Making Sense of Media Stories about COVID-19: studies of treatment and prevention

Centre For Inquiry Canada
June 13 2020

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DALHOUSIE UNIVERSITY Inspiring Minds

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1

Disclaimer

This session is intended as an introduction to medical research studies.

It is not intended to give you specific medical advice.

Decisions about your health care should be made in consultation with a health professional.

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2

Outline

1. Review research study designs
2. Relate study design to levels of evidence, guideline recommendations
3. Discuss examples
   - Masks
   - Vitamin D
   - Vitamin K
   - Remdesivir
   - Hydroxyquinolone

3

3

Study Design

- **Exposure**
  - Observational study: The potential risk
    - An actual exposure e.g., environmental tot
    - A behaviour e.g., sedentary lifestyle,
    - An individual attribute e.g., age
    - Face mask
  - Experimental study: The intervention applied to study subjects e.g., a drug or other treatment – or face mask, social distancing, hand washing
- **Outcome**
  - The disease or other outcome that is being investigated in relation to the exposure e.g., blood pressure, heart attack, stroke, COVID-19 infection, death

Compare the frequency of the outcome in people who do and do not have the exposure.

4

4

Observational vs Experimental Study

- Observational study
  - The researchers do not control the exposure status of the subjects
  - May show association between exposure and outcome but not necessarily causation
- Experimental study
  - The researchers employ some type of intervention (exposure) to determine its effect on an outcome
  - Implies causation

5

5

Observational studies

- Ecological studies (7)
  - Study populations defined geographically or temporally
  - Looks at populations not individuals
  - E.g. use of face masks vs COVID-19 cases in different countries
- Case reports or series of case reports (6)

6

6

Observational studies

- Case-control studies (5)
  - Pick subjects based on **outcome** and see what they were **exposed** to
    - Did more COVID-19 patients who died have high blood pressure compared to COVID-19 patients who did not die?
      - Outcome
      - Exposure
- Cohort studies (4)
  - Pick subjects based on **exposure** and see if they developed the **outcome**
    - Were COVID-19 patients who had high blood pressure more likely to die compared to those who did not have high blood pressure?
      - Exposure
      - Outcome

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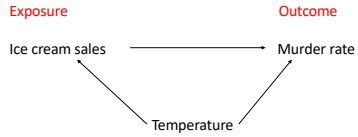
Observational studies - Confounders



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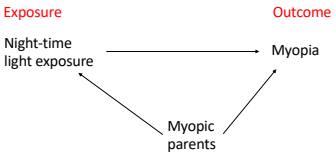
Observational studies - Confounders



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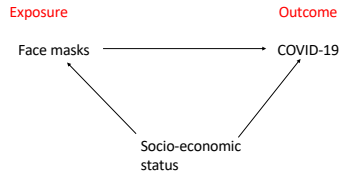
Observational studies - Confounders



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Experimental studies

- Case reports or case series (6)
- Control = comparison group
  - Important to know what it is
    - Placebo
    - Usual drug
    - Usual treatment
  - Randomized or non-randomized

Randomization avoids confounders

Double blinded

Double blinded randomized controlled **trial** (2)

Unblinded = open label (3)

11

11

Other categories

- In vitro – "test tube" – mostly experimental (10)
- Animal (9)
- Modelling studies – "quasi-experimental" (8)
- Systematic review (1)
- Meta-analysis – mostly experimental (1)
  - Statistically pool results of several studies on same topic to identify overall results

12

12

Modelling Studies

- Predict COVID-19 outcomes based on
  - People susceptible to catching virus
  - Exposed
  - Asymptomatic carriers
  - People infected
  - People who have recovered or died
- Depends on how people move from one group to another
  - Infection rate
  - Incubation time
  - Recovery time

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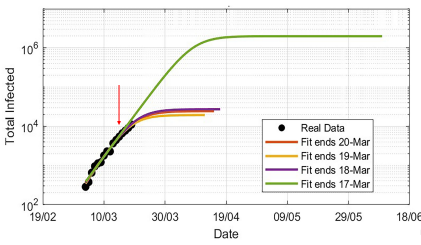
13

Modeling COVID-19 data must be done with extreme care, scientists say



https://phys.org/news/2020-05-covid-extreme-scientists.html

14

14

Modelling Studies – Canada

	Cases	Deaths
• April 28		
– Predicted by May 5	53,200 – 66,835	3,277 – 3,883
– Actual May 5	62,046	4,043
• June 4		
– Predicted by June 15	97,990 – 107,454	7,700 – 9,400
– Actual June 12		

CTV News June 4 2020

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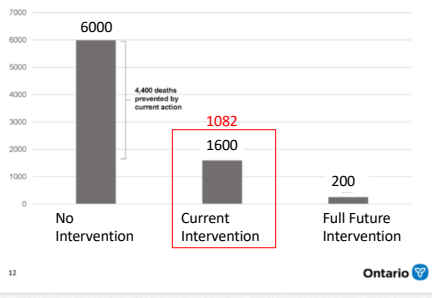
Projected Ontario Deaths by April 30, 2020

CBC April 4 2020



Ontario

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16

THE GLOBE AND MAIL*

WORLD

Sweden's hands-off approach to tackling coronavirus resulted in too many deaths, top epidemiologist says

PAUL WALDIE
LONDON
PUBLISHED JUNE 3 2020, 6:38PM
UPDATED JUNE 4 2020, 9:58AM

Paul Franks, an epidemiologist at Lund University in Malmo, Sweden, said Dr. Tegnell's strategy made sense at first, but has become too rigid given how much more is known about the virus.

"There hasn't been a willingness to change direction based on credible data," Dr. Franks said.

Dr. Tegnell insisted that he stood by his overall approach and that strict lockdowns were not sustainable.

"This is a bit like having an ocean liner and trying to steer it with a lag of three or four weeks.

I think we are too early to both say that Sweden was right or anybody else was right."

17

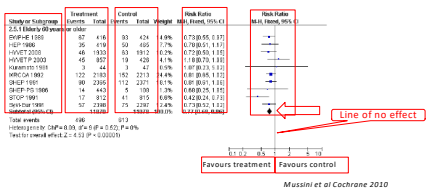
17

Meta-analysis

Statistically pool results of several studies on same topic to identify overall results

Exposure: Effect of blood pressure medications on
Outcome: death from cardiovascular disease in patients 60 years old and older

Figure 3. Cardiovascular mortality in elderly patients with hypertension



Mussini et al Cochrane 2010

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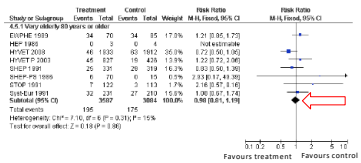
Meta-analysis

Effect of blood pressure medications on death from cardiovascular disease in patients 80 years old and older

Figure 6. Cardiovascular mortality in the very elderly patients



Mussini et al Cochrane 2010

19

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Other categories

- Drug studies
  - Phase 0 Small dose of test drug given to 10-15 people to assess how drug is processed by the body
  - Phase 1 Test drug on **healthy** subjects for dose ranging and safety
  - Phase 2 Test drug on small number **patients** for safety and effectiveness
  - Phase 3 Test drug on larger number of patients with a control group to further assess safety and effectiveness – *double-blind randomized controlled trial*
  - Post-marketing Observational studies of drug in real-world use

20

20

Outcomes

Surrogate (intermediate)	**Clinical**
• Cholesterol →	• Heart attack
• Blood pressure →	• Stroke
• Blood sugar →	• Loss of vision
• Bone density →	• Fractures
	• Death
	• Quality of life

21

21

Outcomes – COVID-19

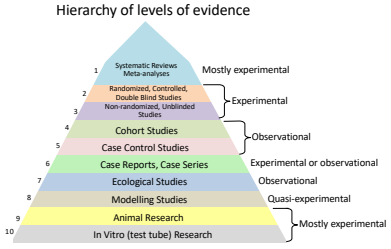
Surrogate (intermediate)
- Symptoms
- Improvement on scale
- Negative test
- Viral shedding

Clinical
- Hospitalization
- Intensive care
- Death

22

22

Hierarchy of levels of evidence



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Use of Levels of Evidence

Diabetes Canada 2018

- **Level 1A**
  - Systematic overview or meta-analysis of high-quality randomized control trials OR
  - Appropriately designed randomized control trial
- **Level 1B** - Non-randomized clinical trial or cohort study with indisputable results
- **Level 2** - Randomized controlled trial or systematic overview that does not meet Level 1 criteria
- **Level 3** - Non-randomized clinical trial or cohort study; systematic overview or meta-analysis of level 3 studies
- **Level 4** – Other case control studies, case reports, expert opinion

25

25

Use of Levels of Evidence
Diabetes Canada 2018

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- **Level 3** - Non-randomized clinical tria overview or meta-analysis of level 3 s
- **Level 4** – Other case control studies,

Strength of Recommendation
Grade A
Grade B
Grade C
Grade D

26

26

Use of Levels of Evidence - GRADE

- High quality evidence
  - Consistent evidence from well performed randomized controlled trial or overwhelming evidence of some other form
- Moderate quality evidence
  - Evidence from randomized controlled trials with important limitations
    - Inconsistent results
    - Flaws in methods
    - Imprecise results
- Low quality evidence
  - Evidence from observational studies, unsystematic clinical experience, randomized controlled trials with ~~serious flaws~~

Strong or Conditional recommendation For or Against

29

29

Use of Levels of Evidence – GRADE
2019 American Guideline for Osteoarthritis of Hand, Knee, Hip

- Chondroitin sulfate is **strongly recommended against** in patients with knee and/or hip osteoarthritis
- Exercise is **strongly recommended for** patients with knee, hip, and/or hand osteoarthritis

Arthritis & Rheumatology Vol. 72, No. 2, February 2020, pp 220–233 DOI 10.1002/art.41142

30

30

Questions
Discussion
Practice

31

31

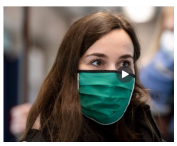
Study 1	Yes	No	Uncertain
1. What type of study is this? *(Experimental studies are usually better.)*			
• Observational			
• Experimental			
2. What is the exposure? *(What is the risk factor or intervention being reported on?)*			
3. What is the outcome? *(What effects can be expected from the exposure?)*			
• Clinical outcome (e.g., heart attack, stroke)			
• Surrogate outcome (e.g., blood pressure, cholesterol)			
4. What level on the evidence pyramid is this study?			

32

32

CTV NEWS

'Convincing' evidence suggests cloth masks may help reduce COVID-19 transmission



Jonathan Forani
CTVNews.ca Writer
Published May 25, 2020 11:52 a.m. ET
Updated May 26, 2020 7:54 a.m. ET

Face masks made with multiple layers of cloth may help prevent further transmission of COVID-19, according to an international team of researchers who examined a century's worth of mask studies.

Homemade cloth masks aren't perfect, they found, but may help provide a "modest reduction in transmission" if widely used, according to the opinion paper published in the Annals of Internal Medicine on May 22.

https://www.ctvnews.ca/health/coronavirus/convincing-evidence-suggests-cloth-masks-may-help-reduce-covid-19-contamination-1.4953351

34

34

Face Masks CTV News May 26 2020

- The team's full review of mask research has yet to be published but is currently being peer-reviewed.
- The scientists looked at 100 years of research, going back to the 1918 Spanish flu pandemic.
- A century later, there is still lack of evidence to support the effectiveness of homemade masks in preventing community transmission.
- "There are no clinical studies that show wearing a mask out in the community is definitely going to reduce the transmission of a viral illness," said the lead author Clase.

35

35

Face Masks CTV News May 26 2020

- "Although no direct evidence indicates that cloth masks are effective in reducing transmission of SARS-CoV-2, the evidence that they reduce contamination of air and surfaces is **convincing** and should suffice to inform policy decisions on their use in this pandemic pending further research."

In vitro studies
Animal studies

36

36

WHO June 5 2020

who.int/emergencies/diseases/novel-coronavirus-2019/advice-for-public/when-and-how-to-use-masks

- At present, there is no direct evidence (from studies on COVID-19 and in healthy people in the community) on the effectiveness of universal masking of healthy people in the community to prevent infection with respiratory viruses, including COVID-19
- However, taking into account
  - studies evaluating pre- and asymptomatic transmission
  - growing **observational** evidence on the use of masks by the general public in several countries
  - individual values and preferences
  - difficulty of physical distancing in many contexts

  WHO advises that to prevent COVID-19 transmission in community areas, governments should encourage the general public to wear masks in specific situations and settings

40

40

41

41