Integrity and Transparency of Decisions on Essential Medicines

24th Expert Committee on the Selection and Use of Essential Medicines | Geneva, April 24, 2023

Holger Schünemann, MD, MSc, PhD, FRCPC

Professor of Medicine and Clinical Epidemiology

WHO Collaborating Center for Infectious Diseases, Research Methods, McMaster University

Disclosures

- No direct financial conflicts
- GRADE Working Group Co-Chair
- Cochrane Canada - Director
- Guideline International Network – vice chair
- Research grants from Canadian Institutes of Health Research and WHO
- Consultant to WHO, MSIF
- Views expressed my own

Thanks to:

- T. Piggott (whose thesis work is instrumental for this presentation)!
- Theory of everything collaborators
- L. Moja, B. Huttner

Today's talk

1. Considerations about transparency of EML selection by building on decision-making frameworks

2. Opportunities for how transparency may ensure integrity of the selection and how we can learn from other disciplines

Background

- We submitted an application for inclusion of new oral anticoagulants (direct oral anticoagulants/DOACs) in WHO EML 2015 – rejected: need in LMIC? Cost differential to alternatives (warfarin)?

- Higher cost medicines such as direct acting antivirals for hepatitis C are included, but cancer medicines of similar cost have not been included

Concerns about the EML – use of evidence and reporting

1) Search strategy, reasons for inclusion or exclusion of data

2) Target population, comparison groups, and outcomes of interest

3) Quantitative summaries of overall treatment effects for each comparison and outcome

4) Quality of supporting evidence

5) Conflicts of interest: reporting and management

Criticism of the EML process

The composition of WHO's expert committee on essential medicines needs more scrutiny

Craig Welch *health policy consultant*

Garran, Australian Capital Territory, Australia

Barbui and Purgato call for reforms to both the standard of applications to and the clarity of reporting of decisions by the World Health Organization expert committee on essential medicines.[1] But they don't go far enough. It isn't just the decisions that need more scrutiny but the composition of the committee too.

We are told only that the committee is made up of experts, "appointed by the WHO director general," who meet "every two years to review applications with expert assessors and decide which medicines are added or deleted." Just try to find out from the WHO website who the committee members are before a committee meeting—as opposed to when the meeting report is published—let alone their qualifications, fitness for the role, or conflicts of interest. Why is there never a call for nominations to the committee? The list of current members smacks of croneyism, the appointments process is opaque, and the decisions lack clarity. Transparency is its own reward; WHO should, indeed, try leading by example.

Competing interests: None declared.

1   Barbui C, Purgato M. Decisions on WHO's essential medicines need more scrutiny. *BMJ* 2014;349:g4798. (31 July.)

Cite this as: *BMJ* 2014;349:g5211

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thebmj.com
▶ Listen to a podcast interview with the authors at thebmj.com/podcasts

ANALYSIS

Decisions on WHO's essential medicines need more scrutiny

Global endorsement as a WHO essential medicine is a big step. But **Corrado Barbui** and **Marianna Purgato** find that the quality of applications for antidepressants and antipsychotics is poor and call on applicants and WHO to raise standards

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Viewpoint

October 24, 2022

Reforming the World Health Organization's Essential Medicines List
Essential but Unaffordable

Thomas J. Hwang, MD[1,2]; Aaron S. Kesselheim, MD, JD, MPH[2]; Kerstin N. Vokinger, MD, JD, PhD[2,3]

☐ Author Affiliations | Article Information

So how can one efficiently …

a) enhance the transparency in how medicines are included in the EML?

b) describe and manage any potential biases (including conflicts) that could influence the process?

c) foster practical use of the EML in settings different income settings and legal frameworks?

d) increase the efficiency in the preparation of applications?

2021 anti-PD1 inhibitor application from ESMO used a non-systematic summary of the evidence - a Cochrane review on the exact same question was published Dec. 2020 – the month the application was submitted

A striking similarity to …

Practice guidelines and their history at WHO and other decision makers in health

NEWS

Storm over W

Feb 4 saw the London
of the 1999 WHO–Inter
Society of Hypertension (ISH
lines for the management of
tension. But just hours bet
launch, WHO faxed a press re
health editors headed "UF

THE LANCET · Vol 353 · February

Use of evidence i

Andrew D Oxman, John N Lavis, Atle Fre

Summary
Background WHO regulations,
recommendations. However, the
for evidence of effects, processe
values), and evidence-informed
particularly evidence of effects, i

Health Research Policy and Systems

Articles

BioMed Central

Open Access

Review

Improving the use of research evidence in guideline development: 1. Guidelines for guidelines

Holger J Schünemann*[1], Atle Fretheim[2] and Andrew D Oxman[2]

Address: [1]INFORMA, S.C. Epidemiologia, Istituto Regina Elena, Via Elio Chianesi 53, 00144 Rome, Italy and [2]Norwegian Knowledge Centre for the Health Services, P.O. Box 7004, St. Olavs plass, N-0130 Oslo, Norway

Email: Holger J Schünemann* - hjs@buffalo.edu; Atle Fretheim - atle.fretheim@nokc.no; Andrew D Oxman - oxman@online.no

* Corresponding author

Learn from guideline science

The process from prioritization to a recommendation and decision is now largely transparent and "reproducible"

GRADE Working Group DECIDE project 2011 – 2015 with WHO, NICE & partners

Evidence to decision frameworks to enhance transparency of the process and decision … also for the EML

GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. 2: Clinical practice guidelines

GRADE Guidelines: 16. GRADE evidence to decision frameworks for tests in clinical practice and public health

GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. 1: Introduction

The GRADE evidence-to-decision framework: a report of its testing and application in 15 international guideline panels

The GRADE Evidence to Decision (EtD) framework for health system and public health decisions

GRADE EVIDENCE TO DECISION (EtD) FRAMEWORK FOR COVERAGE DECISIONS

Original EtD Framework (allows tailoring)

Discuss evidence

QUESTION

Should Intermediate intensity anticoagulation, therapeutic intensity anticoagulation vs. prophylactic intensity anticoagulation be used in Patients with COVID-19-related acute illness who do not have confirmed or suspected VTE?

Population: Patients with COVID-19-related acute illness who do not have confirmed or suspected VTE

Intervention: Intermediate intensity anticoagulation, therapeutic intensity anticoagulation

Comparison: prophylactic intensity anticoagulation

Main outcomes: Mortality; Pulmonary Embolism - representing the moderate PE marker state; Proximal Deep Vein Thrombosis - representing the moderate proximal DVT marker state; Major Bleeding;

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2 Desirable Effects ⓘ
How substantial are the desirable anticipated effects?

JUDGEMENT

- ○ Trivial
- ○ Small
- ○ Moderate
- ○ Large
- ○ Varies
- ○ Don't know

Detailed judgements

RESEARCH EVIDENCE

Plain language statements `OFF` | Absolute effect `ON` | Relative effect `ON` | Visual overview `ON`

Outcomes	Absolute Effect — With Prophylactic intensity	Absolute Effect — With DOACs, LMWH, UFH, Fondaparinux, Argatroban, or Bivalirudin at intermediate-intensity or therapeutic-intensity	Differences in outcomes (Fewer/Less with DOACs, LMWH, UFH, Fondaparinux, Argatroban, or Bivalirudin at intermediate-intensity or therapeutic-intensity ◄ ► More with Prophylactic intensity)	Relative effect (95% CI)	Certainty of the evidence GRADE
Mortality Follow-up: range 14 days to 22 days	236 per 1000	184 per 1000 — Difference: 52 fewer per 1000 patients (95% CI: 143 fewer to 116 more per 1000 patients) Based on data from 141 patients in 1 study	52 fewer per 1000 patients	OR 0.73 (0.33 to 1.76)	⊕◯◯◯ VERY LOW Due to serious risk of bias. Due to very serious imprecision.
Pulmonary embolism Follow-up: range 14 days to 20 days	98 per 1000	10 per 1000 — Difference: 88 fewer per 1000 patients (95% CI: 96 to 40 fewer per 1000 patients) Based on data from 82 patients in 1 study	88 fewer per 1000 patients	OR 0.09 (0.02 to 0.57)	⊕◯◯◯ VERY LOW Due to serious risk of bias. Due to very serious imprecision.
Deep Venous Thrombosis of the upper leg (Proximal lower extremity DVT) Follow-up: range 14 days to 20 days					
Venous thromboembolism Follow-up: range 18 days to 28 days					
Major bleeding Follow-up: mean 16 days	84 per 1000	260 per 1000 — Difference: 176 more per 1000 patients (95% CI: 33 to 400 more per 1000 patients) Based on data from 141 patients in 1 study	176 more per 1000 patients	OR 3.84 (1.44 to 10.21)	⊕◯◯◯ VERY LOW Due to serious risk of bias. Due to very serious imprecision.

ADDITIONAL CONSIDERATIONS

Add relevant considerations

QUESTION

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Detailed judgements

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Make judgments

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How substantial are the desirable anticipated effects?

JUDGEMENT

○ Trivial
○ Small
○ Moderate
○ Large

○ Varies
○ Don't know

Detailed judgements

RESEARCH EVIDENCE

Plain language statements OFF | Absolute effect ON | Relative effect ON | Visual overview ON

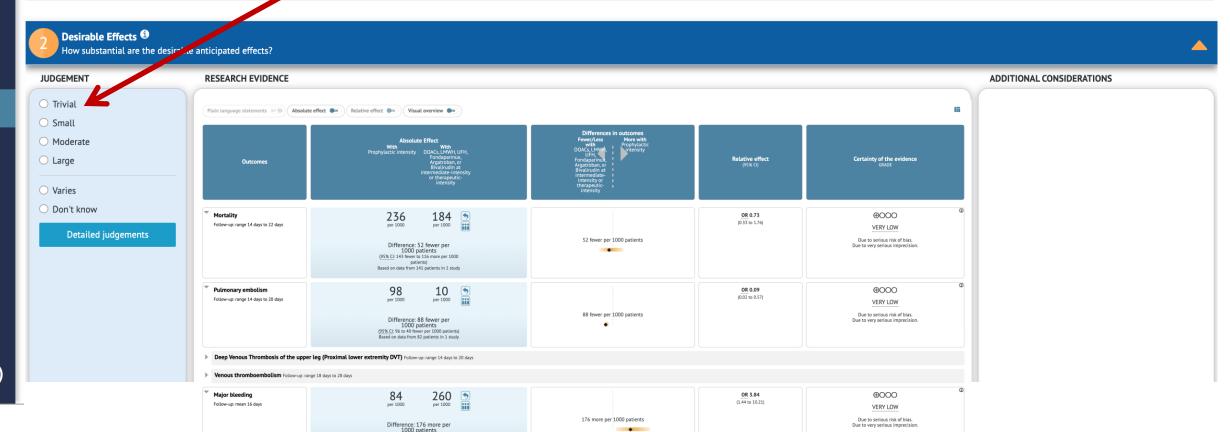| Outcomes	Absolute Effect With Prophylactic intensity	With DOACs, LMWH, UFH, Fondaparinux, Argatroban, or Bivalirudin at intermediate-intensity or therapeutic-intensity	Differences in outcomes Fewer/Less with DOACs, LMWH, UFH, Fondaparinux, Argatroban, or Bivalirudin at intermediate-intensity or therapeutic-intensity — More with Prophylactic intensity	Relative effect (95% CI)	Certainty of the evidence GRADE
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ADDITIONAL CONSIDERATIONS

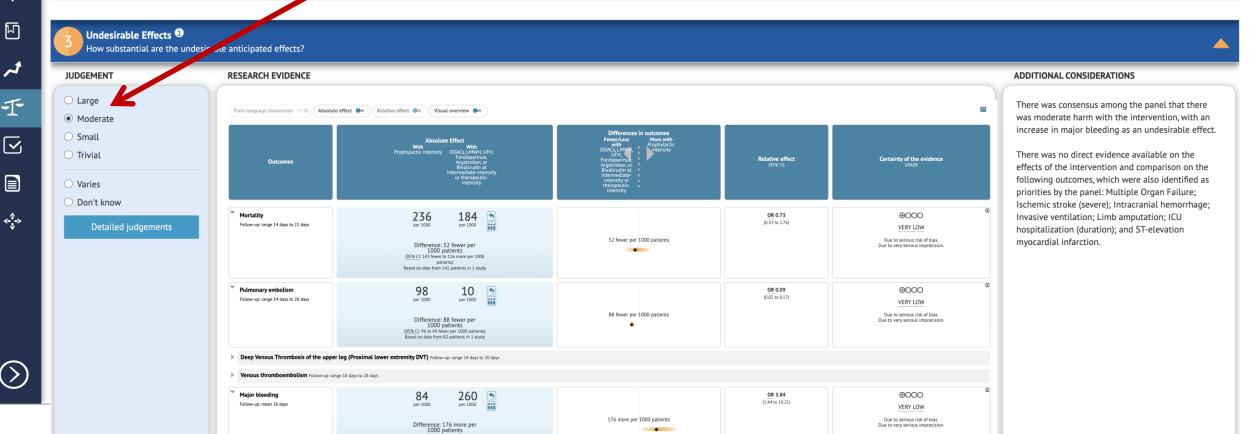# Make judgments

No conflicts of interest

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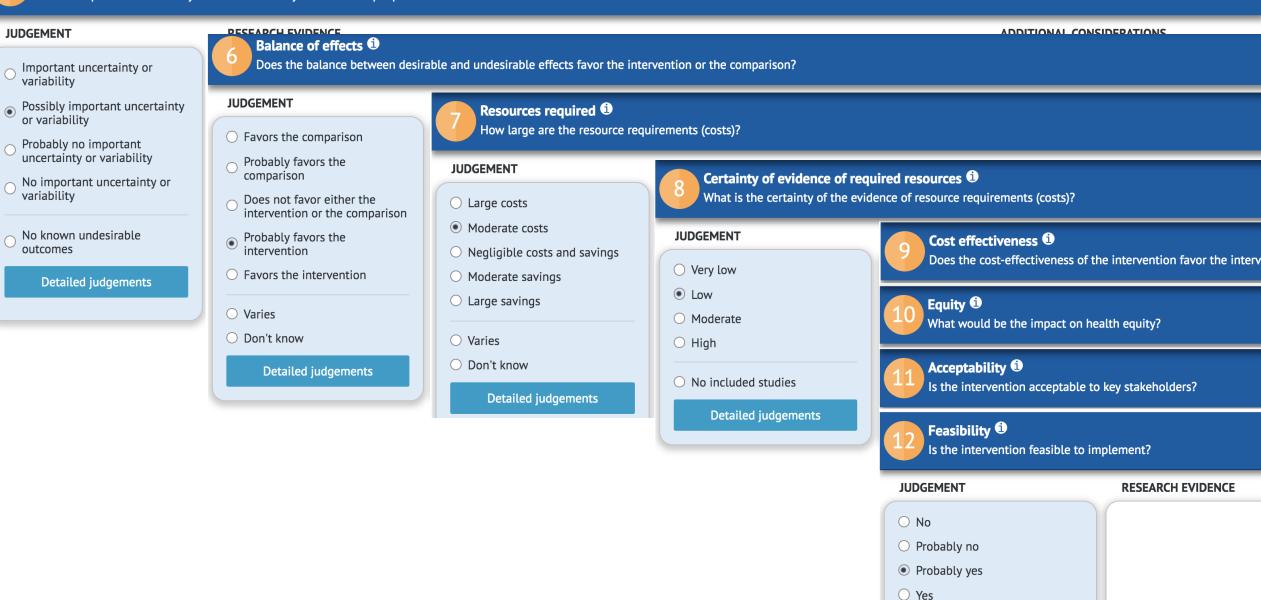
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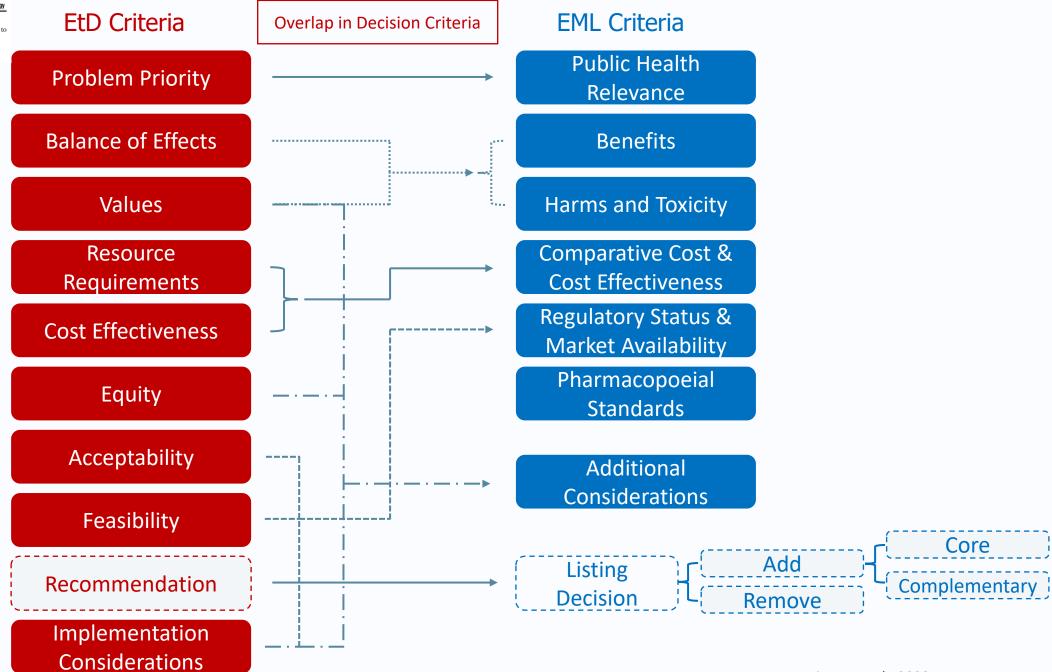
3 Undesirable Effects ⓘ
How substantial are the undesirable anticipated effects?

JUDGEMENT

- ○ Large
- ● Moderate
- ○ Small
- ○ Trivial
- ○ Varies
- ○ Don't know

[Detailed judgements]

RESEARCH EVIDENCE

Plain language statements OFF | Absolute effect ON | Relative effect ON | Visual overview ON

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ADDITIONAL CONSIDERATIONS

There was consensus among the panel that there was moderate harm with the intervention, with an increase in major bleeding as an undesirable effect.

There was no direct evidence available on the effects of the intervention and comparison on the following outcomes, which were also identified as priorities by the panel: Multiple Organ Failure; Ischemic stroke (severe); Intracranial hemorrhage; Invasive ventilation; Limb amputation; ICU hospitalization (duration); and ST-elevation myocardial infarction.

5 Values ⓘ
Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT

RESEARCH EVIDENCE

- ○ Important uncertainty or variability
- ● Possibly important uncertainty or variability
- ○ Probably no important uncertainty or variability
- ○ No important uncertainty or variability
- ○ No known undesirable outcomes

[Detailed judgements]

6 Balance of effects ⓘ
Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT

- ○ Favors the comparison
- ○ Probably favors the comparison
- ○ Does not favor either the intervention or the comparison
- ● Probably favors the intervention
- ○ Favors the intervention
- ○ Varies
- ○ Don't know

[Detailed judgements]

7 Resources required ⓘ
How large are the resource requirements (costs)?

JUDGEMENT

- ○ Large costs
- ● Moderate costs
- ○ Negligible costs and savings
- ○ Moderate savings
- ○ Large savings
- ○ Varies
- ○ Don't know

[Detailed judgements]

8 Certainty of evidence of required resources ⓘ
What is the certainty of the evidence of resource requirements (costs)?

JUDGEMENT

- ○ Very low
- ● Low
- ○ Moderate
- ○ High
- ○ No included studies

[Detailed judgements]

9 Cost effectiveness ⓘ
Does the cost-effectiveness of the intervention favor the interve

10 Equity ⓘ
What would be the impact on health equity?

11 Acceptability ⓘ
Is the intervention acceptable to key stakeholders?

12 Feasibility ⓘ
Is the intervention feasible to implement?

JUDGEMENT

RESEARCH EVIDENCE

- ○ No
- ○ Probably no
- ● Probably yes
- ○ Yes
- ○ Varies
- ○ Don't know

ADDITIONAL CONSIDERATIONS

Piggott et al., 2023

2021 EML Applications

Should anti-PD1 immune-checkpoint inhibitors vs. chemotherapy be used for "non-oncogene- addicted" (EGFR, ALK, and ROS1 wild type) locally advanced and metastatic non-small cell lung cancer (NSCLC)?

POPULATION:	"non-oncogene- addicted" (EGFR, ALK, and ROS1 wild type) locally advanced and metastatic non-small cell lung cancer (NSCLC)
INTERVENTION:	anti-PD1 immune-checkpoint inhibitors
COMPARISON:	chemotherapy
MAIN OUTCOMES:	Overall survival; Progression-free survival; Overall response rate; Adverse Events grade 3-4; Quality of Life;
SETTING:	
PERSPECTIVE:	
BACKGROUND:	
CONFLICT OF INTERESTS:	

ASSESSMENT

Problem
Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ No ○ Probably no ○ Probably yes ● Yes ○ Varies ○ Don't know	**From Pentheroudakis MLEM Application** Lung cancer is the most diagnosed and the first cause of death for cancer worldwide, estimating 2 million new cases and 1.7 related deaths in 2018, according to Global Cancer Observatory 2018 (5). Lung cancer is a highly lethal malignancy, with an economic impact estimated around $8 billion productivity lost in the BRICS countries (6). Moreover, in the absence of a wide coverage of an effective screening programme in place on global scale, lung cancer diagnoses occur in advanced stages (i.e. III and IV, TNM 8th) in more than 60% of cases, with highly regional variability (7-9). Lung cancer is the leading cause of cancer-related mortality in the United States and worldwide. Over 80% of the lung cancers are classified as NSCLC. Although targeted therapies have redefined the therapeutic landscape for patients with molecularly druggable NSCLC (e.g. epidermal growth factor receptor [EGFR] mutations, anaplastic lymphoma kinase [ALK] rearrangements, ROS1 rearrangements, BRAF mutations, HER2 mutations or amplifications, NTRK1-3 fusions), these therapies are ineffective in those tumours lacking such genetic alterations, the majority of NSCLC patients. However, ICI therapy has become part of the treatment of such patients, which has led to improvements in survival and quality of life. The ICI target and reactivate the immune-competent cells, i.e. T-lymphocytes and antigen-presenting cells, by inhibiting the immunosuppressive ligand PD-L1 or its receptor, PD-1, in the tumour-induced immunosuppressant milieu or by strengthening the immune-activating signals of immune-response (e.g. GITR, pro-inflammatory interleukins, interferon-gamma) (10). The approval of ICIs in NSCLC addresses an unmet need for patients considered to have a poor prognosis in advanced stage, in the absence of an indication of targeted therapy."	

Desirable Effects
How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
○ Trivial ○ Small ○ Moderate ● Large ○ Varies ○ Don't know	**From Dec 2020 Cochrane Review** https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013257.pub2/full	Evidence from original application. Large desirable effects for expression ≥50%.

Outcomes	Nº of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with chemotherapy	Risk difference with anti-PD1 immune-checkpoint inhibitors

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ESMO – WHO EML Submission 2020

Application for the inclusion of the anti-PD1 immune-checkpoint inhibitors in the WHO Model list of ESSENTIAL MEDICINES for the treatment of "non-oncogene- addicted" (EGFR, ALK, and ROS1 wild type) locally advanced and metastatic non-small cell lung cancer (NSCLC).

List of Contributors: George Pentheroudakis, MD PhD

1.   Name of the focal point in WHO submitting or supporting the application

Andrè Ilbawi, WHO Department for Management of Noncommunicable Diseases, Disability, Violence and Injury Prevention (NVI).

2.   Name of the organization(s) consulted and/or supporting the application

European Society for Medical Oncology (ESMO)

Medicine — **Anti-PD1 Inhibitors** [nivolumab, pembrolizumab]

Benefits — **Compared to chemotherapy (per 1,000):**
119 fewer deaths (⊕⊕⊕O)
16 more progression free survival (⊕⊕OO)
115 more overall response rate (⊕⊕OO)
135 more higher Quality of Life (⊕⊕OO)

Values — No important uncertainty or variability in how people value the main outcomes

Problem — Lung Cancer — 2 million cases/year — 1.8 million deaths/year

Harms — **Compared to chemotherapy (per 1,000):**
244 fewer grade 3/4 adverse events (⊕⊕OO)

Balance — Favours Anti-PD1 Inhibitors vs chemotherapy

Resources — **Large Costs**

Drug costs alone over $100,000 per patient.

Lung CA prevalent and therefore budget impact higher than for less common cancers.

Cost-Effectiveness — **Favours chemotherapy**

ICER approximately $100,000 per QALY gained

Equity — **Reduced**

If this drug is listed it would decrease health equity unless pricing decreases substantially.

Acceptability — **Probably Yes**

These drugs are likely acceptable to patients and healthcare providers due to effectiveness and less undesirable effects than alternative regimens.

These drugs are likely not acceptable to decision-makers in most settings due to the cost.

Feasibility — **No**

This intervention is feasible and already implemented in many high-income settings.

Globally this intervention is not currently feasible across most settings.

GRADE interactive Evidence to Decision Frameworks

Settings
Tasks
Team
Scope
References
Prognosis
Comparisons
Multi comparisons
PanelVoice
Document sections
Dissemination

Question
- Details – PICO Subgroups
- Background and conflicts of interest

Assessment
- Criteria
- Judgements
- Research evidence (HTA and Systematic Reviews)
- Additional considerations

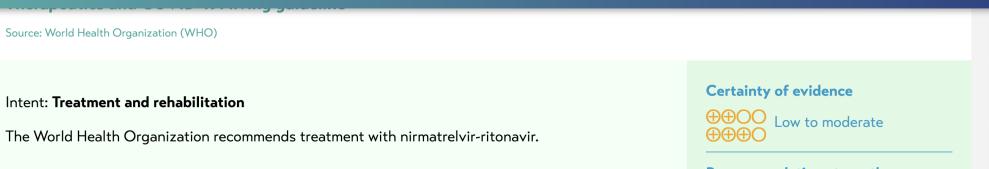## Conclusions
- Type of decision - recommendation
- Justification
- Implementation considerations - monitoring and evaluation
- Research considerations

Presentation
- Group meeting processes & informing coverage decisions
- Database of decision frameworks
- Decision Aids, apps

Source: World Health Organization (WHO)

Recommendation

Additional information

Summary of choices

iSoF

EtD

Source of recommendation

Intent: **Treatment and rehabilitation**

The World Health Organization recommends treatment with nirmatrelvir-ritonavir.

Certainty of evidence

⊕⊕◯◯ Low to moderate
⊕⊕⊕⊕

Recommendation strength

✅ strong

AGREE II score ⓘ

Scope and purpose: 86.1%
Rigor of development: 88.5%
Editorial Independence: 91.7%

Request for adolopment

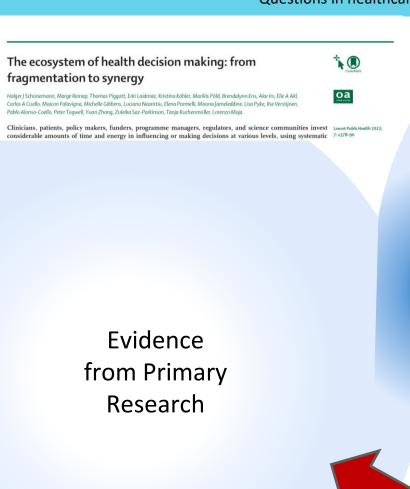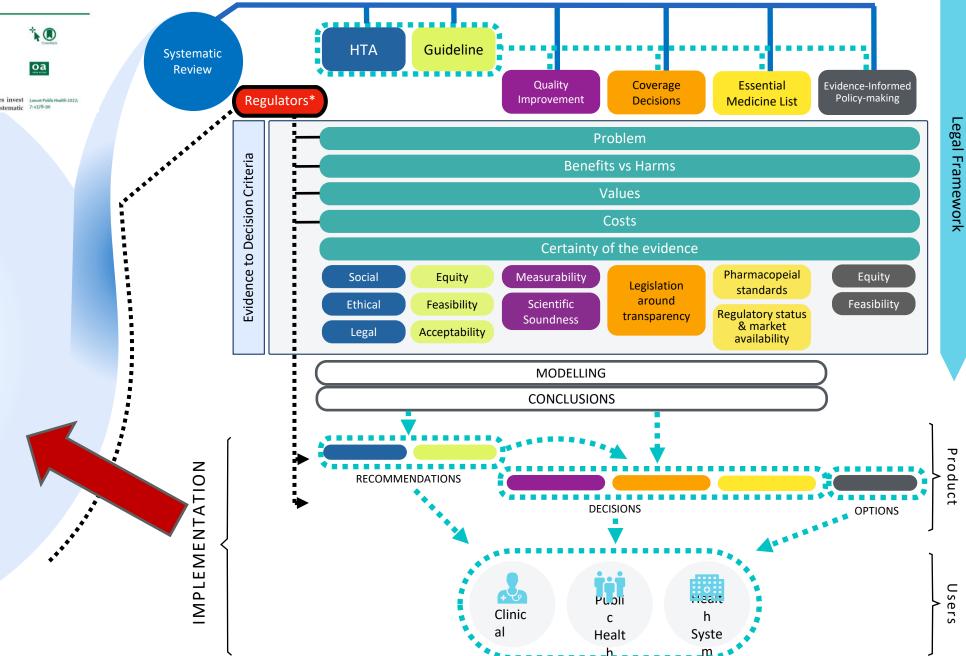| Population/Health problem	Patients with non-severe COVID-19 at highest risk of hospitalization
Intervention	Nirmatrelvir-ritonavir
Links to WHO Model List of Essential Medicines	https://list.essentialmeds.org/?query=ritonavir ▭EML
Relevant evidence from L·OVE platform	Relevant evidence from L·OVE platform L☼VE

Ledipasvir + sofosbuvir

Section: 6. Anti-infective medicines > 6.4. Antiviral medicines > 6.4.4. Antihepatitis medicines > 6.4.4.2. Medicines for hepatitis C >
6.4.4.2.2. Medicines for hepatitis C > Non-pangenotypic direct-acting antiviral combinations

ATC codes: J05AP51

Indication	Chronic hepatitis C ICD11 code: 1E91.1
INN	Ledipasvir + sofosbuvir
Medicine type	Chemical agent
List type	Core
Formulations	Oral > Solid: 90 mg + 400 mg tablet
EML status history	First added in 2015 (TRS 994)
Sex	All
Age	Adolescents and adults
Therapeutic alternatives	The recommendation is for this specific medicine
Patent information	Read more about patents.
Wikipedia	Ledipasvir + sofosbuvir
DrugBank	Ledipasvir, Sofosbuvir

Questions in healthcare systems: Problem/Populations, Interventions, Comparators, and Outcomes (PICO)

The ecosystem of health decision making: from fragmentation to synergy

Holger J Schünemann, Marge Reinap, Thomas Piggott, Erki Laidmäe, Kristina Köhler, Mariliis Põld, Brendalynn Ens, Alar Irs, Elie A Akl, Carlos A Cuello, Maicon Falavigna, Michelle Gibbens, Luciana Neamtiu, Elena Parmelli, Mouna Jameleddine, Lisa Pyke, Ilse Verstijnen, Pablo Alonso-Coello, Peter Tugwell, Yuan Zhang, Zuleika Saz-Parkinson, Tanja Kuchenmüller, Lorenzo Moja

Clinicians, patients, policy makers, funders, programme managers, regulators, and science communities invest considerable amounts of time and energy in influencing or making decisions at various levels, using systematic

Lancet Public Health 2022; 7: e378–90

Evidence from Primary Research

Beyond guidelines: Evidence ecosystem of health decision-making

Systematic Review

Regulators*

HTA · Guideline

Quality Improvement · Coverage Decisions · Essential Medicine List · Evidence-Informed Policy-making

Legal Framework

Evidence to Decision Criteria

Problem
Benefits vs Harms
Values
Costs
Certainty of the evidence

Social · Equity · Measurability · Legislation around transparency · Pharmacopeial standards · Equity
Ethical · Feasibility · Scientific Soundness · Regulatory status & market availability · Feasibility
Legal · Acceptability

MODELLING
CONCLUSIONS

IMPLEMENTATION

RECOMMENDATIONS

DECISIONS

OPTIONS

Product

Clinical · Public Health · Health System

Users

Key visions for enhancing EML transparency

1. Improve the quality and evaluation of applications → EtD framework like process for all applications, rapid updating, cost-considerations?

2. Is it time to re-assess 2001 criteria for decision making (EB109/8): missing equity and feasibility (availability)?

3. Work with medicine funders to align financing with EML decision-making?
- Move from comparative cost-effectiveness medication classes to affordability of medicines?

4. Strengthen the link with WHO guidelines and other norms and standards products → increase efficiency as there is much work to do

5. Work with the evidence-informed policy making to ensure essential medicine list decisions are translated into political priorities and policy decisions directly and indirectly

6. Improve dissemination and capacity building for both WHO and national EMLs

Summary

Little justification to do less than is demanded from guideline recommendations

- with regards to evidence to decision process, engagement and transparency to achieve integrity of the list

- consider the visions over the next days

Thank you

Thomas Piggott, Marge Reinap, Erki Laidmäe, Kristina Köhler, Elie A. Akl, Carlos A. Cuello, Maicon Falavigna, Michelle Gibbens, Mouna Jameleddine, Tanja Kuchenmüller, Luciana Neamtiu, Elena Parmelli, Mariliis Pōld, Lisa Pyk, Ilse Verstijnen, Ray Zhang, Peter Tugwell, Benedikt Huttner, Lorenzo Moja

@schunemann_mac

schuneh@mcmaster.ca

In the meantime…

Examples of synergy between different decision-making bodies taught us how to enhance related processes:

Estonia national guideline making conditional recommendation for DOACs in atrial fibrillation – cost too high for strong recommendation based on systematic review and HTA

Price negotiations with Estonian Health Insurance Fund – manufacturer lowering price → strong recommendation

And, our repeat submission to the 2019 EML (directly based on our guideline with decision-making support) → Listing of DOACs, the evidence accumulated

- but did not change dramatically in terms of cost or need in LMIC

Different types of decisions

Table 1 | Criteria for EtD frameworks for five different types of decisions

	Clinical recommendations–individual perspective	Clinical recommendations–population perspective	Coverage decisions	Health system and public health recommendations/decisions	Diagnostic, screening, and other tests*
Priority of the problem	Is the problem a priority?				
Test accuracy	Not applicable				How accurate is the test?
Benefits and harms	How substantial are the desirable anticipated effects?				
	How substantial are the undesirable anticipated effects?				
Certainty of the evidence	What is the overall certainty of the evidence of effects?				What is the certainty of the evidence of: - Test accuracy? - Any critical or important direct benefits, adverse effects, or burden of the test? - Effects of the management that is guided by the test results? - Link between test results and management decisions? - Effects of the test?
Outcome importance	Is there important uncertainty about or variability in how much people value the main outcomes?				Is there important uncertainty about or variability in how much people value the main outcomes, including adverse effects and burden of the test and downstream outcomes of clinical management that is guided by the test results?
Balance	Does the balance between desirable and undesirable effects favour the intervention or the comparison?				Does the balance between desirable and undesirable effects favour the test or the comparison?
Resource use	—	How large are the resource requirements (costs)?			
	—	What is the certainty of the evidence of resource requirements (costs)?			
	Does the cost effectiveness of the intervention (the out-of-pocket cost relative to the net benefits) favour the intervention or the comparison?	Does the cost effectiveness of the intervention favour the intervention or the comparison?	Does the cost effectiveness of the option favour the option or the comparison?		Does the cost effectiveness of the test favour the test or the comparison?
Equity	—	What would be the impact on health equity?			
Acceptability	Is the intervention acceptable to patients, their care givers, and healthcare providers?	Is the intervention acceptable to key stakeholders?	Is the option acceptable to key stakeholders?		Is the test acceptable to key stakeholders?
Feasibility	Is the intervention feasible for patients, their care givers, and healthcare providers?	Is the intervention feasible to implement?	Is the option feasible to implement?		Is the test feasible to implement?

*Tests cover clinical and public health recommendations at individual and population perspectives.

GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare