TARTU ÜLIKOOL

Sissejuhatus GRADE metoodikasse

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Eriline tänu: Holger Schünemann ja GRADE working group

www.gradeworkinggroup.org

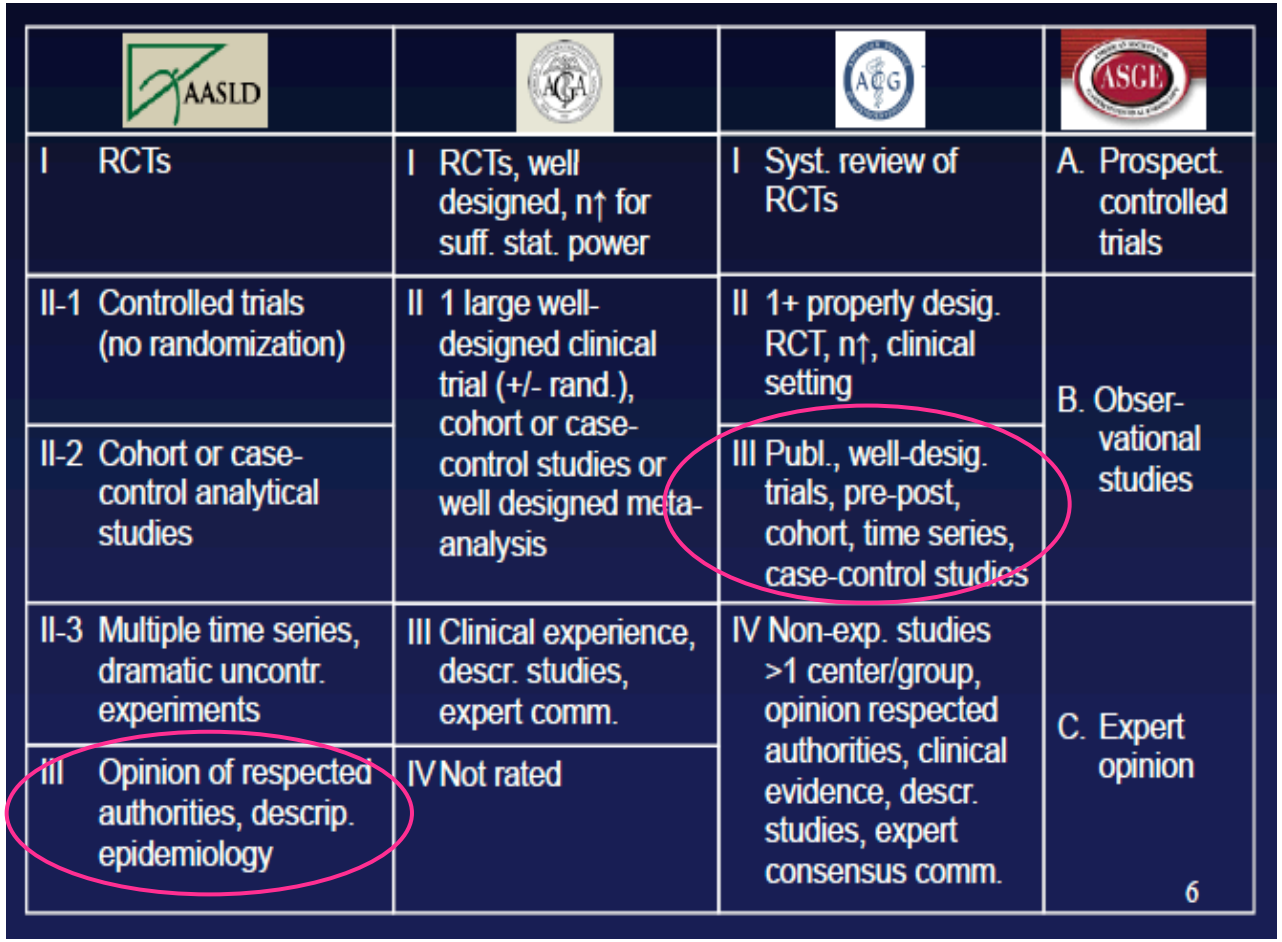
Kaja-Triin Laisaar

TÜ peremeditsiini ja rahvatervishoiu instituut

kaja-triin.laisaar@ut.ee

Tallinn 17.02.2017

Erinevad tõendusmaterjali hindamise süsteemid



AASLD	AGA	ACG	ASGE
I RCTs	I RCTs, well designed, n↑ for suff. stat. power	I Syst. review of RCTs	A. Prospect. controlled trials
II-1 Controlled trials (no randomization)	II 1 large well-designed clinical trial (+/- rand.), cohort or case-control studies or well designed meta-analysis	II 1+ properly desig. RCT, n↑, clinical setting	B. Obser-vational studies
II-2 Cohort or case-control analytical studies		III Publ., well-desig. trials, pre-post, cohort, time series, case-control studies	
II-3 Multiple time series, dramatic uncontr. experiments	III Clinical experience, descr. studies, expert comm.	IV Non-exp. studies >1 center/group, opinion respected authorities, clinical evidence, descr. studies, expert consensus comm.	C. Expert opinion
III Opinion of respected authorities, descrip. epidemiology	IV Not rated		

6

hindama − ingl *grade*

AASLD – American Association for the Study of Liver Diseases
AGA – American Gastroenterological Association
ACG – American College of Gastroentrology
ASGE – American Society for Gastrointestinal Endoscopy

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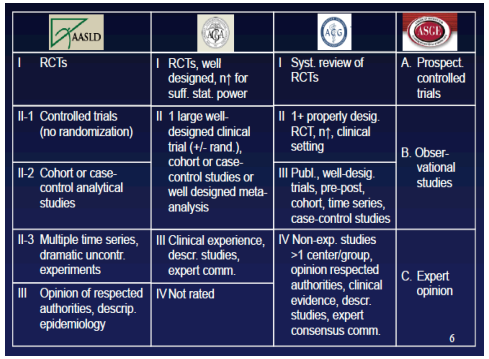
Erinevad tõendusmaterjali hindamise süsteemid

- tõenduse kvaliteet *versus* kliinilise soovituse tugevus?
- kindel raamistik?
- (hindamis)kriteeriumid selged ja läbipaistvad?



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GRADE metoodika

1. (ravi)juhendi koostamise protsess on põhjalik ja intensiivne
2. paigas on kindel kontseptuaalne* raamistik
3. (hindamis)kriteeriumid on põhjalikud** ja läbipaistvad
4. tõendust hinnatakse iga kliinilise küsimuse iga olulise tulemi kohta ning kokkuvõtvalt
5. kasutajaskond (organisatsioonid, asutused) järjest laieneb

* mõisteline, ingl *conceptual*
** kõikehõlmavad, ingl *comprehensive*

GRADE: tulemite valimine

Patsiendi seisukohast olulised tulemid!

Ühe kliinilise küsimuse kohta max 7 tulemit

Iga tulemusi suhteline olulisus (kliinilise otsuse langetamisel) 9-pallisel skaalal:

- 1−3 ebaoluline
- 4−6 oluline
- 7−9 kriitilise tähtsusega / väga oluline

Tulemid, mille alusel saab vastata kliinilisele küsimusele

Systematic review

Formulate question

Select outcomes

Rate importance

P
I
C
O

Outcome — Critical

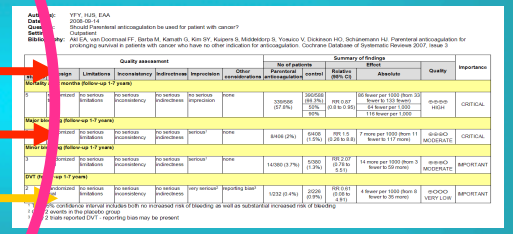
Outcome — Critical

Outcome — Important

Outcome — Not important

Outcomes across studies

Create evidence profile with GRADEpro



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Moderate
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Very low

RCT start high, obs. data start low

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Formulate recommendations:
- For or against (direction)
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By considering:
- ❑ Quality of evidence
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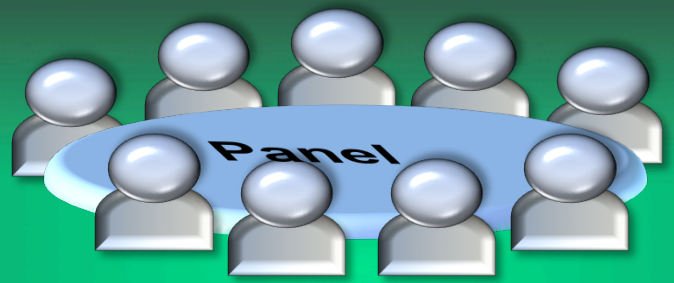
- ❑ Values and preferences

Revise if necessary by considering:
- ❑ Resource use (cost)



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of ***critical*** outcomes

- "We recommend using…"
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- "We suggest against using…"

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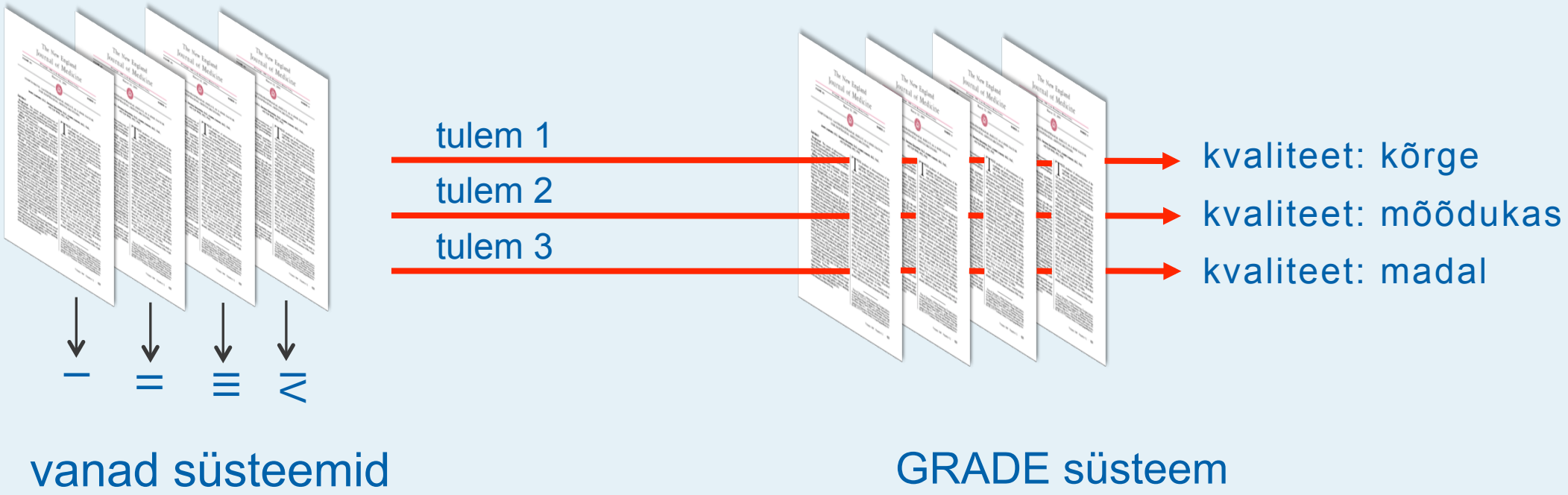
GRADE: tõendust vaadataks tulemite kaupa



Tõendus – et vastata kliinilisele küsimusele

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GRADE: etapid

1. **Tõenduse kvaliteedi taseme hindamine** (4 taset)
    - kõrge
    - mõõdukas
    - madal
    - väga madal

2. **Kliiniliste soovituste liigi hindamine** (2 liiki)
    - tugev
    - nõrk

hindama − ingl *to grade*

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1.1. GRADE: tõenduse kvaliteedi mõiste

Mida kvaliteetsem on tõendus, seda kindlamad me saame olla, et hinnang sekkumise mõjule on tõene

The quality of evidence reflect the extent of our confidence that the estimates of the effect are correct

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1.2. GRADE: tõenduse kvaliteedi tasemed

Tõenduse kvaliteet	Määratlus
⊕⊕⊕⊕ **kõrge**	Oleme väga kindlad, et sekkumise tegelik mõju on väga lähedane uuringutes antud hinnangule
⊕⊕⊕◯ **mõõdukas**	Oleme mõõdukalt kindlad, et sekkumise tegelik mõju on lähedane uuringutes antud hinnangule, ent see võib ka oluliselt erineda
⊕⊕◯◯ **madal**	Me ei ole kindlad sekkumise mõjule antud hinnangus, tegelik mõju võib hinnangust oluliselt erineda
⊕◯◯◯ **väga madal**	Me ei ole üldse kindlad sekkumise mõjule antud hinnangus, tegelik mõju on tõenäoliselt hinnangust oluliselt erinev

GRADE: tõenduse kvaliteedi kriteeriumid

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Uuringukavand	Tõenduse kvaliteedi algne tase	Langeta tõenduse kvaliteedi taset, kui uuringutes	Tõsta tõenduse kvaliteedi taset, kui uuringutes	Tõenduse kvaliteedi lõplik tase
randomiseeritud kontrollitud uuring	kõrge →	esinevad piirangud – nihke võimalus(ed) tulemused on • mittekooskõlalised • kaudsed • ebatäpsed • avaldatud valikuliselt	mõju/seos on suur esineb annus-vastus seos	kõrge
			kõik tõenäolised segavad tegurid ja nihked • oleks vähendanud sekkumise mõju • kirjeldavad võimalikke põhjuseid, kui sekkumise mõju ei täheldatud	mõõdukas
vaatlusuuring	madal →			madal
				väga madal

TARTU ÜLIKOOL 1632

1.4. GRADE: tõenduse profiil (ingl *evidence profile*)

Author(s): Elie Akl & Holger Schunemann **Date:** 2008-09-11
Question: Should parenteral anticoagulation be used in prolonging survival of patients with cancer? **Settings:** Outpatient
Bibliography: EA Akl, FF van Doormaal, M Barba, G Kamath, SY Kim, S Kuipers, S Middeldorp, V Yosuico, H Dickinson, HJ Schünemann. Parenteral anticoagulation for prolonging survival in patients with cancer who have no other indication for anticoagulation. CDSR Reviews. 2007 Issue 3

Quality assessment							Summary of findings					
							No of patients		Effect		Quality	Importance
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	anticoagulation	control	Relative (95% CI)	Absolute		
Survival at 12 months (study follow up)												
5	randomised trials	no serious limitations[1]	no serious inconsistency	no serious indirectness[2]	no serious imprecision	none	339/586 (57.8%)	390/588 (60%)	RR 0.87 (0.8 to 0.95)	78 fewer per 1000 (from 30 to 120 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
Survival (overall - study follow up at 24 to 84 months)												
5	randomised trials	no serious limitations[1]	no serious inconsistency	no serious indirectness	no serious imprecision	none	477/586 (81.4%)	520/588 (85%)	HR 0.77 (0.65 to 0.91)	82 fewer per 1000 (from 28 to 141 fewer)	⊕⊕⊕⊕ HIGH	CRITICAL
DVT												
2	randomised trials	no serious limitations[1]	no serious inconsistency	no serious indirectness	very serious[3]	reporting bias[4]	1/232 (0.4%)	2/226 (4%)	RR 0.61 (0.08 to 4.91)	16 fewer per 1000 (from 37 fewer to 156 more)	⊕OOO VERY LOW	CRITICAL
Major bleeding												
3	randomised trials	no serious limitations[1]	no serious inconsistency	no serious indirectness	serious[3]	reporting bias[5]	8/406 (2%)	6/408 (1.5%)	RR 1.50 (0.26 to 8.8)	7 more per 1000 (from 11 fewer to 117 more)	⊕⊕OO LOW	CRITICAL
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[1] Unclear concealment in one of the five trials did not lead to downgrading the quality of evidence.
[2] The studies used different LMWHs but indirectness is not likely given the similiarity in results across studies.
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GRADE's software for Summary of Findings tables, Health Technology Assessment and Guidelines

LOG IN / SIGN UP

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I
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Outcome — Critical

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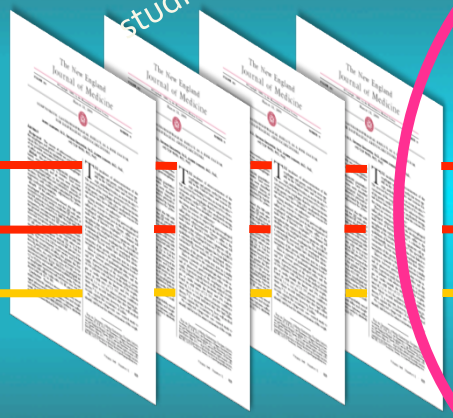

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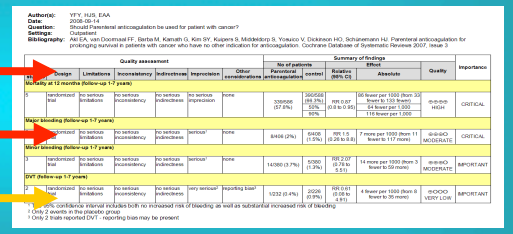

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Systematic review

Guideline development

Formulate recommendations:

- For or against (direction)
- Strong or weak (strength)

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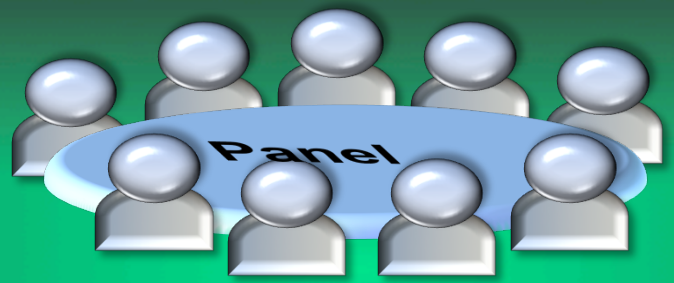

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2. Kliinilise soovituse liik: tugev vs nõrk

Soovituse tugevus näitab seda, mil määral saab olla kindel, et soovituse järgimisest tulenevad soovitud mõjud ületavad soovimatuid mõjusid

Soovitus võib olla nii sekkumise poolt kui ka selle vastu

2.1. Kaalule sekkumise soovitud ja soovimatud mõjud

- suremusele
- haiguse ja selle ravi kestusele
- ravikoormusele
- ravikulule
- elukvaliteedile

jmt-le

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2.3. Kliinilise soovituse tugevust mõjutavad tegurid

- tõenduse kvaliteet ingl *quality of evidence*
- soovitud ja soovimatute mõjude (kasu-kahju) tasakaal ingl *balance between desirable and undesirable effects*
- väärtushinnangud ja eelistused ingl *values and preferences*
- kulud (ressursikasutus) ingl *costs (resource allocation*)
- õigluse (võrdsuse) põhimõte ingl *equity*
- vastuvõetavus ingl *acceptability*
- teostatavus ingl *feasibility*

2.4. Tugeva soovituse tähendus

- **patsientidele**: valdav enamik* sellises olukorras olevaid inimesi tahaks soovitatud sekkumist ning ainult vähesed ei tahaks
- **tervishoiutöötajatele**: valdava enamiku* patsientide ravis peaks kasutama soovitatud sekkumist
- **tervishoiukorraldajatele**: soovitust on võimalik enamikes olukordades rakendada

** ≥ 85%*

2.5. Nõrga soovituse tähendus

- **patsientidele**: enamik sellises olukorras olevaid inimesi tahaks soovitatud sekkumist, kuid paljud siiski mitte
- **tervishoiutöötajatele**: peab olema valmis aitama patsiente sellise otsuse langetamisel, mis oleks kooskõlas nende (endi) väärtushinnangutega; valmis jagatud vastutusega otsustusprotsessiks
- **tervishoiukorraldajatele**: on vajadus põhjaliku arutelu ja huvitatud osapoolte kaasamise järele

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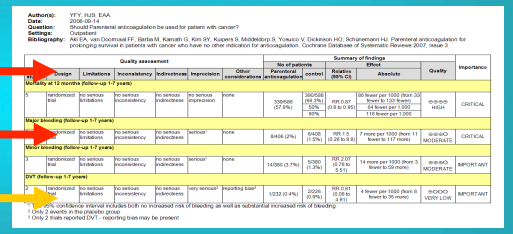

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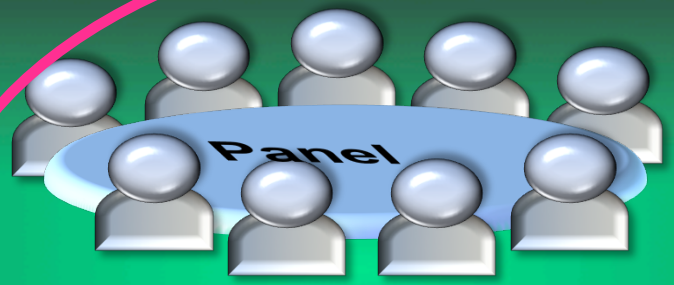

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