



**University of
Zurich^{UZH}**

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





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





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)



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 \geq 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 \geq 4% 10-year risk of CHD
- 60–69 year old if \geq 9% 10-year risk of CHD
- 70–79 year old if \geq 12% 10-year risk of CHD

(A recommendation)



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

European Society of Cardiology

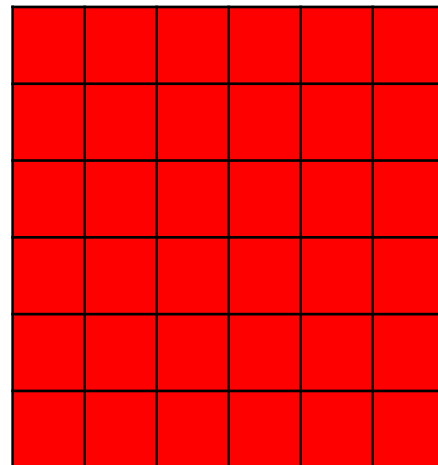
WHO

US Preventive Services Task Force

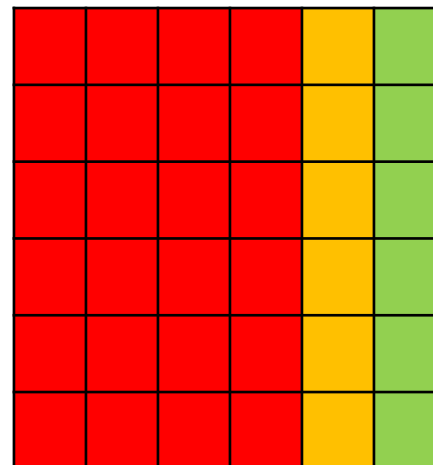
>15

10-year risk of severe GI bleed in %

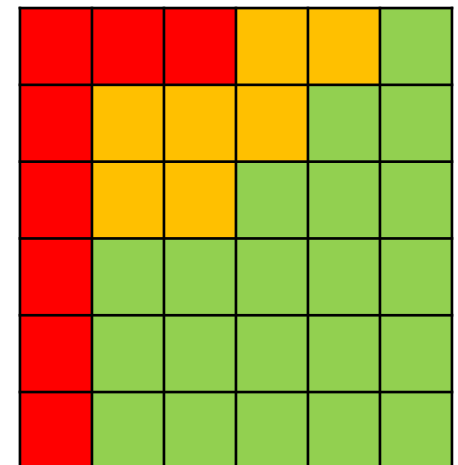
≤3



≤5 5-10 >30



≤5 5-10 >30



≤5 5-10 >30

10 year risk of MI in %

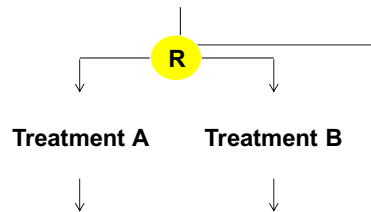


A useful tool to explore how sensitive a decision is to needs and preferences

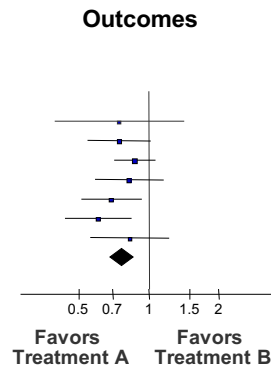


Quantitative benefit harm assessments

Evidence generation



Evidence synthesis



Decision makers

Patients and health care providers

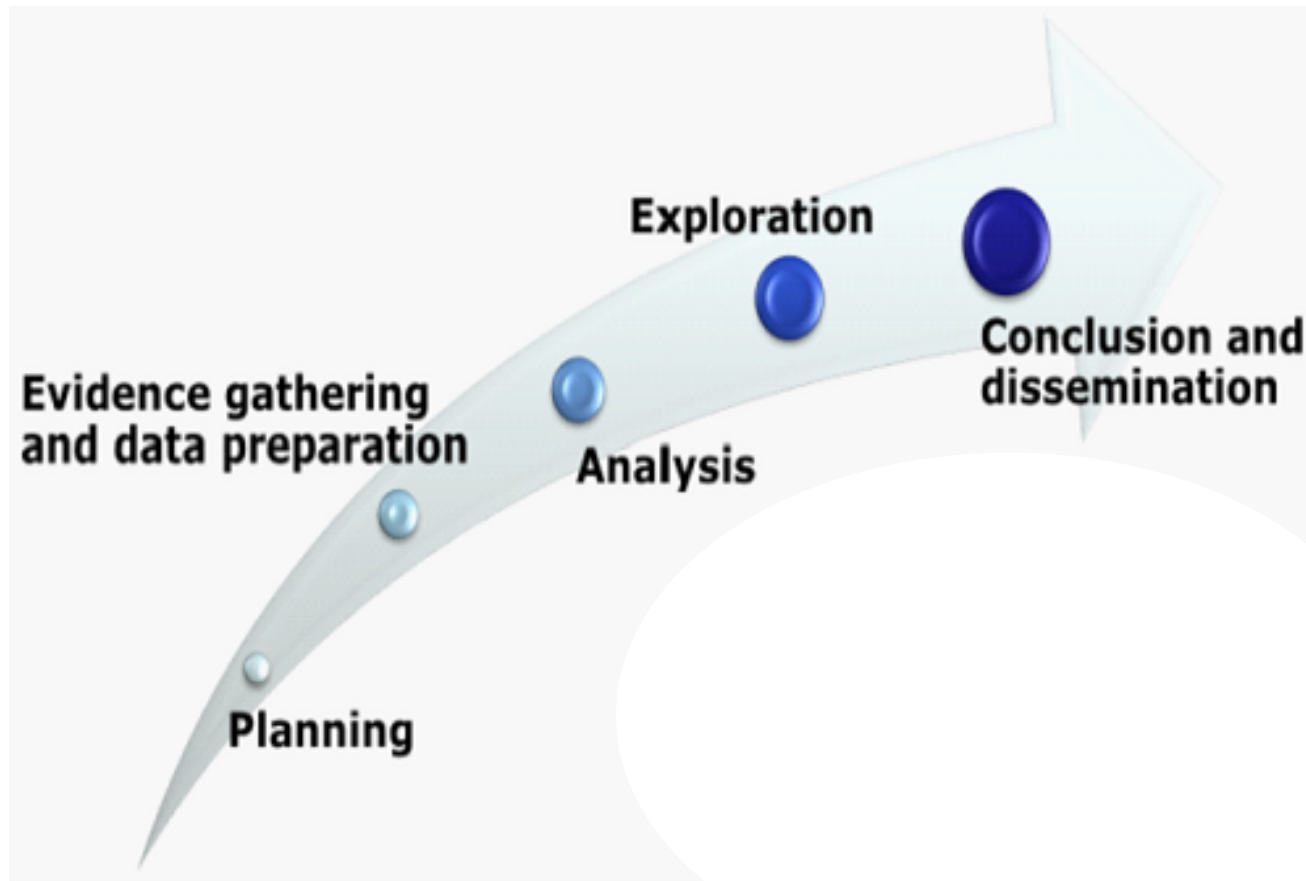
Guideline developers

Regulatory agencies

Policy makers

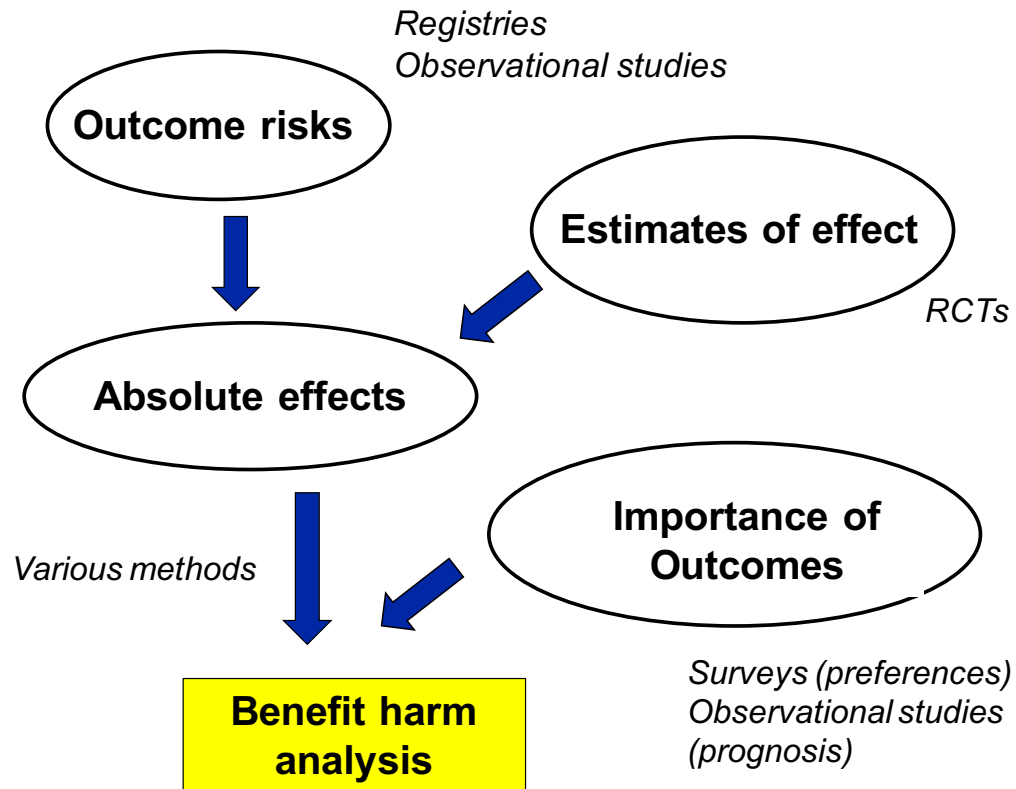


Process of benefit harm assessments



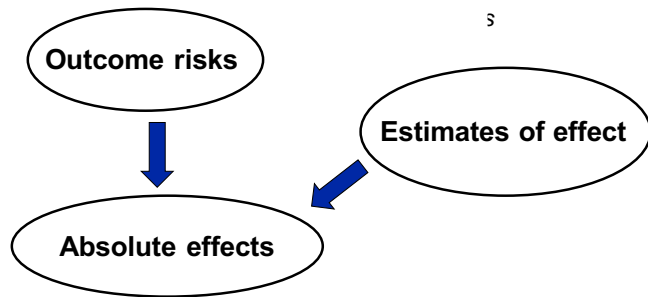


Evidence gathering and preparation





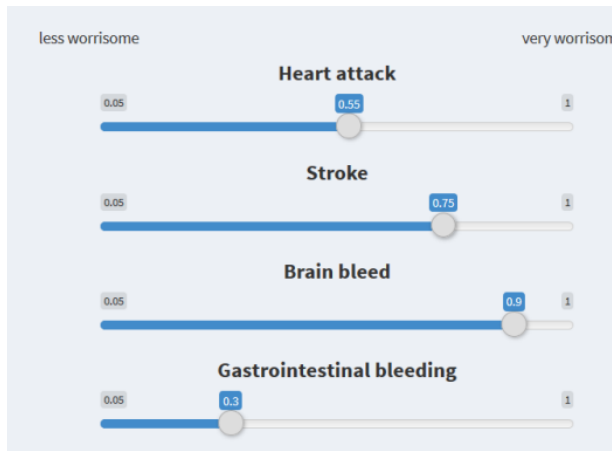
Analysis: Estimate absolute numbers of events to be expected



Number of expected events over 10 years per 1,000 men									
Men	45–54		55–64		65–74		75–84		
Age (years)	No	Yes	No	Yes	No	Yes	No	Yes	
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	



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



Men	Number of expected events over 10 years per 1,000 men			
	55–64		65–74	
Age (years)				
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:

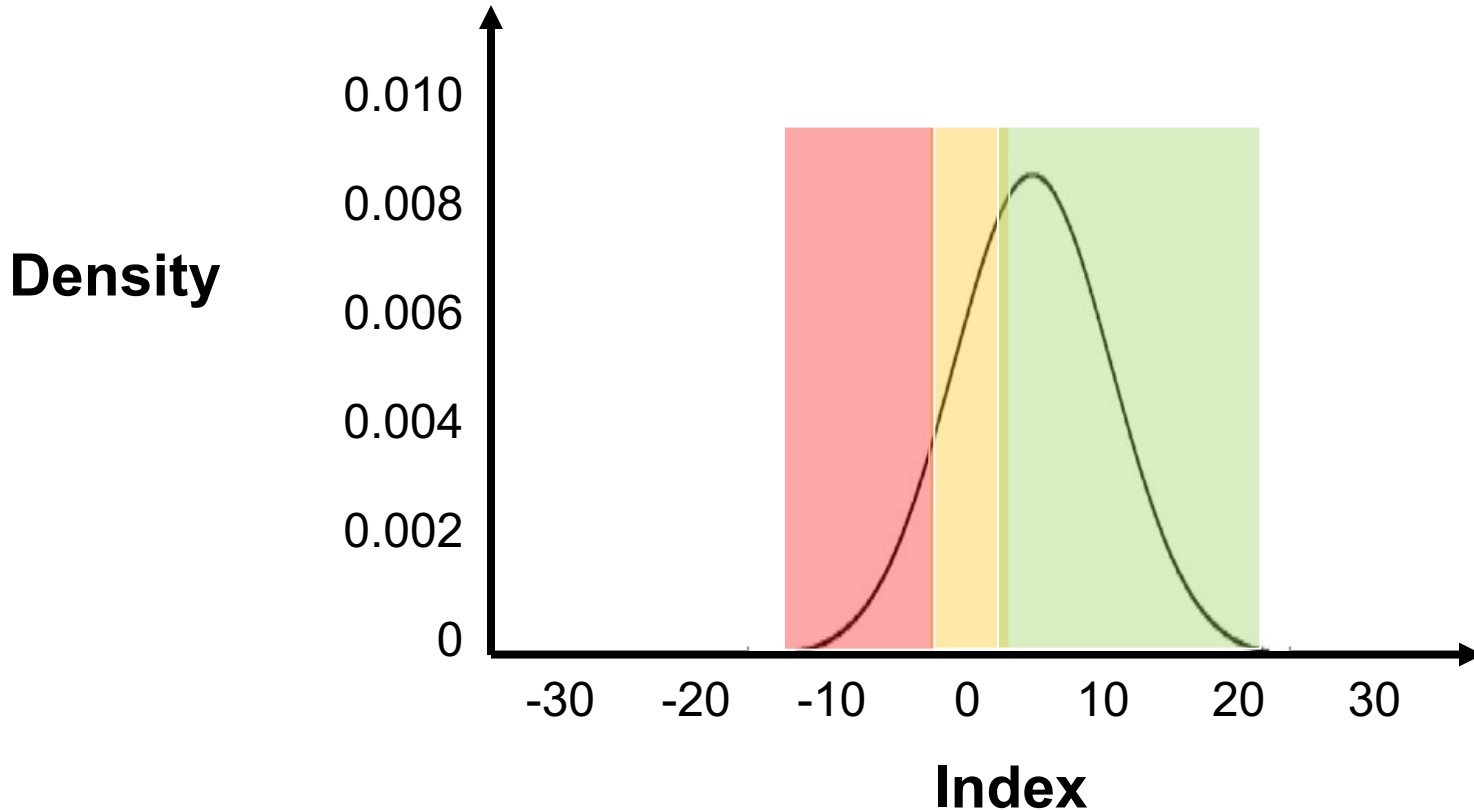
$$Index = \sum Wx * Nx$$

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



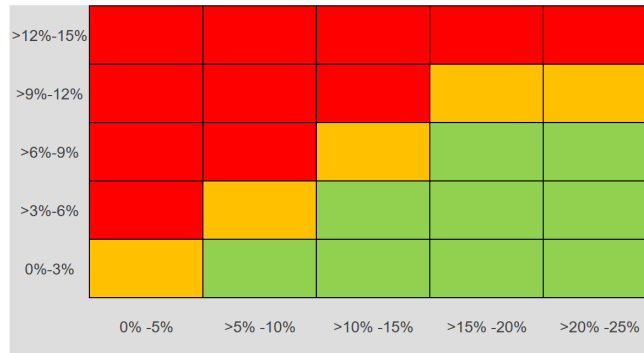
For a single scenario, e.g. 55 year old men at 10 year
CVD risk of 10% and GI risk of 3%



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

Outcomes weighted the same

Men, Age 55-64



10-year risk of severe GI bleed in %

10 year risk of MI in %

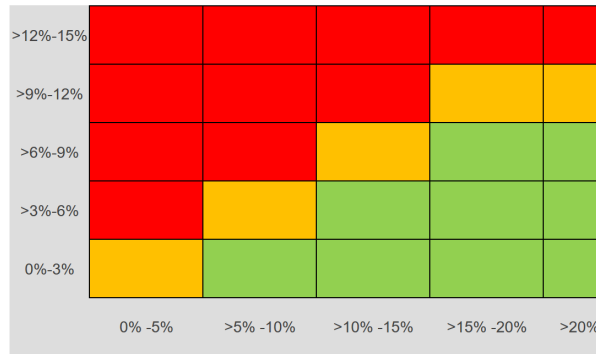


Benefit harm balance of low dose aspirin varies according to needs and preferences of 55 year old men

Outcomes weighted the same

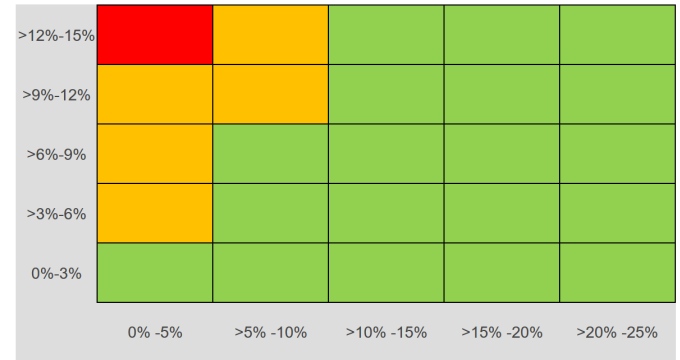
Stroke weighted most, followed by MI, then GI bleeds

Men, Age 55-64



10 year risk of MI in %

Men, Age 55-64



10 year risk of MI in %

10-year risk of severe GI bleed in %



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]

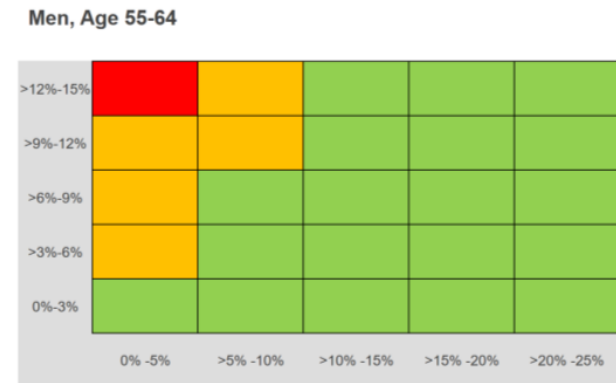
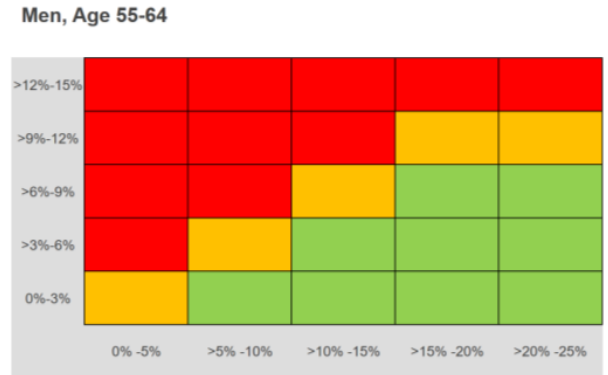
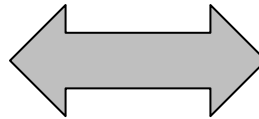
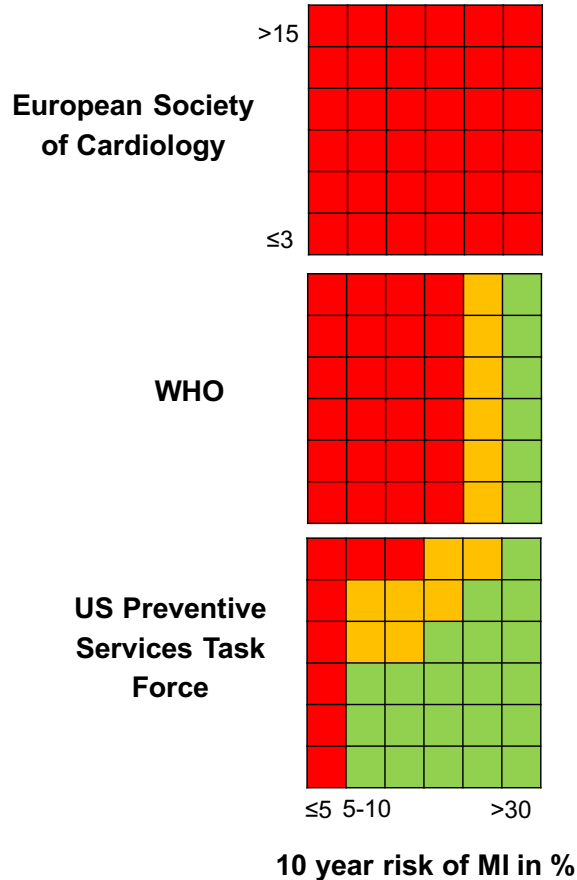
0.61 [0.59, 0.61]

New drug for COPD (roflumilast)

0.0	0.0	0.0	0.0	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0
0.0	0.0	0.0	0.0	0.0	0.0



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



10 year risk of MI in %



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



Your Decision to Take

Research has shown that taking low-dose aspirin daily reduces the risk of having a heart attack or a stroke in people who have no history of cardiovascular disease. It might also prevent certain types of cancer. However, aspirin also has side effects and can cause severe bleedings. This tool will help you decide whether or not taking low-dose aspirin could be an option for you.

You will find some of the most frequently asked questions (FAQ) below:

What is aspirin? How does it work?



Why consider aspirin? What are the benefits?



What are the possible harms and side-effects of aspirin?



The positive effects of low-dose aspirin have to be carefully weighed against its possible harms. As aspirin reduces blood clotting, it also increases the risk of bleeding. Most importantly, the risk of a gastrointestinal bleeding (bleeding in the stomach or bowels) or a bleeding in the head are higher when taking low-dose aspirin. People with a history of a stomach or duodenal ulcer, or regularly taking certain pain killers (non-steroidal anti-inflammatory drugs, NSAIDs), have a higher risk of gastrointestinal bleeding when using aspirin. Also, the risk of suffering from a severe cerebral bleed is higher when taking



Web-base decision aid



The Benefits and Harms Explained

Now please read some further information about the health conditions associated with the benefits and harms of aspirin.

Heart attack



Stroke



Brain bleed



Gastrointestinal bleeding



A gastrointestinal bleeding is very variable in severity. In mild forms it can be almost unnoticed and you might only have black stool as a symptom. More severe forms, on the other side, are an emergency situation and can lead to shock or rarely to death due to a significant loss of blood. You will receive emergency treatment and will usually have to stay at the hospital for about 2-4 days. You will have a gastroscopy and/or colonoscopy. In very severe cases, transfusions of blood or a stay in the intensive care unit is necessary. You might feel short of breath or unusually tired for the weeks following the bleeding. But usually, you will not have long-term consequences.



with preference elicitation



Home

Information

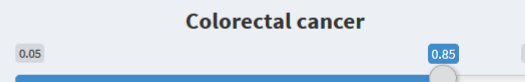
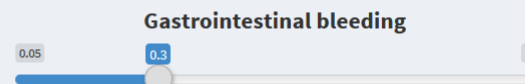
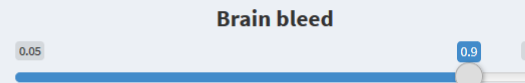
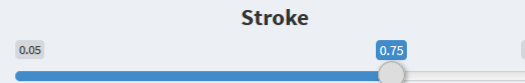
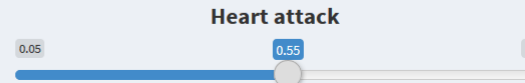
Terms of Use

Your Preference Overview

You will now see an overview of your preferences on the health conditions associated with the benefits and harms of aspirin. How they stand relative to each other is based on your answers on the previous page.

You can now adjust your rating for all health conditions, depending on how worrisome they are for you. Please press "next" when you think the sliders correctly show your preferences.

less worrisome very worrisome





risk assessment



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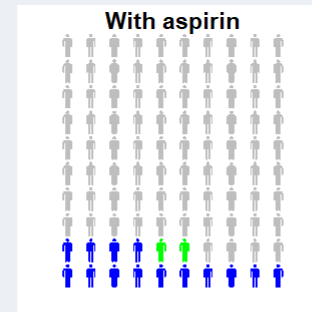
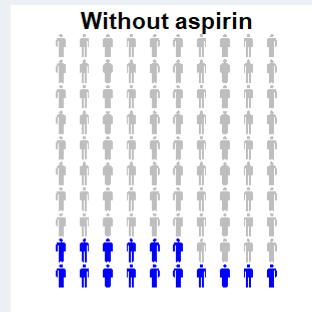
Your Individual Risk

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

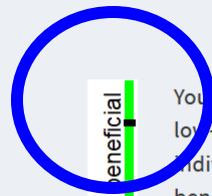


and an individualized estimate for the benefit harm balance



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Your Benefit-Harm-Assessment



Aspirin is beneficial

Aspirin is harmful

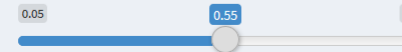
You would have a benefit from taking low-dose aspirin. Based on your individual risk and your weighing of the benefits and harms of aspirin, the benefits seem to exceed the harms for you.

To come to a decision, you should consider how strong the benefit would be and whether you are ready to take low-dose aspirin daily. Also remember that there could be other minor side-effects. You should not start taking low-dose aspirin without talking to your doctor.

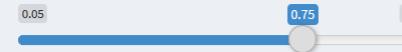
A healthy lifestyle should always be the first step before considering taking medication. The risk can change during the lifetime. Therefore, the balance of benefits and harms might change later in life when your risk increases.

You can change your rating of the different health conditions to see how the balance of benefits and harms changes. On the summary page, you will see the result based on your previous rating.

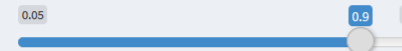
Heart attack



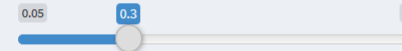
Stroke



Brain bleed



Gastrointestinal bleeding



Colorectal cancer

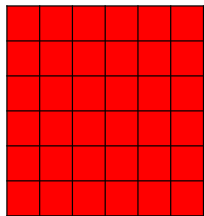


recalculate

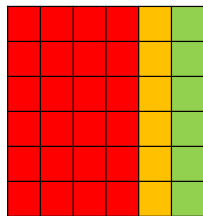


Benefit harm assessment on group and individual level may support need- and preference-based decisions

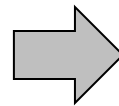
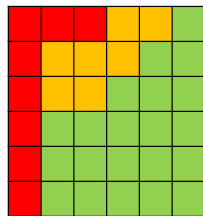
European Society of Cardiology



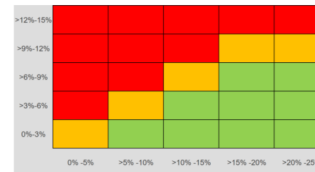
WHO



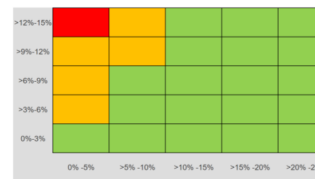
US Preventive Services Task Force



Men, Age 55-64



Men, Age 55-64



Your Benefit-Harm-Assessment

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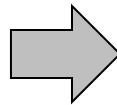
Heart attack

Stroke

Brain bleed

Gastrointestinal bleeding

Colorectal cancer





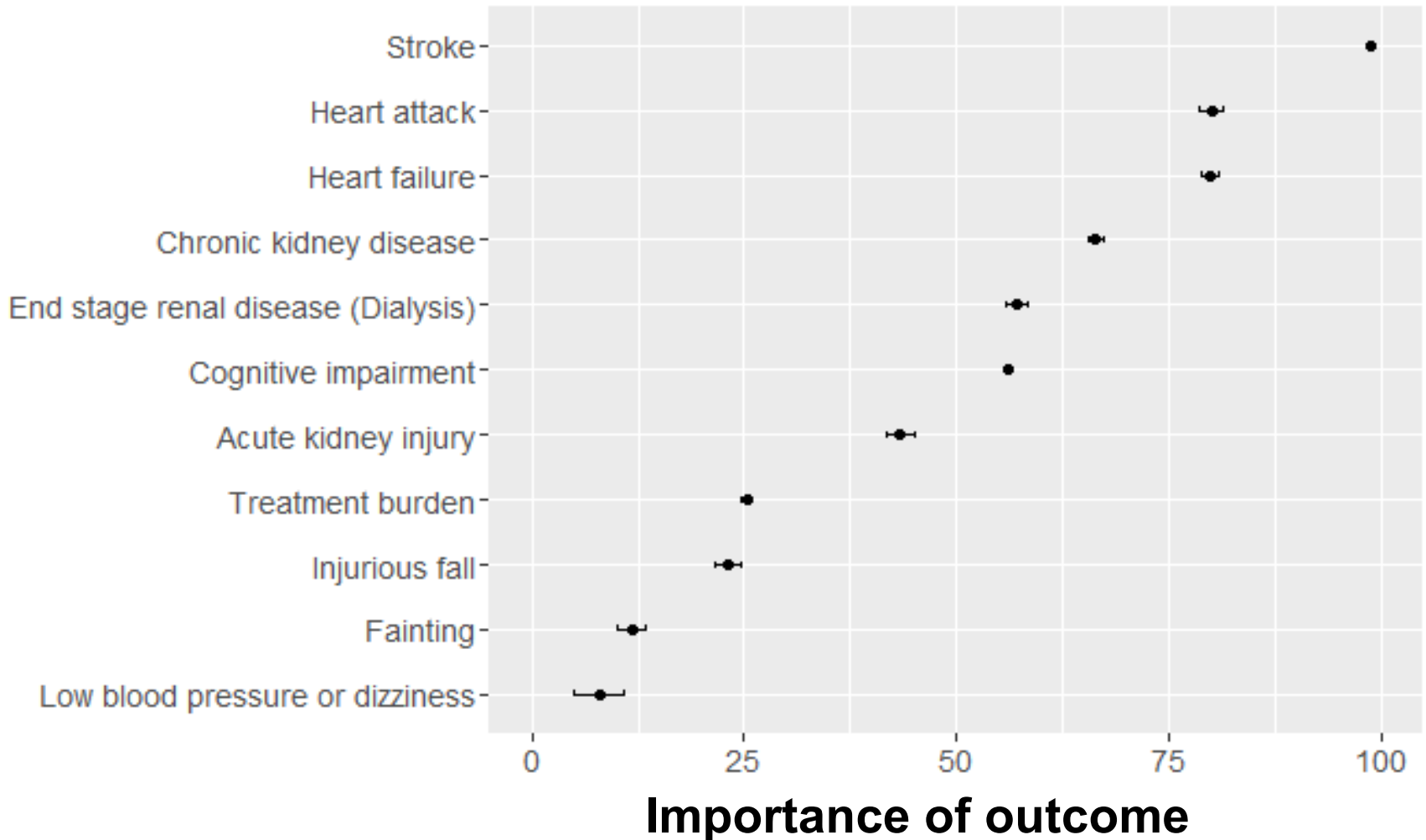
Number of methods to elicit preferences e.g. best worst scaling survey

Problem	Most worrisome (choose one)	Least worrisome (choose one)
Acute kidney injury	<input type="checkbox"/>	<input type="checkbox"/>
Low blood pressure with dizziness	<input type="checkbox"/>	<input checked="" type="checkbox"/>
Fall	<input type="checkbox"/>	<input type="checkbox"/>
Cognitive impairment	<input type="checkbox"/>	<input type="checkbox"/>
Heart failure	<input checked="" type="checkbox"/>	<input type="checkbox"/>

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



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