Feasibility of targeted screening for melanoma

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Cancer Council Queensland

ASSC Melanoma Screening Summit
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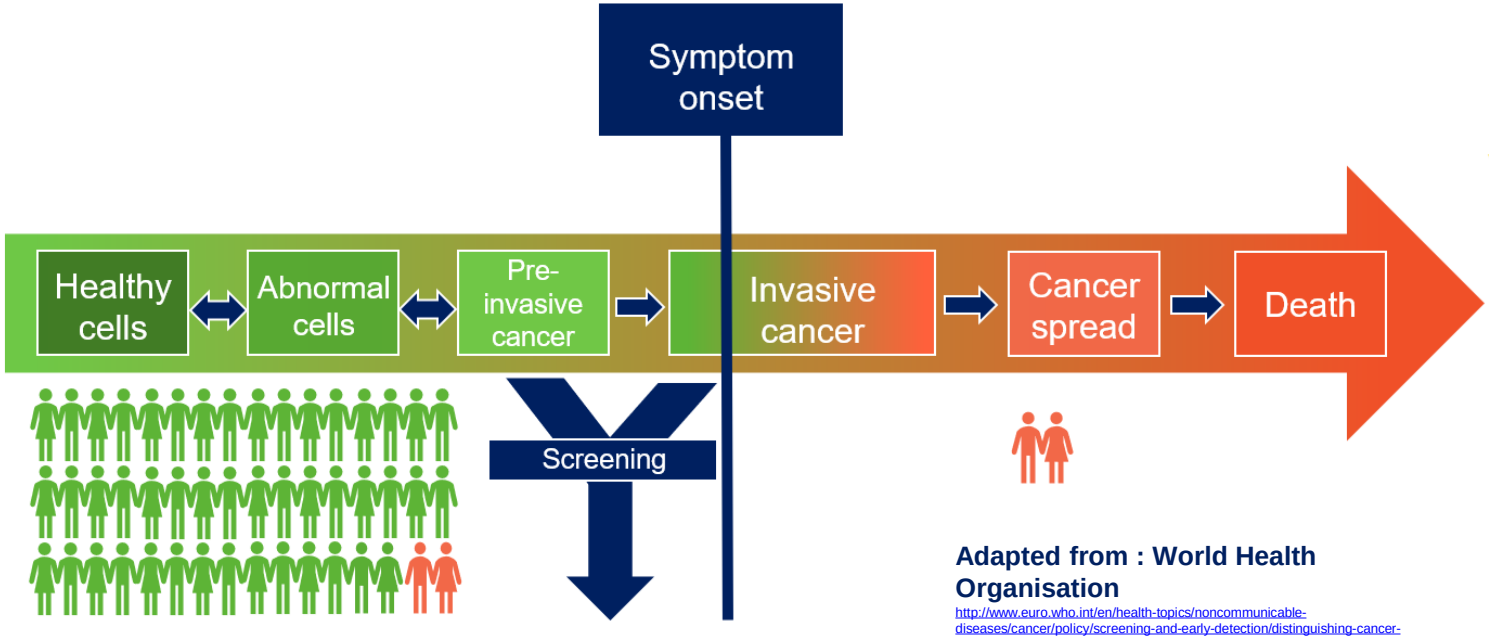
What is population screening?

Population screening: a test that is offered systematically to all individuals in a target group, usually defined by age, as part of an organised program

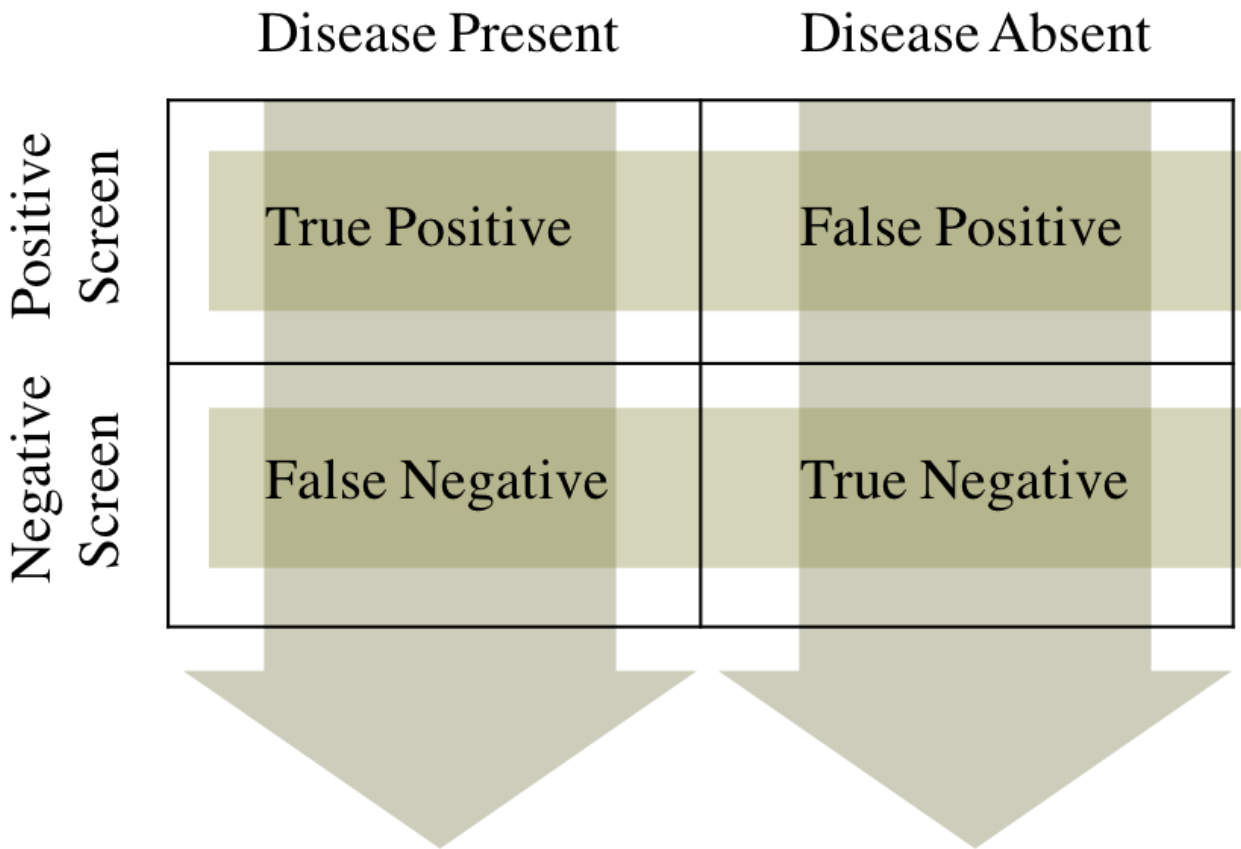
Department of Health, Australian Government



Adapted from : World Health Organisation

http://www.euro.who.int/en/health-topics/noncommunicable-diseases/cancer/policy/screening-and-early-detection/distinguishing-cancer-screening-from-early-diagnosis

Measures of screening effectiveness



Positive Predictive Value

$$\text{PPV} = \frac{TP}{TP + FP}$$

Negative Predictive Value

$$\text{NPV} = \frac{TN}{TN + FN}$$

Sensitivity

$$= \frac{TP}{TP + FN}$$

Specificity

$$= \frac{TN}{TN + FP}$$

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Adoption of population screening

$$\textbf{Positive Predictive Value} = \frac{\text{Sensitivity X } \textbf{\textit{Prevalence}}}{\text{Sensitivity x } \textbf{\textit{Prevalence}} + \left[(1\text{-Specificity}) \text{ x } (1 - \textbf{\textit{Prevalence}})\right]}$$

- **For same specificity and sensitivity, lower prevalence means lower Positive Predictive Value (PPV)**
- **Screening is more feasible when the screened population has a higher prevalence of the disease**

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RCTs for screening

- **Randomised controlled trials (RCT) provide the only definitive evidence for the effectiveness of screening**

- **Prevalence rate of outcome measure is important in sample size calculations (Intervention and Control Groups) for the RCT**

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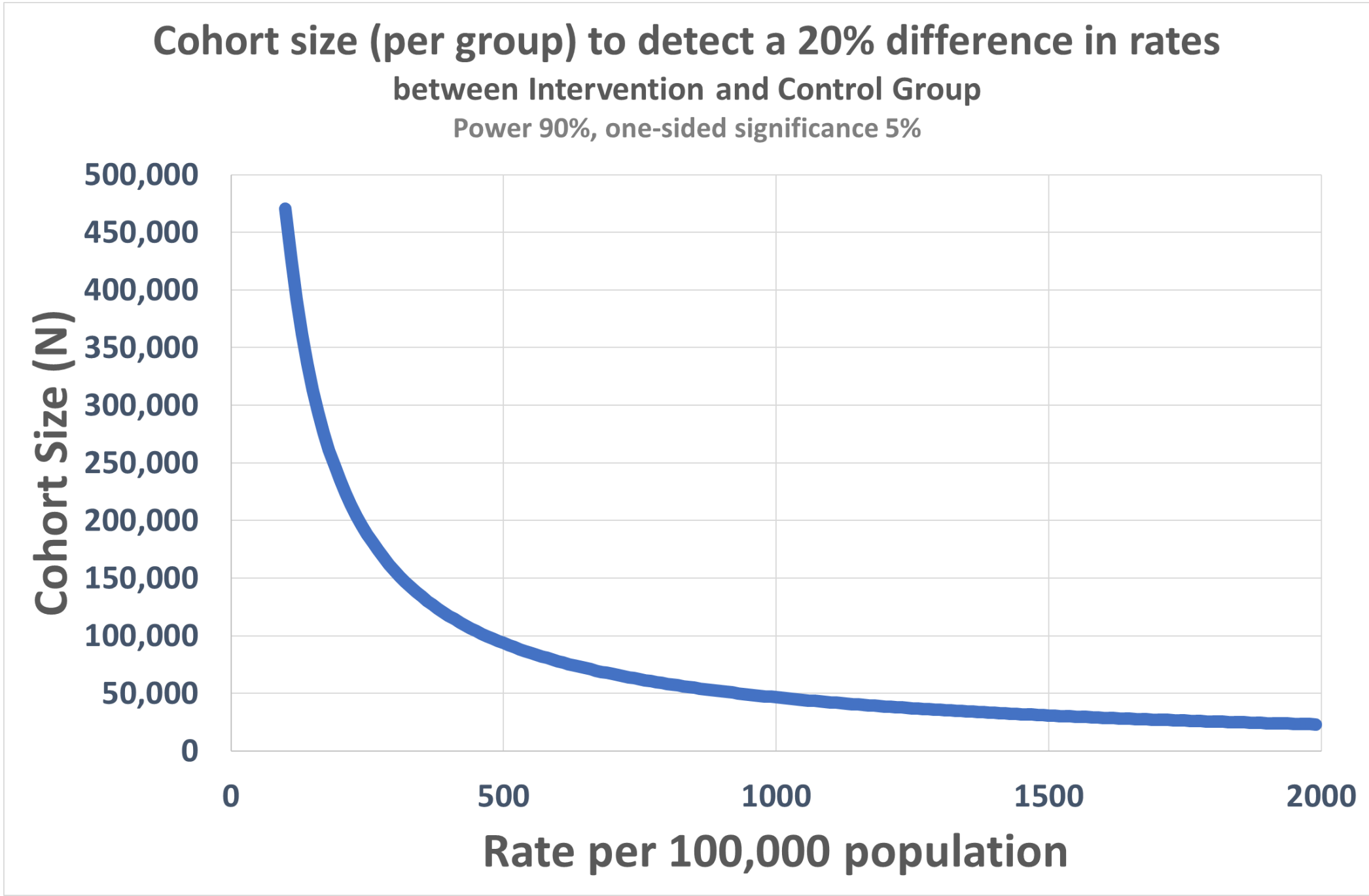
Cohort size (per group) to detect a 20% difference in rates
between Intervention and Control Group
Power 90%, one-sided significance 5%
Cohort Size (N)
500,000
450,000
400,000
350,000
300,000
250,000
200,000
150,000
100,000
50,000
0
0
500
1000
1500
2000
Rate per 100,000 population

RCTs for melanoma screening

- Optimal design would be based on a reduction in melanoma mortality
- Often not feasible due to the generally high survival (low mortality) and long time lag between diagnosis and death
- An alternative is to use an intermediate outcome – for example, a reduction in the incidence of thick melanoma
- Extrapolate to estimate impact of this on melanoma mortality

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Sample size PER GROUP to detect a 20% reduction in incidence of “thick” melanoma over 10 years (chosen at ≥2mm for demonstration purposes)

Population group	≥ 2.00mm		Estimated number needed to screen to prevent ONE melanoma death
	10-year cum. incidence rate / 100,000	Required cohort size PER GROUP	
All women	101	465,000	22,400
All people	147	320,000	13,800
All men	197	240,000	9,800
Women 50+	259	181,000	8,800
Men 50+	573	82,000	3,500

Note: Queensland data, 2011-2015, 90% power, one sided 5% significance

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How to ensure the population being screened has a high enough prevalence of the disease?

Targeted cancer screening uses information about who are most at risk of the outcome to separate those who are more likely to benefit from screening from those who are less likely to benefit.

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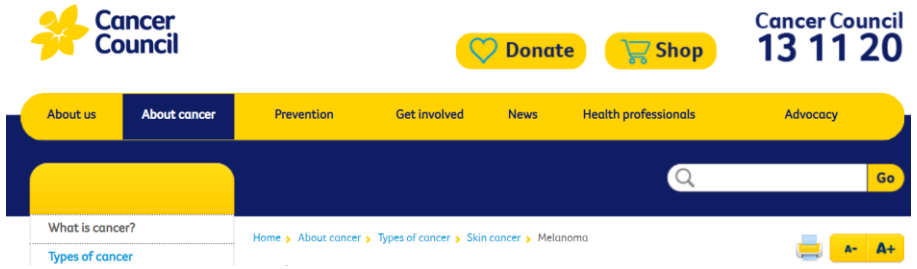
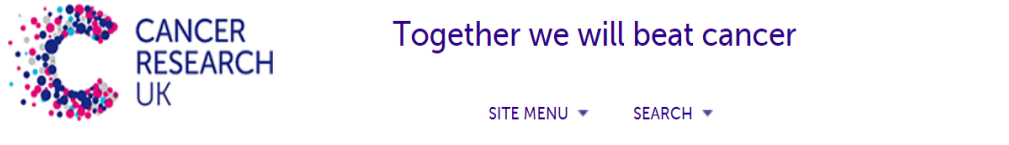
Advocating for targeted screening for melanoma



Screening for melanoma

There is no organised screening program for melanoma. However, individuals at high risk of melanoma should be taught to check their skin for irregular or changing lesions, and have annual checks by a dermatologist.

Download Cancer Council's skin cancer identification poster to help identify potential skin cancers.



Melanoma skin cancer

Some people have a much higher than normal risk of melanoma and should have regular checks by a skin cancer specialist. This includes people who:

- have 2 family members with melanoma and also have a lot of large, irregularly shaped moles
- were born with a very large mole (bigger than 20cm across)
- have 3 or more people in their family diagnosed with melanoma or pancreatic cancer
- have had more than 1 melanoma

US Preventive Services Task Force | EVIDENCE REPORT

Screening for Skin Cancer in Adults
Updated Evidence Report and Systematic Review for the US Preventive Services Task Force

Karen J. Wernli, PhD, MS; Nora B. Henrikson, PhD, MPH; Caitlin C. Morrison, MPH; Matthew Nguyen, MPH; Gaia Pocobelli, PhD; Paula R. Blasi, MPH

CONCLUSIONS AND RELEVANCE Only limited evidence was identified for skin cancer screening, particularly regarding potential benefit of skin cancer screening on melanoma mortality. Future research on skin cancer screening should focus on evaluating the effectiveness of targeted screening in those considered to be at higher risk for skin cancer.

26 July 2016

AAD statement on USPSTF recommendation on skin cancer screening

Statement from Abel Torres, MD, JD, FAAD, President, American Academy of Dermatology: — SCHAUMBURG, Ill. (July 26, 2016) — "In its Recommendation Statement on Screening for Skin Cancer, the U.S. Preventive Services Task Force — a group that provides guidance for primary care physicians — has determined that

"The AAD encourages everyone to serve as their own health advocate by regularly conducting skin self-exams. Individuals who notice any unusual spots on their skin, including those that are changing, itching or bleeding, should make an appointment with a board-certified dermatologist. In addition, individuals with an increased risk of melanoma — including men older than 50; people with more than 50 moles, or large or unusual moles; individuals with fair skin; and those with a history of skin cancer — should talk to a dermatologist about how often they should receive a skin exam from a doctor."

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Targeted screening for melanoma

- Identify what characterises a population at “high risk”
- Risk factor information available in population cancer registries is limited
- Reliant on research studies, particularly those using a cohort design

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Targeted screening

OXFORD

JNCI J Natl Cancer Inst (2018) 110(10): djy023

doi: 10.1093/jnci/djy023
First published online March 11, 2018
Article

QSKIN Cohort study

- QLD residents, 40-69 years
- N=41,954
- Median follow up of 3.4 years
- No previous history of skin cancer
- Risk of invasive melanoma diagnosis
- n=257 invasive melanomas (thin and thick combined)

ARTICLE

Risk Stratification for Melanoma: Models Derived and Validated in a Purpose-Designed Prospective Cohort

Catherine M. Olsen, Nirmala Pandeya, Bridie S. Thompson, Jean Claude Dusingize, Penelope M. Webb, Adele C. Green, Rachel E. Neale, David C. Whiteman; for the QSkin Study

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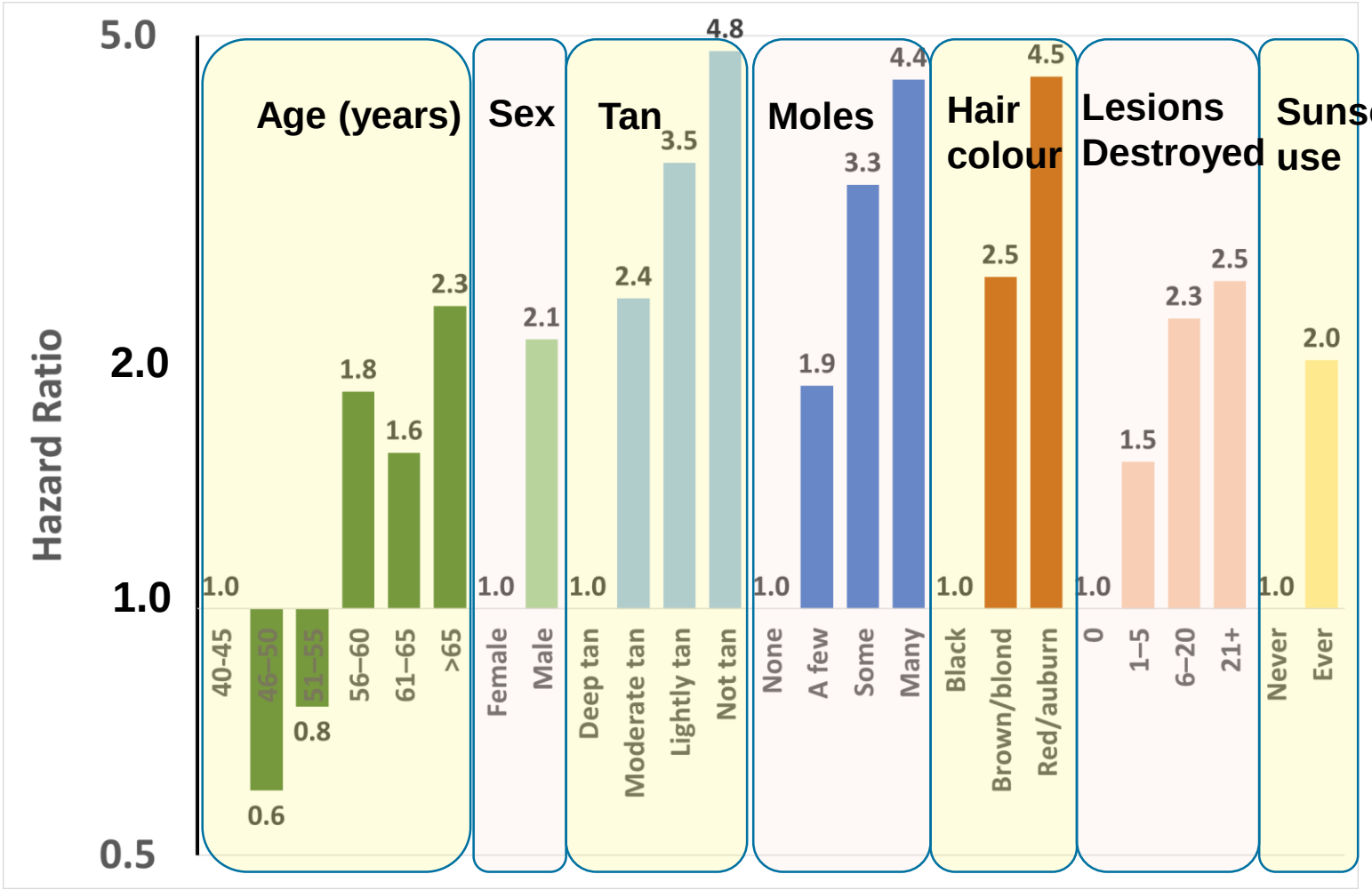
Risk factors predicting diagnosis of invasive melanoma (QSKIN) – 40 to 69 year old



Predicted risk of invasive melanoma derived from multivariate model

Source: Olsen, Pandeya, Thompson, Dusingize, Webb, Green, Neale, Whiteman.
Risk Stratification for Melanoma: Models Derived and Validated in a Purpose-Designed Prospective Cohort. J Natl Cancer Inst, 2018

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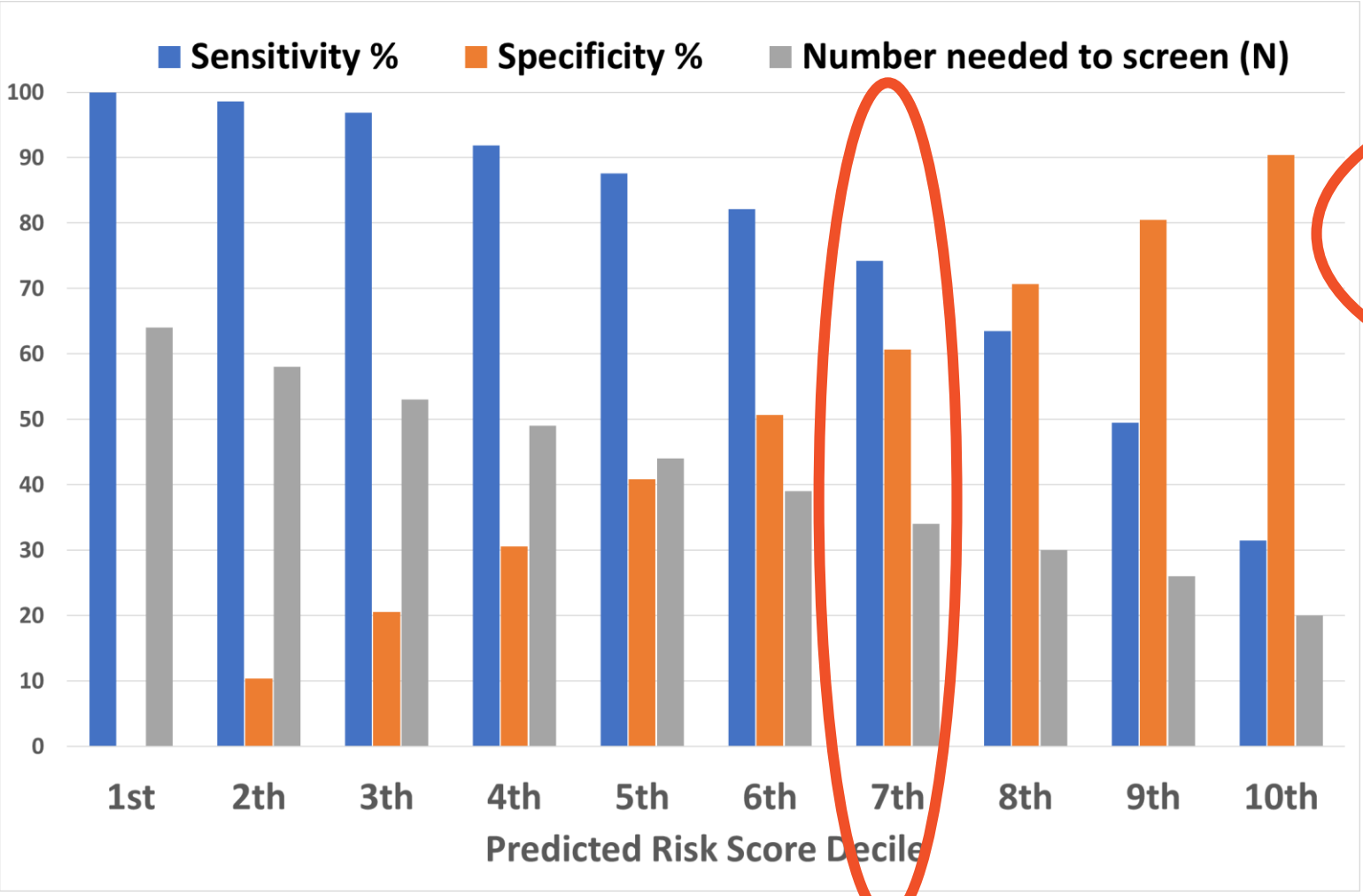
Risk factors predicting diagnosis of invasive melanoma – 40 to 69 year olds



- 7th decile of risk score
- Of 34 people meeting the threshold, one person would develop melanoma
- Detect 74% of future cases

- 5th decile of risk score
- Of 44 people meeting the threshold, one person would develop melanoma
- Detect 88% of future cases

Source: Olsen, Pandeya, Thompson, Dusingize, Webb, Green, Neale, Whiteman.
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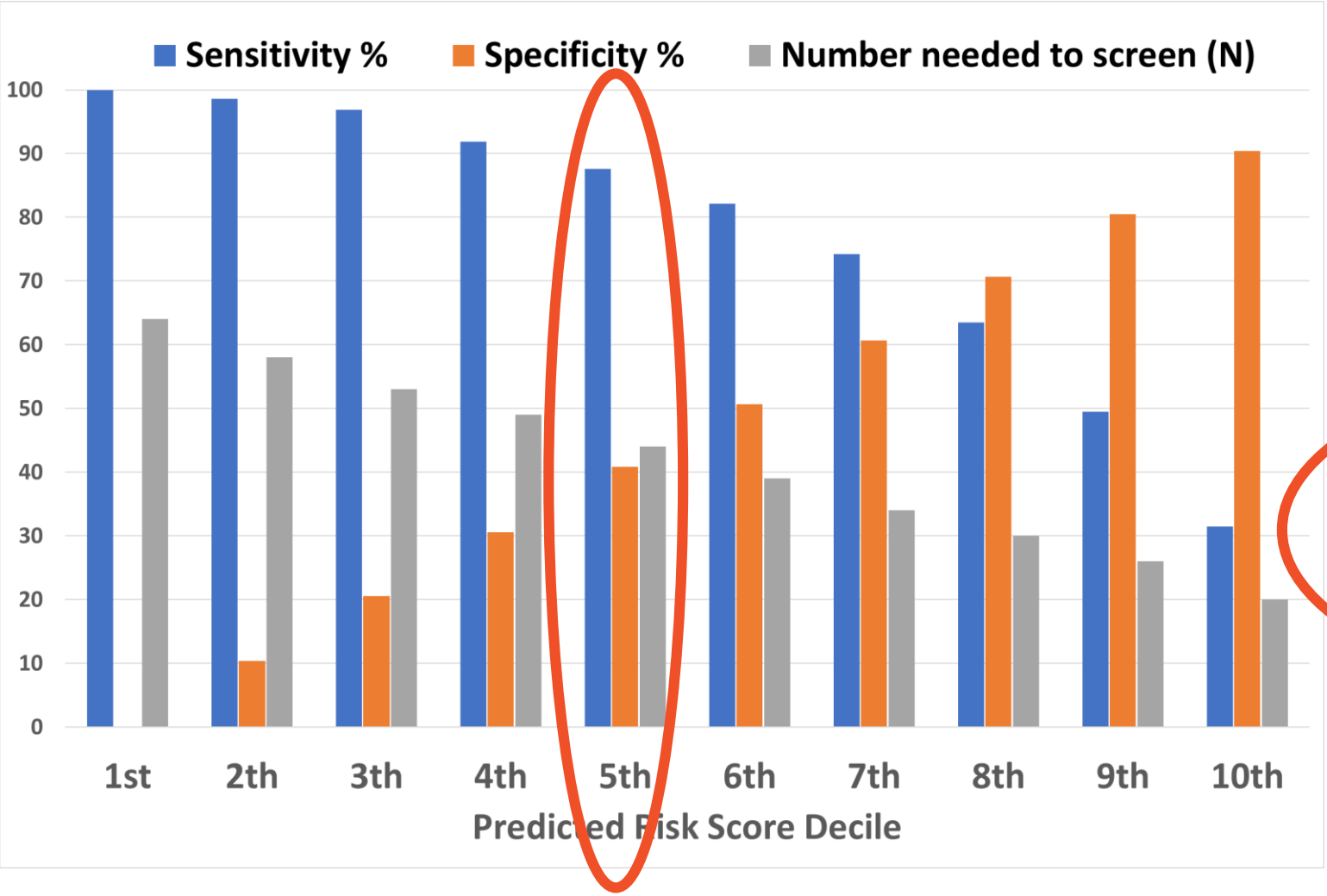

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Risk factors predicting diagnosis of invasive melanoma

However,

- Small numbers of invasive melanomas diagnosed (n=257)
  - Substantial uncertainty associated with the risk estimates
  - Not possible to model “thick” melanomas (n=23 ≥ 2mm) separately
- Still unclear what the key risk factors for a diagnosis of “thick” melanomas are

Source: Olsen, Pandeya, Thompson, Dusingize, Webb, Green, Neale, Whiteman.
Risk Stratification for Melanoma: Models Derived and Validated in a Purpose-Designed Prospective Cohort. J Natl Cancer Inst, 2018

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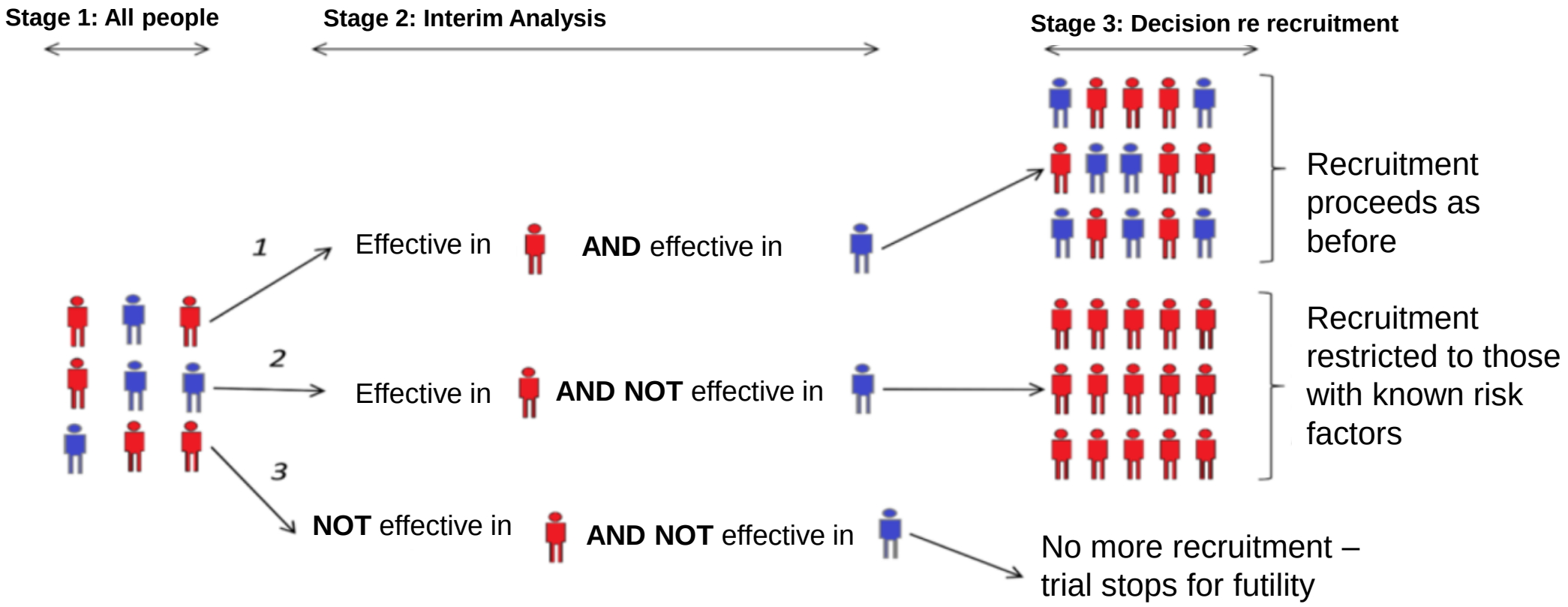
Selecting “high risk” cohort: Adaptive enrichment method



Participant has known risk factors

Participant has no known risk factors

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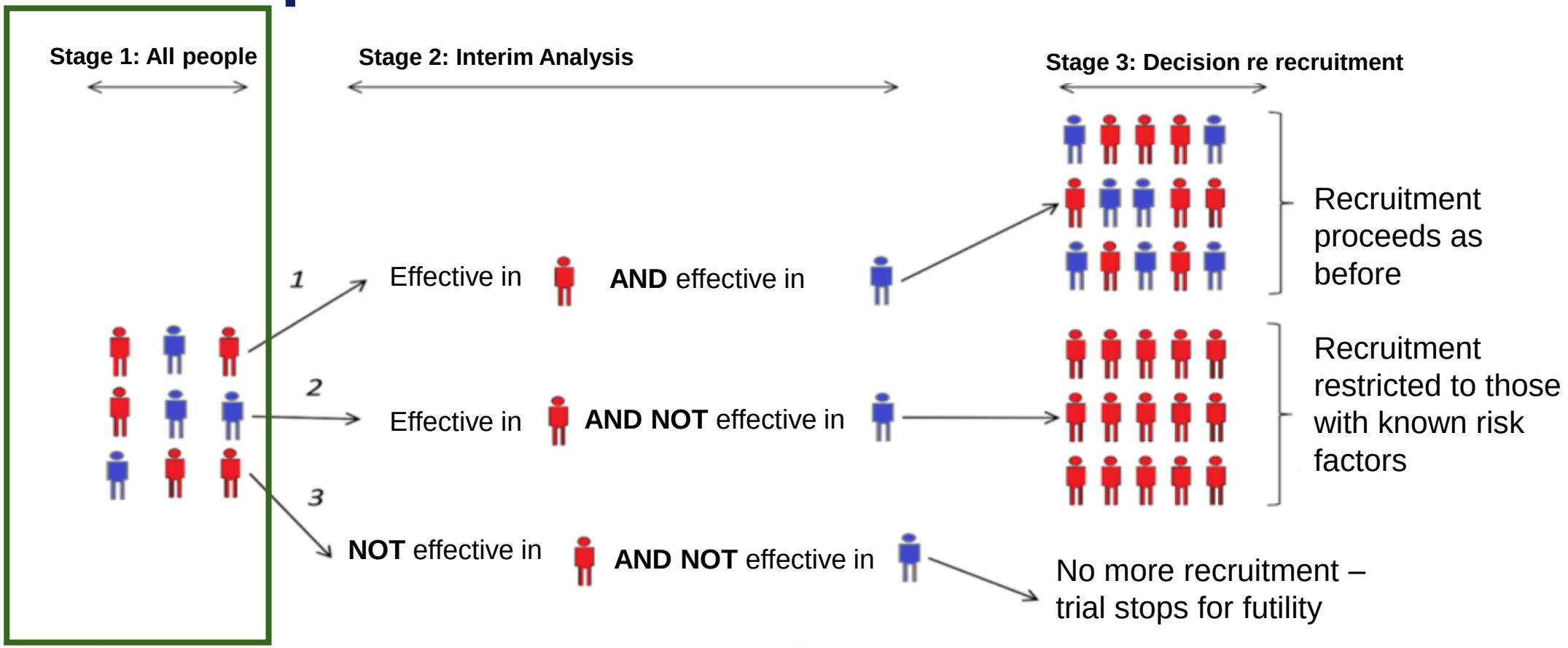

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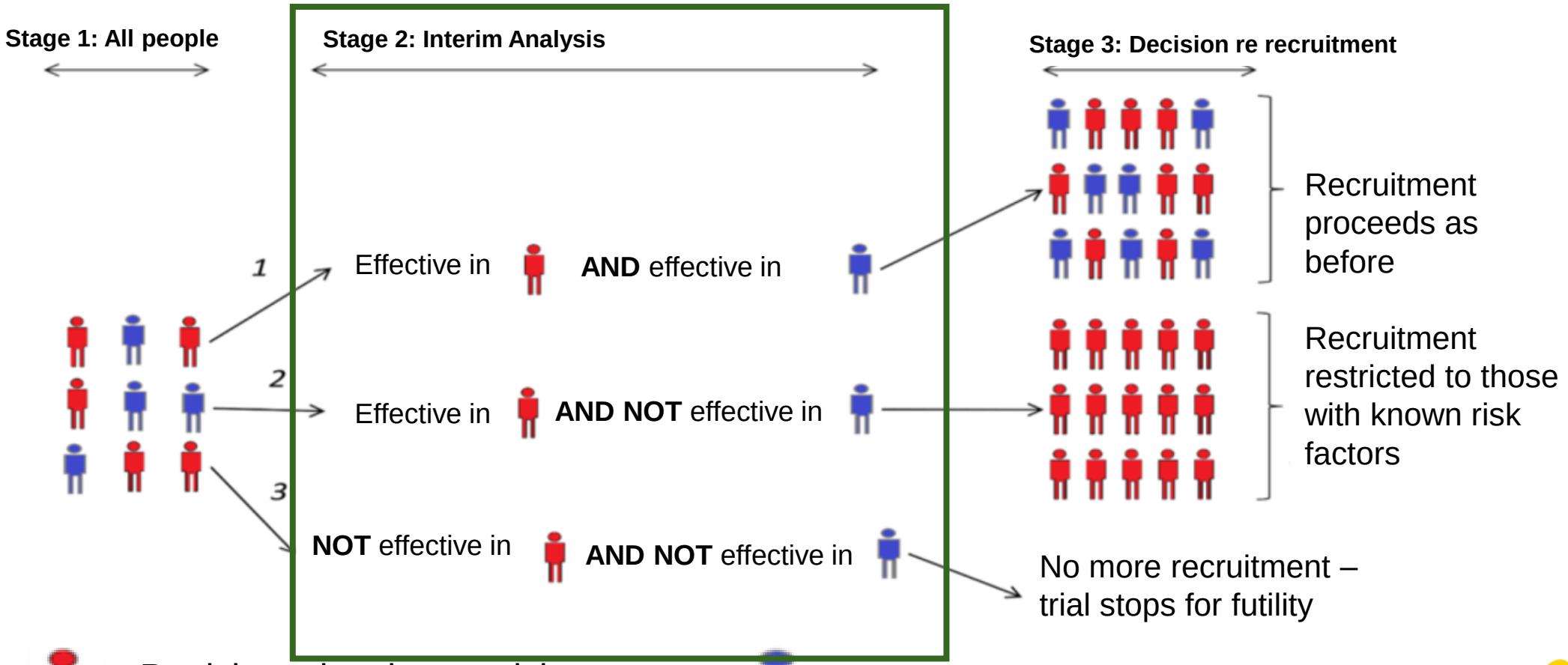

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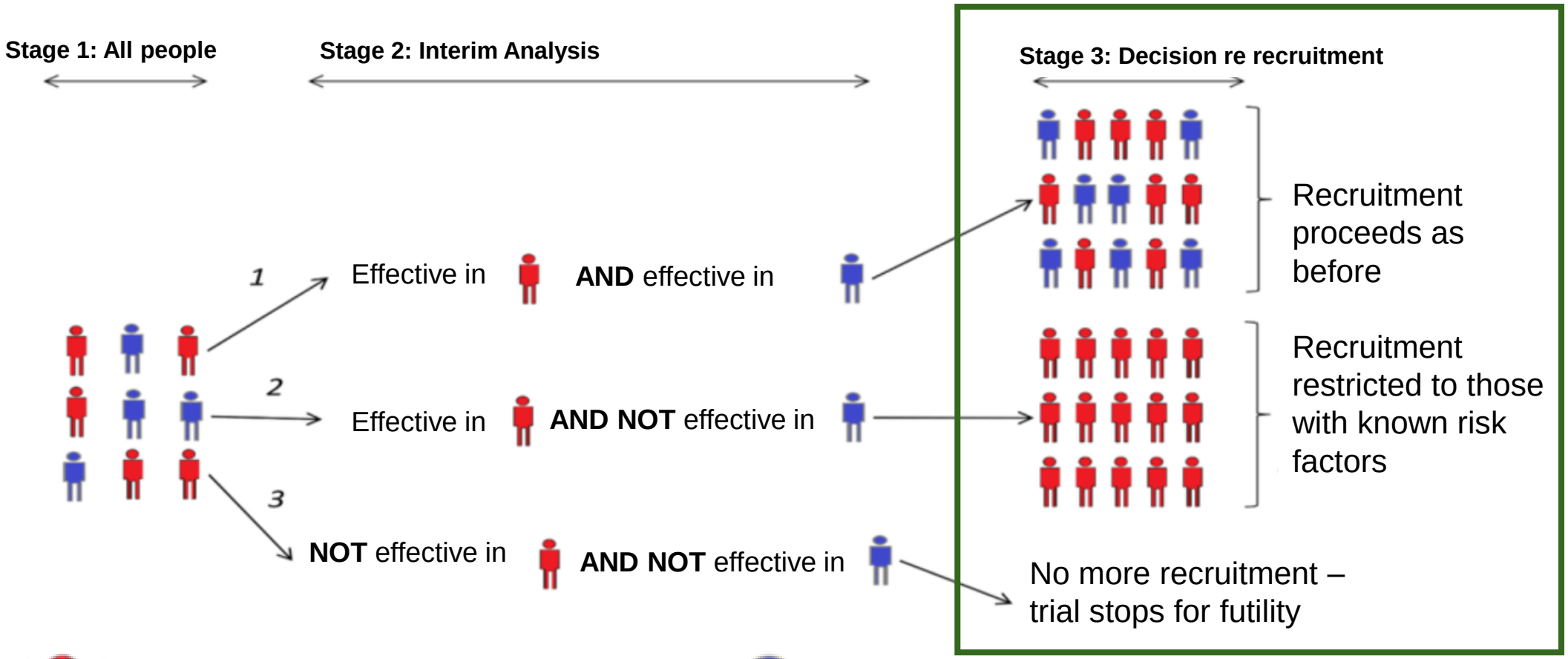

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Key issues to consider with targeted screening for melanoma

- **Greater clarity around the optimal outcome measure for a trial of melanoma screening**
  - Reducing incidence of “thick” melanoma (at diagnosis)?
  - Reducing melanoma mortality (multiple years after diagnosis)?
  - Others?

- **Determine the risk factors that predict “high risk” for this outcome**

- **Identification of “high risk” groups in the population**

- **Determine the optimal trade off between screening cost, performance and potentially missing some melanomas**

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Thank you

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