

Initial disclaimer...

- Only involved in four COVID-19 studies this far
 - Two manuscripts – none through peer review yet

Large differences in community COVID-19 testing across geographic areas in a Swedish region with 385,000 inhabitants

Beatrice Kennedy ^{1*}, Mats Martinelli ^{2,3*}, Ulf Hammar ¹, Vera van Zoest ⁴, Robert S Kristiansson ^{2,3}, Hugo Fitipaldi ⁵, Nelli Tsereteli ⁵, Georgios Varotsis ¹, Koen F Dekkers ¹, Jonas Björk ^{6,7}, Tove Fall ¹

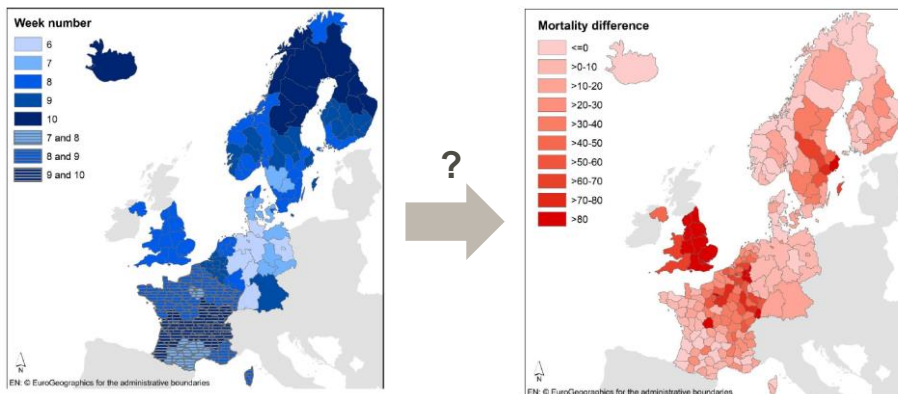
Excess mortality across regions of Europe during the first wave of the COVID-19 pandemic – impact of the winter holiday travelling and government responses

Jonas Björk ^{1,2}, professor, Kristoffer Mattisson ¹, PhD, Anders Ahlbom ³, professor



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Diversity of COVID-19 studies

A population-based cohort study of socio-demographic risk factors for COVID-19 deaths in Sweden

Sven Dridal¹, Matthew Wallace¹, Eleonora Mussino¹, Södärtha Aradhya¹, Martin Kolk^{1,2}, Maria Brandén^{1,3}, Bo Malmberg⁴, Gunnar Andersson⁵

School closures and SARS-CoV-2. Evidence from Sweden's partial school closure

Jonas Vlachos^{*}, Edvin Hertegård¹, Helena Svaleryd^{2*}

The effect of smoking on COVID-19 severity: A systematic review and meta-analysis

Humoral Immune Response to SARS-CoV-2 in Iceland

Oxford-AstraZeneca COVID-19 vaccine efficacy

Seroprevalence of anti-SARS-CoV-2 IgG antibodies in Geneva, Switzerland (SEROCoV-POP): a population-based study

Lockdown, quarantine measures, and social distancing: Associations with depression, anxiety and distress at the beginning of the COVID-19 pandemic among adults from Germany

Explaining the homogeneous diffusion of COVID-19 nonpharmaceutical interventions across heterogeneous countries

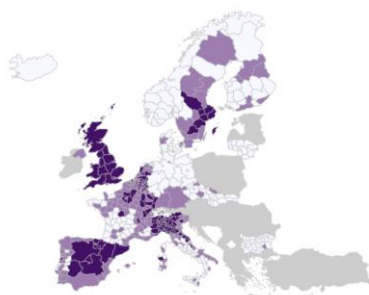


Reflection #1 – Population studies

- Population studies can be conducted quite fast, based on readily available data

Excess deaths in Europe

Total excess deaths since the start of the pandemic



- European Data Journalism Network

– Instrumental for our study on winter holidays

N.B. Countries have reported up to different dates

Source: Eurostat, Destatis, ONS, NRS, NISRA, IRCIII, CBS

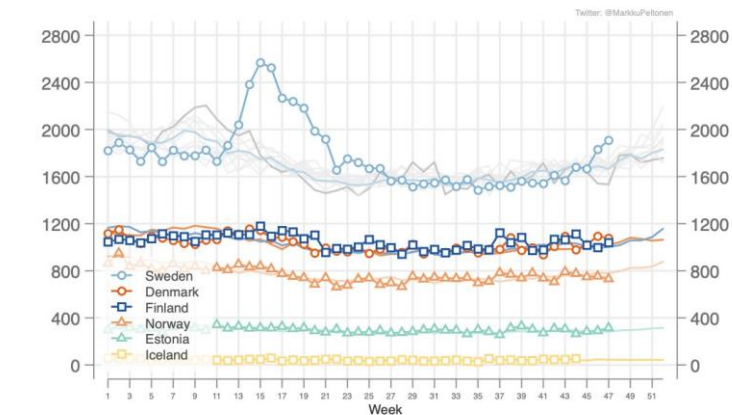


- Much of the data are available on region level
 - NUTS 2 or NUTS 3 (“län” in Sweden)
 - Both exposure and outcome data

(NUTS = Nomenclature of Territorial Units)

1a. Weekly total mortality in the nordic countries and Estonia

Number of deaths per week during year 2020 vs. average 2015-2019. 20201210.



Sources: Eurostat: <https://ec.europa.eu/eurostat/tgm/table.do?tab=table&init=1&language=en&code=sdg-11-6-2>
 Tilastokeskus: https://pxnet2.stat.fi/PXWeb/pjweb/Kokokeiliset_blastot/Kokokeiliset_blastot_vamuu_koko/taffin_vamuu_pnt_12ng.px
 Data for year 2020 is preliminary, it will change. Grey fainted lines are individual years 2010-2019 for Sweden. Influenza season 2018 was severe; marked with darker grey in the figure.

Reflection #2 – Country comparisons

- “Cherry-picked” comparisons usually not so meaningful
 - *Pandemic effect worse in Sweden than in Norway...*
 - but.. *Pandemic effect worse in UK than in Sweden*
- **But... Comparisons between countries are essential for the control of COVID-19**

Neil Pearce ^{1*}, Deborah A Lawlor^{2,3} and Elizabeth B Brickley¹

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²MRC Integrative Epidemiology Unit at the University of Bristol, Bristol, UK and ³Population Health,
 Bristol Medical School, University of Bristol, Bristol, UK

Finally, the COVID-19 epidemic shows the need for epidemiology to go back to its roots—thinking about populations.³ Studying disease occurrence by person, place and time (often referred to as ‘descriptive epidemiology’) is usually taught in introductory courses, even if this approach is then paid little attention subsequently. COVID-19 is a striking example of how we can learn a great deal from comparing countries, states, regions, time trends and persons, despite of all the difficulties. Epidemiology is a process of

(Pearce et al. *Int Jn Epi* 2020)



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Reflection #3 – Revival of Epidemiology

Epidemiology is about disease in populations

Anders Ahlbom^{1,2} 

The advent of the Covid-19 pandemic has not only promoted epidemiology and incorporated the word in everyday language, it has also provided numerous examples of the difficulties that may be attached to the seemingly trivial concept of identifying cases of disease and an underlying population properly. The purpose of this text is not to criti-

(Ahlbom Eur Jrn Epi 2020)

- The study of distribution and determinants of disease in humans
- Relies on Biostatistics – but adjusted to epidemiology
- Has its own theory and methods
- Subject matter knowledge is required.



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Reflection #4 - Ecological studies

- Unit of observation is on group-level rather than on individual-level
 - Regions, neighborhoods, occupations, schools, etc.
 - Sometimes *partially ecological*, some data on individual-level some on group-level
 - Sometimes exposure is *purely ecological* (no analogue on the individual-level)
 - » Existence of fire station or hospital in a small town
 - » Living in a region with winter holiday in week 9
- Most COVID-19 population studies conducted early were “ecological” in some sense



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Reflection #4 - Ecological studies (cont.)

- Bad reputation within Epidemiology, misunderstood in contacts with other disciplines
 - Aggregated population studies more easy to understand
 - Usually only provide weak evidence for causality (at best)
 - » Ecological fallacy
 - Mismatch between group-level association and causal mechanisms on the individual-level
 - » Quality can of course vary
 - Several migration studies have provided useful results regarding environmental vs. genetic causes of disease




Smoking and COVID-19 hospitalization

What is Happening with Smokers and COVID-19? A Systematic Review and a Meta-Analysis

Jesus Gonzalez-Rubio , Carmen Navarro-Lopez , Elena Lopez-Najera , Ana Lopez-Najera , Lydia Jiménez-Díaz 
 *, Juan D. Navarro-López , Alberto Nájera 

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Abstract

SARS-CoV-2 is a new coronavirus that has caused a worldwide pandemic. It produces severe acute respiratory disease (COVID-19), which is fatal in many cases, characterised by cytokine release syndrome (CRS). According to the World Health Organization (WHO), those who smoke are likely to be more vulnerable to infection. Here, in order to clarify the epidemiologic relationship between smoking and COVID-19, we present a systematic literature review until 28 April 2020 and a meta-analysis. It includes 18 recent COVID-19 clinical and epidemiological studies based on smoking patient status from 720 initial studies in China, USA, and Italy. The percentage of hospitalised current smokers was 7.7% (95%CI: 6.9-8.4) in China, 2.3% (95%CI: 1.7-2.9) in the USA and 7.6% (95%CI: 4.2-11.0) in Italy. These percentages were compared to the smoking prevalence of each country and statistically significant differences were found in them all ($p < 0.0001$). By means of the meta-analysis, we offer epidemiological evidence showing that smokers were statistically less likely to be hospitalised (OR=0.18, 95%CI: 0.14-0.23, $p < 0.01$). CRS and exacerbated inflammatory response are associated with aggravation of hospitalised patients. In this scenario, we hypothesise that nicotine, not smoking, could ameliorate the cytokine storm and severe related inflammatory response through the cholinergic-mediated anti-inflammatory pathway.



- What goes wrong here?

It gets even worse...

What is Happening with Smokers and COVID-19? A Systematic Review and a Meta-Analysis

✉ Jesús González-Rubio ¹, ✉ Carmen Navarro-López ², ✉ Elena López-Nájera ³, ✉ Ana López-Nájera ⁴, ✉ Lydia Jiménez-Díaz ⁵, ✉ Juan D. Navarro-López ⁶, ✉ Alberto Nájera ⁷

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Abstract

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Article

A Systematic Review and Meta-Analysis of Hospitalised Current Smokers and COVID-19

Jesús González-Rubio ^{1,†}, Carmen Navarro-López ², Elena López-Nájera ³, Ana López-Nájera ⁴, Lydia Jiménez-Díaz ^{5,†}, Juan D. Navarro-López ^{6,†} and Alberto Nájera ^{7,†}

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Abstract: SARS-CoV-2 is a new coronavirus that has caused a worldwide pandemic. It produces severe acute respiratory disease (COVID-19), which is fatal in many cases, characterized by the cytokine release syndrome (CRS). According to the World Health Organization, those who smoke are likely to be more vulnerable to infection. Here, in order to clarify the epidemiologic relationship between smoking and COVID-19, we present a systematic literature review until 28 April 2020 and a meta-analysis. We included 18 recent COVID-19 clinical and epidemiological studies based on smoking patient status from 720 initial studies in China, the USA, and Italy. The percentage of hospitalized current smokers was 7.7% (95%CI: 6.9-8.4) in China, 2.3% (95%CI: 1.7-2.9) in the USA and 7.6% (95%CI: 4.2-11.0) in Italy. These percentages were compared to the smoking prevalence of each country and statistically significant differences were found in them all ($p < 0.0001$). By means of the meta-analysis, we offer epidemiological evidence showing that smokers were statistically less likely to be hospitalized (OR = 0.18, 95%CI: 0.14-0.23, $p < 0.01$). In conclusion, the analysis of data from 18 studies shows a much lower percentage of hospitalized current smokers than expected. As more studies become available, this trend should be checked to obtain conclusive results and to explore, when appropriate, the underlying mechanism of the severe progression and adverse outcomes of COVID-19.



Reflection #5 – Preprints and Peer review

- Peer review no guarantee for scientific quality
- Preprints
 - A version of a scholarly or scientific paper that precedes formal peer review and publication... (Wikipedia)
 - Accepted by most journals. Explosion during the pandemic.
 - Caution required in contacts with media

Caution: Preprints are preliminary reports of work that have not been certified by peer review. They should not be relied on to guide clinical practice or health-related behavior and should not be reported in news media as established information.

(medRxiv)





Foto: Paul Kleiven/NTB

COVID-19

▶ Studie: Ökad dödlighet kopplad till sportlovsvecka

2:00 min [Min sida](#) [Dela](#)

Publicerat onsdag 2 december kl 21.10

- Regioner som hade sportlov vecka 9 har drabbats mycket hårdare av covid-19 än de som hade lov en annan vecka, visar preliminära resultat från en studie som undersökt flera hundra europeiska regioner.
- Många av dödsfallen i till exempel Stockholm kan bero på det.
- "Ungefär en tredjedel av överdödligheten i de här regionerna kan tillskrivas det faktum att de hade sportlov vecka 9", säger Jonas Björk, professor i epidemiologi vid Lunds universitet till Ekot.



Preprint – may lead to 100's of informal reviews

- Other researchers, journalists, interested general public

Excellent paper and very interesting - congrats! Perhaps add some more background info if possible on differences week 9 -10 - was travel to Alps still going on in week 10? What could explain the specific associations with week 9?

Looks interesting. I don't know if it makes any difference, but the winter holiday in Copenhagen wasn't in week 8 as the map seems to indicate, but in week 7

föreställer mig att länders policy för hemkarantän bland lov-resenärer, testning, etc kunde minska lov-effekten. Förstod inte helt om ni lyckats väga in det? I så fall blir det väl en åtgärd som modifierar lov-effekten och kanske minskar den?

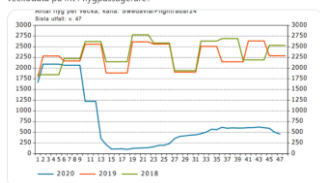
Anekdotiskt så åker folk från norra halvan av Sverige inte till Alperna på sportlov.



Preprint – may lead to 100's of informal reviews (cont.)

- Other researchers, journalists, interested general public

Men är det internationella resandet signifikant större i sportlovveckorna? Annars finns väl ingen särskild anledning att kolla på "sportlov"? Finns det veckodata på int'l flygpassagerare?



Bara spontant ang artikeln: Ni har inte med antal som reser, var man reser i texten? Är det inte en brist att man inte vet hur stor importen av fall därmed verkligen varit?

Och om man missat det – kan man då bedöma effekten av åtgärder?

Tack för pre-printen! Snubblade över din mening:

Belgium, Sweden and UK stood out as the three countries in our study area that, according to our estimates, may have experienced lower excess mortality by intervening earlier.

Jag liste första gången på helt fel sätt och blev förvirrad -- But, they didn't experience lower excess mortality and they didn't intervene early! tänkte jag.

föreslår ändring till ...might have experienced lower excess mortality if interventions had been implemented earlier.

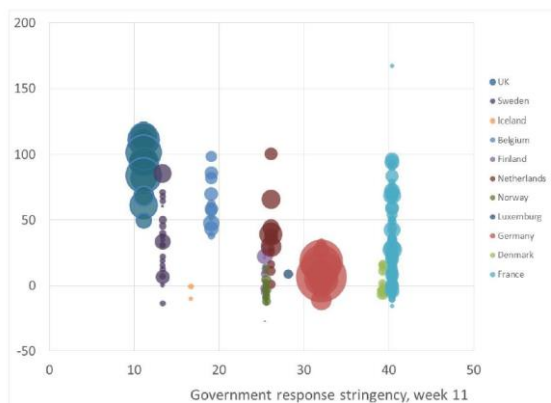
Intressant! Vet man varför det dör så många fler v.8 varje år än runtomkring liggande veckor? Det är ju 3-4 gånger fler som dör då.



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Reflection #6: Ecological regression

Weekly
Mortality
difference
2020 vs.
2015 - 2019



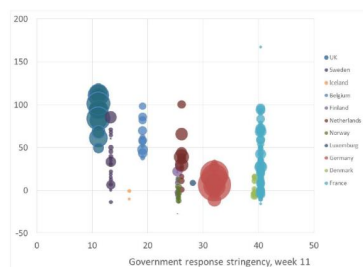
(Björk et al. Submitted for publication)



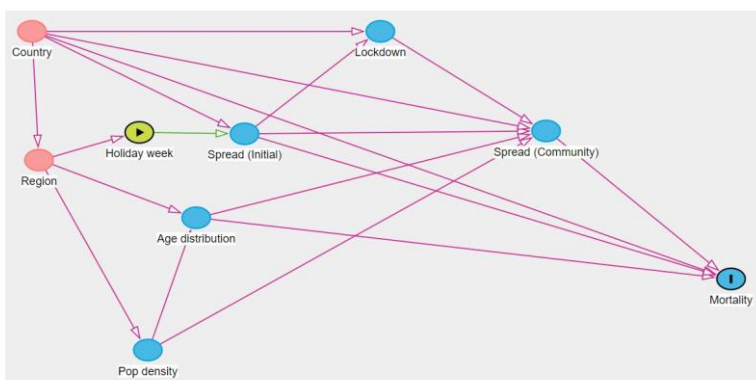
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Reflection #6: Ecological regression

- Few data points
- Generally high statistical precision behind each data point
- Results extremely sensitive to choice of adjustment variables
 - Important to have clear causal diagram in mind
 - Sensitivity analyses, transparent reporting crucial



Our tentative causal diagram (DAG)



→ Adjustment for country, population density and age distribution



Summary of reflections

- Population studies
 - Can be conducted quite fast based on available data
- Country comparisons
 - Range: Meaningless → Useful
- Revival of Epidemiology
- Ecological studies
 - Range: Meaningless → Useful
- Preprint and peer reviews
 - Be careful with both
- Ecological regressions
 - Must be planned rigorously. Be careful in interpretation.

