Evaluating Evidence for Emerging Therapies during a Pandemic

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Disclosure

- No industry conflicts of interest to declare

- Previous members of Alberta Expert Committee on Drug Evaluation and Therapeutics

- Current member of AHS Drugs & Therapeutics Committee
Objectives:

• Understand what a pandemic does to the usual evidence evaluation process
• With limited evidence on specific interventions, understand how can an evidence informed decision be made
• How to account for harms when making decisions using limited evidence
• Put forward a recommendation for a pandemic related intervention
COVIDmab

COVIDmab is our imaginary drug we will use as an example.

Any resemblance to actual drugs, on or off the Canadian market, is purely coincidental.
Appreciate During a Pandemic

• It is a difficult and emotional time
• Everyone is trying to do the best for their patients
• We have a bias to do something to help
What does a pandemic mean for EBM?

Are we:

• Suspending it’s use as EBM doesn’t apply in a time like this?
• Adapting our exceptions of the evidence but holding to the principles?
• Standing firm, nothing changes
## What does a Pandemic do to us?

<table>
<thead>
<tr>
<th></th>
<th>“Normal” times</th>
<th>Pandemic times</th>
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<tbody>
<tr>
<td><strong>Efficacy</strong></td>
<td>Review literature in detail</td>
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<td>Determine the value of an incremental investment</td>
<td>If drug not available, we’ve failed our patients</td>
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<td>If drug not available, why would we list?</td>
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STEDT Program

Short Term Exceptional Drug Therapy Program

Evidence informed review process for rare life, limb and organ threatening cases

For more information, visit:
https://www.cadth.ca/creating-criteria-using-patient-experience-high-cost-rare-use-drugs-limited-evidence
Efficacy data

We can’t just state the evidence is weak, promising, emerging, or the best we have. We need to outline what the evidence is:

COVIDmab has:

• Three open label trials (all N<50) that measure recovery time after treatment
• There are two case reports of use in this condition
• In vitro data of activity

Interesting, but not evidence

• There is a large scale randomized trial looking at the effectiveness of COVIDmab in this condition
Harms

Hippocratic Oath:
• “……and abstain from whatever is deleterious and mischievous.”

Of the Epidemics:
• “……and have two special objects in view with regard to disease, namely, to do good or to do no harm.”
How good are we at estimating harms?

“Clinicians rarely had accurate expectations of benefits or harms, with inaccuracies in both directions. However, clinicians more often underestimated rather than overestimated harms and overestimated rather than underestimated benefits.”

1
Quantifying Harms

“The drug is well tolerated”

Compared to what?

- Full course of cisplatin
- A single dose of acetaminophen 325mg
Quantifying Harms

We cannot accurately assess whether the risks of the drug are suitable for a patient population unless we are specific.

COVIDmab has the following side effect profile:

- **Common**: flu like symptoms – nausea, vomiting, dizziness, chills
- **Rare**: thrombocytopenia, allergic reaction, increased risk of infection
Sustainability (costs)

• During a pandemic, costs are often overlooked
• However costs still need to be understood

COVIDmab has the following cost implications:
• Costs $1000 for a course of treatment
• Is an add on therapy
• New lab costs are $50 per patient
• We estimate treating 500 patients
• Total cost is estimated to be $525,000
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What does a pandemic mean for EBM?

Are we:

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What does a pandemic mean for EBM?

Given the severity and urgency of the situation we may have to accept lower levels of evidence to make the best informed decision at the time:

– Case studies
– Open label trials
– In vitro data

However we still keep EBM principles and require solid evidence before we support using a drug.
If Expert Opinion is all we have......

Expert opinion is:

• A form of evidence (at the bottom of the hierarchy)
• Critical to making an informed decision

However expert opinion should be informing evidence above it in the hierarchy, not be the only source of evidence to build a case to use a therapy
# Making the Case for COVIDmab

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<td>• There is limited but emerging evidence for this drug</td>
<td>• Three open label trials (all N&lt;50) that measure recovery time after treatment</td>
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<td>• It is being studied in other countries for its possible role</td>
<td>• There are two case reports of use in this condition</td>
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<td>• The drug has a favorable side effect profile</td>
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<td>• Rare: thrombocytopenia, allergic reaction, increased risk of infection</td>
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<td>• Acceptable costs for the circumstances we are in</td>
<td>• The incremental cost to introducing therapy is $525,000</td>
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Bottom line

- Discussing treatment options during a pandemic is emotional & stressful for everyone
- Bringing objective information to discussions helps reduce emotion and focus the discussion on solutions
- While we may be accepting lower levels of evidence, we shouldn’t be accepting:
  - Items that are not actually evidence
  - Only expert opinion evidence as direction
- Ideally make treatment decision for the system before a case presents, not waiting until a case presents
Discussion/Questions

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Reference

Clinicians’ Expectations of the Benefits and Harms of Treatments, Screening, and Tests
doi:0.1001/jamainternmed.2016.8254

Link

Background presentation on the Short Term Exceptional Drug Therapy Program
https://www.cadth.ca/creating-criteria-using-patient-experience-high-cost-rare-use-drugs-limited-evidence