Evidence-Based Clinical Practice Guidelines

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Introduction

- Clinical practice guidelines are recommendations for optimizing patient care that are developed by systematically reviewing the evidence and assessing the benefits and harms of health care interventions.
- These interventions may include not only medications but other types of therapy, such as radiation, surgery, and physical therapy.
- Clinical practice guidelines are developed by a variety of groups and organizations including federal and state government, professional associations, managed care organizations, third-party payers, quality assurance organizations, and utilization review groups.

- Clinical practice guidelines should be developed using rigorous evidence-based methodology with the strength of evidence for each guideline explicitly stated.
- Clinical practice guidelines should be feasible, measurable, and achievable.
- Clinical practice guidelines, from which quality performance measures will be developed, should be reviewed by representatives of the pharmacist they will impact.
- Clinical performance measures may be developed from clinical practice guidelines and used in quality improvement initiatives. When these performance measures are incorporated into public reporting, accountability, or pay for performance programs, the strength of evidence and magnitude of benefit should be sufficient to justify the burden of implementation.
- In the clinical setting, implementation of clinical practice guidelines should be prioritized to those that have the strongest supporting evidence, and the most impact on patient population morbidity and mortality.
- Research should be conducted on how to effectively implement clinical practice guidelines, and the impact of their use as quality measures.
- Clinical practice guidelines, from which quality performance measures have been developed, should be updated as new evidence is available, and the producers of the performance measures should be notified of the work in progress.

The purpose of guidelines
Methods used to develop guidelines
Format of the document
Strategy for implementation

Vary

Evidence-based medicine (EBM) and Clinical Practice Guidelines

- Evidence-based medicine (EBM) is a philosophy of practice and an approach to decision making in the clinical care of patients that involves making individual patient care decisions based on the best currently available evidence.

Why Does EBM Matter?

- Increases audience confidence in the value, objectivity, effectiveness and reproducibility of the tests or procedures
- Increases transparency
- Provides a balanced approach
- Protects patients from ineffective or risky care
- Increases cost-effectiveness and value

To be trustworthy, guidelines should…

- Be based on a systematic review of the existing evidence
- Be developed by a knowledgeable, multidisciplinary panel of experts and representatives from key affected groups
- Consider important patient subgroups and patient preferences as appropriate
- Be based on an explicit and transparent process that minimizes distortions, biases, and conflicts of interest
- Provide a clear explanation of the logical relationships between alternative care options and health outcomes, and provide ratings of both the quality of evidence and the strength of recommendations
- Be reconsidered and revised as appropriate when important new evidence warrants modifications of recommendations.

Institute of Medicine (IOM) ???

- The IOM proposed 8 standards for developing evidence-based clinical practice guidelines.

1. Establishing transparency
2. Managing 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. Articulation of recommendations
7. External review
8. Updating

Developed and Funded

1. Establishing Transparency

The processes by which a clinical practice guideline (CPG) is developed and funded should be detailed explicitly and publicly accessible.

explicit

[Transparency]

* explicit tool ⇐ (Beer's criteria)

assessment of appropriate medical tools → explicit tool / emplicit tool

Ref1. chapter 7_Thank you

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2. Conflict of Interest (COI)

- A set of circumstances that creates a risk that professional judgment or actions regarding a primary interest will be unduly influenced by a secondary interest
- A divergence between an individual's private interests and his or her professional obligations such that an independent observer might reasonably question whether the individual's professional actions or decisions are motivated by personal gain, such as financial, academic advancement, clinical revenue streams, or community standing.
- Intellectual COI: academic activities that create the potential for an attachment to a specific point of view that could unduly affect an individual's judgment about a specific recommendation.

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Scanned by CamScanner

[*] Community COI ⇐ Financical : شخص ما عنده
acidemic : ولا عنده
← نسبه ابنه مدير شركة أدوية كذا ← هاي اسمها
⇐ الصورة السيئة
[nepotism] قرابة الأقارب
منظمها هو

Experts with Conflicts

ع كانه * even cometment of COI
عندي :

The most knowledgeable individuals regarding the subject matter addressed by a CPG are frequently conflicted.

(واحد بشتغل حقليته)
↓
الشركات الداعية بتمنع هاد الشيء

These "experts" often possess unique insight into guideline relevant content domains.

They may be aware of relevant information about study design and conduct that is not easily identified.

* انه أحكي انه هاد الشخص حاز برعاية شركة كذا

Strategies for Managing COI

∴ هاد الاعلان نازل على التلفاز برعاية شركة كذا
{*} هاي محاولة لحل اختلاف ⇐ على الشخص أو الحدث

- Simple disclosure ⇐ أسهل حل
- Exclude from leadership roles ⇒ .... {*} مثلاً علماء دفعوا للشركة وأخذت خبراء من مختلف العالم ودكاترة
- Participation in certain restricted recommendations ⇐ تعبير آخر عنها
- Formal or informal consultation
- Fully exclude conflicted members from panel participation

{*} اذا قدرنا نعمل هيك
يفضل الجرح ← يكون قائم على البحث
مثلاً رئيس اللجنة تابعة التصنيع مثلاً أو رئيس اللجنة
لي يقرر شراء الدواء أو لا

[*] يستحيل نروح نقابة ما فيها COI ⇐ بس نحاول نعمل تقليل على

∴ leadership roles.

≥ * ⇒ in Jornals ⇐ حنلاحظ انه الأمريكان ⇐ بحبوا يعملوا
Sitation to Amirican Jornals
فيها COI سواء كان أو مش بالجد

Managing conflict of interest

a. 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.

b. 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 their work.
- Each panel member should explain how their COI could influence the CPG development process or specific recommendations.
- Each panel member will update any COI at each meeting of the GDG.
- COI conflicts will be reviewed and resolved by the GDG chair and staff. The resolution may involve having the panel member recuse themselves from relevant discussion and/or voting.

c. Divestment

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

d. 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 not represent a majority of the GDG.
- The chair or co-chairs should not be a person(s) with COI.
- Funders should have no role in CPG development.

3. Composition of Guideline Development Group (GDG)

1. The GDG should be multidisciplinary and balanced, including methodological experts, clinicians, and populations expected to be affected
2. Include (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
3. Adopt strategies to increase effective participation of patient and consumer representatives

4. Intersection of Clinical Practice Guideline and Systematic Review

1. Use systematic reviews that meet standards set by the institute of medicine's committee (e.g IOM Committee) on Standards for Systematic Reviews
2. The GDG and systematic review team should interact.

Standards for Systematic Reviews

- RIGOROUS recommendations for:
  - Initiating a systematic review
  - Finding and assessing individual studies
  - Synthesizing body of evidence – Reporting

5. Establishing Evidence Foundations and Rating Strength of Recommendations

For each recommendation provide:

1. A summary of relevant available evidence, description of the quality, quantity, and consistency of the aggregate available evidence.
2. A clear description of potential benefits and harms.
3. An explanation of the part played by values, opinion, theory, and clinical experience in deriving the recommendation.
4. A description of any differences of opinion regarding the recommendation.
5. A rating of the level of confidence in the evidence
6. A rating of the strength of the recommendation

[*] evidance → strength of evidance
→ quality of evidance ⇐ (Biases) ↘ بتتأثر بال

Determinants of Evidence Quality GRADE Collaboration

- Randomized controlled trails (RCTs) start high ⇐ أعطاها أعلى قيمة ⇐ الجيد منه
- Observational studies start low] ⇐ أعطاها قيمة منخفضة
-

(RCT > Observation ⇓ cohort > Case control - - -)

5 factors that Can lower quality	Factors increase confidence in quality
1. Bias 2. Inconsistency 3. Indirectness 4. Imprecision 5. Publication bias	1. Large effect 2. Dose response

↘ [*] عندي 35 أنوع Bias

[*] ريكورد 15

* ⇐ إذا كان عندي دراستين معمولات على RCT كل وحدة بتطرش شكل معين رح اعتمدها؟

Grading of the strength of the recommendation

if you understand [GRADE] you understand how to use evidence to inform practice

⇓ معناها (درجات)

↘ [*] بنفس الوقت هو اختصار ل 5 كلمات

GRADE

Plan

- GRADE background
- two steps
  - confidence in estimates (quality of evidence)
  - strength of recommendation
- evidence profiles
- an exercise in applying GRADE

Proliferation of systems
Common international grading

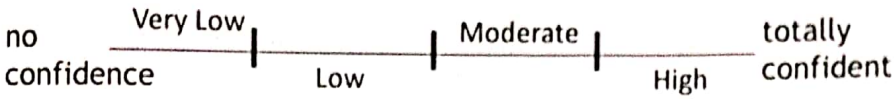
- GRADE (Grades of recommendation, assessment, development and evaluation)
- international group
  - Australian NMRC, SIGN, USPSTF, WHO, NICE, Oxford CEBM, CDC, CC
- ~ 40 meetings over last 16 years
- **The** system – over 100 organizations thus far

* تقريباً لا الأوبساء العلمية متفقين عليه

* وزارة الصحة الأمريكية والبريطانية

What are we grading?

two components



strength of recommendation:
strong and weak

Determinants of confidence

- RCTs start high
- Observational studies start low
- What can Lower, Higher confidence?

* Adequacy of allocation : ⇒ • allocation ⇓ هي توزيع

Concealment

[عينة البحث ↓ على مجموعات البحث] ← تابع

(Sample) عينة study ↓ على group of the study.

* لو عينة الناس في group A ⇐ مجموعة عام و في مجموعة مش عام ⇓ group B
الهدف التوزيع مش صح

12/15/2019

Grading Recommendation Strength

TABLE 7-2. GRADE SYSTEM TO RATING CONFIDENCE IN EFFECT ESTIMATES[28]

1. Establish initial level of confidence		2. Consider lowering or raising level of confidence		3. Final level of confidence rating
Study design	Initial confidence in an estimate of effect	Reasons for considering lowering or raising confidence ↓ Lower if	↓ Higher if	Confidence in an estimate of effect across those considerations
Randomized trials →	High confidence	Risk of bias −1 Serious −2 Very serious Inconsistency −1 Serious −2 Very serious Indirectness −1 Serious −2 Very serious	Large effect +1 Large +2 Very large Dose response +1 gradient found	High ⊕⊕⊕⊕ Moderate ⊕⊕⊕○ Low ⊕⊕○○ Very low ⊕○○○
Observational studies →	Low confidence	Imprecision −1 Serious −2 Very serious Publication bias −1 Likely −2 Very likely		

الجدول ⇐ ... متوقف منه في المجمل

لو وزعت وأنا ما شوف مين في رح يروح على group A أو group B

احتمالية انه الشخص ممكن يروح على group A / B واني أنا مش شايفة
هذا هو ⇐ اسمها (Concealment) ⇐

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[*] يكون هاد ما الأهداف للدراسة يكون خارج عند وجود معلم

[*] هادي كل دراسة لها نوع منه risk of Bias

[*] كل دراسة لها Bias ولازم الباحث يكون فاهم هاي (Bias)

What can lower confidence (RCT)

1. Risk of bias (results whereby the expected value of the results differs from the true underlying parameter, more than 30 types)
   - (P) • Study design bias and implementation bias
     - Adequacy of allocation concealment, blinding, loss to follow-up, stopping early for benefit, unvalidated outcome measures,
   - (U) • Publication bias; selective outcome reporting
   - (R) • Researcher bias: Selection bias, Observation bias
   - (S) • Responders bias: Hawthorne effect, Recall bias

انه في شارك بالدراسة أو باحث ما يكون عارف مجموعات البحث زي placebo

الجدول Bias for RCT

العينة في بتتفرق منها للدراسة في Criteria هي تدخل عند ... (Bias)

2. Inconsistency between different studies. (على العينة)
   - Point estimates of the results vary widely across the studies
   - Confidence intervals shows minimal overlap
   - Statistical tests for heterogenicity are significant and differences are not explained.

3. Indirectness ⇐ ... المقارنات المباشرة والغير مباشرة [*] ⇐
   - Patients, interventions, outcomes are similar to the target population for a given treatment.
   - Indirect comparisons ... * ليش بدي اعمل على دراسة معينة إذا

* عشان العين ما يعرفوا اذا هم بأخذوا دواء أو placebo

4. Imprecision ⇐ (imprecise) or (precise) هي

Assessment of the confidence intervals for the results ← في حجم الدقة هي CI ⇐ هي أداة تقاس الدقة

↓ * متناقصة ↑ Blinding ↑ قوة الدراسة

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* Stopping early for Benifit ⇓

* في بعض الدراسات توقفت على النتيجة بتوقف عامل للدراسة مع سببه وقف عند الـ Benfit

[∴ Howthrein effect]

[⇐ Blinding was implemented to minimized Howthrin effect]
⇓
انه الشخص يعمل علاقة بطاقة تحت مراقبة من جهة معينة

* ⇐ [allocation concealment]
هيك صار عندي

⇓

توزيع عينة البحث على مجموعات البحث بدون توجيه مسبق من الباحث

≈ [أي] والفرصة لكل عينة بأنها تكون مجموعة A أو B متساوية ...

≈ * adequacy of allocation concealment ⇐ إنه تكون كل هاي العملية (adequate) ⇐ محترمة ومنطقية

[كل randomization → ال adequacy parameter]

حتى لما عملت ∴ Parallel Randomization → ليش عملته
شو الجهاز لي استخدمته
ليش عملت
هيك allocation

≈ Loss to follow up ⇐ ≈ * follow up to intervention
أنه بأي فترة زمنية

مهمة

كل ما كان في follow up أكثر كان أحسن

≈ * وهل مجرد ما خلص الدوا سكرت الدراسة ولا عملت follow up ⇓ لمدة سنة

≈ [*] أيضاً في follow up on the [idivinual studies.]

في بالتحليل اسمه اسمه

[إذا دخل بالدراسة 100 شخص اللي ضل منهم 50 وعملت عليهم تحليل] ← * Per Protocol

* intentional to treat. ⇐ [لما أبدأ بالدراسة ⇐ كل اللي دخلوا معي بالدراسة احسبهم] ⇐ عملت تحليل على كل واحد دخل بالدراسة

intention to treat

* selection Bias ⇐ صفة الدكتور عامل دراسة على طلابه جامعة هاي الصورة عندي ⇐ (بعرفه طلابه وهم بعرفوه) ⇐ [*]

Bias
⇓
selection

Blind ⇐ {*} الدكتور لو رحت على عينة ما بعرفها وهاوه بعرفني

الهدف الدراسة صارت أحسن *

Observation Bias ⇒ (Publication Bias) زي

⇓
صفة بتروح بتابع فاعلية الدوا وبنسى الأحياء الثانية عينة ...

≈ * Recall Bias ⇐ مرتبطة ارتباط وثيقة بـ

Case control study

⇓

{*} إنه المريض ما بتذكر الأحداث اللي صارت معه أو بتذكر بشغلة معينة بس

② inconsistancy between different studies

↓ عدم الاستمرارية

→ [P] Point estimate of results vary widely across the studies.

بالعادة معناها ③ أحصاء

(1) دراسة

(2) دراسة — الهن واحد هل جذري

(3) دراسة

دراسة (1) * ⇐ هل يستطيع هذا الدواء تنزيل الوزن 5 كيلو

← هاي هي [Point of estimate.]

دراسة (2) * ⇐ هل يستطيع هذا الدوا تنزيل الوزن 8 كيلو

← صورت هاي هي [Point of estimate.]

دراسة (3) * ⇐ " " " " " 25 كيلو

⇐ Point estimate.

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* الصورة Point of estimate مش ثابتة ⇐ لذلك هي (inconsistancy)

هون تكون consistancy ⇐ انه تكون Point of estimate

(1) —— 5 kg

(2) —— 5 kg

(3) —— 5 kg

(*) لما يكون عندي مجموعة من الدراسات بتقيس نفس مفهوم الـ Outcome بدي اشوف هل هم متساويات بال Outcome ولا لاء

ما [١١] **Confidance interval** shows minimal ovarlap.

CI

range زي مبدأ

دراسة (١)	5 kg	(4 - 6)	مافي Overlap بينهم
دراسة (٢)	5kg	(-20 - 20)	
دراسة (٣)	5 kg	(-80 - 80)	

⇓ الجدول confidance interval ⇐ (inconsistancy.)

مثال أوضح

15	(20 - 30)	⇐ مافي بينهم (overlap)
8	(1 - 16)	

الجدول overlap minimal مافي بينهم أي علاقة

⇐ لكن لو كانت ⇒

1 - 3
3 - 7
7 - 9
⇐ Overlap بينهم متشابهات

الأرقام والفترات داخلات ببعضها (maximal ovarlap) ⇒ Consistancy.

ما [١٢] Statistical test of [**heterogenicity**] ⇐ كل ما كانت الدراسات ↑ Heterogenicity ↑ inconsistant

⇓ الاختلاف بالدراسات *

مثلاً تخفيف الوزن ⇐
- الدراسة على السيدات [١]
- الدراسة على الأطفال [٢]
- الدراسة على الرجال [٣]

⇐ هاي الدراسة Hetergenicity

⇐ إذا كانت الدراسات الثلاث على السيدات بين عمر (٤٠ - ٦٠) سنة ما هاي **Homogenicity.** ⇐ هاي أحسن ⇐ ↑ Homogenicity ↑ consistancy.

* Univalidated outcome analysis :-

- قياس الطول ≡ الوحدة [Cm] ⇐ يعني Valide measure to length.
- الوزنه ≡ [kg] ⇐ valide measure to weight

* ⇐ لو درست أو شفت دراسة كاتبة فيها :-

الي أخذوا antibiotic → بعد أسبوع صاروا يمشوا !!

صار في بين فاعلية (antibiotic و المشي) أي علاقة

↳ هاي اسمها **Unvalidated measure.** ⇐ في شي أبحاث بتترك الجوهر تاع البحث وبتشتغل على هاد الاشي

↓

مثلاً حكوا انه عدد الناس الي اشتروا الصيدلي (70%)

↳ هاي Unvalide measure to effecacy of drug. (A) ⇐

** ⇐ لذلك Outcomes للأبحاث (related to input)

* ⇒ مثلاً

عامل بحث على الحمية السكري → outcome :→ هاي الدراسات

إنه هاي الأدوية ممكن تزيد أو تقلل الوزنه ⇐ هاي (*) ⇐ (Unvalide measure.)

→ Valide measure (*) to these Drug ⇐ ↓ Sugar in Blood.

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(5) ⇒ impresion ⇐ مثلاً 5 CI (3 - 7)

(5) ⇐ هاي جاي بالنص (-10 - 10) ⇓ أعم CI 95%

⇐ CI 95% mean = 5 أعم

دراسة (1) → (more presise)

دراسة (2)

* (Confidance interval => mean ± Standerd Diviation)

وكم بحث => Precise :: الدراسة الفردية قدية الهي

:: الدراسة الجماعية قدية الهي . Consistancy

في عنوانها الجدول بسبب الحادي يمهما

What can raise confidence?

for observation studies

* ريليفو ١٦

- **Large treatment effect**
  - Can rate up one level (twofold increase or decrease in [Odds ratio (OR) or Relative Risk (RR).]
  - Up two levels (if fivefold differences in OR , RR)

Note: (OR) and RR are measure of association between an exposure and an outcome.

The OR represents the *odds* that an outcome will occur given group compare to other group.

The RR: probability of an event occurring in one group compared to the probability of an event occurring in the other group.

تستخدم حتى نقدر نحكم على قوة الدليل العلمي بالدراسات وخاصة [Observation] ⇓ Study بعطيه قوة

- **Dose response relationship** ⇐ دليل على علاقة أو تأثير بالنتيجة ...
- **Common criteria** ⇐ مشترك في التعميم
  - everyone used to do badly
  - almost everyone does well
  - quick action

indirectness 12 كبير إذا اختلفوا ⇐

Ref1. chapter 7_Thank you 27

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*

[*] indirectness => كل ما كانت الدراسات تقارن أشياء نفسه بالإمباشرة وبرايتة (Direct) مباشرة ⇐ تابع للسلايد ٣٦

يشمل Similar يكونوا I Patient intervention outcome. ⇐ إذا تحققوا لهم => ↑ Directness

Certainty assessment criteria

Study Design	Confidence in estimates	Lower if	Higher if
Randomized trials	High	Risk of bias -1 Serious -2 Very serious	Large Effect +1 Large +1 Very large
	Moderate	Inconsistency -1 Serious -2 Very serious	Dose response +1 Evidence of a gradient
Observational studies	Low	Indirectness -1 Serious -2 Very serious Imprecision -1 Serious -2 Very serious	
	Very Low	Publication bias -1 Likely -2 Very likely	

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إذا لم ادرس ساعة ولا عشر ساعات ونفس العلاقة صحيحة صارت موضع شك

(*) Dose response relationship —> أعطيت الانسولين ونزل السكر بمقدار 1 Unit

مثال

⇓ علاقة طردية = علاقة عكسية

↑ الانسولين ↑ نزول السكر

(*) في علاقة طردية سببية قوية ⇐ إذا درست ساعة ← بتجيب 20 ساعتين ← 25 ⇐ أخرته في الثبات

Odds ratio :→

ما

عدد الحالات الي قيد الدراسة

٢٤ طالب → يعني ٢٤ - ٦ = (١٨) ⇐ (ما نجح)

↓

odds for succes ⇒ ٦ منهم نجح →

odds ratio = عدد الي نجح / عدد الي ما نجح

$= \frac{6}{18} = \frac{1}{3}$

relative risk :→

ما = عدد الي نجح / العدد الكلي = $\frac{6}{24}$ = 0.25

مش شروط تكون دوا يعني ⇐

نجح عندي

بدي 2 comparing groups

Treatment group

مش أعطيهم ناجح

Control group

∴ لذلك

Odds ratio — relative risk

⇐ بقسمهم على بعض

Odds ratio — relative risk

↓ هي للمقارنة مش شرط إنها Drug

⇒

هاد مش كاع

- odds ratio 6/18
- relative 6/24

* لو حكيت عندي مادة صعبة وحكيت انه نجح

↓ هاد لـ Treatment group { بدي (Control group)

quality of the study level

= (1)

إذا كانت * ⇐ Odds ratio أو relative risk بمقدار ⇒ • (1 أو 2)

= (2) أقوى بـ two level

• (3 أو 4 أو 5) ⇐ (أغلب الأبحاث بتعتمد لحد (3))

x ⇐ مثلاً = واحد طلع معه قيمة odds ratio = 3.5 ⇐ معناها قوة هالبحث الدراسة زد تزيد = (2) level

relative resk = 1.3 ⇐ معناها بتزيد قوة الدراسة بمقدار (One level) ⇐

هاد أفضل ⇐ (observation studies) بطبيعتها هي صنفية يُفضل اخذها level (2) كحد أدنى

(*) ⇐ كل ما كانت Odds ratio أو relative resk ⇐ كل ما كانت هاد أفضل

إذا كانت ⇐ odds ratio أكبر من 5 ⇐ معناها الدولة غنية ؟

rational Drug use.

EXAMPLE: Beta blockers in non-cardiac surgery

Quality Assessment							Summary of Findings		
Outcome	Number of participants (studies)	Risk of Bias	Consistency	Directness	Precision	Publication Bias	Quality	Relative Effect (95% CI)	Absolute risk difference
Myocardial infarction	10,125 (9)	No serious limitations	No serious imitations	No serious limitations	No serious limitations	Not detected	High	0.71 (0.57 to 0.86)	1.5% fewer (0.7% fewer to 2.1% fewer)
Mortality	10,205 (7)	No serious limitations	Possibly inconsistent	No serious limitations	Imprecise	Not detected	Moderate or low	1.23 (0.98 – 1.55)	0.5% more (0.1% fewer to 1.3% more)
Stroke	10,889 (5)	No serious limitaions	No serious limitations	No serious limitations	No serious limitations	Not detected	High	2.21 (1.37 – 3.55)	0.5% more (0.2% more to 1.3% more0

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Strength of Recommendation

- strong recommendation
  - benefits clearly outweigh risks/hassle/cost
  - risk/hassle/cost clearly outweighs benefit

- what can downgrade strength?
- low confidence in estimates
- close balance between up and downsides

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