The HPV screening policy

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Sensitivity of a screening test

	Disease of interest		
	Present	Absent	
Test positive	a	b	a + b
Test negative	c	d	c + d
Total	a + c	b + d	T

$$\text{Sensitivity} = \frac{a}{a + c} = \text{probability of detection in those with the disease}$$

Comparing two screening tests

- The disease of interest for the tests should be the same
- If one test detects disease over a greater period of time, sensitivity will be increased without improved detection of advanced cellular changes
- When regression is a major part of the natural history of the disease, increased sensitivity need not translate into increased detection of advanced disease as it can be due to increased detection of disease that will regress
- The tests may produce different amounts of overdiagnosis

- “For comparing the sensitivities of two screening tests, the single cohort paired design is problematic, as individual test sensitivities and overdiagnosed cases cannot be determined. Formulating screening policy based on this study design is precarious.”

- Prorok PC, Kramer BS, Miller AB. Study designs for determining and comparing sensitivities of disease screening tests. J Med Screen 2015, Vol. 22(4) 213–220

Trials of HPV testing versus cytology

- Four trials, the main disease of interest reported was CIN2 and CIN3 combined
- CIN2 and CIN3 have quite different natural histories, progression and regression
- CIN3 should be the target for cervical screening
- Only one trial compared the New Zealand test of LBC with HPV testing
- Two trials clearly indicate that, after 6 years of screening, HPV testing detects the same cumulative number of CIN3 abnormalities as cytology, not more.

Swedish RCT: Elfstrom KM et al BMJ 2014;348:g130 doi: 10.1136/bmj.g130

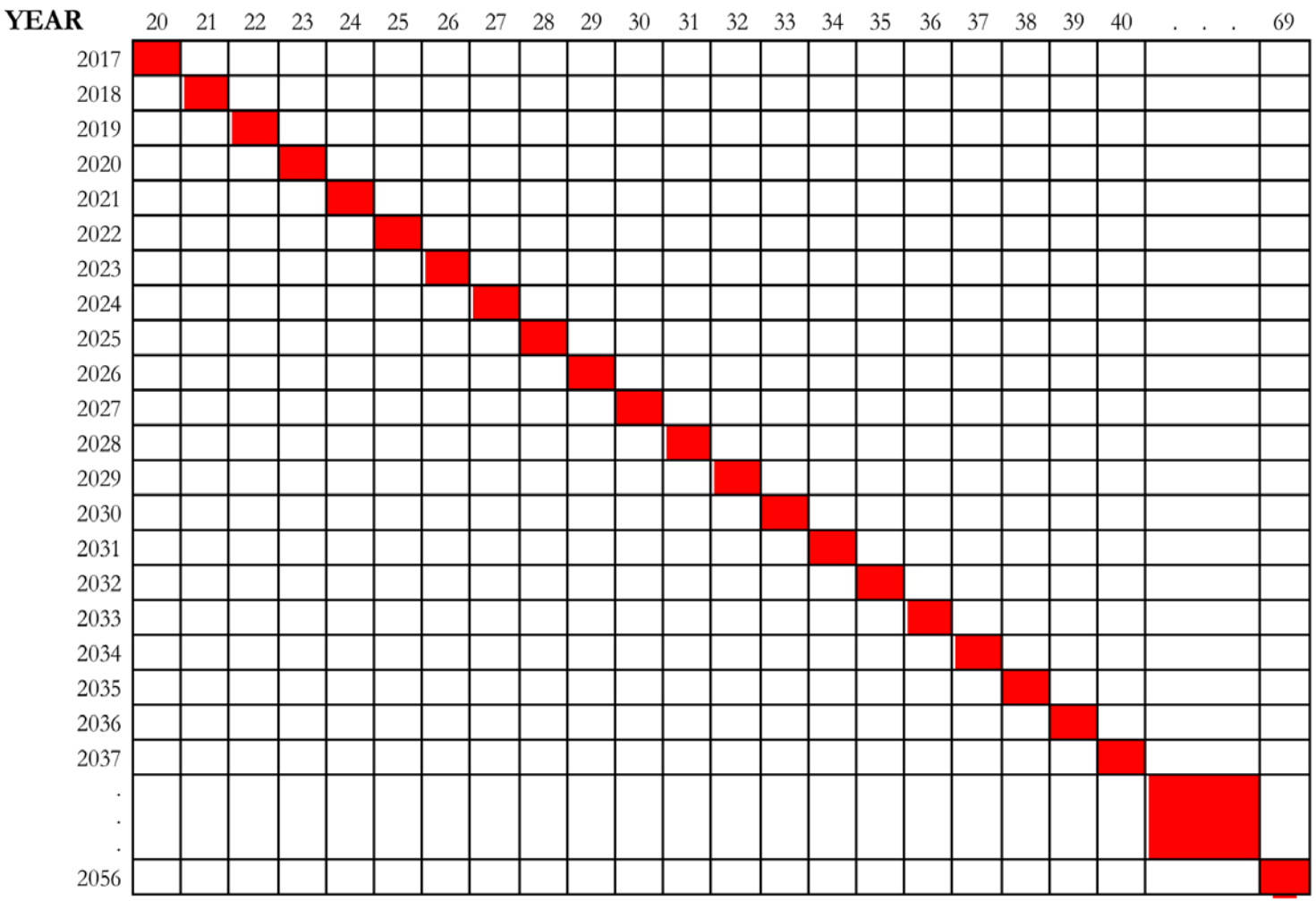
- "During the first six years of follow-up, the cumulative incidence of CIN3+ was greater in the intervention arm (fig 3), reflecting that women persistently positive for HPV and with negative cytology had been referred to colposcopy, resulting in additional cases of CIN3+ detected. However, after six years of follow-up the CIN3+ rates did not differ, suggesting that the additional CIN3+ cases detected are more likely to reflect early diagnosis rather than overdiagnosis."

5-yearly HPV testing versus 3-yearly LBC

Simulation models

- The Ministry of Health have paid for the Australian simulation method. This simulates the screening experience of women born 1997 through to the year 2056 (when they would be aged 59) has been what has guided policy
- The annual experience of women currently aged 40 in 2017 is then assumed to be the same as the simulated experience of the cohort in 2037

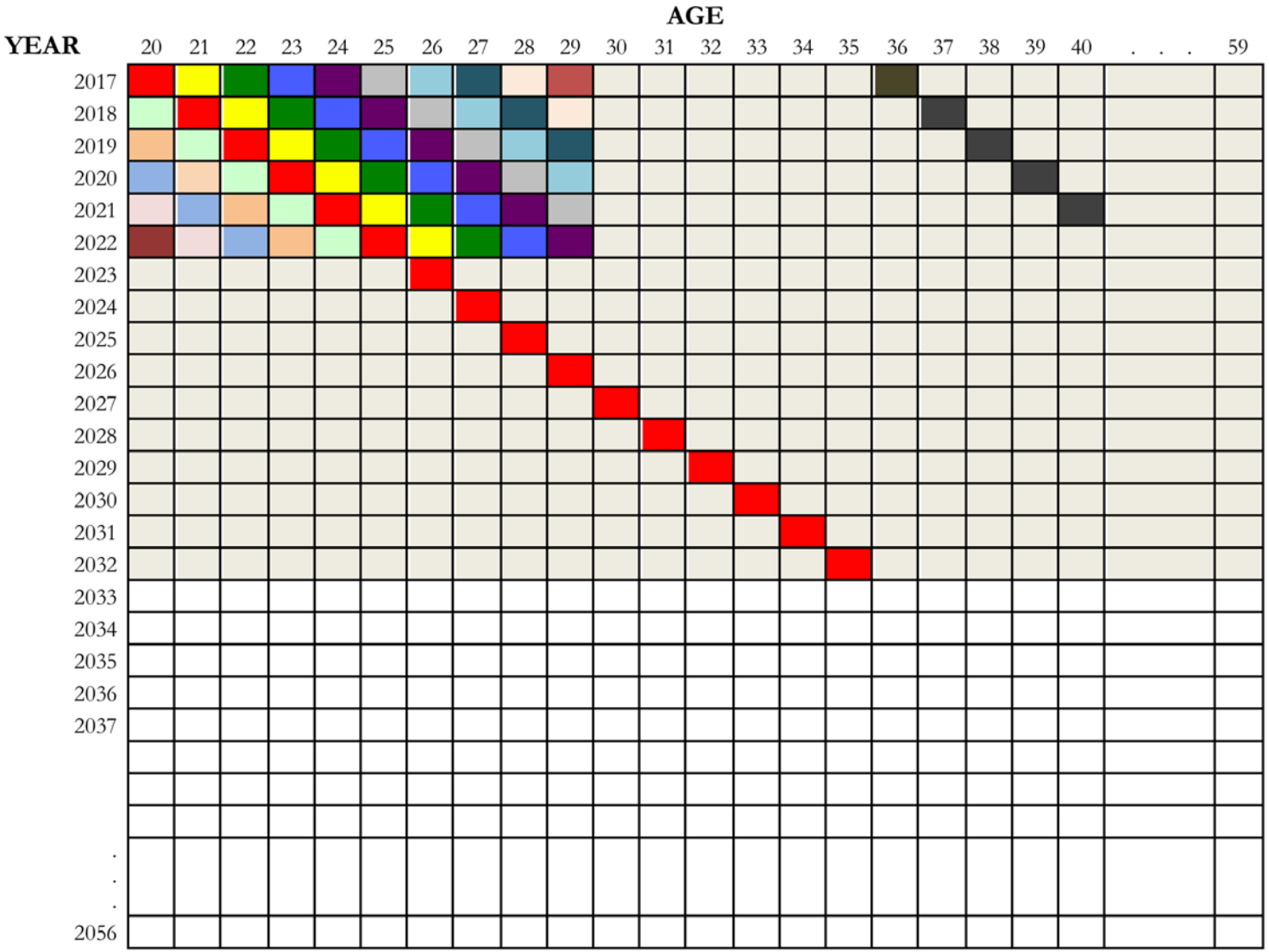
Cohort born 1997



New Zealand simulation model

- Based on the model of Parkin DM and Moss S
- Uses a health service approach and simulates everyone over the ensuing 15 years
- The model accurately estimated the effects of the introduction of the NCSP and the introduction of LBC
- Recently adapted to incorporate oncogenic HPV infection vaccine and assessment of HPV testing

Cohorts at different stages of screening and at different risk



Comparative effects of screening policies

Policy	Relative protection (RP)	Proportional change in RP
Current LBC with vaccination	61%	reference
HPV 98.4% sensitivity, 80% coverage, 5 yearly and vaccination	58%	-4.9%
HPV 85% sensitivity, 80% coverage, 5-yearly and vaccination	57%	-6.6%
HPV 98.4% sensitivity, current coverage 5-yearly and vaccination	58%	-5.0%