NACB/AACC
Laboratory Medicine Practice Guidelines

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National Academy of Clinical Biochemistry (NACB)

- NACB was founded in 1976: symposia, journal, guidelines → 1998 Standards of Laboratory Practice (SOLP); 2000 Laboratory Medicine Practice Guidelines (**LMPG**).
- NACB merged with and became the academy of AACC in 2006: **AACC(NACB) Academy** →LMPG, educational, research, advocacy.
- In 2010, a new combined AACC/NACB Evidence-Based Laboratory Medicine Committee **(EBLMC)**
- LMPG: recommendations for best practices on using clinical laboratory tests to diagnose, monitor, and optimize care of patients with various specified disorders.

Final Version: January 2014

Standard Operating Procedures for: Preparing, Publishing and Revising National Academy of Clinical Biochemistry Laboratory Medicine Practice Guidelines

Including Review and Approval of External Society/Organization Guidelines for Endorsement and Support by AACC/NACB

- The purpose is to provide guidance for members of NACB and others for new LMPGs, revision of previously published LMPGs or review and approval of other societies' and organizations' CPGs external to NACB and the AACC.
- NACB LMPGs will be developed to address, incorporate and/or conform to the standards explicitly stated in the 2011 IOM report.
- Please note that CPGs and LMPGs are considered similar guidelines although not truly identical: not all elements of the IOM standards articulated in the 2011 report may always be applicable

IOM Clinical Practice Guidelines

- CPGs are "systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances."

IOM 1990

- CPGs are 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.

IOM 2011

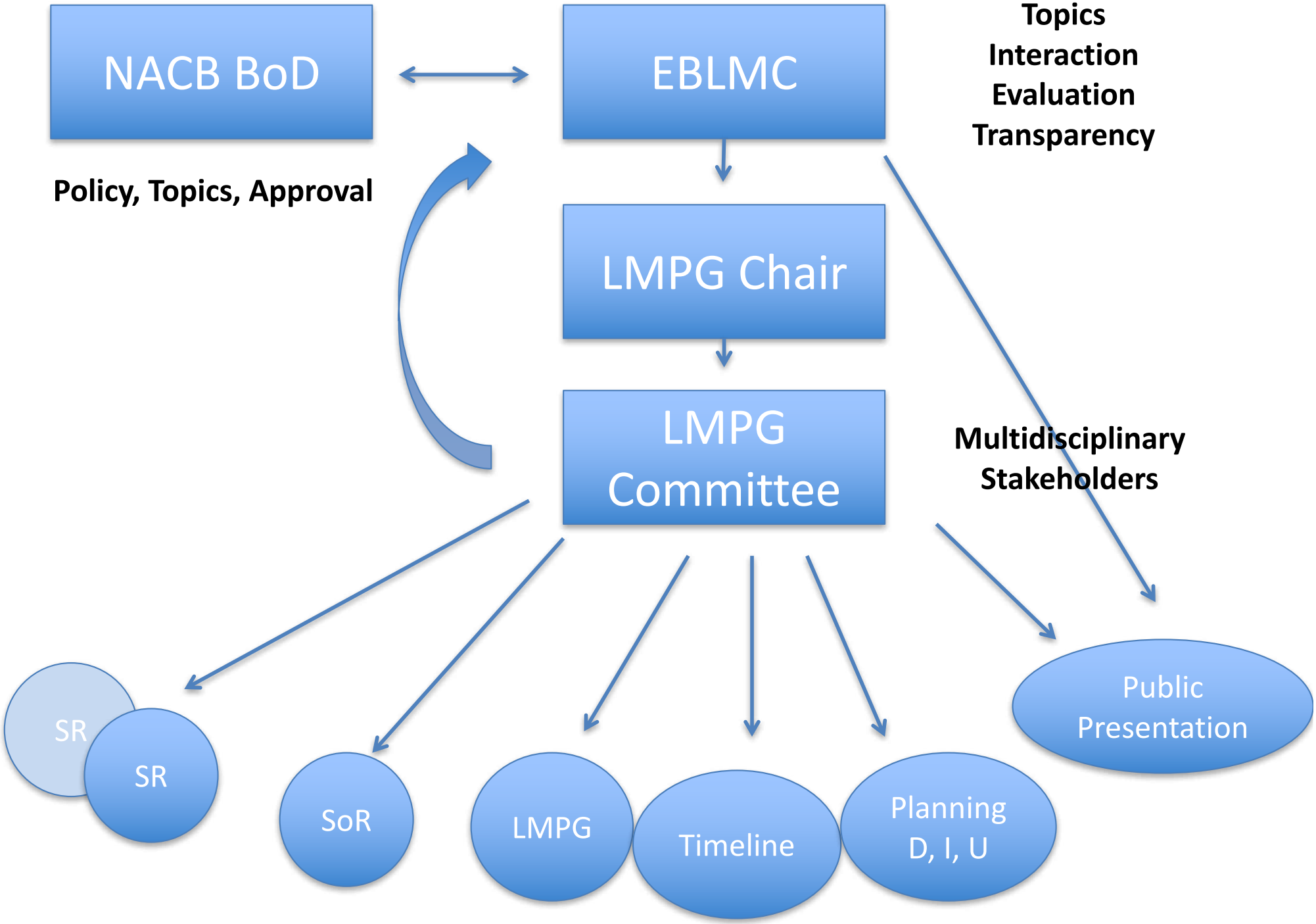
IOM CPGs Attributes

- Validity (strength of evidence; estimated outcomes)
- Reliability/reproducibility
- Clinical applicability
- Clinical flexibility
- Clarity
- Multidisciplinary process
- Scheduled review
- Documentation

IOM 1992

- Transparency
- Conflict of Interest
- Group composition
- CPG-SR intersection
- Evidence Foundations/Strenghth of Recommendations
- External Review
- Updating

IOM 2011


NACB BoD
EBLMC
Topics
Interaction
Evaluation
Transparency
Policy, Topics, Approval
LMPG Chair
LMPG Committee
Multidisciplinary Stakeholders
SR
SR
SoR
LMPG
Timeline
Planning D, I, U
Public Presentation

Evaluating and developing LMPG: AGREE II

Domain 1: Scope and Purpose
1. The overall objective(s) of the guideline is (are) specifically described.
2. The health question(s) covered by the guideline is (are) specifically described.
3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described
Domain 2: Stakeholder Involvement
4. The guideline development group includes individuals from all relevant professional groups.
5. The views and preferences of the target population (patients, public, etc.) have been sought.
6. The target users of the guideline are clearly defined.
Domain 3: Rigour of Development
7. Systematic methods were used to search for evidence.
8. The criteria for selecting the evidence are clearly described.
9. The strengths and limitations of the body of evidence are clearly described.
10. The methods for formulating the recommendations are clearly described.
11. The health benefits, side effects, and risks have been considered in formulating the recommendations.
12. There is an explicit link between the recommendations and the supporting evidence.
13. The guideline has been externally reviewed by experts prior to its publication.
14. A procedure for updating the guideline is provided.

Evaluating and developing LMPG: AGREE II

Domain 4: Clarity of Presentation
15. The recommendations are specific and unambiguous
16. The different options for management of the condition or health issue are clearly presented.
17. Key recommendations are easily identifiable.
Domain 5: Applicability
18. The guideline describes facilitators and barriers to its application.
19. The guideline provides advice and/or tools on the recommendations can be put into practice.
20. The potential source implications of applying the recommendations have been considered.
21. The guideline presents monitoring and/or auditing criteria.
Domain 6: Editorial Independence
22. The views of the funding body have not influenced the content of the guideline.
23. Competing interests of guideline development group members have been recorded and addressed
Rate the overall quality of this guideline
I would recommend this guideline for use (Yes; Yes, with modifications; No)

AGREE Reporting Checklist
2016

AGREE REPORTING CHECKLIST

This checklist is intended to guide the reporting of clinical practice guidelines.

CHECKLIST ITEM AND DESCRIPTION	REPORTING CRITERIA	Page #
DOMAIN 1: SCOPE AND PURPOSE		
1. OBJECTIVES *Report the overall objective(s) of the guideline. The expected health benefits from the guideline are to be specific to the clinical problem or health topic.*	☑ Health intent(s) (i.e., prevention, screening, diagnosis, treatment, etc.) ☑ Expected benefit(s) or outcome(s) ☑ Target(s) (e.g., patient population, society)	40 Evidenze, 41 Risultati, 46 Conclusioni
2. QUESTIONS *Report the health question(s) covered by the guideline, particularly for the key recommendations.*	☑ Target population ☑ Intervention(s) or exposure(s) ☑ Comparisons (if appropriate) ☑ Outcome(s) ☑ Health care setting or context	37-41 SCA, POCT cTn, Evidenze
3. POPULATION *Describe the population (i.e., patients, public, etc.) to whom the guideline is meant to apply.*	☐ Target population, sex and age ☑ Clinical condition (if relevant) ☑ Severity/stage of disease (if relevant) ☐ Comorbidities (if relevant) ☑ Excluded populations (if relevant)	idem
DOMAIN 2: STAKEHOLDER INVOLVEMENT		
4. GROUP MEMBERSHIP *Report all individuals who were involved in the development process. This may include members of the steering group, the research team involved in selecting and reviewing/rating the evidence and individuals involved in formulating the final recommendations.*	☑ Name of participant ☑ Discipline/content expertise (e.g., neurosurgeon, methodologist) ☑ Institution (e.g., St. Peter's hospital) ☑ Geographical location (e.g., Seattle, WA) ☐ A description of the member's role in the guideline development group	36 Autori, 40 MM
5. TARGET POPULATION PREFERENCES AND VIEWS *Report how the views and preferences of the target population were sought/considered and what the resulting outcomes were.*	☐ Statement of type of strategy used to capture patients'/publics' views and preferences (e.g., participation in the guideline development group, literature review of values and preferences) ☐ Methods by which preferences and views were sought (e.g., evidence from literature, surveys, focus groups) ☐ Outcomes/information gathered on patient/public information ☐ How the information gathered was used to inform the guideline development process and/or formation of the recommendations	No o NA?
6. TARGET USERS *Report the target (or intended) users of the guideline.*	☑ The intended guideline audience (e.g. specialists, family physicians, patients, clinical or institutional leaders/administrators) ☑ How the guideline may be used by its target audience (e.g., to inform clinical decisions, to inform policy, to inform standards of care)	41 Risultati

DOMAIN 3: RIGOUR OF DEVELOPMENT		
7. SEARCH METHODS *Report details of the strategy used to search for evidence.*	☑ Named electronic database(s) or evidence source(s) where the search was performed (e.g., MEDLINE, EMBASE, PsychINFO, CINAHL) ☑ Time periods searched (e.g., January 1, 2004 to March 31, 2008) ☐ Search terms used (e.g., text words, indexing terms, subheadings) ☑ Full search strategy included (e.g., possibly located in appendix)	40 MM
8. EVIDENCE SELECTION CRITERIA *Report the criteria used to select (i.e., include and exclude) the evidence. Provide rationale, where appropriate.*	☑ Target population (patient, public, etc.) characteristics ☑ Study design ☑ Comparisons (if relevant) ☑ Outcomes ☐ Language (if relevant) ☑ Context (if relevant)	40 MM
9. STRENGTHS & LIMITATIONS OF THE EVIDENCE *Describe the strengths and limitations of the evidence. Consider from the perspective of the individual studies and the body of evidence aggregated across all the studies. Tools exist that can facilitate the reporting of this concept.*	☑ Study design(s) included in body of evidence ☑ Study methodology limitations (sampling, blinding, allocation concealment, analytical methods) ☑ Appropriateness/relevance of primary and secondary outcomes considered ☑ Consistency of results across studies ☑ Direction of results across studies ☑ Magnitude of benefit versus magnitude of harm ☑ Applicability to practice context	37-40
10. FORMULATION OF RECOMMENDATIONS *Describe the methods used to formulate the recommendations and how final decisions were reached. Specify any areas of disagreement and the methods used to resolve them.*	☑ Recommendation development process (e.g., steps used in modified Delphi technique, voting procedures that were considered) ☑ Outcomes of the recommendation development process (e.g., extent to which consensus was reached using modified Delphi technique, outcome of voting procedures) ☐ How the process influenced the recommendations (e.g., results of Delphi technique influence final recommendation, alignment with recommendations and the final vote)	40 MM, 41 Risultati, 45 Discussione, 46 Conclusioni
11. CONSIDERATION OF BENEFITS AND HARMS *Report the health benefits, side effects, and risks that were considered when formulating the recommendations.*	☑ Supporting data and report of benefits ☑ Supporting data and report of harms/side effects/risks ☑ Reporting of the balance/trade-off between benefits and harms/side effects/risks ☑ Recommendations reflect considerations of both benefits and harms/side effects/risks	37-40
12. LINK BETWEEN RECOMMENDATIONS AND EVIDENCE *Describe the explicit link between the recommendations and the evidence on which they are based.*	☑ How the guideline development group linked and used the evidence to inform recommendations ☑ Link between each recommendation and key evidence (text description and/or reference list) ☑ Link between recommendations and evidence summaries and/or evidence tables in the results section of the guideline	40 MM, 41-45 Risultati

13. EXTERNAL REVIEW *Report the methodology used to conduct the external review.*	☑ Purpose and intent of the external review (e.g., to improve quality, gather feedback on draft recommendations, assess applicability and feasibility, disseminate evidence) ☑ Methods taken to undertake the external review (e.g., rating scale, open-ended questions) ☑ Description of the external reviewers (e.g., number, type of reviewers, affiliations) ☐ Outcomes/information gathered from the external review (e.g., summary of key findings) ☐ How the information gathered was used to inform the guideline development process and/or formation of the recommendations (e.g., guideline panel considered results of review in forming final recommendations)	40 MM
14. UPDATING PROCEDURE *Describe the procedure for updating the guideline.*	☐ A statement that the guideline will be updated ☐ Explicit time interval or explicit criteria to guide decisions about when an update will occur ☐ Methodology for the updating procedure	NO
DOMAIN 4: CLARITY OF PRESENTATION		
15. SPECIFIC AND UNAMBIGUOUS RECOMMENDATIONS *Describe which options are appropriate in which situations and in which population groups, as informed by the body of evidence.*	☑ A statement of the recommended action ☑ Intent or purpose of the recommended action (e.g., to improve quality of life, to decrease side effects) ☑ Relevant population (e.g., patients, public) ☑ Caveats or qualifying statements, if relevant (e.g., patients or conditions for whom the recommendations would not apply) ☑ If there is uncertainty about the best care option(s), the uncertainty should be stated in the guideline	41-45 Risult ati
16. MANAGEMENT OPTIONS *Describe the different options for managing the condition or health issue.*	☐ Description of management options ☐ Population or clinical situation most appropriate to each option	?
17. IDENTIFIABLE KEY RECOMMENDATIONS *Present the key recommendations so that they are easy to identify.*	☑ Recommendations in a summarized box, typed in bold, underlined, or presented as flow charts or algorithms ☑ Specific recommendations grouped together in one section	42 Sintes i
DOMAIN 5: APPLICABILITY		
18. FACILITATORS AND BARRIERS TO APPLICATION *Describe the facilitators and barriers to the guideline's application.*	☑ Types of facilitators and barriers that were considered ☑ Methods by which information regarding the facilitators and barriers to implementing recommendations were sought (e.g., feedback from key stakeholders, pilot testing of guidelines before widespread implementation) ☑ Information/description of the types of facilitators and barriers that emerged from the inquiry (e.g., practitioners have the skills to deliver the recommended care, sufficient equipment is not available to ensure all eligible members of the	41-45 Risult ati

	population receive mammography) ☐ How the information influenced the guideline development process and/or formation of the recommendations	41-45 Risult ati
19. IMPLEMENTATION ADVICE/TOOLS *Provide advice and/or tools on how the recommendations can be applied in practice.*	☑ Additional materials to support the implementation of the guideline in practice. For example: ☐ Guideline summary documents ☐ Links to check lists, algorithms ☐ Links to how-to manuals ☐ Solutions linked to barrier analysis (see Item 18) ☐ Tools to capitalize on guideline facilitators (see Item 18) ☐ Outcome of pilot test and lessons learned	41-45 Risult ati
20. RESOURCE IMPLICATIONS *Describe any potential resource implications of applying the recommendations.*	☐ Types of cost information that were considered (e.g., economic evaluations, drug acquisition costs) ☐ Methods by which the cost information was sought (e.g., a health economist was part of the guideline development panel, use of health technology assessments for specific drugs, etc.) ☐ Information/description of the cost information that emerged from the inquiry (e.g., specific drug acquisition costs per treatment course) ☐ How the information gathered was used to inform the guideline development process and/or formation of the recommendations	?
21. MONITORING/ AUDITING CRITERIA *Provide monitoring and/or auditing criteria to measure the application of guideline recommendations.*	☑ Criteria to assess guideline implementation or adherence to recommendations ☐ Criteria for assessing impact of implementing the recommendations ☑ Advice on the frequency and interval of measurement ☐ Operational definitions of how the criteria should be measured	45 racc 15
DOMAIN 6: EDITORIAL INDEPENDENCE		
22. FUNDING BODY *Report the funding body's influence on the content of the guideline.*	☐ The name of the funding body or source of funding (or explicit statement of no funding) ☐ A statement that the funding body did not influence the content of the guideline	NO
23. COMPETING INTERESTS *Provide an explicit statement that all group members have declared whether they have any competing interests.*	☐ Types of competing interests considered ☐ Methods by which potential competing interests were sought ☐ A description of the competing interests ☐ How the competing interests influenced the guideline process and development of recommendations	46 Col

From:
Brouwers MC, Kerkvliet K, Spithoff K, on behalf of the AGREE Next Steps Consortium. The AGREE Reporting Checklist: a tool to improve reporting of clinical practice guidelines. *BMJ* 2016;352:i1152. doi: 10.1136/bmj.i1152.

For more information about the AGREE Reporting Checklist, please visit the AGREE Enterprise website at www.agreetrust.org.

How can we improve guideline use? A conceptual framework of implementability

Domain/Element	Statistic	Overall (n = 20)
Adaptability		
Journal version	n (%)	10 (50.0)
PDA version	n (%)	5 (25.0)
Short version	n (%)	9 (45.0)
Patient version	n (%)	4 (20.0)
Usability		
Table of contents	n (%)	15 (75.0)
Number of pages	mean	120.2
	med	72.5
	min	21.0
	max	878.0
Number of recommendations	mean	71.7
	med	41.5
	min	8.0
	max	214.0
Recommendation summary	n (%)	11 (55.0)
Recommendation algorithm	n (%)	13 (65.0)
Validity		
Number of references	mean	452.0
	med	230.5
	min	15.0
	max	3,487.0
Evidence graded	n (%)	19 (95.0)
Evidence format	narrative	15 (75.0)
	narrative + tabular	5 (25.0)

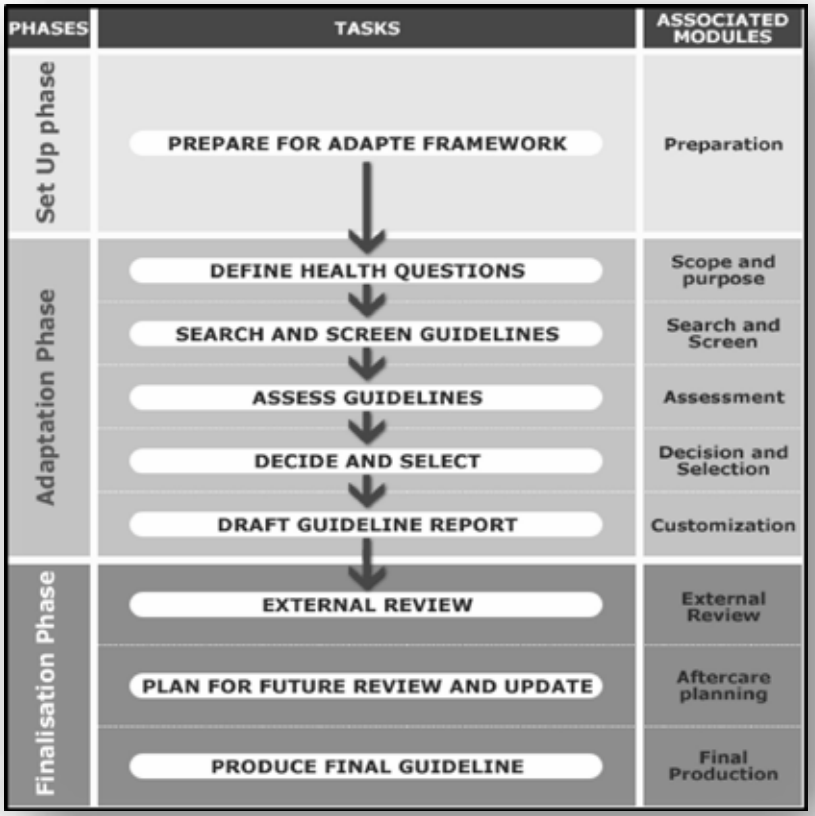
Domain/Element	Overall (n = 20)	
	n	%
Applicability		
Individualization	18	90.0
Communicability		
Patient informed care	10	50.0
Accommodation		
Objectives:		
Clinical	20	100.
Education	1	0
Policy	—	5.0
Quality improvement	2	—
		10.0
Users	12	60.0
User needs/values	0	0.0
Technical	9	45.0
Regulatory	3	15.0
Human resources	1	5.0
Professional	4	20.0
Impact	0	0.0
Costs	0	0.0
Implementation		
Barriers	3	15.0
Tailoring instructions	2	10.0
Point-of-care tools/forms	6	30.0
Implementation strategies	9	45.0
Evaluation		
Evaluation instructions	0	0.0
Performance measures	10	50.0

AR Gagliardi et al 2011

Guideline ADAPTATION

A **systematic process** that guides local groups to identify, evaluate, adapt and use already available guidelines for their own purposes.

- An alternative to denovo development; reduces duplication of effort while maintaining the validity of recommendations
- Encourages participative approach involving all key stakeholders to foster local ownership of recommendations and promote utilization
- Ensures consideration of (regional and local) contextual factors to ensure relevance for practice and improve uptake by targeted users
- Improves guideline quality:
  - Increases knowledge and commitment to evidence-based principles by using reliable methods to ensure quality and validity of adapted guidelines
  - Promotes explicitness and transparency in documenting recommendations



http://www.g-i-n.net/working-groups/adaptation

ADAPTATION PHASE
Customization Module

Tool 15: Evaluation sheet – Acceptability/Applicability

Health question 1	Guideline #1			Guideline #2		
	Yes	Unsure	No	Yes	Unsure	No
Overall, the recommendation is acceptable	○	○	○	○	○	○
The strength of evidence and the magnitude of effect adequately support the grade of the recommendation	○	○	○	○	○	○
There is sufficient benefit of the intervention, compared with other available management	○	○	○	○	○	○
The recommendation is compatible with the culture and values in the setting where it is to be used	○	○	○	○	○	○
	Comments			Comments		
	Yes	Unsure	No	Yes	Unsure	No
Overall, the recommendation is applicable	○	○	○	○	○	○
The intervention is applicable to the patients in the context of use	○	○	○	○	○	○
The intervention/equipment is available in the context of use	○	○	○	○	○	○
The necessary expertise is available in the context of use	○	○	○	○	○	○
There are no constraints, legislation, policies, or resources in the health care setting of use that would impede the implementation of the recommendation	○	○	○	○	○	○
	Comments			Comments		

(Process is repeated as needed for additional health questions)

http://www.g-i-n.net/working-groups/adaptation

Strength of Recommendations and Grading of the Evidence

Strength of Recommendations:

A. The NACB strongly recommends adoption; there is good evidence that it improves important health outcomes and concludes that benefits substantially outweigh harms.

B. The NACB recommends adoption; there is at least fair evidence that it improves important health outcomes and concludes that benefits outweigh harms.

C. The NACB recommends against adoption; there is evidence that it it is ineffective or that harms outweigh benefits.

I. The NACB concludes that the evidence is insufficient to make recommendations; evidence that it is effective is lacking, of poor quality, or conflicting and the balance of benefits and harms cannot be determined.

Grading the Quality of the Recommendations:

NACB grades the quality of the overall evidence on a 3-point scale:

I: Evidence includes consistent results from well-designed, well-conducted studies in representative populations.

II: Evidence is sufficient to determine effects, but the strength of the evidence is limited by the number, quality, or consistency of the individual studies; generalizability to routine practice; or indirect nature of the evidence.

III: Evidence is insufficient to assess the effects on health outcomes because of limited number or power of studies, important flaws in their design or conduct, gaps in the chain of evidence, or lack of information.

Altri metodi

Evidenze → Criteri di valutazione della qualità → Raccomandazione con grading (IA, IB, etc…)

GRADE

Evidenze → Votazione degli outcome → Qualità delle evidenze: stime di benefici & rischi, rischio di bias, trasferibilità, … → Rapporto benefici / rischi, considerando costi, accessibilità e fattibilità → Raccomandazione forte o debole

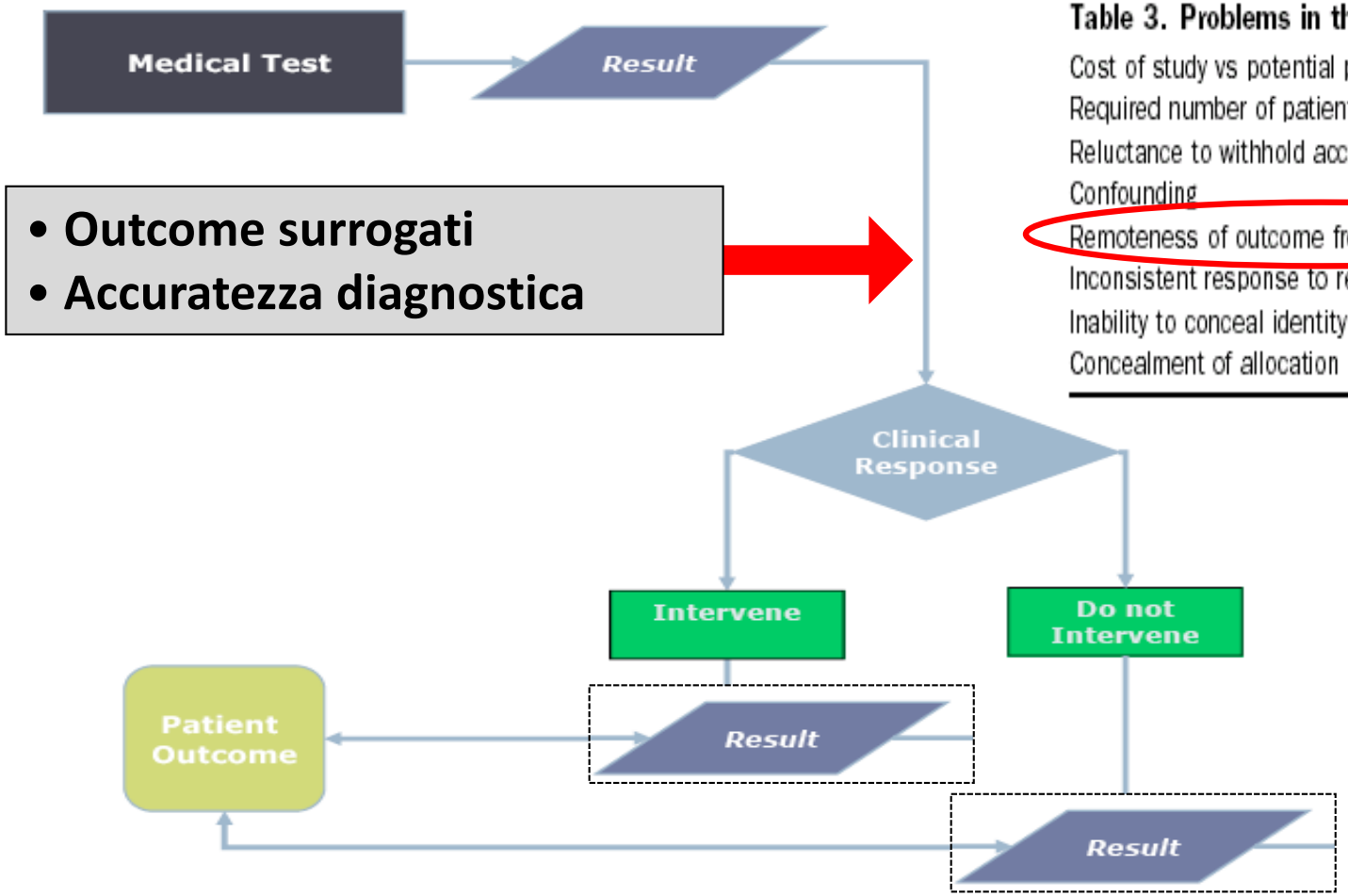
GRADE for diagnostic tests and strategies

Table 2 | Factors that decrease quality of evidence for studies of diagnostic accuracy and how they differ from evidence for other interventions

Factors that determine and can decrease quality of evidence	Explanations and differences from quality of evidence for other interventions
Study design	Different criteria for accuracy studies—Cross sectional or cohort studies in patients with diagnostic uncertainty and direct comparison of test results with an appropriate reference standard are considered high quality and can move to moderate, low, or very low depending on other factors
Limitations (risk of bias)	Different criteria for accuracy studies—Consecutive patients should be recruited as a single cohort and not classified by disease state, and selection as well as referral process should be clearly described.[7] Tests should be done in all patients in the same patient population for new test and well described reference standard; evaluators should be blind to results of alternative test and reference standard
Indirectness:	
Outcomes	Similar criteria—Panels assessing diagnostic tests often face an absence of direct evidence about impact on patient-important outcomes. They must make deductions from studies of diagnostic tests about the balance between the presumed influences on patient-important outcomes of any differences in true and false positives and true and false negatives in relation to complications and costs of the test. Therefore, accuracy studies typically provide low quality evidence for making recommendations owing to indirectness of the outcomes, similar to surrogate outcomes for treatments
Patient populations, diagnostic test, comparison test, and indirect comparisons	Similar criteria—Quality of evidence can be reduced if important differences exist between populations studied and those for whom recommendation is intended (in previous testing, spectrum of disease or comorbidity); if important differences exist in tests studied and diagnostic expertise of people applying them in studies compared with settings for which recommendations are intended; or if tests being compared are each compared with a reference (gold) standard in different studies and not directly compared in same studies
Important inconsistency in study results	Similar criteria—For accuracy studies, unexplained inconsistency in sensitivity, specificity, or likelihood ratios (rather than relative risk or mean differences) can reduce quality of evidence
Imprecise evidence	Similar criteria—For accuracy studies, wide confidence intervals for estimates of test accuracy or true and false positive and negative rates can reduce quality of evidence
High probability of publication bias	Similar criteria—High risk of publication bias (for example, evidence from small studies for new intervention or test, or asymmetry in funnel plot) can lower quality of evidence

Schuenemann et al 2008

Evidence-based Laboratory Medicine



- Outcome surrogati
- Accuratezza diagnostica

Table 3. Problems in the performance of outcomes studies.

Cost of study vs potential profit or perceived savings
Required number of patients/volunteers (sample size)
Reluctance to withhold accepted test
Confounding
Remoteness of outcome from biochemical test
Inconsistent response to result of testing
Inability to conceal identity of tested vs not-tested participants
Concealment of allocation

DE Bruns 2001

Carenza di evidenze

Qualità delle evidenze

POCT: where is the evidence?
A systematic survey

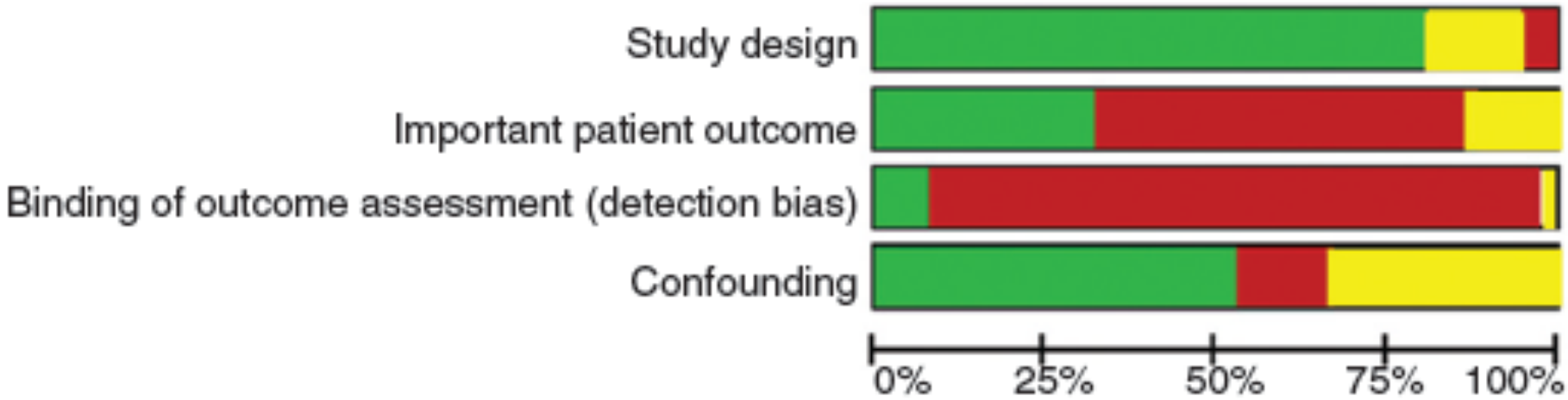
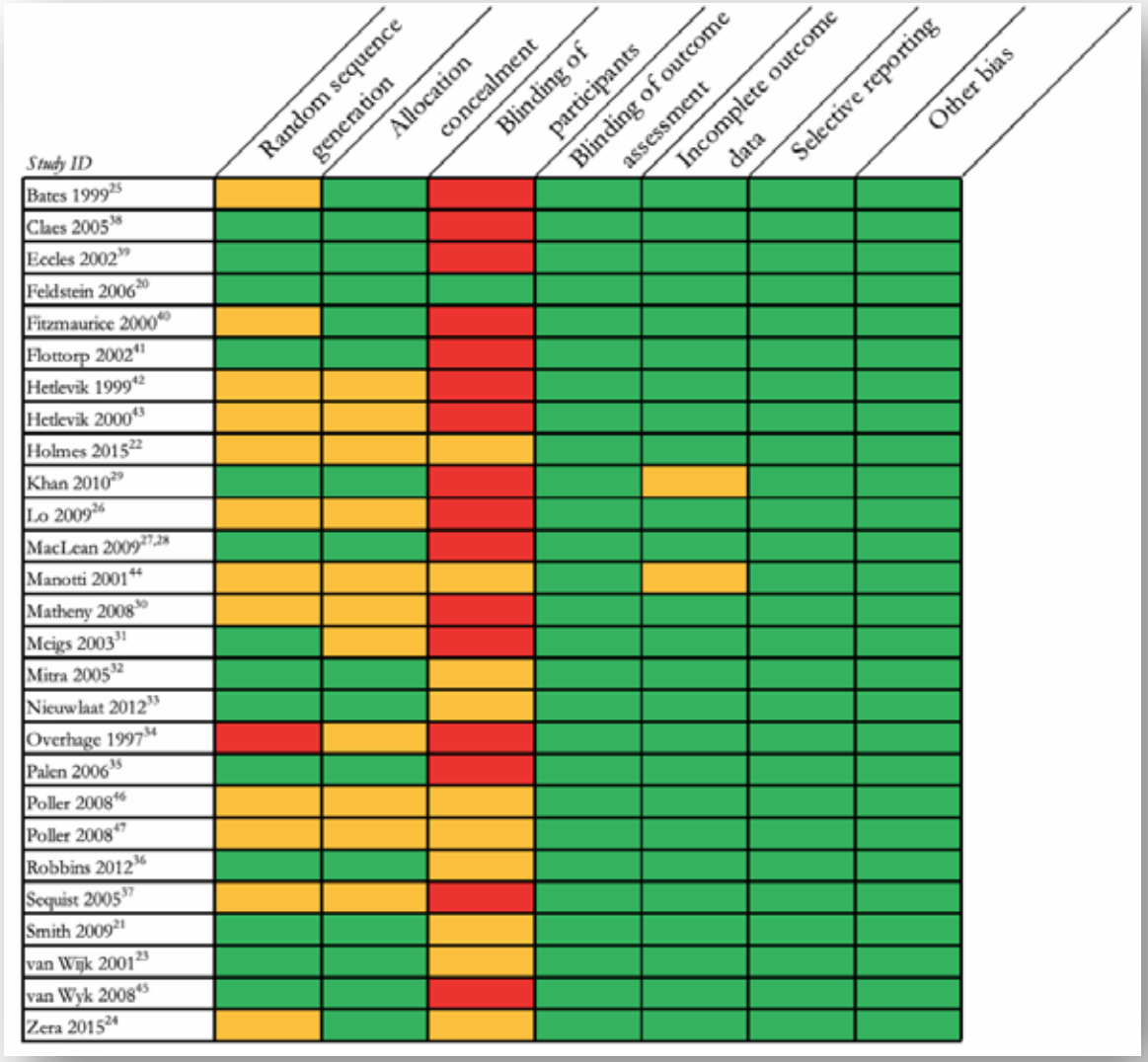


Figure 2 Risk of bias.
Red, high risk of bias; yellow, unknown risk of bias; green, low risk of bias.

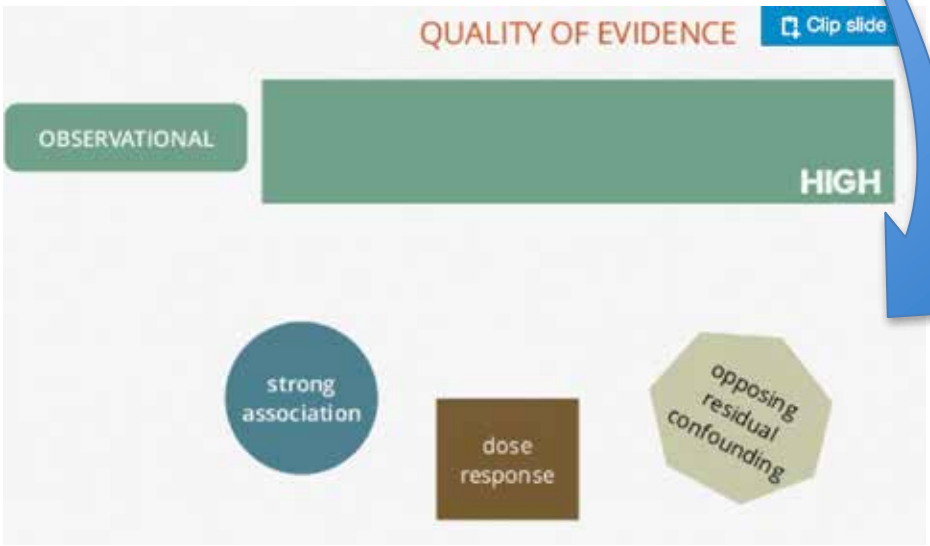
V Pecoraro et al 2014

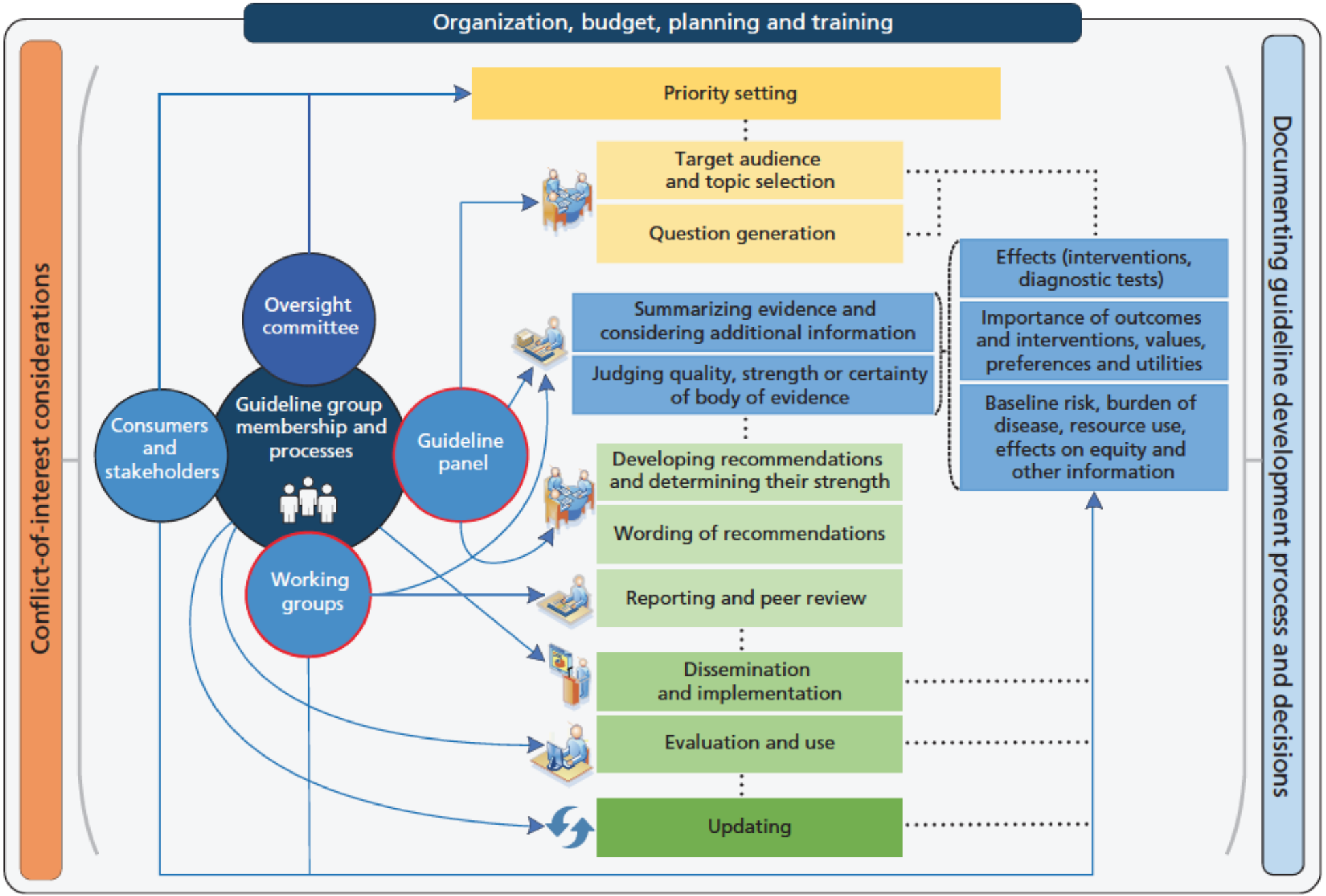
The Effects of Computerized Clinical Decision Support Systems on Laboratory Test Ordering A Systematic Review



Delvaux et al 2017

Experts' opinions





Schuenemann et al 2014

Laboratory investigation in CGL

Pre-analytical phase	Target population for use	All relevant information (Table 2) should be included
	Indication for using the test	All relevant information (Table 2) should be included
	Clinical performance	Sensitivity
		Specificity
		Positive outcome of testing
		Negative outcome of testing
	Sampling procedures	Fasting required
		Time from clinical event
Analytical phase	Methodology	Recommended method
	Biological interferences	All relevant information (Table 2) should be included
	Quality issues	Allowable bias, imprecision and total error
Post-analytical phase		Commenting on reported results
		Diagnostic cut-off value
		Therapeutic target (if relevant)
		Information about clinical meaningful changes based on RCVs and clinical outcome studies when available

Table 3 Laboratory issues that should be addressed in all clinical practice guidelines when laboratory testing is recommended.

KM Aakre et al 2013

Topic	Laboratory medicine specialist involved	Laboratory medicine specialist not involved	p-Value of difference
Sample type	3/4	0/8	0.02
Sample transportation	2/4	0/8	0.09
Sample pre-treatment (maximum delay)	2/4	0/8	0.09
Analytical variation	3/4	1/8	0.07
Maximum storage time (at specified temperature)	2/4	0/8	0.09
Recommended to comment on reported results	2/4	0/8	0.09

Table 4 Number of guidelines that included information about a topic stratified according to involvement of laboratory medicine specialist in the development process (n=12).

Una proposta per SIPMeL

- Obiettivi: appropriatezza/effectiveness; standard of practice; guidance
- LG: adopte & adapt (G-I-N); nuove
- Regole: IOM (CoI); riferimento SOP NACB 2014; (auto)valutazione AGREE II; SoR/LoE NACB/GRADE (specificare); GdS + multidisciplinarietà; revisione 5/6 a.
- Percorso (Giunta →) GdS → CN; pubblicazione RIML; sito (specifica area pubblica)

Appendice

Clinical Practice

Guidelines We Can Trust

IOM 2011

CPGs IOM 2011

STANDARDS FOR DEVELOPING TRUSTWORTHY CLINICAL PRACTICE GUIDELINES (CPGS)

1. Establishing Transparency
   1.1 The processes by which a CPG is developed and funded should be detailed explicitly and publicly accessible.

2. Management of Conflict of Interest (COI)

2.1 Prior to selection of the guideline development group (GDG), individuals being considered for membership should declare all interests and activities potentially resulting in COI with development group activity, by written disclosure to those convening the GDG:

- Disclosure should reflect all current and planned commercial (including services from which a clinician derives a substantial proportion of income), non-commercial, intellectual, institutional, and patient–public activities pertinent to the potential scope of the CPG.

2.2 Disclosure of COIs within GDG:

- All COI of each GDG member should be reported and discussed by the prospective development group prior to the onset of his or her work.
- Each panel member should explain how his or her COI could influence the CPG development process or specific recommendations.

2.3 Divestment

- Members of the GDG should divest themselves of financial investments they or their family members have in, and not participate in marketing activities or advisory boards of, entities whose interests could be affected by CPG recommendations.

2.4 Exclusions

- Whenever possible GDG members should not have COI.
- In some circumstances, a GDG may not be able to perform its work without members who have COIs, such as relevant clinical specialists who receive a substantial portion of their incomes from services pertinent to the CPG.
- Members with COIs should represent not more than a minority of the GDG.
- The chair or cochairs should not be a person(s) with COI.
- Funders should have no role in CPG development.

3. Guideline Development Group Composition
   - 3.1 The GDG should be multidisciplinary and balanced, comprising a variety of methodological experts and clinicians, and populations expected to be affected by the CPG.
   - 3.2 Patient and public involvement should be facilitated by including (at least at the time of clinical question formulation and draft CPG review) a current or former patient, and a patient advocate or patient/consumer organization representative in the GDG.
   - 3.3 Strategies to increase effective participation of patient and consumer representatives, including training in appraisal of evidence, should be adopted by GDGs.
4. Clinical Practice Guideline–Systematic Review Intersection
   - 4.1 Clinical practice guideline developers should use systematic reviews that meet standards set by the Institute of Medicine's Committee on Standards for Systematic Reviews of Comparative Effectiveness Research.
   - 4.2 When systematic reviews are conducted specifically to inform particular guidelines, the GDG and systematic review team should interact regarding the scope, approach, and output of both processes.

5. Establishing Evidence Foundations for and Rating Strength of Recommendations

5.1 For each recommendation, the following should be provided:

- An explanation of the reasoning underlying the recommendation, including
  - a clear description of potential benefits and harms;
  - a summary of relevant available evidence (and evidentiary gaps), description of the quality (including applicability), quantity (including completeness), and consistency of the aggregate available evidence;
  - an explanation of the part played by values, opinion, theory, and clinical experience in deriving the recommendation.
- A rating of the level of confidence in (certainty regarding) the evidence underpinning the recommendation
- A rating of the strength of the recommendation in light of the preceding bullets
- A description and explanation of any differences of opinion regarding the recommendation

7. External Review

7.1 External reviewers should comprise a full spectrum of relevant stakeholders, including scientific and clinical experts, organizations (e.g., health care, specialty societies), agencies (e.g., federal government), patients, and representatives of the public.

7.2 The authorship of external reviews submitted by individuals and/or organizations should be kept confidential unless that protection has been waived by the reviewer(s).

7.3 The GDG should consider all external reviewer comments and keep a written record of the rationale for modifying or not modifying a CPG in response to reviewers' comments.

7.4 A draft of the CPG at the external review stage or immediately following it (i.e., prior to the final draft) should be made available to the general public for comment. Reasonable notice of impending publication should be provided to interested public stakeholders.

8. Updating

8.1 The CPG publication date, date of pertinent systematic evidence review, and proposed date for future CPG review should be documented in the CPG.

8.2 Literature should be monitored regularly following CPG publication to identify the emergence of new, potentially relevant evidence and to evaluate the continued validity of the CPG.

8.3 CPGs should be updated when new evidence suggests the need for modification of clinically important recommendations. For example, a CPG should be updated if new evidence shows that a recommended intervention causes previously unknown substantial harm; that a new intervention is significantly superior to a previously recommended intervention from an efficacy or harms perspective; or that a recommendation can be applied to new populations.