Primary Health Care Specialist Group
British Computer Society

9 November 2023, Chester

Values-based practice: the less-travelled path that would make all the difference

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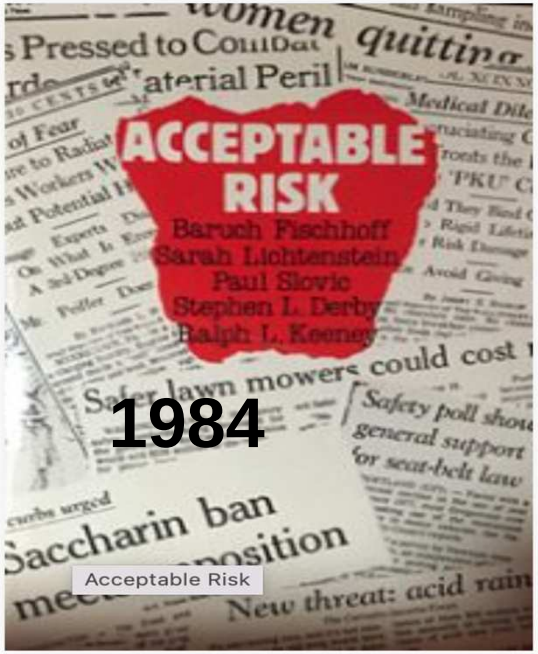
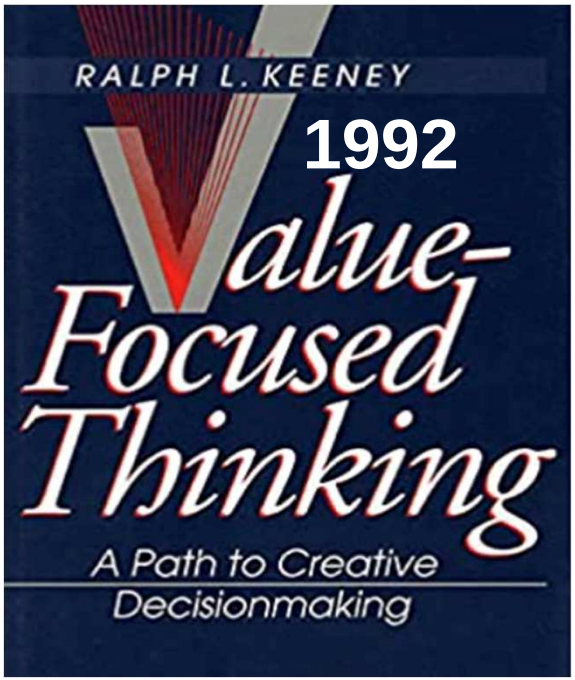
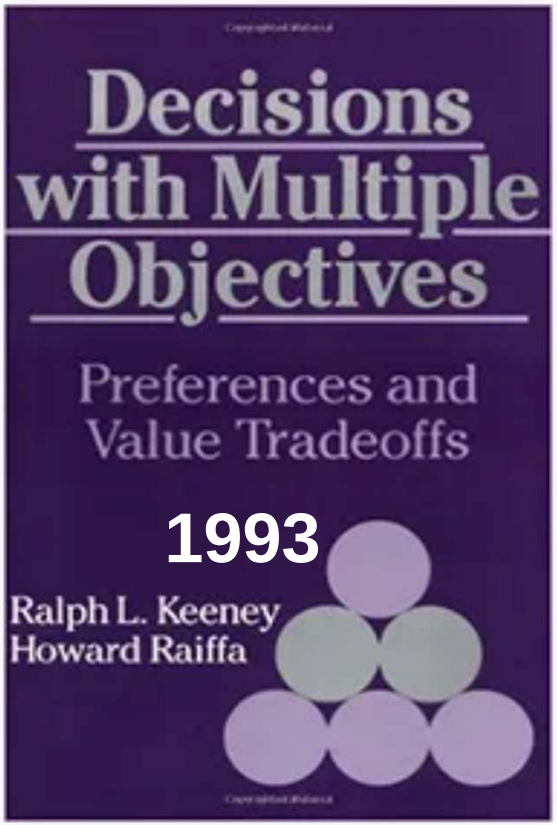
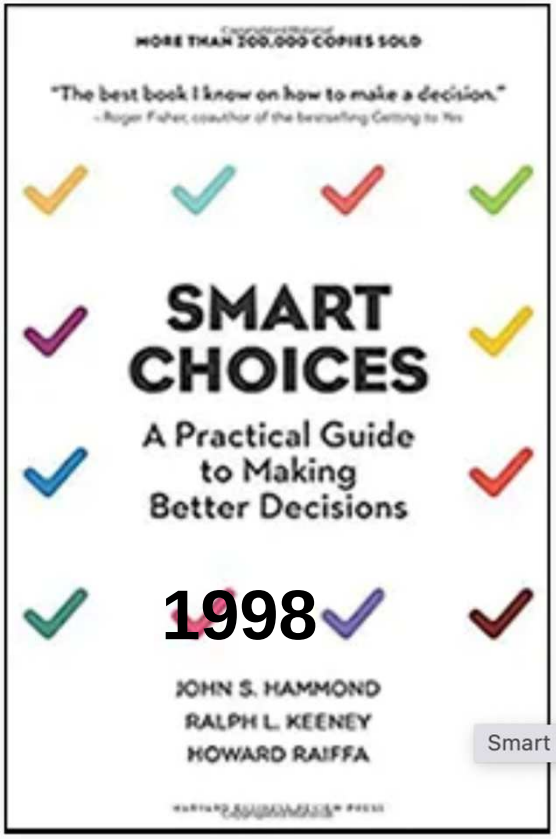
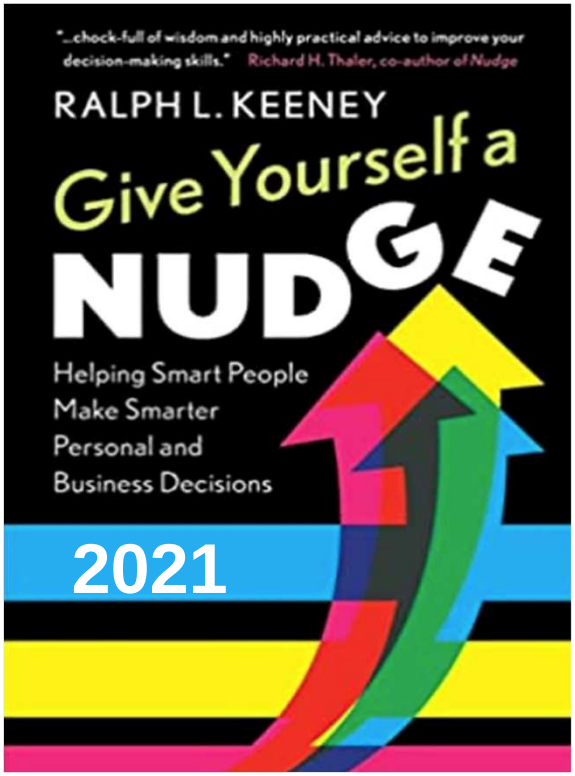
Ralph Keeney











Prof. Ralph Keeney: Decision Analysis and Value-focused Thinking |

https://www.youtube.com/watch?v=xaQse9MomOA

Move from well-beaten path
Alternatives/**Options/Evidence**-Based Medicine
(OBM for short)

to less travelled path
Objectives/**Values/Preference-**Based Medicine
(VBM for short)

"The fundamental basis for decision-making should be values, not alternatives... Your interest in any decision is to avoid undesirable consequences and achieve desirable ones. The desirability of consequences is based on values."

Not either/or, structuring/sequencing/emphasis

OPTIONS/EVIDENCE-Based Medicine

Options
(medications, surgery, lifestyle changes)
Evidence

↓

Objectives
Preferences
(outcomes importance weights)

VALUES/PREFERENCE-Based Medicine

Objectives
Preferences
(outcomes importance weights)

↓

Options
(medications, surgery, lifestyle changes)
Evidence

Values “follow the science”

Science “follows the values”

- In *decision-framed* VBM. the preferences **of the individual** over ***outcomes*** drives the decision-making process *from the start*
- Not, as in *problem-framed* OBM, after priority is given to communicating *information* about the patient's options and evidence on them.
- This sequencing minimises 'contamination' of their preferences by information containing embedded preferences, as do most evidence-based guidelines
- Prevents the discussion being later segued into the patient's **option** preferences, rather than their **outcome** preferences, which are the preferences needed to arrive at an informed and preference-based decision regarding the best option

Options/Evidence BM

- problem framed
- clinician centred
- diagnosis/testing focused
- reasoning based
- research driven (practice)
- statistical theory: classical
- group frequencies
- guideline as first resort
- decision support optional
- Decision Curve Analysis (DCA)
- maximand: ‘clinical utility’
- group preferences (DCE)
- treatment: ‘is-ought’ segue
- *OverDiagnosis/Treatment*

Values/Preference BM

- decision framed
- patient-as-person centred
- prognosis/treatment focused
- modelling/calculation based
- practice driven (research)
- statistical theory: Bayesian
- individual probabilities
- guideline as last resort
- decision support essential
- (Multicriteria) Decision Analysis
- maximand: patient’s utility
- individual’s preferences
- treatment: no ‘oughtism’ risk
- *No OverDiagnosis/Treatment*

- The big picture: VBM would help ensure :

- clinical medicine is not confused with public health
- clinical medicine is not metamorphosed into population medicine (oxymoron!), un/intentionally, by whatever means, however well-motivated

- the patient's rights as individual are respected, and distinguished from their rights and obligations as citizen/resident of a social collectivity (e.g., NHS)

- it is understood/accepted that information / knowledge / evidence can only **inform** decisions

It is preferences that <u>make</u> decisions

Are you becoming anxious?

Maybe you have
Generalised Anxiety Disorder?

Please score yourself on GAD-7 while I screen myself

GAD-7 Anxiety

Over the last two weeks, how often have you been bothered by the following problems?	Not at all	Several days	More than half the days	Nearly every day
1. Feeling nervous, anxious, or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it is hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3
7. Feeling afraid, as if something awful might happen	0	1	2	3

Column totals _____ + _____ + _____ + _____ =

Total score 7

Cut-offs, Thresholds and me

US Preventive Services Task Force 2023

- The USPSTF concludes with moderate certainty that screening for anxiety disorders in adults has a moderate net benefit... recommends screening for anxiety disorders in adults [defined as <65]

- The USPSTF concludes that the evidence is insufficient on screening for anxiety disorders in older adults [65 and over]

USPSTF 2023 – evidence on key test

- GAD-7 (range, 0-21), demonstrated adequate accuracy for detecting Generalized Anxiety Disorder.
- Three studies reported test accuracy for the GAD-7 at cutoffs of 8, 9 and 10
- Cut-off of 10 has ‘best balance’ of Sensitivity and Specificity [i.e., greatest accuracy]

Preferences are embedded in cut-offs

- Imagine a 64yo trying to make a decision which reflects their personal risk preferences over the consequences of screen and no screen
- Take the example from Plummer's 2016 Systematic Review of GAD instruments
  - prevalence of GAD is 5%
  - sensitivity is 74% .
  - specificity is 84%.

What is the embedded preference trade-off between being Falsely Alarmed and Falsely Reassured at a cutoff of 10, where the test is most accurate?

Cutoff 10	GAD	Not GAD	Total		
GAD+	37	161	198	0.81	False Alarm Rate
GAD-	13	789	802	0.02	False Reassurance Rate
	50	950	1000		
	0.74	0.83		**50.17**	FAR/FRR
	Sens	**Spec**			

Plummer's conclusion (in line with OBM)

"The GAD-7 could be a useful tool if the clinical pathway is able to cope with the 161 false positive patients identified and it is deemed clinically acceptable to miss 13 patients with GAD."

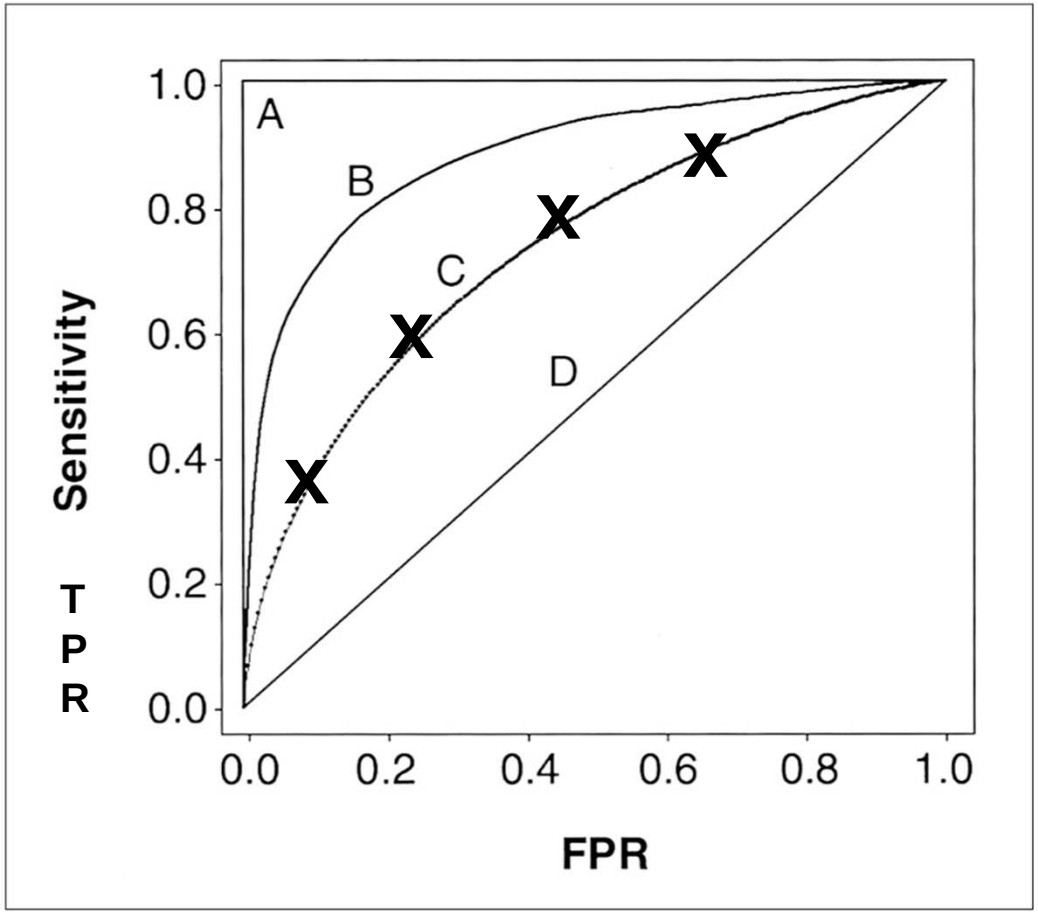
Plummer F, Manea L, Trepel D, McMillan D. Screening for anxiety disorders with the GAD-7 and GAD-2: a systematic review and diagnostic metaanalysis. Gen Hosp Psychiatry. 2016 Mar-Apr;39:24-31.

VBM says

- There is no place for a ‘clinically acceptable’ ratio to determine ‘*the* optimal’ FA/FR trade-off and hence ‘*the* optimal’ cut-off

- In fact, there is no optimal cut-off (except in ‘population medicine’), other than the patient’s personally optimal trade-off

- So, it is up to me (if I were 20 years younger) whether I want 10 or 7 used as the GAD-7 cutoff to determine whether I should be referred for further investigation and treatment

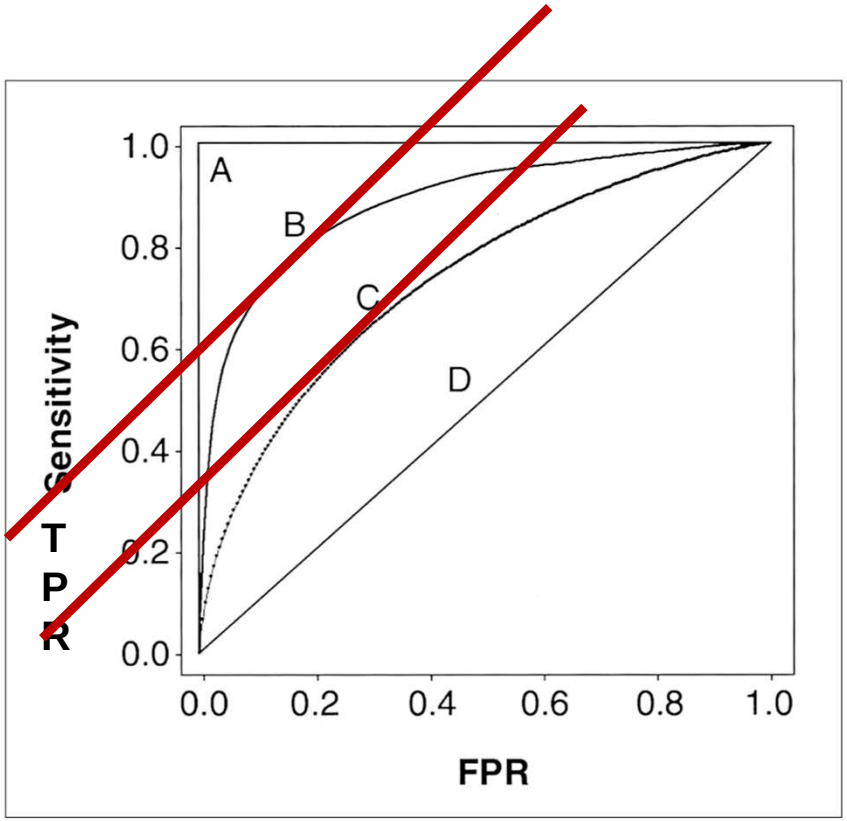


Discriminatory Power of a test is measured by Area Under Curve (AUC) formed by plotting its TPR and FPR at possible cutoffs (**Xs)** and fitting

D is a worthless test (TPR = FPR at all cutoffs); C is useful test, but B is better; A is perfect but utopian

A scalar test does not have **A** Sensitivity (TPR) or **A** Specificity (TNR)

A test's **accuracy** - treating TPR and FPR as equally important and seeking the 'best balance' of them - is irrelevant in screening/testing

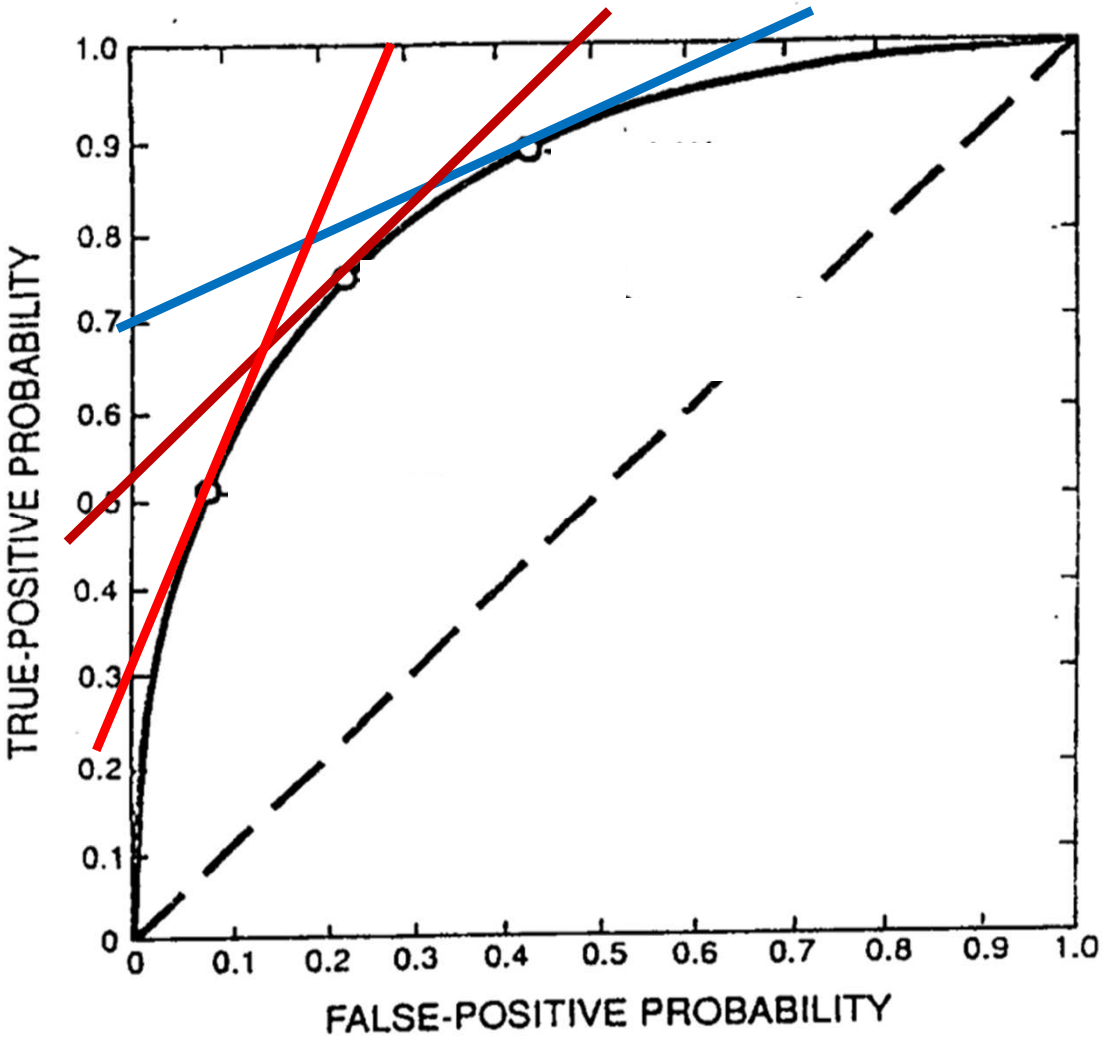


Different trade-off preferences produce different cutoffs

Same preferences produce different cutoffs on different tests

The characteristics and quality of a test are irrelevant to the determination of tradeoff preference and hence cutoff

We choose the cut-off to use by deciding our TPR/FPR trade-off preference – slope of trade-off line – and seeing where it is tangent to curve



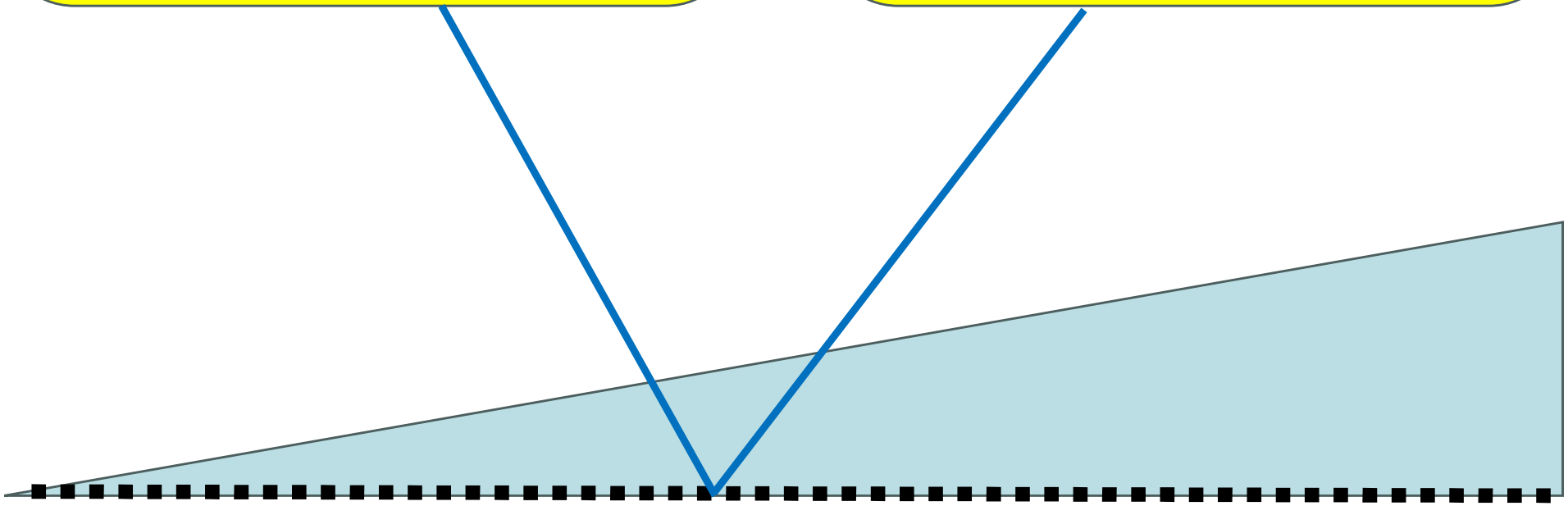
So, in VBM trade off preference is established FIRST

Requires knowledge of probability/content OF CONSEQUENCES at every cut off

Preferences are over these prognoses

Probabilistic Consequences of NOT X at THIS point:
60% chance of **8** years survival
40% chance of **4** years survival
[EV 6.4]

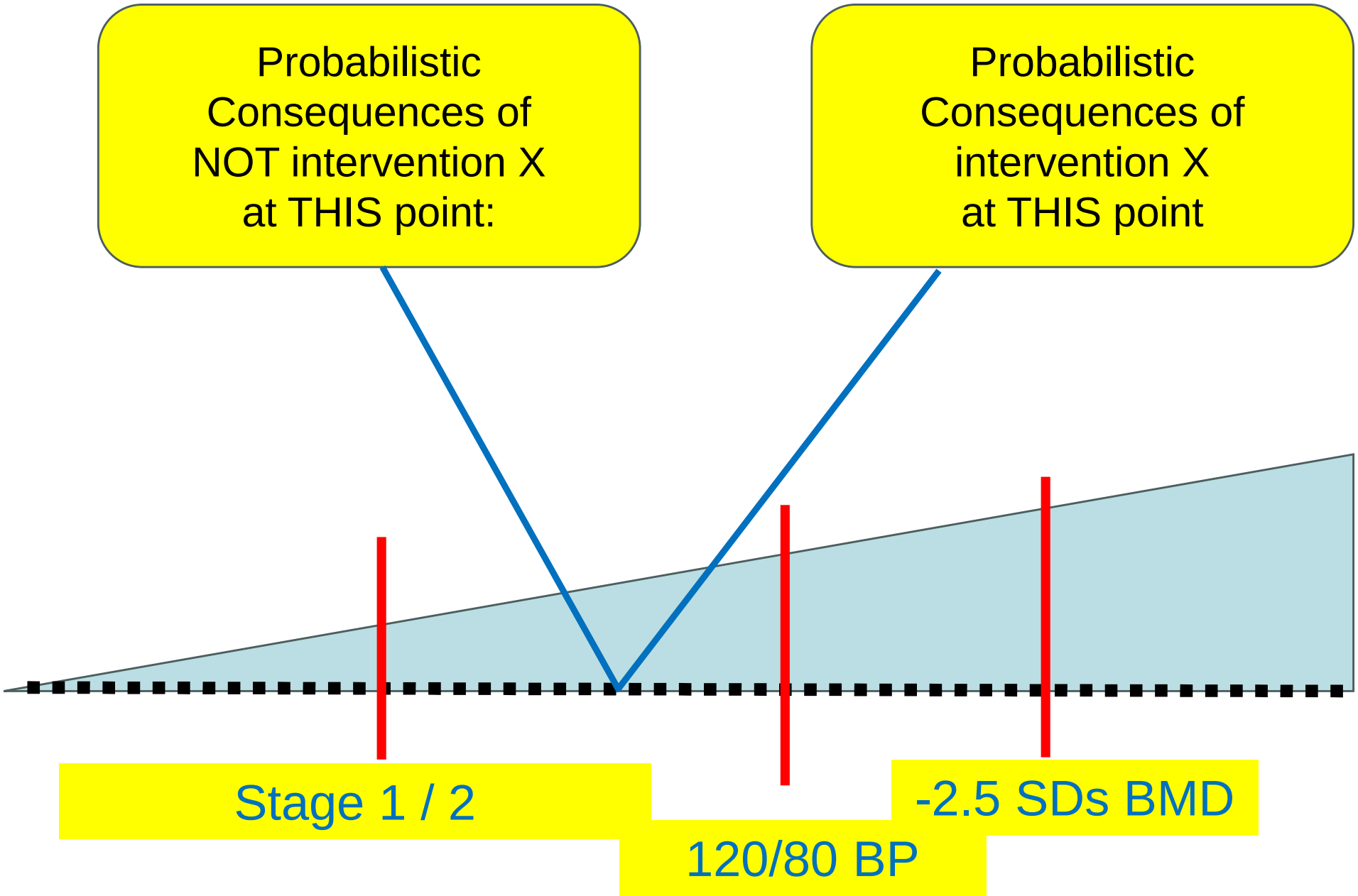
Probabilistic Consequences of intervention X at THIS point
40% chance of **12** years survival
60% chance of **3** years survival
[EV 6.6]



and different patient's trade-off preferences between them will produce different patient's decisions at this point

Diagnostic cutoffs (and diagnoses) are irrelevant in VBM

All cut-off diseases are preference-sensitive constructs



Example 2 – Bone Fragility

National Osteoporosis Guideline Group (NOGG)
FRAX-based age-specific action thresholds

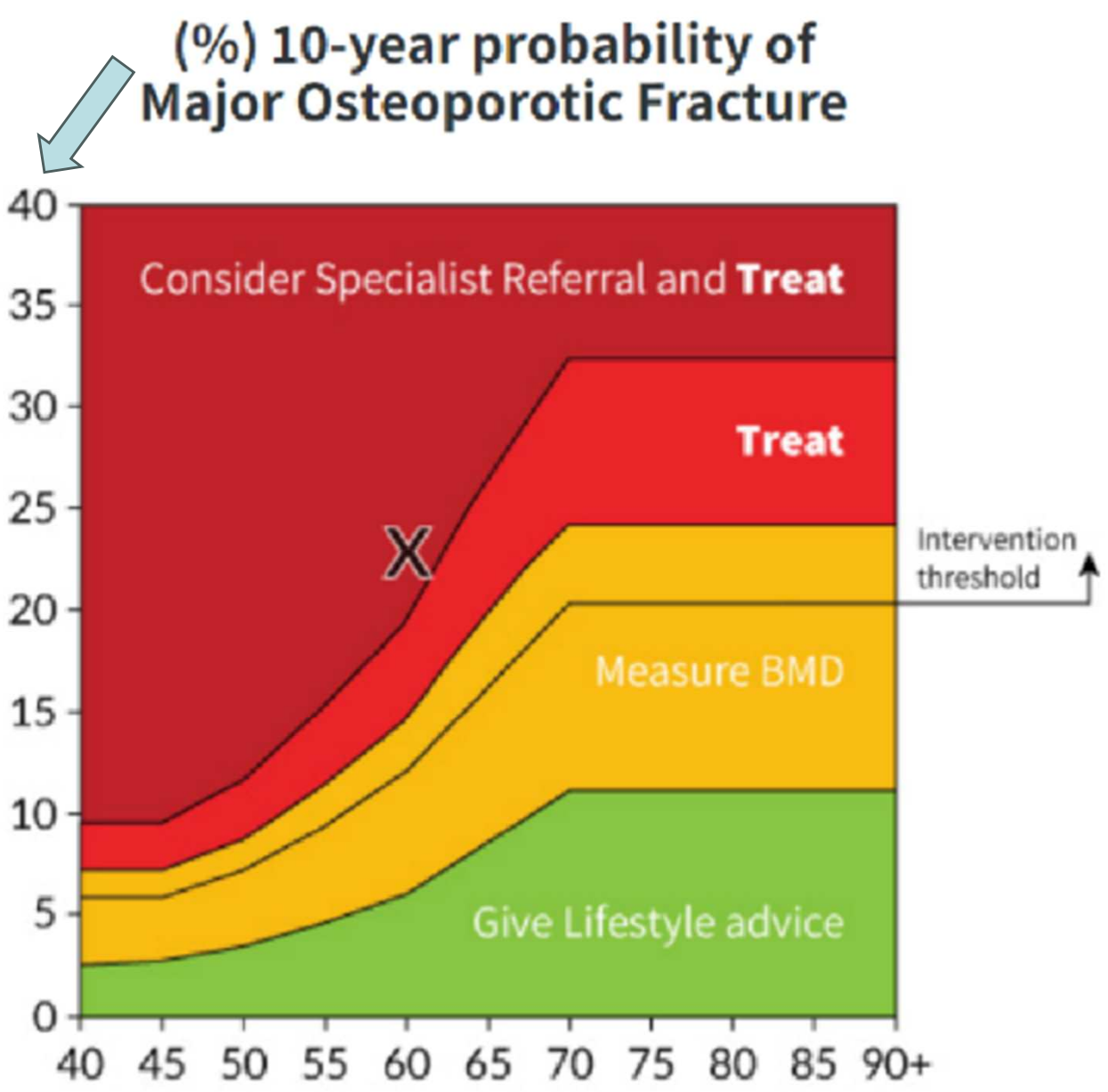


Table 4 Numerical values for NOGG thresholds for major osteoporotic fracture and hip fracture probabilities based on FRAX. LAT and UAT refer to the lower and upper assessment thresholds, respectively, between which a BMD is indicated. The intervention threshold (IT) and very high-risk threshold (VHRT) denote the thresholds for high and very high risk

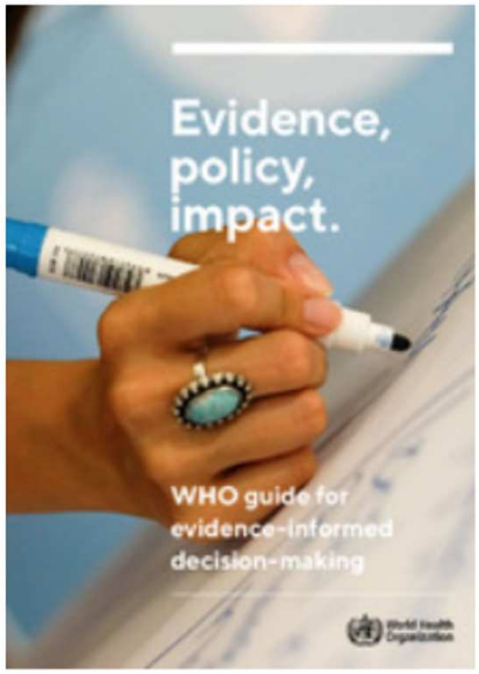
Age (years)	LAT	IT	UAT	VHRT
Major osteoporotic fracture				
50	3.4	7.3	8.8	11.7
55	4.5	9.5	11.4	15.2
60	6.0	12.2	14.6	19.4
65	8.6	16.5	19.8	26.4
70	11.1	20.3	24.4	32.5
	Don't Reassure-DEXA	High Risk	Treat without DEXA	Very High Risk

How are NOGG (preference-sensitive) thresholds set?

- For men and women, the high risk intervention threshold up to 70 is set at a risk equivalent to that of a woman of the same age with a prior fracture, in line with current clinical practice, and hence rises with age. **Whose value judgement/preference?**
- A threshold that characterises person at high and very high fracture risk has also been established using FRAX probabilities; very high risk is identified as a FRAX-based fracture risk that exceeds the intervention threshold by 60%**Whose value judgemer**
- This approach is underpinned by cost-effectiveness analysis with oral or intravenous bisphosphonates as the intervention.

Whose value judgement/preference?

At the global level



Evidence, policy, impact: WHO guide for evidence-informed decision-making

"With its new Guide on evidence-**informed** decision-making and the related online repository of tried and tested WHO tools, WHO is now providing users with comprehensive hands-on guidance so that rigorous systematic and transparent methods are applied for the creation and application of research evidence...

"At the core of the Guide and repository is its evidence ecosystem for impact framework,.. providing guidance on how to apply rigorous systematic and transparent methods for evidence-**informed** decision-making"

Evidence, policy, impact. WHO guide for evidence-informed decision-making.WHO; 2021.

EPI Guide and repository

World Health Organization

The WHO EIDM Repository

Evidence for impact

Welcome to the EIDM Repository! Here you can explore the latest WHO tools and best practices for knowledge translation and evidence-informed decision-making (EIDM). Each tool in our repository has been carefully selected and arranged according to the policy/action cycle of the WHO EIDM Guide. This dynamic repository complements the written guidance by providing you easy access to practical tools curated for each step of the EIDM process. Click here to learn more

To get started, make use of the policy/action cycle to the right or the search bar below to access the tools.

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https://evidence-impact.org

Why are values/preferences ‘blanked’?

- Straightforward desire to avoid accepting the uncomfortable fact that all assessments of the ‘benefits’ and ‘harms’ of an intervention are always preference-sensitive and therefore in no way ‘objective’, even at the population level.
- Worrying desire to avoid accepting that preferences are ontologically and epistemologically independent of empirical information / evidence / knowledge / ’science’ about options
- *Diagnostically identical individuals equipped with exactly the same knowledge about the prognostic consequences will take different decisions if they have different preferences*.
- Attempts are often made to imply that information has implications for preferences. (“Your test result is above threshold x, so treatment y is appropriate”.)
- This is the ‘oughtism’ fallacy (or tactic) – the implication that a prescriptive ought can be derived from a descriptive is.

Screening

August 28, 2023

Estimated Lifetime Gained With Cancer Screening Tests

A Meta-Analysis of Randomized Clinical Trials

Michael Bretthauer, MD, PhD[1]; Paulina Wieszczy, MSc, PhD[1,2]; Magnus Løberg, MD, PhD[1]; et al

» Author Affiliations

JAMA Intern Med. Published online August 28, 2023. doi:10.1001/jamainternmed.2023.3798

... current evidence does not substantiate the claim that common cancer screening tests [for breast, colorectal, lung and prostate cancer] save lives by extending lifetime, except possibly for colorectal cancer screening with sigmoidoscopy.

William Dahut, chief scientific officer for the American Cancer Society, said, “Cancer screening was never really designed to increase longevity. Screenings are really designed to decrease premature deaths from cancer.”

JAMA Internal Medicine | Viewpoint

August 28, 2023

The Future of Cancer Screening—Guided Without Conflicts of Interest

Hans-Olov Adami, MD, PhD; Mette Kalager, MD, PhD; Michael Bretthauer, MD, PhD

Abstract | Full Text

ONLINE FIRST *JAMA Intern Med. 2023; 10.1001/jamainternmed.2023.4064*

“Beware reification” (says VBM)

- It is common for screening guidelines to reify what are actually preference-sensitive constructs
- They talk of ‘*the* benefits’ and ‘*the* harms’, *the* ‘net benefits/harms’, whether ‘its benefits exceed its harms’, whether it is a ‘high or low benefit’
- Separating ‘benefits and harms’ from ‘values and preferences’ as if they are not preference-sensitive
- e.g., WHO evidence-informed guideline handbook
  - intervention efficacy and effectiveness
  - intervention harms
  - the values and preferences of the individuals affected by an intervention

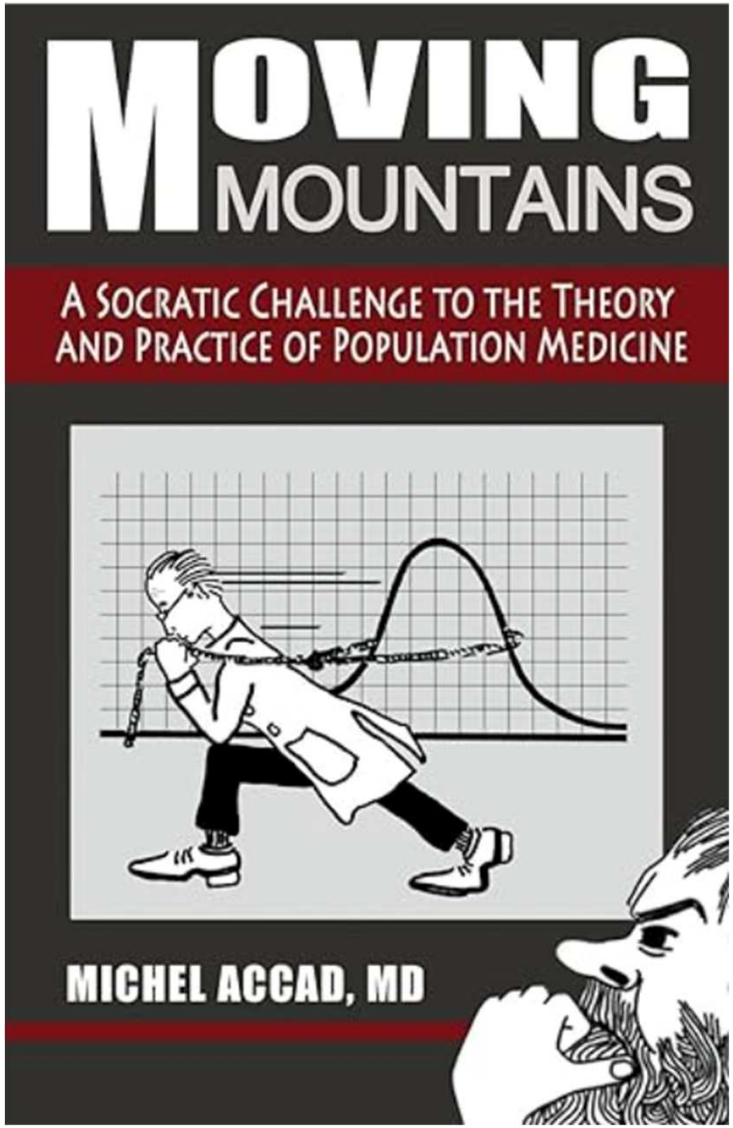
WHO handbook for guideline development. (2nd ed.) 2014

- VBM implies that the goal of maximising the uptake of a screening test is unacceptable

- ‘Preference heterogeneity' should not be addressed by clustering research to design group-targeted strategies to increase population uptake

- Simply calling it ‘heterogeneity’ frames it as deviation from a norm and therefore a ‘public health problem’ - which it is not

- ‘Population medicine' – ‘moving mountains’ of individuals to achieve a supra-individual goal - is ethically questionable (Georges Canguilhem vs Geoffrey Rose) .



thebmj

Head To Head

Does evidence based medicine adversely affect clinical judgment?

BMJ 2018; 362 doi: https://doi-org.proxy1-bib.sdu.dk/10.1136/bmj.k2799 (Published 16 July 2018)
Cite this as: BMJ 2018;362:k2799

Michel Accad, cardiologist[1], Darrel Francis, professor of cardiology[2]

HPLS (2021) 43:111
https://doi.org/10.1007/s40656-021-00463-x

ORIGINAL PAPER

Can populations be healthy? Perspectives from Georges Canguilhem and Geoffrey Rose

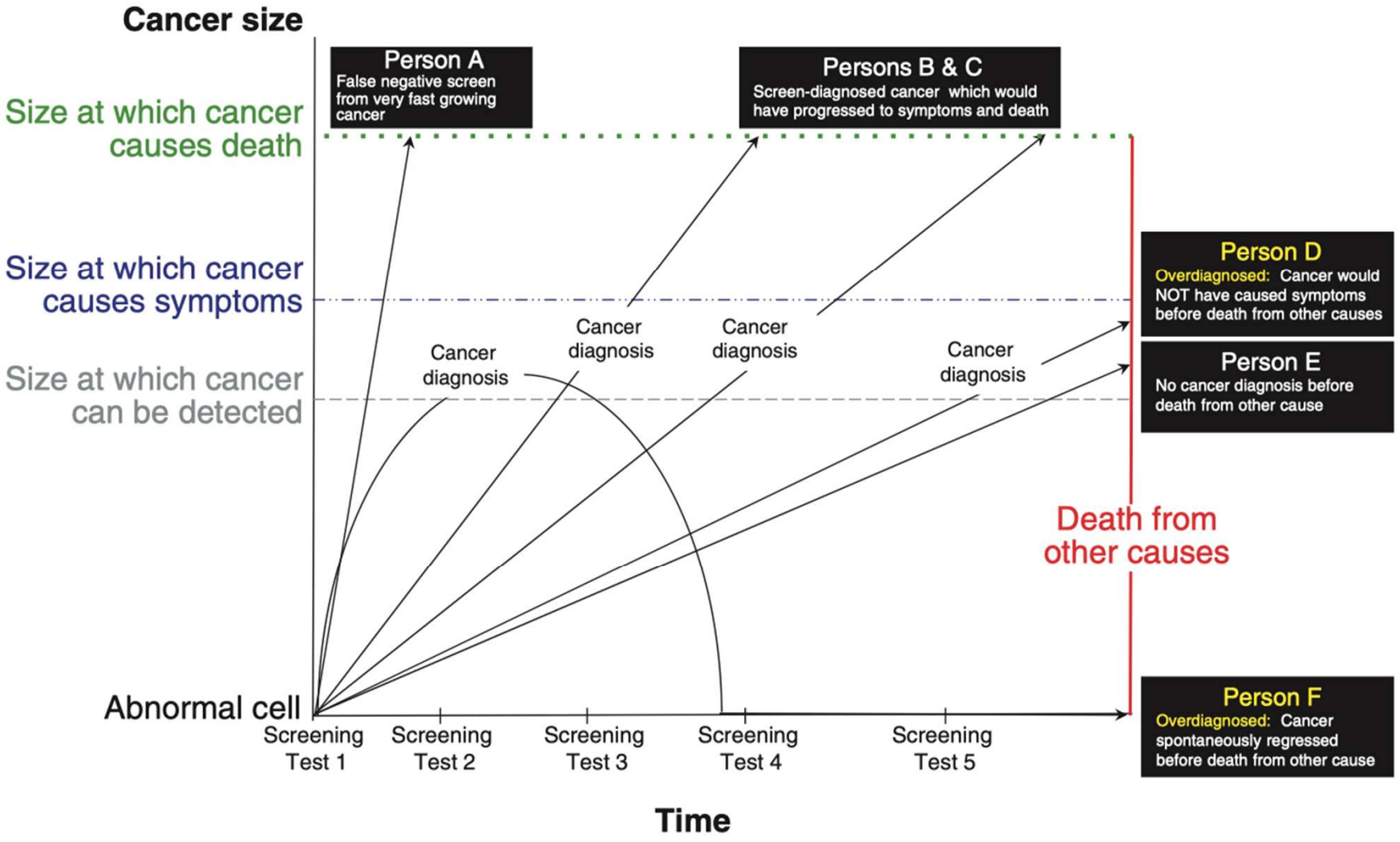
Élodie Giroux[1]

Accad M *Moving Mountains: A Socratic Challenge to the Theory and Practice of Population Medicine* 2017 Huntsville, TX: Green Publishing House. ISBN 978-1-63432-030-6.
Accad M, Francis D. Does evidence-based medicine adversely affect clinical judgment? *BMJ.* 2018 Jul 16;362:k2799. doi: 10.1136/bmj.k2799. PMID: 30012642.
Giroux É. Can populations be healthy? Perspectives from Georges Canguilhem and Geoffrey Rose. *Hist Philos Life Sci.* 2021 Oct 20;43(4):111. doi: 10.1007/s40656-021-00463-x. PMID: 34671888; PMCID: PMC8527978.

- Individuals should be provided - using the resources freed from group screening - with individualised and personalisable decision support
- ... in order that each can make an optimal informed and preference-sensitive decision about screening - as they are legally entitled to with any other test (or treatment)
- The False Alarm/False Reassurance ratio implicit in the cutoff of an offered test must be supplied
- If this trade-off is not acceptable to the person, there can be no justification for trying to impose it, since it reflects only the value judgments / preferences of content experts

- There is no ‘expertise’ in value judgments

Overdiagnosis and OverTreatment



Brodersen J, Schwartz LM, Woloshin S. Overdiagnosis: how cancer screening can turn indolent pathology into illness. APMIS. 2014 Aug;122(8):683-9

- Assume the indolent prevalence is 50%. If 100 asymptomatic individuals are all sufficiently 'risk averse' to be unwilling to accept the 50% chance of having a non-indolent tumour, they will all opt for screening+. The rate of 'overdiagnosis' found on their deaths will be 50%
- Make indolent prevalence only 10%. If all are sufficiently risk-averse to be unwilling to accept even the 10% chance of having a non-indolent tumour, they will all go for screening+. The OD rate found on their deaths will be 10%!
- Generalising, 'overdiagnosis' will always be found in a group, its extent being the simple arithmetic consequence of the indolent prevalence and the average degree of risk aversion assuming they are informed of this prevalence.
- BTW, suppose the indolent prevalence is 90% and all are willing to accept the 10% chance of non-indolence. None will go for screening and as a simple consequence the rate of '**under**diagnosis**'** found on their deaths will be 10%!

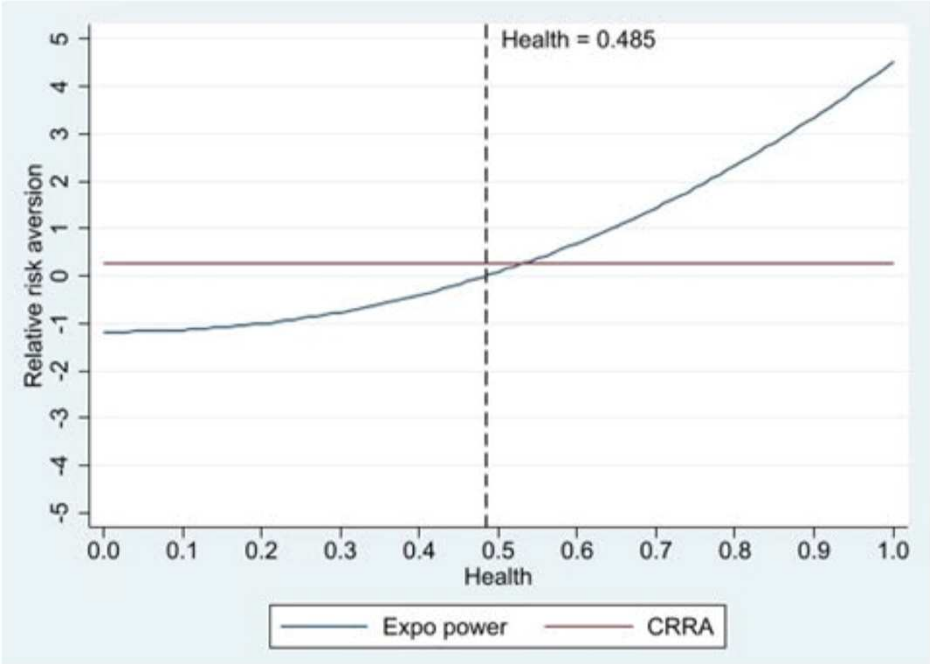
- Following guidelines will also normally and inevitably produce ODOT because the guideline panel will *embed risk-averse preferences at all decision nodes in the guideline*.
- No problem. The issues VBM has with guidelines are:
  - that the embedded risk preferences have no valid empirical basis, at best being the panel opinion of the the risk aversion of the 'representative patient'.
  - that no panel will be willing to expose its embedded preference trade-off between False Alarms and False Reassurances (should vary with regional prevalence)
  - that clinical medicine should not be paying attention to guidelines based on average preferences, *even if they were to be validly derived and publicly available*
- Clinical medicine should be using patient's preferences not patients' preferences. The apostrophe's positioning matters.

- Using individual patient's preferences throughout clinical practice will also inevitably produce population level ODOT, if they are on average risk averse. But are they?

- Phelps, Lakdawalla et al. have recently produced results that are highly pertinent to the present argument

  - "Although there is a substantial degree of individual heterogeneity in risk preferences over health, we find minimal evidence that risk preferences are correlated with common demographic covariates [age, sex, ethnicity...]

  - The estimates indicate relative risk aversion is increasing in health... individuals in the worst health state exhibit risk seeking preferences, switch to risk-averse preferences at health equal to 0.485 [on a 0 to 1 scale], and reach their maximum risk-aversion when their health is perfect [i.e.,1]



Mulligan 2023
Figure 1

- The degree of risk aversion *increases* with health, being greatest among those in perfect health.
- Means that the healthier you are, the more you contribute to population level ODOT, as measured.
- Those in poor health are, on average, risk *seeking*.
- Means the less healthy you are, the less you contribute to population level ODOT,... and more likely to UnderDUnderT

Lakdawalla DN, Phelps CE. Health technology assessment with risk aversion in health. *J Health Econ.* 2020 Jul; 72:102346.
Mulligan K, Baid D, Doctor JN, Phelps CE, Lakdawalla DN. Risk Preferences Over Health: Empirical Estimates and Implications for Healthcare Decision-Making *NBER Working Paper* No. 31524 August 2023

To summarise

- The higher the average degree of risk aversion in the asymptomatic population, the higher will be the uptake of screening and the higher the accepted False Alarm to False Reassurance trade-off, given the screen result.
- And the higher, therefore, will be the amount of ODOT at the population level that should be regarded as the simple arithmetic consequence of respecting individual's (probably also the clinician's) risk averse preferences
- If the individual's risk preferences entered into their decision are not based on requisite information about the prognostic consequences. ***that*** is the problem to be addressed.

- To have informed preferences you need to take preferences much more seriously than research-driven OBM does

Why not VBM-driven research
instead of research-driven OBM?

- The human being's values-based preferences - the core of their humanness - are anathema for 'scientific' research seeking 'the truth'
- (Publishable, rewardable, fundable) 'scientific' research/analysis cannot be done on me
- Interventional science (establishing causality) can only be done on **bits** of humans (organs,cells, DNA)
- Observational 'science'/analysis (inferring causality) can only be done on **groups** of humans
- Reluctance to accept that all causal **inference** is preference-sensitive - to **whose** preferences are controlling/censoring the causal model

Rajput VK, Kaltoft MK, Dowie J. Inferring Causality Is Preference-Sensitive: We Need a Book of Who as Well as Why. Stud Health Technol Inform. 2023 Oct 20;309:38-42. doi: 10.3233/SHTI230735. PMID: 37869802.

Special Topic Conference STC 2023 EFMI
ww.stc2023.org/home-page

EFMI 45 EUROPEAN FEDERATION MEDICAL INFORMATICS

Torino, Italy

25-27 October 2023

Inferring causality is preference-sensitive - we need a Book of Who as well as Why

Vije Kumar Rajput[1,2], Mette Kjer Kaltoft[3], Jack Dowie[2,3]

Stonydelph Medical Centre[1], London School of Hygiene and Tropical Medicine[2]

University of Southern Denmark[3]

LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

SDU University of Southern Denmark

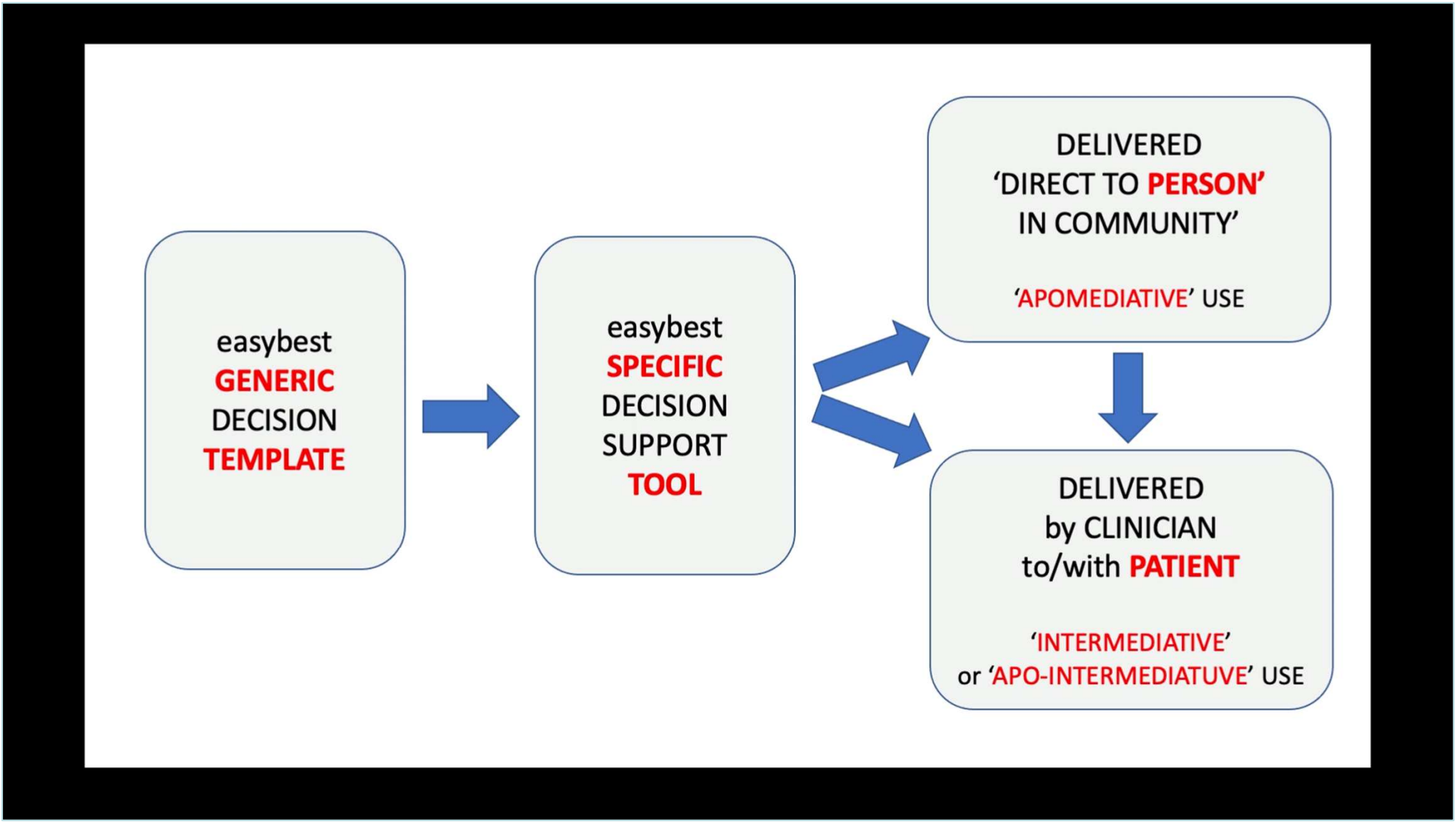
But, no need to be anxious– VBM won't happen !

- Formidable opposition is socio-psycho-ideo-logical
- Would expose the preference-sensitivity of the threshold-based **construction** of **most** diseases
- Would expose full extent of values heterogeneity and require its addressing, rather than avoiding/blanking by various means
- And politico-economic : current reward systems, in research particularly, but also practice, would be seriously threatened, especially by VBM supported by Bayesian Multicriteria Decision Analysis
- Requires neither empirical science nor guideline production of the orthodox sort, which are basically designed for 'population medicine'.

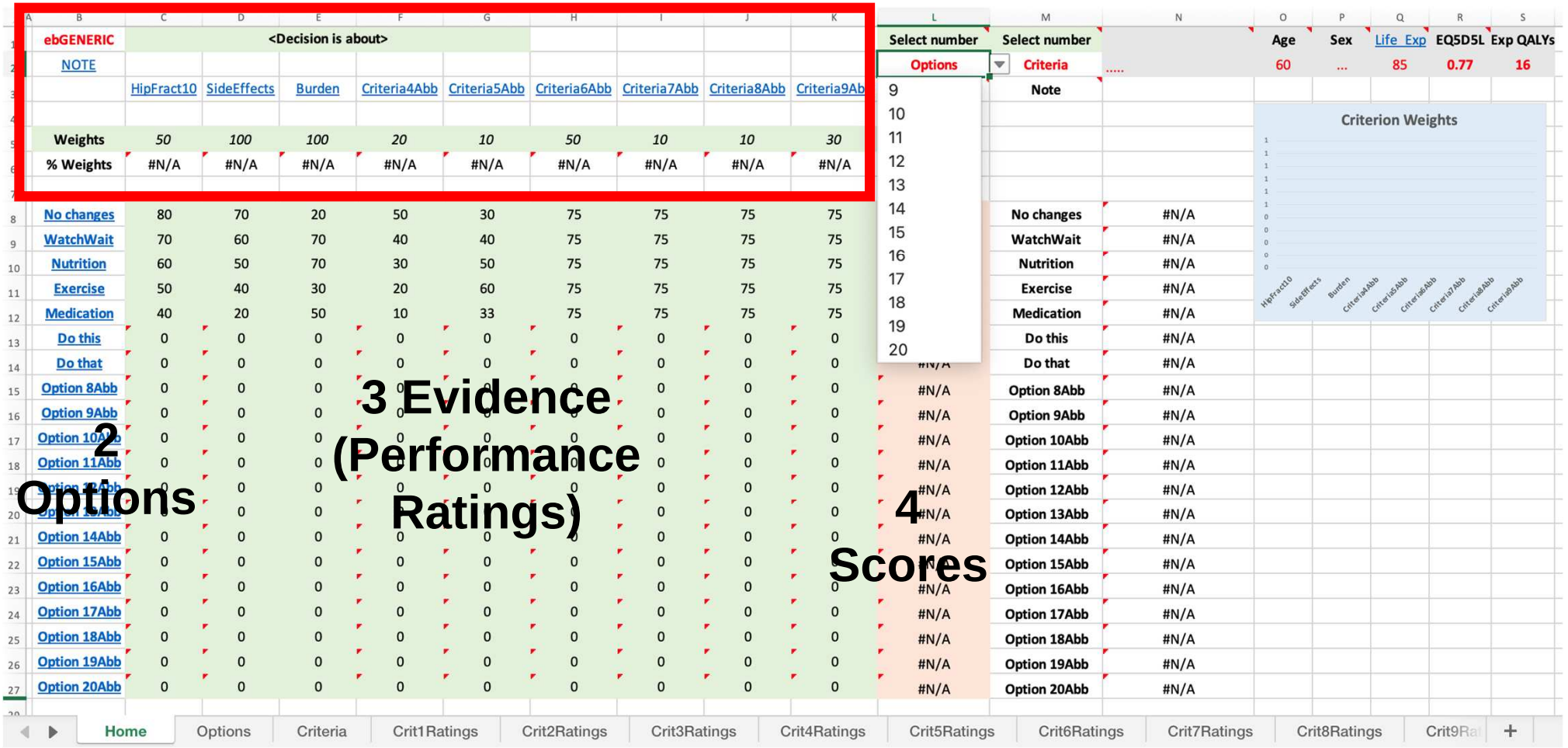
Why WHY not HOW ?

Why Why, not How?

- I’m often asked about why I focus on Why VBM, instead of showing How VBM could be practised and trialing it against OBM in a proper evaluation
- That is the OBM question!
- The answer is implicit in VBM itself: Objectives first, then Options to achieve them
- Unless you are convinced that the Objective, based on your values and preferences, is VBM, there’s no point in considering Options to deliver it or the evidence on them
- If you are convinced, we do offer one approach to HOW... referred to as easybest


easybest
GENERIC
DECISION
TEMPLATE
easybest
SPECIFIC
DECISION
SUPPORT
TOOL
DELIVERED
'DIRECT TO PERSON'
IN COMMUNITY'
'APOMEDIATIVE' USE
DELIVERED
by CLINICIAN
to/with PATIENT
'INTERMEDIATIVE'
or 'APO-INTERMEDIATUVE' USE

1. Objectives, Preferences
Criteria Importance Weightings



ebGENERIC	<Decision is about>								
NOTE									
	HipFract10	SideEffects	Burden	Criteria4Abb	Criteria5Abb	Criteria6Abb	Criteria7Abb	Criteria8Abb	Criteria9Ab
Weights	50	100	100	20	10	50	10	10	30
% Weights	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
No changes	80	70	20	50	30	75	75	75	75
WatchWait	70	60	70	40	40	75	75	75	75
Nutrition	60	50	70	30	50	75	75	75	75
Exercise	50	40	30	20	60	75	75	75	75
Medication	40	20	50	10	33	75	75	75	75
Do this	0	0	0	0	0	0	0	0	0
Do that	0	0	0	0	0	0	0	0	0
Option 8Abb	0	0	0	0	0	0	0	0	0
Option 9Abb	0	0	0	0	0	0	0	0	0
Option 10Abb	0	0	0	0	0	0	0	0	0
Option 11Abb	0	0	0	0	0	0	0	0	0
Option 12Abb	0	0	0	0	0	0	0	0	0
Option 13Abb	0	0	0	0	0	0	0	0	0
Option 14Abb	0	0	0	0	0	0	0	0	0
Option 15Abb	0	0	0	0	0	0	0	0	0
Option 16Abb	0	0	0	0	0	0	0	0	0
Option 17Abb	0	0	0	0	0	0	0	0	0
Option 18Abb	0	0	0	0	0	0	0	0	0
Option 19Abb	0	0	0	0	0	0	0	0	0
Option 20Abb	0	0	0	0	0	0	0	0	0

Select number	Select number		Age	Sex	Life_Exp	EQ5D5L	Exp QALYs
Options	Criteria	.....	60	...	85	0.77	16
	Note						
No changes	#N/A						
WatchWait	#N/A						
Nutrition	#N/A						
Exercise	#N/A						
Medication	#N/A						
Do this	#N/A						
Do that	#N/A						
Option 8Abb	#N/A						
Option 9Abb	#N/A						
Option 10Abb	#N/A						
Option 11Abb	#N/A						
Option 12Abb	#N/A						
Option 13Abb	#N/A						
Option 14Abb	#N/A						
Option 15Abb	#N/A						
Option 16Abb	#N/A						
Option 17Abb	#N/A						
Option 18Abb	#N/A						
Option 19Abb	#N/A						
Option 20Abb	#N/A						

9 10 11 12 13 14 15 16 17 18 19 20

Criterion Weights

HipFract10 SideEffects Burden Criteria4Abb Criteria5Abb Criteria6Abb Criteria7Abb Criteria8Abb Criteria9Abb

Home | Options | Criteria | Crit1Ratings | Crit2Ratings | Crit3Ratings | Crit4Ratings | Crit5Ratings | Crit6Ratings | Crit7Ratings | Crit8Ratings | Crit9Rat

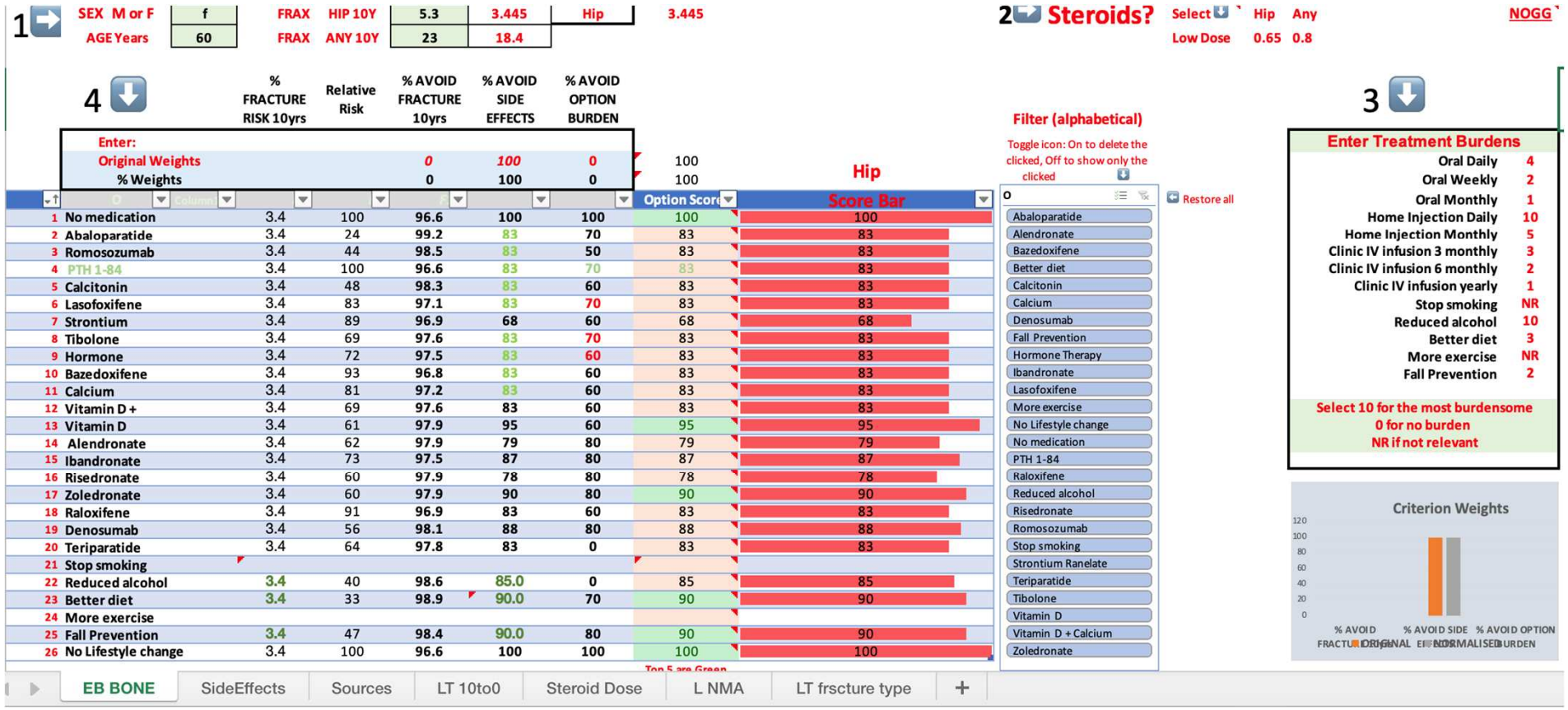
2 Options

3 Evidence (Performance Ratings)

4 Scores

VBM Sequence

bone health application



A comparative evaluation?

Since VBM and OBM are paradigms,
and paradigms are incommensurable,
trialing is out.

Choice between them is ultimately
a matter of preference

and many would **prefer** to deter us from
taking the less-travelled path

Appendix: ODOT papers without ”preference/s”

Brodersen J, Schwartz LM, Woloshin S. Overdiagnosis: how cancer screening can turn indolent pathology into illness. *APMIS*. 2014 122(8):683-9

Esserman LJ, Thompson IM, Reid B, et al. Addressing overdiagnosis and overtreatment in cancer: a prescription for change. *Lancet Oncol*. 2014 15(6): e234-42.

Brodersen J, Schwartz LM, Heneghan C, et al. Overdiagnosis: what it is and what it isn't. *BMJ Evid Based Med*. 2018 23(1):1-3.

Bell K, Doust J, Sanders S, et al. A novel methodological framework was described for detecting and quantifying overdiagnosis. *J Clin Epidemiol*. 2022 48: 146-159

Ryser MD, Lange J, Inoue LYT, et al. Estimation of Breast Cancer Overdiagnosis in a U.S. Breast Screening Cohort. *Ann Intern Med*. 2022175(4): 471-478

Vickers A, O'Brien F, Montorsi F, et al. . Current policies on early detection of prostate cancer create overdiagnosis and inequity with minimal benefit. *BMJ*. 2023 381: e071082.

Gard CC, Lange J, Miglioretti DL, et al.. Risk of cancer versus risk of cancer diagnosis? Accounting for diagnostic bias in predictions of breast cancer risk by race and ethnicity. *J Med Screen*. 2023 12: 969141323118002 8.