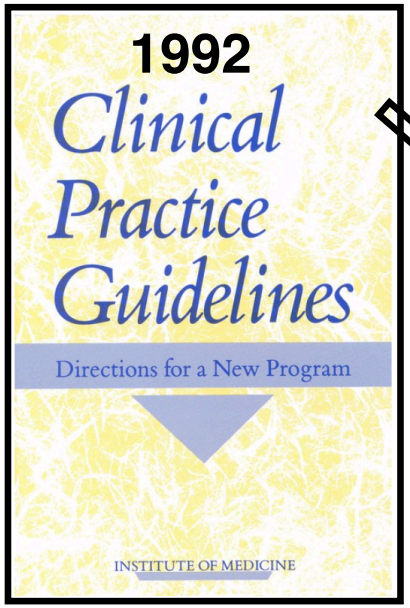
An evidence-based look
(as much as possible)
at Clinical Practice Guidelines (CPGs)

James McCormack, BSc(Pharm), Pharm D
Professor, Faculty of Pharmaceutical Sciences, UBC



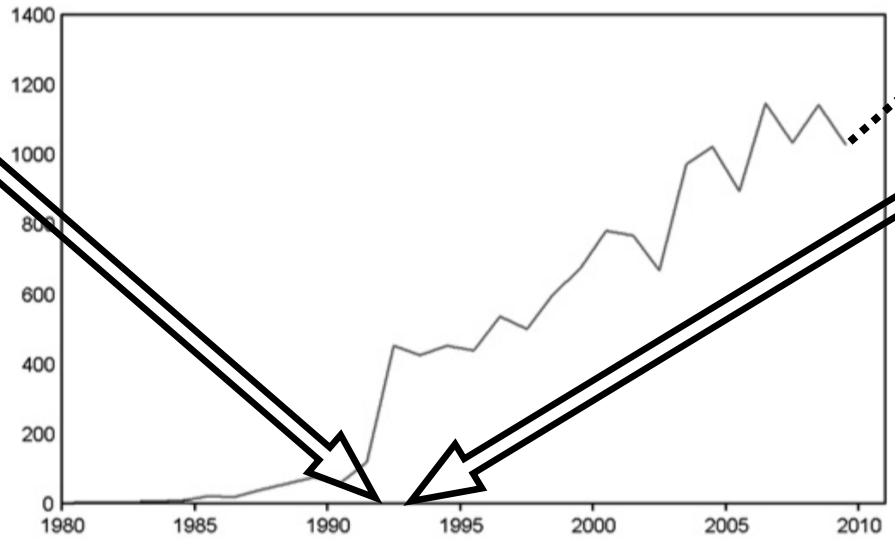
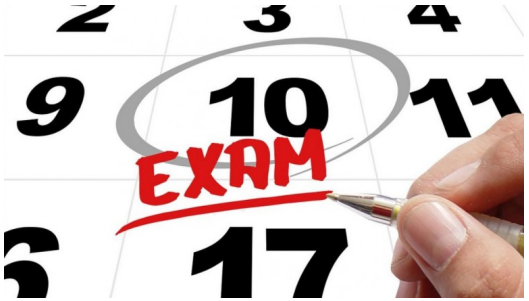


Figure 1 Number of guidelines in PubMed.

2018
~~1500

1993
Cochrane

Handout - https://therapeuticseducation.org/handouts


9
10
11
EXAM
17


FOLLOW THE
GUIDELINES


FOLLOW THE
GUIDELIINES


KEEP
CALM
AND
FOLLOW
GUIDELINES


FOLLOW THE
GUIDELINES

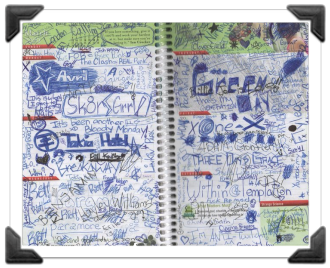

Guidelines


FOLLOW
THE GUIDELINES

Using Guidelines

not all good and not all bad

The (my) Agenda



Describe the issue/problem of CPGs/chronic disease state guidelines

Specifically the evidence around:

- How evidence-based are they?
- Who writes/sponsors them?
- How well do they incorporate patient values/preferences?

The “magnitudinous” problem

Legal aspects

Suggest some ideas for going forward

Show examples of a some well-done CPGs

Hear from you

What is a Clinical Practice Guideline (CPG)?

The Institute of Medicine definition:

"…statements that include recommendations, intended to optimize patient care, that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options”

1998-2018

The Number of Guidelines

Diseases/conditions - 2,983

Treatments/interventions - 7,364

Spectrum of Decisions

Immediate life-threatening issues or very “technical” work - surgery, dispensing etc - YES

Guidelines, even policies, are likely very useful

Symptom treatment (e.g. migraines, pneumonia) - SORT OF

Each person is an experiment - just need to know what has the potential to work and the harm/cost/convenience

Risk factor interventions (e.g. lipids, glucose, HTN) - NO

At least not what CPGs are now

Guidelines would be awesome if they…

Were developed primarily by, and definitely for, the people that ultimately end up using them

Were a credible synopsis of the best available evidence (obtained via a systematic review) presented in a way that clinicians could easily access and interpret

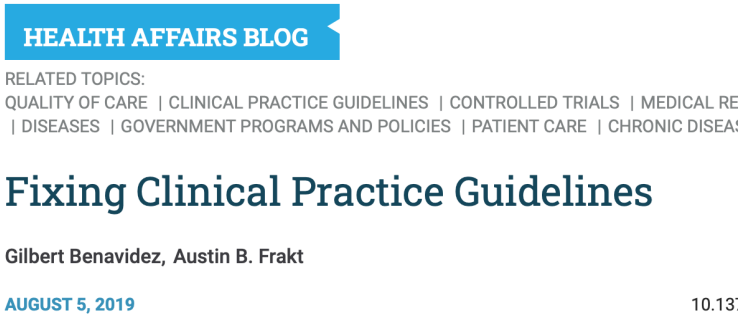
Allowed patient values and preferences to be taken into account

Wrong guidelines: why and how often they occur

Primiano Iannone,[1] Nicola Montano,[2] Monica Minardi,[3] James Doyle,[3] Paolo Cavagnaro,[4] Antonino Cartabellotta[5]

"Unfortunately, depending on how their reliability is measured, up to 50% of guidelines can be considered untrustworthy. This carries serious consequences for patients' safety, resource use and health economics burden."

EBM 2017;22:1-3



HEALTH AFFAIRS BLOG

RELATED TOPICS:
QUALITY OF CARE | CLINICAL PRACTICE GUIDELINES | CONTROLLED TRIALS | MEDICAL RE
| DISEASES | GOVERNMENT PROGRAMS AND POLICIES | PATIENT CARE | CHRONIC DISEA

Fixing Clinical Practice Guidelines

Gilbert Benavidez, Austin B. Frakt

AUGUST 5, 2019 10.13

Three decades later, we still haven't figured out how to reliably produce high-quality guidelines

Two core issues that lead to a host of problems

1) a lack of centralized authority to coordinate, vet, approve, and catalog guidelines

   there is an absence of a universal methodology to create guidelines—every professional organization promulgating guidelines today generally decides freely which, if any, framework they will use to construct guidelines

   Enforce A Rigorous, Universal Methodology For Creating Guidelines

CARDIOVASCULAR PERSPECTIVE

Professional Societies Should Abstain From Authorship of Guidelines and Disease Definition Statements

Blogs > Revolution and Revelation

When Did Guidelines Become Holy Writ?

— Milton Packer wonders whether our opinions should be worshipped

VIEWPOINT

Evidence vs Consensus in Clinical Practice Guidelines

Benjamin Djulbegovic, MD, PhD
City of Hope, Duarte, California.

Gordon Guyatt, MD, MS
McMaster University, Hamilton, Ontario, Canada.

All clinical practice guideline recommendations, whether the available evidence is considered as being of high quality or very low quality, require both:

a judicious consideration of the relevant evidence and consensus from the panel regarding both the interpretation of the evidence and,

the tradeoff between the benefit vs the harm or burden of the recommended health intervention

"guideline panels are challenged with evaluating the evidence regarding patients' values and preferences and deciding whether all or almost all fully informed individuals would make the same choice - or if not, what would the majority choose?"

JAMA July 19, 2019

How to appraise CPGs

Appraisal Tools for Clinical Practice Guidelines: A Systematic Review **2013**

“the most comprehensively validated appraisal tool is the AGREE II instrument

PLoS ONE 8(12): e82915. doi:10.1371/journal.pone.0082915

Appraisal of Guidelines for Research and Evaluation (AGREE) II

DOMAIN 1. SCOPE AND PURPOSE

DOMAIN 2. STAKEHOLDER INVOLVEMENT

DOMAIN 3. RIGOUR OF DEVELOPMENT

DOMAIN 4. CLARITY OF PRESENTATION

DOMAIN 5. APPLICABILITY

DOMAIN 6. EDITORIAL INDEPENDENCE

OVERALL GUIDELINE ASSESSMENT

Factors Associated With High-Quality Guidelines for the Pharmacologic Management of Chronic Diseases in Primary Care

A Systematic Review

Caroline de Godoi Rezende Costa Molino, MS[1]; Nathalia Celini Leite-Santos, BS[1]; Franciele Cordeiro Gabriel, MS[1]; et al

» Author Affiliations

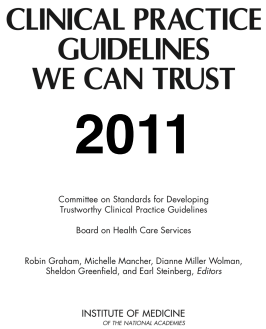
JAMA Intern Med. 2019;179(4):553-560. doi:10.1001/jamainternmed.2018.7529

Heart disease
Lung disease
Diabetes
Osteoporosis
Depression
Osteoarthritis
Dementia
GERD
BPH

AGREE II

421 CPGs (July 2011-August 2017) for the management of common non-communicable disease in primary care

24% were rated as high quality
lowest median domain scores
applicability (22%) and rigour of development (33%)



"AGREE Tool inadequately reflects the full range of quality CPG development" - they focus on development rather than quality of evidence and strength of recommendations

8 STANDARDS

1. Establishing transparency
2. Management of conflict of interest
3. Guideline development group composition
4. Clinical practice guideline–systematic review intersection
5. Establishing evidence foundations for and rating strength of recommendations
6. Standardized articulation of recommendations
7. External review
8. Updating

GRADE

Grading of Recommendations
Assessment, Development and Evaluation

QUALITY

Table 5.1: Quality of Evidence Grades	
Grade	Definition
High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
Very Low	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

GRADE

Grading of Recommendations
Assessment, Development and Evaluation

RECOMMENDATIONS (for or against)

Table 6.1. Implications of strong and weak recommendations for different users of guidelines		
	Strong Recommendation	Weak Recommendation
For patients	Most individuals in this situation would want the recommended course of action and only a small proportion would not.	The majority of individuals in this situation would want the suggested course of action, but many would not.
For clinicians	Most individuals should receive the recommended course of action. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.	Recognize that different choices will be appropriate for different patients, and that you must help each patient arrive at a management decision consistent with her or his values and preferences. Decision aids may well be useful helping individuals making decisions consistent with their values and preferences. Clinicians should expect to spend more time with patients when working towards a decision.

"A strong recommendation is one for which the guideline panel is confident the desirable effects of an intervention outweigh its undesirable effects"

When I use a word, it means just what I choose it to mean—neither more nor less.

Table 6.1. Implications of strong and weak recommendations for different users of guidelines		
	Strong Recommendation	Weak Recommendation
For patients	Most individuals in this situation would want the recommended course of action and only a small proportion would not.	The majority of individuals in this situation would want the suggested course of action, but many would not.

SOME DEFINITIONS

Most - means more than half (51-99%)

Majority - means more than half (51-99%)

Many - a large but indefinite number, but also the majority

Most is more than many

GRADE

Grading of Recommendations Assessment, Development and Evaluation

Table 6.4. Suggested representations of quality of evidence and strength of recommendations		
Quality of Evidence	**Symbol**	**Letter** (varies)
High	⊕⊕⊕⊕	A
Moderate	⊕⊕⊕◯	B
Low	⊕⊕◯◯	C
Very low	⊕◯◯◯	D
Strength of Recommendation	Symbol	Number
Strong for an intervention	↑↑	1
Weak for an intervention	↑?	2
Weak against an intervention	↓?	2
Strong against an intervention	↓↓	1

COMPARISON OF BENEFITS AND HARMS

For the elderly - about 65 years and older

No thyroid hormones	No important difference	Thyroid hormones

After 1 year		**EQ-5D score: -0.59-1 (High better)**		**Evidence quality**	
General quality of life	0.85	No important difference	0.83	★★★★ High	More
		Mean score: 0-100 (Low better)			
Thyroid-related symptoms	16.7	No important difference	16.5	★★★★ High	More
Fatigue / tiredness	28.6	No important difference	29.0	★★★★ High	More
		Mean score: 0-21 (Low better)			
Depressive symptoms	3.3	No important difference	3.6	★★★★ High	More
After 1.5 years		**Mean score: 0-infinity (High better)**			
Cognitive function	27.1	No important difference	28.1	★★★★ High	More
After 2 years		**Events per 1000 people**			
Mortality ⚠	14	No important difference	27	★★☆☆ Low	More
Cardiovascular events ⚠	54	No important difference	48	★★☆☆ Low	More
		Mean score: 0-100 (Low better)			
Side effects	10.3	No important difference	10.9	★★★☆ Moderate	More

See all outcomes MAGIC app | See patient decision aids MAGIC app

For younger people (such as 65 and younger)

No thyroid hormones	No important difference	Thyroid hormones

After 1 year		**EQ-5D score: -0.59-1 (High better)**		**Evidence quality**	
General quality of life	0.85	No important difference	0.82	★★★☆ Moderate	More
		Mean score: 0-100 (Low better)			
Thyroid-related symptoms	16.7	No important difference	16.4	★★★★ High	More
Fatigue / tiredness	28.6	No important difference	29.0	★★★☆ Moderate	More
		Mean score: 0-21 (Low better)			
Depressive symptoms	3.3	No important difference	3.6	★★★★ High	More
After 1.5 years		**Mean score: 0-infinity (High better)**			
Cognitive function	27.1	No important difference	29.7	★★☆☆ Low	More
After 2 years		**Events per 1000 people**			
Mortality	14	No important difference	27	★☆☆☆ Very low	More
Cardiovascular events	54	No important difference	48	★☆☆☆ Very low	More
		Mean score: 0-100 (Low better)			
Side effects	10.3	No important difference	10.9	★★☆☆ Low	More

See all outcomes MAGIC app | See patient decision aids MAGIC app

What evidence is behind CPG recommendations?

Typically “evidence-based” guideline recommendations are not based on “solid” evidence

Scientific Evidence Underlying the ACC/AHA Clinical Practice Guidelines

Pierluigi Tricoci; Joseph M. Allen; Judith M. Kramer; et al.

JAMA. 2009;301(8):831-841 (doi:10.1001/jama.2009.205)

Analysis of Overall Level of Evidence Behind Infectious Diseases Society of America Practice Guidelines

Dong Heun Lee, MD; Ole Vielemeyer, MD

Arch Intern Med. 2011;171(1):18-22

Clinical Endocrinology (2013) 78, 183–190 doi: 10.1111/j.1365-2265.2012.04441.x

METHODOLOGICAL ASSESSMENT IN ENDOCRINOLOGY

A comparative quality assessment of evidence-based clinical guidelines in endocrinology

EVIDENCE LEVEL	Cardiology	Infectious disease	Endocrinology
1 or A based on RCTs	11%	14%	6%
3 or C based on opinion	48%	55%	35%

Levels of Evidence Supporting American College of Cardiology/American Heart Association and European Society of Cardiology Guidelines, 2008-2018

41 ACC/AHA or ESC guidelines - classification of 6329 recommendations

9%/14% - LOE A - multiple RCTs or single large RCT

50%/31% - LOE B - observational or single RCT

42%/55% - LOE C - expert opinion

Current guidelines with prior versions - LOE A

ACC/AHA - **9%** [current] vs **12%** [prior]

ESC - **15%** [current] vs **18%** [prior]

JAMA. 2019;321(11):1069-1080. doi:10.1001/jama.2019.1122

Systematic review of clinical practice guidelines recommendations about primary cardiovascular disease prevention for older adults

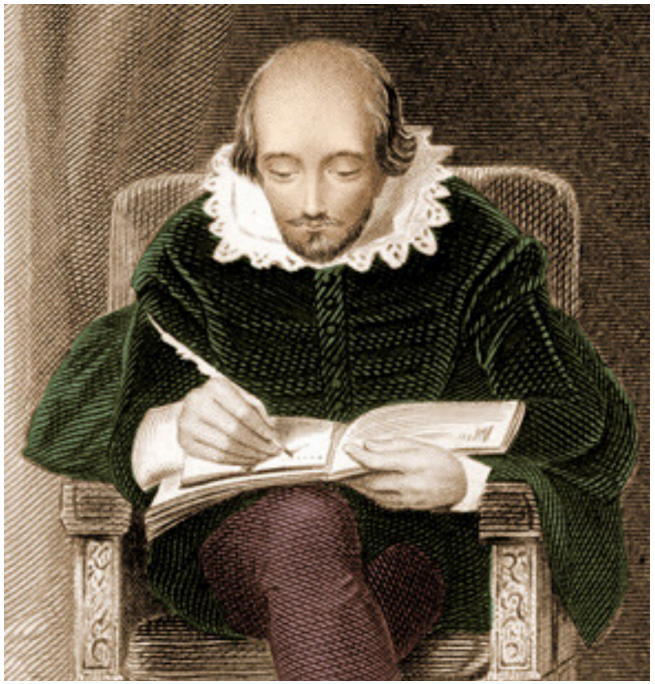
Jesse Jansen[1,2*], Shannon McKinn[1,2], Carissa Bonner[1,2], Les Irwig[1], Jenny Doust[1,3], Paul Glasziou[1,3], Brooke Nickel[1,2], Barbara van Munster[4,5] and Kirsten McCaffery[1,2]

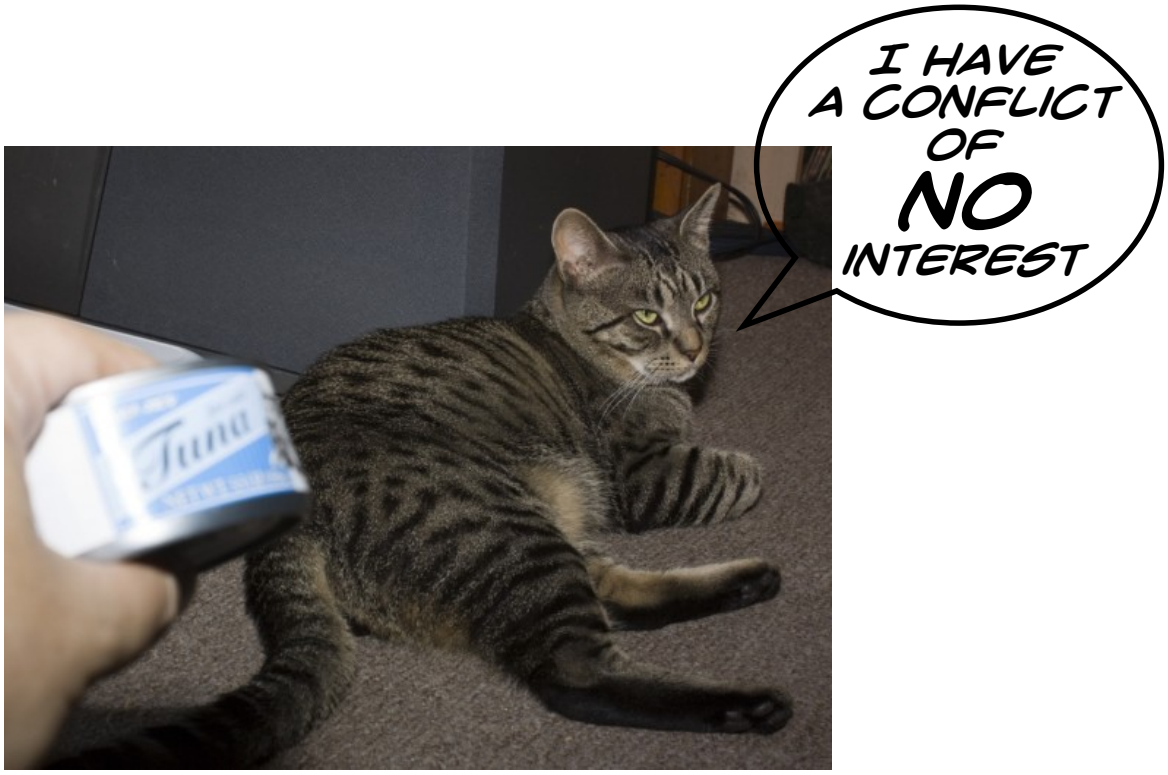
47 guidelines	Discussed benefits	Discussed harms
CVD assessment and harms	19%	17%
Medications	32-33%	15-19%
Lifestyle	15%	0%

Desprescribing mentioned - 0%

BMC Family Practice (2015) 16:104 DOI 10.1186/s12875-015-0310-1

Who writes/sponsors guidelines?





Research

Contributors to primary care guidelines

What are their professions and how many of them have conflicts of interest?

G. Michael Allan MD CCFP Roni Kraut Aven Crawshay Christina Korownyk MD CCFP
Ben Vandermeer MSc Michael R. Kolber MD CCFP MSc

176 PRIMARY CARE guidelines in the CMA database

CONTRIBUTORS

54% non–family physician specialists
17% family physicians - 8% if industry sponsored
11% other clinicians
8% non-clinician scientists
6% nurses
3% pharmacists

69% of guidelines didn't report conflicts of interest

Can Fam Physician 2015;61:52-8

Guideline sponsorship

2009 - 2,300 guidelines in the National Guideline Clearinghouse

Guideline development

- 41% - medical speciality societies
- 22% - government agencies/nonprofit
- 17% - professional associations
- 9% - disease specific societies
- 4% - independent expert panels

at least 2/3 are being developed by groups with a clear potential for important biases

http://www.ncbi.nlm.nih.gov/books/NBK22928/

Prevalence of financial conflicts of interest among panel members producing clinical practice guidelines in Canada and United States: cross sectional study

~50-80% of panel members on guidelines have financial COIs

BMJ 2011;343:d5621 doi: 10.1136/bmj.d5621

EVIDENCE BASED MEDICINE

Why we can't trust clinical guidelines **BMJ 2013:346**

Despite repeated calls to prohibit or limit conflicts of interests among authors and sponsors of clinical guidelines, the problem persists. **Jeanne Lenzer** investigates

Major Medical Associations Feud Over Diabetes Guidelines

npr

March 5, 2018 · 5:01 PM ET

CLINICAL GUIDELINES | 6 MARCH 2018

Hemoglobin A_{1c} Targets for Glycemic Control With Pharmacologic Therapy for Nonpregnant Adults With Type 2 Diabetes Mellitus: A Guidance Statement Update From the American College of Physicians

"Clinicians should aim to achieve an HbA1c level **between 7% and 8% in most patients** with type 2 diabetes"

Because of harms - primarily internists

Canadian Guidelines

Most <7%
<6.5% if low risk for hypoglycaemia

CJD April 2018

CONSENSUS STATEMENT BY THE AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS AND AMERICAN COLLEGE OF ENDOCRINOLOGY ON THE COMPREHENSIVE TYPE 2 DIABETES MANAGEMENT ALGORITHM – *2018 EXECUTIVE SUMMARY*

"**An A1C level of ≤6.5% is considered optimal** if it can be achieved in a safe and affordable manner, but higher targets may be appropriate for certain individuals and may change for a given individual over time."

Because of benefits - primarily endocrinologists

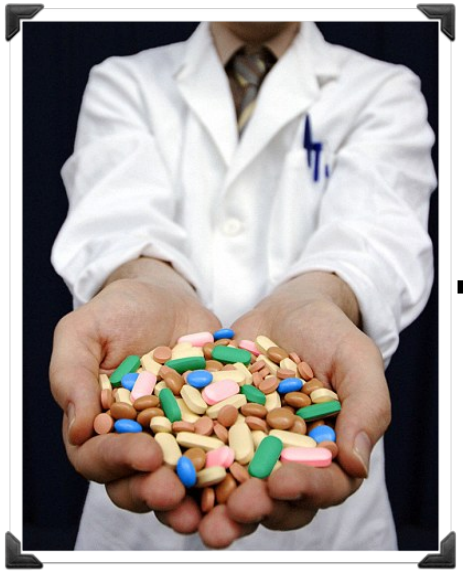
Can we agree to disagree?

Table 2. Guidelines for Target HbA_{1c} Levels in T2D

Guideline	HbA_{1c} Target for Most Patients, %	HbA_{1c} Target in Selected Patients If It Can Be Achieved Safely Without Hypoglycemia, %	HbA_{1c} Target for Patients With Comorbid Conditions, Shortened Lifespan, or History of Severe Hypoglycemia, %*
AACE/ACE	<6.5	–	7–8
ADA	<7	<6.5	<8†
ICSI	<7	–	<8
NICE	<6.5‡	–	Relax target HbA_{1c}
SIGN	<7	<6.5 at diagnosis	–
VA/DoD	6–7	–	8–9
ACP	7–8	–	Avoid targeting HbA_{1c} level

Ann Intern Med 2019;171:505-513

How well do guidelines address patient values and preference?



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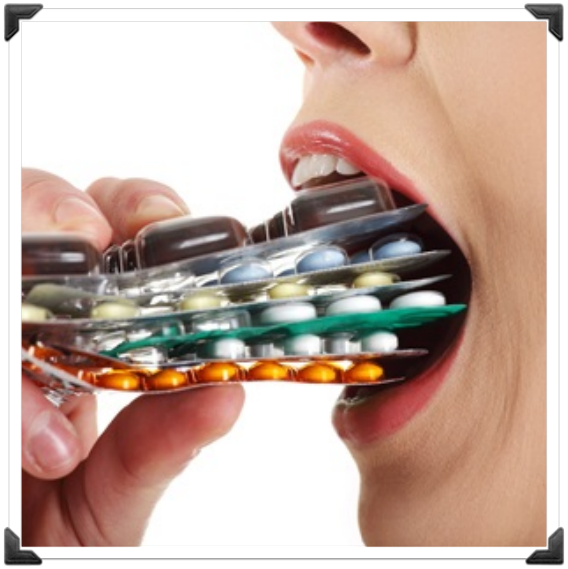


Adding "value" to clinical practice guidelines

James P. McCormack PharmD Peter Loewen PharmD

5 Canadian Guidelines for
blood pressure, cholesterol, glucose, and bone density

197 PAGES - 90,000 WORDS

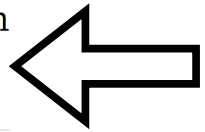
99(0.1%) words - relevant to
patients' values and preferences

Can Fam Physician 2007;53:1326-27

Management of Hyperglycemia in Type 2 Diabetes, 2015: A Patient-Centered Approach

Update to a Position Statement of the American Diabetes Association and the European Association for the Study of Diabetes

Diabetes Care 2015;38:140–149 | DOI: 10.2337/dc14-2441



Diabetes Care
THE JOURNAL OF CLINICAL AND APPLIED RESEARCH AND EDUCATION
January 2015 Volume 38, Supplement 1

Standards of Medical Care in Diabetes—2015

Diabetes Care January 2015

113 PAGES

Looked for info on

- Risk estimation (magnitude)
- Impact of treatment on risk
- Potential harms (magnitude)

"The information presented in these documents is glucose-centric and not organized or presented in a way that could be construed as supporting shared decision making"

Diabetes Care 2015;38:e141–e142 | DOI: 10.2337/dc15-0074

Guidelines

Hypertension Canada's 2016 Canadian Hypertension Education Program Guidelines for Blood Pressure Measurement, Diagnosis, Assessment of Risk, Prevention, and Treatment of Hypertension

~11,800 words - 20 pages

Total mention of values and preferences - 0.19% of the words

"Practitioners are advised to consider patient preferences, values, and clinical factors when determining how to best apply these recommendations at the bedside"

"In the absence of Canadian data to determine the accuracy of risk calculations, **avoid using absolute levels of risk** to support treatment decisions"

ACP American College of Physicians℠ Leading Internal Medicine, Improving Lives **2017** CLINICAL GUIDELINE

Treatment of Low Bone Density or Osteoporosis to Prevent Fractures in Men and Women: A Clinical Practice Guideline Update from the American College of Physicians

~8,700 words - 27 pages

Benefits

No numbers whatsoever for fracture risk or fracture benefit

Do present info in an appendix - new studies

Harms 2017

28 numeric mentions of side effects

6 absolute numbers

22 relative numbers

One mention of patient preferences

Recommendation 6: *ACP recommends that clinicians should make the decision whether to treat osteopenic women 65 years of age or older who are at a high risk for fracture based on a discussion of patient preferences, fracture risk profile, and benefits, harms, and costs of medications. (Grade: weak recommendation; low-quality evidence)*

"clinicians should make the decision whether to treat osteopenic women 65 years of age or older"

2018 Clinical Practice Guidelines Committees

The following committee members contributed to the development of the *Diabetes Canada 2018 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada.*

325 PAGES

Risks of diabetes complications - couldn't ballpark CVD, renal, blindness, amputation risk etc

Benefits of treatment - most are described as relative benefits

Harms of treatment - some tables of harms - but magnitude typically missing

"Where available, … NNT or NNH was considered in assessing the impact of a particular intervention"

MENTIONED ONCE - STENO trial

Mention of clinical trials - this was helpful

3 DPP - 4 trials - no benefit

Insulin - no benefit

Empagliflozin - 12.1% vs 10.5%

Canagliflozin - 32.5/1000 vs 26.9/1000

Liraglutide -14.9% vs 13%

Semaglutide - 8.9% vs 6.6

Table with relative effects of the three new classes

Patient benefit expectations

Patient preferences for shared decisions: A systematic review

Betty Chewning [a,*], Carma L. Bylund [b], Bupendra Shah [c], Neeraj K. Arora [d], Jennifer A. Gueguen [e], Gregory Makoul [f]

"the number of patients who prefer participation has increased over the past three decades so that the majority of patients prefer to participate in decisions"

Patient Educ Couns (2011), doi:10.1016/j.pec.2011.02.004

Factors involved in deciding to start preventive treatment: qualitative study of clinicians' and lay people's attitudes

David K Lewis, Jude Robinson, Ewan Wilkinson **BMJ 2003;327:841**

"Many of the preferences expressed by the clinicians and lay people in this study are at odds with recommendations in guidelines"

Differing perceptions of intervention thresholds for fracture risk: a survey of patients and doctors **Osteoporos Int 2012;23:2135–40**

77% of doctors would recommend treatment
21% of our patient cohort would consider treatment justified

The Magnitudinous Problem

More
Increased
Reduced
Improved
Decreased
Higher
Lower
High
Low
Significant
Less
Fewer
Worsened

Better
Worse
Greater
Uncommon
Superior
Rare
Smaller
Larger
Least
Common
Quicker
Slower
Important

Considerable
Strong
Moderate
Minor
Big
Unimportant
Huge
Tiny
Inferior
Lesser
Small
Bigger
Major

Severe
Weak
Strong
Different
Faster
Shorter
Longer
Shortened
Lengthened
Extreme
Unlikely
Short

Convey a story but not really the evidence

All these words mean something different to everyone

Clinical guidelines on antidepressant withdrawal urgently need updating

James Davies *reader*[1], John Read *professor*[2], Michael P Hengartner *senior lecturer*[3], Fiammetta Cosci *associate professor*[4], Giovanni Fava *professor*[5], Guy Chouinard *professor*[6], Jim van Os *professor*[7], Antonio Nardi *professor*[8], Peter Gøtzsche *professor*[9], Peter Groot *researcher*[10], Emanuela Offidani *assistant professor*[11], Sami Timimi *visiting professor*[12], Joanna Moncrieff *reader*[13], Marcantonio Spada *professor*[14], Anne Guy *researcher*[15]

National Institute for Health and Care Excellence (NICE), which state that "[withdrawal] symptoms are usually mild and self-limiting over about 1 week."

They added the evidence

for over two weeks in 55% of patients
at least six weeks in 40%
at least 12 weeks in 25%
one to 13 weeks in 58%
studies finding mean durations of 11 days and 43 days

Its not that difficult

Medication Class	Medication
Insulin	Insulin
Biguanides	Metformin
	Phenformin
Sulfonylureas	Tolbutamide
	Chlorpropamide
	Glyburide/ glibenclamide
	Gliclazide
	Glipizide
	Glimepiride
Glitazones	Rosiglitazone
	Pioglitazone
Meglitinides	Repaglinide
	Nateglinide
Other	Acarbose
	Aleglitazar
GLP's	Exenatide
	Dulaglutide
	Albiglutide
	Lixisenatide
	Liraglutide
	Semaglutide
DPP4's	Sitagliptin
	Saxagliptin
	Linagliptin
	Alogliptin
	Omarigliptin
Gliflozins	Dapagliflozin
	Empagliflozin
	Canagliflozin
	Ertugliflozin

All the large RCTs evaluating the impact of glucose lowering medications on CVD Outcomes

RCTs evaluating the impact of medications on CVD outcomes in T2DM

YEAR	NAME		MEDICATION	RESULT	OUTCOME CHANGED	ABSOLUTE DIFFERENCE/TIME
1970	UGDP	SU	tolbutamide (Orinase)	NEGATIVE	CVD mortality	↑8%/5 years
1971		BG	phenformin (DBI)	NEGATIVE	Mortality	↑ 6%/5-8 years
1976		SU	tolbutamide (Orinase)	NEGATIVE	Fatal MI	↑ 5%/5 years
1982		IN	insulin	NEUTRAL		
1998	UKPDS 33/34	IN,SU	insulin, chlorpropamide, glyburide/glibenclamide, glipizide	NEUTRAL		
1998		IN,SU,BG	metformin, insulin, chlorpropamide, glyburide/glibenclamide, glipizide	NEUTRAL except POSITIVE for metformin	Mortality MI	↓7%/11 years ↓ 6%/11 years
2003	STOP-NIDDM	OTH	acarbose (Precose)	POSITIVE	MI	↓ 1.5%/3 years
2005	PROACTIVE	GLIT	pioglitazone (Actos)	POSITIVE	MI	↓ 1.5%/3 years
2007	RECORD	GLIT	rosiglitazone (Avandia)	NEGATIVE	Heart failure	↑ 1%/4 years
2012	ORIGIN	IN	insulin	NEUTRAL		
2013	EXAMINE	DPP4	alogliptin (Nesina)	NEUTRAL		
2014	SAVOR-TIMI 53	DPP4	saxagliptin (Onglyza)	NEGATIVE	Heart failure	↑ 1%/2 years
2014	ALECARDIO	OTH	aleglitizar	NEUTRAL		
2015	ELIXA	GLP	lixisenatide (Adlyxin)	NEUTRAL		
2015	TECOS	DPP4	sitagliptin (Januvia)	NEUTRAL		
2015	EMPA-REG	GLIF	empagliflozin (Jardiance)	POSITIVE	Mortality Heart failure	↓ 2.5%/3 years ↓ 1.5%/3 years
2016	SUSTAIN 6	GLP	semaglutide (Ozempic)	POSITIVE	Combined outcome	↓ 2%/2 years
2016	LEADER	GLP	liraglutide (Victoza)	POSITIVE	Mortality Combined outcome	↓ 1%/4 years ↓ 2.5%/4 years
2017	CANVAS	GLIF	canagliflozin (Invokana)	POSITIVE	Combined outcome Heart failure Amputations	↓ 2%/3.5years ↓ 1%/3.5 years ↑ 1%/3.5 years
2017	EXSCEL	GLP	exenatide (Byetta)	NEUTRAL		
2017	ACE	OTH	acarbose (Procose)	NEUTRAL		
2017	Omarigliptin	DPP4	omarigliptin	NEUTRAL		
2018	HARMONY	GLP	albiglutide (Tanzeum)	POSITIVE	Combined outcome	↓ 2%/2 years
2018	CARMELINA	DPP4	linagliptin (Tradjenta)	NEUTRAL		
2018	DECLARE-TIMI 58	GLIF	dapagliflozin (Farxiga)	POSITIVE	Combined outcome (primarily heart failure)	↓ 1%/4 years
2019	REWIND	GLP	dulaglutide (Trulicity)	POSITIVE	Combined outcome Renal outcomes	↓ 1.5%/5.4 years ↓ 2.5%/5.4 years
2019	PIONEER 6	GLP (oral)	semaglutide (Ozempic)	POSITIVE	CVD mortality Mortality	↓ 1%/1.5 years ↓ 1.5%/1.5 years
2019	CREDENCE	GLIF	canagliflozin (Invokana)	POSITIVE	Combined CVD outcome Combined renal outcome outcomes	↓ 2.5%/2.6 years ↓ 3%/2.6 years

mystudies.org ~300 studies

MyStudies beta

Study Results at Your Fing

You want to use evidence in your clinical practi
studies that change practice. Your patient come
greatest study. How can you quickly and easily
MyStudies help.

You are at a presentation and you start to wonder if the presenter is really
know about a study. Did they just present relative numbers? Did they onl
of harms? Did they come up with conclusions that don't really match the

A Comparison of Two LDL Cholesterol Targets after Ischemic Stroke.

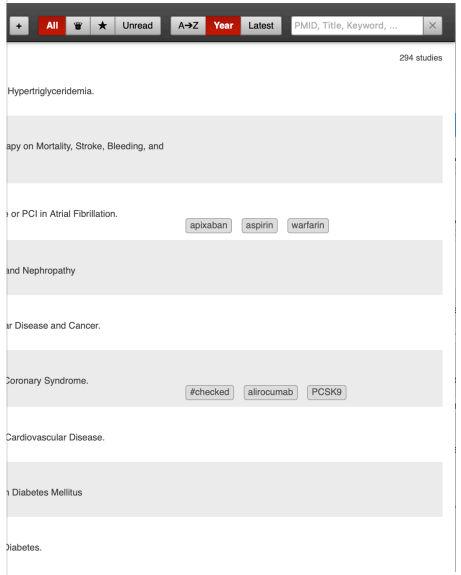
Study	
Blinded	**n**
Duration	**3.5 years**
ITT	**y**

Baseline	
Average Age	**67 yr**
Dyslipidemia	**61 %**
Hypertension	**66 %**
Index event - TIA	**14 %**
Index event - ischemic stroke	**86 %**
Male	**68 %**
Previous Smokers	**23 %**
Smokers	**30 %**
Type 2 diabetics	**23 %**

Labs	
A1c	**6.3 %**
Avg DBP	**80 mmHg**
Avg SBP	**141 mmHg**
BMI	**26 kg/m²**
HDL	**50 mg/dL**
LDL	**135 mg/dL**
Total chol	**210 mg/dL**
Triglycerides	**122 mg/dL**

	Higher-Target 2.3-2.8 mmol/L or 90-110 mg/dL **1430** subjects	Lower-Target 1.8 mmol/L or <70 mg/dl **1430** subjects	ARR (%)	RRR (%)	NNT
Comparator	●	○			
Control	○	●			
Any revascularization procedure	**6.9** n = 99	**6.6** n = 94	-0.3	-5	n/s
CVD mortality	**1.7** n = 24	**1.2** n = 17	-0.5	-41	n/s
Ischemic stroke, myocardial infarction, new symptoms leading to urgent coronary or carotid revascularization, or death from cardiovascular causes	**10.9** n = 156	**8.5** n = 121	-2.4	-29	-41
Mortality	**6.5** n = 93	**6.2** n = 88	-0.3	-6	n/s
Non-fatal acute coronary syndrome	**1.6** n = 23	**1.0** n = 15	-0.6	-53	n/s
Non-fatal cerebral infarction or stroke	**7.0** n = 100	**5.7** n = 81	-1.3	-23	n/s

Show n
95% CI 99% CI
Show only statistically significant



McCormack *et al. BMC Medical Research Methodology* 2013, **13**:134
http://www.biomedcentral.com/1471-2288/13/134

BMC
Medical Research Methodology

DEBATE Open Access

How confidence intervals become confusion intervals

James McCormack[1], Ben Vandermeer[2] and G Michael Allan[3*]

BMC Medical Research Methodology 2013;13:134

Do statins reduce mortality in primary prevention?

Need to look at meta-analyses

Do statins reduce mortality in primary prevention?

Studer et al.: “reduced risks of overall and cardiac mortality” **YES**

Thavendiranathan et al.: [does not decrease]”overall mortality” **NO**

Mills et al.: “an important role in preventing all-cause mortality” **YES**

Brugts et al.: “associated with significantly improved survival” **YES**

Ray et al.: “did not find evidence for the benefit … on all-cause mortality” **NO**

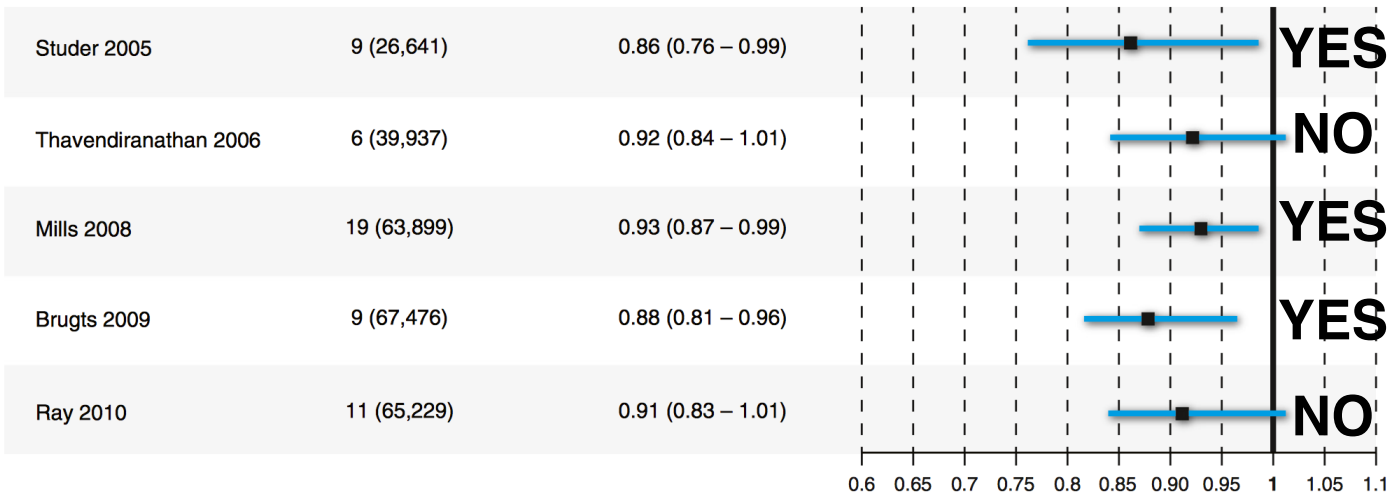


Figure 1 Comparison of 5 meta-analyses examining relative risk of overall mortality with statin use in primary prevention. Footnote: Brugts 2009 point estimate and confidence intervals are odds ratios (not relative risks).

Guidelines and the Law

Guidelines and the Law

"As per the Canadian Medical Association Handbook on Clinical Practice Guidelines, guidelines should NOT be used as a legal resource in malpractice cases as "their more general nature renders them insensitive to the particular circumstances of the individual cases."

CJD
Canadian Journal of Diabetes

A Publication of the Professional Section of Diabetes Canada

Une publication de la Section professionnelle de Diabète Canada

CONTENTS: April 2018 ▪ Volume 42 ▪ Supplement 1

CMPA
Empowering
better healthcare

The Bottom Line

Sep 2011

Even an authoritative CPG may NOT be found to be determinative of a standard of care.

It is prudent for physicians to be aware of authoritative clinical practice guidelines relevant to their practices. If a clinical decision may be perceived as being contrary to a recognized and accepted CPG, a physician, where appropriate, may consider the following steps: consult with a colleague or relevant specialist, discuss reasonable treatment options with the patient, and document the patient's consent for the chosen treatment.

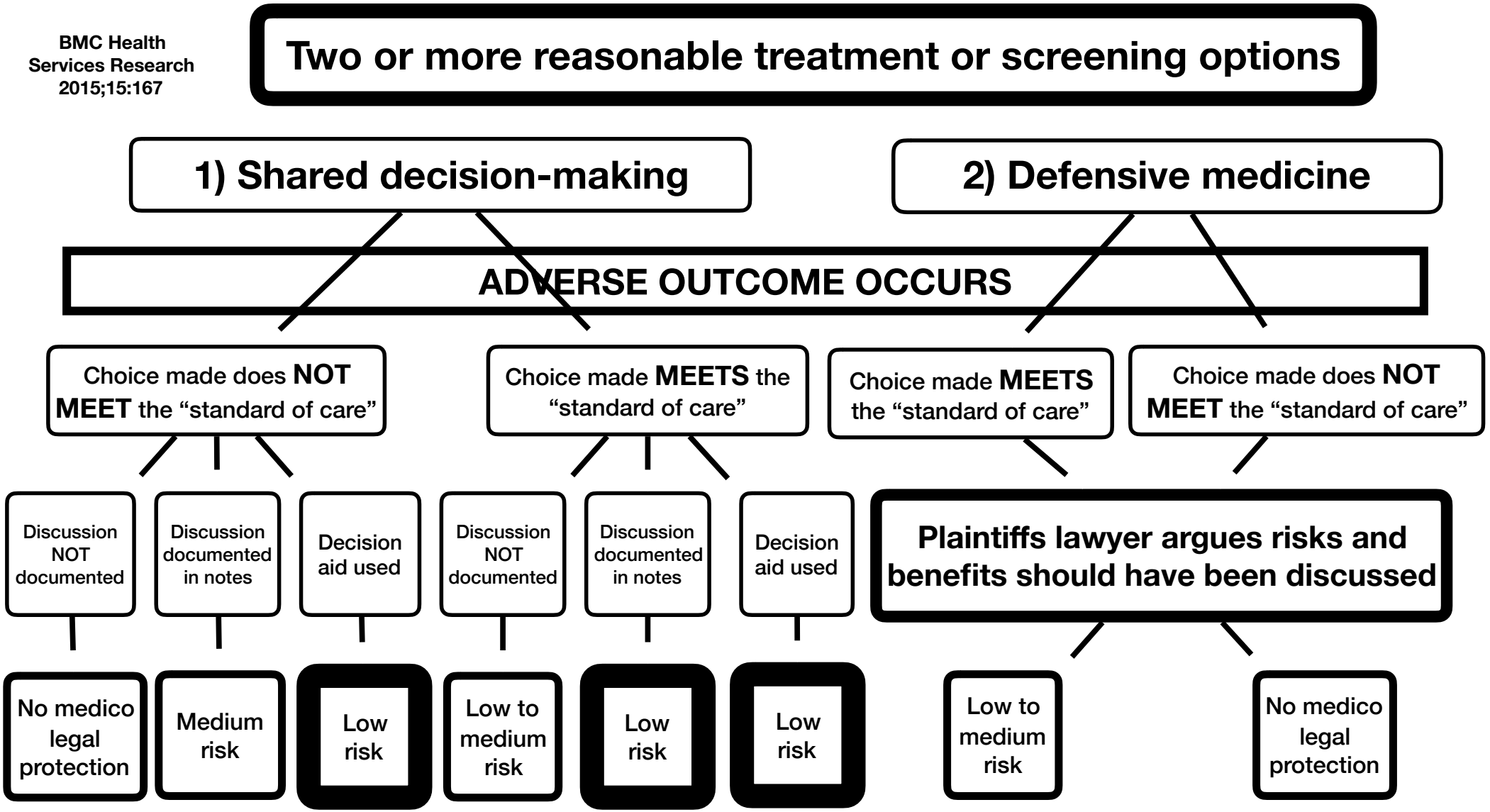
If deviating from an established CPG, physicians should consider documenting the rationale for doing so, as well as any discussions with the patient about such variance.

Many courts (UK, US, CA)

"The reasonable-patient standard … requires physicians and other health care practitioners to disclose all relevant information about the risks, benefits, and alternatives of a proposed treatment that an **OBJECTIVE PATIENT** would find material in making an intelligent decision as to whether to agree to the proposed procedure"

JAMA 2016;315:2063-4

BMC Health Services Research 2015;15:167



Defensive model (guidelines/standard of care)

NEVER get to a low litigation risk

Reducing litigation risk

2 THINGS to DO

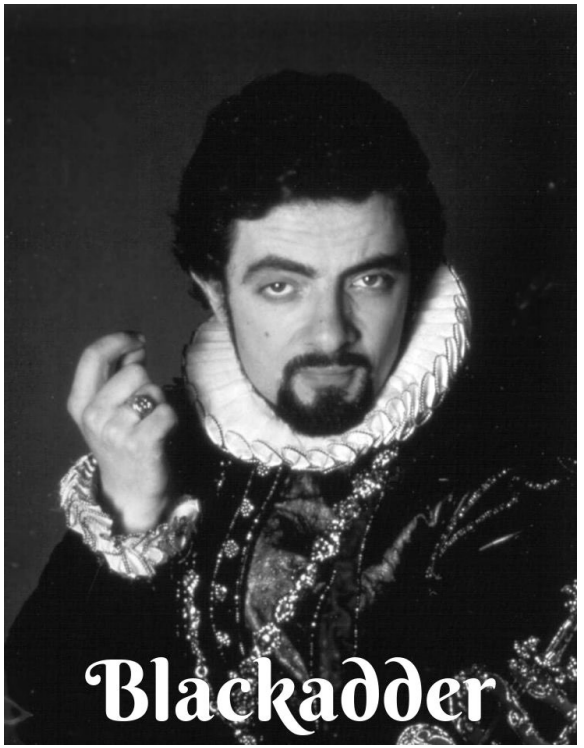
Shared decision-making model

1) Use a decision aid

2) Document decision

The Guideline Solution?

“I've got a plan so cunning,
you could put a tail on it
and call it a weasel”



Guidelines would be awesome if they…

Were developed primarily by, and definitely for, the people that ultimately end up using them

Were a credible synopsis of the best available evidence (obtained via a systematic review) presented in a way that clinicians could easily access and interpret

Allowed patient values and preferences to be taken into account

Guidelines should provide
ballpark estimates
of what happens if
you DON'T treat/test/screen
and if
you DO treat/test/screen

“I would rather know evidence and try to apply it to each patient, than memorize guidelines and try to apply them to all patients”

Mark McConnell

Simplified lipid guidelines

Prevention and management of cardiovascular disease in primary care

G. Michael Allan MD CCFP Adrienne J. Lindblad ACPR PharmD Ann Comeau MN NP CCN(C) John Coppola MD CCFP
Brianne Hudson MD CCFP Marco Mannarino MD CCFP Cindy McMinis Raj Padwal MD MSc
Christine Schelstraete Kelly Zarnke MD MSc FRCPC Scott Garrison MD PhD CCFP Candra Cotton
Christina Korownyk MD CCFP James McCormack PharmD Sharon Nickel Michael R. Kolber MD CCFP MSc

Can Fam Phy 2015;61:857-67

CLINICAL PRACTICE GUIDELINES

Simplified guideline for prescribing medical cannabinoids in primary care

G. Michael Allan MD CCFP Jamil Ramji Danielle Perry Joey Ton PharmD Nathan P. Beahm PharmD
Nicole Crisp RN MN NP-Adult Beverly Dockrill RN Ruth E. Dubin MD PhD FCFP DCAPM Ted Findlay DO CCFP FCFP
Jessica Kirkwood MD CCFP Michael Fleming MD CCFP FCFP Ken Makus MD FRCPC Xiaofu Zhu MD FRCPC
Christina Korownyk MD CCFP Michael R. Kolber MD CCFP MSc James McCormack PharmD Sharon Nickel
Guillermina Noël MDes PhD Adrienne J. Lindblad ACPR PharmD

Can Fam Phy 2018;64:111-120

CLINICAL PRACTICE GUIDELINES

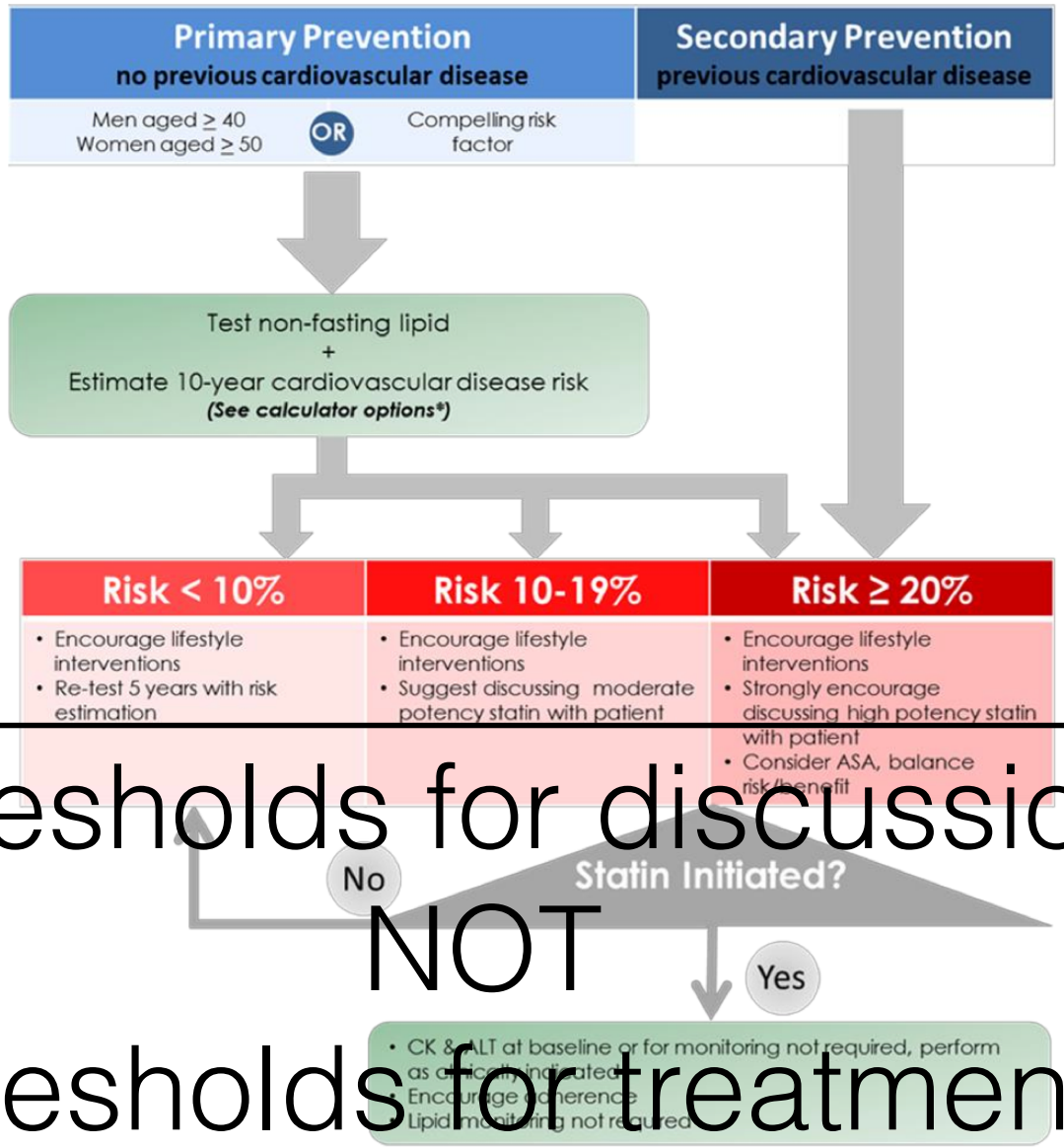
Managing opioid use disorder in primary care

PEER simplified guideline

Christina Korownyk MD CCFP Danielle Perry Joey Ton PharmD Michael R. Kolber MD CCFP MSc
Scott Garrison MD CCFP PhD Betsy Thomas BScPharm G. Michael Allan MD CCFP Cheryl Bateman PSW
Raquel de Queiroz NP Dorcas Kennedy MD CCFP FCFP Wiplove Lamba MD FRCPC Dip ABAM Jazmin Marlinga MD CCFP(AM)
Tally Mogus MD CCFP(AM) Tony Nickonchuk BScPharm Eli Orrantia MD MSc CCFP FCFP Kim Reich RSW
Nick Wong MD CCFP(AM) FCFP Nicolas Dugré PharmD MSc Adrienne J. Lindblad ACPR PharmD

Can Fam Phy 2019;65:321-30

All informed by questions identified by primary care clinicians
All informed by a systematic review
All benefits and harms were presented as absolute numbers in calculators and/or evidence tables
All promoted shared decisions as an integral part of the guideline
All provided patient material



Thresholds for discussion NOT thresholds for treatment

Reducing Your Risk for Heart Attacks & Strokes

A SHIFT IN THINKING...

What's Changed?

If you asked anyone how to reduce your risk of a heart attack or stroke you'd likely hear them mention the need to lower your cholesterol.

CHOLESTEROL ONLY TELLS US PART OF YOUR HEART HEALTH STORY

However, many studies have shown improving cholesterol does not always reduce risk of cardiovascular disease (heart attack or stroke). By worrying only about cholesterol we might miss helping the right people because cholesterol is only one risk

Medication

Statin therapy should be discussed with all people with moderate to high cardiovascular risk (10% or more). Your healthcare provider can explain your risk and how statins can reduce that risk by 25-35%.

STATINS CAN REDUCE YOUR RISK OF HEART ATTACK AND STROKE BY 25% TO 35%

A low-dose of ASA (Aspirin®) may also be recommended for further risk reduction if you are at high cardiovascular risk (20% or more) or have had a heart attack or stroke. ASA reduces cardiovascular risk by about 12.5% (half or third as effective as statins). Note – ASA can cause bleeding.

What are the side effects of statins?

All drugs come with

Most Common

1 in every 10 to 20 people – muscle aches or stiffness*

1 in every 10,000

Are statins right for you?

You decide. Speak with your healthcare provider about your risk of cardiovascular disease and the benefits and risks of taking statins. Regardless of your decision, your healthcare provider will support you!

This number is an educated guess of your chances of developing cardiovascular disease in the next 10 years. For example, a 10% risk means you have about a 1 in 10 chance of having a heart attack or stroke in the next 10 years.

What can you do to reduce your risk of heart attack or stroke?

Eat healthy – be active – don't smoke

These lifestyle choices reduce your risk of cardiovascular disease and benefit your overall health.

EXERCISE OR A MEDITERRANEAN DIET CAN REDUCE YOUR RISK OF HEART ATTACK AND STROKE BY 30%

tested?

Not taking a statin → You should continue to have your cholesterol tested every 5 years.

Taking a statin → No. Once you have decided to take a statin a cholesterol test is unnecessary – statins help to reduce your cardiovascular risk no matter what your cholesterol level. So knowing your cholesterol level would not change your treatment plan.

Are statins right for you?

You decide. Speak with your healthcare provider about your risk of cardiovascular disease and the benefits and risks of taking statins. Regardless of your decision, your healthcare provider will support you!

Alberta College of Family Physicians

The College of Family Physicians of Canada | Le Collège des médecins de famille du Canada

TOP Toward Optimized Practice

Tools to help clinicians discuss benefits and harms with patients

Languages: English (EN)

The Absolute CVD Risk/Benefit Calculator

Framingham
US Data, 10 Year Risk
Heart attacks + angina/coronary insufficiency + heart failure + strokes + intermittent claudication

QRISK®2-2014
UK Data, 10 Year Risk
Heart attacks + strokes

ACC/AHA ASCVD
US Data, 10 Year Risk
CHD death + nonfatal heart attacks + fatal/nonfatal strokes

PREDICT
New Zealand Data, 5 Year Risk
Heart attacks + angina + heart failure + strokes/TIAs + peripheral vascular disease

Age 50 years

Gender Male / ✔ Female

Smoker Yes / ✔ No
CVD risk is reversed after 5-10 years of no smoking

Diabetes Yes / ✔ No

Systolic Blood Pressure 120 mmHg
Enter present blood pressure regardless of treatment
120 mmHg is used for baseline risk

On treatment for BP Yes / ✔ No
Click YES if taking blood pressure medication
Only applies if SBP is greater than 120 mmHg

Total Cholesterol 3 mmol/L
Cholesterol should be prior to drug treatment
3 mmol/L is used for baseline risk.
Click to change to mg/dL.

HDL Cholesterol 1.3 mmol/L
HDL should be prior to drug treatment

Relative Benefit: 0%

Benefit often has *nothing* to do with the effect on the surrogate marker. At present, you can only select one intervention at a time.

- Physical Activity
- Mediterranean Diet vs Low fat
- Vitamin/Omega-3 supplements
- BP meds (not atenolol/doxazosin)
- Low-mod intensity statins
- High intensity statins
- Fibrates
- Niacin
- Ezetimibe
- Metformin
- Sulfonylureas
- Insulins
- Glitazones
- GLPs
- DPP-4s
- Meglitinides
- SGLT2
- Smoking Cessation
- ASH

Benefit Estimate Details

Risk Time Period

10 years

97.9%	No event
2.1%	Total with an event
0.0%	Number who benefit from treatment
NNT ∞	Number needed to treat
2.1%	Baseline events using baseline factors alone
0.0%	Additional events "caused" by risk factors

As with all risk calculators, calculated risk numbers are +/- 5% at best. More information.

Comparing Treatment Options for Pain: The C-TOP Tool

Neuropathic Pain | Osteoarthritis Pain (Coming Soon) | Back Pain (Coming Soon)

Medication Options

- **Amitriptyline** (Elavil®)
- **Cannabinoids** (Nabiximols, nabilone, medical marijuana)
- **Duloxetine** (Cymbalta®)
- **Gabapentin** (Neurontin®)
- **High-Dose Opioids** (morphine, oxycodone)
- **Pregabalin** (Lyrica®)
- **All Treatments** (comparison)

Curious about capsaicin, botox, tramadol, carbamazepine, or venlafaxine for neuropathic pain? Click here to learn more.

Meaningful Pain Relief from Amitriptyline
(30% reduction in pain scores)

Amitriptyline Benefit	Placebo Benefit	No Benefit
25% (ranges 13% to 45%)	25%	50%

A typical placebo group response seen in pain studies is **25%** but this can be adjusted in the FAQ section.

Meaningful Pain Relief

An example of a **30% reduction** in pain scores is a decrease from **6** to **4** on a **10** point pain scale

Amitriptyline Harms

Dry mouth	34%	6% (placebo)
Sleepiness	34%	9% (placebo)
Balance problems	20%	3% (placebo)
Stopped due to side effects	16%	7% (placebo)

Other Considerations

- Typically taken at bedtime due to sleepiness effects
- Approximate cost (CAD) for 30-day supply (without dispensing fee): **$1.50 to $3.50**

Making evidence based medicine work for individual patients 2016

Margaret McCartney and colleagues argue that new models of evidence synthesis and shared decision making are needed to accelerate a move from guideline driven care to individualised care

Margaret McCartney *general practitioner*[1], Julian Treadwell *general practitioner*[2], Neal Maskrey *visiting professor*[3], Richard Lehman *senior advisory fellow in primary care*[4]

The guideline was praised in a BMJ article for its simplicity and that it “offers lifestyle and drug options without judging which is best for an individual with links to attractive risk calculators”

BMJ 2016;353:i2452 doi: 10.1136/bmj.i2452 (Published 16 May 2016)

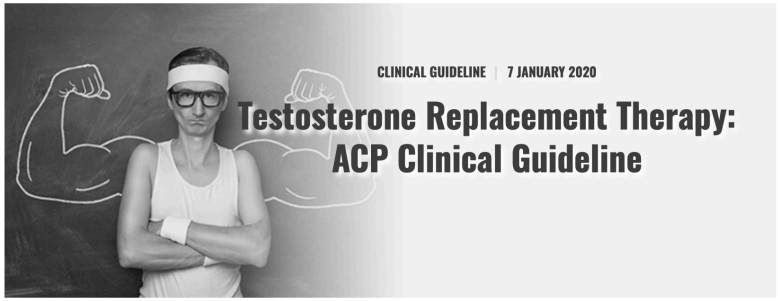
ACP

ACP American College of Physicians℠ Leading Internal Medicine, Improving Lives

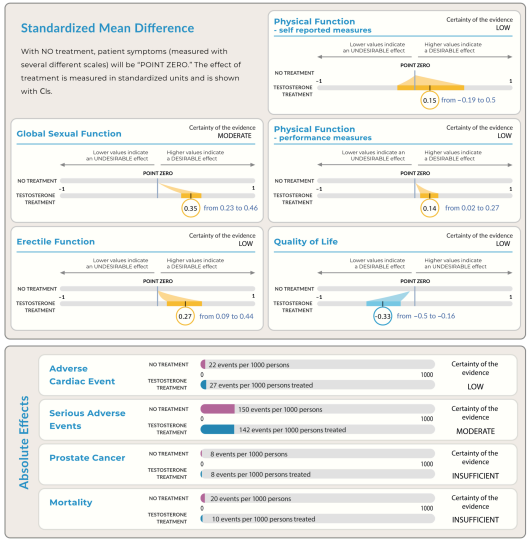
CLINICAL GUIDELINE

Testosterone Treatment in Adult Men With Age-Related Low Testosterone: A Clinical Guideline From the American College of Physicians

Amir Qaseem, MD, PhD, MHA; Carrie A. Horwitch, MD, MPH; Sandeep Vijan, MD, MS; Itziar Etxeandia-Ikobaltzeta, PhD; and Devan Kansagara, MD, MCR; for the Clinical Guidelines Committee of the American College of Physicians*



Outcomes Evaluated



BMJ

thebmj

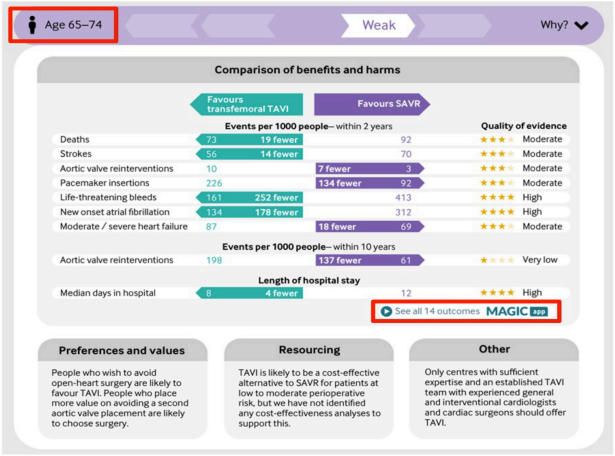
BMJ 2016;354:i5191 doi: 10.1136/bmj.i5191 (Published 29 September 2016)

EDITORIALS

Introduction to *BMJ* Rapid Recommendations

New BMJ collaboration accelerates evidence into practice to answer the questions that matter quickly and transparently through trustworthy recommendations

Reed A Siemieniuk *methodologist*[1 2], Thomas Agoritsas *assistant professor*[1 3], Helen Macdonald *acting head of education section*[4], Gordon H Guyatt *distinguished professor*[1 5], Linn Brandt *methodologist*[6], Per O Vandvik *associate professor*[6 7]



There are LOTS of guidelines

Often don't provide a solid synopsis/systematic review of the best available evidence

Often don't provide sufficient information to do shared-decision-making or even support the concept

Many "conflicts" and ownership issues

Patient expectations are often at odds with guideline recommendations

Legal precedents are leaning in favour of benefit/harm communication

Useful guidelines can be written