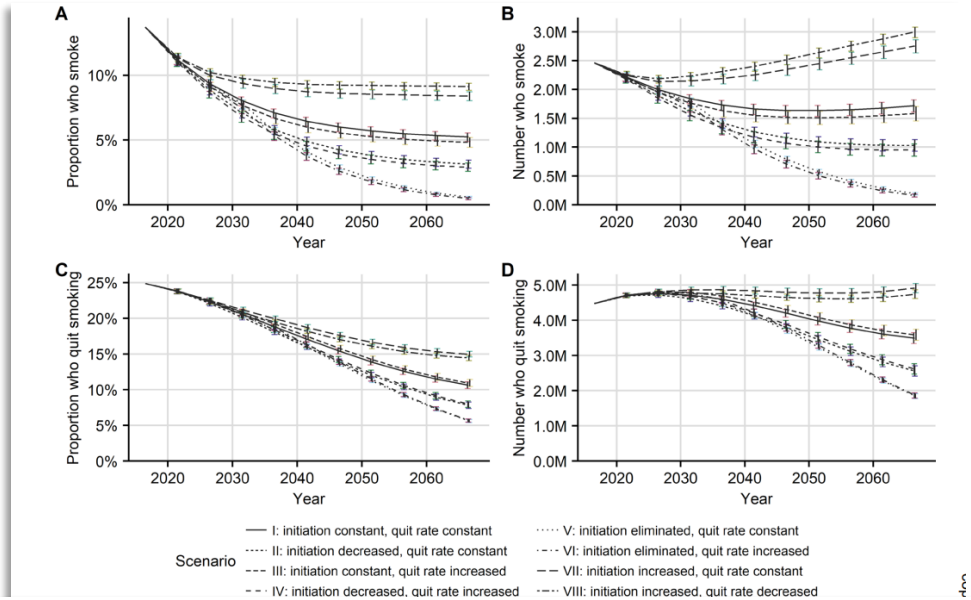


Table 1 Hypothetical scenarios of smoking initiation and cessation trends and modelled estimates of daily smoking prevalence 2017–2066 in the Australian population

Scenario	Proportion that initiated smoking	Smoking cessation rate	Daily smoking prevalence in 2066 (%) (90% EI)	Adults smoking daily in 2066, n (90% EI)	Year when daily smoking prevalence is 5% (90% EI)
I	Kept constant from 2017 to 2066	Kept constant from 2017 to 2066	5.24 (4.90–5.55)	1.72 m (1.61–1.82 m)	>2066
II	Downward trend continued for 10 years	Kept constant from 2017 to 2066	3.14 (2.84–3.45)	1.03 m (0.93–1.13 m)	2041 (2039–2043)
III	Kept constant from 2017 to 2066	Upward trend continued for 10 years	4.83 (4.44–5.20)	1.58 m (1.46–1.71 m)	2058 (≥2049)
IV	Downward trend continued for 10 years	Upward trend continued for 10 years	2.90 (2.58–3.23)	0.95 m (0.85–1.06 m)	2039 (2037–2041)
V	Set to 0 for individuals born after 2010	Kept constant from 2017 to 2066	0.59 (0.53–0.65)	0.19 m (0.17–0.21 m)	2038 (2038–2039)
VI	Set to 0 for individuals born after 2010	Upward trend continued for 10 years	0.49 (0.41–0.57)	0.16 m (0.14–0.19 m)	2037 (2036–2038)
VII	Trend reversed 10 years to 2007	Kept constant from 2017 to 2066	8.40 (8.03–8.73)	2.76 m (2.64–2.86 m)	>2066
VIII	Trend reversed 10 years to 2007	Trend reversed 10 years to 2007	9.14 (8.83–9.39)	3.00 m (2.90–3.08 m)	>2066

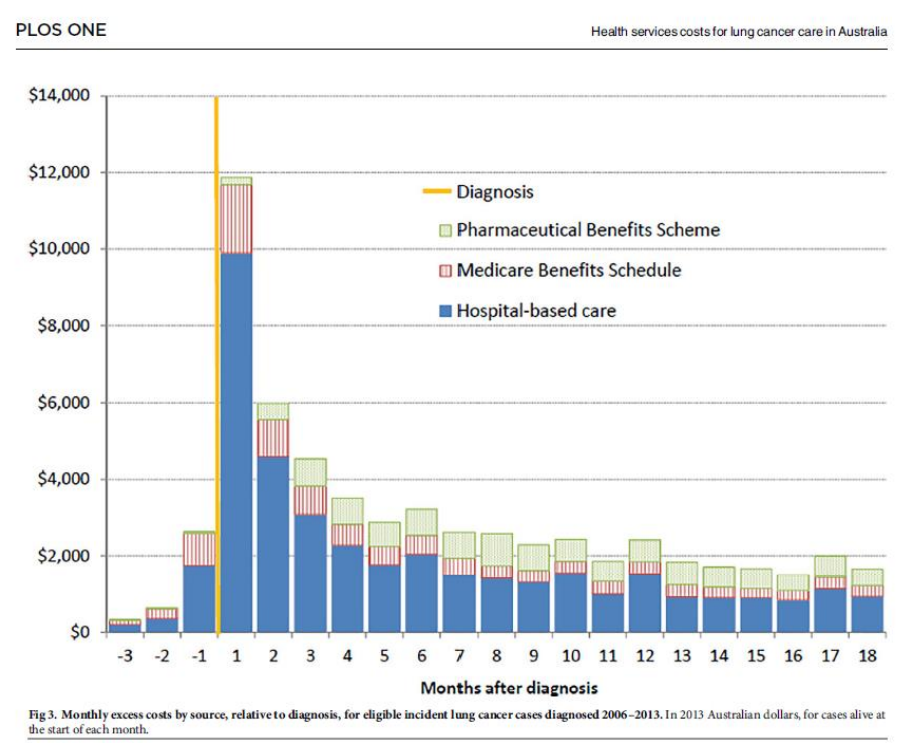
.EI, equal-tailed interval; m, million.

Wade S, *et al*. *Tob Control* 2023;**0**:1–7. doi:10.1136/tc-2022-057624 5

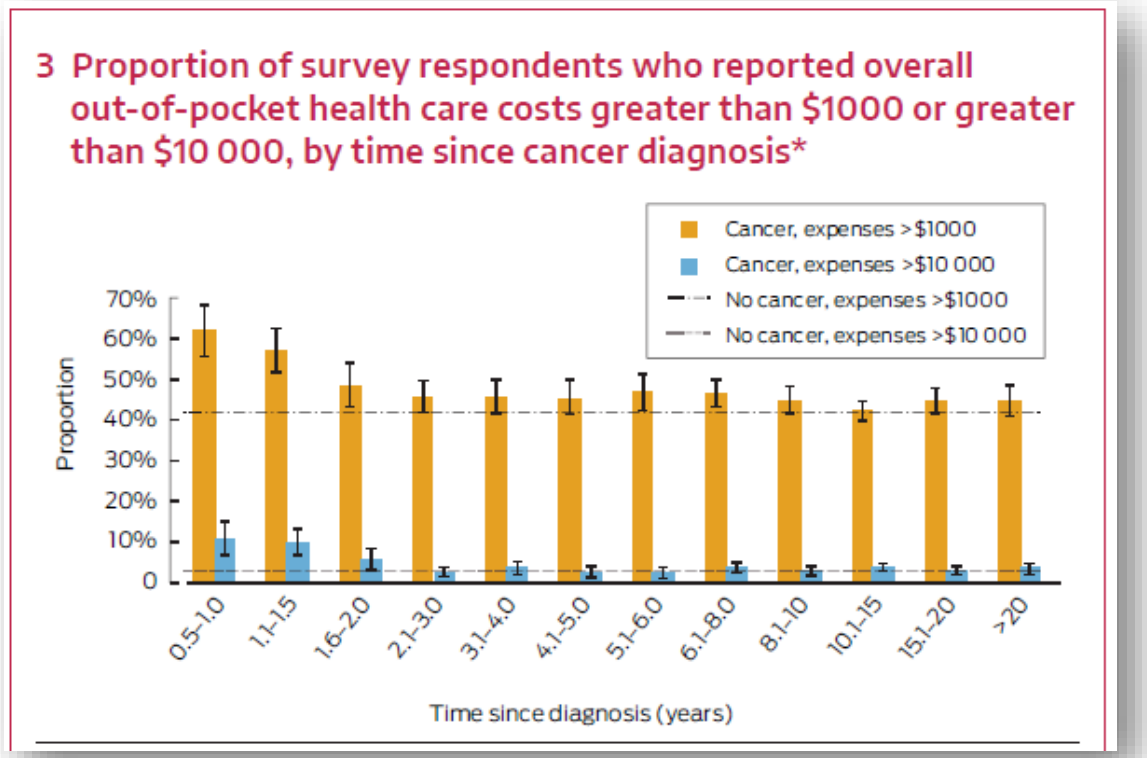
"A 5% adult daily smoking prevalence target cannot be achieved by the year 2030 based on current trends. Urgent investment in concerted strategies that prevent smoking initiation and facilitate cessation is necessary to achieve 5% prevalence by 2030."

Wade S, et al.Tob Control. 2023 May 22:tc-2022-057624.

Costs of cancer: health services and OOP



Goldsbury DE, Weber MF, Yap S, Rankin NM, Ngo P, Veerman L, Banks E, Canfell K, O'Connell DL. Health services costs for lung cancer care in Australia: Estimates from the 45 and Up Study. PLoS One. 2020 Aug 31;15(8):e0238018.



Goldsbury DE, Haywood P, Pearce A, Collins LG, Karikios D, Canfell K, Steinberg J, Weber MF. Out-of-pocket health care expenses for people with and without cancer, New South Wales, 2020: a cross-sectional study. Med J Aust. 2024 Jun 25

Assessing eligibility criteria for screening

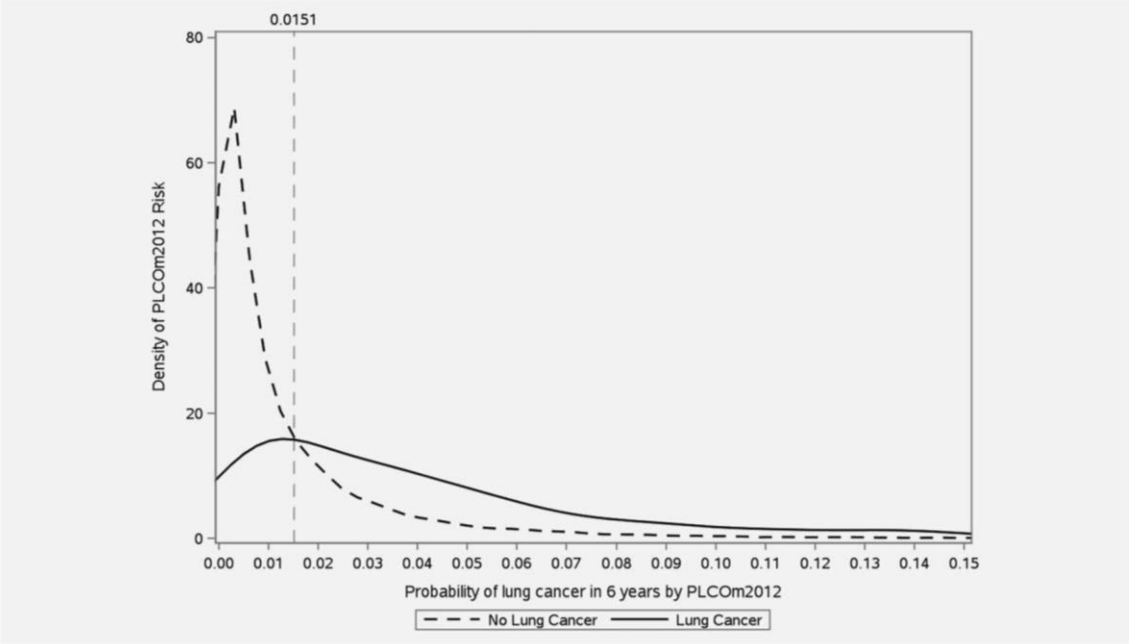


Figure 2. Distribution of PLCOm2012 risk for those aged 55–74 years in the 45 and up study (age at 2006–2008) for those with and without lung cancer diagnosed within 5–6 years of follow-up. The risk threshold value of 0.0151 is indicated by the vertical dashed line. The graph is right truncated to allow direct comparison with the original validation model.[22]

- Using risk classification tools might better select those at highest risk, who will benefit from screening → potential to enhance both the effectiveness and efficiency of the program
- For example PLCOm2012 is a risk assessment tool incorporating sociodemographic and health factors into screening eligibility criteria
- We have performed validation in Australian context, using 45 and Up data

Weber M, Yap S, Goldsbury D, Manners D, Tammemagi M, Marshall H, Brims F, McWilliams A, Fong K, Kang YJ, Caruana M, Banks E, Canfell K. Identifying high risk individuals for targeted lung cancer screening: Independent validation of the PLCOm2012 risk prediction tool. *Int J Cancer*. 2017 Jul 15;141(2):242-253.

Quantifying disability, distress & QoL after cancer

a. Severe physical functioning limitations

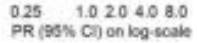
Type of cancer	% (n/N)	PR (95% CI)
Multiple myeloma	46.7 (70/150)	3.10 (2.56- 3.77)
Lung	48.5 (189/390)	2.81 (2.50- 3.15)
Kidney	25.5 (102/400)	1.64 (1.39- 1.94)
Oesophagus	27.7 (18/65)	1.60 (1.09- 2.36)
NHL	25.4 (171/673)	1.56 (1.37- 1.78)
Uterus (female only)	26.1 (102/390)	1.54 (1.31- 1.82)
Leukaemia	22.8 (72/316)	1.47 (1.21- 1.79)
Thyroid	18.0 (52/289)	1.36 (1.07- 1.72)
Bladder	27.6 (91/330)	1.34 (1.12- 1.59)
Breast (female only)	19.7 (721/3657)	1.23 (1.16- 1.32)
Colorectal	22.1 (547/2476)	1.20 (1.12- 1.29)
Prostate (male only)	16.7 (834/5003)	1.11 (1.04- 1.19)
Melanoma	15.9 (471/2960)	1.02 (0.94- 1.10)
Other cancer	24.5 (465/1900)	1.57 (1.46- 1.70)
Any cancer	20.6 (3911/19025)	1.28 (1.25- 1.32)
No cancer	12.6 (26717/212030)	1

b. Moderate/High psychological distress

Type of cancer	% (n/N)	PR (95% CI)
Lung	34.6 (136/393)	1.67 (1.46- 1.92)
Multiple myeloma	31.9 (45/141)	1.53 (1.20- 1.96)
NHL	25.8 (171/663)	1.20 (1.05- 1.36)
Kidney	24.1 (100/414)	1.17 (0.98- 1.38)
Thyroid	27.1 (82/302)	1.11 (0.92- 1.33)
Prostate (male only)	20.1 (991/4942)	1.09 (1.02- 1.15)
Oesophagus	20.9 (14/67)	1.06 (0.67- 1.68)
Uterus (female only)	24.8 (99/400)	1.05 (0.88- 1.24)
Leukaemia	21.8 (66/303)	1.03 (0.84- 1.28)
Bladder	19.7 (60/304)	1.03 (0.82- 1.29)
Colorectal	19.7 (477/2420)	0.97 (0.89- 1.05)
Melanoma	20.6 (609/2963)	0.96 (0.89- 1.03)
Breast (female only)	23.0 (856/3718)	0.95 (0.90- 1.01)
Other cancer	26.8 (502/1875)	1.22 (1.13- 1.32)
Any cancer	22.2 (4213/18933)	1.05 (1.02- 1.08)
No cancer	23.5 (51130/217282)	1

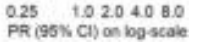
c: Poor/Fair self-rated health

Type of cancer	% (n/N)	PR (95% CI)
Multiple myeloma	48.2 (81/168)	3.11 (2.64- 3.66)
Lung	46.5 (216/465)	2.81 (2.54- 3.12)
Leukaemia	31.4 (114/363)	2.02 (1.73- 2.36)
Oesophagus	30.8 (24/78)	1.92 (1.38- 2.69)
NHL	29.6 (229/775)	1.91 (1.71- 2.13)
Kidney	26.7 (123/460)	1.68 (1.45- 1.96)
Thyroid	20.6 (67/325)	1.57 (1.28- 1.94)
Uterus (female only)	21.4 (98/459)	1.54 (1.30- 1.84)
Colorectal	23.1 (659/2859)	1.39 (1.30- 1.49)
Bladder	25.0 (95/380)	1.33 (1.12- 1.59)
Breast (female only)	17.9 (740/4132)	1.33 (1.24- 1.42)
Prostate (male only)	20.5 (1158/5643)	1.24 (1.17- 1.31)
Melanoma	15.5 (509/3286)	1.00 (0.92- 1.08)
Other cancer	28.9 (618/2142)	1.87 (1.75- 2.00)
Any cancer	22.0 (4738/21562)	1.41 (1.37- 1.45)
No cancer	13.5 (31767/235530)	1



d: Poor/Fair self-rated quality of life

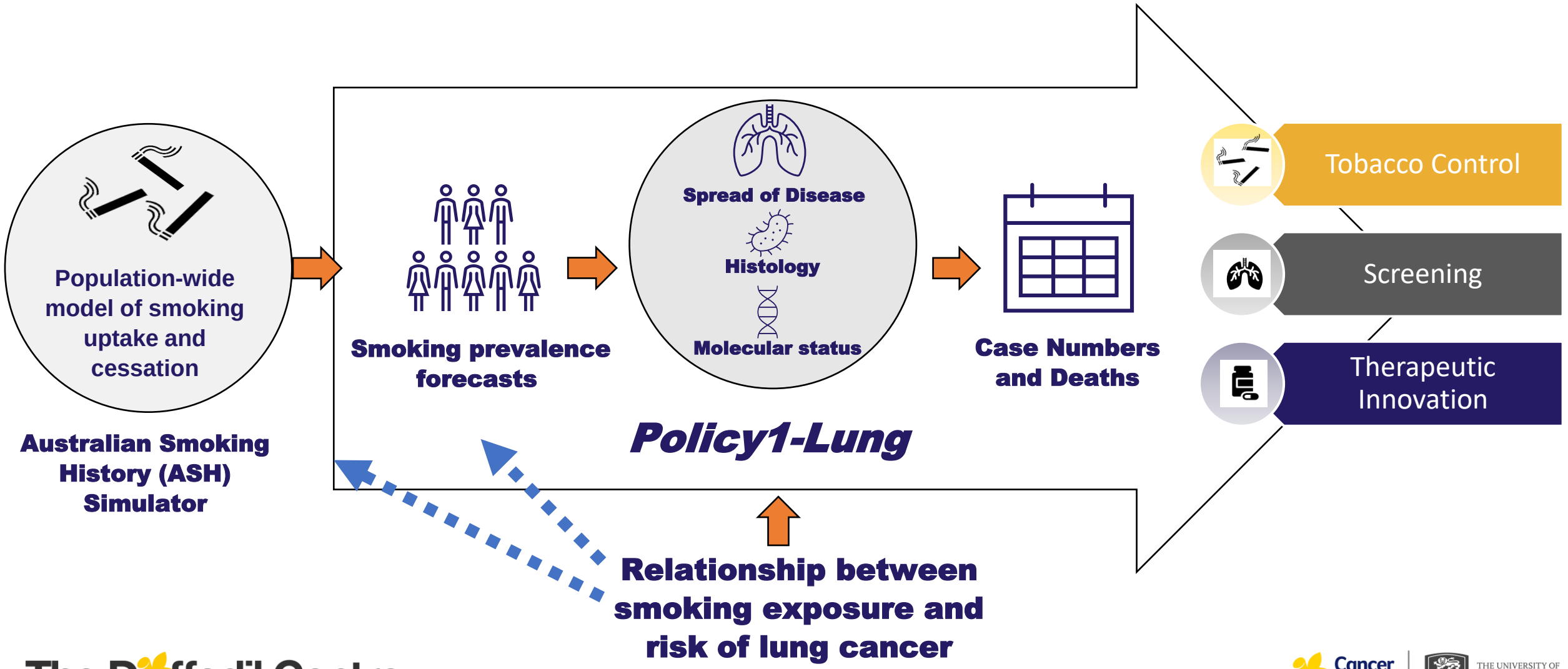
Type of cancer	% (n/N)	PR (95% CI)
Lung	31.9 (145/455)	2.53 (2.21- 2.91)
Multiple myeloma	27.9 (46/165)	2.40 (1.87- 3.07)
NHL	19.6 (149/760)	1.66 (1.44- 1.92)
Leukaemia	18.8 (66/351)	1.59 (1.28- 1.98)
Kidney	18.6 (85/456)	1.54 (1.27- 1.86)
Oesophagus	18.7 (14/75)	1.53 (0.96- 2.45)
Thyroid	15.1 (48/318)	1.52 (1.18- 1.96)
Bladder	19.9 (73/366)	1.39 (1.13- 1.71)
Uterus (female only)	14.5 (65/448)	1.38 (1.10- 1.72)
Colorectal	15.8 (443/2803)	1.25 (1.14- 1.36)
Prostate (male only)	14.4 (802/5554)	1.15 (1.08- 1.23)
Breast (female only)	11.8 (480/4064)	1.15 (1.05- 1.25)
Melanoma	10.9 (351/3232)	0.92 (0.83- 1.01)
Other cancer	21.1 (443/2104)	1.80 (1.66- 1.96)
Any cancer	15.2 (3214/21178)	1.28 (1.24- 1.32)
No cancer	10.2 (23664/231263)	1



- Age- and sex-adjusted prevalence ratios (PRs) for adverse person-centred outcomes in participants with versus without cancer, for 13 cancer types

Joshy G, Thandrayen J, Koczwara B, Butow P, Laidsaar-Powell R, Rankin N, Canfell K, Stubbs J, Grogan P, Bailey L, Yazidjoglou A, Banks E. Disability, psychological distress and quality of life in relation to cancer diagnosis and cancer type: population-based Australian study of 22,505 cancer survivors and 244,000 people without cancer. *BMC Med.* 2020 Dec 1;18(1):372.

Modelling Platform: *Policy1-Lung* microsimulation



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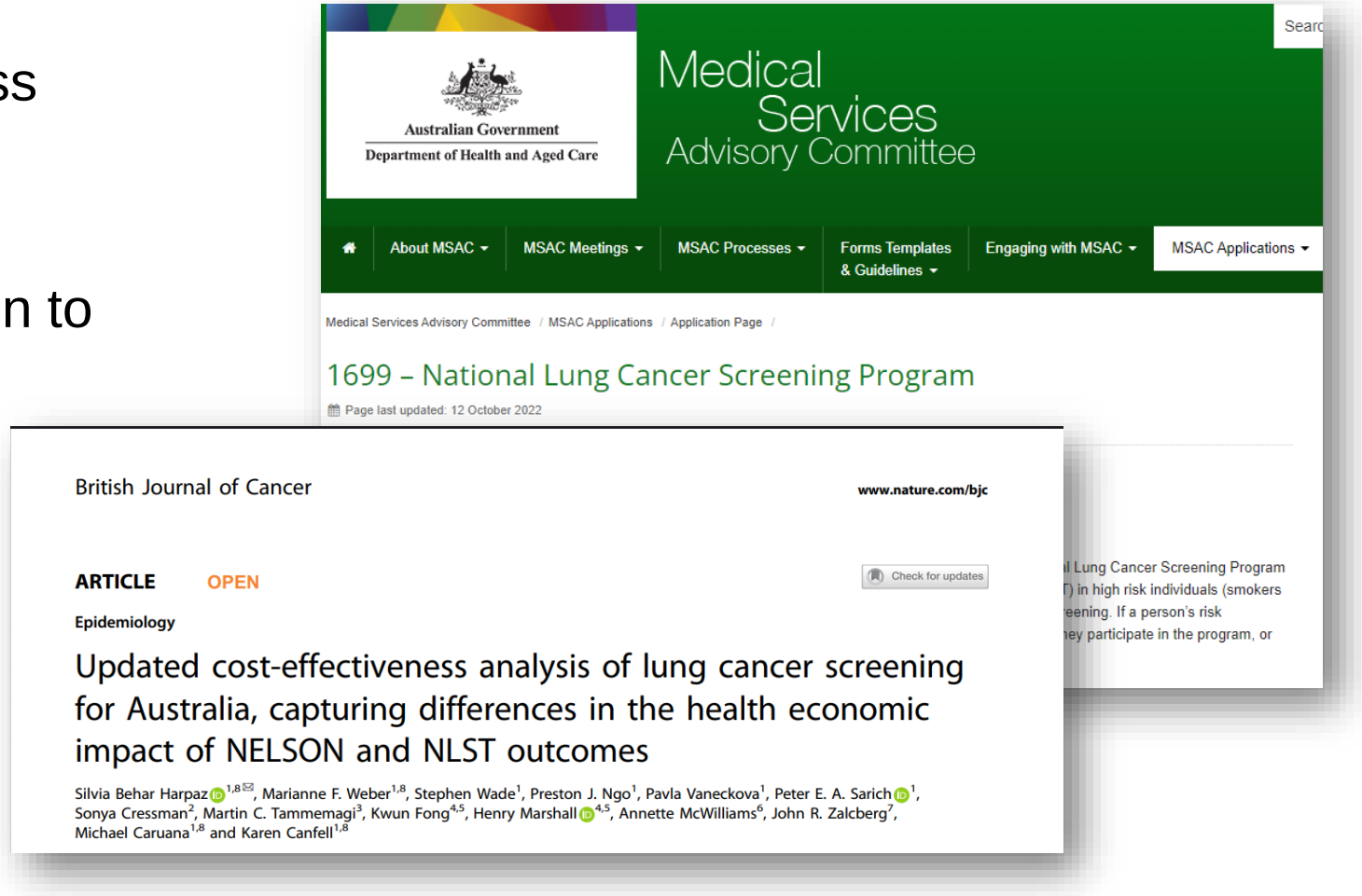
Cost-effectiveness of lung cancer screening.

- Favourable cost-effectiveness evaluation in Australia: $39,250/QALY
- Supported a national decision to introduce lung screening.



Behar Harpaz S, Weber MF, Wade S, Ngo PJ, Vaneckova P, Sarich PEA, Cressman S, Tammemagi MC, Fong K, Marshall H, McWilliams A, Zalcberg JR, Caruana M, Canfell K. Updated cost-effectiveness analysis of lung cancer screening for Australia, capturing differences in the health economic impact of NELSON and NLST outcomes. *Br J Cancer*. 2023 Jan;128(1):91-101.

Are traditional cohorts outdated?

- What's 'traditional' is evolving!
- Building in linkage and complementary activities – if feasible - greatly enhances the long-term value of cohorts
- Let's act as advocates, to:
  - Explain the incredible value of 'enhanced cohorts' and their flexibility – using case study examples
  - Push for funding mechanisms that enable continuity of funding for large-scale and long-term platforms, with aligned activities.

Acknowledgements and Funding: Lung Cancer

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This work was done in collaboration with Henry Marshall[1, 2], Renee Manser[3, 4], Shalini Vinod[5], Kwun Fong[1, 2]

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This work was done in collaboration with David Manners[1], Martin Tammemagi[2], Henry Marshall, Fraser Brims[3], Annette McWIlliams[4], Kwun Fong, and Emily 5

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