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Using the GRADE Methodology in Clinical Practice Guidelines: Theory and Practice

Использование методологии GRADE в клинических рекомендациях: теория и практика

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Janne Estill – Declaration of conflicts of interest (and research interests in general!)

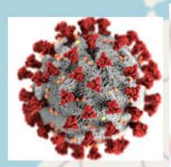
EPIDEMIOLOGY CONSULTING

UNIVERSITÉ DE GENÈVE

$$\frac{dS}{dt} = bN - \beta\frac{SI}{N} - \mu S$$

$$\frac{dI}{dt} = \beta\frac{SI}{N} - (\gamma + \mu + \delta)I$$

$$\frac{dR}{dt} = \gamma I - \mu P$$



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RIGHT
Reporting Items for Practice Guidelines in Healthcare

No relevant financial conflicts of interest

What is evidence-based medicine?

- What would be “non-evidence-based medicine”?
- What is evidence?

*Meaning of **evidence** in English*

evidence

noun [U]

UK /ˈev.ɪ.dᵊns/ US /ˈev.ə.dᵊns/

Add to word list

B2

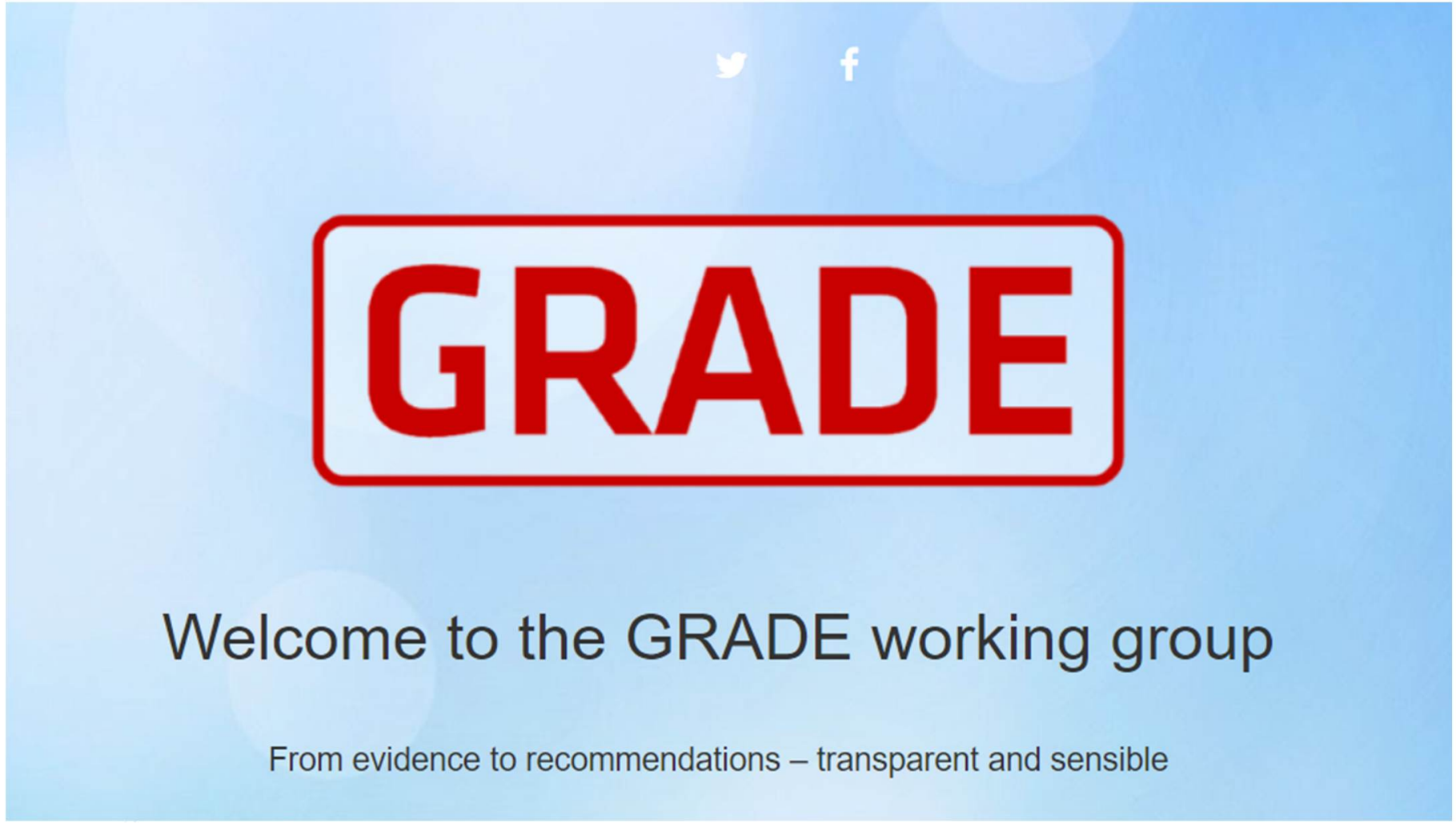
facts, information, documents, etc. that give reason to believe that something is true:

to provide evidence (= facts, information, etc. that give reasons for believing) that something is true or present:

anything that helps to prove that something is or is not true:

objects, documents, official statements, etc. that are used to prove something is true or not true, especially for legal or insurance purposes:

GRADE – a systematic approach to evaluate the evidence and recommendations



GRADE – a systematic approach to evaluate the evidence and recommendations

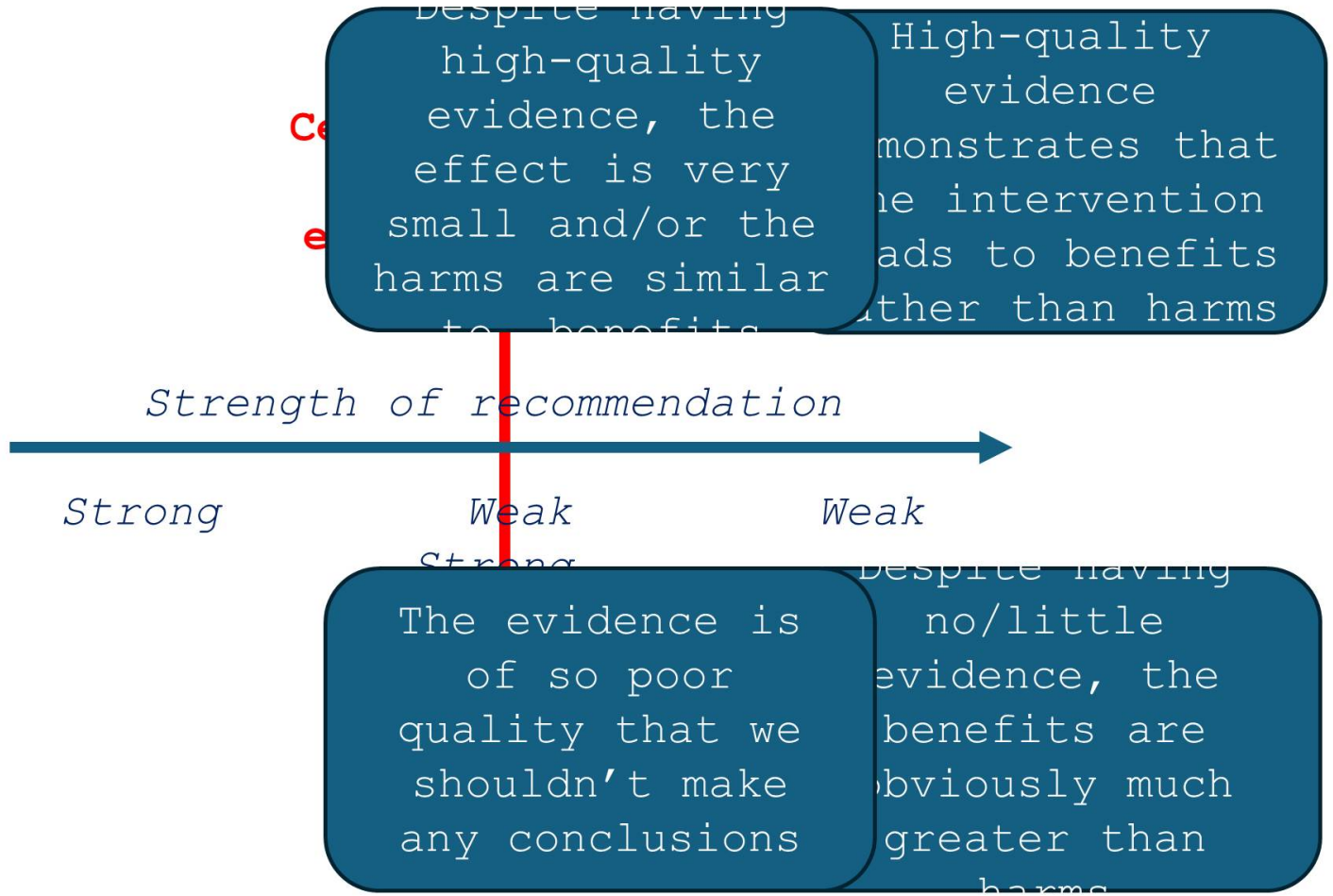
Certainty of evidence

- High
- Moderate
- Low
- Very low

Strength of recommendations

- Strong for
- Weak/conditional for
- Weak/conditional against
- Strong against

GRADE – a systematic approach to evaluate the evidence and recommendations



Example: the COVID-19 pandemic

We were faced with a previously unknown virus – what could we do?

- Indirect evidence (e.g. SARS and MERS – or even other respiratory viral infections)
- Common sense

Example: the COVID-19 pandemic

Are these interventions more likely to benefit than harm?

- Washing hands
  - Is certainly not harmful – and can have many other positive effects!
  - Finally, not very effective against COVID-19 (that spreads through droplets and aerosols – not through surfaces)

- Wearing masks
  - Not harmful for health
  - Some undesirable effects (environmental pollution, uncomfortable…) – but in an emergency situation, we need to prioritize

Example: the COVID-19 pandemic

Guidelines for the prevention and management of children and adolescents with COVID-19

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ORIGINAL ARTICLE

Guidelines for the prevention and management of children and adolescents with COVID-19

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Abstract

Children are the future of the world, but their health and future are facing great uncertainty because of the coronavirus disease 2019 (COVID-19) pandemic. In order to improve the management of children with COVID-19, an international, multidisciplinary panel of experts developed a rapid advice guideline at the beginning of the outbreak of COVID-19 in 2020. After publishing the first version of the rapid advice guideline, the panel has updated the guideline by including additional stakeholders in the panel and a comprehensive search of the latest evidence. All recommendations were supported by systematic reviews and graded using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system. Expert judgment was used to develop good practice statements supplementary to the graded evidence-based recommendations. The updated guideline comprises nine recommendations and one good practice statement. It focuses on the key recommendations pertinent to the following issues: identification of prognostic factors for death or pediatric intensive care unit admission; the use of remdesivir, systemic glucocorticoids and antipyretics, intravenous immunoglobulin (IVIG) for multisystem inflammatory syndrome in children, and high-flow oxygen by nasal cannula or non-invasive ventilation for acute hypoxemic respiratory failure; breastfeeding; vaccination; and the management of pediatric mental health.

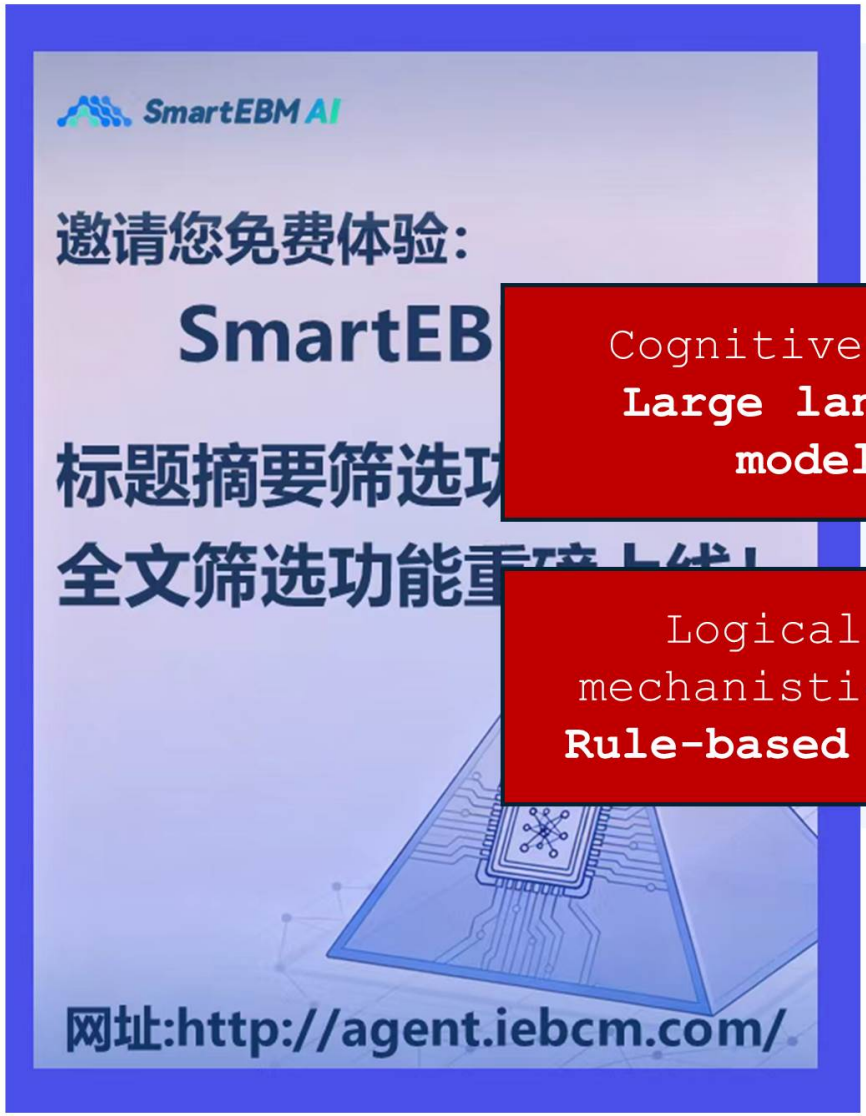
Conclusion: This updated evidence-based guideline intends to provide clinicians, pediatricians, patients and other stakeholders with evidence-based recommendations for the prevention and management of COVID-19 in children and adolescents. Larger studies with longer follow-up to determine the effectiveness and safety of systemic glucocorticoids, IVIG, noninvasive ventilation, and the vaccines for COVID-19 in children and adolescents are encouraged.

Recommendations	Status
Recommendation 1: We suggest that pediatricians and other guideline users should identify the presence of prognostic factors for death or PICU admission in children and adolescents with COVID-19 at an early stage. The main prognostic factors for death are MIS-C complications and AKI; the prognostic factors for PICU admission include AKI, ARDS, MIS-C complications, chronic pulmonary disease, and congenital heart disease *(Conditional recommendation, very low certainty of evidence)*	New
Recommendation 2: We suggest standard care without remdesivir to treat children and adolescents with COVID-19 *(Conditional recommendation, very low certainty of evidence)*	Modified
Recommendation 3: We suggest that antipyretics (ibuprofen or paracetamol) can be used to relieve fever and pain in children and adolescents with COVID-19 *(Conditional recommendation, very low certainty of evidence)*	New
Recommendation 4: We suggest low-dose, short-course of dexamethasone therapy for children and adolescents with severe COVID-19 *(Conditional recommendation, low certainty of evidence)*	Modified
Recommendation 5.1: We suggest IVIG for children and adolescents with MIS-C *(Conditional recommendation, very low certainty of evidence)*	New
Recommendation 5.2: We suggest using glucocorticoids in combination with IVIG for children and adolescents with MIS-C who have a severe clinical presentation at the time of diagnosis (acute left ventricular dysfunction, immediate admission to PICU care, or hemodynamic support requirement) *(Conditional recommendation, very low certainty of evidence)*	New
Recommendation 6: We suggest HFNC or NIV (CPAP or BiPAP) as the initial modality of therapy for acute hypoxic respiratory failure in hospitalized children and adolescents with COVID-19 *(Conditional recommendation, low certainty of evidence)*	New
Recommendation 7: We recommend that mothers with COVID-19 continue to breastfeed their babies if their health condition permits, while taking appropriate precautions *(Strong recommendation, low certainty of evidence)*	Unchanged
Recommendation 8: We suggest COVID-19 vaccination for children and adolescents aged 3–17 years if a COVID-19 vaccine is available and approved by local health authorities for their age and health condition, while closely monitoring for potential side effects after vaccination *(Conditional recommendation, moderate certainty of evidence)*	New
Good practice statements	**Status**
Good practice statement: We suggest pediatricians, parents, and caregivers should explore possible mental health problems among children and adolescents with COVID-19 and provide them with the optimal support that is feasible in the local setting	New

How to grade evidence using GRADE?

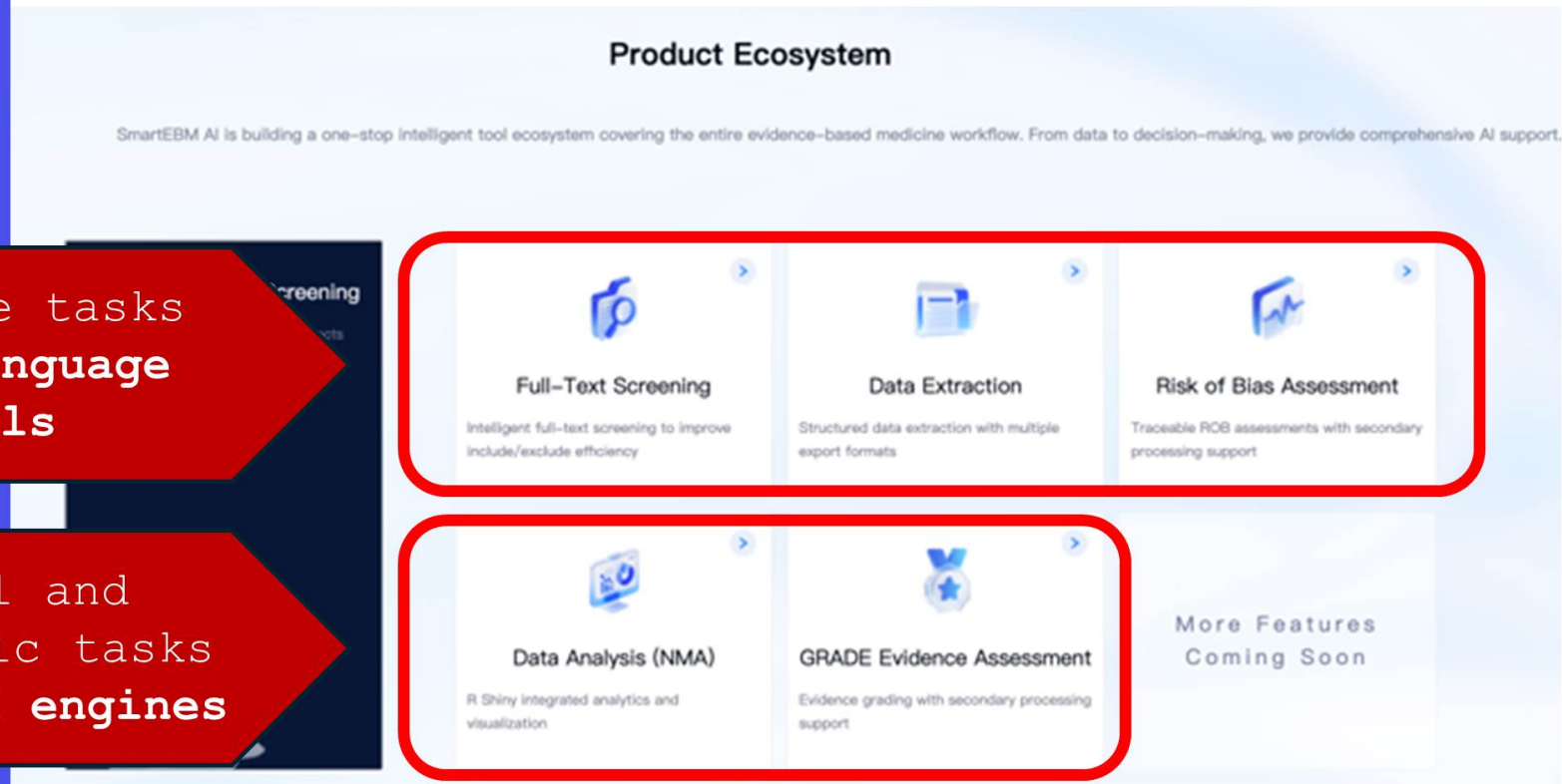
- Choose the starting point (high quality from RTCs – low quality from observational studies only)
- Up- or downgrade according to specified factors

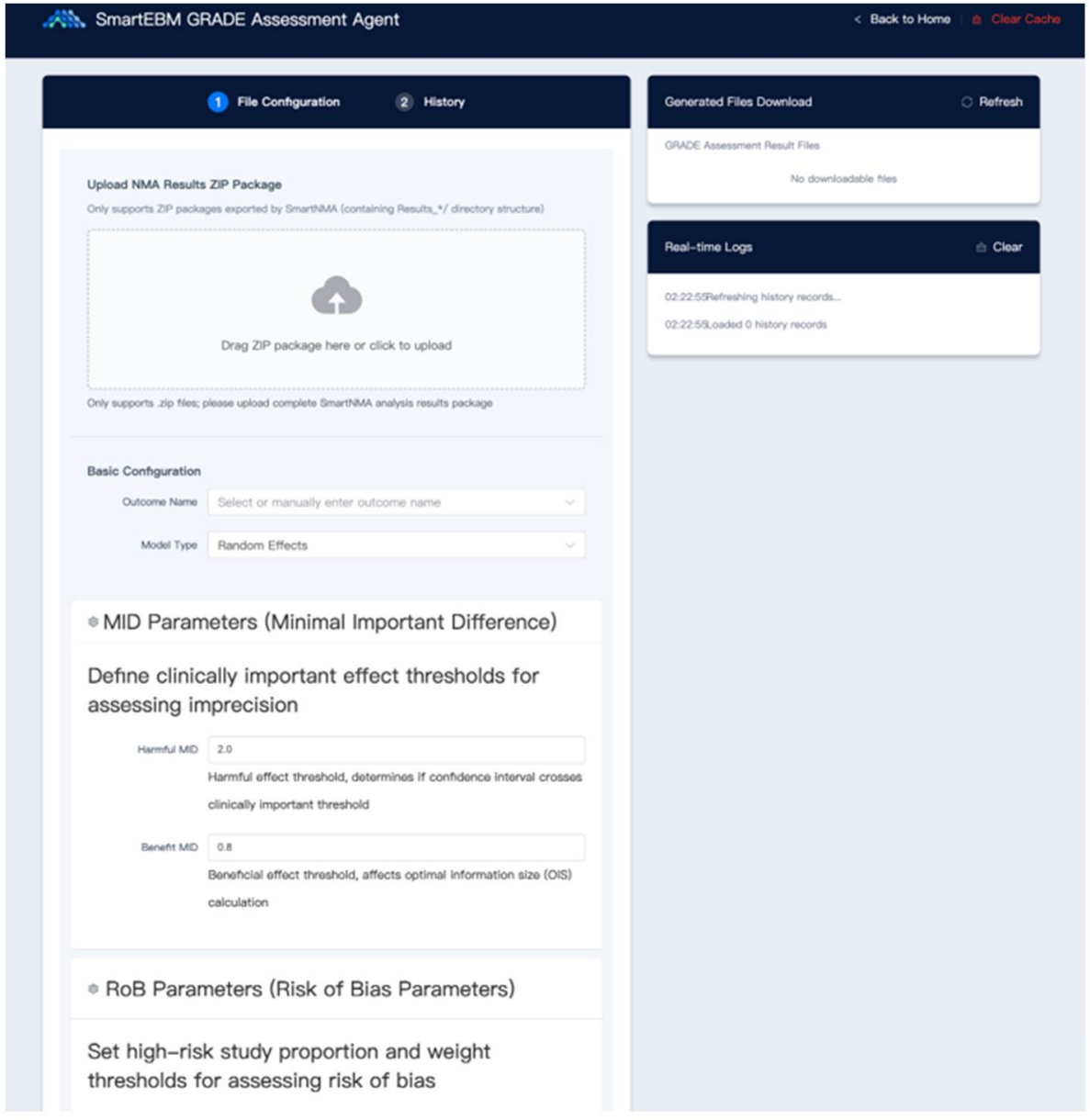
How to grade evidence using GRADE?

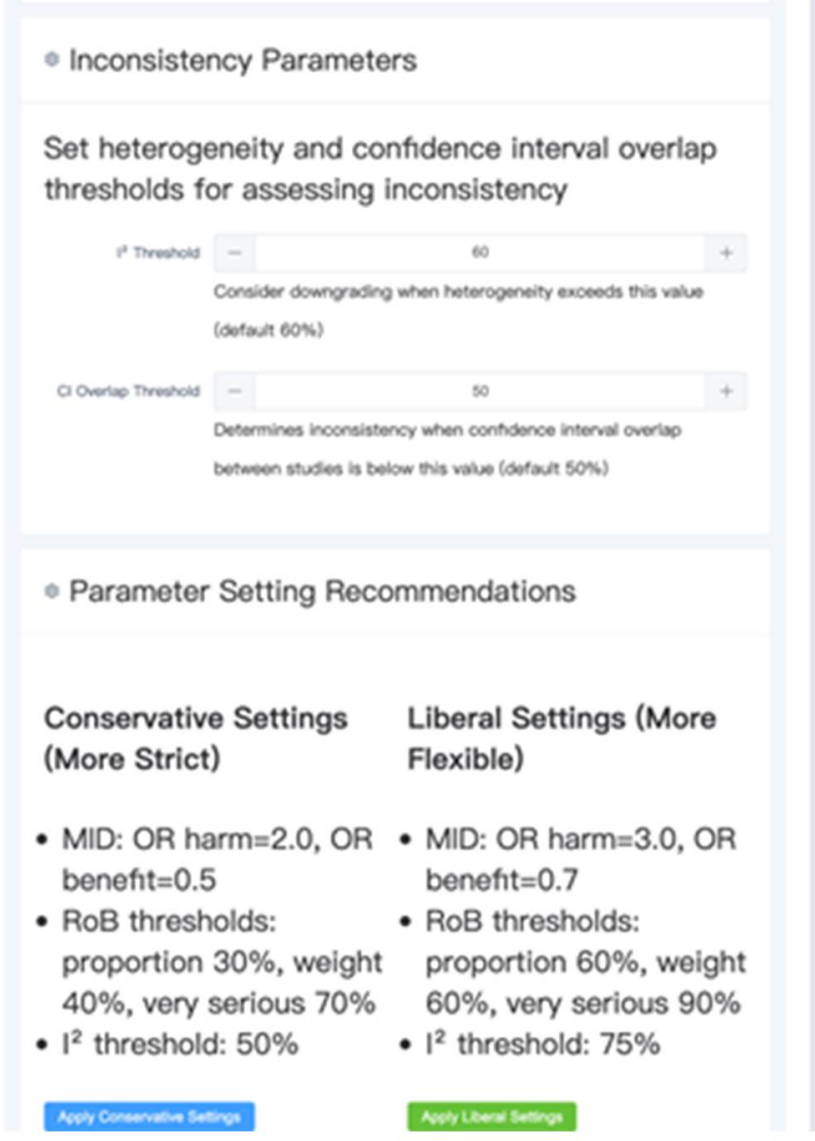


Cognitive tasks
Large language models

Logical and mechanistic tasks
Rule-based engines




SmartEBM GRADE Assessment Agent
Back to Home
Clear Cache
1 File Configuration
2 History
Upload NMA Results ZIP Package
Only supports ZIP packages exported by SmartNMA (containing Results_*/ directory structure)
Drag ZIP package here or click to upload
Only supports .zip files; please upload complete SmartNMA analysis results package
Basic Configuration
Outcome Name
Select or manually enter outcome name
Model Type
Random Effects
MID Parameters (Minimal Important Difference)
Define clinically important effect thresholds for assessing imprecision
Harmful MID
2.0
Harmful effect threshold, determines if confidence interval crosses clinically important threshold
Benefit MID
0.8
Beneficial effect threshold, affects optimal information size (OIS) calculation
RoB Parameters (Risk of Bias Parameters)
Set high-risk study proportion and weight thresholds for assessing risk of bias
Generated Files Download
Refresh
GRADE Assessment Result Files
No downloadable files
Real-time Logs
Clear
02:22:55 Refreshing history records...
02:22:55 Loaded 0 history records


Inconsistency Parameters
Set heterogeneity and confidence interval overlap thresholds for assessing inconsistency
I² Threshold
60
Consider downgrading when heterogeneity exceeds this value (default 60%)
CI Overlap Threshold
50
Determines inconsistency when confidence interval overlap between studies is below this value (default 50%)
Parameter Setting Recommendations
Conservative Settings (More Strict)
MID: OR harm=2.0, OR benefit=0.5
RoB thresholds: proportion 30%, weight 40%, very serious 70%
I² threshold: 50%
Liberal Settings (More Flexible)
MID: OR harm=3.0, OR benefit=0.7
RoB thresholds: proportion 60%, weight 60%, very serious 90%
I² threshold: 75%
Apply Conservative Settings
Apply Liberal Settings

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Thank you!
Спасибо за внимание!

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