


Novel Multi-level Outcomes: Increasing the value of your trial

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Disclosures

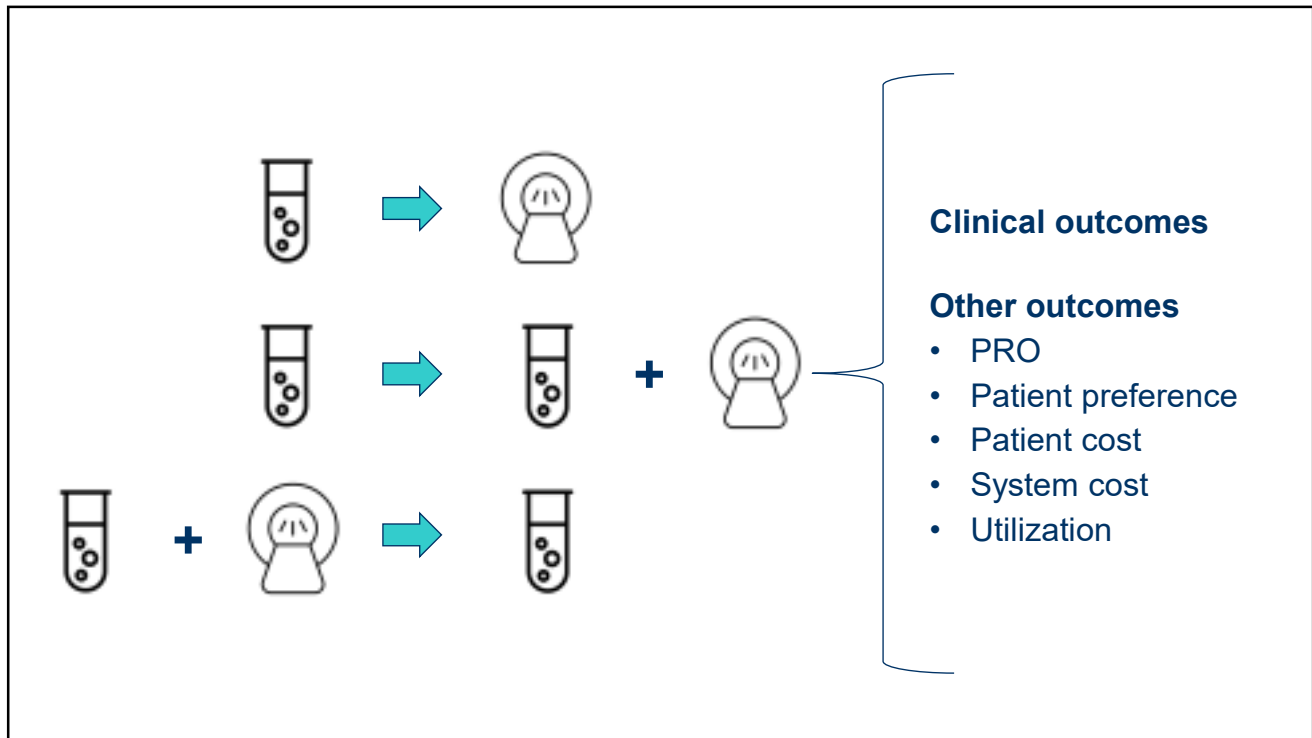
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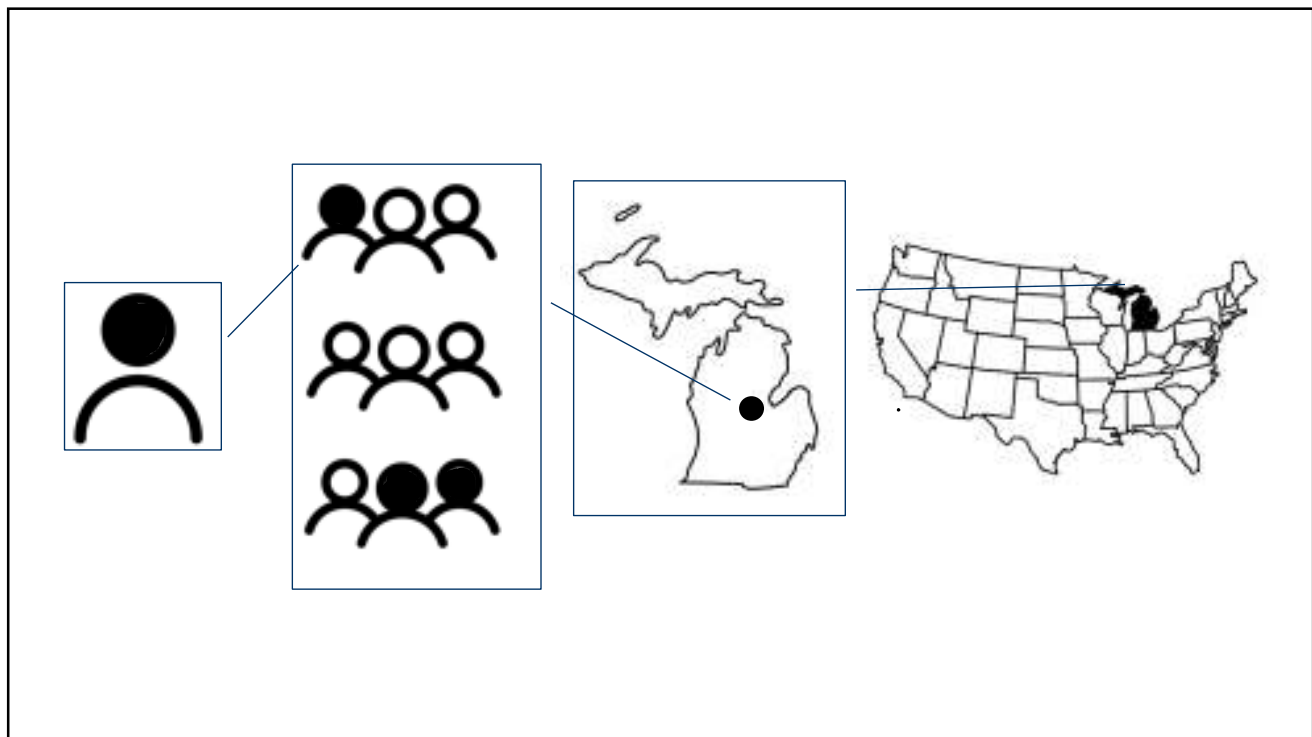
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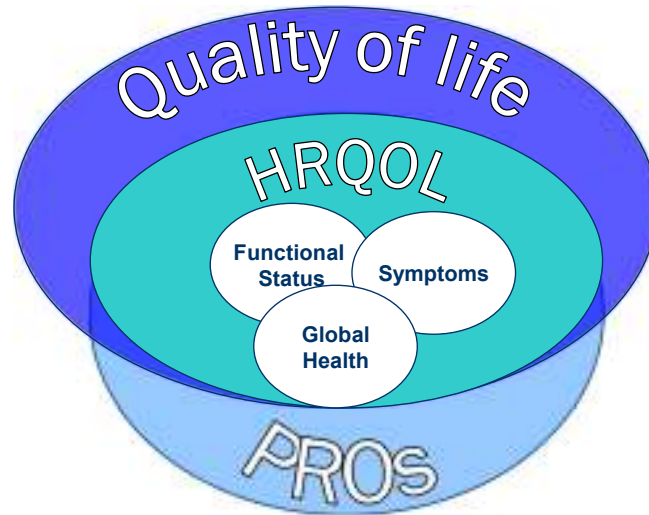
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What is health-related quality of life?

HRQoL focuses on the impact of disease, disability or disorder on one's wellbeing



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Why measure HRQOL?



Measure disease impact on an individual patient or groups of patients



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Why measure HRQOL?



Shared decision-making
Treatment choice in early-stage prostate ca
Prophylactic mastectomy in BRCA+



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HRQOL Measures: Disease-specific scales



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Selecting disease-specific measures

Assessing knee pain interventions:

PAIN: Multi-dimensional

- Severity (average pain vs. worst pain)
- Temporality (worst at night)
- Quality (dull vs. sharp)
- Use of pain medication

FUNCTION: Multi-dimensional

- Physical
- Emotional



GLOBAL ASSESSMENT OF IMPROVEMENT

Initiative on Methods, Measurements and Pain Assessment in Clinical Trials (IMMPACT)

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Selecting disease-specific measures

	AKSS	WOMAC	HSS	OKS
Pain severity	1	5 (diff activities)	2 (rest, walking)	2 (aver, standing)
Pain med	-	-	-	-
Pain quality	-	-	-	-
Temporality of pain	1 (occ/cont)	1 (at night)	-	1 (at night)
Physical function	1 (walk/stand)	4 (walk, climb, sit, stand)	1 (walk)	3 (nl work, distance before severe, stand)
Emotional function				2 (troubled at night, unbearable pain)

AKSS=American Knee Society Score

WOMAC=Western Ontario and McMaster Univ OA Index

HSS=Hospital for Special Surgery Knee Score

OKS=Oxford Knee Score



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Generic Health Status

Measures the broad scope of HRQOL

Measures domains important to all using multiple scales

Can be used in a wide variety of settings, areas, diseases, populations

Allow broad comparison of relative impact of various health care programs

Mosquito control vs HIV medication vs organ transplantation

May be insufficiently sensitive to changes in a specific condition

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Generic Measures



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HRQOL: Adjusting for quality of a life-year

Cost-effectiveness studies need to quality adjust for number of years spent in one health state vs another.

Health utility: preference for a specific health related outcome

Measure **directly** using standard gamble or time trade-off

“Would you take the magic pill if the chance of blindness were 1 % and the chance of perfect vision were 99 %, or would you prefer to remain in your present state of health wearing glasses (contacts)?”

“Instead of spending 30 years in your present state of health wearing glasses (contacts), you can trade 5 years and spend 25 years with perfect vision. Would you accept?”

Measure **indirectly** by adjusting generic instruments (SF-36, PROMIS-10, EQ5D)

Summarized as a single number representing the continuum between death (0) and perfect health (1)

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HRQOL Utilities in temporary health states

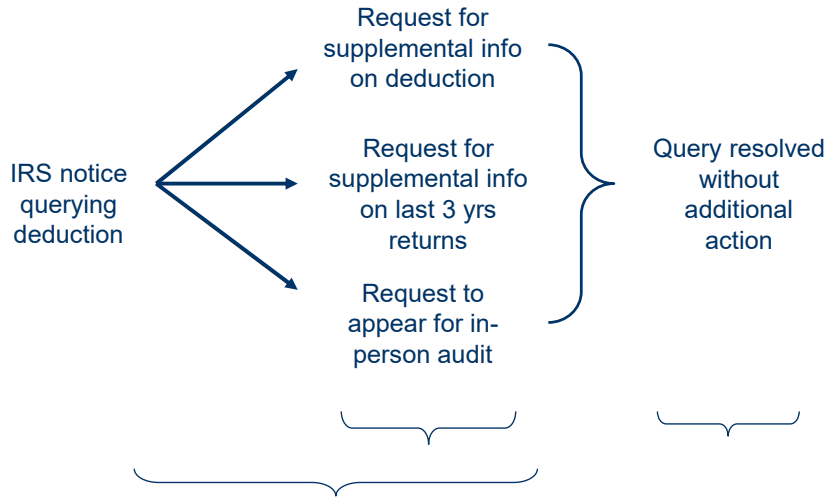
Standard utilities measure long-term or permanent states

Many health states are temporary (<1 year)

- Infection, vaccination, short term medications and procedures, screening and diagnostic tests
- Health state duration influences patient preference

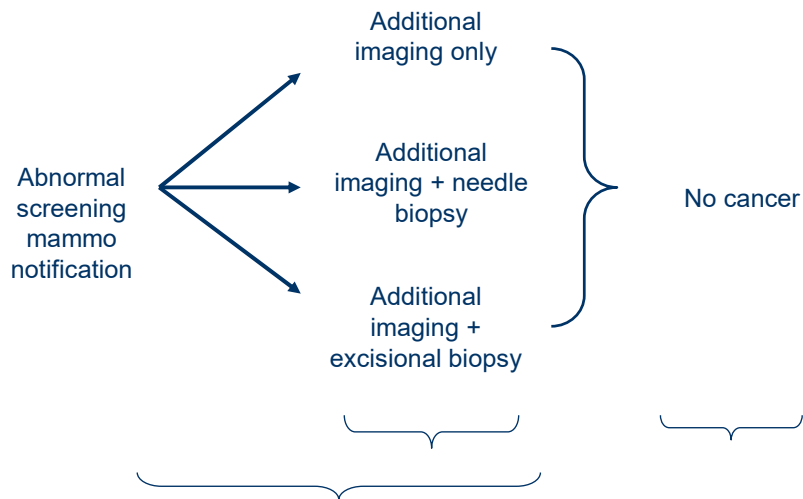
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Temporary health states: example



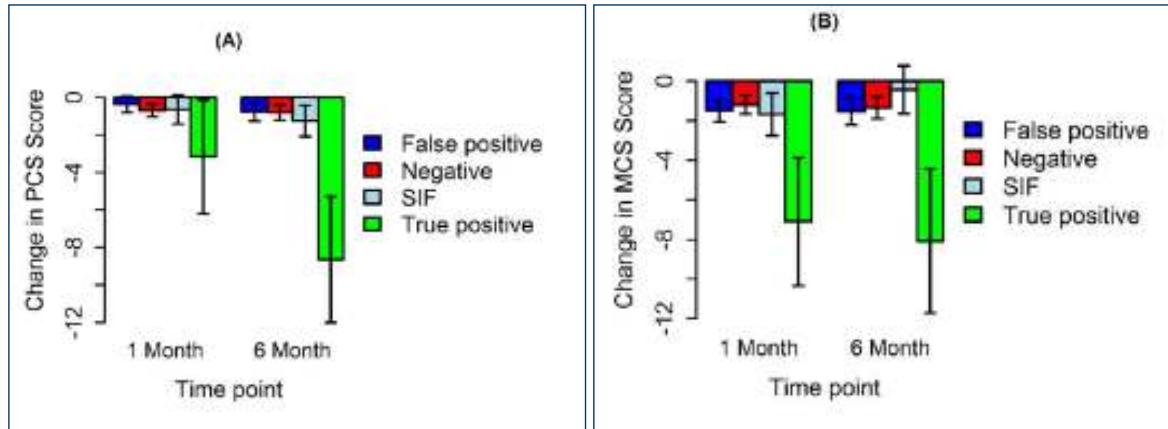
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Temporary health states: example



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HRQOL: NLST



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HRQOL: Temporary Utilities Index

7 items

Physical: pain of prep, pain of test, role function after test

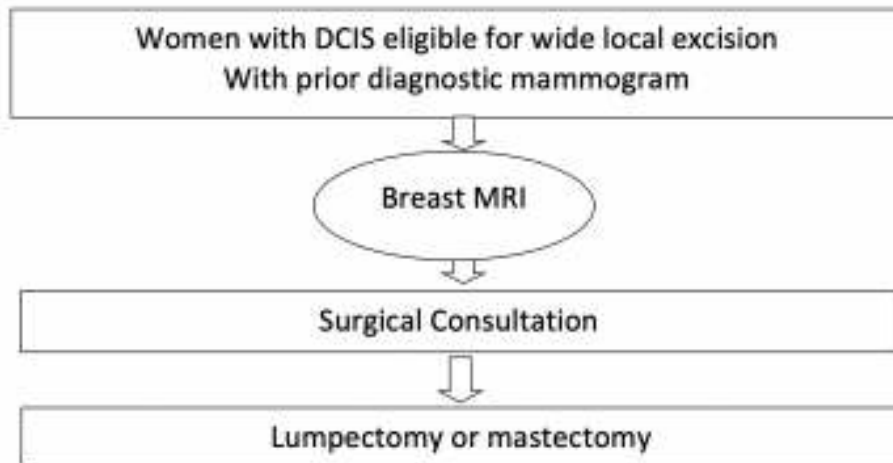
Mental: fear about test (before), fear during test, embarrassment during test, role function after test

Applicable to screening tests, unlike WTO



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E4112



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E4112: TMI → Higher score=less distress

	Mammography Mean (SD)	Breast MRI Mean (SD)	P-value ¹
Summary Utility scores (0-100)	90.0 (8.7)	85.9 (10.6)	<0.0001
Component scores (0-100 scale)			
Before (pain, anxiety)	92.3 (12.0)	82.0 (16.4)	<0.0001
During (pain, embarrassment, anxiety)	84.5 (12.5)	82.7 (13.8)	0.06
After (mental, physical impact)	96.1 (9.7)	94.8 (11.8)	0.13



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Prostate MRI vs biopsy



TMI Results	MRI (n = 55)	Biopsy (n = 55)	P Value
Domain-level scores (1-5 scale)*			
Pain before	1.1 (95% CI: 1-1.2)	1.4 (95% CI: 1.2-1.5)	.003 [†]
Fear or anxiety before	1.4 (95% CI: 1.2-1.5)	2.1 (95% CI: 1.9-2.3)	<.0001 [†]
Pain during	1.3 (95% CI: 1.1-1.5)	2.6 (95% CI: 2.4-2.8)	<.0001 [†]
Embarrassment	1.0 (95% CI: 1-1.1)	1.6 (95% CI: 1.4-1.8)	<.0001 [†]
Fear or anxiety during	1.3 (95% CI: 1.1-1.4)	1.8 (95% CI: 1.6-2.1)	<.0001 [†]
Mental impact after	1.1 (95% CI: 1-1.2)	1.1 (95% CI: 1-1.3)	.725
Physical impact after	1.1 (95% CI: 1-1.2)	1.4 (95% CI: 1.2-1.7)	.022
Summary utility score (0-1 scale) [‡]	0.95 (95% CI: 0.94-0.97)	0.82 (95% CI: 0.79-0.85)	<.0001 [‡]

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Eliciting preferences: Conjoint analysis

Which of the following ice-creams would you buy?

200g Frosty Vanilla \$2.90	200g Strawberry Galore \$2.90
150g Mango Ice \$3.50	None of these

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Which imaging center will you choose?



4.5* reviews \$400	2.5* reviews \$50
4.5* reviews 87% accurate \$50	4.5* reviews 96% accurate \$50-3500
96% accurate \$50-3500	2.5* reviews \$50

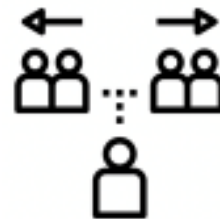
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HRQOL: Making PROs actionable

FACT-G: GP5 "I am bothered by side effects of treatment"



GP5 ~ CTCAE



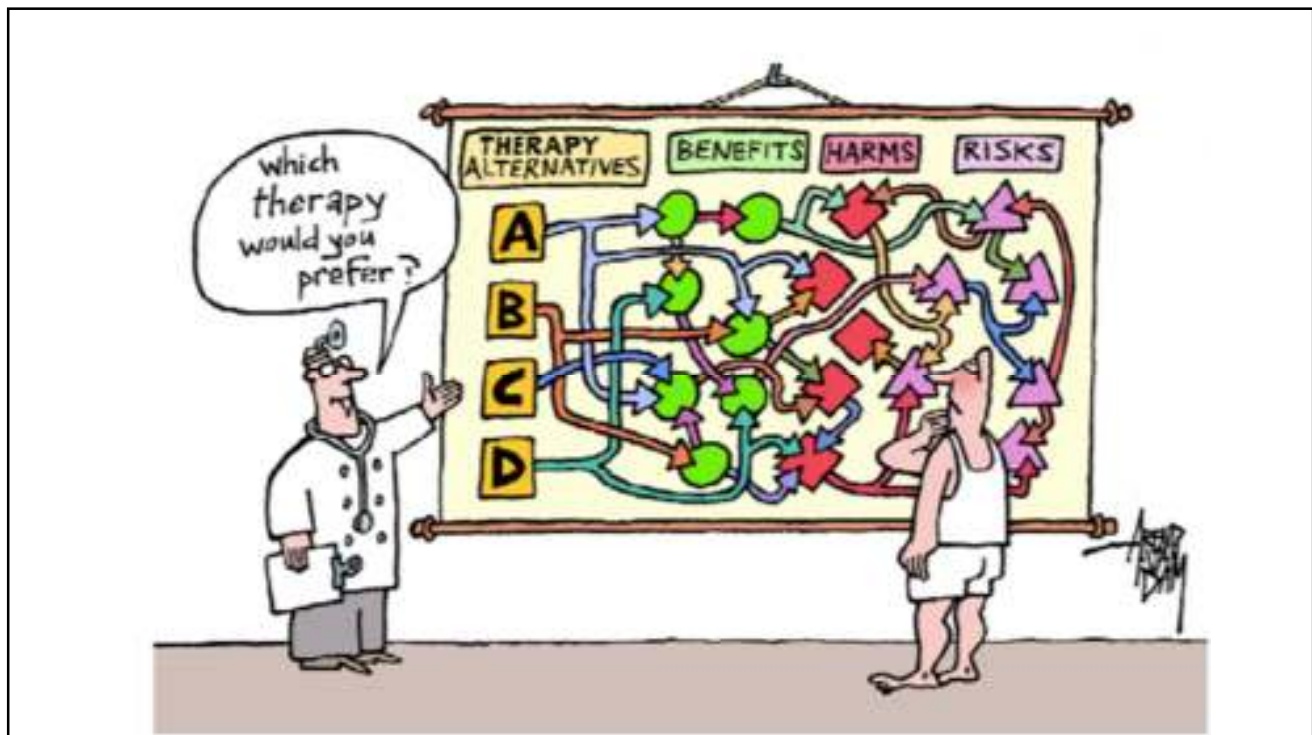
Wagner et al, 2011

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HRQOL: Selecting a measure

Study Goal	Possible measures
Assess diagnostic imaging test or imaging-based treatment efficacy	Disease-specific measure, wait trade-off, toxicity symptoms, global health, health utilities
Minimize disease symptoms	Disease-specific measure, toxicity symptoms, global health, functional status, health utilities
Cure disease	Survival, health utilities, toxicity symptoms, functional status
Palliate / Prolong survival	Survival, functional status, disease-specific measure, global rating, health utilities
Characterize illness burden in a population	Generic health status profile
Characterize illness burden in a specific patient	Generic health status profile, domain-specific measures
Predict outcomes	Baseline HRQOL
CEA/CUA	Health Utilities

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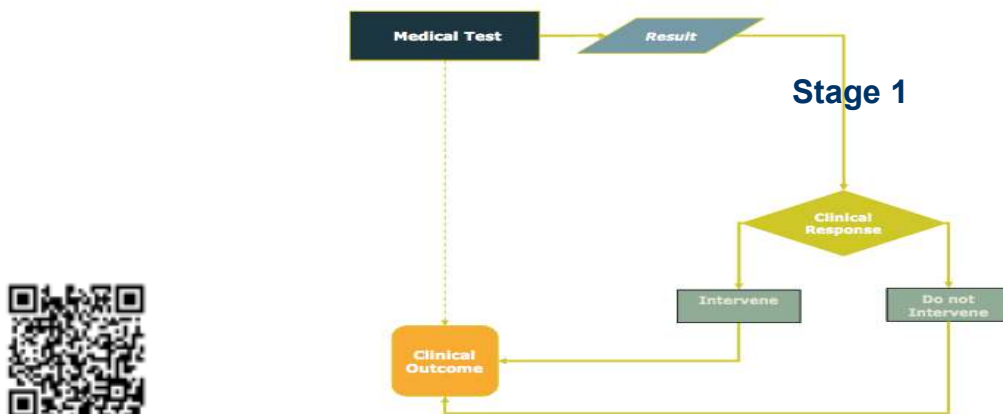
The perfect test for breast cancer



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Effect on Patient Outcomes

EX: Breast cancer

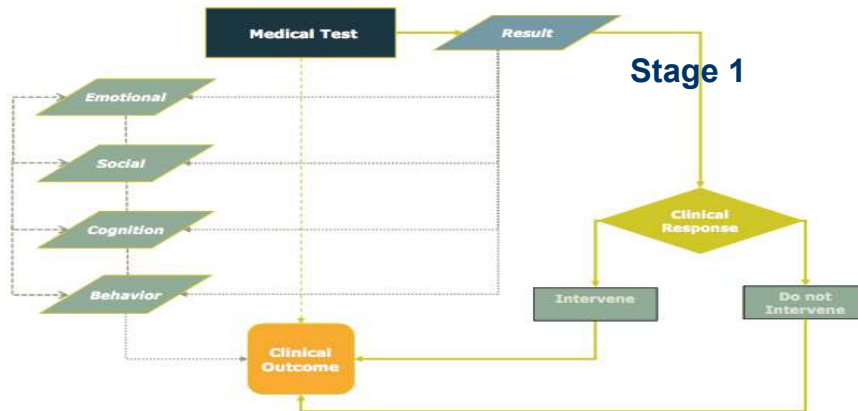


P.M. Bossuyt and K. McCaffery, MDM, 2009

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Effect on Patient Outcomes

EX: Breast cancer

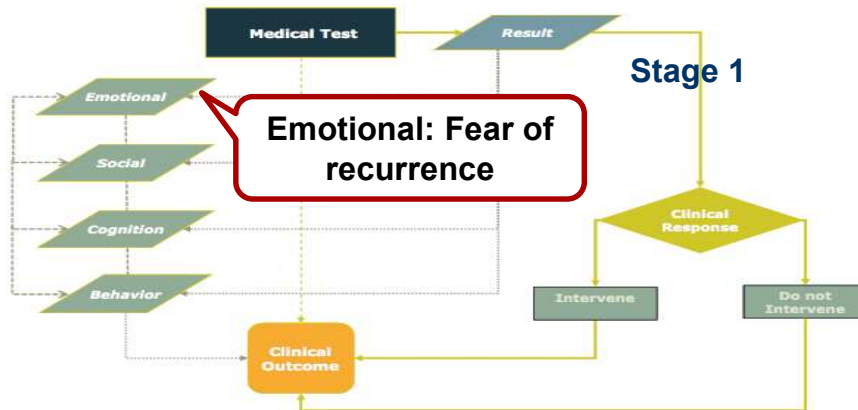


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Effect on Patient Outcomes

EX: Breast cancer

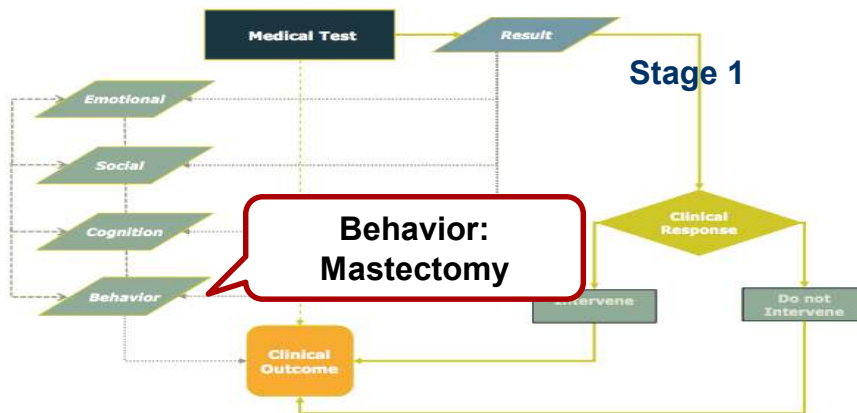


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Effect on Patient Outcomes

EX: Breast cancer

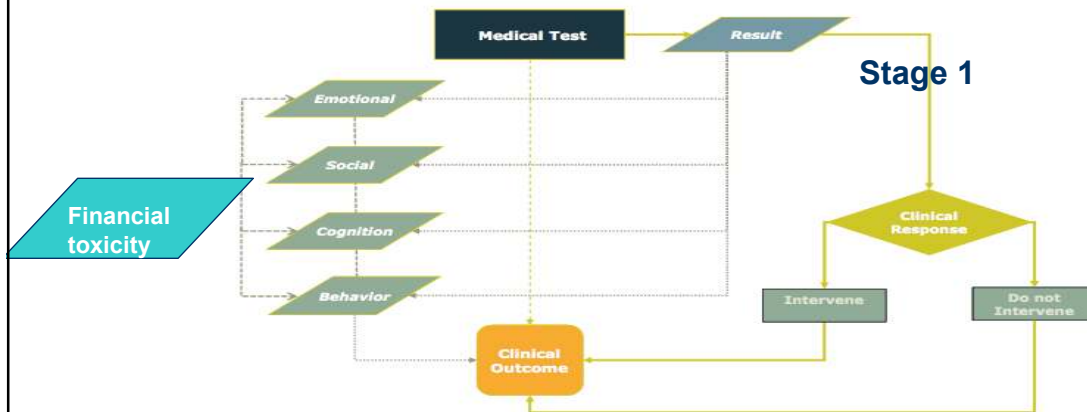


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Effect on Patient Outcomes

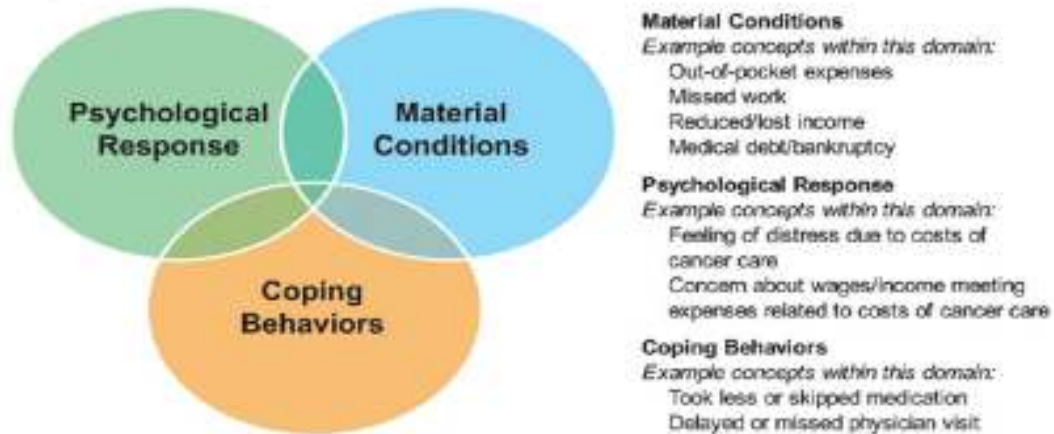
EX: Breast cancer



P.M. Bossuyt and K. McCaffery, MDM, 2009

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HRQOL: Financial toxicity as AE of care



Aguiar. JNCI 2017

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Financial burden in cancer survivors



High out of pocket costs (28% survivors v 16%)
Productivity loss / **unemployment** (missed 22.3 d more)



Asset depletion and **medical debt**
33-88% used savings for medical expenses
2-34% borrowed to pay for care
Bankruptcy (1.7% of cancer survivors within 5 years after dx)



Financial stress, distress or worry
22.5% - 64% reported worry about paying bills
28.2% worry about rent or mortgage
22.7% worry about food

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PRO Consequences of financial burden

Treatment adherence: Higher copays → increased non-adherence
Imatinib for CML; AI for ER/PR+ early stage breast cancer

QOL: Increased reported symptom burden, pain if <12 months of
financial reserves in lung and colorectal cancer

Poorer physical health and mental health; lower QOL

Lathan et al, 2016

Debt and bankruptcy

Survival → WA SEER increased mortality with bankruptcy

aHR 2.1 prostate, aHR 2.5 colon

Ramsey et al, 2015

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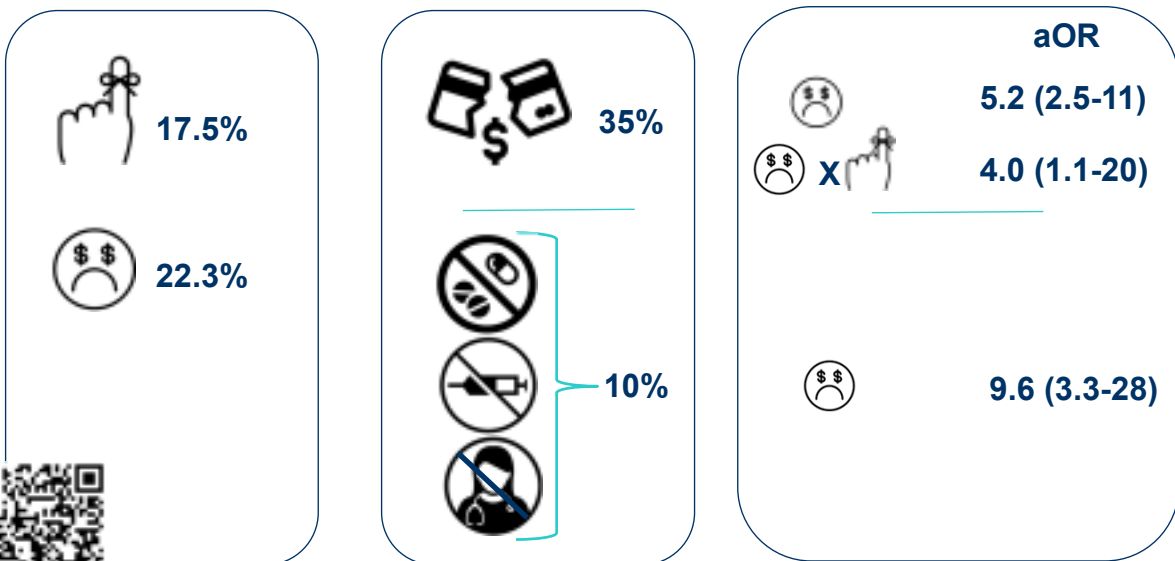
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Ramsey et al, 2015

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Financial burden of advanced imaging (FAIR)



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Measuring financial distress and impact

Worry: COmprehensive Score for financial Toxicity (COST)

Care non-adherence (foregone visits, tests, tx/less med dose/script non-filling)

Material resource modification (debt, savings expenditure)

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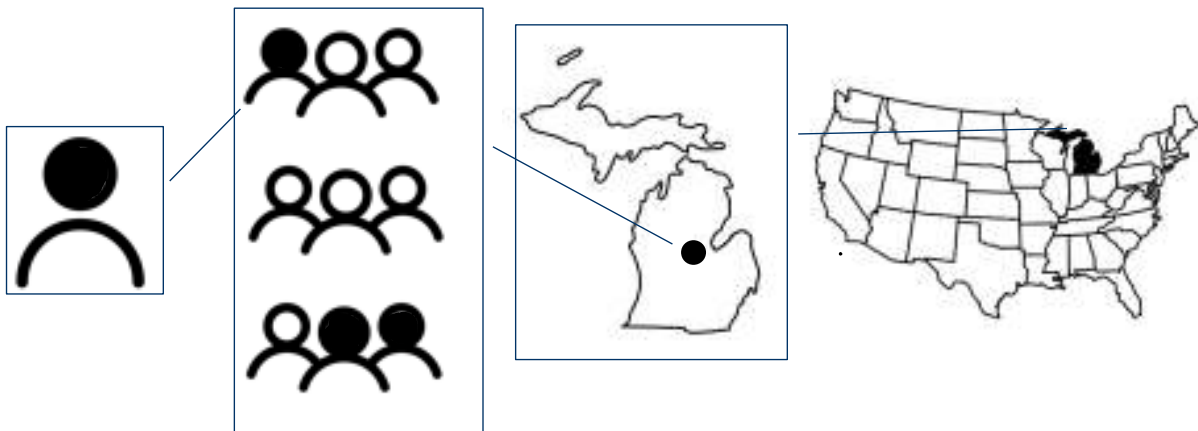
Health equity: measuring what matters

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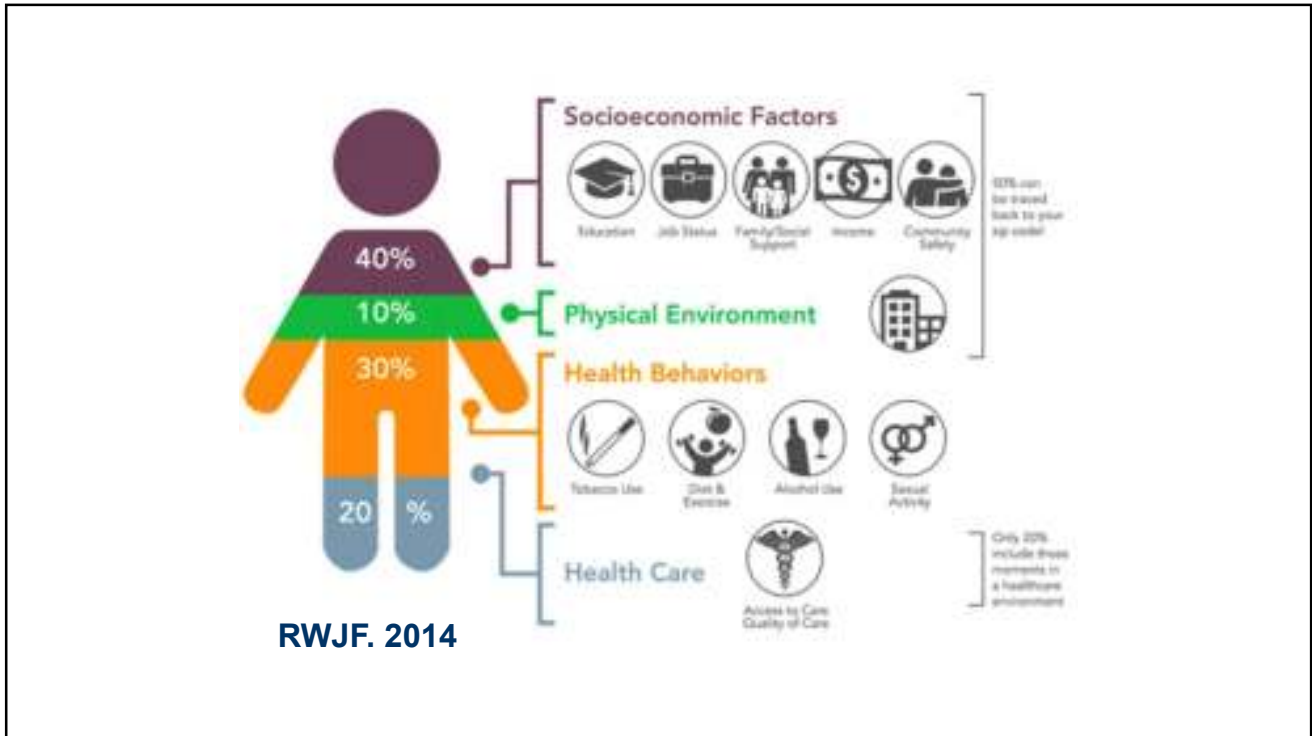
E4112

Independent Variables	T0 Mental Health [Baseline T score]		T2 Mental Health [Change from baseline]	
	Est (SE) ¹	p-value	Est (SE) ¹	p-value
Age (per 5-year increment)	0.15 (0.24)	0.51	-0.50 (0.26)	0.06
Race:				
White	Ref	Ref	Ref	Ref
Black/African American	0.86 (1.18)	0.47	-5.35 (1.33)	<0.001 ***
Other	1.05 (1.52)	0.49	-3.33 (1.74)	0.06
Surgery received				
>1 surgery	--	--	Ref	Ref
1 WLE	--	--	1.63 (1.04)	0.12
Mastectomy	--	--	4.37 (1.68)	0.01 *
Concordance between T1 surgery preference and surgery received	--	--	6.92 (2.67)	0.01 *
ASC cancer worry subscale	-1.67 (0.50)	0.001 **	-1.20 (0.60)	0.046 *

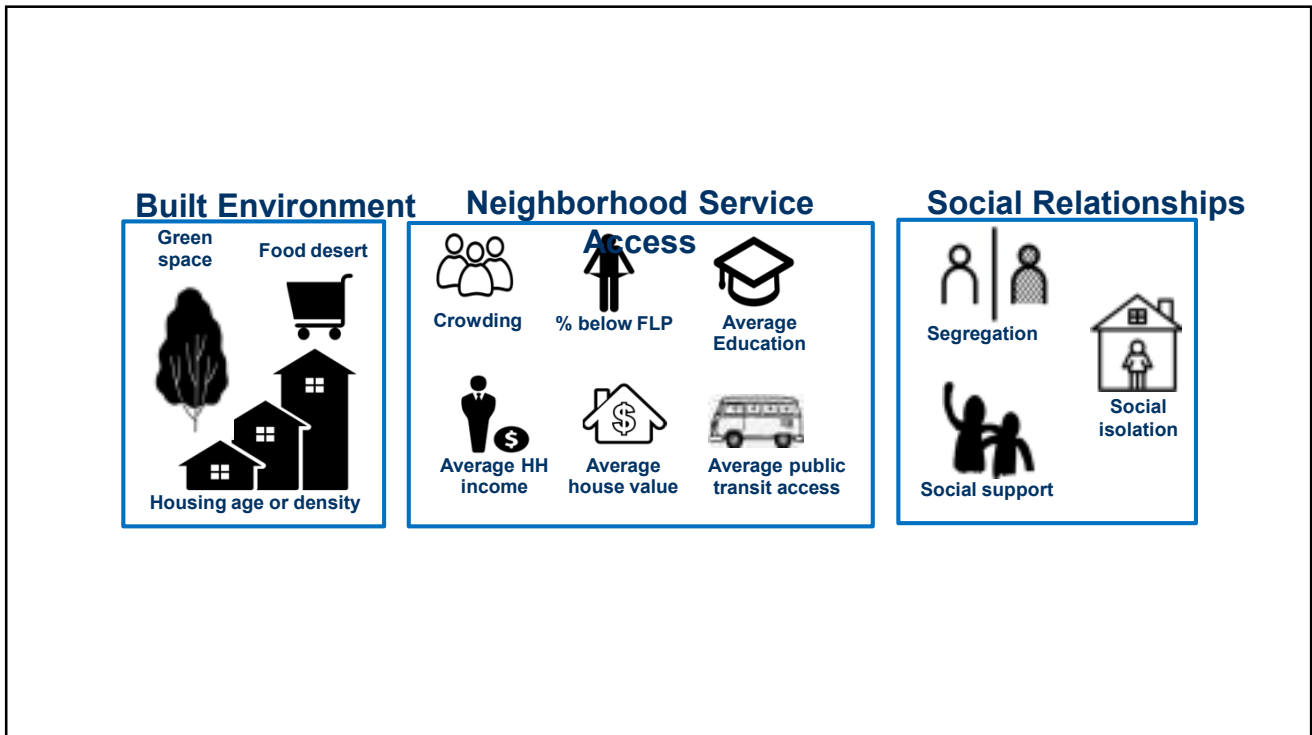
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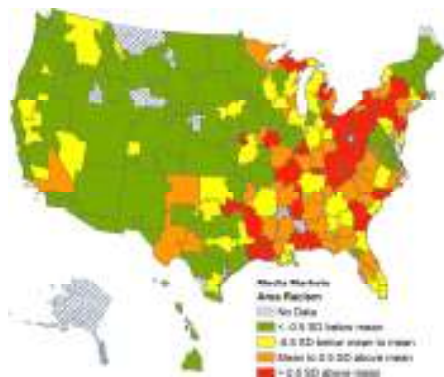
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Association of structural racism using residential segregation measures on clinical and biological outcomes



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Interpersonal racism



Racial animus

Discriminative variable ^a	Health service use model ^b				Multi-stage models ^c			
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Mean discrimination score	Base outcome		1.23	0.99-1.54	1.28	1.05-1.55	0.85	0.54-0.86
Individual discrimination items	"treated with less courtesy"	Base outcome	1.09	0.89-1.26	1.12	0.95-1.31	0.98	0.70-0.91
	"receive poorer service"	Base outcome	1.09	0.88-1.41	1.13	0.88-1.45	0.78	0.67-0.93
	"you are not smart"	Base outcome	1.18	0.96-1.46	1.11	1.08-1.20	0.81	0.71-0.92
	"people are afraid of you"	Base outcome	1.15	0.91-1.47	1.32	1.09-1.60	0.88	0.66-0.93
	"discarded or ignored"	Base outcome	1.19	0.98-1.39	1.23	0.99-1.50	0.71	0.39-0.89

Experience of discrimination

Chae 2015, Dekhordy 2009

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Physiology of scarcity



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Take-home points

- No perfect PRO measure
- Choice driven by research question
- Independent variables at the community, state and national level can influence clinical and PRO outcomes
- Social determinants of health key component

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