Kritična analiza strokovne literature

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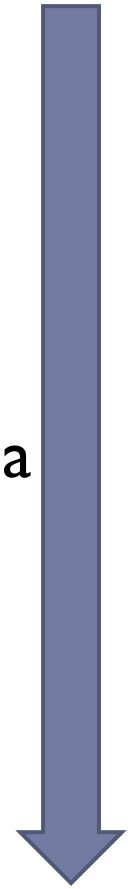
Proces odgovora na klinično vprašanje

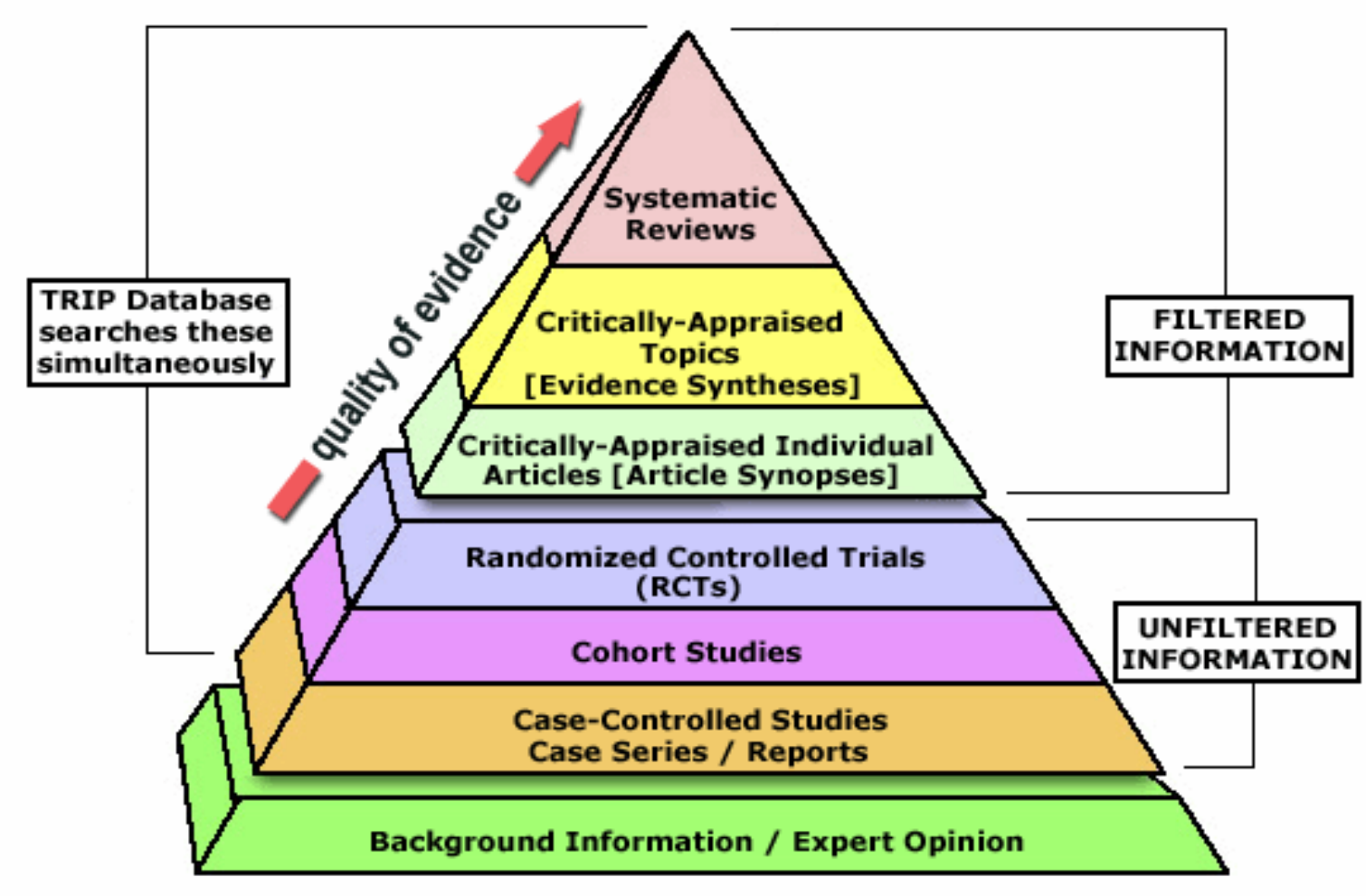
- Klinični scenarij
- Oblikovanje kliničnega vprašanja (PICO)
- Iskanje literature
- **Kritična analiza virov (npr. člankov)**
- Predstavitev ključnih virov
- Prenos na dokazih temelječih ugotovitev v prakso (na klinični primer)



Različni viri

- **Primarni viri**
  - Enostavni primarni viri (članki o diagnostiki, terapiji in prognozi)
  - Sestavljeni primarni dokumenti: Metaanalize, sistematični pregledi literature, smernice
- **Sekundarni viri** (povzemajo primarne vire):
  - Učbeniki
  - Zborniki
  - Časopisni članki
  - …

Piramida dokazov

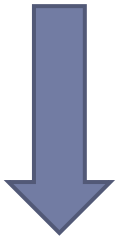


Najboljši dokazi za posamezen tip kliničnega vprašanja

Level	Treatment	Prognosis	Diagnosis
I	*Systematic Review of …*	*Systematic Review of …*	*Systematic Review of …*
II	Randomised trial	Inception Cohort	Cross sectional
III			

Kritična analiza virov

- Naslov
- Izvleček
- **Celotno besedilo**



Naslov in izvleček sta ključna, ker nas vodita k odločitvi, ali bomo članek sploh pridobili in ga ocenili!

Elementi primarnega dokumenta

IMRAD

- Naslov
- Izvleček/Abstract
- **U**vod
- Namen, cilji, hipoteza
- **M**etode in preiskovanci
- **R**ezultati
- **R**azprava
- Sklepi in predlogi
- Zahvala
- Finančna podpora
- Literatura
- Priloge

Kaj ocenjujemo?

1. Relevantnost (ali članek odgovarja na naše klinično vprašanje?)
2. Veljavnost (metode/izbor preiskovancev)
3. Predstavitev rezultatov
4. Zaključke

Ocenjevanje članka o terapiji - relevantnost

1. V čem je uporabnost rezultatov?	
2. Je članek relevanten za primarno raven?	
3. Ali bo vplival na moje odločanje v ambulanti?	

Ocenjevanje članka o terapiji- veljavnost (metode/preiskovanci)

4. Ali tip razikave ustreza raziskovalnemu vprašanju?	
5. Če je šlo za randomizirano raziskavo: ali je bila randomizacija ustrezna ?	
6. Ali je razvidno, kako so izbirali bolnike?	
7. Je velikost vzorca zadostna?	
8. Je bil odstotek odgovorov zadosten?	
9. Ali so uporabljene statistične metode primerne/zadostno opisane	

Ocenjevanje članka o terapiji- predstavitev rezultatov

10. Ali je prikaz rezultatov ustrezen (NNT, ARR, tabele) ali zavajajoč (RRR)	
11. Ali so podani intervali zaupanja?	

Ocenjevanje članka o terapiji - zaključki

12. Ali se sklepi nanašajo na rezultate?	
13. Ali se avtor(ji) zaveda(jo) omejitev in možnih prostranosti?	
14. Ali je podana praktična uporabnost/ideje za nadaljnje raziskovanje	

Meta-analiza in sistematični pregled literature

- **Meta-analiza** je statistična metoda pregledovanja in kombiniranja rezultatov več neodvisnih raziskav
- **Sistematični pregledi so natančni povzetki najboljših dokazov,** ki se nanašajo na določena vprašanja – so metaanalize v širšem smislu (Cochrane Collaboration Centres, PRIZMA kriteriji)

literature/metaanaliza: pregled literature

Razpr. 1. *Razlika med metaanalizo (sistematičnim pregledom) in pripovedovalnimi pregledi (povzeto po 9).*

Table 1. *Differences between Meta-analysis (Systematic Reviews) and Narrative Reviews.*

Značilnost Feature	Pripovedni neformalni pregledi Narrative Review	Metaanaliza (Sistematični pregled) Meta-analysis (Systematic Review)
Namen Question	zelo široki often broad in scope	natančno opredeljena vprašanja often a focused clinical question
Viri in način pregledovanja Sources and search	niso natančno določeni, velikokrat podvrženi publikacijski neobjektivnosti not usualy specified, potentially biased	obsežni viri in opredeljena strategija pregledovanja comprehensive sources and explicit search strategy
Izbira Selection	ni natančno določena, subjektivna not usualy specified, potentially biased	na določenih merilih temelječa izbira, podvržene vse študije criterion-based selection, uniformly applied
Ocena Appraisal	variabilna variable	stroga kritična ocena rigorous critical appraisal
Sinteza Synthesis	kvalitativna qualitative summary	kvantitativna (metaanaliza) quantitative (meta-analysis)
Povzetki Inferences	včasih dokazno naravnani sometimes evidence-based	po navadi dokazno naravnani usually evidence-based

Kako“beremo“ sistematični pregled oz. Metaanalizo

Najprej:

- Relevantnost za naše klinično vprašanje
- Ustreznost metod

Nato:

Ocena rezultatov:

- Kako verjetno je, da je da se v uporabljenih virih pojavljajo pristranosti?
- Ali so predstavljeni intervali zaupanja
- Ali so rezultati študij enotni
- Kako natančni so rezultati (kako širok je interval zaupanja)
- Ali obstajajo razlogi, ki bi vplivali na interval zaupanja

Prikaz in interpretacija rezultatov

JAMA 2014; 312(2):171-179.

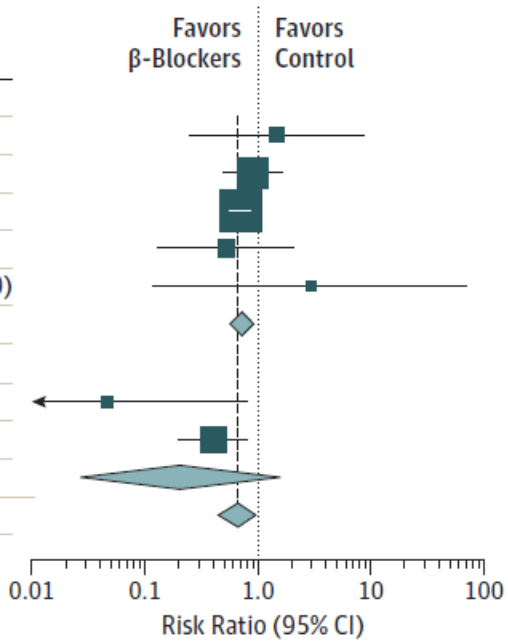
Figure. Results of a Meta-analysis of the Outcomes of Nonfatal Infarction, Death, and Nonfatal Stroke in Patients Receiving Perioperative β-Blockers

A Nonfatal myocardial infarction

Source	β-Blockers Events, No.	β-Blockers Total, No.	Control Events, No.	Control Total, No.	RR (95% CI)
Low risk of bias					
DIPOM	3	462	2	459	1.49 (0.25-8.88)
MaVS	19	246	21	250	0.92 (0.51-1.67)
POISE	152	4174	215	4177	0.71 (0.58-0.87)
POBBLE	3	55	5	48	0.52 (0.13-2.08)
BBSA	1	110	0	109	2.97 (0.12-72.19)
Subtotal (I^2 = 0%; P = .70)					0.73 (0.61-0.88)
High risk of bias					
Poldermans	0	59	9	53	0.05 (0.00-0.79)
Dunkelgrun	11	533	27	533	0.41 (0.20-0.81)
Subtotal (I^2 = 57%; P = .13)					0.21 (0.03-1.61)
Overall					0.67 (0.47-0.96)

I^2 = 29%; P = .21

Interaction test between groups, P = .22



B Death

Prikaz in interpretacija rezultatov

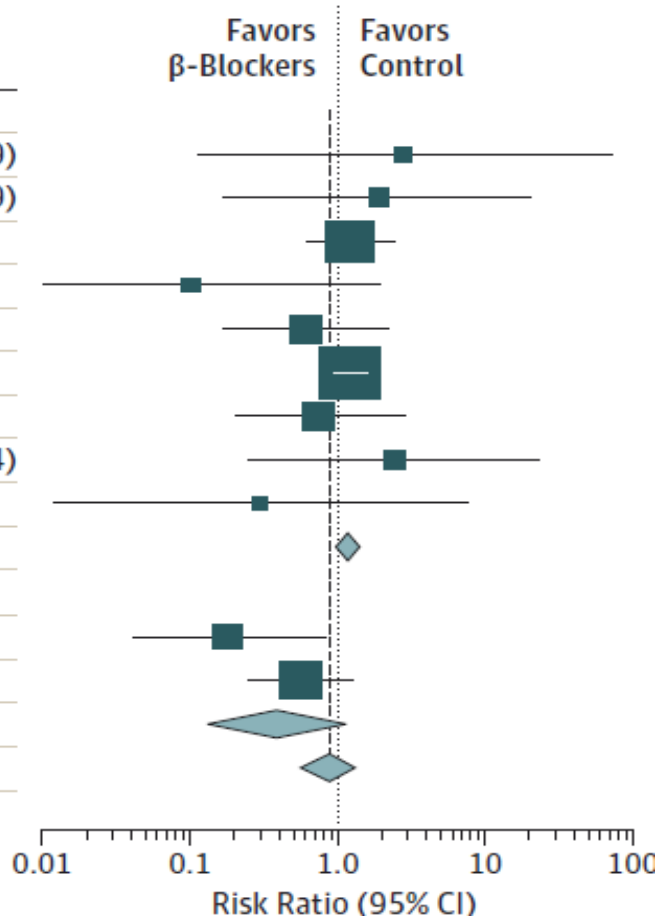
JAMA 2014; 312(2):171-179.

B | Death

Source	β-Blockers Events, No.	β-Blockers Total, No.	Control Events, No.	Control Total, No.	RR (95% CI)
Low risk of bias					
BBSA	1	110	0	109	2.97 (0.12-72.19)
Bayliff	2	49	1	50	2.04 (0.19-21.79)
DIPOM	20	462	15	459	1.32 (0.69-2.55)
MaVS	0	246	4	250	0.11 (0.01-2.09)
Neary	3	18	5	20	0.67 (0.19-2.40)
POISE	129	4174	97	4177	1.33 (1.03-1.73)
Mangano	4	99	5	101	0.82 (0.23-2.95)
POBBLE	3	55	1	48	2.62 (0.28-24.34)
Yang	0	51	1	51	0.33 (0.01-8.00)
Subtotal (I^2 = 0%; P = .68)					1.27 (1.01-1.60)
High risk of bias					
Poldermans	2	59	9	53	0.20 (0.05-0.88)
Dunkelgrun	10	533	16	533	0.63 (0.29-1.36)
Subtotal (I^2 = 44%; P = .18)					0.42 (0.15-1.23)
Overall					0.94 (0.63-1.40)

I^2 = 30%; P = .16

Interaction test between groups, P = .04



Prikaz in interpretacija rezultatov

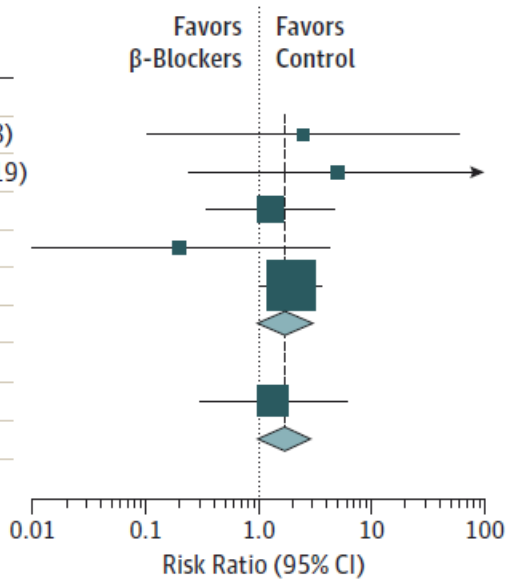
JAMA 2014; 312(2):171-179.

C | Nonfatal stroke

Source	β-Blockers Events, No.	β-Blockers Total, No.	Control Events, No.	Control Total, No.	RR (95% CI)
Low risk of bias					
POBBLE	1	53	0	44	2.50 (0.10-59.88)
DIPOM	2	462	0	459	4.97 (0.24-103.19)
MaVS	5	246	4	250	1.27 (0.35-4.67)
Yang	0	51	2	51	0.20 (0.01-4.07)
POISE	27	4174	14	4177	1.93 (1.01-3.68)
Subtotal (I^2 = 0%; P = .60)					1.73 (1.00-2.99)
High risk of bias					
Dunkelgrun	4	533	3	533	1.33 (0.30-5.93)
Overall					1.67 (1.00-2.80)

I^2 = 0%; P = .71

Interaction test between groups, P = .75



Prikaz in interpretacija rezultatov

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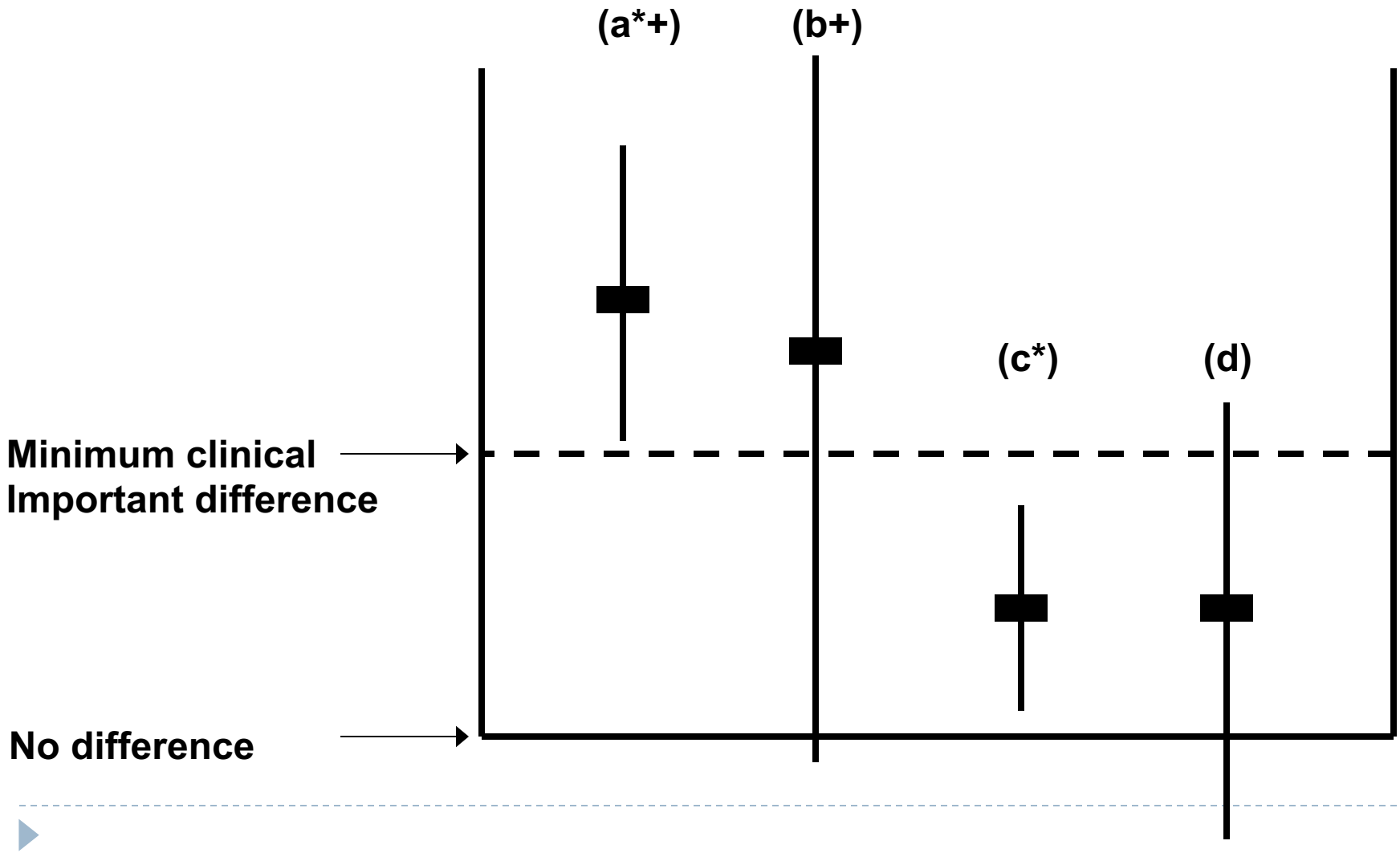
Table. Evidence Summary of the Perioperative β-Blockers Question

Outcome	No. of Participants (Trials)	Confidence	Relative Effect (95% CI)	Risk Difference per 1000 Patients[a]
Nonfatal myocardial infarction	10 189 (5)	High	0.73 (0.61-0.88)	14 fewer (6 fewer to 20 fewer)
Stroke	10 186 (5)	Moderate	1.73 (1.00- 2.99)	2 more (0 more to 6 more)
Death	10 529 (9)	Moderate	1.27 (1.01-1.60)	6 more (0 more to 13 more)

Ali gre za za statistično in/ali klinično pomemben rezultat?



Klinična smernica

- Smernica je:

sistematično zbrano in oblikovano gradivo o ustrezni oskrbi na določenem področju dela.

Namen smernic (priporočil)

- Oblikovati z dokazi podprta priporočila in jih približati uporabnikom
- Olajšati in narediti odločitev bolj objektivno (poenotenje)
- Standard za oceno strokovnosti dela
- Razmejitve dela med nivoji (družinski zdravnik-klinični specialist)
- Izobraževanje bolnikov in strokovnjakov o načelih dobre prakse
- Povečanje stroškovne učinkovitosti
- Orodje za izvajanje zunanje kontrole

Zakaj uporabljati smernice (priporočila)

- Zmanjšanje razlik pri delu
- Zmanjšanje negotovosti pri odločanju
- Olajšan prenos novega znanja
- Zagotovljena uporaba najboljšega razpoložljivega znanja
- Vir kazalcev, meril in smernic
- Predstavljajo želeno raven kakovosti

Na kaj moramo biti pozorni pri uporabi smernic

- So odraz mnenja strokovnjakov in ne odraz z dokazi podprte medicine
- So odraz povprečja in ne dobre prakse
- Omejujejo individualen pristop
- Smernice (mednarodne, nacionalne) niso ustrezne za okolje, kjer naj bi jih uporabljali
- Smernice, oblikovane na sekundarnem nivoju niso uporabne za primarni nivo
- Zloraba smernic v politične namene (določenim strokovnjakom dajejo veliko moč)
- Zastarelost smernic ovirajo uvajanje novih pristopov k zdravljenju

Dva elementa ocene – 1. nivo dokazov

Table 1.2 Level of evidence

Level of evidence A	**Data derived from multiple randomized clinical trials or meta-analyses.**
Level of evidence B	**Data derived from a single randomized clinical trial or large non-randomized studies.**
Level of evidence C	**Consensus of opinion of the experts and/or small studies, retrospective studies, registries.**

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Dva elementa ocene – 2. stopnja priporočil

Classes of recommendations

Classes of recommendations	Definition	Suggested wording to use
Class I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Is recommended/is indicated
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.	
Class IIa	*Weight of evidence/opinion is in favour of usefulness/efficacy.*	Should be considered
Class IIb	*Usefulness/efficacy is less well established by evidence/opinion.*	May be considered
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.	Is not recommended

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Stopnja dokazov

- A: Priporočilo podpira več randomiziranih raziskav ali meta-analiza
- B: Priporočilo podpira ena randomizirana raziskava ali velike nerandomizirane raziskave
- C: Priporočilo podpirajo mnenja strokovnjakov, manjše retrospektivne raziskave, registri...

Stopnja priporočil na osnovi teže dokazov

- **Razred 1:** Dokazi, da je zdravljenje (postopek) koristen in/ali učinkovit
- **Razred 2**: nasprotni dokazi in/ali razhajajoča mnenja glede koristnosti
- **Razred 2a**:Količina dokazov/mnenj je v prid koristi/učinkovitosti
- **Razred 2b**: Koristnost/učinkovitost je manj podprta z dokazi
- **Razred 3**: Dokazi in/ali soglasje, da zdravljenje ni koristno in je lahko v posameznih primerih škodljivo

Primer- zdravljenje srčnega popuščanja

Recommendations	Class [a]	Level [b]	Ref [c]
Diuretics			
Diuretics are recommended in order to improve symptoms and exercise capacity in patients with signs and/or symptoms of congestion.	I	B	178, 179
Diuretics should be considered to reduce the risk of HF hospitalization in patients with signs and/or symptoms of congestion.	IIa	B	178, 179
Angiotensin receptor neprilysin inhibitor			
Sacubitril/valsartan is recommended as a replacement for an ACE-I to further reduce the risk of HF hospitalization and death in ambulatory patients with HFrEF who remain symptomatic despite optimal treatment with an ACE-I, a beta-blocker and an MRA[d]	I	B	162
I_f-channel inhibitor			
Ivabradine should be considered to reduce the risk of HF hospitalization and cardiovascular death in symptomatic patients with LVEF ≤35%, in sinus rhythm and a resting heart rate ≥70 bpm despite treatment with an evidence-based dose of beta-blocker (or maximum tolerated dose below that), ACE-I (or ARB), and an MRA (or ARB).	IIa	B	180
Ivabradine should be considered to reduce the risk of HF hospitalization and cardiovascular death in symptomatic patients with LVEF ≤35%, in sinus rhythm and a resting heart rate ≥70 bpm who are unable to tolerate or have contra-indications for a beta-blocker. Patients should also receive an ACE-I (or ARB) and an MRA (or ARB).	IIa	C	181
ARB			
An ARB is recommended to reduce the risk of HF hospitalization and cardiovascular death in symptomatic patients unable to tolerate an ACE-I (patients should also receive a beta-blocker and an MRA).	I	B	182
An ARB may be considered to reduce the risk of HF hospitalization and death in patients who are symptomatic despite treatment with a beta-blocker who are unable to tolerate an MRA.	IIb	C	-

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Primer- zdravljenje srčnega popuščanja

Recommendations	Class [a]	Level [b]	Ref [c]
Secondary prevention An ICD is recommended to reduce the risk of sudden death and all-cause mortality in patients who have recovered from a ventricular arrhythmia causing haemodynamic instability, and who are expected to survive for >1 year with good functional status.	I	A	223–226
Primary prevention An ICD is recommended to reduce the risk of sudden death and all-cause mortality in patients with symptomatic HF (NYHA Class II–III), and an LVEF ≤35% despite ≥3 months of OMT, provided they are expected to survive substantially longer than one year with good functional status, and they have:			
• IHD (unless they have had an MI in the prior 40 days – see below).	I	A	149, 156, 227
• DCM.	I	B	156, 157, 227
ICD implantation is not recommended within 40 days of an MI as implantation at this time does not improve prognosis.	III	A	158, 228
ICD therapy is not recommended in patients in NYHA Class IV with severe symptoms refractory to pharmacological therapy unless they are candidates for CRT, a ventricular assist device, or cardiac transplantation.	III	C	229–233
Patients should be carefully evaluated by an experienced cardiologist before generator replacement, because management goals and the patient's needs and clinical status may have changed.	IIa	B	234–238
A wearable ICD may be considered for patients with HF who are at risk of sudden cardiac death for a limited period or as a bridge to an implanted device.	IIb	C	239–241

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Zaključek

- Informacij je ogromno, njihova kakovost in uporabnost pa različna
- Analiza kakovosti članka zahteva nekaj vaje!
- Če obstajajo najboljši možni dokazi (sistematični pregled literature/metaanaliza) izberite le te
- Naslednja stopnja je prenos najboljšega razpoložljivega znanja na našega pacienta – potrebno je ločiti med statistično značilnostjo in klinično uporabnostjo!