Studies of Medical Treatment and Prevention: study design and statistics

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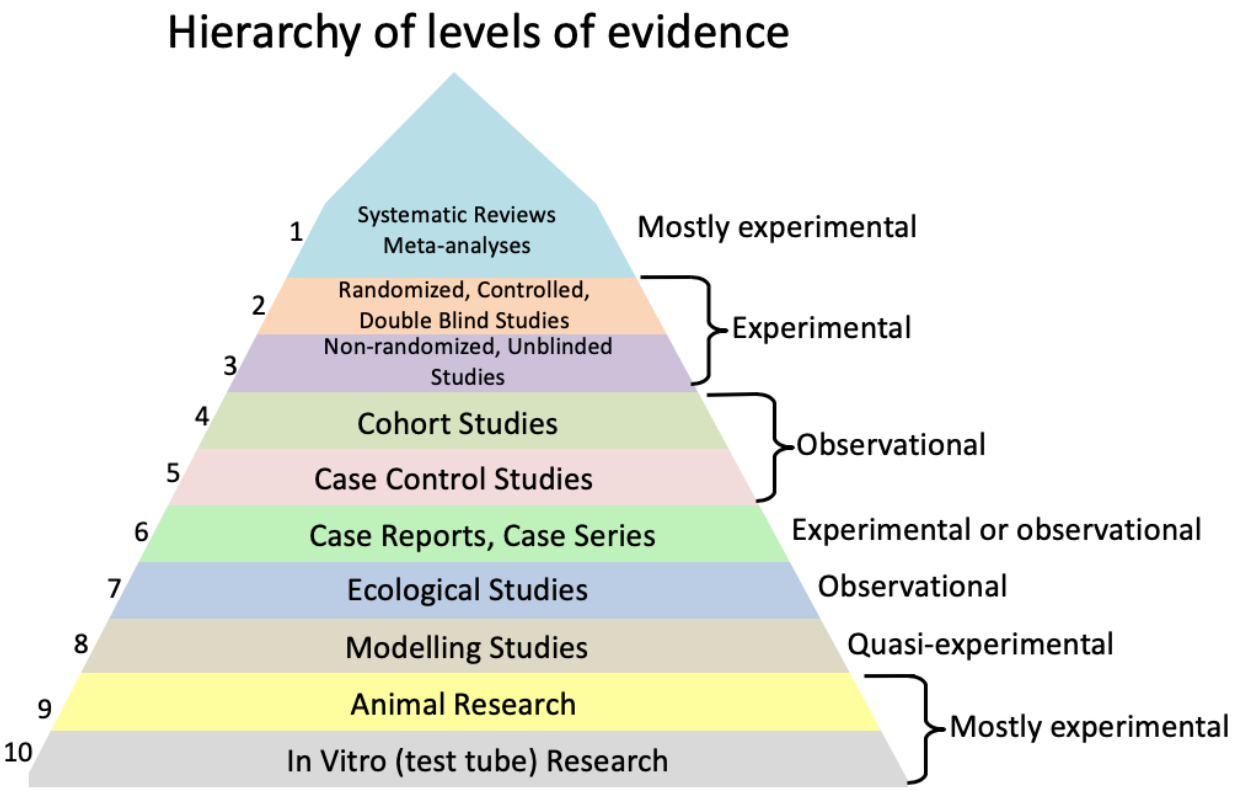

Useful Websites

Sources of Evidence-based Health Information

Cochrane Library https://www.cochrane.org

Canadian Agency for Drugs and Technology in Health https://www.cadth.ca

National Institute for Health and Care Excellence https://www.nice.org.uk

COVID-19 Evidence Alerts from McMaster PLUS™ https://plus.mcmaster.ca/COVID-19/

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?			

Masks probably slow the spread of covid-19
The Economist May 28 2020

1. Although scientists cannot experiment on human beings deliberately, some wonder if the world is now carrying out a natural experiment that tests the value of mask-wearing.
2. Many people in East Asia took immediately to wearing masks when the epidemic started.
3. Countries that adopted masks early on did not, by and large, shut their economies down.
4. Yet they suppressed the disease more effectively than those that locked down but did not wear masks.
5. According to Patricia Greenhalgh, professor of primary health care sciences at Oxford University, "there is not a single country in which mask wearing was introduced early and with high compliance, where the disease wasn't quickly brought under control."
6. Sceptics point out that this does not prove masks work, since countries in which they are widely worn also tend to be those which have been threatened by epidemics in the past, and therefore have well-established systems of testing and contact tracing.

Not masking a lot
Growth of covid-19, by country or region
First 60 days after reaching 30 confirmed cases

Region/ country	Total cases	Avg. daily growth rate, %	Measures taken
Beijing	558	4.7	Lockdown, masks
Hong Kong	989	5.6	Masks
Japan	4,618	6.9	Masks
S. Korea	10,635	10.3	Masks
Germany	158,758	14.5	Lockdown
France	164,589	15.0	Lockdown
Britain	171,253	15.2	Lockdown
America	903,882	17.7	Lockdown

Sources: De Kai et al.; Johns Hopkins University CSSE; *The Economist*

Study 2	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?)*			
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4. What level on the evidence pyramid is this study?			

Vitamin D deficiency may be linked to more severe cases of COVID-19, studies suggest
CTV News May 13 2020
https://www.ctvnews.ca/health/coronavirus/vitamin-d-deficiency-may-be-linked-to-more-severe-cases-of-covid-19-studies-suggest-1.4937535

1. Researchers found that patients from countries with high COVID-19 mortality rates, such as Italy, Spain and the U.K., had lower levels of vitamin D compared to patients in countries that were not as severely affected.
2. The study, which has not been peer-reviewed, was pre-printed April 30 in the online journal medRxiv.
3. Researchers looked at data from hospitals and clinics across China, France, Germany, Italy, Iran, South Korea, Spain, Switzerland, the U.K. and the U.S. They compared this with data on the levels of vitamin D in the population in those countries before the pandemic.
4. The study found a correlation between vitamin D deficiency and a complication known as a cytokine storm, which occurs when the immune system goes into overdrive, as well as a correlation between vitamin D deficiency and mortality rates.
5. Vitamin D modulates the response of white blood cells and can prevent them from releasing too many inflammatory cytokines. COVID-19 can cause an excess of these cytokines.
6. "Cytokine storm can severely damage lungs and lead to acute respiratory distress and death," Ali Daneshkhah, lead author of the study, said. "This is what seems to kill a majority of COVID-19 patients, not the destruction of the lungs by the virus itself."
7. However, the researchers stress that this does not mean that everyone -- especially those without a known deficiency -- need to start increasing their intake of vitamin D.
8. "While I think it is important for people to know that vitamin D deficiency might play a role in mortality, we don't need to push vitamin D on everybody," researcher Vadim Backman said. "This needs further study, and I hope our work will stimulate interest in this area."

Study 3	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?)*			
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4. What level on the evidence pyramid is this study?			

Vitamin K found in some cheeses could help fight Covid-19, study suggests
The Guardian June 5 2020
https://www.theguardian.com/science/2020/jun/05/vitamin-k-could-help-fight-coronavirus-study-suggests

1. Patients who died or had been admitted to intensive care with Covid-19 were found to be deficient in a vitamin found in spinach, eggs, and hard and blue cheeses, raising hopes that dietary change might be one part of the answer to combating the disease.
2. Researchers studying patients admitted to hospital in the Dutch city of Nijmegen have discovered a link between Vitamin K deficiency and the worst coronavirus outcomes.
3. Covid-19 causes blood clotting and leads to the degradation of elastic fibres in the lungs. Vitamin K, which is ingested through food and absorbed in the gastrointestinal tract, is key to the production of proteins that regulate clotting and can protect against lung disease.
4. The research, undertaken in partnership with the Cardiovascular Research Institute Maastricht studied 134 patients hospitalised for Covid-19 between 12 March and 11 April, alongside a control group of 184 age-matched patients who did not have the disease.
5. The Dutch researchers are now seeking funding for a clinical trial, but Dr Rob Janssen, a scientist working on the project, said that in light of the initial findings he would encourage a healthy intake of vitamin K, except to those on blood-thinning medications such as warfarin.
6. He said: “We are in a terrible, horrible situation in the world. We do have an intervention which does not have any side effects, even less than a placebo. There is one major exception: people on anti-clotting medication. It is completely safe in other people.
7. Jona Walk, a second researcher on the study, which was submitted for peer review on Friday, said: “We want to take very sick Covid-19 patients and randomise them so that they get a placebo or vitamin K. We want to give vitamin K in a significantly high enough dose that we really will activate the protein that is important for protecting the lungs, and check if it is safe.”

Study 4	Yes	No	Uncertain
1. What type of study is this? *(Experimental studies are usually better.)*			
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3. What is the outcome? *(What effects can be expected from the exposure?)*			
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More evidence remdesivir helps some coronavirus patients
CNN June 2 2020
https://www.cnn.com/2020/06/01/health/remdesivir-coronavirus-phase-iii-trial-gilead-study/index.html

1. A 5-day course of the antiviral drug remdesivir sped recovery in moderately ill patients with pneumonia from Covid-19, drugmaker Gilead Sciences announced.
2. The results from the Phase III clinical trial led and funded by Gilead have not been published in a peer-reviewed medical journal.
3. Researchers randomly assigned 600 moderately ill patients to receive either the current standard of care for Covid-19; 5 days of remdesivir in addition to standard care; or 10 days of remdesivir plus standard care.
4. Patients who received a 5-day course of remdesivir were more likely to improve by at least 2 points on a tracking scale compared to those who received standard care alone.
5. However, while patients who received a 10-day course of remdesivir improved, the results were not statistically significant, suggesting just 5 days of treatment may be enough.
6. 134 of the 191 patients (70%) given 5 days of remdesivir improved and none died.
   126 of the 193 patients (65%) given 10 days of remdesivir improved but 2 died.
   122 of the 200 patients (61%) who received only standard care improved and 4 died.
7. When asked why 10 days of treatment was no better than standard care an infectious disease expert said, it "could be a toxicity from the longer dosing" or "a fluke of open-label design and physician behavior, where clinicians treat sicker patients for longer."
8. Stephen Evans, professor of pharmacoepidemiology at the London School of Hygiene & Tropical Medicine said “These improvements are not dramatic but at least there is some evidence of improvement. For the patients it is good news that few died, but the evidence that remdesivir improves mortality in these patients is uncertain and limited."

Study 5	Yes	No	Uncertain
1. What type of study is this? *(Experimental studies are usually better.)*			
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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?)*			
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4. What level on the evidence pyramid is this study?			

Hydroxychloroquine fails to prevent COVID-19 in those at high risk, trial shows
CBC June 4 2020
https://www.cbc.ca/news/health/covid19-hydroxychloroquine-who-1.5596689

1. Hydroxychloroquine, which has been the subject of heated debate as a potential treatment for COVID-19, was not effective in preventing the disease in Canadians and Americans at risk, according to the first gold standard clinical trial.
2. In the New England Journal of Medicine, researchers reported on testing the use of hydroxychloroquine in 821 adults in the U.S. and in Quebec, Manitoba and Alberta.
3. The participants did not have symptoms but were exposed to someone with confirmed COVI9-19 in a health-care or household setting.
4. The exposures were considered high risk because the subjects were less than 2 metres away from a confirmed case for more than 10 minutes without wearing a mask or face shield.
5. The goal of the randomized trial was to see if hydroxychloroquine could prevent symptoms of infection, known as post-exposure prophylaxis, compared with taking a sugar pill.
6. "In this trial, high doses of hydroxychloroquine did not prevent COVID-19 when initiated within four days after a high-risk or moderate-risk exposure," the study's authors wrote.
7. Half of participants were randomly assigned to the drug and half to the placebo without investigators knowing to avoid bias in interpreting any symptoms or their resolution.
8. Overall, 107 of 821 of participants developed COVID-19 based on a swab or compatible symptoms during 14 days of followup.
9. Of those who received hydroxychloroquine, investigators said 49 developed the disease compared with 58 in the placebo group, a difference that could simply be random.
10. Two patients were hospitalized, one in each group. No deaths occurred.
11. Side-effects such as nausea and abdominal discomfort were more common for patients taking hydroxychloroquine compared to placebo (40 per cent versus 17 per cent), but there were no serious adverse reactions were including heart arrhythmia.

Study 6	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?)*			
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• Surrogate outcome (e.g., blood pressure, cholesterol)			
4. What level on the evidence pyramid is this study?			

New study shows potential link between bad quality sleep and Alzheimer's in Hispanics
https://www.miamiherald.com/living/health-fitness/article235945087.html
October 9 2019

1. Hispanics who have trouble sleeping may be at a higher risk of Alzheimer's disease or other dementias, according to a new study.
2. The study found a possible link between insomnia, prolonged sleep duration (more than nine hours of sleep) and a decline in neurocognitive functioning, which could precede Alzheimer's disease or other dementias
3. During the study, researchers analyzed a variety of sleep disturbances including sleep apnea — which has been linked to impaired cognition — among 16,000 Latinos from urban centers in Chicago, Miami, San Diego and the Bronx in New York City.
4. The participants were selected from the nationwide Hispanic Community Health Study/Study of Latinos, considered to be the most comprehensive study of Hispanic/Latino adults in the United States. Fifty-five percent were women.
5. In the study, 5,247 people between 45 and 75 years old were selected to represent the "snapshot" of U.S. Latinos.
6. Participants were given a neurocognitive test, which examined their mental status, verbal episodic learning and memory, word and verbal fluency and their processing speed. Seven years later, they were tested again.
7. The study found that prolonged periods of sleep and chronic insomnia symptoms led to declines in memory, executive function and processing speed. Those measures can precede the development of mild cognitive impairment and Alzheimer's disease.
8. Insomnia affected memory more while abnormal periods of sleep affected executive functions and processing speed, which is how the mind organizes and understand information.
9. It's too early to tell, at this point in the ongoing study, who will be diagnosed with symptoms of Alzheimer's or dementia. But the findings are a good indicator of vulnerability.

Study 7	Yes	No	Uncertain
1. What type of study is this? *(Experimental studies are usually better.)*			
• Observational			
• Experimental			
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3. What is the outcome? *(What effects can be expected from the exposure?)*			
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4. What level on the evidence pyramid is this study?			

Treating acutely ill patients with too much oxygen can be life threatening, Canadian study finds
CBC April 28 2018 https://www.cbc.ca/news/health/second-opinion-too-much-oxygen-mcmaster-study-1.4638395

1. Oxygen is given to millions of patients around the world every day, but too much of it can be harmful and life-threatening, according to a new Canadian scientific paper that in one expert's view "is a very significant landmark study."
2. McMaster University researchers were interested in testing the widely held belief that traditional oxygen therapy is harmless.
3. Their study, published this week in The Lancet medical journal, shows supplemental oxygen, when given liberally to acutely ill patients, increases the risk of death in people with sepsis, stroke, cardiac arrest, as well as those with trauma or requiring emergency surgery.
4. In their meta-analysis, the researchers systematically reviewed 25 randomized controlled trials of more than 16,000 adult patients that compared the use of liberal (supplemental oxygen) and conservative oxygen (room air) therapies.
5. They concluded that for every 71 patients treated with excessive oxygen, an additional death occurs in hospital.
6. "What this is suggesting is that we need to move away from being too liberal with oxygen," said the study's lead author Dr. Derek Chu, who is a clinical fellow at McMaster University. "Maybe we need to be a bit more modest, frequently recheck if we can decrease how much oxygen a patient is requiring. And that's a simple intervention that could save a number of lives."
7. The study also found that supplemental use of oxygen:

   Didn't decrease any infections.

   Didn't improve a patient's length of hospital stay.

   Didn't improve the level of disability for stroke patients or those with brain injuries.
8. Cardiologist John William McEvoy believes the results will likely lead to a reconsideration of guideline recommendations around supplemental oxygen.