Supplementary file for "The impact of low dose CT screening for lung cancer on ethnic health inequities in New Zealand: a cost-effectiveness analysis"

Contents

Appendix A Methods

List of model and parameter updates for Waitematā/Auckland model

A number of key parameters and assumptions in the BODE[3] model were updated with varying impacts on the ICER. We have grouped these changes into those that incorporate NELSON RCT evidence, updates of New Zealand data, and changes in model assumptions. The table below indicates the impact of each of these changes on the ICER (Table A).

1. Incorporation of NELSON RCT findings

Screening **sensitivity and specificity** have been updated to NELSON parameters to account for improvements in specificity from changes to nodule management protocol (nodule volumes and volume doubling time). Improving the specificity of screening had the direct impact of reducing the number of false positives test results that required diagnostic tests – and therefore the cost of diagnostic testing decreased. *This change reduced ICERS.*

The **nodule management** protocol resulted in a small (2%) increase in the number of CT scans – so we weighted up CT scan costs by 2%. *This change increased ICERS.*

The **stage shift** in the original BODE[3] model assumed a proportionate stage shift, equal to what was found in the NLST study. This resulted in a stage distribution of screened patients that was inconsistent with the distributions that have been observed in virtually all LDCT screening trials. We instead assumed that the final stage distribution achieved in the NELSON study represented what was achievable by a CT lung cancer screening programme with nodule management, and we therefore used the NELSON final stage distribution as the stage distribution achieved in the screening arm of our model.

Diagnostic test adherence in NELSON varied: round 1 95.9%[1], round 1-2: 92.2%, round 2-3: 87.5%, and round 3-4: 80.7%.[2] in the model we used the median of the values, which was also the value reflecting a 2 year screening interval.

In the NELSON trial, an **excess-incidence overdiagnosis rate of 8.9%** (bootstrapped 95% CI, −18.2 to 32.4) for screening-detected was found 11 years after randomization (5.5 years after the final screening round).[3] In the model, overdiagnosis was accounted for in stage shift by removing 8.9% of local stage cancers in the screening arm.

In our model we assumed that 7.5% of CT scans produced an **incidental finding** that required further investigation, at a cost of $500 (approximately that of an abdominal U/S). This aligns with the recent NELSON evidence 7% had a clinically relevant incidental finding.[3]

2. Updated epidemiologic parameters and costs

The original BODE³ model **stage at diagnosis** drew on NZ cancer registry data which has a high proportion of unknown stage [4, 5] those with unknown stage had been distributed evenly across local, regional and distant extent of disease. We incorporated new data on stage at diagnosis from the Midland Lung Cancer Registry, provided by Professor Lawrenson, which has used a combination of clinical records and cancer registry data to provide a near complete set of stage data by extent of disease in the Midland region. We used the International Cancer Benchmarking Partnership (ICBP) algorithm [6, 7]with TNM values (7th edition) within the register to generate SEER disease extent values (localised, regional and distant) and produce a baseline stage distribution. The proportion of distant extent of disease in this database was considerably higher than that which was used in the BODE[3] model based on the cancer registry data alone (64% versus 34%) and the proportion of patients with localised disease extent was lower (13% versus 31%). In the Midland Lung cancer registry there was no significant difference in stage at diagnosis between Māori and non-Māori. *More distant extent of disease in the baseline reduced the ICER.*

The Waitematā/Auckland model includes a new analysis of **stage-specific survival** to address the implausibly high stage-specific survival from lung cancer in the original BODE[3] model. The data was from 2006-2016 cancer registry with vital status followed until 31 March 2018. Life tables were provided by Statistics NZ. Mortality rates in the Statistics NZ life tables for 2014-2018 were smoothed using the Ewbank 4 parameter model, fitting them to the 2013 life table as the standard. Lung cancer cases were identified from the cancer registry as those where the first 3 characters of the site variable was recorded as "C33" or "C34". SEER summary extent was classified using the ICBP algorithm where TNM data was available. Where it was not, the SEER summary extent recorded in the cancer registry was used. The Cancer Registry patients with extent C (Invasion of adjacent tissue or organ) were classified as having localised disease (this was based on an analysis PS conducted comparing survival rates in that group with those of the TNM classified patients). Net survival was calculated using the Pohar Perme method with the stns command.[8] The log-normal survival function was fitted to observed survival. Parameters were solved with minimising difference between 5-year survival values. Log normal parameters are ethnicity, sex and age group specific The Waitematā/Auckland model stage-specific net survival ratios are consistent with the aggregate

relative survival ratios produced by the Ministry of Health. *This change increased the ICER (by worsening the survival for those that shifted to localised disease)*

Cost of CT scans. Three quotes from local providers were sought for the provision of LDCT tests ($250, $350-400 and $800 per scan), with the middle quote ($400) used as the base case, and sensitivity analyses undertaken to examine different LDCT costs.

The rate of **complications per diagnostic test** was set at 6% of invasive diagnostic tests and costed for a pneumothorax requiring hospitalisation.[9, 10] Sensitivity analyses of a higher complication rate (15%) and double this cost were undertaken.

3. Updated model assumptions

The original **screening coverage** parameters of screened per round and proportion never screened were differential, with lower screening coverage for Māori. We set screening coverage in the base case to be equal for Māori and non-Māori – thereby not building in an expectation for unequal treatment by ethnicity. *This change slightly increased the ICER for Māori.*

The **smoking cessation rate** in the model determines the continuing eligibility of the original population and the risk of lung cancer that reduces from time of quitting. The original BODE^3 model based its cessation assumptions on 2013 census data that have since been shown to overestimate cessation rates, as compared to New Zealand Health Survey data.[11] We updated the cessation rates to better align with current evidence by using the pessimistic scenario for cessation from the 2013 census analyses. The impact of this change primarily impacted on the continuing eligibility of our cohort to be screened – that is – fewer people in the cohort fell below the 30 pack year history eligibility criterion, or saw a reducing risk of lung cancer from cessation of smoking.

Table A: The impact of stepwise changes from BODE3 model to Waitematā/Auckland model on costs, HALYs and ICERs

	BODE^3 model results	Baseline stage, stage shift, sensitivity and specificity	AND stage-specific survival	AND equal coverage	AND CT costs	AND diagnostic test adherence	AND complication rate	AND nodule cost weight	AND cessation rate	Waitematā / Auckland model
Māori										
Base Costs (NZ$ mill)	513	516	465	465	465	465	465	465	464	464
Total Int costs (NZ$ mill)	546	543	490	493	486	486	486	486	482	482
Int costs (NZ$ mill)	25	17	17	18.	11	11	11	11.	9.3	9.3
HALY base	57100	57100	57100	57100	57100	57100	57100	57100	57100	57100
HALY intervention	58000	58300	57900	57900	57900	57900	57900	57900	57800	57800
Cost Difference	33	27	26	28	21	21	21	22	18	18
HALYS gained	870	1170	760	830	830	830	830	830	660	660
ICER	**37900**	**22800**	**33900**	**34200**	**25700**	**25700**	**25800**	**26000**	**27100**	**27100**
non-Māori										
Base Costs (NZ$ mill)	3570	3582	3446	3446	3446	3446	3446	3446	3445	3445
Total Int costs (NZ$	3759	3720	3589	3589	3546	3546	3546	3547	3533	3533
Int costs (NZ$ mill)	91	61	61	61	37	37	37	38	33	33
HALY base	469000	469000	469000	469000	469000	469000	469000	469000	469000	469000

	BODE^3 model results	Baseline stage, stage shift, sensitivity and specificity	AND stage-specific survival	AND equal coverage	AND CT costs	AND diagnostic test adherence	AND complication rate	AND nodule cost weight	AND cessation rate	Waitematā / Auckland model
HALY intervention	471900	473000	472200	472200	472200	472200	472100	472100	471700	471700
Cost Difference	190	138	143	143	99	99	100	101	89	89
HALYS gained	2668	3761	2954	2954	2954	2954	2952	2952	2476	2476
ICER	**71000**	**36700**	**48300**	**48300**	**33700**	**33600**	**33800**	**34000**	**35800**	**35800**

References

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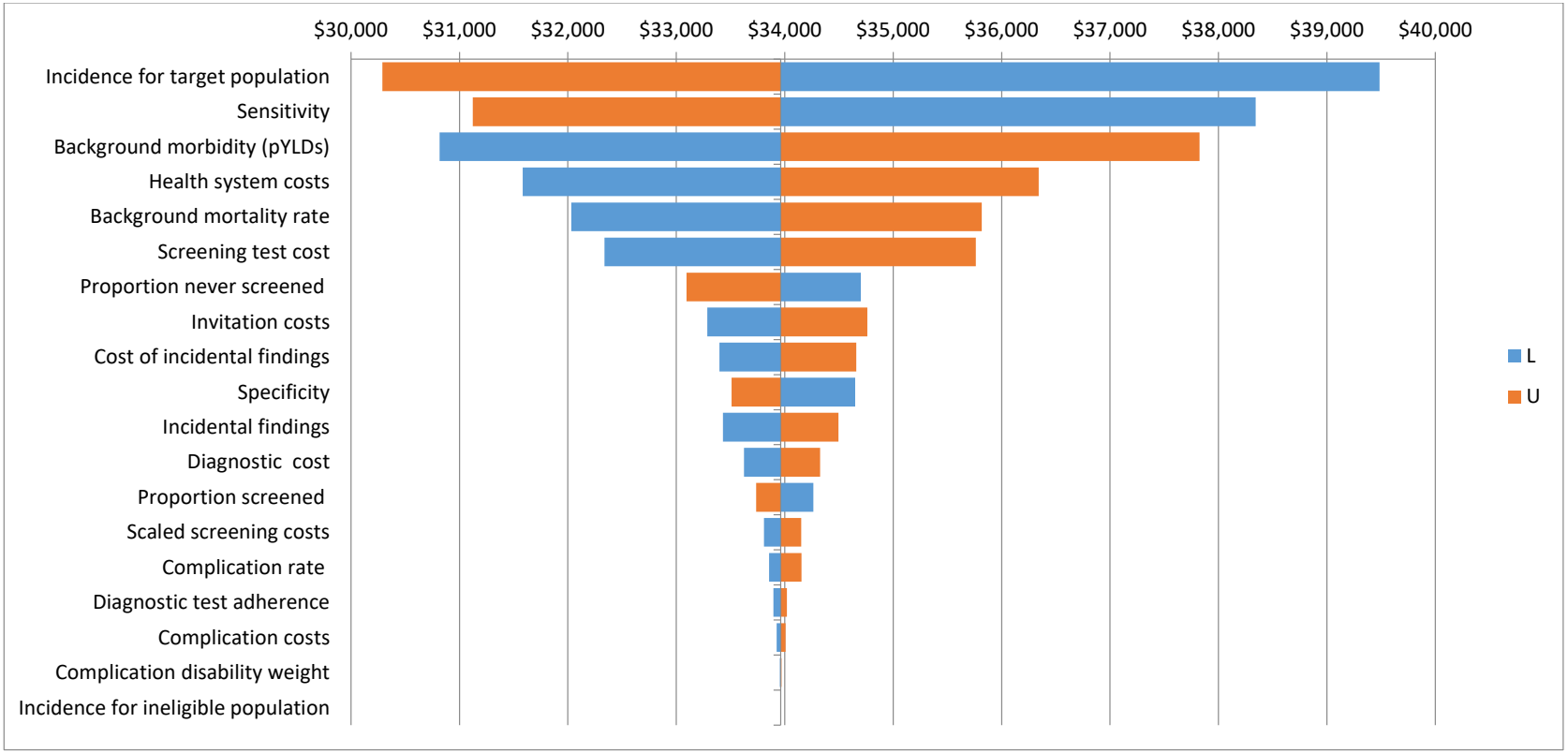
7. Walters S, Maringe C, Butler J, et al. Comparability of stage data in cancer registries in six countries: lessons from the International Cancer Benchmarking Partnership. *Int J Cancer* 2013;132:676-685.
8. Perme MP, Stare J, Esteve J. On estimation in relative survival. *Biometrics* 2012;68:113-120.
9. Nanavaty P, Alvarez MS, Alberts WM. Lung cancer screening: advantages, controversies, and applications. *Cancer Control* 2014;21:9-14.
10. Wiener RS, Schwartz LM, Woloshin S, et al. Population-based risk for complications after transthoracic needle lung biopsy of a pulmonary nodule: an analysis of discharge records. *Ann Intern Med* 2011;155:137-144.
11. van der Deen FS, Ikeda T, Cobiac L, et al. Projecting future smoking prevalence to 2025 and beyond in New Zealand using smoking prevalence data from the 2013 Census. *N Z Med J* 2014;127:71-79.

Appendix B Additional figures and tables

Figure S1 Tornado plot for ICER



NOTE: The incidence, prevalence and mortality costs were adjusted as a set.

Figure S2 Tornado plot for HALYs

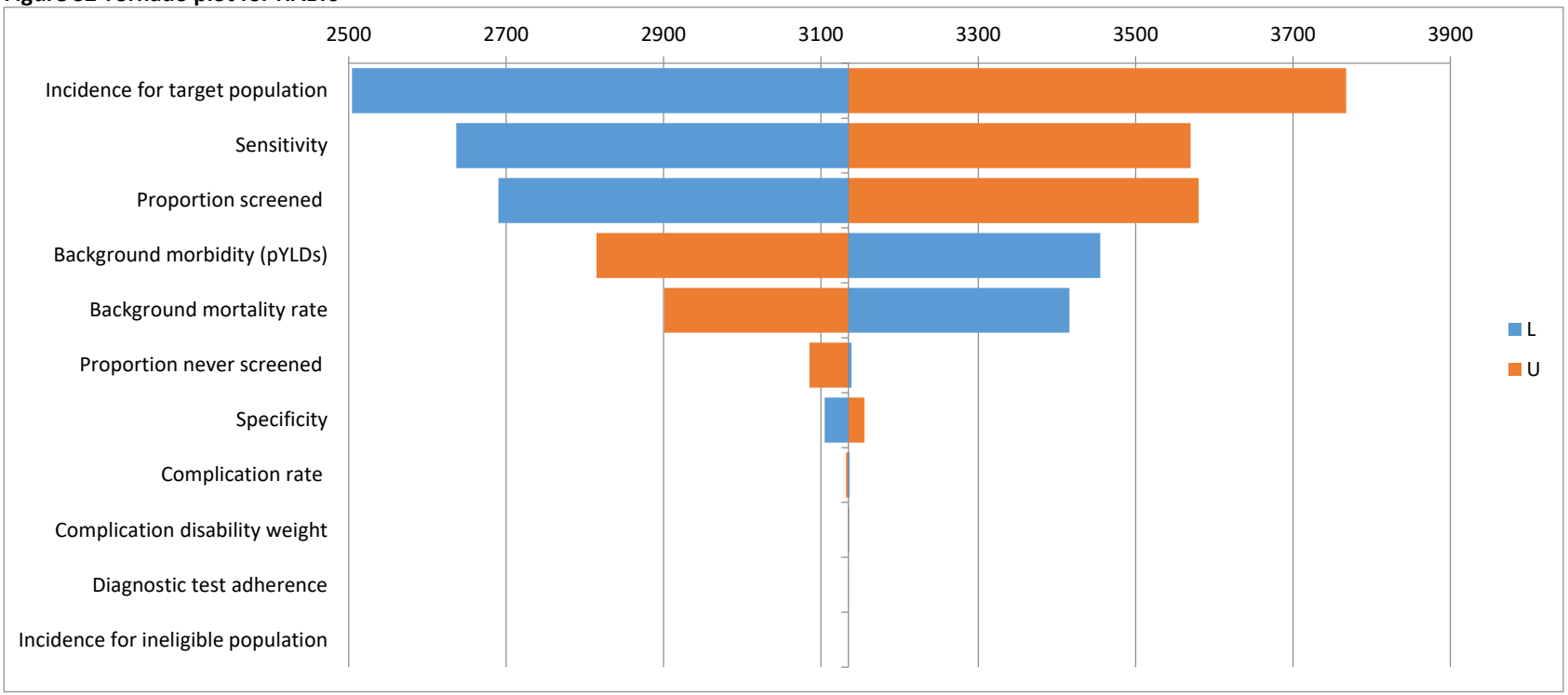


Figure S3 Tornado plot for incremental costs (NZ$ million)

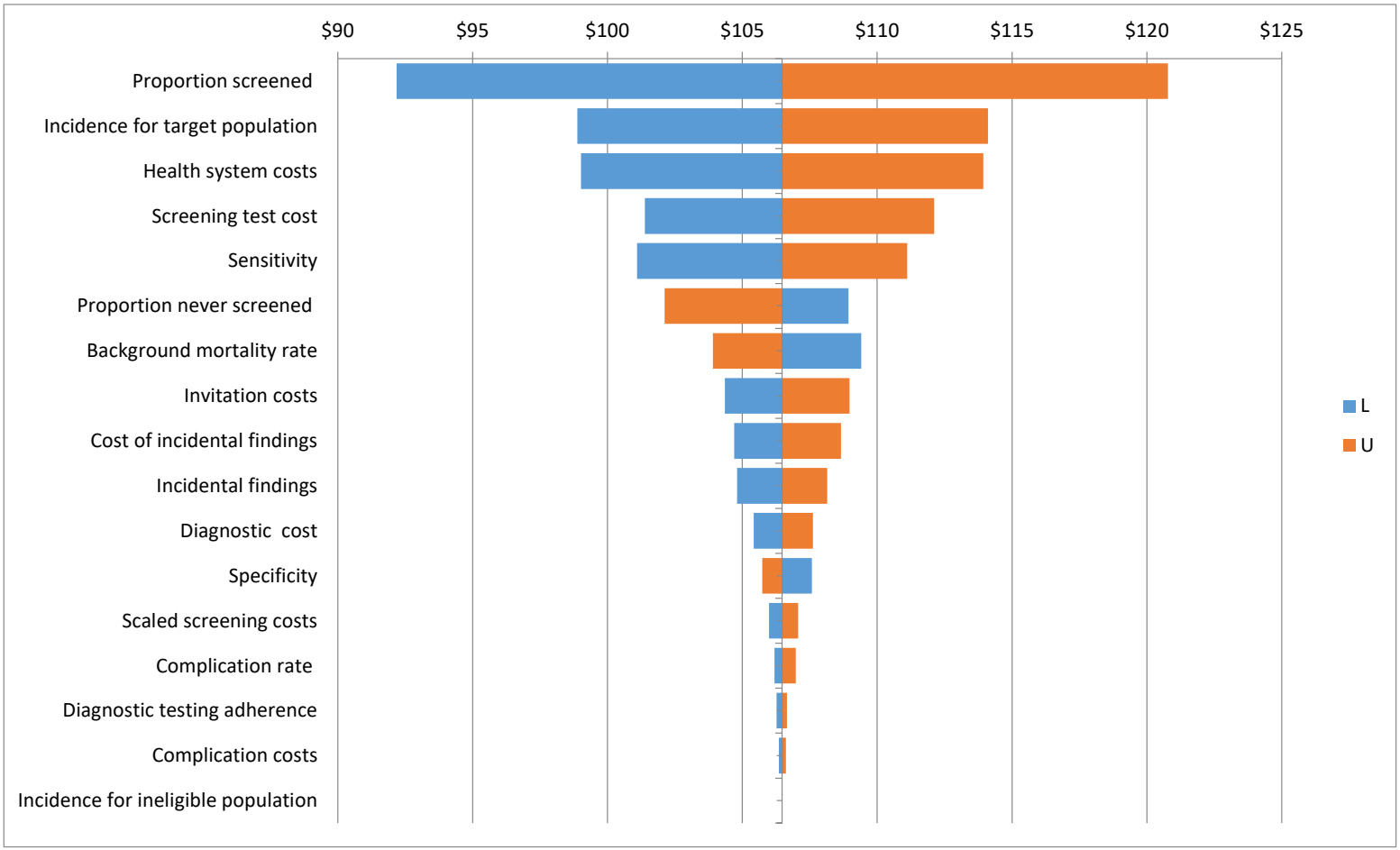


Table S1 Lung cancer mortality rates and HALEs <u>with equal stage specific survival from the intervention</u>, in the 55-59 year eligible and total population: rate differences (RD) and ratios (RR), for Māori compared to non-Māori at baseline and with CT lung screening, by sex.

	Male				Female			
Lung cancer mortality in the screening eligible population, per 1000 aged 55-59 years	non-Māori	Māori	M:NM RD	M:NM RR	non-Māori	Māori	M:NM RD	M:NM RR
Baseline	86.7 (73.5 to 100.6)	236 (197 to 277)	148.9 (122.6 to 178)	2.72 (2.60 to 2.90)	112.0 (95 to 129)	297 (249 to 346)	188 (154 to 218)	2.65 (2.57 to 2.73)
Intervention	79.1 (67.1 to 91.8)	220 (183 to 260)	140 (115 to 169)	2.77 (2.60 to 2.90)	10 (89 to 120)	277 (233 to 325)	17 (144 to 206)	2.67 (2.58 to 2.75)
Lives saved Māori over non-Māori as a result of CT lung screening (per 1000 aged 55-59 yrs)	8.5 (6. to 10.6				11.3 (8.7 to 14.0)			
Lives saved Māori over non-Māori as a result of CT lung screening weighted to the total population (per 1000 aged 55-59 yrs)	1.2 (0.9 to 1.5)				1.7 (1.3 to 2.)			
HALE per eligible individual aged 55-59 yrs	non-Māori	Māori	M:NM QD	M:NM QR	non-Māori	Māori	M:NM QD	M:NM QR
Baseline	17.8 (16.2 to 19.6)	12.6 (10.9 to 14.4)	-5.2 (-5.4 to -5.1)	0.71 (0.68 to 0.74)	19.8 (17.9 to 21.7)	14.6 (12.8 to 16.6)	-5.1 (-5.2 to -5.1)	0.74 (0.71 to 0.77)
Intervention	17.9 (16.3 to 19.7)	12.8 (11.1 to 14.7)	-5.2 (-5.3 to -5)	0.71 (0.68 to 0.74)	19.9 (18.0 to 21.9)	14.9 (13.0 to 17.0)	-5.0 (-5 to -4.9)	0.75 (0.72 to 0.78)
Healthy days gained by Māori over non-Māori as a result of CT lung screening (per individual **eligible population** aged 55-59 yrs)	31.2 (21.2 to 42.6)				59.8 (41.9 to 79.5)			
Healthy days gained Māori over non-Māori as a result of CT lung screening weighted to the total population (per individual aged 55-59 yrs)	4.6 (3.2 to 6.2)				9.0 (6.4 to 11.9)			