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Quantitative Benefit Harm Assessment to Explore Preference Sensitive Treatment Decisions

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Low dose aspirin for primary prevention

Use in people 40+ in the USA vs. Europe

Prev Med Rep. 2017 Mar; 5: 183–186. Prev Med. 2008 Feb;46(2):137-44

Reasons for variation: Different population needs, preferences, evidence base, or other?

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Evidence on the benefits and harms of aspirin ≤100 mg/d

Benefits		Harms	
Less non-fatal MI	RR 0.83 (0.74-0.94)	More severe GI bleeds	OR 1.59 (1.32-1.91)
Less non-fatal strokes	RR 0.86 (0.76-0.98)	More hemorrhagic strokes	OR 1.33 (1.03-1.71)
Less CVD mortality	RR 0.97 (0.85-1.10)		
Less all-cause mortality	RR 0.95 (0.89-1.01)		

Ann Intern Med. 21 June 2016 Vol: 164, Issue 12

Discrepant guidelines for aspirin for primary prevention

European Society of Cardiology	Not recommended because of risk of bleeds (Class of recommendation III B)
WHO	CVD 10 y risk <20%: aspirin not recommended CVD 10 y risk 20 to <30%: aspirin rather not recommended CVD 10 y risk ≥30% aspirin recommended (1++, A)
US Preventive Services Task Force	Stratified, e.g. men 45 to 79 y aspirin recommended if risk reduction for MI > excess of GI bleeds – 45–59 year old if ≥4% 10-year risk of CHD – 60–69 year old if ≥9% 10-year risk of CHD – 70–79 year old if ≥12% 10-year risk of CHD (A recommendation)

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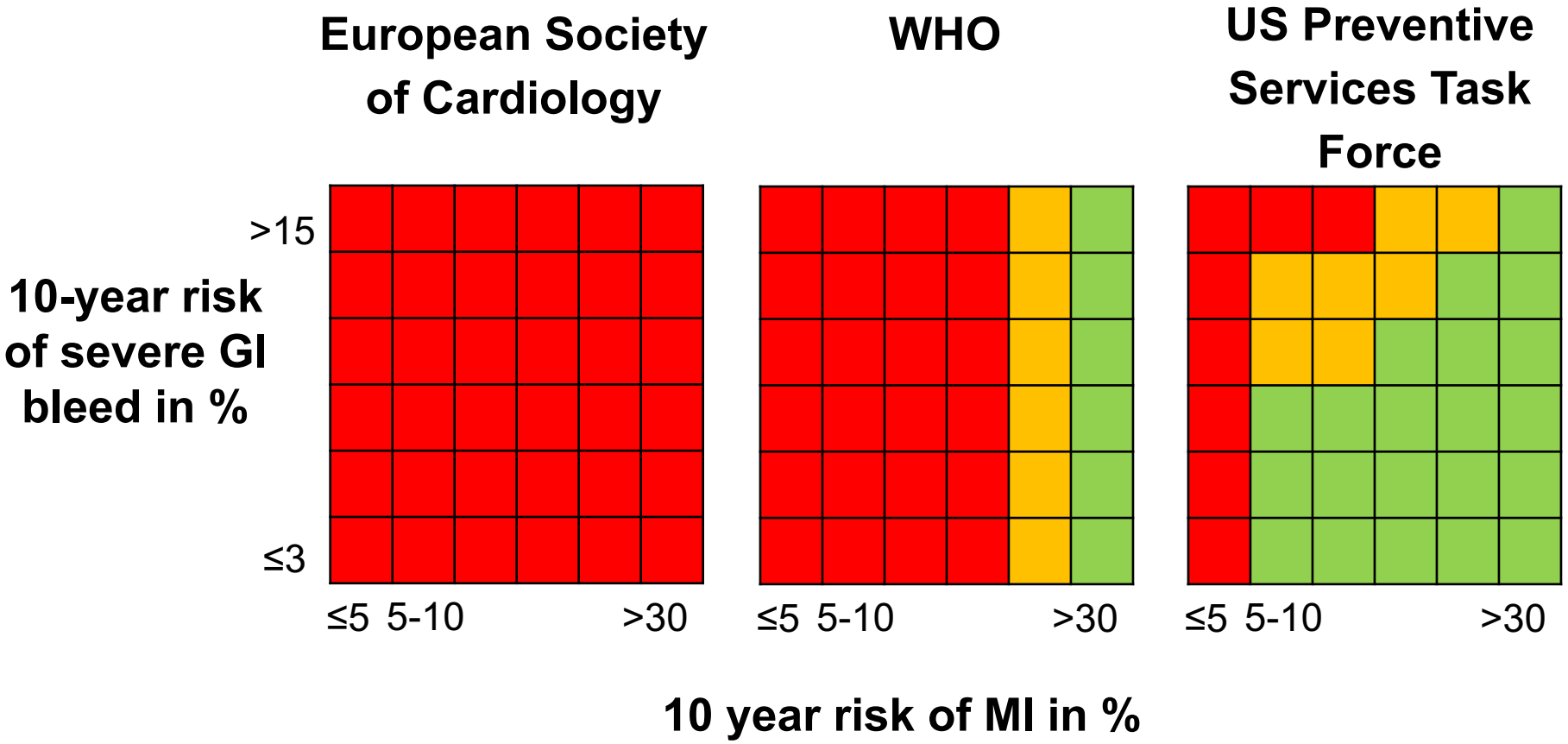
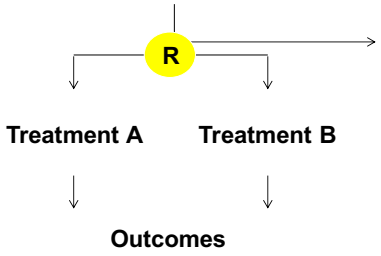
What this means for (e.g.) 55 year old men



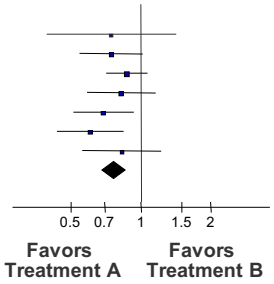
A useful tool to explore how sensitive a decision is to needs and preferences

Quantitative benefit harm assessments

Evidence generation



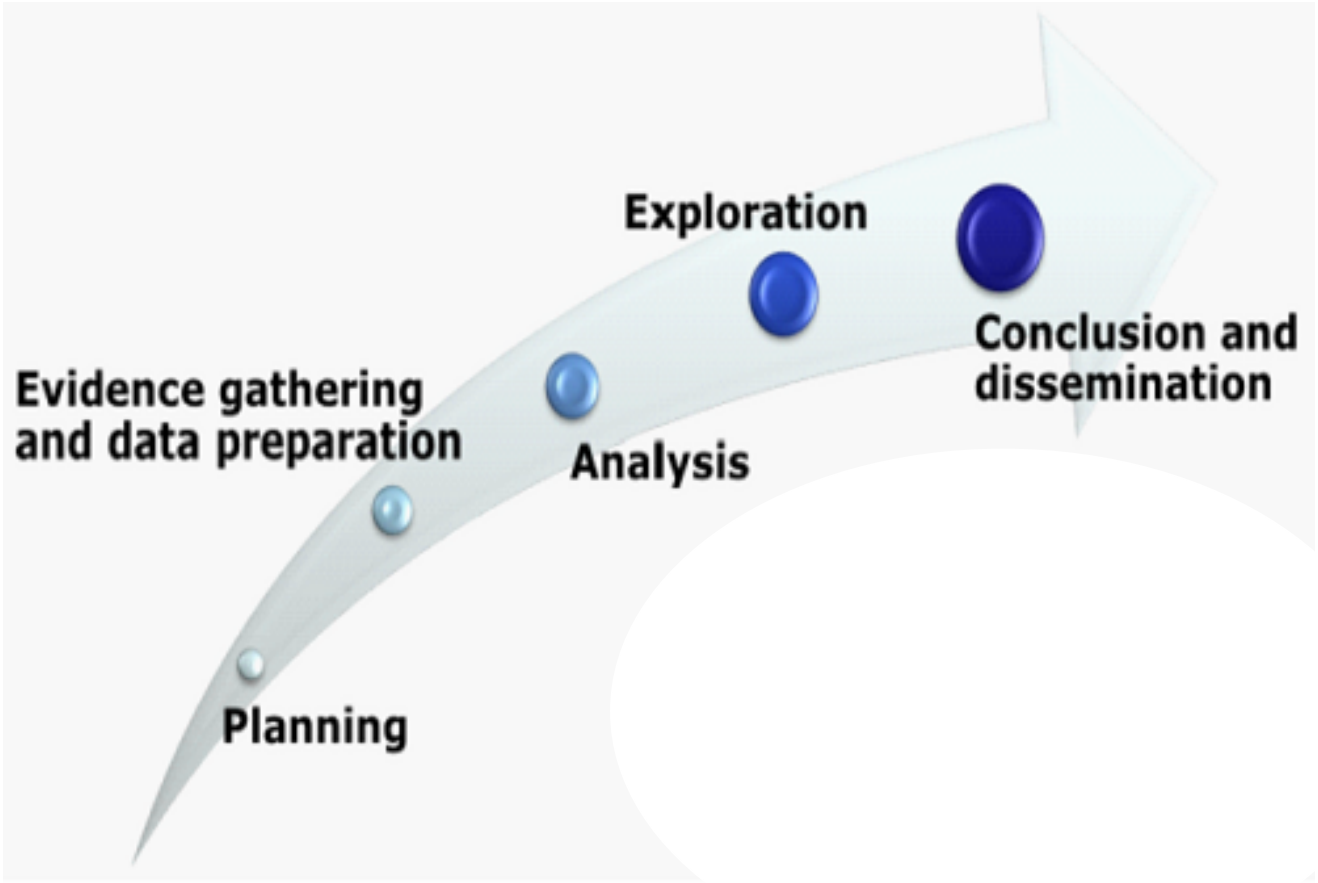
Evidence synthesis



Decision makers

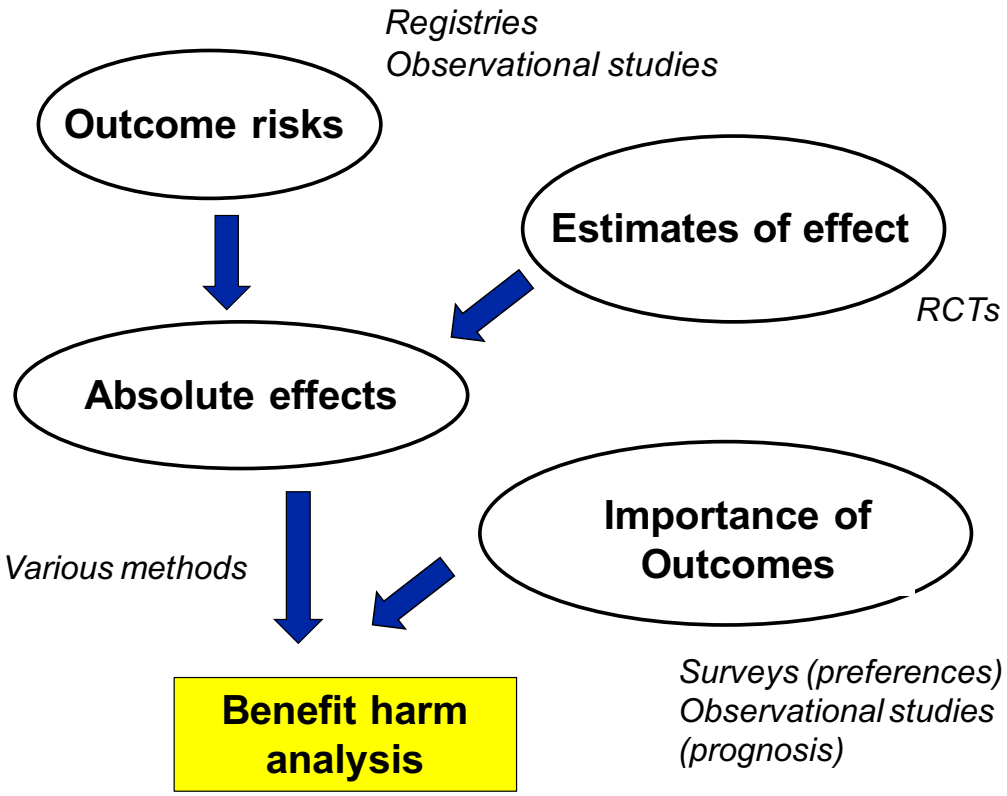
- Patients and health care providers
- Guideline developers
- Regulatory agencies
- Policy makers

Process of benefit harm assessments



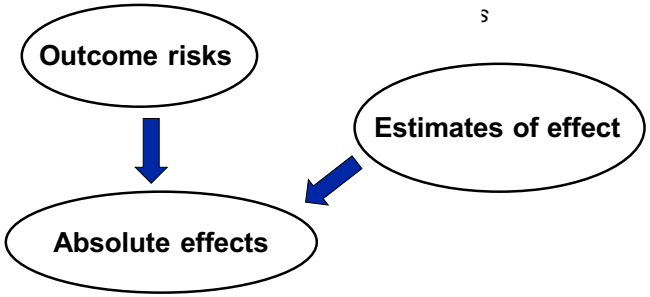
http://www.protectbenefitrisk.eu/

Evidence gathering and preparation



Puhan et al. BMC Med Res Meth 2012, 12:173; Boyd, et al. AHRQ 2012 .12(13)-EHC150-EF, http://www.protectbenefitrisk.eu/; Fain et al. J Clin Epi 2016; 74:151-7

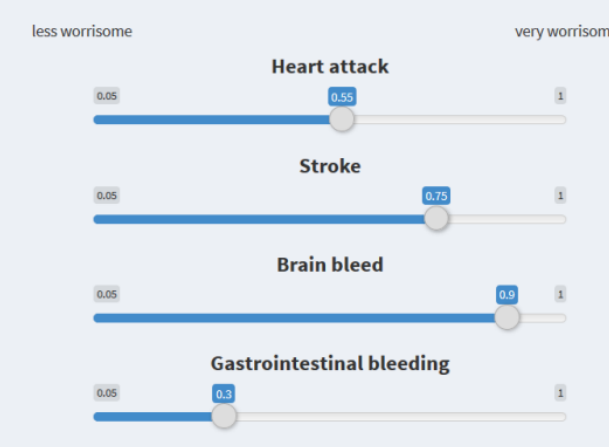
Analysis: Estimate absolute numbers of events to be expected



	Number of expected events over 10 years per 1,000 men							
Men								
Age (years)	45–54		55–64		65–74		75–84	
Aspirin (no or yes)	No	Yes	No	Yes	No	Yes	No	Yes
Myocardial infarction	38	33	57	49	79	68	96	83
Major ischemic stroke	12	10	24	20	48	42	75	66
Major haemorrhagic stroke	2	3	4	5	7	10	12	16
Major gastrointestinal bleeding	12	19	24	38	42	68	56	89

PLoS ONE 2015; 10(7): e0127194

Combine and weigh expected number of events without and with low-dose aspirin in men



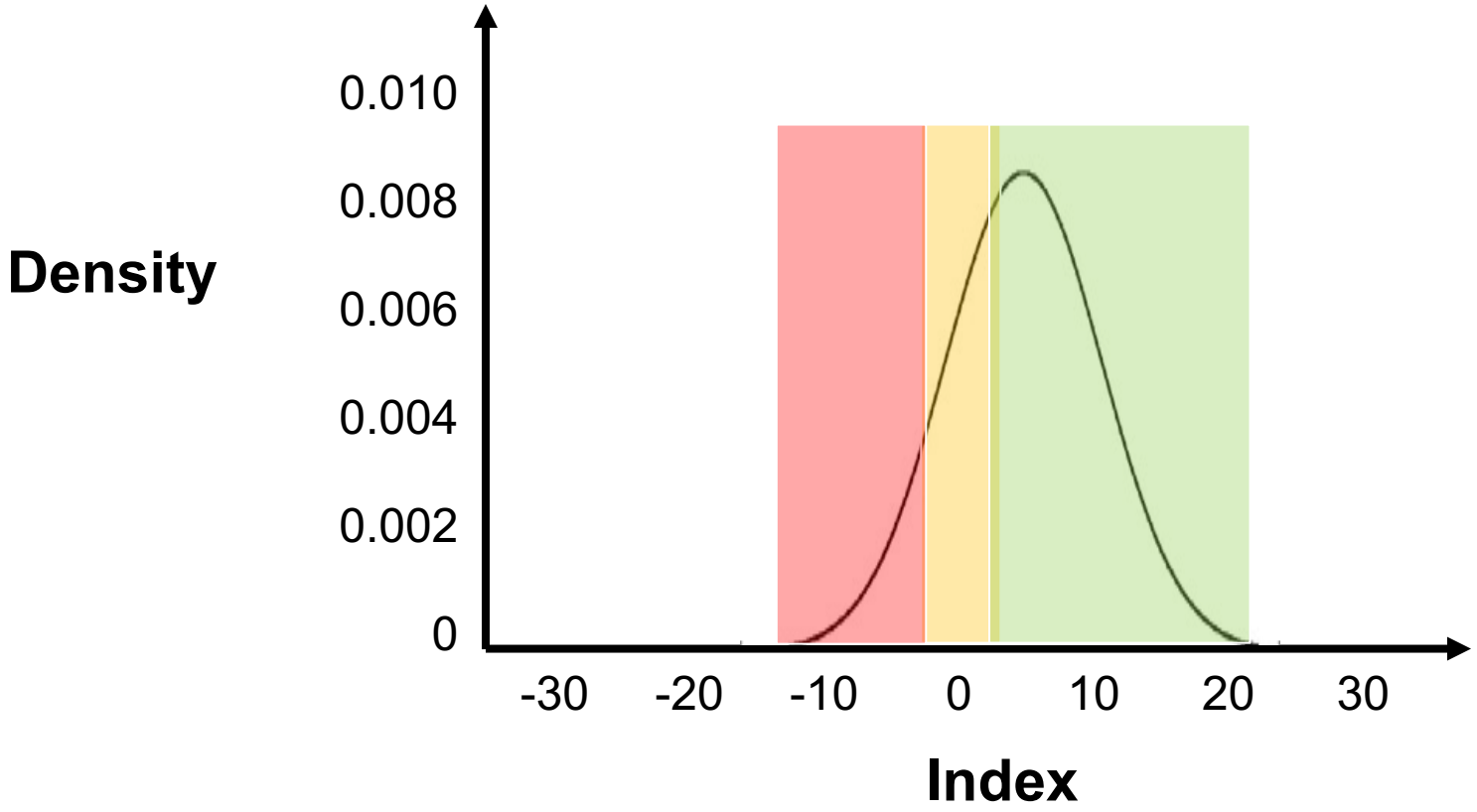
	Number of expected events over 10 years per 1,000 men			
Men				
Age (years)	55–64		65–74	
Aspirin (no or yes)	No	Yes	No	Yes
Myocardial infarction	57	49	79	68
Major ischemic stroke	24	20	48	42
Major haemorrhagic stroke	4	5	7	10
Major gastrointestinal bleeding	24	38	42	68

Analysis step 1: $Index = \sum Wx * Nx$

Analysis step 2: **Probability that index shows in certain direction**

(step 1 repeated 100’000 times with sampling from distributions to consider statistical uncertainty)

Distribution of index and interpretation



For a single scenario, e.g. 55 year old men at 10 year CVD risk of 10% and GI risk of 3%

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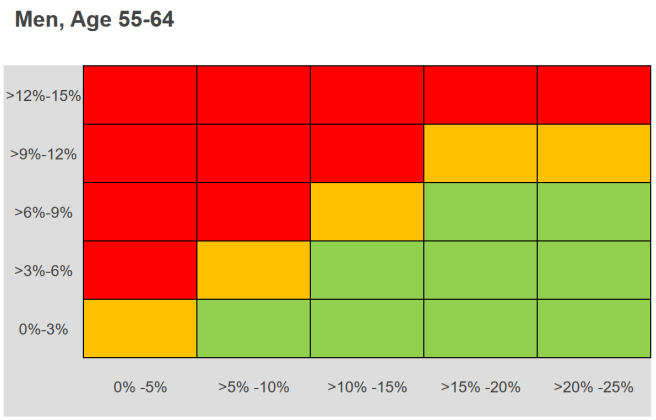
Benefit harm balance of low dose aspirin varies according to needs of 55 year old men

Outcomes weighted the same



10-year risk of severe GI bleed in %

10 year risk of MI in %

Puhan et al. BMC Med. 2015 Oct 1;13:250.

→ **See** http://www.benefit-harm-balance.com/

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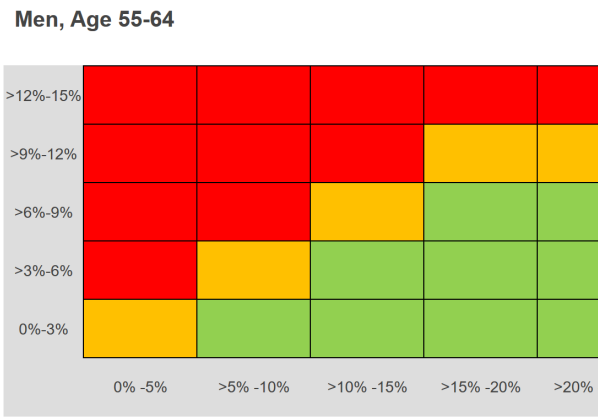
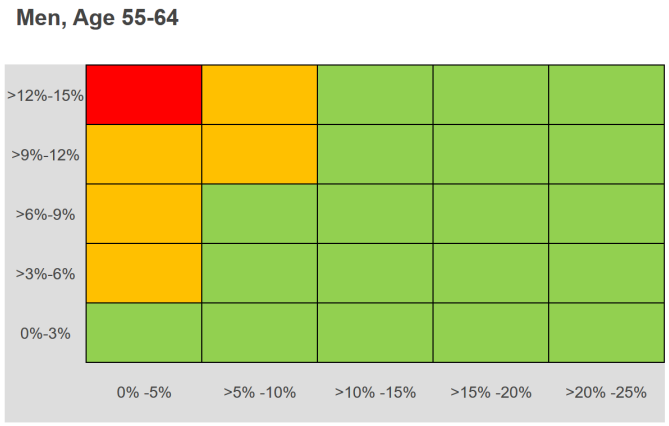
Benefit harm balance of low dose aspirin varies according to needs and preferences of 55 year old men

Outcomes weighted the same



Stroke weighted most, followed by MI, then GI bleeds



10-year risk of severe GI bleed in %

10 year risk of MI in %

10 year risk of MI in %

Puhan et al. BMC Med. 2015 Oct 1;13:250.

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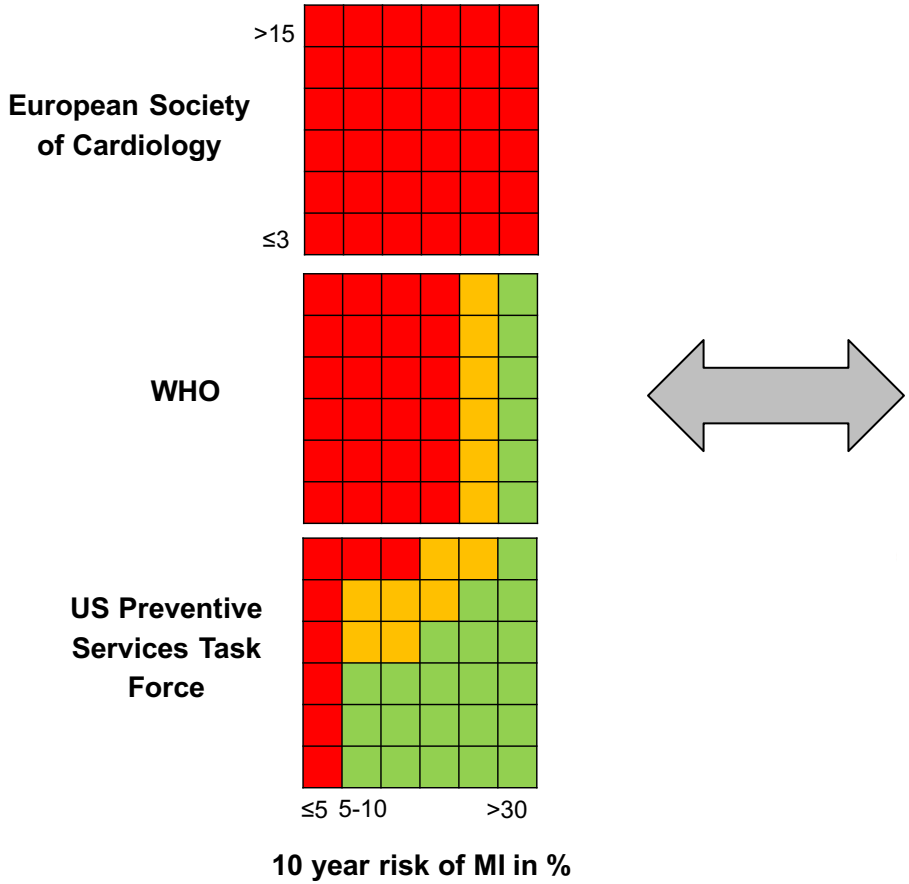
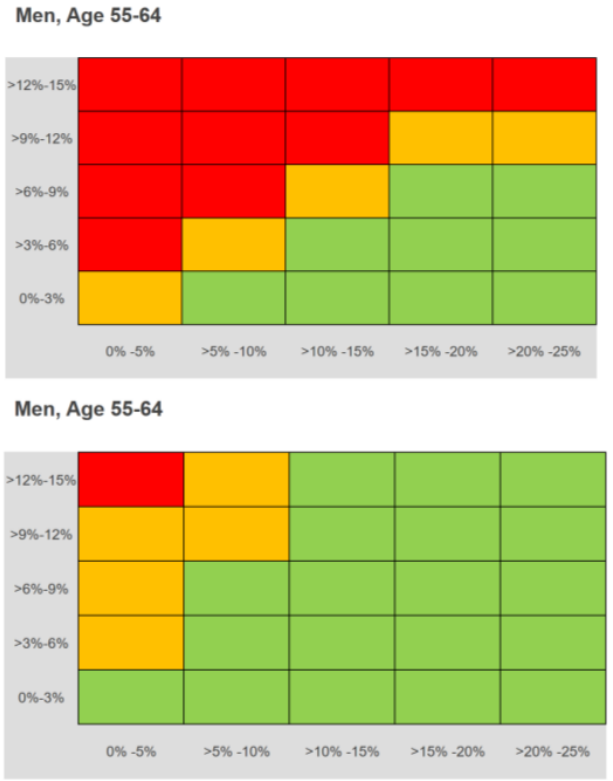
Do low dose aspirin recommendations make sense to meet needs and preferences?





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Benefit harm balance often but not always depends on needs or preferences

Blood pressure target 140 vs 120 mm Hg

0.44	0.1	0.02
0.87	0.59	0.34
0.35	0.03	0.01
0.88	0.58	0.38
0.49	0.17	0.07
0.7	0.28	0.25
0.74	0.4	0.27
0.45	0.13	0.14

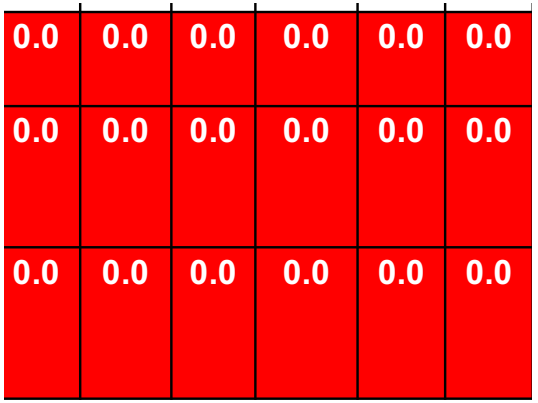
0.05	0.01	0
0.45	0.24	0.13
0.04	0	0
0.6	0.24	0.15
0.13	0.06	0.03
0.29	0.07	0.08
0.5	0.18	0.12
0.18	0.04	0.06

Second line diabetes drugs

0.31 [0.14, 0.31]
0.45 [0.34, 0.45]
0.54 [0.48, 0.54]

0.53 [0.45, 0.53]
0.58 [0.54, 0.58]
0.61 [0.59, 0.61]

New drug for COPD (roflumilast)



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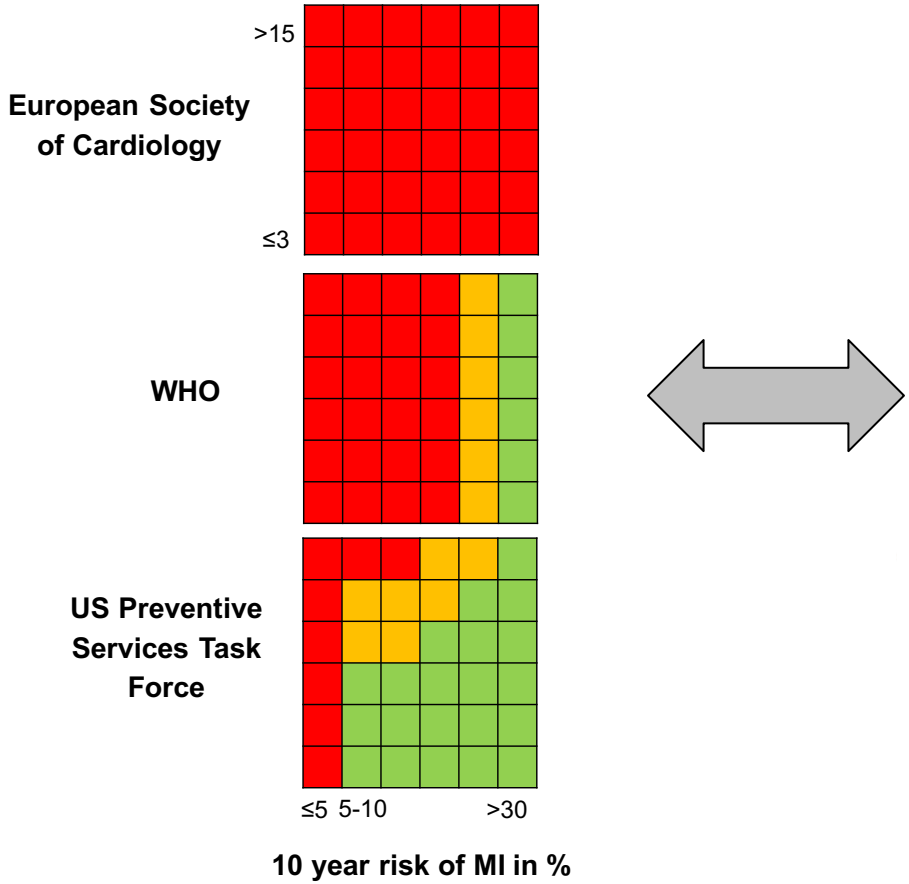
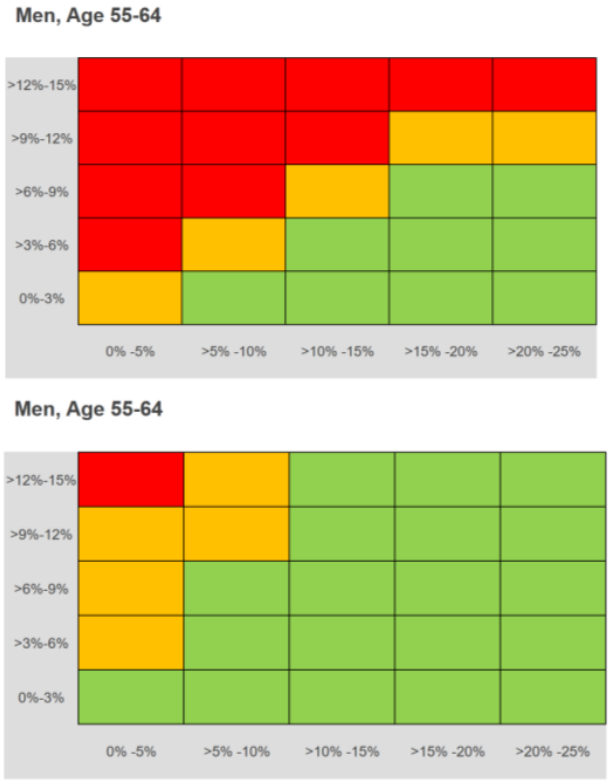
Do low dose aspirin recommendations make sense to meet needs and preferences?





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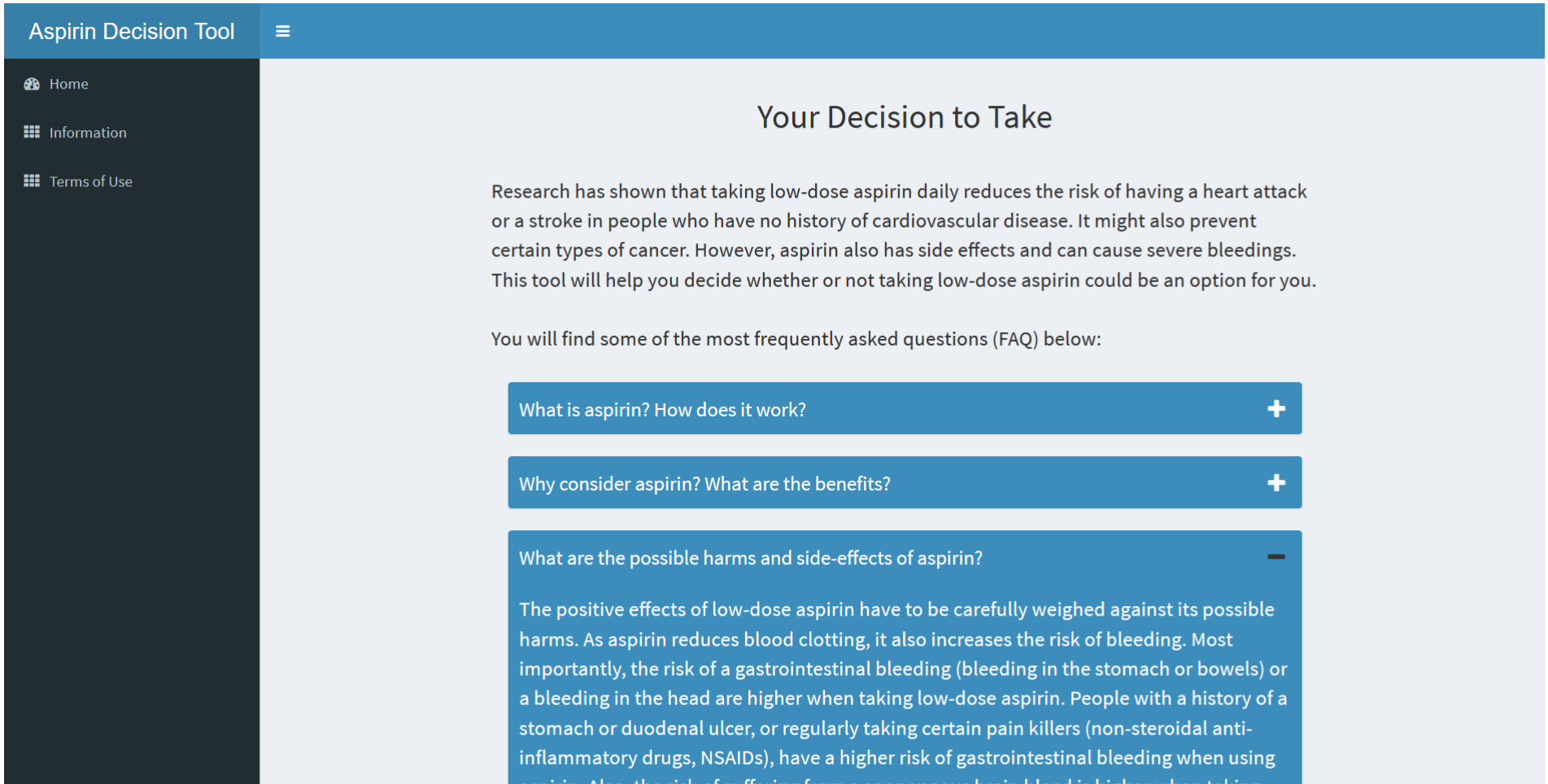
Individual risk-stratified and preference-sensitive prevention, rather than guidelines?



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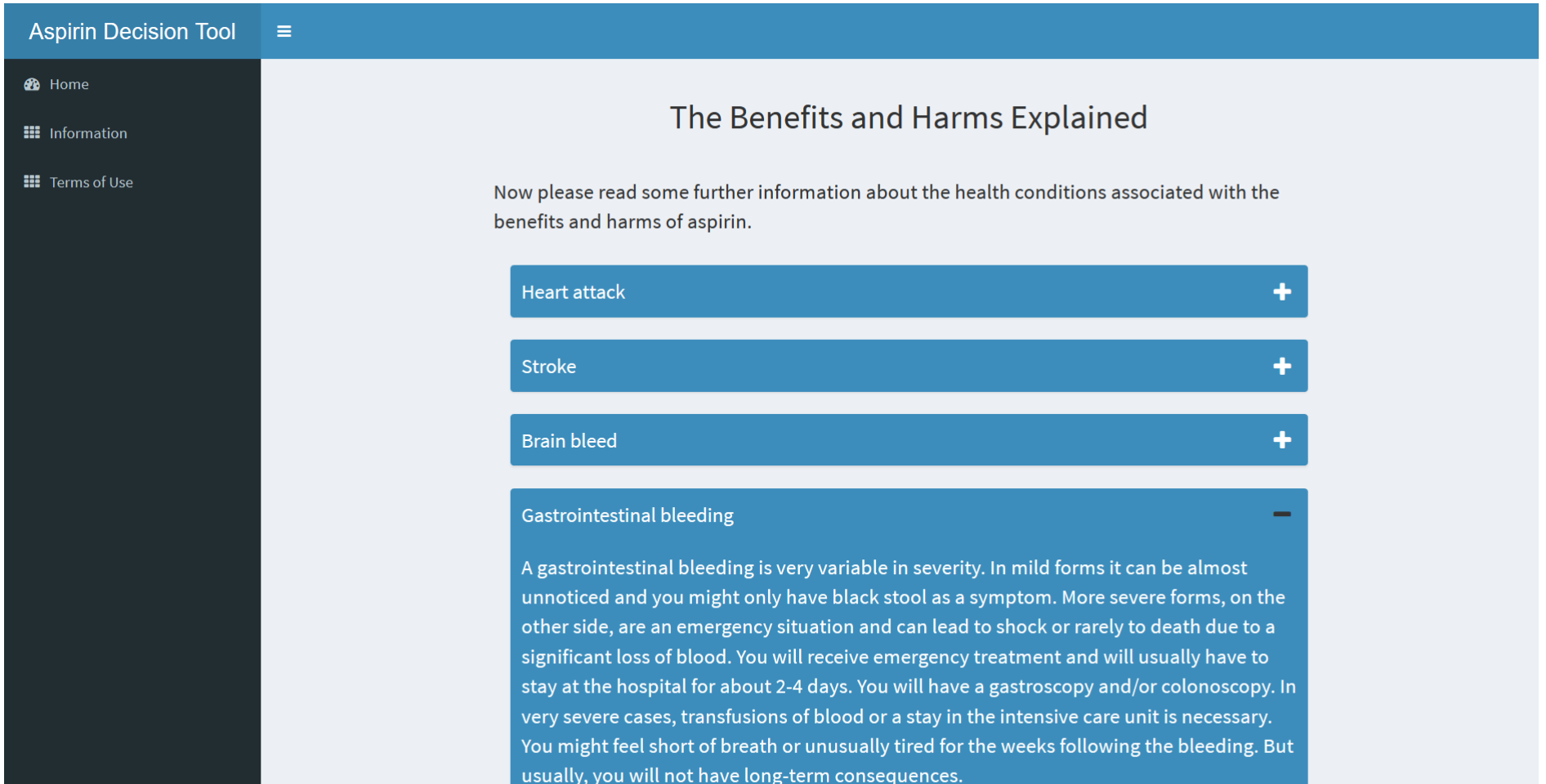
Web-base decision aid



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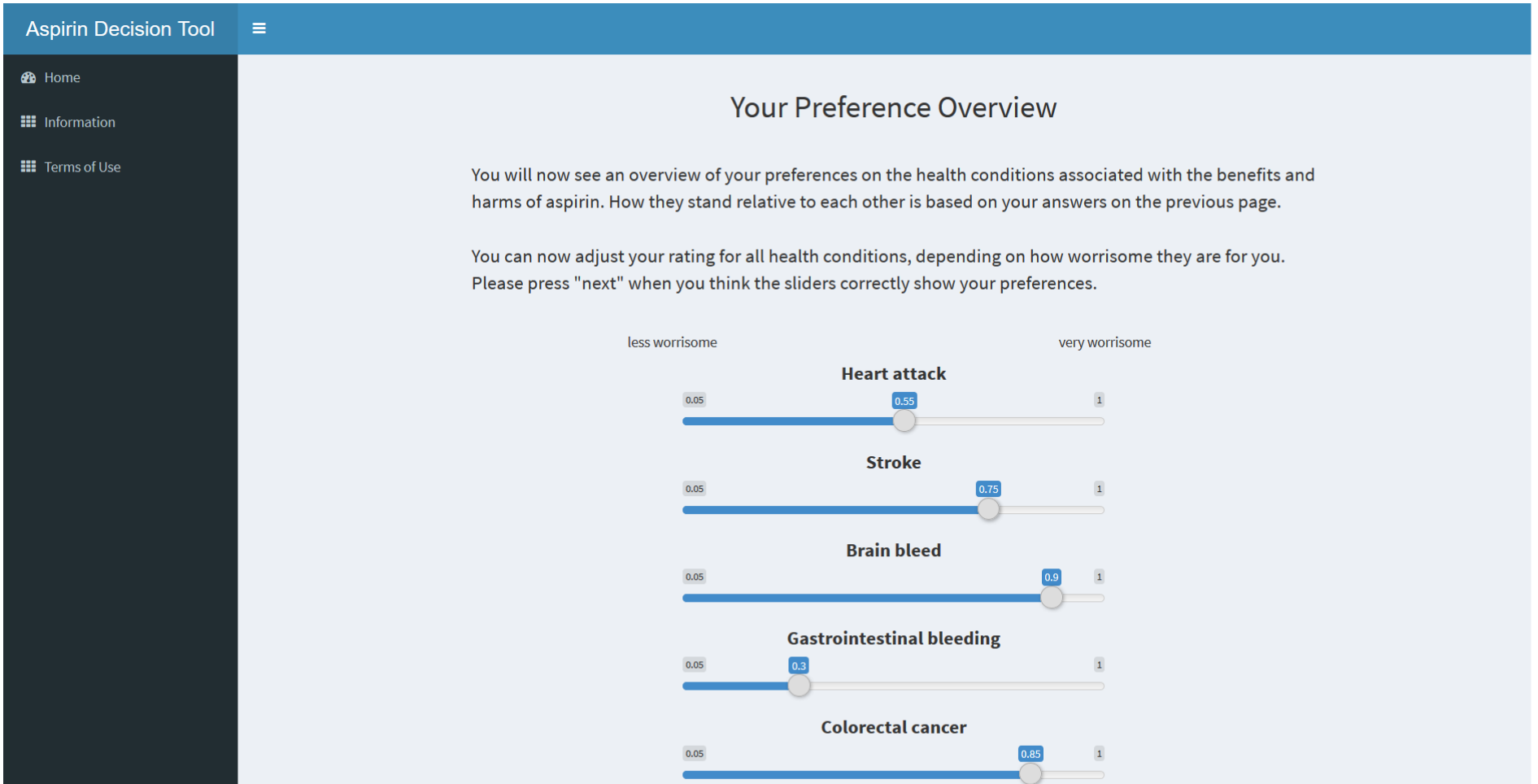
with preference elicitation



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risk assessment

Aspirin Decision Tool

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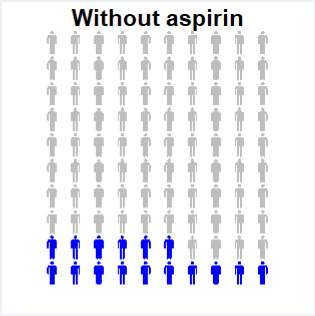
Your Individual Risk

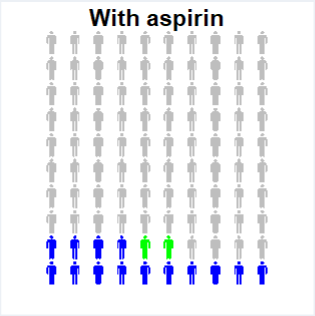
This page shows your individual risk for the health conditions you have weighed against each other before.

On the left side, you will see how many out of 100 people with your risk will get the condition in the next 10 years. On the right side you will see what the effect of taking low-dose aspirin daily would be.

Heart attack

16 out of 100 people with your risk will have a heart attack in the next 10 years. **84** will not have a heart attack. **2** will avoid having a heart attack because of taking low-dose aspirin.





Stroke

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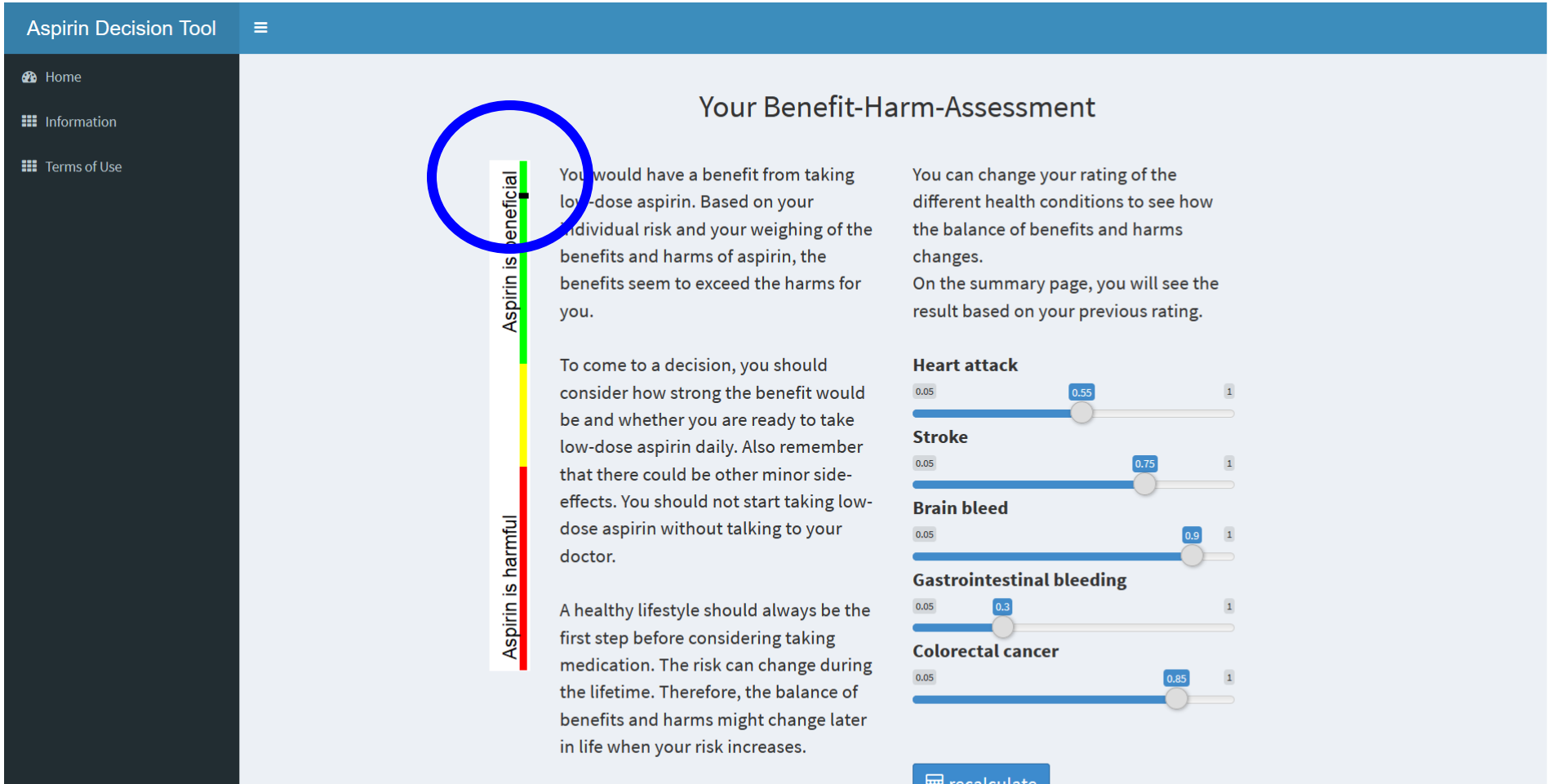
and an individualized estimate for the benefit harm balance



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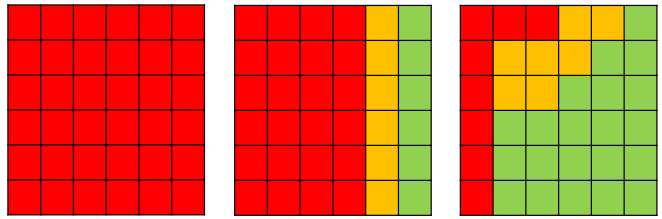
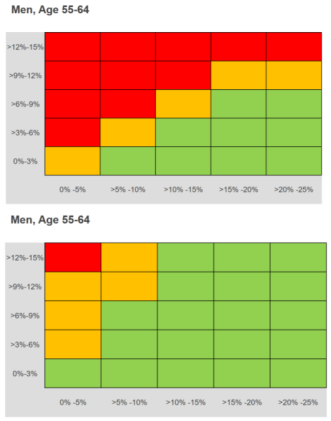
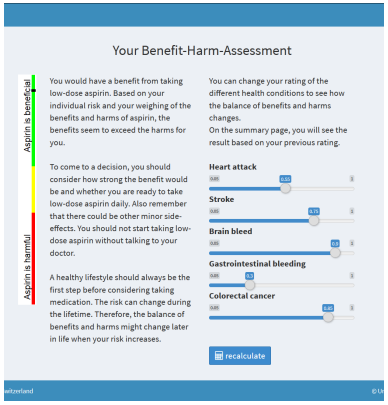
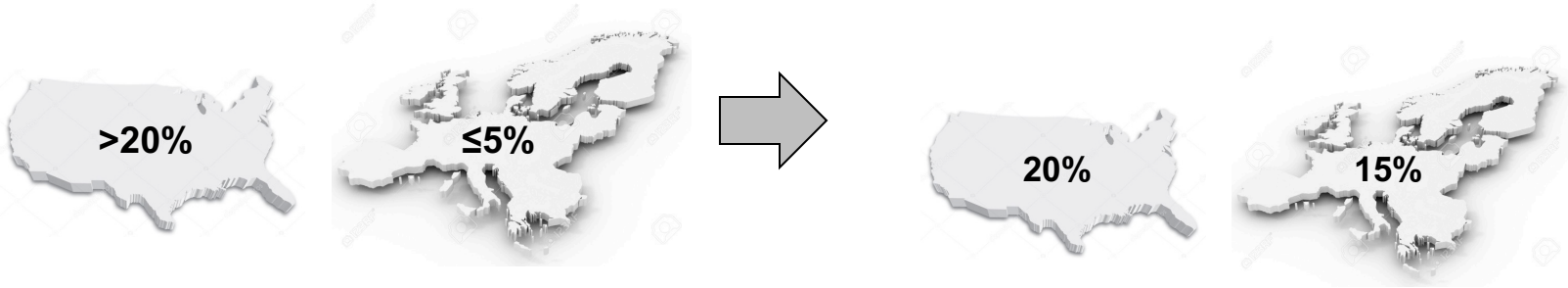
Benefit harm assessment on group and individual level may support need- and preference-based decisions









Number of methods to elicit preferences e.g. best worst scaling sruvey

Problem	Most worrisome (choose one)	Least worrisome (choose one)
Acute kidney injury	☐	☐
Low blood pressure with dizziness	☐	☑
Fall	☐	☐
Cognitive impairment	☐	☐
Heart failure	☑	☐

The person who answered this question is most worried about “heart failure” and least worried about “low blood pressure with dizziness”.

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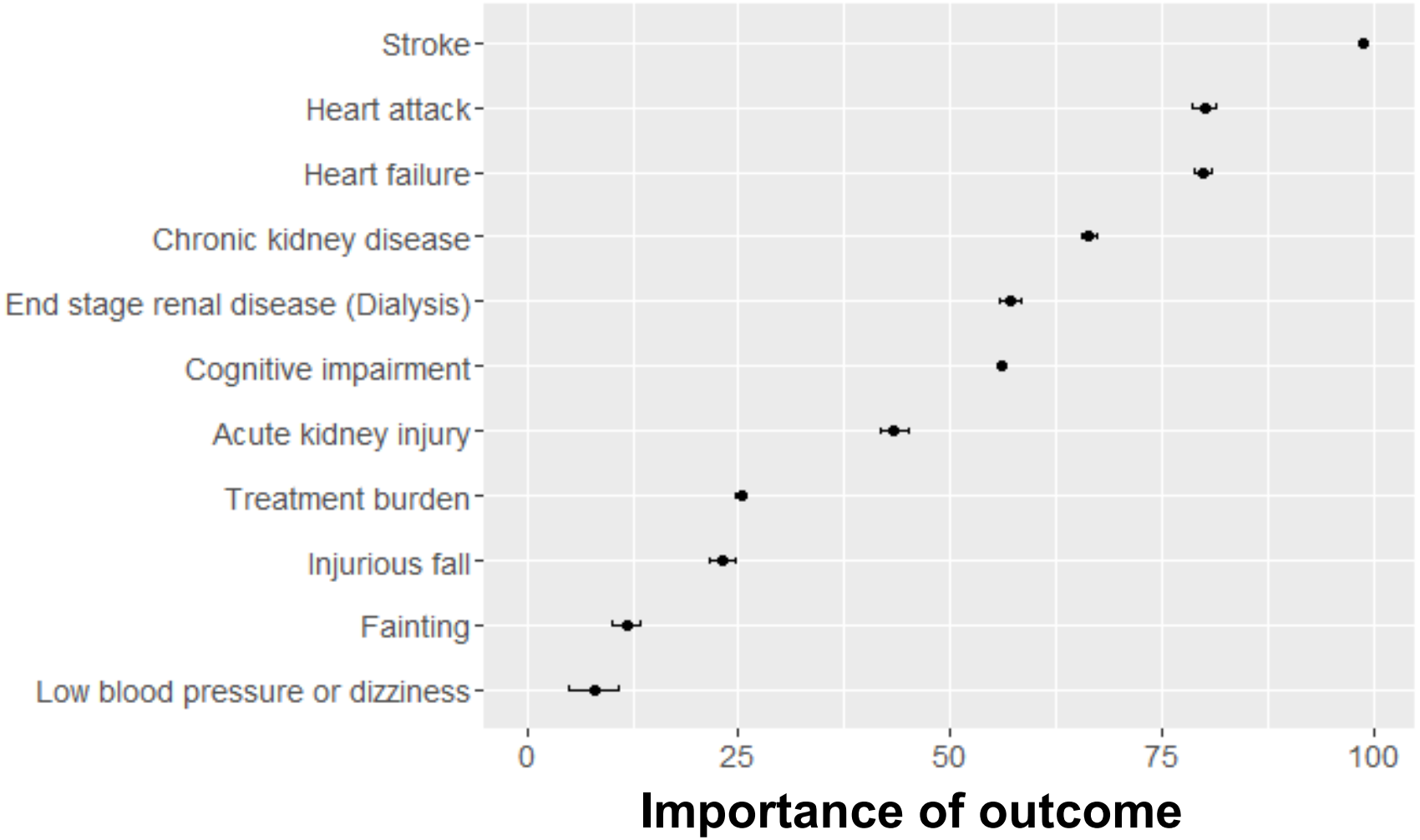
Preference elicitation survey for hypertension outcomes



Challenges for data gathering

Outcome risks	Various cohorts and trials are needed (subgroups)
	Applicability of outcome risks (studies vs. real world)
	Consistency of outcome risks across subgroups
Treatment effects	Sparse data → imprecise estimates
	No data for certain outcomes that patients and caregivers identify as important
Importance of outcomes	THE weights do not exist
	Deriving weights from preference-elicitation surveys