“Responding to the Pandemic Together” Programme
Episode 27: Evidence-based practice during the COVID-19 pandemic: More important now than ever

Delivered by the FIP Pharmacy Practice Research Special Interest Group in Collaboration with Research in Social and Administrative Pharmacy and the Social and Administrative Pharmacy Section
Moderator(s)

Victoria Garcia Cardenas

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• Chair, FIP Pharmacy Practice Research SIG
• Associate Editor, Research in Social and Administrative Pharmacy

Email: Victoria.GarciaCardenas@uts.edu.au

@VGC_AF
Welcome to the “Responding to the Pandemic Together” events
FIP’s Special Online Programme on COVID-19

These webinars aim to:

I. Provide relevant information and interim guidelines for pharmacists and the pharmacy workforce on Coronavirus SARS-CoV-2/COVID-19 pandemic.

II. Share and discuss strategies adopted by pharmacy leaders and workers - including our Member Organisations – in response to the pandemic.

III. Describe sector or area-specific implications, innovations and approaches adopted across pharmaceutical science, practice and education.

IV. Engage frontline workers of the health and pharmacy workforce to know about the realities facing them around the world.

V. Discuss the implications of the pandemic on issues such as safety, supply, shortages that have been exacerbated by COVID-19, and

VI. Consider the impact of this disease on patients across age groups and with concurrent conditions.

VII. Assess and discuss the evidence behind treatments and the process of developing therapies, vaccines and tests.

To share ideas on webinar topics we should feature, or if you’d like to share your story on dealing with the pandemic please email lina@fip.org
Important Links & Resources

FIP Covid-19 Information Hub
A comprehensive FIP webpage containing all of our resources and outputs relating to COVID-19, including recordings of previous webinars.
Link: https://www.fip.org/coronavirus

FIP Facebook Group: “COVID-19 & pharmacy”
Link: https://www.facebook.com/groups/covid19andpharmacy/
Announcements

FIP Digital Events House Rules

1. This webinar is being recorded and live streamed on Facebook
2. The recording will be freely available at www.fip.org/coronavirus and on our YouTube channel
3. You may ask questions by typing them into the Q&A box
4. Your feedback is welcome (webinars@fip.org)

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Learning Objectives

• To differentiate between the different levels of evidence
• To identify the types of evidence that can be used to inform practice
• To critically assess the published studies related to COVID-19 and be able to use them to inform practice, where appropriate
Evidence Based Practice

The concept and relevance of the webinar

- Evidence based practice requires that healthcare decisions are made based on the best available, current, valid, and relevant evidence and is essential to deliver high quality patient care.

- Critical during the current COVID-19 pandemic

Speaker 1: Levels of evidence
Speaker 2: Critical appraisal of evidence
Speaker 3: Economic evidence to inform decision making
Speaker 1

Filipa Alves da Costa, PhD

- Public health Consultant, WHO Regional Office for Europe
- IUEM, Associate Professor
- FFUL, Invited Professor
- RON (National Oncology Register), Researcher in therapeutic effectiveness
- Associate Editor of International Journal of Clinical Pharmacy
- Chair Education Committee, European Society of Clinical Pharmacy
- iPACT Board

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What is evidence?

What are opinions?

- **Opinion evidence** refers to evidence of what the witness thinks, believes, or infers in regard to facts, as distinguished from personal knowledge of the facts themselves. In general, witnesses should testify only as to the facts observed and should not give opinion\(^1\).

- **Evidence** (noun): the available body of facts or information indicating whether a belief or proposition is true or valid\(^2\).

- **Evidence-based medicine** the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients. The practice of evidence-based medicine means integrating individual clinical expertise with the best available external clinical evidence from systematic research\(^3\).

Hierarchy of Evidence

How to judge the quality of evidence provided by different studies
"Expert consensus statement" implies review by recognized organizations and widespread expert agreement. It should reflect a broad-based consensus representing more than author opinions. It should not reflect the views of a few self-selected individuals, even if after conducting literature. Recommendations issued ought to be supported by existing evidence, the highest available to date. E.g. WHO recommendations consider only systematic reviews; there are published studies with recommendations based on a single published report of 10 cases.

Case study and Case Series

Case presentation

…On 11 February 2020, a 37-year-old man presented to Wuhan Huo Shen Shan Hospital with a history of fever, dry cough and chest pain since 10 January 2020. The chest CT of this patient on 08 February showed multiple infiltrations in both lungs, consistent with viral infection. But the RT-PCR amplification of SARS-Cov-2 virus nucleic acid from a nasopharyngeal swab was negative. He denied any other diseases before this onset. The initial physical examination revealed a body temperature of 38.8 °C, oxygen saturation (SPO₂) 85–90% under ambient air, respiratory rate of 40 breaths/minute, blood pressure of 145/93 mmHg, and pulse of 119 bpm. The laboratory results reflected normal lymphocytes, normal procalcitonin (0.04 ng/mL) and elevated C-reactive protein (CRP, 96.5 mg/L), a-hydroxybutyrate dehydrogenase (a-HBDH, 318 IU/L) and glutamyl transpeptidase (GGT, 136 IU/L)…. 

Cross-sectional studies

General characteristics

• Measure the prevalence of conditions or characteristics of people in a population at a point in time or over a short period
• Classified as descriptive studies for large populations, but can also explore risk factors associated with particular illness or behaviour
• Useful for planning public health interventions.

Some examples

1. Online survey of 4,850 Malaysian residents, 13 knowledge items, 3 on attitudes and 3 on practices. >80% taking precautions to avoid crowds, hand hygiene; face masks by 51%.

2. Online self-reported survey from 3,388 people from South Arabia. Older adults are likely to have better knowledge and practices, than younger people (p>0.001).

3. UK bathers were more likely to report skin ailments (AOR=2.64 {95%CI: 1.23 to 5.65}, ear ailments (AOR=3.77 {95%CI: 1.84-7.73} and any symptoms of illness (AOR=3.73 {95%CI: 2.63-5.29}).

Hernández-Garduño, E. Obesity is the comorbidity more strongly associated for Covid-19 in Mexico. A case-control study. *Obesity Research & Clinical Practice* 2020
Cohort studies

How long will we be monitoring you?

Roughly 20 years...

Researchers

20 years later...

Exposed

Unexposed

Time for the count

Researchers

Relative Risk Hazard Function

Clinical Trials

News releases from National Institute of Allergy and Infectious Diseases (NIAID): Phase 3 clinical trial of investigational vaccine for COVID-19 begins. *Multi-site trial to test candidate developed by Moderna and NIH.*
### Clinical Trials

<table>
<thead>
<tr>
<th>TrialID</th>
<th>Public title</th>
<th>Date registration</th>
<th>Source Register</th>
<th>web address</th>
<th>Recruitment Status</th>
</tr>
</thead>
</table>

Systematic Reviews

General characteristics

• Research question operationalized using PICOTS
• Intervention must be clearly defined
• Outcomes standardised (eventually divided into primary vs secondary)
• Searches made in ≥ 3 databases
• Study designs should ideally be identical (sometimes not feasible)
• Extracted studies analysed and appraised for quality and risk of bias
• Results may be synthesized narratively and in tabular form

One example (rapid review)

• Ovid MEDLINE, Embase, CINAHL and the WHO Global Index Medicus.
• “As randomization of quarantine is unethical and not feasible for the diseases in question, we considered non-randomized studies of interventions to be the best potentially available empirical evidence…. we also included modelling studies, because, we did not yet expect empirical studies to be available.” Cohort studies, Case-control studies, time series, Interrupted time series, Case series, Mathematical modelling studies


Table 2. Certainty of evidence ratings for the effectiveness of quarantine for individuals who were in contact with a confirmed COVID-19 case

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Number of studies</th>
<th>Risk of bias</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Inconsistency</th>
<th>Other sources of bias</th>
<th>Summary effect size/estimate</th>
<th>Certainty of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence</td>
<td>4 modelling studies (Lee 2020; Zhen 2020; Zou 2020; Yang 2020)</td>
<td>Very uncertain</td>
<td>Direct</td>
<td>Precise</td>
<td>Consistent</td>
<td>None</td>
<td>Summary effect size/estimate</td>
<td>Low</td>
</tr>
</tbody>
</table>
|COVID-19| Co-development simulated the effect of loosening quarantine measures that are already in place. They concluded that if 80% of the people who were previously quarantined were retracted, the risk number of cases would increase by 200% compared to keeping a full quarantine in place.
|Relax 2020 estimated that isolation and quarantine prevented 20% (504) cases and lowered the reproduction number to 1.26 during the COVID-19 outbreak in the Straits Settlements in Singapore.
|Yang 2020 estimated that without any measures, the number of confirmed COVID-19 cases in Wuhan would be 7,772 by the end of January 2020. They estimated that reduced contact by 80% would decrease the number of confirmed COVID-19 cases from 7,772 to 725 (88% reduction). reduced contact by 80% to 771 (89% reduction).
|SARS| Health 2003 states that quarantine is effective in reducing the number of cases (66.5% reduction at the 20% quarantine rate) of SARS that equals quarantining 1 out of 29 people that should be quarantined.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Number of studies</th>
<th>Risk of bias</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Inconsistency</th>
<th>Other sources of bias</th>
<th>Summary effect size/estimate</th>
<th>Certainty of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>2 modelling studies (Tong 2020; Zou 2020)</td>
<td>Very uncertain</td>
<td>Direct</td>
<td>Precise</td>
<td>Consistent</td>
<td>None</td>
<td>Summary effect size/estimate</td>
<td>Low</td>
</tr>
<tr>
<td>COVID-19</td>
<td>Ingham-Brown 2020 estimated that for a timeframe of 4 months, case isolation and household quarantine would decrease deaths in the UK by 20% to 24%.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Meta-analysis

All studies have their place, as long as well conducted.
Speaker 2

Fernanda Stumpf Tonin, PhD

- HEOR Consultant
- Researcher, Federal University of Paraná, Brazil
- Vice-chair, FIP Pharmacy Practice Research SIG
- Member of the Editorial Board, Pharmacy Practice

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@StumpfTonin
Critical appraisal of evidence

To effectively practice as an evidence-based practice provider

Suboptimal research

27% of publications are redundant
20% have methodological flaws
20% are unpublished
17% are decent but not useful
13% misleading conclusions

3% have a scientific/clinical meaning

Critical appraisal of evidence

**COVID-19 era: increasing value, reducing waste**

- To know where to find information
- To be able to identify, select and appraise the best and most up-to-date evidence
- To integrate these findings with your own clinical experience and patients’ values
Critical appraisal of evidence
COVID-19 era: where to find evidence

https://covid-evidence.org/

Find evidence on interventions for COVID-19

COVID-evidence is a continuously updated database of the worldwide available evidence on interventions for COVID-19.

We provide information about worldwide planned, ongoing, and completed trials on any intervention to treat or prevent SARS-CoV-2-infections. We combine automatic search strategies with expert manual extraction of key trial characteristics performed in duplicate.

OPEN THE COVID-EVIDENCE DATABASE
Purpose of critical appraisal

Supporting decision-making

- **Critical appraisal**: process of systematically assessing the outcome of scientific research (evidence) to judge its trustworthiness, value and relevance in each scenario

- Aims to evaluate the level and quality of evidence to **support decision-making**
  - How certain are we about the results? (validity)
  - How applicable are the results to practice? (applicability, translational capacity)

- **Critical appraisal is essential to**:
  - Combat information overload
  - Identify papers that are clinically relevant
  - Continuing professional development

  **Carrying out critical appraisal – basic steps**:
  - Carefully read the study
  - Define study design – evaluate research methods
  - Check minimum standards conduction/reporting (checklists)
  - Address quality, validity of results and compare to other studies

Burls A. What is critical appraisal? London: Hayward Medical Communications. 2016
Enhancing the QUAlity and Transparency Of health Research

Conducting and reporting studies

**Overall recommendations**

**The EQUATOR Network**

- International initiative
- Improve the reliability and value of published health research literature
- Transparent and accurate reporting
- Wider use of robust reporting guidelines

**Library for health research reporting**

- The Library contains a comprehensive searchable database of reporting guidelines and also links to other resources relevant to research reporting.

**Reporting guidelines for main study types**

- Randomised trials
- Observational studies
- Systematic reviews
- Study protocols
- Diagnostic/prognostic studies
- Case reports
- Clinical practice guidelines
- Qualitative research
- Animal pre-clinical studies
- Quality improvement studies
- Economic evaluations

**Join our courses on reporting and research integrity**

**Enhancing the QUAlity and Transparency Of health Research**

http://www.equator-network.org/
Critical appraisal of evidence

Basic steps

Some initial appraisal questions include:

1. Is the evidence from a known, reputable source?
2. Has the evidence been evaluated in any way? If so, how and by whom?
3. How up-to-date is the evidence?
4. Were all important outcomes considered? How were they measured?
5. Is that a reliable way to measure?
6. How large was the effect size?
7. What implications does the study have for your practice? Is it relevant?
8. Can the results be applied into practice (benefit-risk ratio)?
9. Are the benefits worth the costs and potential risks?

References:
Burls A. What is critical appraisal? London: Hayward Medical Communications. 2016
Does Adding of Hydroxychloroquine to the Standard Care Provide any Benefit in Reducing the Mortality among COVID-19 Patients?: a Systematic Review

Tejas K Patel 1, Manish Banvaliya 2, Bhavesh D Kavadiya 3, Parvat B Patel 4, Hira Lai Bhalia 5

Abstract

Hydroxychloroquine has been promoted for its use in treatment of COVID-19 patients based on in-vitro evidence. We searched the databases to include randomized and observational studies evaluating the effect of Hydroxychloroquine on mortality in COVID-19 patients. The outcome was summarized as odds ratios (OR) with a 95% confidence interval (CI). We used the inverse-variance method with a random effect model and assessed the heterogeneity using I^2 test. We used ROBINS-I tool to assess methodological quality of the included studies. We performed the meta-analysis using Review manager software version 5.3. We identified 6 observational studies satisfying the selection criteria. In all studies, Hydroxychloroquine was given as add-on to the standard care and effect was compared with the standard care alone. A pooled analysis observed 231 deaths in 1331 participants of the Hydroxychloroquine arm and 365 deaths in 1577 participants of the control arm. There was no difference in odds of mortality events amongst Hydroxychloroquine and supportive care arm [1.25 (95% CI: 0.65, 2.48); I^2 = 80%]. A similar trend was observed with moderate risk of bias studies [0.95 (95% CI: 0.44, 2.06); I^2 = 85%]. The odds of mortality were significantly higher in patients treated with Hydroxychloroquine + Azithromycin than supportive care alone (2.34 [95% CI: 1.63, 3.34]; I^2 = 0%). A pooled analysis of recently published studies suggests no additional benefit for reducing mortality in COVID-19 patients when Hydroxychloroquine is given as add-on to the standard care. Graphical Abstract.
Systematic review and meta-analysis

COVID-19 evidence

Efficacy and safety of antiviral treatment for COVID-19 from evidence in studies of SARS-CoV-2 and other acute viral infections: a systematic review and meta-analysis

Wen Liu 1, Pengxiong Zhong 1, Ken Chen 1, Zhikang Ye 1, Fang Liu 1, Xiaotong Li 1, Na He 1, Ziyang Wu 1, Qi Zhang 1, Xuexing Gong 2, Qiuqiang Wang 3, Xin Du 1, Yinqiu Yang 1, Xiaohan Xu 1, Yuhai Zhang 1, Jinyu Liu 1, Yun Li 1, Ning Shen 1, Rachel J Couban 1, Quazi I Ibrahim 1, Gordon Guyatt 1, Sunil Zhai 1

Affiliations + expand
PMID: 32493740 DOI: 10.1053/cmaj.2020.06

Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis

Derek K Chu 1, Elie A Akl 2, Stephanie Duda 3, Karla Soo 3, Sally Yaacoub 4, Holger J Schünemann 5, COVID-19 Systematic Urgent Review Group (SURGE) study authors

Collaborators, Affiliations + expand
PMID: 32974310 PMCID: PMC7265314 DOI: 10.1016/S0140-6736(20)31142-9

Effects of four types of integrated Chinese and Western medicines for the treatment of COVID-19 in China: a network meta-analysis

Lairun Jin 1, Yan Xu 1, Hui Yuan 2

Affiliations + expand
PMID: 32696684 DOI: 10.1590/1806-9282.66.6.771
Systematic review and meta-analysis

COVID-19 evidence

Effects of four types of integrated Chinese and Western medicines for the treatment of COVID-19 in China: a network meta-analysis

Network plot: multiple comparisons of interventions

Ranking analysis

<table>
<thead>
<tr>
<th>Treatment</th>
<th>SUCRA</th>
<th>P&lt; Best</th>
<th>Mean rank</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>0.0</td>
<td>0.0</td>
<td>4.9</td>
</tr>
<tr>
<td>B</td>
<td>30.3</td>
<td>1.2</td>
<td>30.0</td>
</tr>
<tr>
<td>C</td>
<td>28.8</td>
<td>0.1</td>
<td>3.8</td>
</tr>
<tr>
<td>D</td>
<td>85.7</td>
<td>54.0</td>
<td>16.0</td>
</tr>
<tr>
<td>E</td>
<td>821</td>
<td>44.7</td>
<td>17.0</td>
</tr>
</tbody>
</table>

Notes: A, Symptomatic and supportive care; B, Symptomatic and supportive care + Qingfei Tussie-Fushuang Rweipe; C, Symptomatic and supportive care + Lianhua Qingwen Granule; D, Symptomatic and supportive care + Lianhua Qingwen Granule; E, Symptomatic and supportive care + Xuebijing Injection.
GRADE
Grading of Recommendations Assessment, Development and Evaluation

- Provides a transparent and structured approach to making **judgments** about the certainty of the evidence
- Offers a transparent process to **making recommendations and decisions**
- Currently used by over 100 organizations globally, including the World Health Organization
- Ideally applied to rate the certainty of a body of evidence in a well-conducted and up-to-date evidence synthesis (e.g. setting, population, intervention, comparator, outcomes) with summary tables
- Although appropriately sophisticated in its full execution, it can answer questions and be relayed to decision-makers by breaking its components down into straightforward questions about:
  - the certainty of evidence
  - the criteria for making decisions or recommendations

www.gradeworkinggroup.org
GRADE
Grading of Recommendations Assessment, Development and Evaluation

Box 3: Definitions of grades of evidence

- **High** = Further research is unlikely to change our confidence in the estimate of effect.
- **Moderate** = Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
- **Low** = Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
- **Very low** = Any estimate of effect is very uncertain.

Box 2: Criteria for assigning grade of evidence

- **Type of evidence**
  - Randomised trial = high
  - Observational study = low
  - Any other evidence = very low

- **Decrease grade if:**
  - Serious (−1) or very serious (−2) limitation to study quality
  - Important inconsistency (−1)
  - Some (−1) or major (−2) uncertainty about directness
  - Imprecise or sparse data (−1)
  - High probability of reporting bias (−1)

- **Increase grade if:**
  - Strong evidence of association—significant relative risk of >2 (<0.5) based on consistent evidence from two or more observational studies, with no plausible confounders (+1)†
  - Very strong evidence of association—significant relative risk of >5 (<0.2) based on direct evidence with no major threats to validity (+2)§
  - Evidence of a dose response gradient (+1)
  - All plausible confounders would have reduced the effect (+1)

Guide recommendations

Strong/Weak Favors/Against

www.gradeworkinggroup.org
Using GRADE in situations of emergencies and urgencies: Certainty in evidence and recommendations matters during the COVID-19 pandemic, now more than ever and no matter what

Holger J. Schünemann,1,2,* Nancy Santibañez, 1 Ganna F. Vidy 3 Carlos Cuvello 1 Jarnara Lotti 1 Shyna Flettore 3 Marina Devoli, 4 Reem Mustafa 5 Joerg J. Meerpohl, 6 Pablo Alonso-Coello, 7 and Elie A. Asli 8

- In situations of emergencies and urgencies, such as the COVID-19 pandemic, GRADE can similarly be used to express and convey certainty in intervention effects, test accuracy, risk and prognostic factors, consequences of public health measures, and qualitative bodies of evidence

- Requirements for emergency, urgency, rapid and routine GRADE assessment may differ but should transition from one to another

Levels of time-based responses using GRADE

- Emergency or ultra-short time responses
- Urgent responses
- Rapid responses
- Routine responses

Time frame

- Ultra-short time responses: needed within hours.
- 1 to 2 weeks to respond.
- Up to 3 months to respond.
- Beyond 3 months. Regular time frame to respond. Living reviews and recommendations

Examples

- Should N95 vs surgical masks be used during the COVID-19 pandemic? Rapid evaluation of evidence from previous coronavirus outbreaks (MERS, SARS).
- Should non-invasive vs invasive mechanical ventilation be used in patients with COVID-19 and hypoxemic respiratory failure? Urgent and complete systematic review.
- Should Remdesivir be used in patients with COVID-19? Rapid reviews and recommendations based on accumulating evidence.
- Should stringent vs loose lockdowns be used during a second COVID-19 outbreak? Question allows routine assessment of the evidence and living approaches.
Implications & Take-home messages

To effectively practice as an evidence-based practice provider

- We should get used to always evaluate the provenance and quality of information
- Critical appraisal looks at the way a study is conducted and evaluates factors such as internal validity, generalizability and relevance
- Evidence and recommendations generation need high quality studies (data confidence)
- Decisions related to patient value and care are carefully made following an essential process of integration of the best existing evidence, clinical experience and patient preference
- GRADEing the certainty of the available evidence is more important than ever because of the unprecedented pressure for action and the large number of people affected by decisions
Speaker 3

Dalia Dawoud, PhD
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Pharmacoeconomics and Outcomes Research,
Research in Social and Administrative Pharmacy (RSAP)
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&
Associate Professor,
Faculty of Pharmacy, Cairo University, Egypt

Email: ddawoud@hotmail.com  @drddawoud
Economic Evidence: The Missing Piece

**Why?**

- No health care system in the world can provide every effective intervention. **Resources** are **limited** and **wants** are **limitless** (**Scarcity**)

- If you provide more of one service, you will have to provide less of another. (**Opportunity cost**)

- **Choices** and **trade-offs** must be made.

*The impact of the COVID-19 pandemic on cancer deaths due to delays in diagnosis in England, UK: a national, population-based, modelling study*

Cornelia Mastegge, James Spicer, Melanie Mowes, Annie Parncuttetham, Ellen Naife, Richard Sullivan, Bernard Haesch, Ajay Aggarwal*
Health economics utilises economic analysis methods to inform decision making regarding the allocation of the scarce resources available by identifying interventions that most likely to provide the best value for every £/$/€ spent (i.e. cost-effective).
Economic Evidence: The Missing Piece

How?

Economic Evaluation:

“The comparative analysis of alternative courses of action in terms of both their costs and consequences.” (Drummond et al. 2015)

• The type of an economic evaluation is largely determined by:
  • The nature and measure of the outcomes considered
  • The presence of evidence (or assumptions made) regarding (non-)equivalence of outcomes
  • How the analysis results are presented
### Economic Evidence: The Missing Piece

#### How?

1. Are both costs (inputs) and consequences (outputs) examined?

<table>
<thead>
<tr>
<th></th>
<th>NO</th>
<th>YES</th>
</tr>
</thead>
<tbody>
<tr>
<td>1A</td>
<td>Examine only consequences</td>
<td>Examine only costs</td>
</tr>
<tr>
<td>2</td>
<td>PARTIAL EVALUATION</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Outcome description.</td>
<td>• Cost description.</td>
</tr>
</tbody>
</table>

2. Are at least 2 alternatives compared?

<table>
<thead>
<tr>
<th></th>
<th>NO</th>
<th>YES</th>
</tr>
</thead>
<tbody>
<tr>
<td>3A</td>
<td>Examine only consequences</td>
<td>Examine only costs</td>
</tr>
<tr>
<td>4</td>
<td>FULL ECONOMIC EVALUATION</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Efficacy or effectiveness evaluation.</td>
<td>• Cost analysis.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Cost-minimisation analysis.</td>
</tr>
</tbody>
</table>

#### Cost-Effectiveness Analysis (CEA)
- Focuses on one primary outcome
- Disease specific expressed in natural units (e.g. number of strokes avoided)

#### Cost-Utility Analysis (CUA)
- Focuses on one primary outcome
- Generis outcome e.g. Quality Adjusted Life Years (QALYs) or Disability Adjusted Life Years (DALYs)

#### Cost-Benefit Analysis (CBA)
- Measures both benefits and costs in monetary terms

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Drummond et al. 2015
Economic Evaluation is most useful after the following:

- **Efficacy studies**: which aim to answer the question “Can the intervention work?"
- **Safety studies**: which aim to answer the question “Does it do more good than harm?”
- **Effectiveness studies**: which answer the question “Does the intervention work when applied?”

The bottom line is that if an intervention is not effective, it is not cost-effective.
**Economic Evidence: The Missing Piece**

**Approaches**

<table>
<thead>
<tr>
<th>A. Alongside a clinical study</th>
<th>B. Using Economic Modelling</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collecting data on both costs and consequences simultaneously from a single study (mostly phase III RCT)</td>
<td>Mathematical simulation of the costs and consequences attached to using each alternative using data from various sources (e.g. Systematic reviews and meta-analysis, epidemiological studies, RCTs, observational studies)</td>
</tr>
</tbody>
</table>

The following are broadly the main steps of conducting a full economic evaluation:

1. Identifying, measuring and valuing **outcomes**
2. Identifying, measuring and valuing **costs**
3. Combining **costs** and **outcomes**
4. Assessing **uncertainty** and drawing conclusions to inform **decision-making**
5. Optional: Assessing **Value of Information** to inform **future research investment**
Economic Evidence: The Missing Piece

Critical Appraisal

- Critical appraisal of published economic evaluation studies allows us to assess the **methodological quality** and **applicability** of these studies and their results to current clinical practice.

- The **Critical Appraisal Skills Program (CASP)** proposed a simple checklist to appraise published economic evaluations in terms of quality, usefulness and applicability.

- This **checklist** prompts the reviewer to answer the following questions:
  - **Is the economic evaluation valid?**
  - **How were costs and consequences assessed and compared?**
  - **Will the results help in purchasing services for local people?**

• Guidelines for conducting economic evaluations also exist to provide a set of methodological standards that should be followed.

• These guidelines are usually proposed by the decision makers who are going to use the results of these studies in their decision making to ensure applicability of the results to their jurisdictions.

• An example of these guidelines is the “Guide to the Methods of Technology Appraisal” published by NICE in April 2013.¹

Economic Evidence: The Missing Piece

Reporting Standards

- The **British Medical Journal, Value in Health, RSAP** and other peer-reviewed journals publishing economic evaluations adopted a 24 item “checklist” for reporting of economic evaluations developed by ISPOR Health Economic Evaluation Publication Guidelines Good Reporting Practices Task Force.

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Economic Evidence: The Missing Piece

Examples

• No economic evaluation of COVID-19 related interventions or strategies published so far.

• One report from USA ICER used economic modeling to establish the value-based price benchmark of remdesivir using economic evaluation (CUA)

• But, a number identified in the literature focused on a large number of mitigation strategies used in previous outbreaks such as H1N1

https://icer-review.org/
Examples

- Screening
- Disease surveillance networks
- Contact tracing
- Face masks
- Hand washing
- Social distancing
- Self-isolation
- Antiviral prophylaxis
- Antiviral treatment
- Antiviral stockpiling
- Vaccination
- Border control
- School closure

“this study estimates that the use of facemasks by 10%, 25%, and 50% of the population could reduce economic losses by $478 billion, $570 billion, and $573 billion, respectively”
Coronavirus: Doctors collapse from exhaustion as virus spreads through South Korea

Stricken Koreans are dying at home while waiting for hospital beds as the government struggles to deploy enough medical staff.
Putting evidence into action

The role of clinical guidance

**Evidence-based Practice**
- Teaching clinicians how to find the evidence to answer clinical questions
- Individual clinicians
- Bottom-up approach

**Clinical Guidelines and HTA**
- Advising clinicians how to practice based on evidence
- Health systems
- Top-down approach

Photo: John Wildgoose/Getty Images
Putting evidence into action

Clinical (Practice) Guidelines

“Statements that include recommendations, intended to optimize patient outcomes, that are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options”¹

¹ Committee on Standards for Developing Trustworthy CPGs. (IOM-AHRQ 2011)
Putting Evidence Into Action

**Rapid Guidelines**

**Rapid guidelines**

Managing symptoms and complications
- Acute kidney injury in hospital - NG175
- Acute myocardial injury - NG171
- Antibiotics for pneumonia in adults in hospital - NG173
- Critical care in adults - NG119
- Managing suspected or confirmed pneumonia in adults in the community - NG165
- Managing symptoms (including at the end of life) in the community - NG163

Managing conditions that increase risk
- Children and young people who are immunocompromised - NG174
- Chronic kidney disease - NG176
- Community-based care of patients with chronic obstructive pulmonary disease (COPD) - NG168
- Cystic fibrosis - NG170
- Dermatological conditions treated with drugs affecting the immune response - NG169
- Gastrointestinal and liver conditions treated with drugs affecting the immune response - NG172
- Interstitial lung disease - NG177
- Rheumatological autoimmune, inflammatory and metabolic bone disorders - NG167
- Severe asthma - NG166

Providing services during the pandemic
- Delivery of radiotherapy - NG162
- Delivery of systemic anticancer treatments - NG161
- Dialysis service delivery - NG169
- Haematopoietic stem cell transplantation - NG164
- Renal transplantation - NG178

**Rapid evidence summaries**

These summaries cover:
- Acute use of non-steroidal anti-inflammatory drugs (NSAIDs) for people with or at risk of COVID-19 - ES23
- Anakinra for COVID-19 associated secondary haemophagocytic lymphohistiocytosis - ES26
- Angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) in people with or at risk of COVID-19 - ES24
- Long-term use of non-steroidal anti-inflammatory drugs (NSAIDs) for people with or at risk of COVID-19 - ES25
- Remdesivir for treating hospitalised patients with suspected or confirmed COVID-19 - ES27
- Vitamin D for COVID-19 - ES28
Putting evidence into action

*Health Technology Assessment (HTA)*

“A multidisciplinary process that uses explicit methods to determine the value of a health technology at different points in its lifecycle. The purpose is to inform decision-making in order to promote an equitable, efficient, and high-quality health system.” O'Rourke et al. 2020
Decision-making under uncertainty and an evolving evidence-base!

Managing uncertainty in a pandemic: five simple rules

1. Most data will be flawed or incomplete. Be honest and transparent about this.
2. For some questions, certainty may never be reached. Consider carefully whether to wait for definitive evidence or act on the evidence you have.
3. Make sense of complex situations by acknowledging the complexity, admitting ignorance, exploring paradoxes and reflecting collectively.
4. Different people (and different stakeholder groups) interpret data differently. Deliberation among stakeholders may generate multifaceted solutions.
5. Pragmatic interventions, carefully observed and compared in real-world settings, can generate useful data to complement the findings of controlled trials and other forms of evidence.

Putting Evidence Into Action

Clinical judgment

• “Guidelines not tramlines!” Sir David Haslam

Your responsibility

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.
Thank You!
Question Time

Please use the chat board to log your questions & comments.
Thank you for participating!

Please provide your feedback through the 4-question survey that will appear to you at the end of the event.