The who, what, why, where, and when of Clinical Practice Guidelines (CPGs)

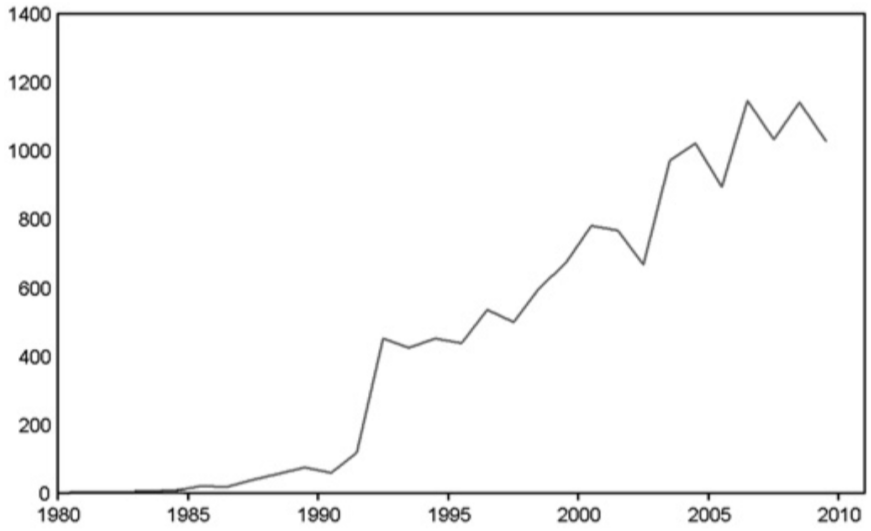

Figure 1 Number of guidelines in PubMed.

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

Grading of Recommendations Assessment, Development and Evaluation (GRADE) - Quality

High Quality (Level A): Further research is very unlikely to change our confidence in the estimate of effect.

Moderate Quality (Level B): Further research is likely to have an important impact on our confidence in the estimate of effect, and may change the estimate.

Low Quality (Level C): Further research is very likely to have an important impact on our confidence in the estimate of effect, and is likely to change the estimate.

Very Low Quality (Level D): Any estimate of effect is very uncertain.

Grading of Recommendations Assessment, Development and Evaluation (GRADE) - Recommendation

Strong recommendation: Most informed patients would choose the option recommended, and clinicians can structure their interactions with patients accordingly.

Weak recommendation: Patient choices will vary based upon their values and preferences, and clinicians must help to ensure that patient care stays true to these values and preferences.

GRADE also allows for “good practice points.” These are recommendations that can be made when it is deemed they will be helpful to the clinician, such as recommendations for shared decision making, but there is no direct evidence to support the recommendation.

COMMENTARY

Guideline panels should not GRADE good practice statements

Gordon H. Guyatt[a,b,*], Holger J. Schünemann[a,b], Benjamin Djulbegovic[c], Elie A. Akl[a,d]

Good practice statements typically represent situations in which a large body of indirect evidence, made up of linked evidence including several indirect comparisons, strongly supports the net benefit of the recommended action.

Box 1 Examples of good practice statement previously mistakenly presented as GRADEd recommendations

For patients with congenital adrenal hyperplasia, we recommend monitoring patients for signs of glucocorticoid excess [5].

Triage (ie, take different courses of action for low vs. higher pretest probability) people with tuberculosis symptoms [6].

Health services should be made available, accessible, and acceptable to sex workers based on the principles of avoidance of stigma, nondiscrimination, and the right to health [7].

In patients presenting with heart failure, initial assessment should be made of the patient's ability to perform routine/desired activities of daily living [8].

Table 1. Questions guideline panels considering good practice statement should ask themselves

i)	Is the statement clear and actionable?
ii)	Is the message really necessary?
iii)	Is the net benefit large and unequivocal?
iv)	Is the evidence difficult to collect and summarize?
v)	If a public health guideline, are there specific issues that should be considered (eg, equity)
vi)	Have you made the rationale explicit?
vii)	Is this better to be formally GRADEd?

A word of caution is required: good practice statements may be subject to abuse.

Journal of Clinical Epidemiology 2015;68:597-600

Levels of Evidence:

IA - Evidence from meta-analysis of randomized controlled trials

IB - Evidence from at least one randomized controlled trial

IIA - Evidence from at least one controlled study without randomization

IIB - Evidence from at least one other type of quasi-experimental study

III - Evidence from non-experimental descriptive studies, such as comparative studies, correlation studies, and case-control studies

IV - Evidence from expert committee reports or opinions or clinical experience of respected authorities, or both

Grades of Recommendations:

A - Directly based on Level I evidence

B - Directly based on Level II evidence or extrapolated recommendations from Level I evidence

C - Directly based on Level III evidence or extrapolated recommendations from Level I or II evidence

D - Directly based on Level IV evidence or extrapolated recommendations from Level I, II, or III evidence

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

JAMA®
Online article and related content current as of March 17, 2009.

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%

BMJQS

The quality of clinical practice guidelines over the last two decades: a systematic review of guideline appraisal studies

Table 2 Appraisal of Guidelines, Research and Evaluation domain scores of guidelines over time (total sample=608)

	1988–1992 (n=9)	1993–1997 (n=102)	1998–2002 (n=291)	2003–2007 (n=206)	p Value for trend
Domain scores		***Top Score = 100%***			
Scope and purpose	44	61	60	71	<0.001
Stakeholder involvement	18	38	33	37	0.01
Rigour of development	14	41	43	44	0.003
Clarity and presentation	32	56	55	68	<0.001
Applicability	10	30	18	23	<0.001
Editorial independence	17	30	28	33	0.26

Engaging the right people, quality of evidence appraisal, providing useful tools, and competing interests have not improved in 14 years (1993-2007)

Qual Saf Health Care 2010;19:e58. doi:10.1136/qshc.2010.042077

Recent examples of Guideline **Quality/Rigour**

AGREE II (Appraisal of Guidelines for Research and Evaluation)

is the instrument typically used ***- 207 guidelines***

avg 55% - neuropathic pain - 16 CPGs - range 27%-88% - BMC Anesthesiology 2016;16:12

avg 30% - hypertension - 11 CPGS - range 8%-86% - PLoS ONE 2013 8(1): e53744

avg 32% - asthma - 18 CPGs - range 8%-64% - Chest 2013 144: 390-7

avg 48% - diabetes - 24 CPGs - range 0%-81% - PLoS ONE 2013 8(4): e58625

avg 20% - vancomycin - 12 CPGs - range 4%-73% - PLoS ONE 2013 9(6): e99044

avg 18% - hypertension (China) - 17 CPGs - range 1-36% - BMJ Open 2015;5:e008099

avg 8% - respiratory (China) - 109 CPGs - range 0%-27%- Chest 2015;148:759-766

August 2016

Original Article

Glycemic Control for Patients With Type 2 Diabetes Mellitus

Our Evolving Faith in the Face of Evidence

René Rodríguez-Gutiérrez, MD, MSc; Victor M. Montori, MD, MSc

Evidence since 1998 for
Tight glycemic control (A1c 6.5%-7%) vs less tight (A1c 7%-8.5%)

Endpoints - End Stage Renal Disease/dialysis, renal death, blindness or clinical neuropathy

5 large trials, 8 meta-analyses, 2 follow-up trials

31 estimates of outcomes

- 2 (6%) suggested benefit
- 29 (94%) suggested NO benefit

Endpoints - all-cause mortality, CV mortality, non-fatal MIs, stroke, amputations/ PVD

5 large trials, 10 meta-analyses, 5 follow-up trials

78 estimates of outcomes

- 10 (13%) suggested benefit
- 64 (82%) suggested NO benefit
- 4 (5%) suggested harm

Circ Cardiovasc Qual Outcomes. 2016;9:00-00. DOI: 10.1161

Overall estimates of benefits and harms (micro and macro)

11% of estimates = a benefit

4% of estimates = harm

85% of estimates = no benefit

despite this, over the last 10 years -
"practice guidelines and published statements offer a consistent and confident consensus, with 100% of the guidelines and 77% to 100% of the statements in favor of tight glycemic control to prevent microvascular complications"

Circ Cardiovasc Qual Outcomes. 2016;9:00-00. DOI: 10.1161

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

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"

Their response

“would like to thank McCormack et al for their thoughtful letter regarding the American Diabetes Association’s Standards of Medical Care in Diabetes”

“agrees that shared decision making is a valuable aspect of diabetes care … that process would be incredibly labor intensive and would make the Standards long and unwieldy”

“Clinical guidelines are the foundation for evidence-based medicine”

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"

Patients' Expectations of the Benefits and Harms of Treatments, Screening, and Tests
A Systematic Review

Tammy C. Hoffmann, PhD; Chris Del Mar, MD, FRACGP

BENEFIT - 88% of study authors concluded that participants **overestimated benefits**

HARM - 67% **underestimated harm**

JAMA Intern Med 2015;175:274-286

Evaluating physician understanding of harms and benefits of common tests and therapies

Paper survey to residents and attending internal medicine physicians
– 18 questions – 117 people responded

	Estimate of benefit in absolute terms						
Green cells are the correct answer	<1%	1 to 5%	5 to 10%	10 to 20%	20 to 45%	45 to 70%	70 to 100%
	Percent of respondents						
Mild HTN 5 years	11	35	28	19	7	1	1
Aspirin with risk factors 5 years	8	32	29	17	8	3	3
Aspirin in CVD 5 years	0	16	29	30	16	8	0
Warfarin Afib 1 year	3	31	29	17	12	8	0
Hip fracture osteoporosis 5 years	3	24	30	24	13	5	0
Death from bleed with PPI 5 years	21	22	20	19	9	9	1
Cancer diagnosis among + screening	4	14	23	35	18	7	0
Major bleeding with ASA 5 years	21	46	21	8	3	0	0
Major bleeding with warfarin 1 year	14	42	30	11	2	2	0
Unneccessary biopsy with screening 10 years	1	9	15	33	26	15	0

79% overestimated benefit

66% overestimated harm

67% were unconfident

JAMA Aug 29 2016

307 subjects using a written questionnaire and interview

Results

Patients	Median acceptable absolute % benefit threshold	% that would take a "safe" drug for 5 years		Absolute % benefit they felt they were getting from their drug	% who wanted to be told percent chance of benefit
		If benefit over 5 years was < 5%	If benefit over 5 years was < 5% AND their MD recommended it		
Post MI patients	20	32	69	70	79
On drugs	20	29	74	68	72
No drugs	30	21	56	-	84

Clin Med 2002;2:527-33

Ability of clinicians to make an estimate of CHD risk

53 residents, 8 fellows, 18 attending physicians

The **mean degree of over-estimation** compared to the Framingham estimate:

low-risk scenarios - **7.8 times**
medium-risk scenarios - **2.8 times**
high-risk scenarios - **1.5 times**

BMC Health Services Research 2003;3:13

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

David K Lewis, Jude Robinson, Ewan Wilkinson

Qualitative study using semi-structured interviews

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

BMJ 2003;327:841

Differing perceptions of intervention thresholds for fracture risk: a survey of patients and doctors

Did NOT ask patients to consider side effects or drug cost, just the dosing regimen, in the decision

"A typical patient in our study required a
50% absolute fracture risk and
50% relative risk reduction (giving an absolute risk reduction of 25%)
before considering long-term drug therapy"

A prominent current guideline …
recommends pharmacologic intervention at thresholds of
10- year risk of 20% for major osteoporotic fracture or
3% for hip fracture

125 (77%) of doctors would recommend treatment
24 (21%) of our patient cohort would consider treatment justified

Osteoporos Int 2012;23:2135–40

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]

"In three quarters of the cancer studies … the majority of patients preferred shared or autonomous decision making. In contrast, this was true for only about half of the studies with non- disease specific study populations"

"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

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 Sections of the Canadian Diabetes Association
Une publication des sections professionnelles de l'Association canadienne du diabète
CONTENTS: April 2013 ▪ Volume 37 ▪ 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

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

An Example of a Guideline that Promotes Discussion Rather than Treatment

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 Physician 2015;61:857-67