

Conflict of interest statement

No conflicts of interest to declare.

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Cost-Effectiveness Analysis of Diagnostic and Screening Strategies: When and How to Compare a Googolplex of Strategies?

A case study in cascade screening for familial hypercholesterolaemia

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The project team includes: Nadeem Qureshi (PI), Beth Woods, Rita Faria, Pedro Saramago, Ed Cox, Jo Leonardi Bee, Laura Condon, Stephen Weng, Ralph K Akyea, Barbara Iyen, Paul Roderick, Steve E, Humphries, William Rowlands, Melanie Watson, Kate Haralambos, Ryan Kenny, Dev Datta, Zosia Miedzybrodzka, Christopher Byrne, and Joe Kai.

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Take home messages

The principle

- Compare all relevant options

In practice

- Identify all options
- Select those to evaluate

Selection criteria

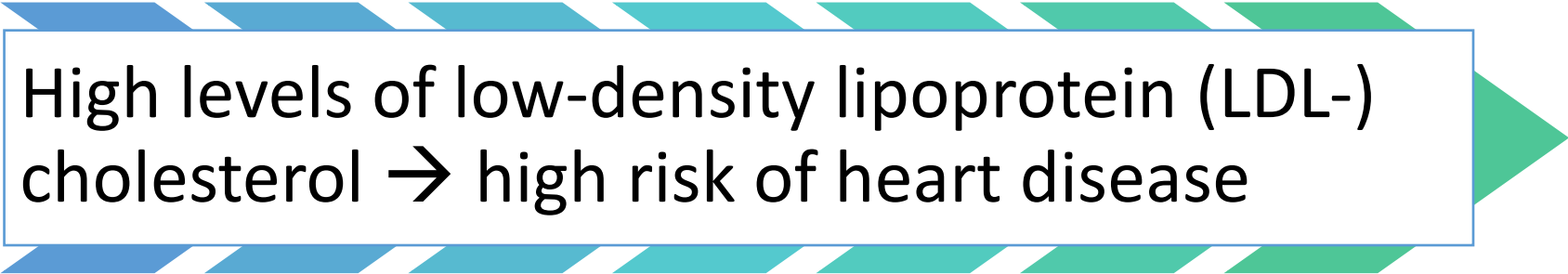
- Based on cost-effectiveness

The mission

**What is the cost-effective protocol
for cascade screening for FH?**

Background

Familial hypercholesterolaemia (FH)

A decorative graphic consisting of a series of overlapping, slanted rectangular blocks in shades of blue and green, forming a large arrow pointing to the right. A white rectangular box is superimposed on the left side of this arrow.

High levels of low-density lipoprotein (LDL-) cholesterol → high risk of heart disease

Background

Familial hypercholesterolaemia (FH)

High levels of low-density lipoprotein (LDL-) cholesterol → high risk of heart disease

Cascade screening

Process of systematically testing people who are at risk of an inherited condition.

What are the “usual” options?

What are the “usual” options?

1

Offer the genetic test to
known individuals with FH

Options about which
clinical score

What are the “usual” options?

1

Offer the genetic test to
known individuals with FH

Options about which
clinical score

2

Contact their relatives:
directly or indirectly

Options about the
method of contact

What are the “usual” options?

1 Offer the genetic test to known individuals with FH

Options about which clinical score

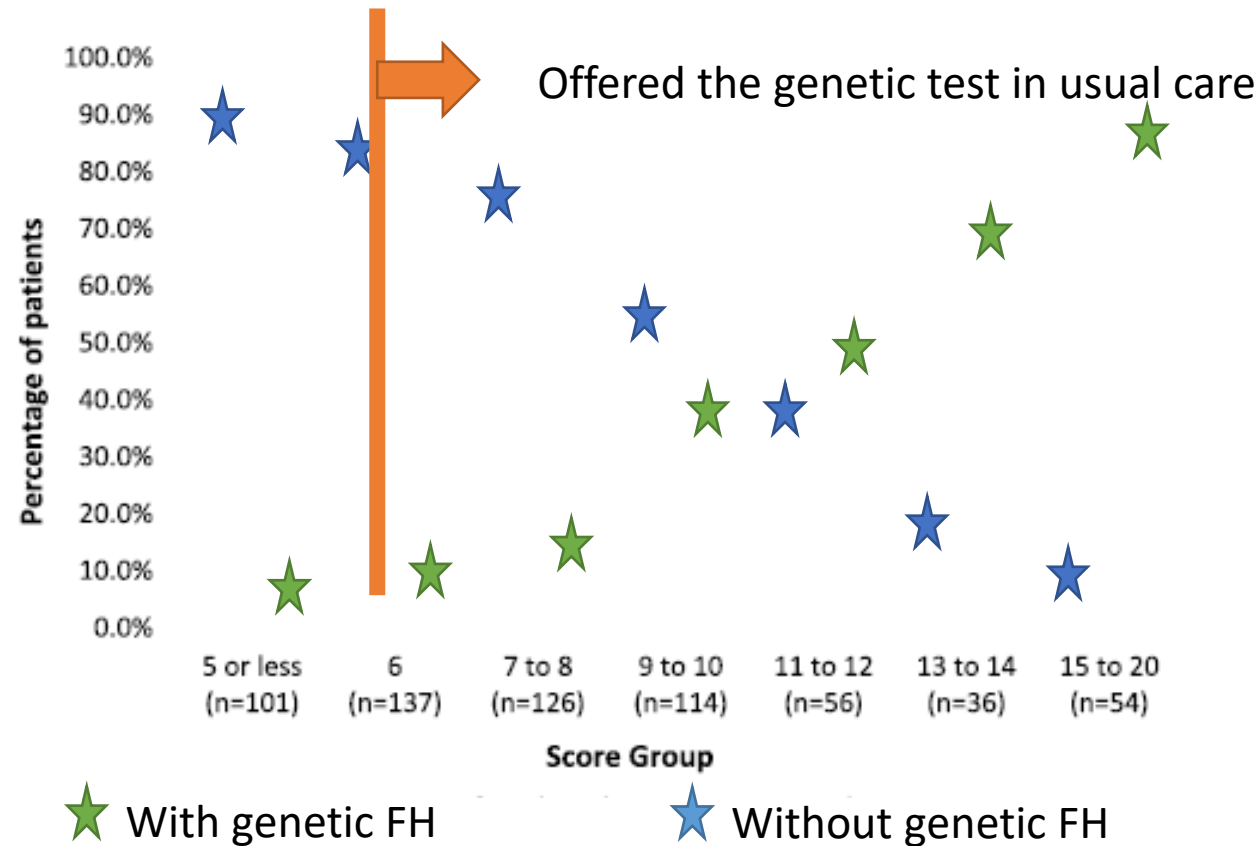
2 Contact their relatives: directly or indirectly

Options about the method of contact

3 Offer their relatives the genetic test

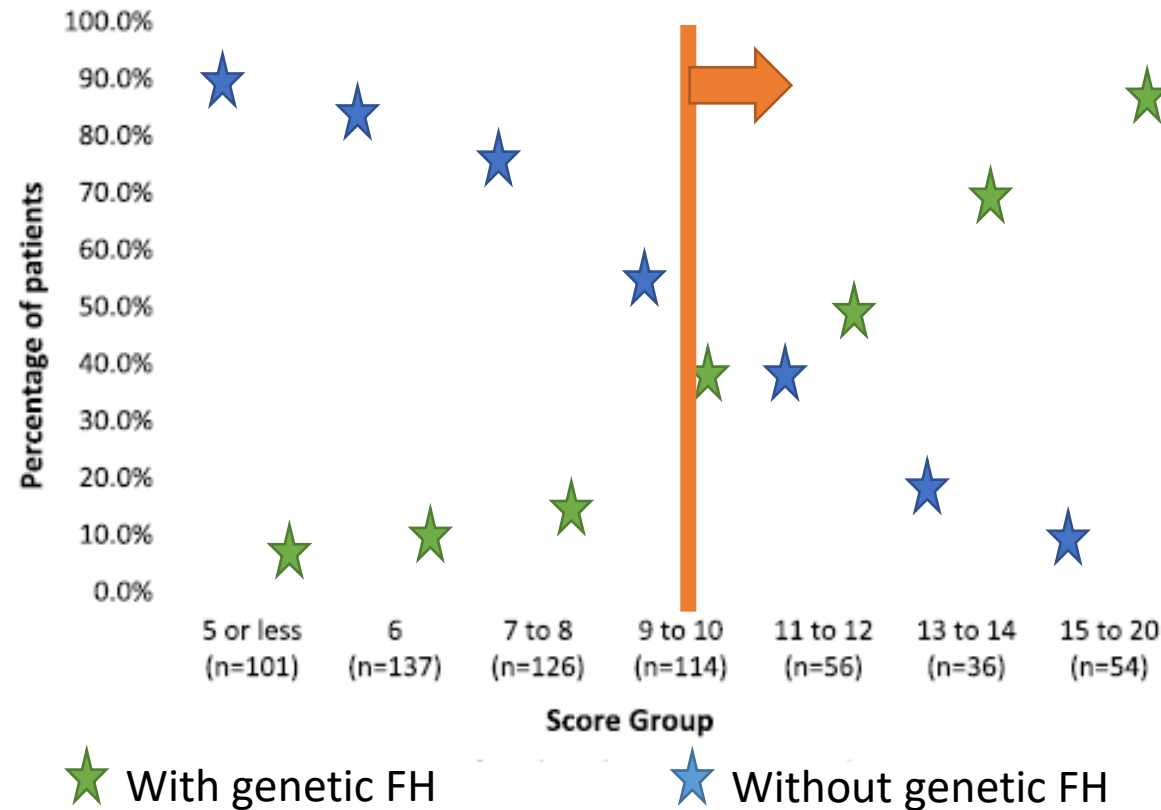
What prompted us to expand our set of options? (1)

More or less restrictive clinical score



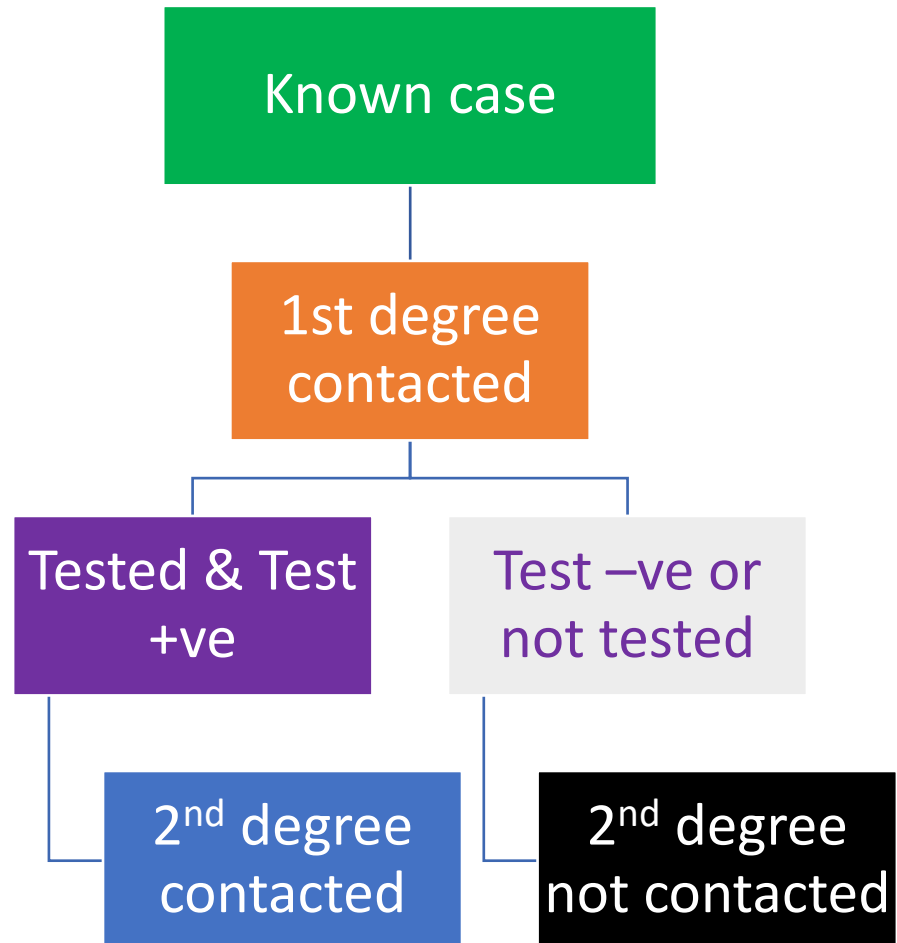
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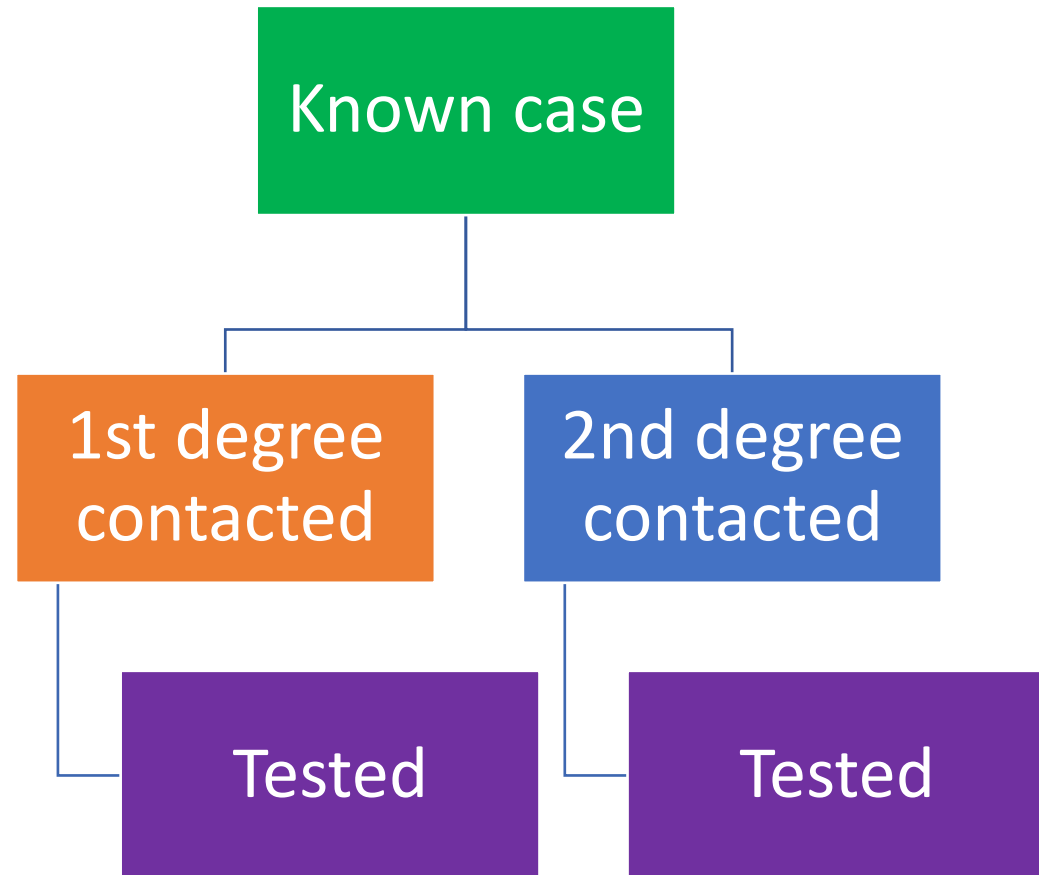
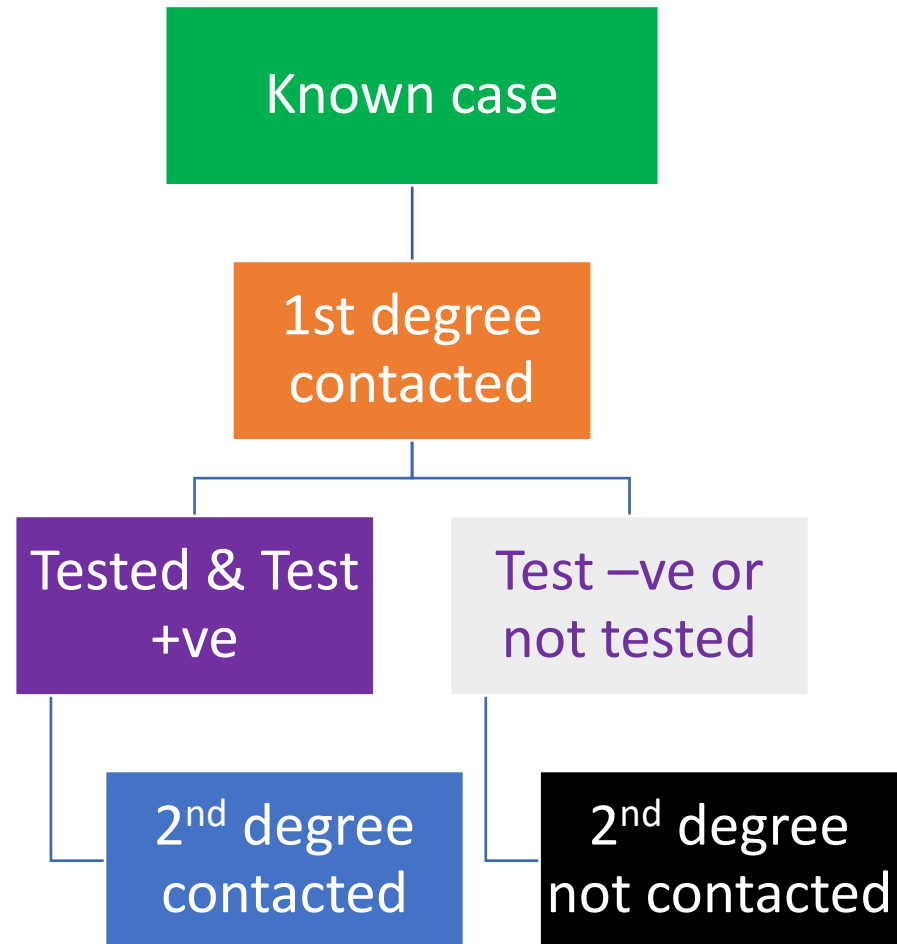
What prompted us to expand our set of options? (2)

Contacting 1st then 2nd degree vs 1st and 2nd degree relatives



What prompted us to expand our set of options? (2)

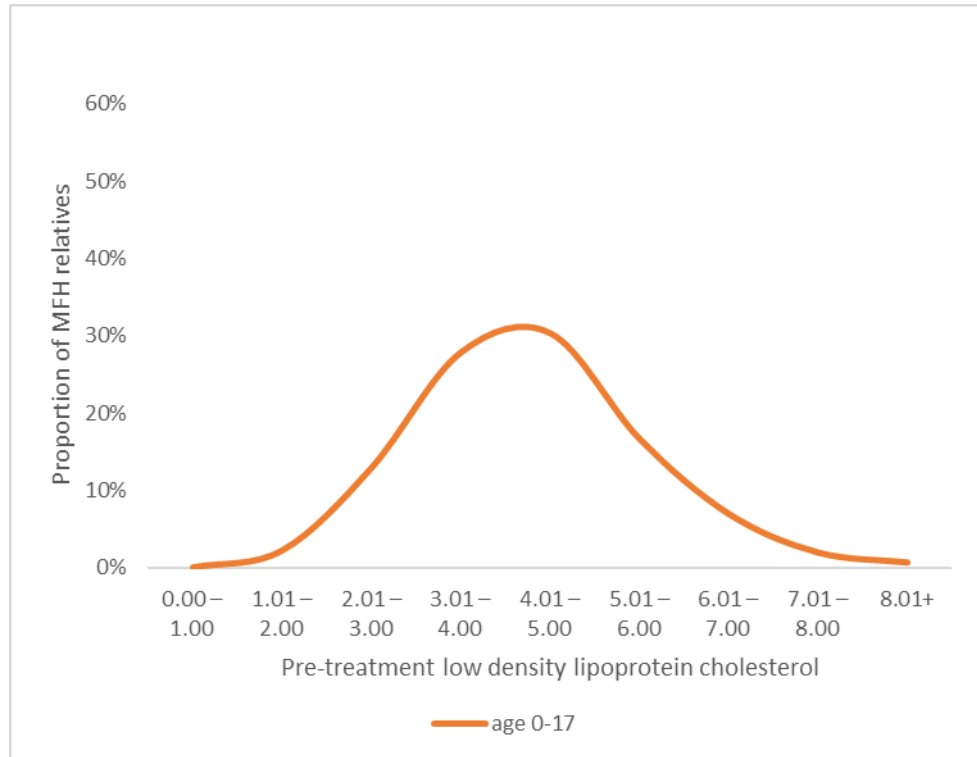
Contacting 1st then 2nd degree vs 1st and 2nd degree relatives



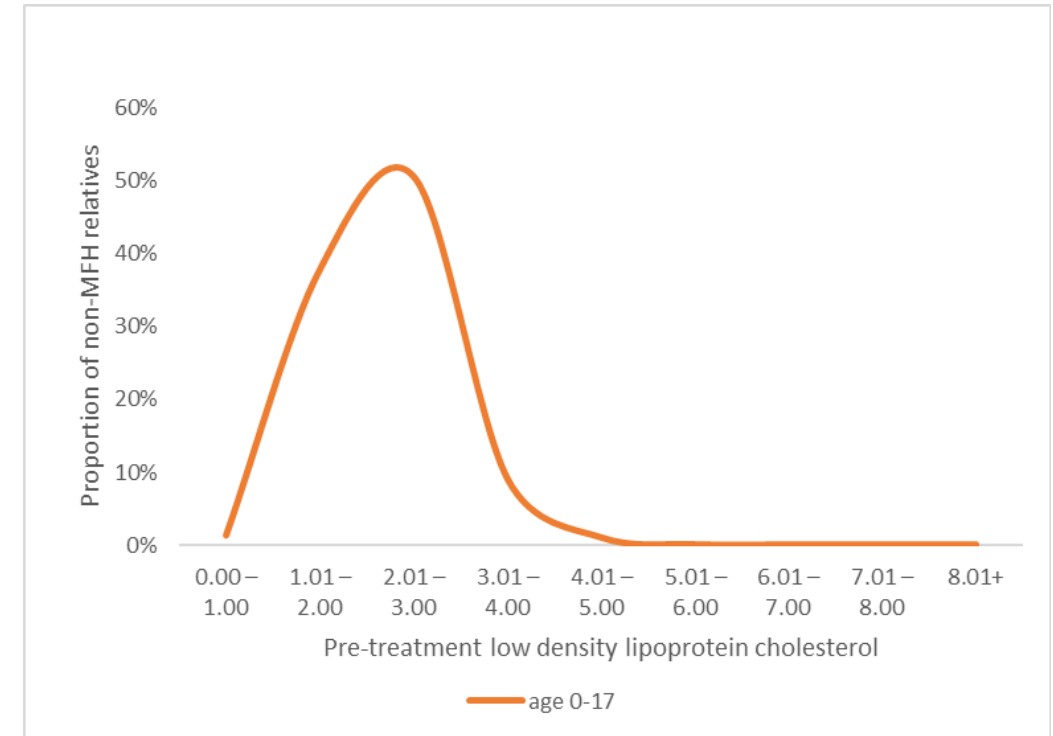
What prompted us to expand our set of options? (3)

Using LDL-cholesterol to screen relatives

Relatives with FH



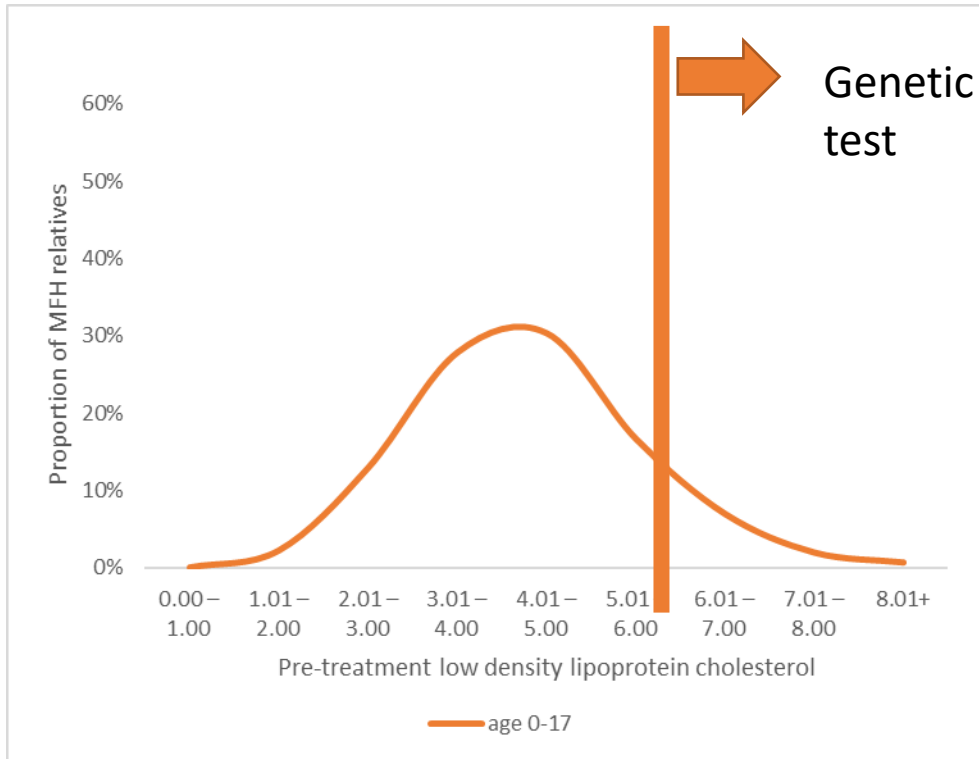
Relatives without FH



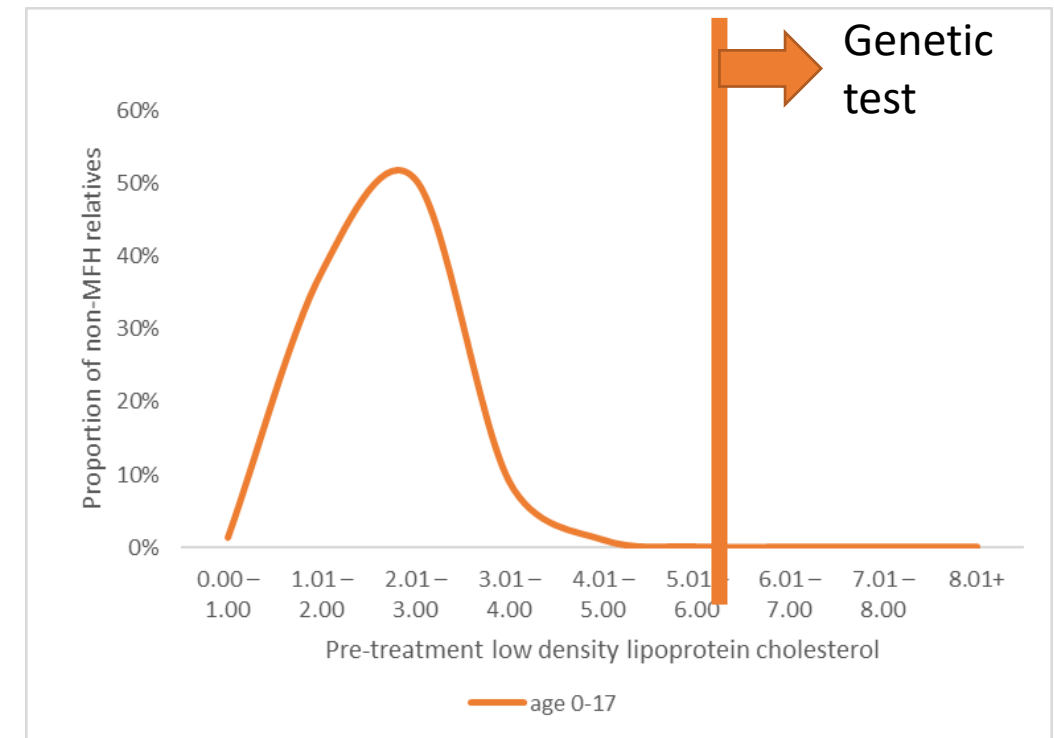
What prompted us to expand our set of options? (3)

Using LDL-cholesterol to screen relatives

Relatives with FH

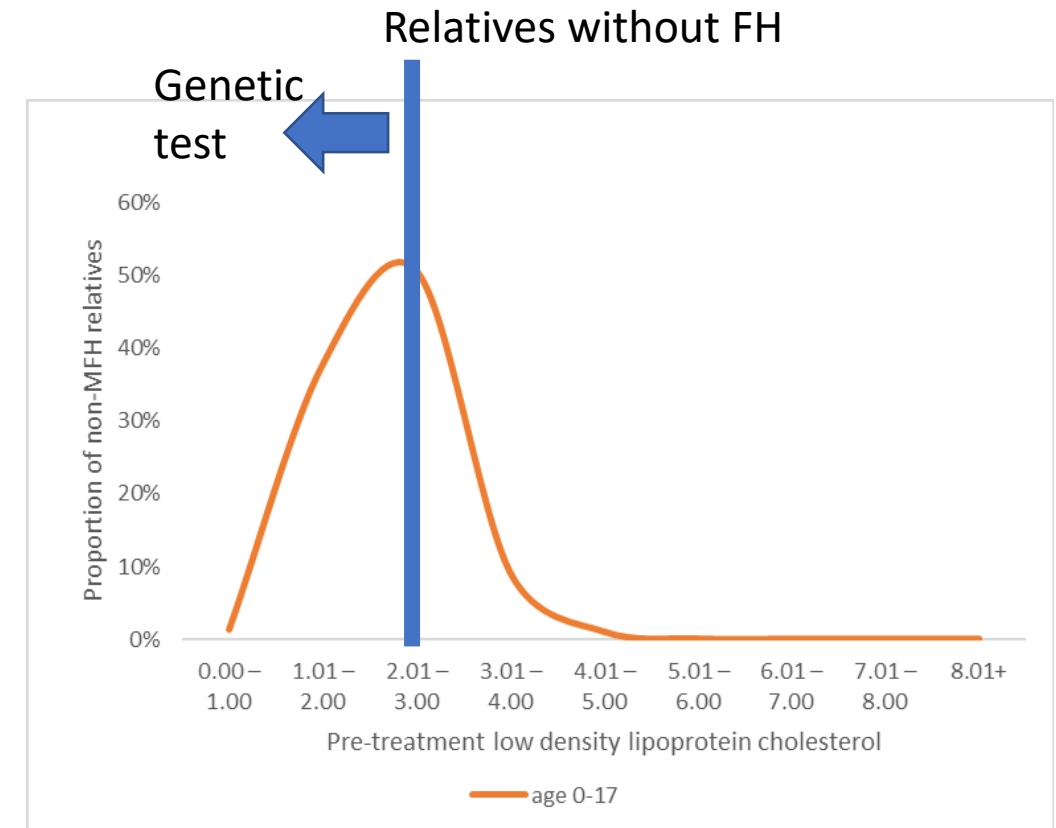
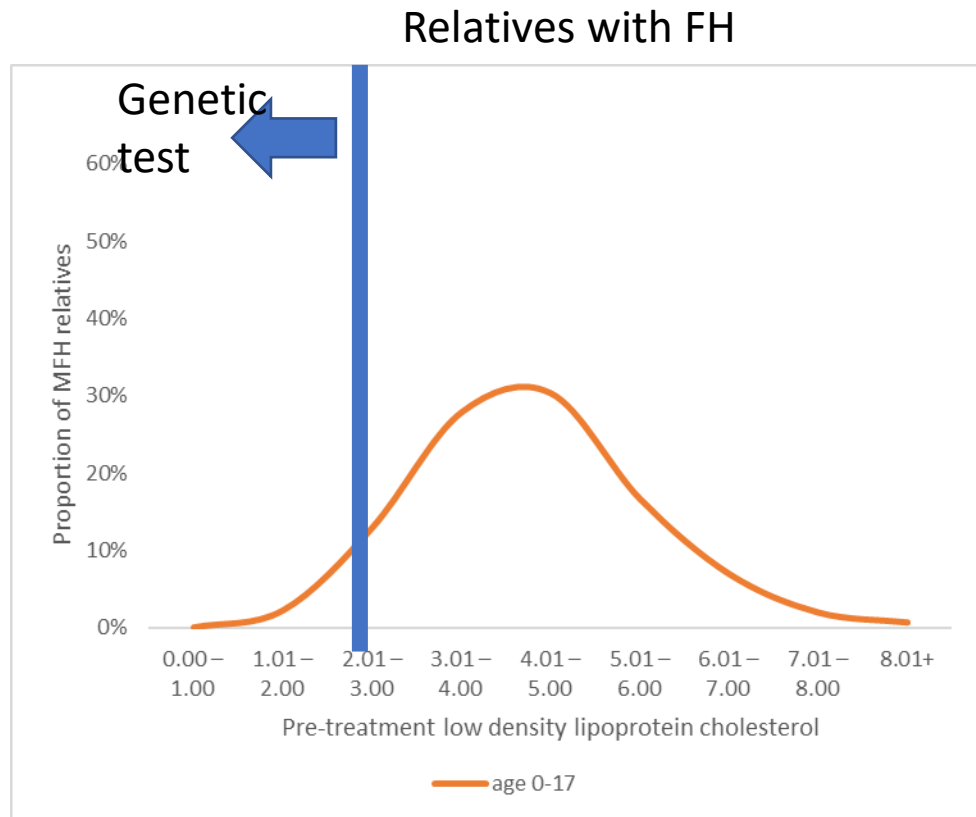


Relatives without FH



What prompted us to expand our set of options? (3)

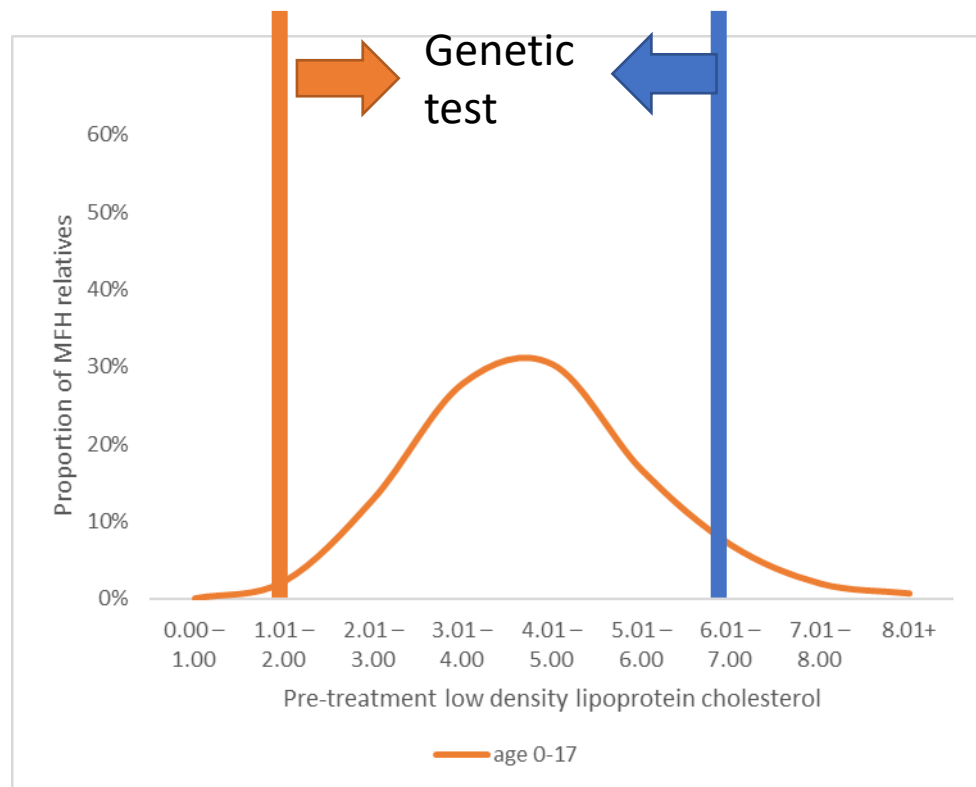
Using LDL-cholesterol to screen relatives



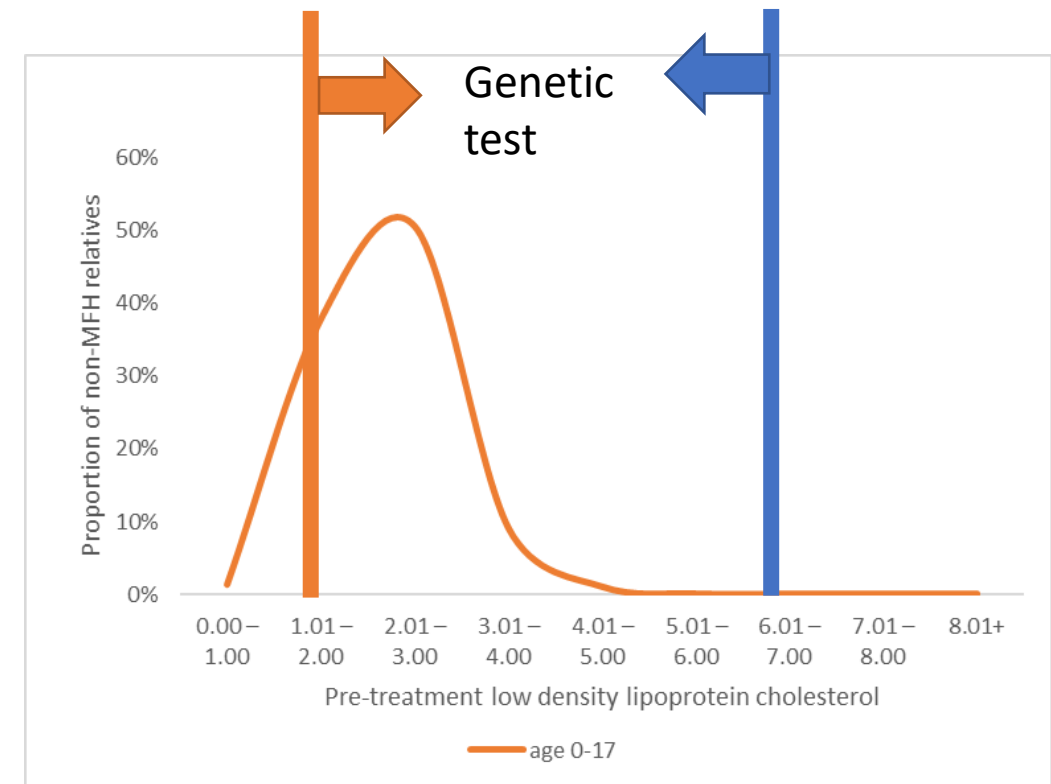
What prompted us to expand our set of options? (3)

Using LDL-cholesterol to screen relatives

Relatives with FH



Relatives without FH



How to reduce the number of options?

- Min and max scores and LDL-cholesterol thresholds
- Simplify options to select known patients
- Pool LDL-cholesterol distributions

Our expanded set of options

1

Offer the genetic test to
known individuals with FH

**Different clinical score
thresholds for the genetic test
= 7 options**

Our expanded set of options

1

Offer the genetic test to
known individuals with FH

7 options

2

Contact their relatives:
directly or indirectly

**Simultaneous vs
sequential contact
= 4 options**

Our expanded set of options

1 Offer the genetic test to known individuals with FH

7 options

2 Contact their relatives: directly or indirectly

= 4 options

3 Offer their relatives the genetic test

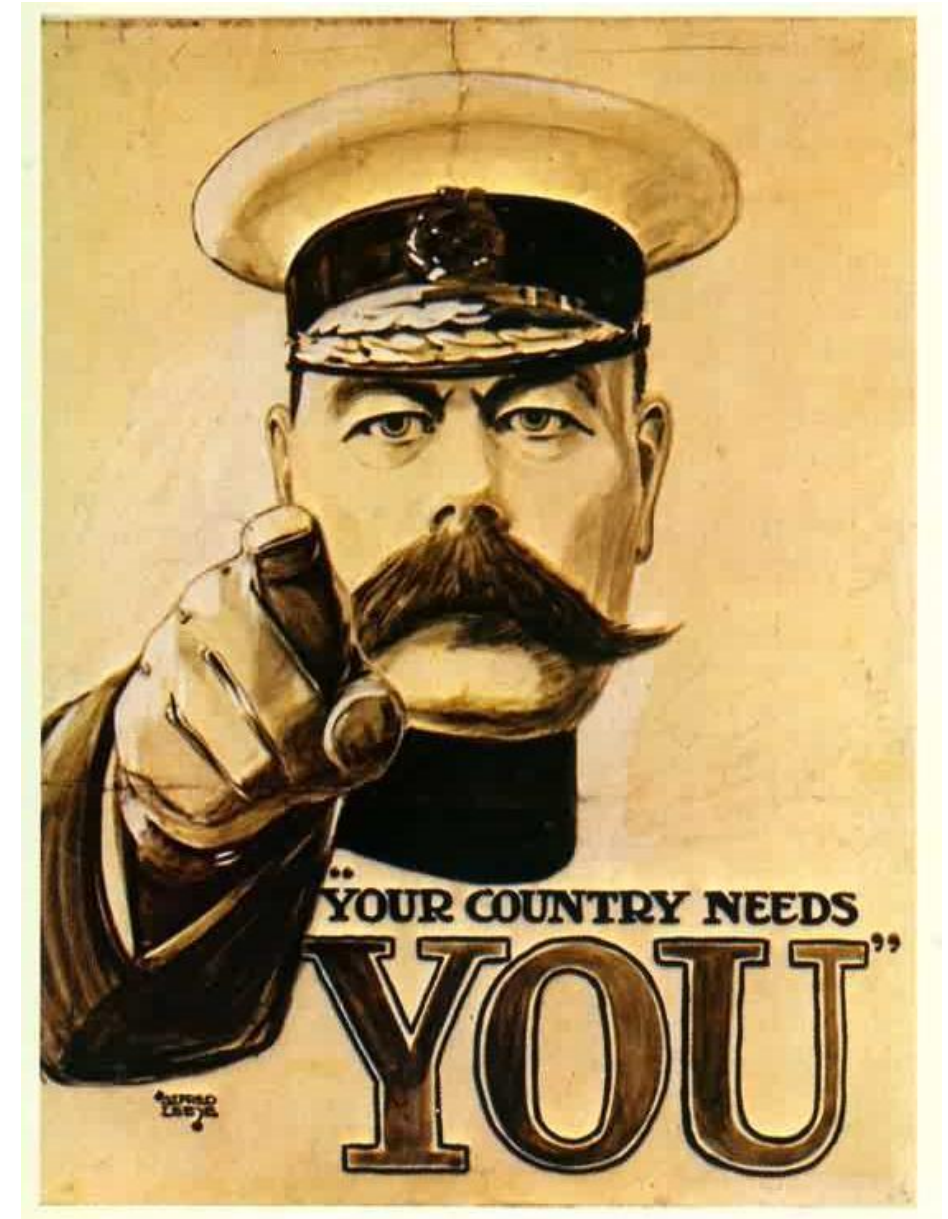
**LDL-cholesterol and treatment to screen prior to genetic test
= 68 options**

Your turn

How many cascade testing strategies given

- 68 testing options for each age group
- 5 age groups

Use “hands up” to vote yes

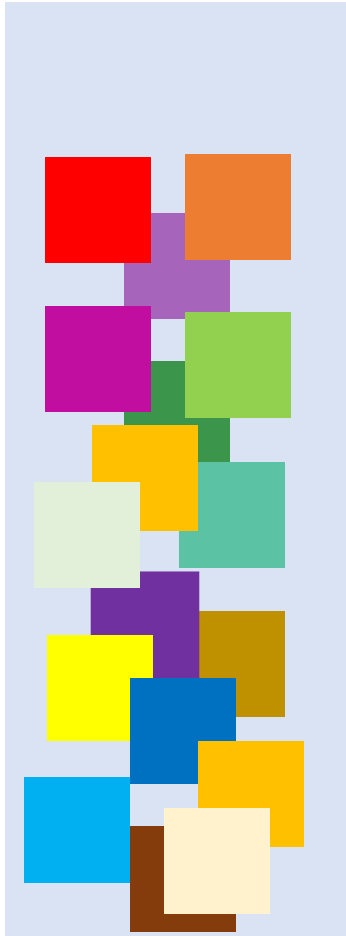


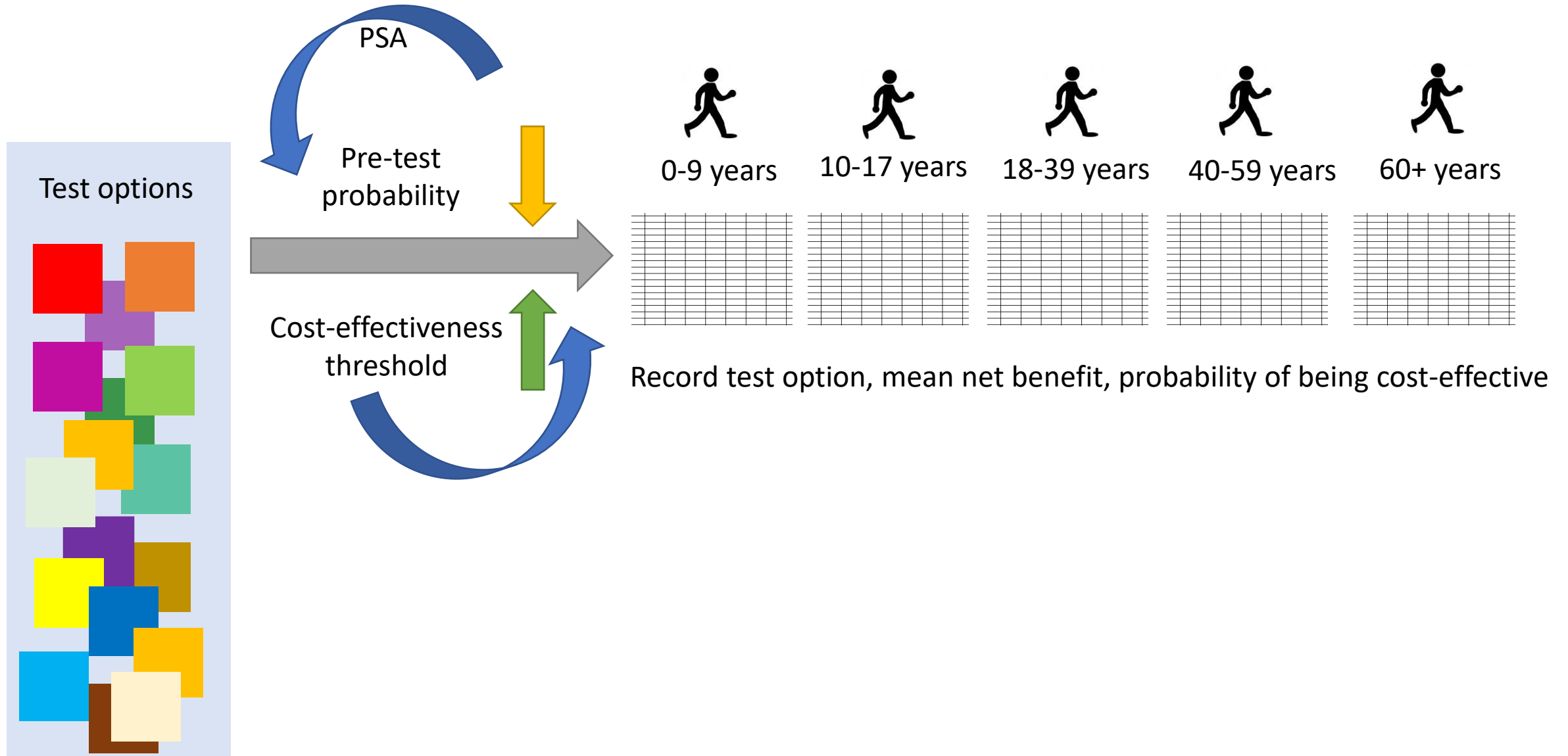


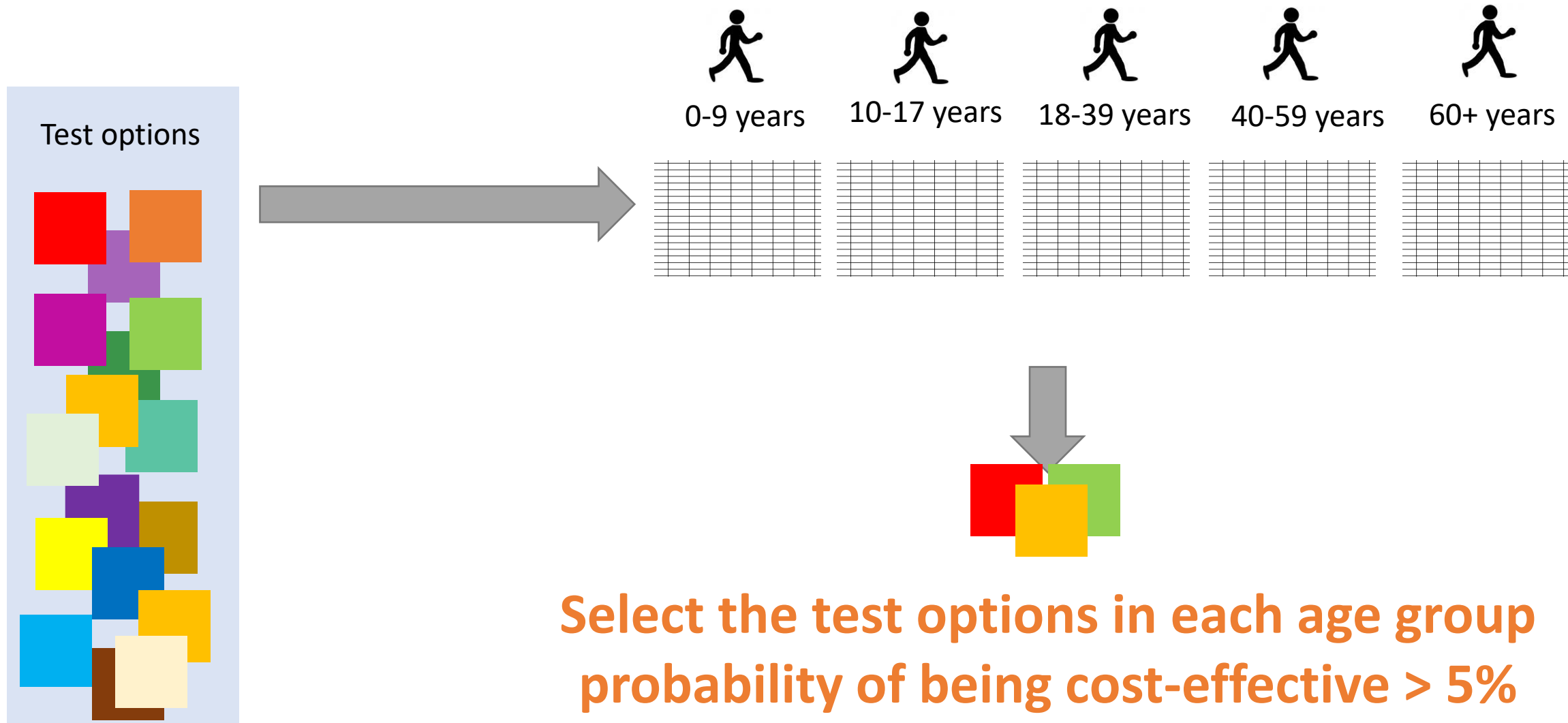
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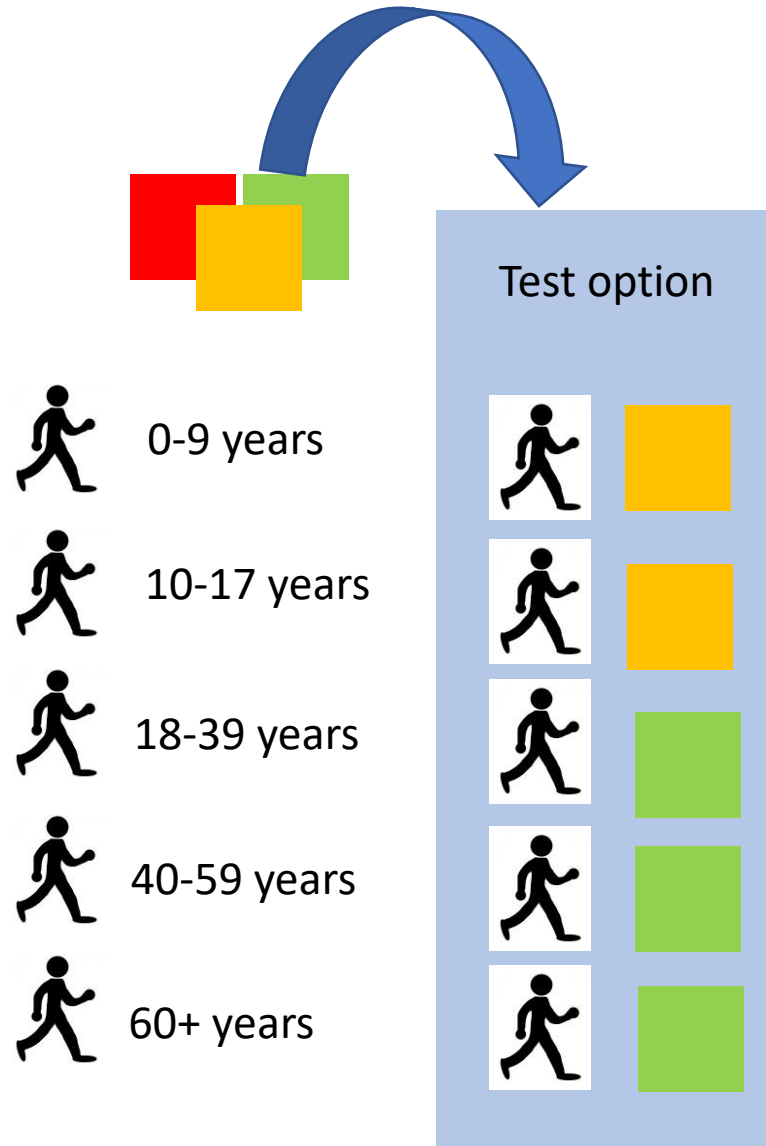
Selecting testing options based on cost-effectiveness criterion

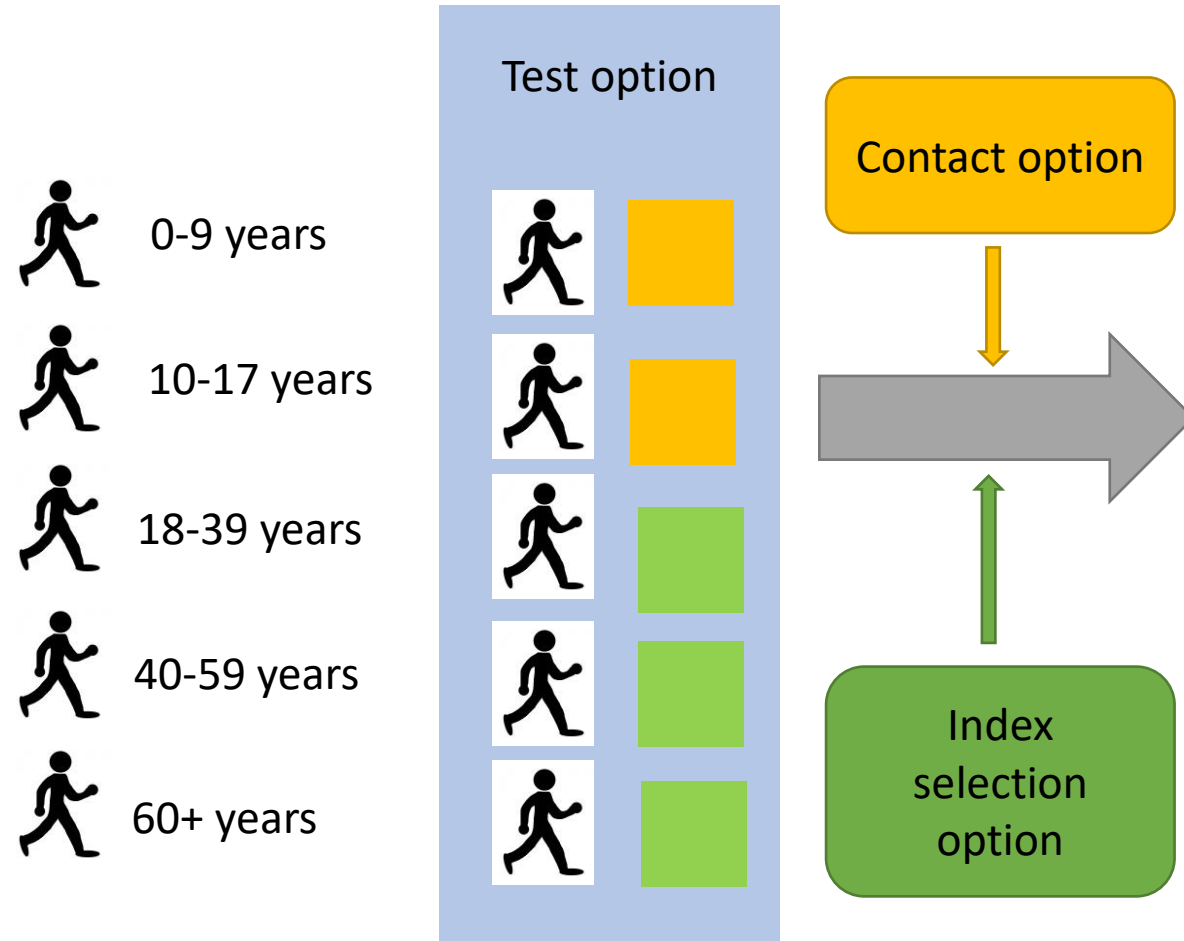
68 Test options
By age group

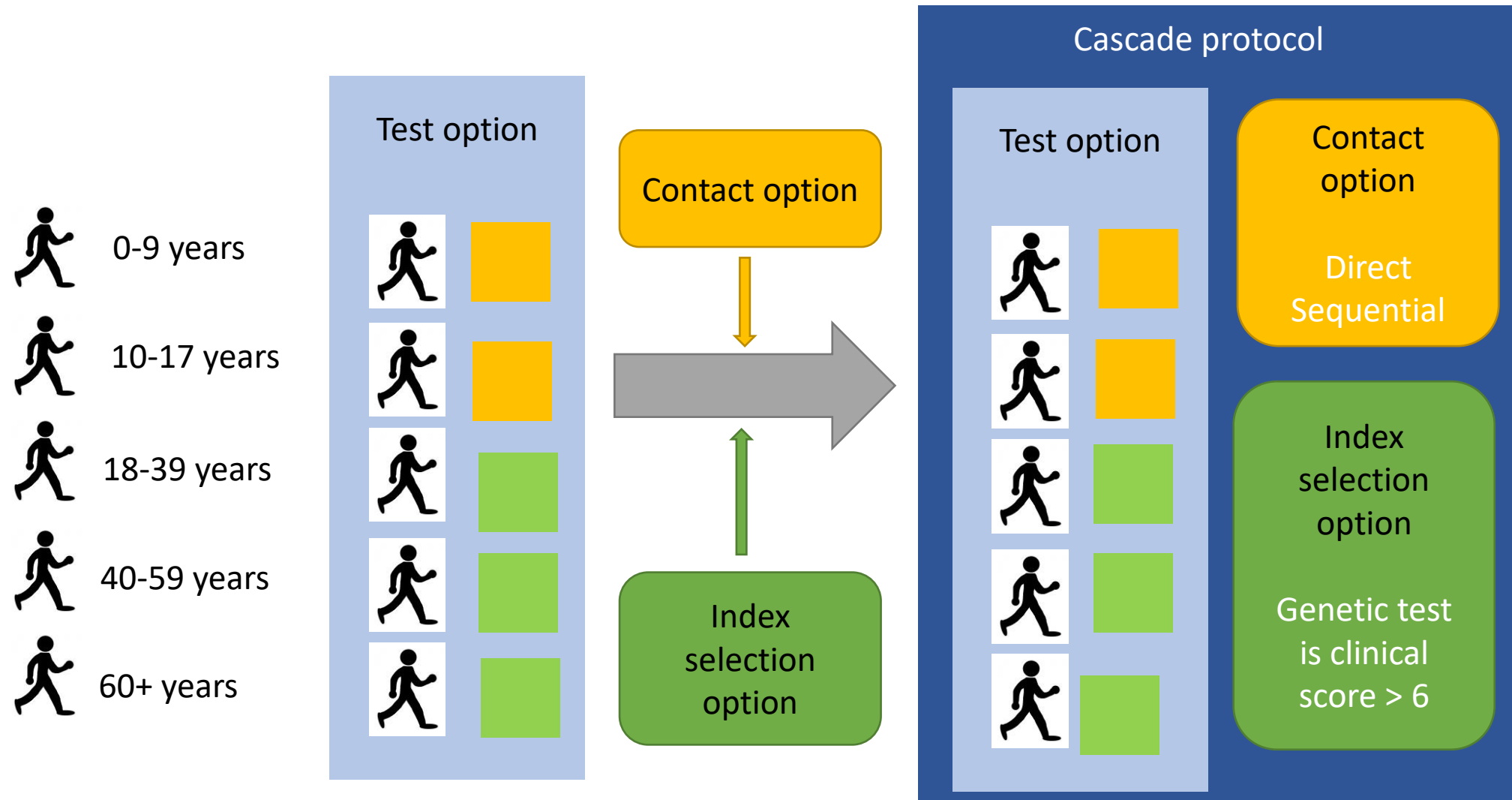












How wrong can we be?

Limitations

- Excluding testing options that had $< 5\%$ probability of cost-effectiveness at the level of the age group
- Not considering strategies with repeated testing
- Data limitations

What if we had only compared strategies in clinical practice?

The cost-effective strategies were not those in clinical practice

- Incremental net health benefit of cost-effective protocol vs usual protocol = 171 QALYs
- 1,175 affected relatives diagnosed vs 808 with usual protocol
- Assumes
 - 3,229 index families could be assessed per year in the UK
 - Usual protocol = sequential indirect contact with genetic testing

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