https://www.coreb.infectiologie.com/

https://reacting.inserm.fr/

EPIDEMIOLOGY

Scientific update on COVID-19

Updated on December 21th 2020

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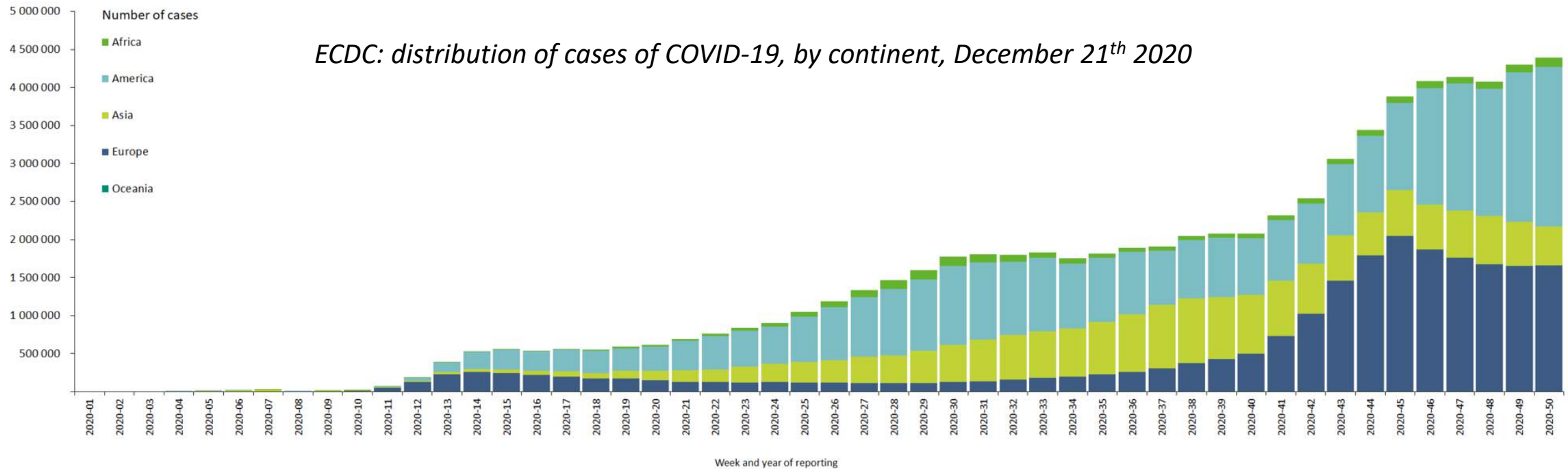Emmanuelle Vidal Petiot – *Inserm, AP-HP Bichat*

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EPIDEMIOLOGY

Questions:

- What is the situation in the World?

- What is the incubation period & R_0?

- What is the impact of non-pharmaceutical intervention on *R*?

- What do we know about the risk of transmission & the mode of transmission?

- What is the impact of the different measures taken by countries?

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Situation update

- **Santé publique France:** https://www.santepubliquefrance.fr/maladies-et-traumatismes/maladies-et-infections-respiratoires/infection-a-coronavirus/articles/infection-au-nouveau-coronavirus-sars-cov-2-covid-19-france-et-monde

- **Johns Hopkins University:** https://reliefweb.int/report/world/coronavirus-covid-19-global-cases-johns-hopkins-csse

- **OMS:** https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports/

- **ECDC :** https://www.ecdc.europa.eu/en/geographical-distribution-2019-ncov-cases

ECDC: distribution of cases of COVID-19, by continent, December 21th 2020
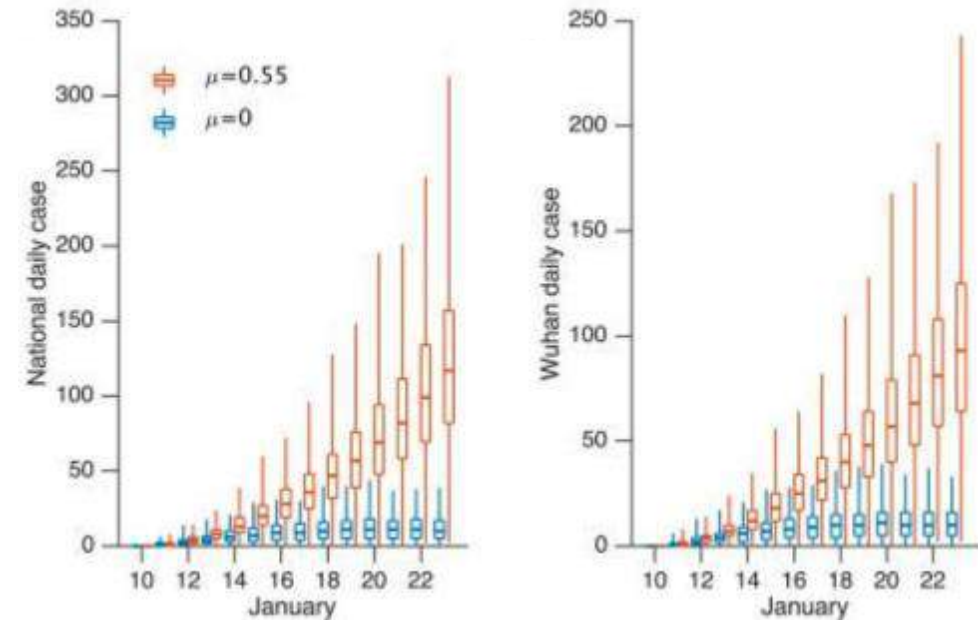
Week and year of reporting

Epidemiology

- Person to person transmission

- Contagious 2 days before symptoms : **pre-symptomatic phase**
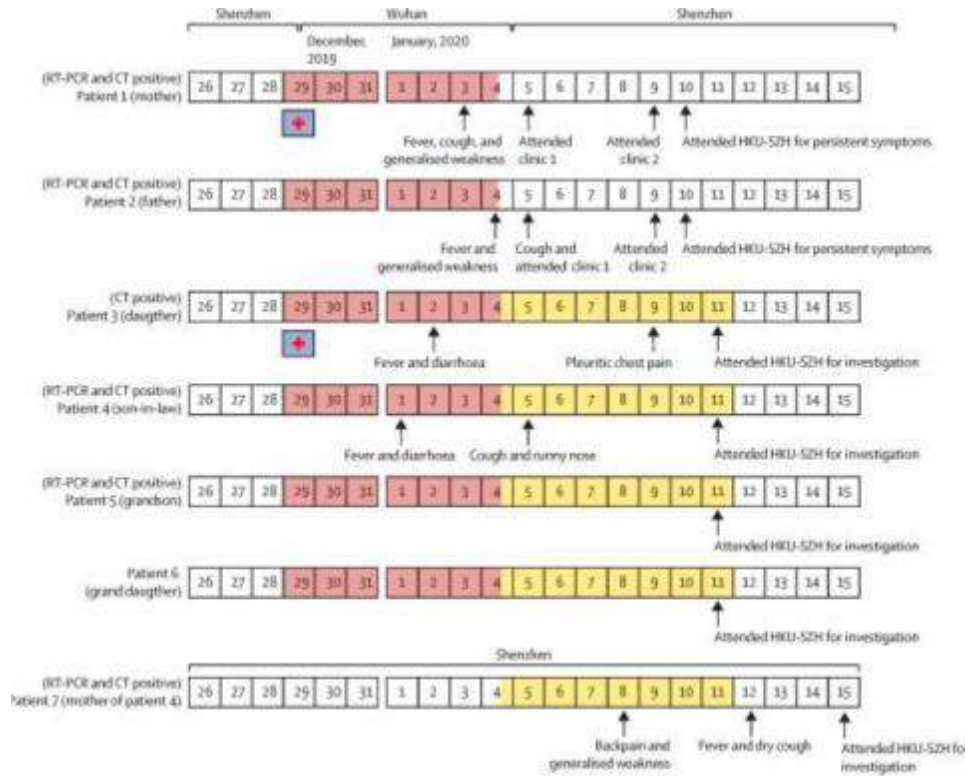
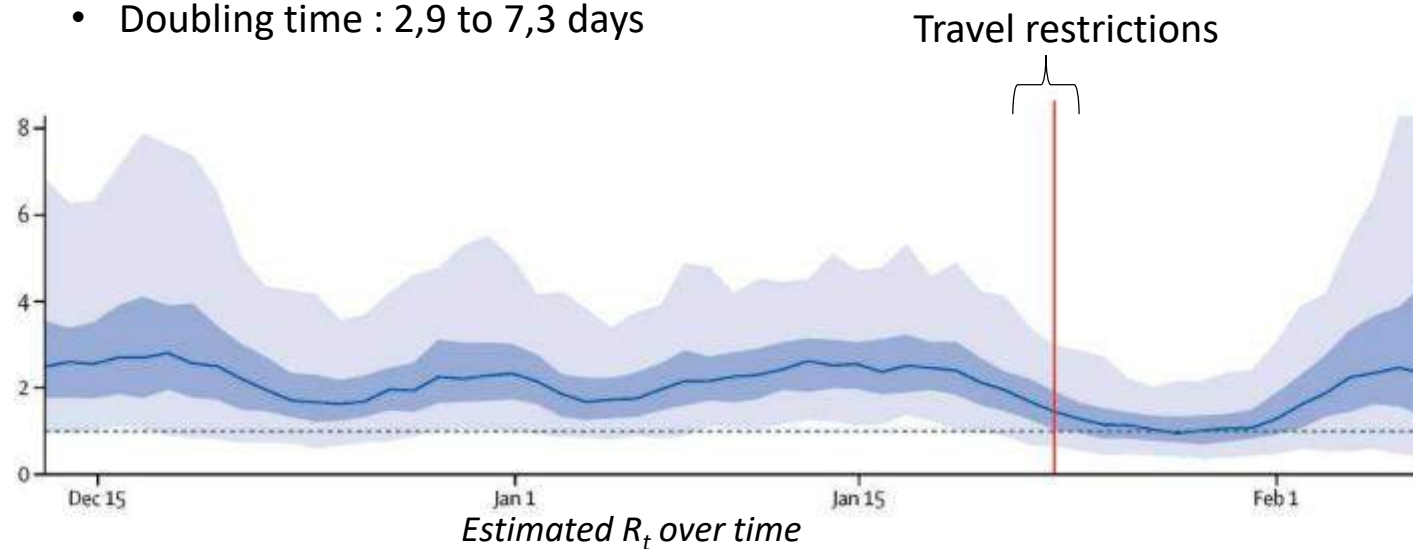*Chronology of symptom onset of the family cluster*

- Very high rate of undocumented infection

- **Dissemination by undocumented infection** (asymptomatic, presymptomatic...)

- <u>He and colleagues</u> estimation (slide 35): 44% ($CI_{95\%}$ [30 – 57%]) of secondary cases were infected during the index cases' presymptomatic stage

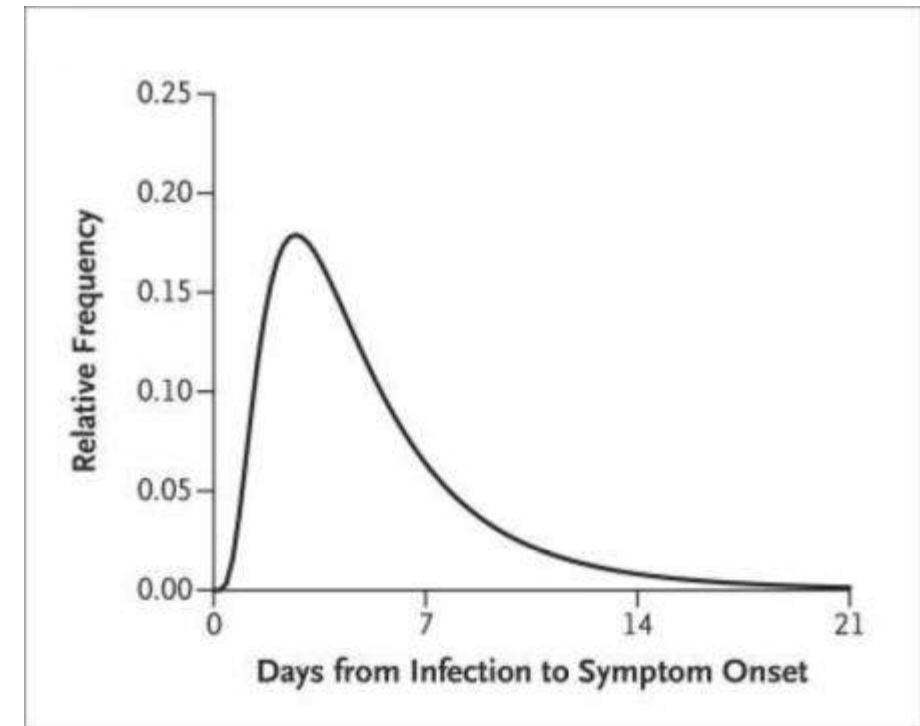Infectiousness was estimated to decline quickly within 7 days

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Epidemiology

At beginning & before controls measures:

- Basic reproduction number **(R_0)**: 2,2 to 6,4

- R_0 depends on
  - Geographic location
  - Stage of outbreak

- R_e depends on
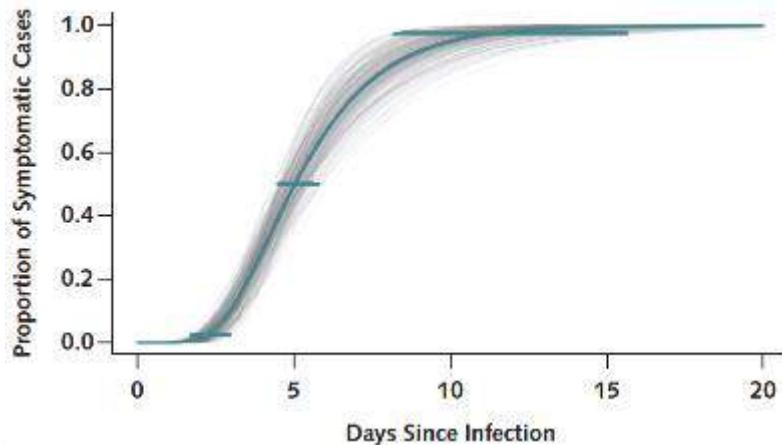 - Control measures

- Doubling time : 2,9 to 7,3 days

- Incubation period SARS-CoV-2
  - Median: 5 days
  - 2 to 14 days

Travel restrictions

Estimated R_t over time

R_t: median daily reproduction number R_e: estimated daily reproduction number

Kucharski AJ *et al. Lancet Infect Dis.* Mar 2020

Li Q et *al. NEJM.* Mar 2020

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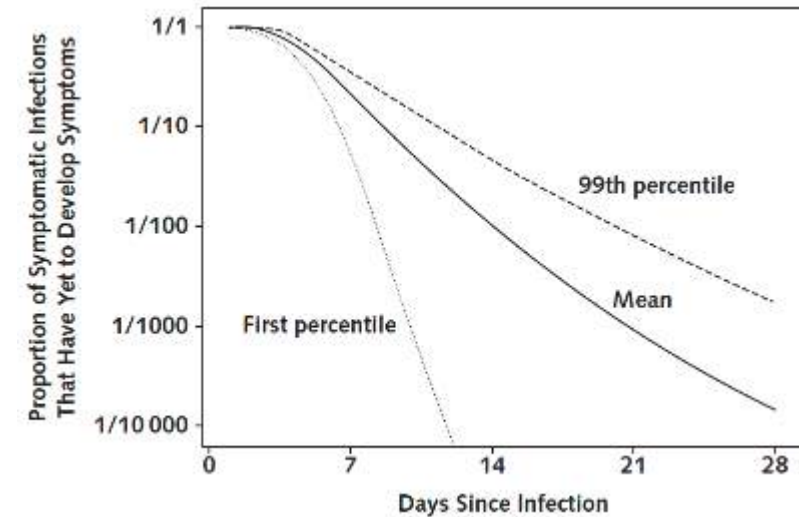targeting emerging infectious diseases

Epidemiology

- 185 cases of confirmed COVID-19 – before Feb 24th

- 24 countries – 89% had recent history of travel to Wuhan

- Median incubation period (days) : 5,1 [4,5 – 5,8]
  - < 2,5% of infected persons will shows symptoms within 2,2 days
  - 97.5% of symptomatic patients developing symptoms within 11.5 days

- Analysis specific for cases detected outside of China
  - Median incubation (days): 5,5 [4,4 – 7,0]
  - 95% range spanning from 2,1 to 14,7 days

- After 14 d → we would not miss a symptomatic infection among high risk persons

Proportion of known symptomatic SARS-CoV-2 infections that have yet to develop symptoms by number of days since infection, using bootstrapped

- High risk = A 1-in-100 chances of developing a symptomatic infection after exposure

Monitoring Duration	Mean Estimated Number of Undetected Symptomatic Infections per 10 000 Monitored Persons (99th Percentile)			
	Low Risk (1 in 10 000)	Medium Risk (1 in 1000)	High Risk (1 in 100)	Infected (1 in 1)
7 d	0.2 (0.4)	2.1 (3.6)	21.2 (36.5)	2120.6 (3648.5)
14 d	0.0 (0.0)	0.1 (0.5)	1.0 (4.8)	100.9 (481.7)
21 d	0.0 (0.0)	0.0 (0.1)	0.1 (0.8)	9.5 (82.5)
28 d	0.0 (0.0)	0.0 (0.0)	0.0 (0.2)	1.4 (17.8)

Lauer SA et *al. Ann Intern Med.* May 2020

Non pharmaceutical interventions and *R*

Temporal association between introducing and lifting non-pharmaceutical interventions (NPIs) and levels of SARS-CoV-2 transmission (*R*) ?

Modelling study – data from 131 countries:

- On country-level estimate *R* from the EpiForecast project
- On country-specific policies on NPIs from the OxCGRT

Jan 1 to July 20, 2020

Definitions:

- Phase: a time period when all of the eight NPIs remained the same
- R_{dayi} as the *R* of the ith day of that phase (ie, since the NPI status changed) and defined R_{day0} as the *R* of the last day of its previous phase
- *R* ratio between R_{dayi} and R_{day0} as a measure of the degree of association of introducing and lifting an NPI with the transmission of SARS-CoV-2
- Modelled the *R* ratio using a log-linear regression

790 phases from 131 countries
- Median duration of phase 11 days

The NPIs
- Stay at home and restriction on internal movements were the most common,
- Closure schools and public events ban were the two first NPIs introduced,
- Stay at home and closure of public transport were the two last NPIs introduced.

Decreasing trend over time in *R* ratio was found in the first 14 days after introducing NPIs

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Non pharmaceutical interventions and *R*

Change over time in the R ratio following the introduction and relaxation of individual NPIs
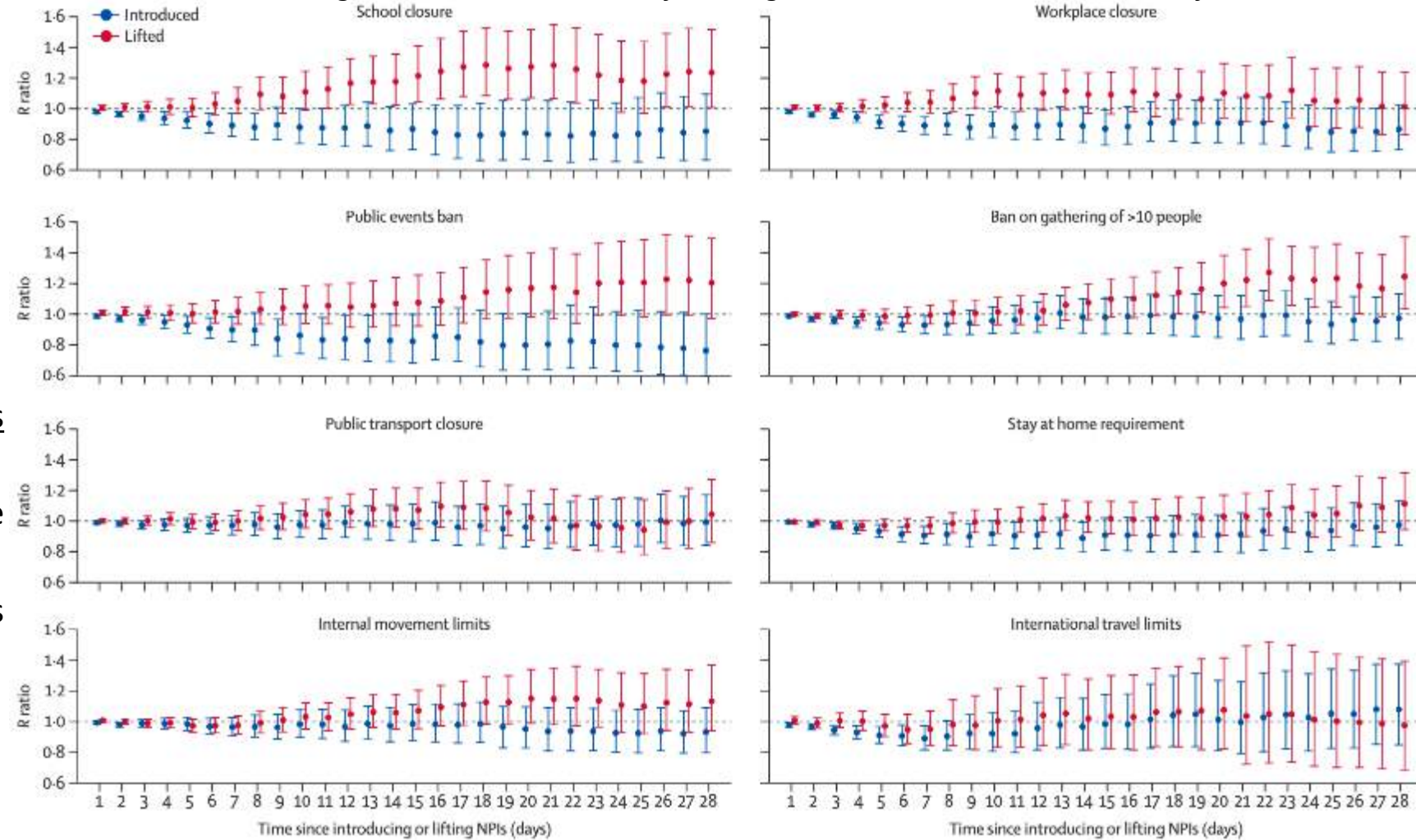
Greatest increase in *R* ratio:

- Relaxation of school closure:

- On day 7 1,05 (CI$_{95\%}$: 0,96–1,14)

- On day 14 1,18 (CI$_{95\%}$: 1,02–1,36)

- Relaxation of a ban on gatherings of >10

- On day 28 1,25 (CI$_{95\%}$: 1,03–1,51)

Time in days needed to reach 60% of its maximum effect:

- Median of 8 days following the indroduction

- Median of 17 days following its relaxation

Greatest reduction in *R*:

	Day 7	Day 14	Day 28
Candidate 4: School and workplace closure plus ban on public events and gatherings of more than ten people plus internal movement limits plus stay at home requirement	0·65 (0·54–0·78)	0·58 (0·42–0·78)	0·48 (0·32–0·71)

Non pharmaceutical interventions and *R*

→ Introducing NPIs were associated with reductions in *R* of 3–24% on day 28 after their introduction

→ Lifting NPIs were associated with increases in *R* of 11-25% on day 28 after their relaxation

→ Effects not immediate & time required to reach certain levels of effect differed by NPI

Several limits:

- Base on control policy rather than on actual population behavior → use of personal hygiene / behavioral change

- Compliance with these NPIs was not examine

- Data on national levels only → vary among different parts of a country

- Heterogeneity across different countries → findings no sensitive to the removal of different lists of countries

- Not consider the role of underlying seasonality or meteorological factors

- The *R* estimate was subject to the specification of parameters

- Change over time in contact/tracing or testing or case definition

- Innate limitation of *R* as measure of transmission

→ Autors: "**The decisions to reintroduce and relax restrictions should be informed by various factors, including the capacity and resilience of the health-care system, and might be best made at provincial or district rather than national levels**"

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Li Y et *al. Lancet Infect Dis.* Oct 2020

Distanciation measures to prevent transmission

The effects of physical distance, face masks, and eye protection on virus transmission?

Systematic revue (172 studies) & meta-analysis (44 comparatives studies)

16 countries & 6 continents

25 697 patients in the meta-analysis

Included COVID-19, SARS & MERS

Did not identify any randomized trials

Unadjusted, adjusted, frequentist, and Bayesian meta-analyses all supported the main findings,

	Studies and participants	Relative effect (95% CI)	Anticipated absolute effect (95% CI), eg, chance of viral infection or transmission		Difference (95% CI)	Certainty*	What happens (standardised GRADE terminology)⁷⁵
			Comparison group	Intervention group			
Physical distance ≥1 m vs <1 m	Nine adjusted studies (n=7782); 29 unadjusted studies (n=10 736)	aOR 0·18 (0·09 to 0·38); unadjusted RR 0·30 (95% CI 0·20 to 0·44)	Shorter distance, 12·8%	Further distance, 2·6% (1·3 to 5·3)	−10·2% (−11·5 to −7·5)	Moderate†	A physical distance of more than 1 m probably results in a large reduction in virus infection; for every 1 m further away in distancing, the relative effect might increase 2·02 times
Face mask vs no face mask	Ten adjusted studies (n=2647); 29 unadjusted studies (n=10 170)	aOR 0·15 (0·07 to 0·34); unadjusted RR 0·34 (95% CI 0·26 to 0·45)	No face mask, 17·4%	Face mask, 3·1% (1·5 to 6·7)	−14·3% (−15·9 to −10·7)	Low‡	Medical or surgical face masks might result in a large reduction in virus infection; N95 respirators might be associated with a larger reduction in risk compared with surgical or similar masks§
Eye protection (faceshield, goggles) vs no eye protection	13 unadjusted studies (n=3713)	Unadjusted RR 0·34 (0·22 to 0·52)¶	No eye protection, 16·0%	Eye protection, 5·5% (3·6 to 8·5)	−10·6% (−12·5 to −7·7)	Low‖	Eye protection might result in a large reduction in virus infection

Population comprised people possibly exposed to individuals infected with SARS-CoV2, SARS-CoV or MERS-CoV

Physical distancing of 1 m or more → lower transmission of viruses compared with a distance of less than 1 m
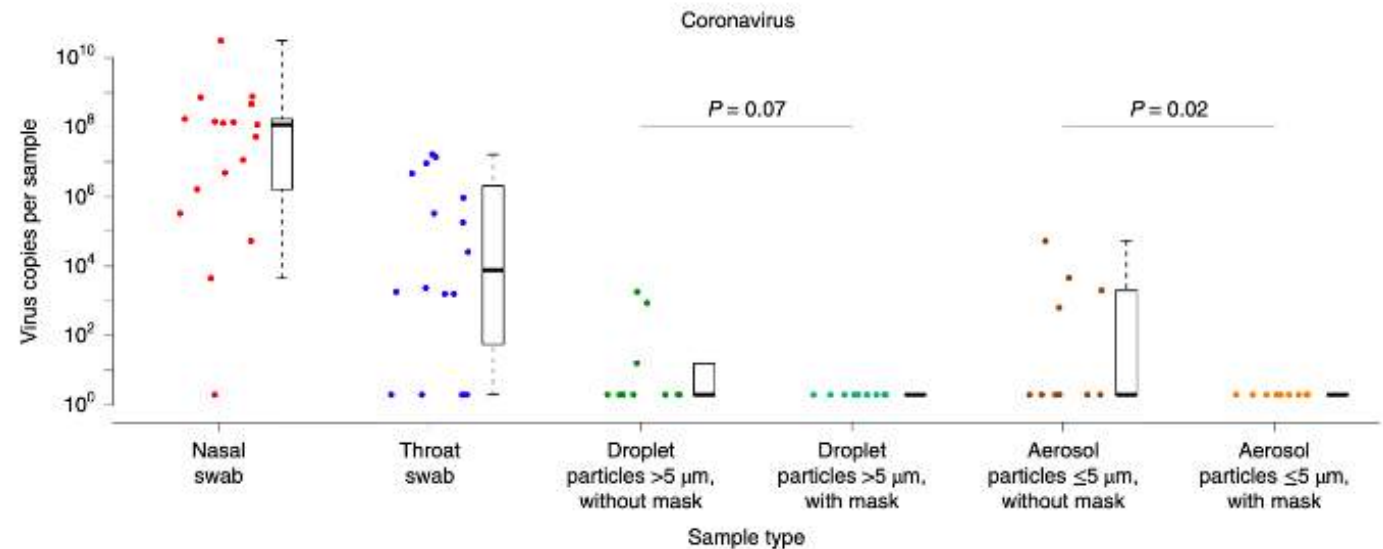Protection was increased as distance was lengthened → **distance of 2 m might be more effective**
The use of face mask → reduction in risk of infection → **wearing face mask protects people**

None of these interventions afforded complete protection from infection when evaluated in isolation

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Chu DK et *al. Lancet*. Jun 2020

Face masks' effectiveness in respiratory viruses

- 246 participants
  - 122 without face masks and 124 with face masks
  - Provided exhaled breath samples

- 123 were infected by
  - HCoV (17), influenza (43) and rhinovirus (54)

- Test viral shedding
  - Nasal swab, throat swab
  - Respiratory droplet sample
  - Aerosol sample

- Detection of coronavirus
  - 30% (droplets) and 40% (aerosol) without mask
  - 0 %(droplet or aerosol) with mask

→Aerosol transmission is possible

→ Face masks reduce coronavirus detection in aerosol (significantly) and respiratory droplet

→ **Face masks could prevent transmission of human coronaviruses and influenza viruses.**

Limits

- Human coronavirus, not SARS-CoV-2

- Large proportion of undetectable viral shedding

- Detected Coronavirus' infectivity not confirmed

Face masks' effectiveness in COVID-19

Event study that examined the effect over different period

- state executive orders or directives signed by governors that mandate use

- Fifteen states + Washington D.C.

- March 31 and May 22, 2020

Estimated the effects of face cover mandates on the **daily county-level COVID-19 growth rate**,

Significant decline in daily COVID-19 growth rate after the mandating of face covers in public

- Increasing over time after the orders were signed

No evidence of declines in daily COVID-19 growth rates with employee-only mandates

Limits:
- Unable to measure the compliance with the mandate
- Examine only confirmed COVID-19 cases
- Other existing social distancing measures

Estimates of the effects of states mandating community face mask use in public on the daily county-level growth rate of COVID-19 cases, 2020

COMMUNITY FACE MASK USE WHEN IN PUBLIC
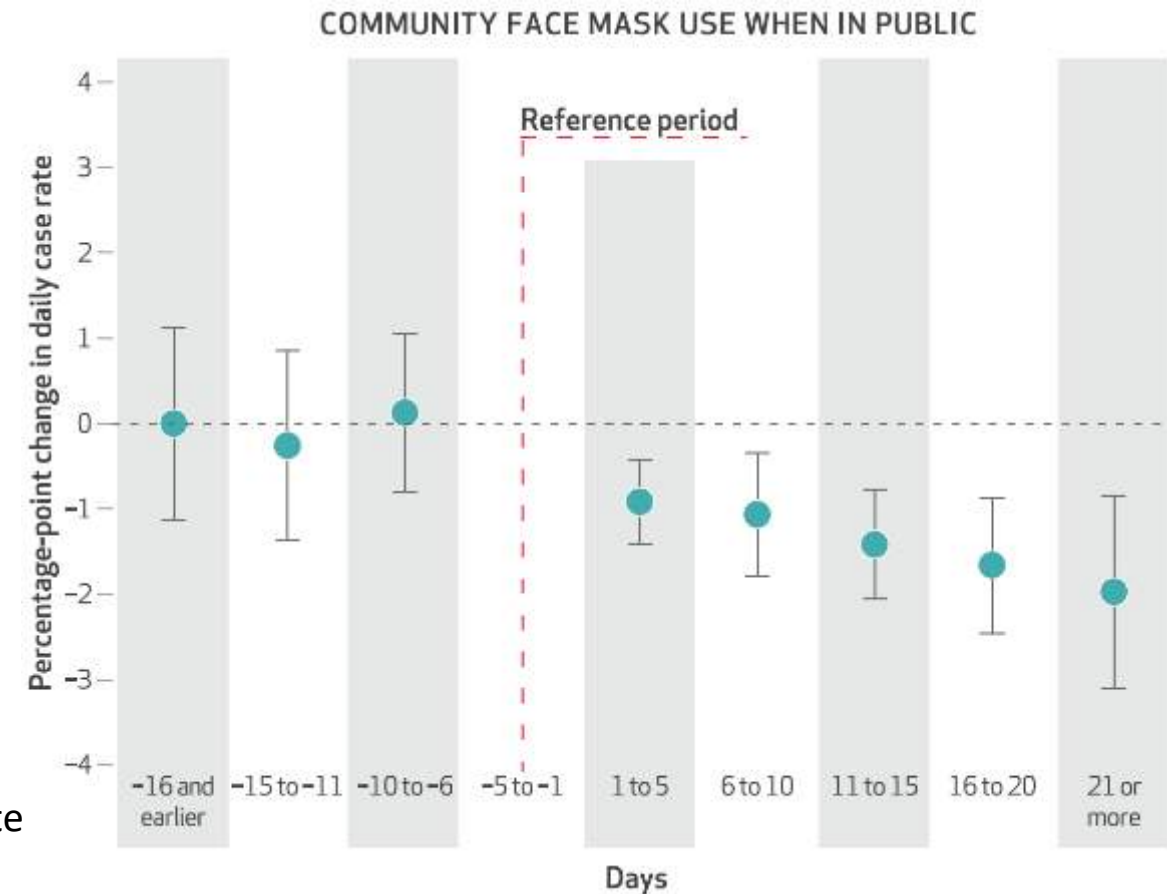
Projection - Transmission dynamics

Model of SARS-CoV-2 transmission

Projected that recurrent wintertime outbreaks will probably occur after the initial outbreak

Used estimates of seasonality, immunity and cross-immunity for beta coronaviruses (OC43 & HKU1)

Post-pandemic transmission dynamics will depend on:
- o Degree of season variation in transmission
- o Duration of immunity
- o Degree of cross-immunity between SARS-CoV-2 and other coronaviruses
- o Intensity and timing of control measures

Presentation of different scenarios

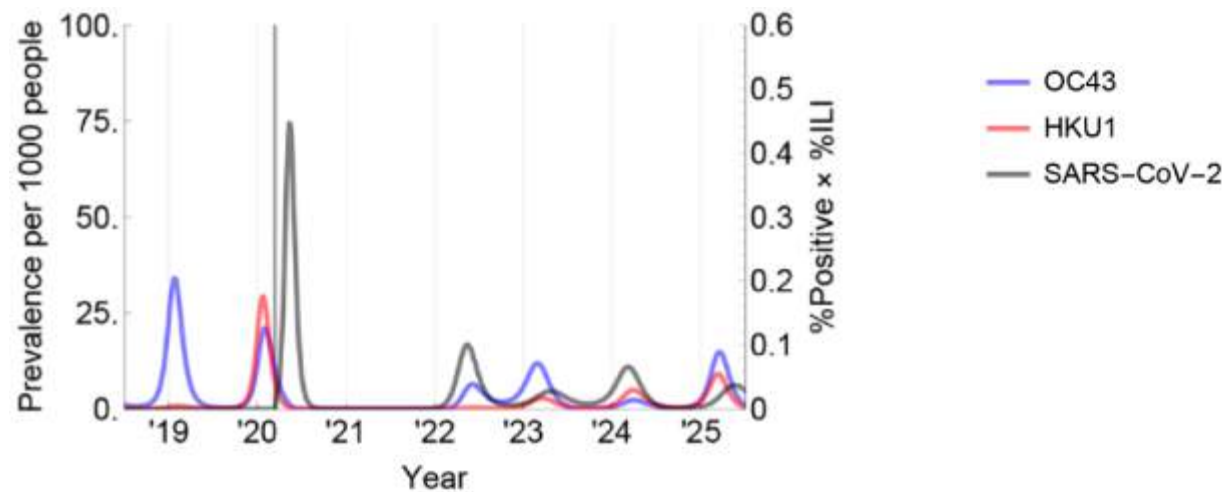*Invasion scenario for SARS-CoV-2 in temperate regions*
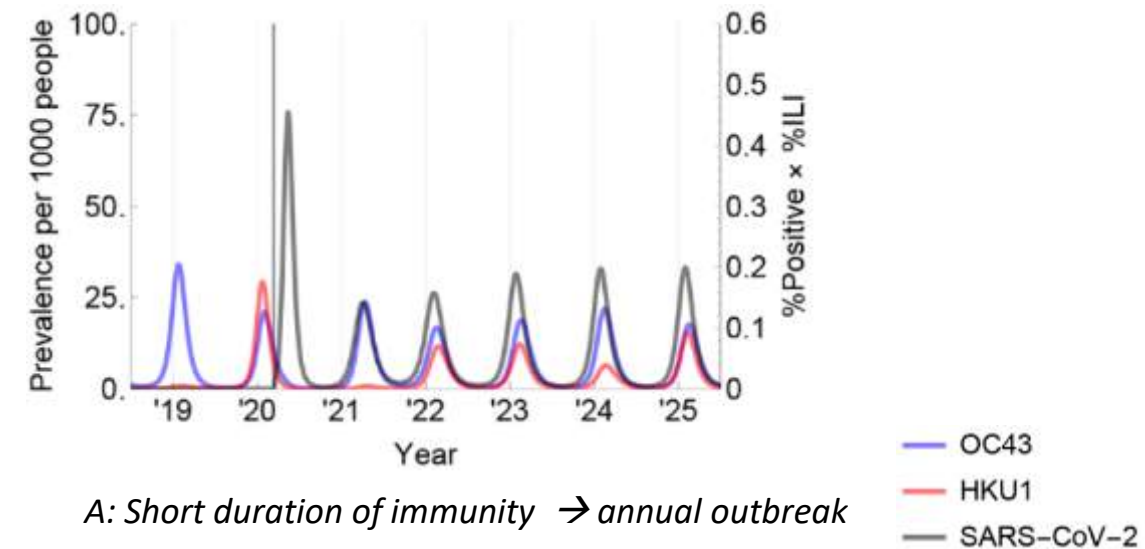
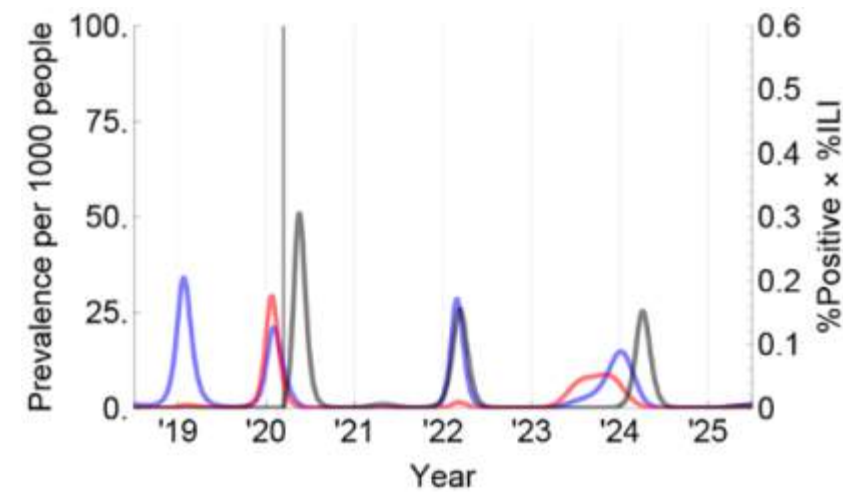*A: Short duration of immunity → annual outbreak*
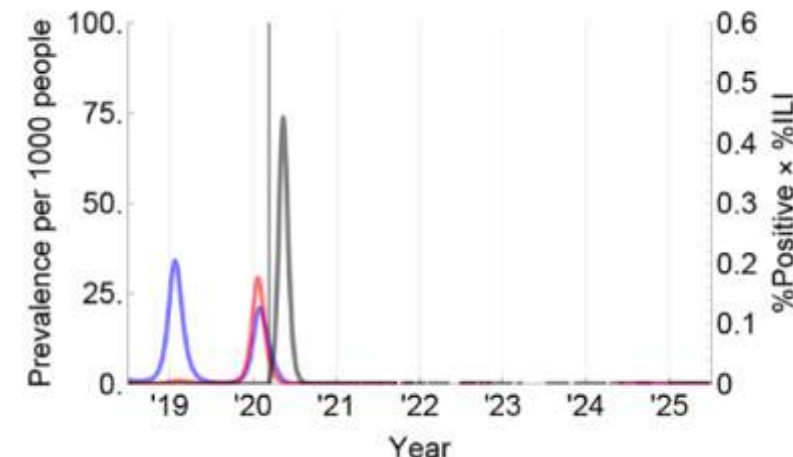
B: Long-term immunity → elimination of the virus

Projection - Transmission dynamics

Invasion scenario for SARS-CoV-2 in temperate regions

*C: Longer-term immunity → biennial outbreaks
Possibly with smaller outbreak*

*D: Higher seasonal variation in transmission → reduce the peak
size of the invasion wave
BUT more severe wintertime outbreaks thereafter compare with C*

<u>Total incidence of COVID-19 illness over next years will depend on</u>
- Regular circulation after the initial pandemic wave
- Duration of immunity that SARS-CoV-2 infection imparts
- Social distancing strategies
- Effective therapeutic

Community and close contact exposures

Comparison between (random sampling 1:2):

- Exposure reported by case-patients: adults with laboratory confirmed COVID-19 (= 154)

- Exposure reported by control-participants (= 160)

All were symptomatic

Identified and contact 14-23 days after results of SARS CoV2 testing.

Interview by telephone:

- Mask-wearing behavior, community activities <14 days before symptom onset (shopping, dining at restaurant, salon, gym, coffee/bar…) …

Case-patients were more likely to have reported dining at restaurant (aOR: 2,4, $IC_{95\%}$: 1,5 – 3,8).

Analysis restricted to 225 participants:

- Dining at restaurant (aOR: 2,8, $CI_{95\%}$: 1,9 – 4,3)

- Going bar/coffee shop (aOR: 3,9, $CI_{95\%}$: 1,5 – 10,1)

Adjusted odds ratio (aOR) and 95% confidence intervals for community exposures

Fisher KA et *al. MMWR.* Sep 2020
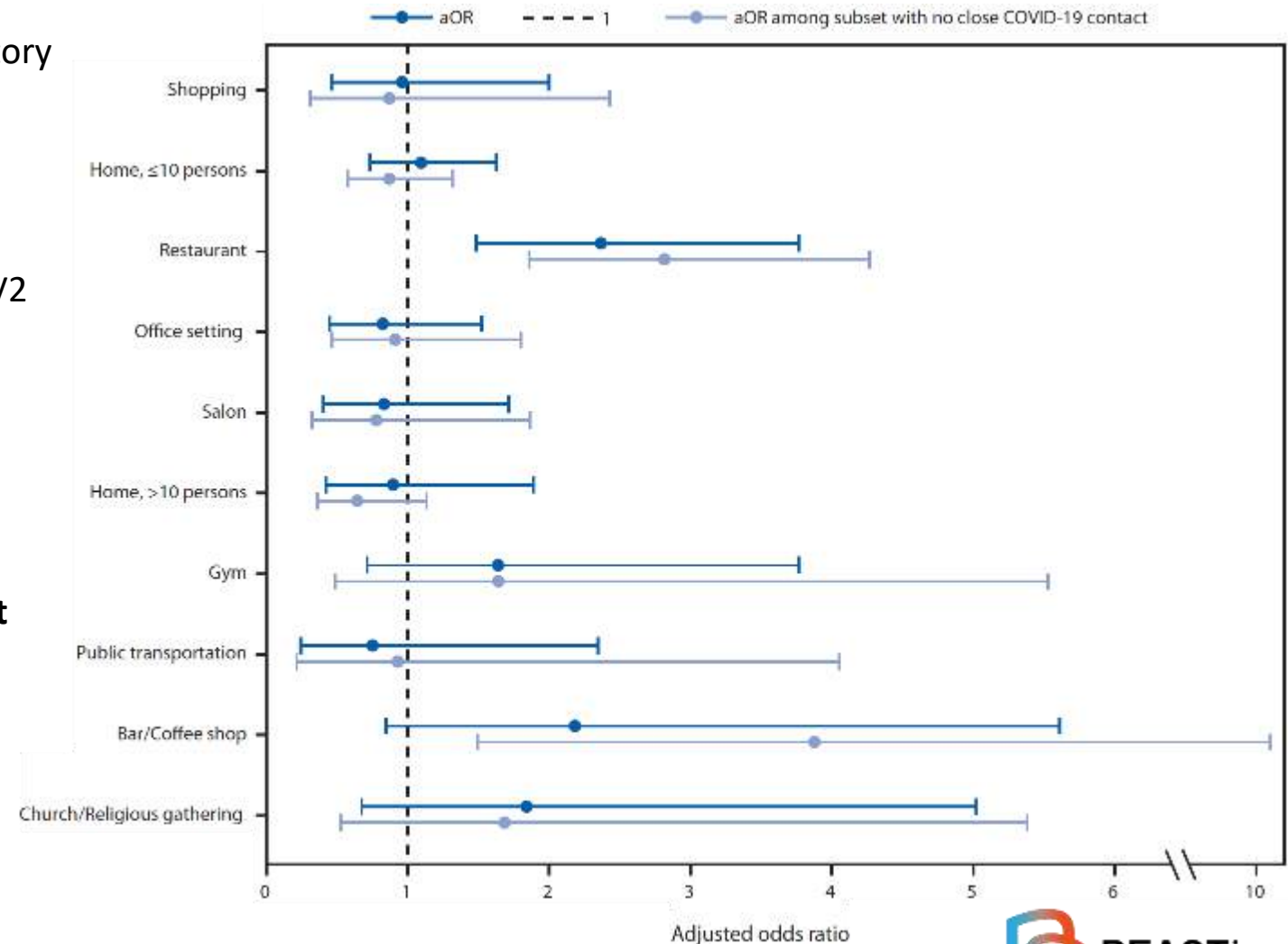
Community and close contact exposures

Most close contact exposures were to family members

Continued assessment of various types of activities and exposures as communities, schools, and workplaces reopen is important

Efforts to reduce possible exposures at location that offer on-site eating and drinking options should be considered

<u>Limits</u>:

- Ratio 1:2 could not be reached → unmatched analysis was performed

- Interview on behaviors one month before → memorization bias

- Participants were aware of their SARS-CoV-2 test results → could influence their responses

- At restaurant: not distinguish between outdoor and indoor

- In coffee shop/bar: not distinguish between venues or service delivery method

- Distanciation measures could not be accounted for restaurant & bar → extrapolate to other countries?

- No explanation about the result difference between dining at restaurant and going to coffee/bar in the full analysis?

COVID-19 & social and leisure activities

Description study of the outbreak in Spain

Transmission declined in early May 2020

Cases' number increased during June and mild July:

- Mild June up to August 2nd: 673 COVID-19 outbreak = 8300 persons

- 76% were small outbreak (<10 cases)

- 2% had more than 100 cases

Social setting = 35% of all active outbreaks

- Family gathering or private party

- Leisure facility

Occupational setting = 20% of all active outbreaks

- Agriculture seasonal worker

Setting		Total				Active			
		Oubreaks		Cases		Oubreaks		Cases	
		N	%	N	%	N	%	N	%
Healthcare facility		20	3.0	274	3.3	17	3.1	219	3.5
Long-term care facility		59	8.8	829	9.9	39	7.1	376	6.1
Vulnerable social group		44	6.5	576	6.9	32	5.8	337	5.4
Family- different households		65	9.7	406	4.8	52	9.4	315	5.1
Occupational	Total	146	21.7	2,331	27.8	110	20.0	1,269	20.4
	Slaughterhouse/meat plant	19	NA	767	NA	12	NA	365	NA
	Agriculture seasonal worker/fruit-vegetable company	45	NA	1,022	NA	31	NA	500	NA
	Other/not specified	82	NA	542	NA	67	NA	404	NA
Social	Total	206	30.6	2,627	31.3	193	35.0	2,546	41.0
	Organised event/public space	31	NA	349	NA	29	NA	324	NA
	Family/friends reunion or private party	120	NA	900	NA	112	NA	854	NA
	Leisure facility (restaurant, bar, club…)	35	NA	1,234	NA	34	NA	1,231	NA
	Other/not specified	20	NA	144	NA	18	NA	137	NA
Mixed		111	16.5	1,218	14.5	92	16.7	1,050	16.9
Other		22	3.3	129	1.5	16	2.9	96	1.5
Total		673	100	8,390	100	551	100	6,208	100

Two main settings to target efforts:
- Social gatherings
- Workers in vulnerable situations

New cases and cumulative incidence are currently increasing in all regions

Infectiousness of children

A nationwide COVID-19 contact tracing program in South Korea

Index patient were eligible if they identified $\geq$ 1 contact.

Compared the difference in detected cases between household and nonhousehold contacts across the stratified age groups.

Index patient age, y	Household	
	No. contacts positive/ no. contacts traced	% Positive (95% CI)
0–9	3/57	5.3 (1.3–13.7)
10–19	43/231	18.6 (14.0–24.0)
20–29	240/3,417	7.0 (6.2–7.9)
30–39	143/1,229	11.6 (9.9–13.5)
40–49	206/1,749	11.8 (10.3–13.4)
50–59	300/2,045	14.7 (13.2–16.3)
60–69	177/1,039	17.0 (14.8–19.4)
70–79	86/477	18.0 (14.8–21.7)
≥80	50/348	14.4 (11.0–18.4)
Total	1,248/10,592	11.8 (11.2–12.4)

Rates of coronavirus disease among household

59 073 contacts of 5 706 COVID-19 index patients:
- 10 592 household contacts → **11,8% (CI$_{95\%}$ [11,2% - 12,4%]) had COVID-19**
  - with an index patient 10–19 years, 18.6% (CI$_{95\%}$ [14.0%–24.0%]) of contacts had COVID-19
- 48 481 nonhousehold contacts → 1,9% (CI$_{95\%}$ [1,8% - 2,0%]) had COVID-19

→ Higher secondary attack rate among household than non household contacts
→ Highest COVID-19 rate for household contacts of school-aged children (10-19y)

Limits:
- Underestimation of the number of cases,
- Exposure outside the household,
- Difference of testing policy between household and nonhousehold contacts,

→ **Transmission potential in both children and adolescents,**
→ **Possibly more effective transmission in adolescents than in adults**.

Risk of COVID-19: health-care workers & general community

Prospective – observational cohort study (UK & USA)
Data from the COVID Symptom Study smartphone application:

- Baseline demographic info
- Daily info on symptoms
- COVID-19 testing

2 135 190 participants, whom 99 795 front-line health-care workers

Primary outcome: positive COVID-19 test (self report)

→ **Recorded 5 545 positive COVID-19 test** over 34 435 272 person-days
→ Testing ratio (health care workers vs general community):
    → UK: ratio 5,5 [1,1 % vs 0,2%]
    → USA: ratio 3,7 [4,1% vs 1,1%]

	Event/person-days	Incidence (30-day)	Multivariate-adjusted hazard ratio (95% CI)	Inverse probability-weighted hazard ratio (95% CI)
Overall (primary analysis)				
General community	3623/32 980 571	0·33%	1 (ref)	1 (ref)
Front-line health-care worker	1922/1 454 701	3·96%	11·61 (10·93–12·33)	3·40 (3·37–3·43)

Front-line health-care workers positive test risk increased 12 fold (HRa: 11,61).

The difference is not related to testing eligibility
→ *(HR model with inverse probability weighting for predictors of testing)*

Compared with the general community, health-care workers initially free of symptoms had an increase risk of predicted COVID-19 (HRa: 2,05) which was higher in the UK than in the USA (2,09 vs 1,31; *p*<0,0001)

Risk of COVID-19: health-care workers & general community

POST-HOC ANALYSIS

	Adequate PPE	Reused PPE	Inadequate PPE
Overall			
Event/person-days	592/332 901	146/80 728	157/60 916
Unadjusted hazard ratio (95% CI)	1 (ref)	1·46 (1·21–1·76)	1·32 (1·10–1·57)
Multivariate-adjusted hazard ratio (95% CI)	1 (ref)	1·46 (1·21–1·76)	1·31 (1·10–1·56)
No exposure to patients with COVID-19			
Event/person-days	186/227 654	19/37 599	48/35 159
Unadjusted hazard ratio (95% CI)	1 (ref)	0·96 (0·60–1·55)	1·53 (1·11–2·11)
Multivariate-adjusted hazard ratio (95% CI)	1 (ref)	0·95 (0·59–1·54)	1·52 (1·10–2·09)
Exposure to patients with suspected COVID-19			
Event/person-days	126/54 676	36/19 378	26/14 083
Unadjusted hazard ratio (95% CI)	2·40 (1·91–3·02)	3·23 (2·24–4·66)	1·87 (1·24–2·83)
Multivariate-adjusted hazard ratio (95% CI)	2·39 (1·90–3·00)	3·20 (2·22–4·61)	1·83 (1·21–2·78)
Exposure to patients with documented COVID-19			
Event/person-days	280/50 571	91/23 751	83/11 675
Unadjusted hazard ratio (95% CI)	4·93 (4·07–5·97)	5·12 (3·94–6·64)	5·95 (4·57–7·76)
Multivariate-adjusted hazard ratio (95% CI)	4·83 (3·99–5·85)	5·06 (3·90–6·57)	5·91 (4·53–7·71)

Health-care workers with inadequate or reused PPE had an increased risk for COVID-19 after multivariable adjustment

Sufficient availability of PPE, quality of PPE, or both reduce the risk of COVID-19.

PPE reuse → self-contamination during repeated application

Increased risk for SARS-CoV-2 infection among health-care workers compared with the general community.

Adequate allocation of PPE is important
Need to ensure proper use of PPE and adherence to other infection control measures.

Limits:
- Details for some exposures were shortened (eg, type of PPE)
- Self-report (risk factor & primary outcome)
- Selection bias (not a random sampling)

Real-world network – COVID-19 control strategies

- Non-pharmaceutical interventions are central to reducing SARS-CoV-2 transmission

- Epidemic model that simulates COVID-19 outbreaks across a real-work network
  - Assess the impact of a range of testing and contact tracing strategies
  - Simulate physical distancing strategies
  - Quantify interaction among physical distancing, contact tracing & testing affects outbreak dynamics
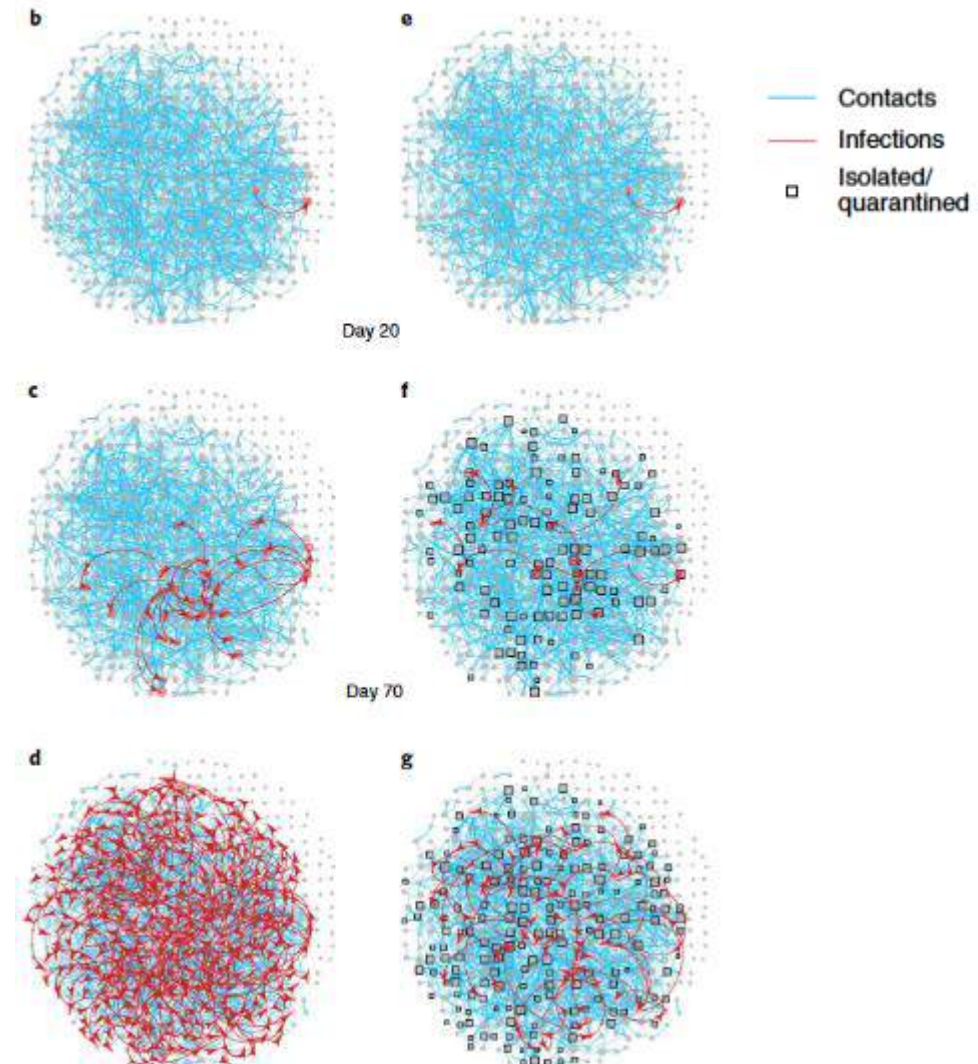
- Uses a publicly dataset on human social interactions

Illustration of the Haslemere network with epidemic simulation predictions.
b–d: Progression of the COVID-19 epidemic under the no-intervention
e-g: under secondary contact tracing scenarios.

Real-world network – COVID-19 control strategies

- From a single infected individual:
  - Uncontrolled outbreak: 75% of the population infected 70 days after the first simulated infection
  - Case isolation: 66% of the population infected
  - Primary tracing: 48% infected
  - Secondary contact tracing: 16% infected after 70 days

  Very high proportion of quarantined individuals
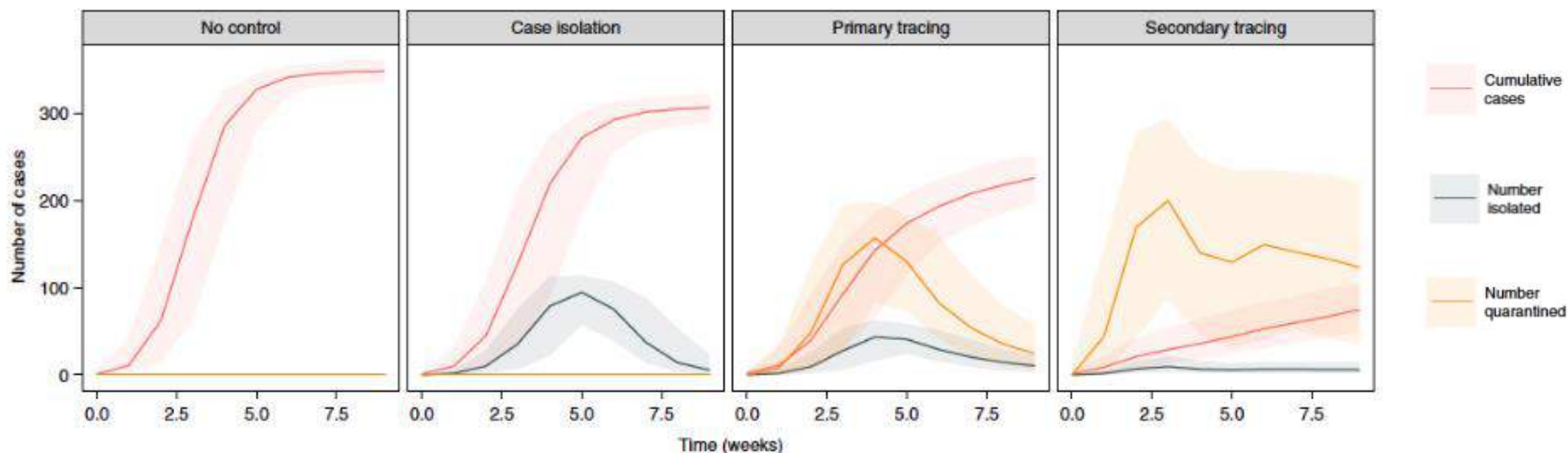
Epidemic model predictions of outbreak size & number of people isolated or quarantined
Cumulative number of cases, number of people isolated and number of people quarantined

Real-world network – COVID-19 control strategies

- Increasing the testing capacity → increases in outbreak size, especially under secondary contact tracing

- Number of quarantined individuals can be reduced through mass testing

Contact tracing & quarantine strategy:

→ Might be more effective than « local lockdown » strategy when contact rates are high

→ Would be most efficient when combined with other control measures such as physical distancing
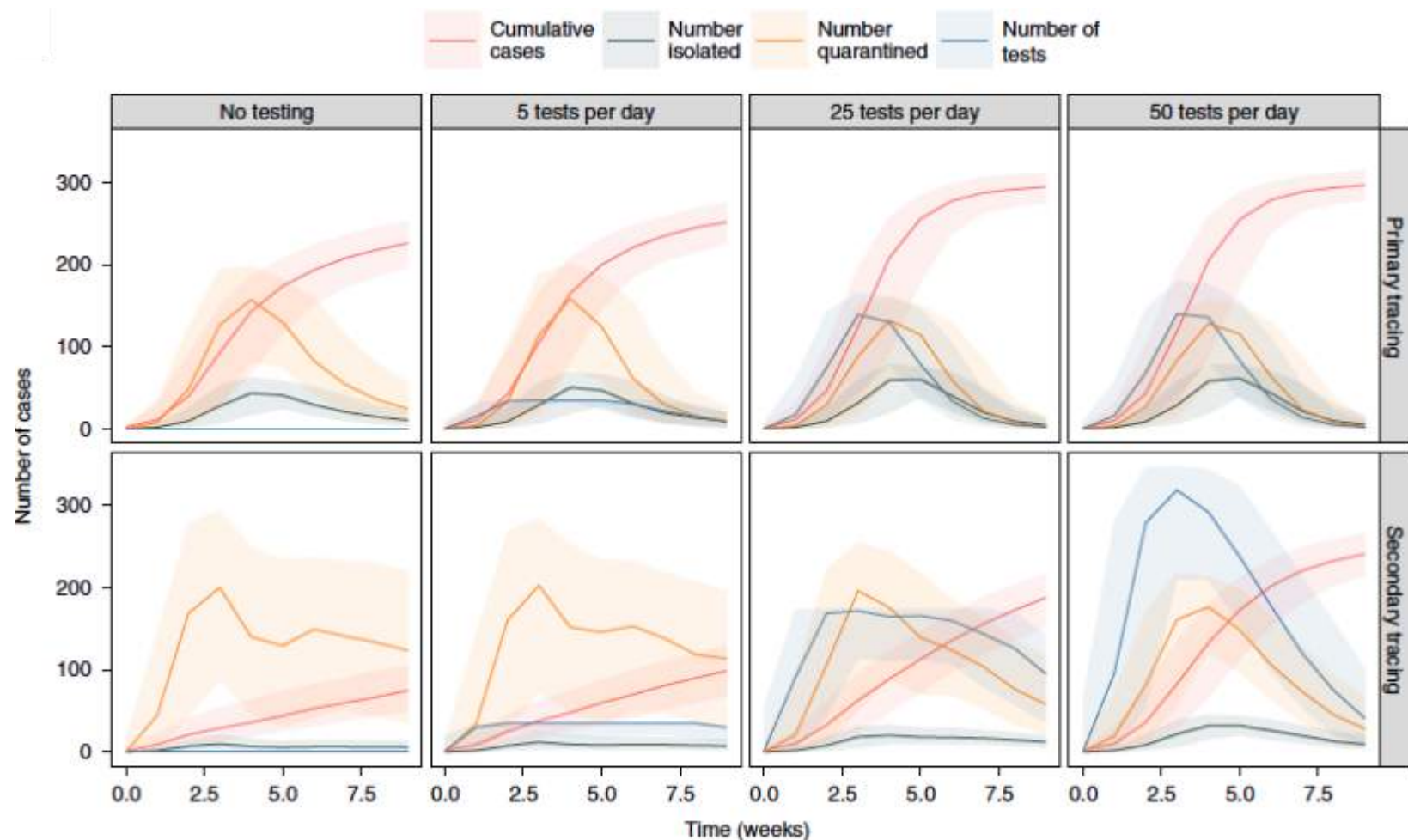
Epidemic model predictions of how testing affect outbreak and qurantine dynamics

# Testing strategies for COVID-19 control

- Mathematical model of SARS-CoV-2 transmission based on:
  - Infectiousness: proportion of infection that are asymptomatic and their infectiousness
  - PCR test sensitivity over time since infection

- Evaluate
  - The impact of self-isolation following either a positive test result or symptom onset
  - The impact of quarantine of contacts of laboratory confirmed cases

- Percentage of reduction in R = expected effectiveness of different testing strategies

- <u>Based on literature</u>: 33% of infections are asymptomatic which have a relative infectiousness off about 50%

- If self-isolation was 100% effective + all individuals with symptoms compatible with COVID-19 self-isolated → reduction in R of 47%; $CI_{95\%}$ [32 – 55]

  - Play an important role in prevention of SARS-CoV-2 transmission

  - No single strategy will reduce R below 1
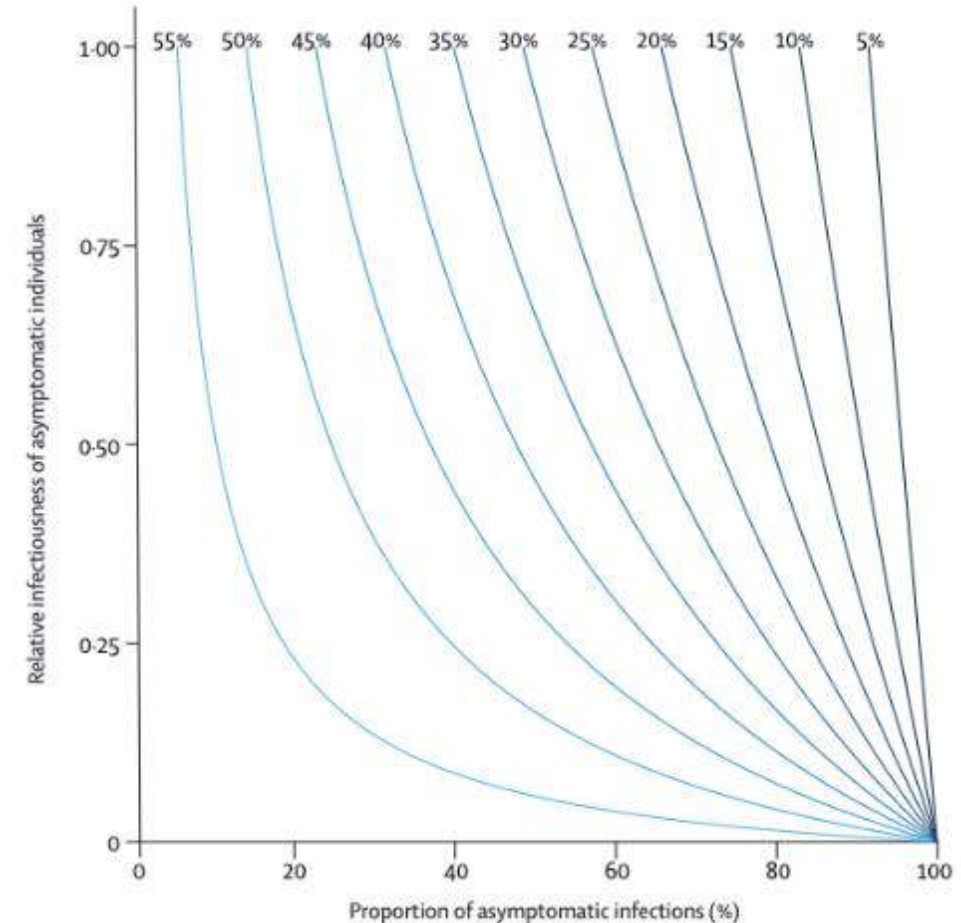
Percentage of reduction in R by self-isolation following onset of symptoms as a function of the proportion of infections that are asymptomatic

Grassly N C et *al. Lancet Infect Dis.* Aug 2020

Testing strategies for COVID-19 control

- Self-isolation following onset symptoms of COVID-19: reduction of their contribution to SARS-CoV-2 transmission
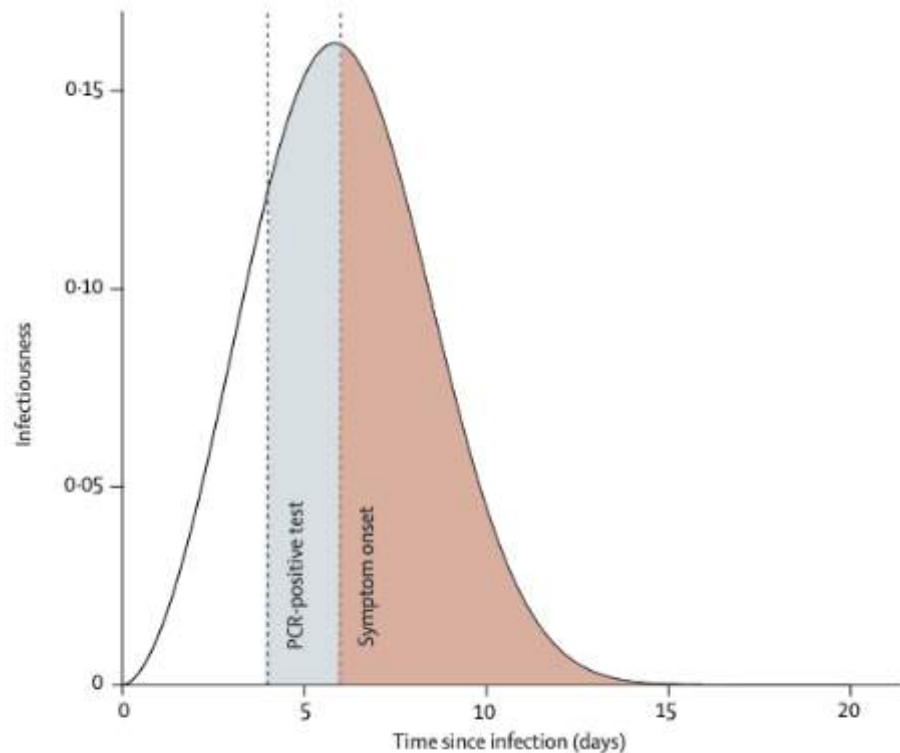
Detection of presymptomatic SARS-CoV-2 infection and subsequent reduction in transmission through self-isolation after a positive PCR test

- PCR testing of symptomatic individuals → reduces the number of individuals needing self-isolate BUT would reduce the effectiveness of self-isolation (false negative)

- Regular PCR testing, irrespective of symptoms, could reduce transmission
 - Depends on the frequency of testing – timeliness of results – sensitivity of the test
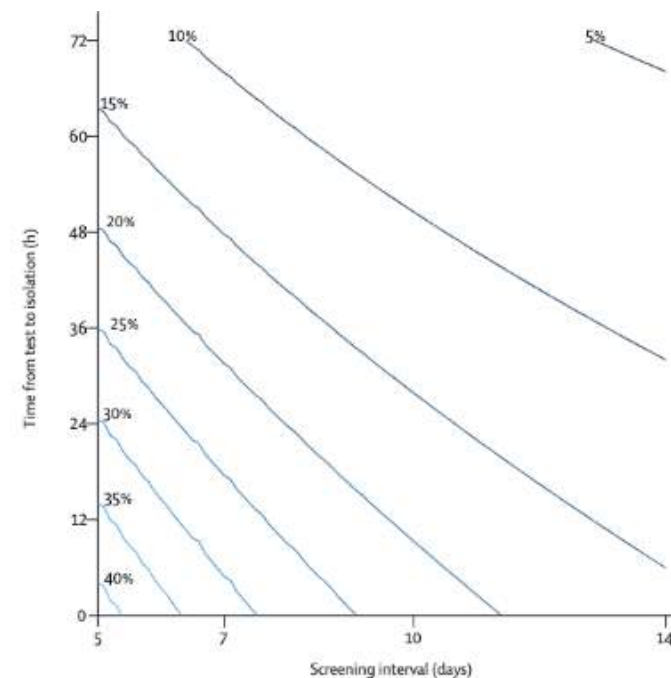
Additional percentage reduction in the R by a policy of repeated PCR testing

Testing strategies for COVID-19 control

- <u>Test-and-trace strategy</u>: Isolating the contact of symptomatic SARS-CoV-2 positive individuals
 - Dependent on:
    - Proportion of symptomatic who are tested
    - Success of tracing their contact
    - Timeless of obtaining test results & identifying & quarantine them
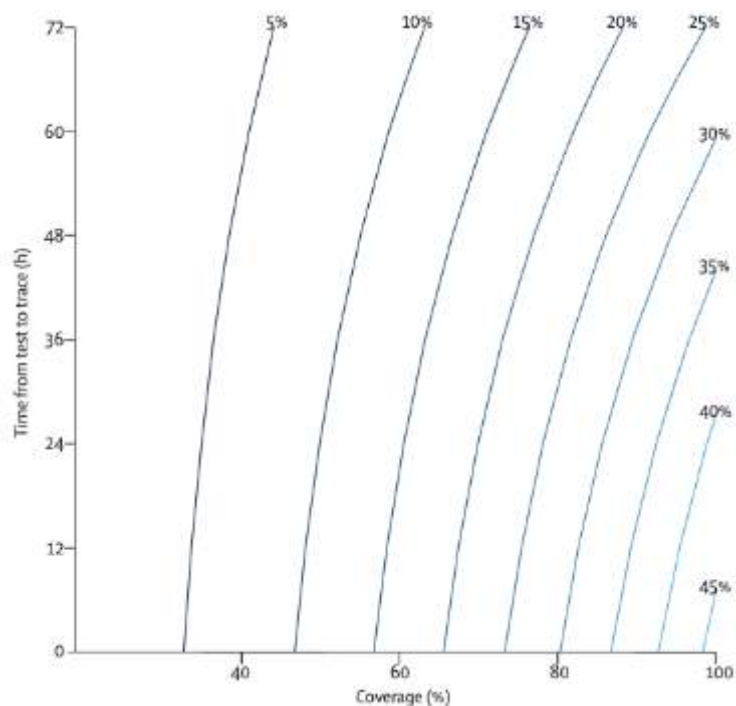
- <u>Test-trace-test strategy</u>: testing contact & only those who tested positive put into isolation
  - Effectiveness is lower than a test-trace strategy
  - High probability of false negative

Test-and-trace strategies
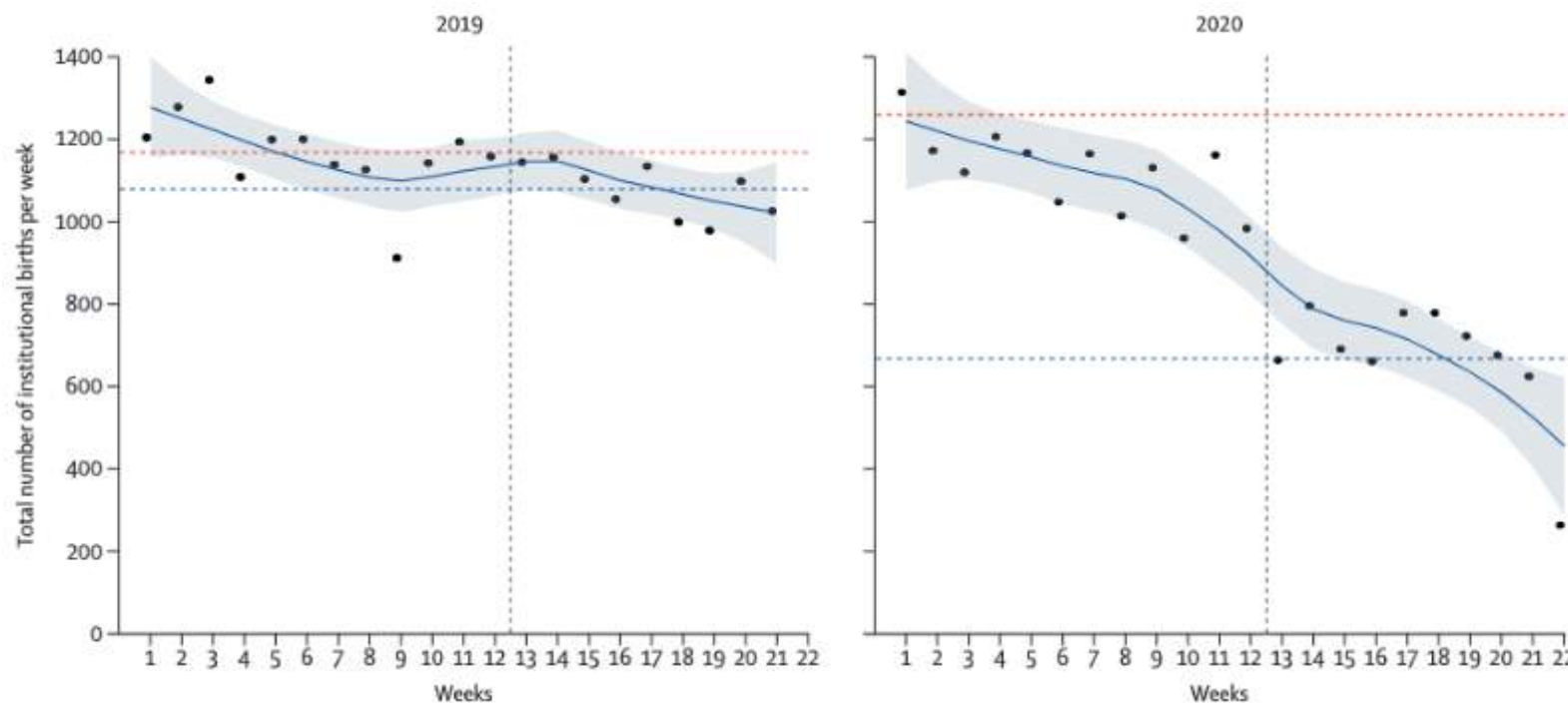
Test-trace-test strategies
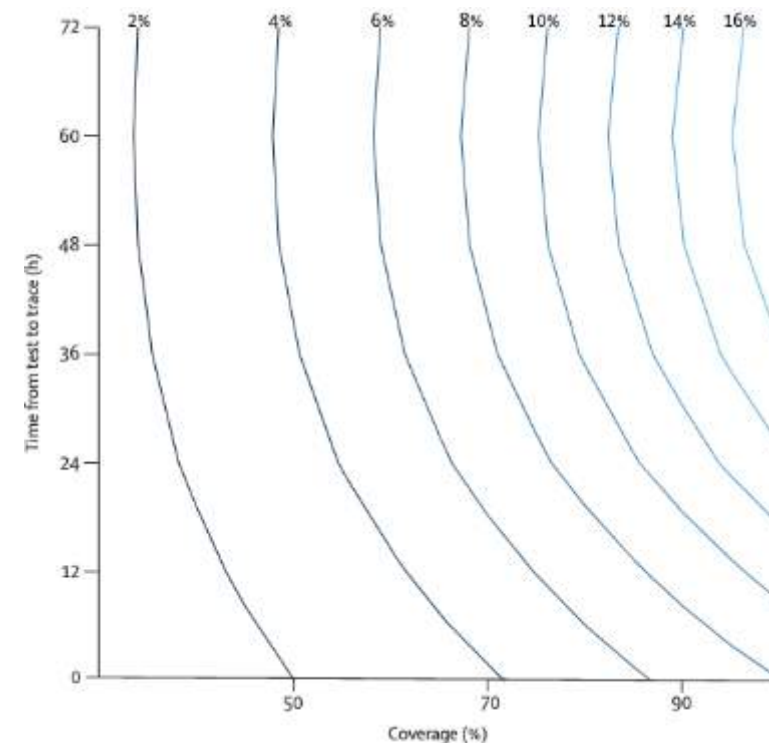
Impact of COVID-19 pandemic response - Nepal

Prospective – observational study in 9 health institutions in Nepal

Data over a period of 5 months: 12,5 weeks before lockdown and 9,5 weeks during lockdown

Women > 22 weeks of gestations + fetal heart sound was heard at the time of admission : 21 763 enrolled & 20 354 gave birth in the hospital

Institutional birth:
- Substantial decrease – especially after week 12,5
- Reduction during lockdown was 7,4%
- **Total decrease of 52,4% by the end of lockdown**

Weekly institutional births for the first 22 weeks of 2019 & 2020

Ashish KC et *al. Lancet Glob Health.* Aug 2020

Impact of COVID-19 pandemic response - Nepal

	Before lockdown	During lockdown	*P value*
Institutional stillbirth (per 1000 total births)	14	21	0,0002
Intitutional neonatal mortality (per 1000 livebirths)	13	40	0,0022
Intrapartum fetal heart rate monitoring (%)	56,8	43,4	<0,0001
Skin to skin contact with the mother's chest (%)	13,0	26,2	<0,0001
Health workers wash hand during childbirth (%)	28,6	41,1	<0,0001

	Preterm birth rate		Institutional stillbirth, rate per 1000 total births		Institutional neonatal mortality rate, per 1000 livebirths	
	Estimate (95% CI)	p value	Estimate (95% CI)	p value	Estimate (95% CI)	p value
Adjusted effect, β						
Baseline risk (risk before lockdown)	0·14 (0·11–0·17)	<0·0001	3 (2–7)	<0·0001	0·9 (0·1–8)	<0·0001
Risk ratio during lockdown vs before lockdown	1·30 (1·20–1·40)	<0·0001	1·46 (1·13–1·89)	0·0042	3·15 (1·47–6·74)	0·0037

- These results raise questions on policies regarding strict lockdown in LMIC
- Pandemic lockdown jeopardize the progress that has been made in the past in Nepal
- Urgent need to protect access to high quality intrapartum care and prevent excess death

Ashish KC et *al. Lancet Glob Health.* Aug 2020

Effect of the first wave on all-cause mortality

Knowledge of the total effect on mortality is needed:
- The true public health effect of the pandemic
- The policy response

→ **Application of 16 Bayesian models to vital statistics data to estimate the all-cause mortality effect of the pandemic for 21 industrialized countries**

Deaths in all countries started to diverge to higher levels in March
(e.g. in 4 countries)

From mild-February through en of May 2020, an **estimated 206,000 more people died** in these 21 countries than would have been expected had the pandemic not occurred
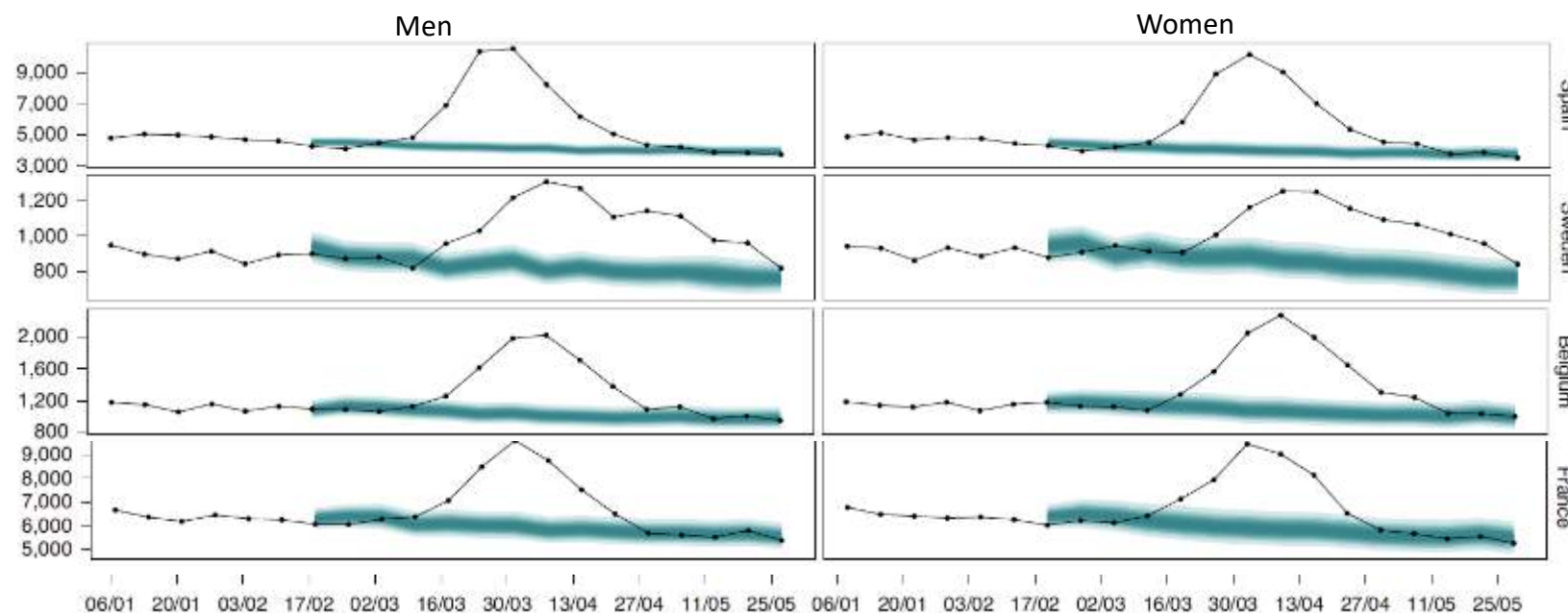
Countries: From Europe and the Pacific
- Total population in 2020 > 4 million
- Up-to-date weekly data on all-cause mortality through May 2020
- Time series of data went back at least to 2015

Weekly number of death from any cause from January 2020 through May 2020

Men   Women

The turquoise-shaded areas show the predictions of how many deaths would have been expected from mid-February had the COVID-19 pandemic not occurred

Effect of the first wave on all-cause mortality

Posterior probability = the inherent uncertainty in how many deaths would have occurred in the absence of the pandemic

The largest rise in mortality was most likely to be in England & Wales followed by Spain and Italy.

For the 21 countries:
- The number of excess deaths from all-causes was 23% (7–38%) higher than the number of deaths assigned to COVID-19 as underlying cause of death.

- The difference between all-cause excess and COVID-19 deaths was largest in Spain and Italy.

- The number of excess deaths for all causes, excess deaths per 100,000 people and relative increase in deaths were similar between men and women in most countries.

4 groups:
- (1): Countries that have avoided a detectable rise
- (2-3): Countries which experienced a low-to-medium effect of the pandemic on overall deaths
- (4): Countries which experienced the highest mortality toll (Belgium, Italy, Scotland, Spain and England and Wales)
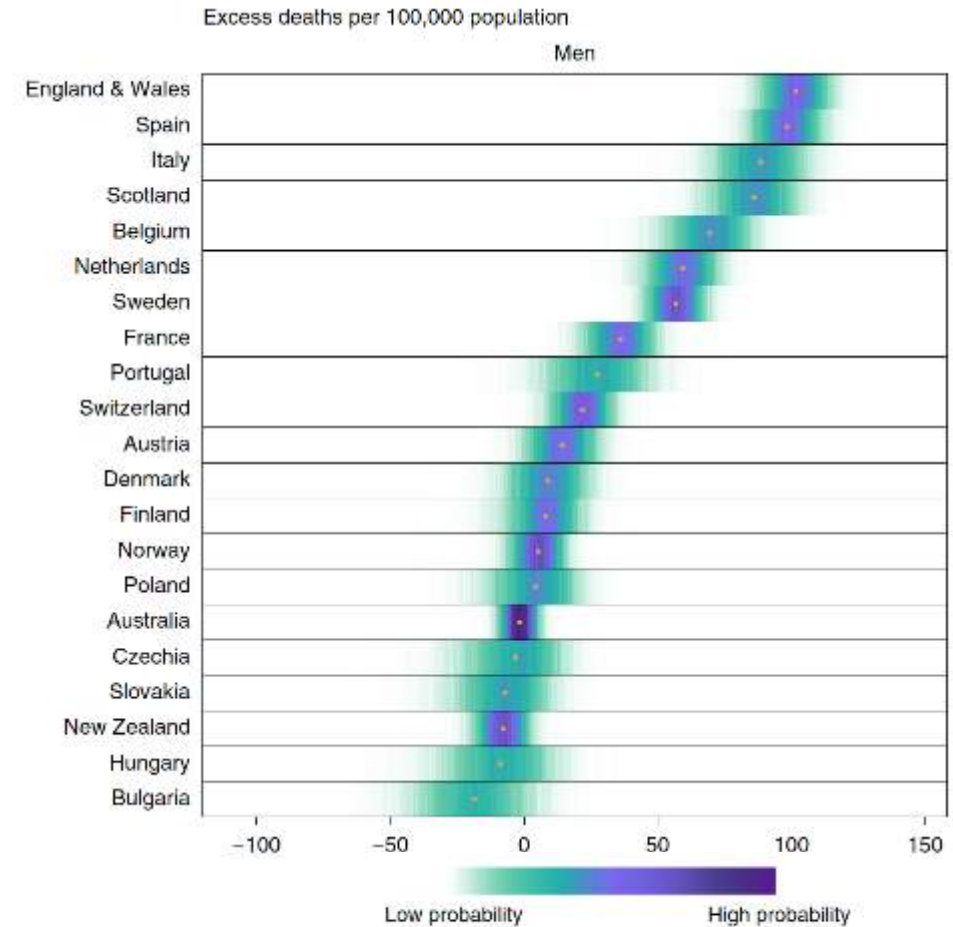
Posterior distribution of excess deaths from any cause per 100,000 people from mid-February to the end of May 2020. Gold dots in the top panels show the posterior medians.
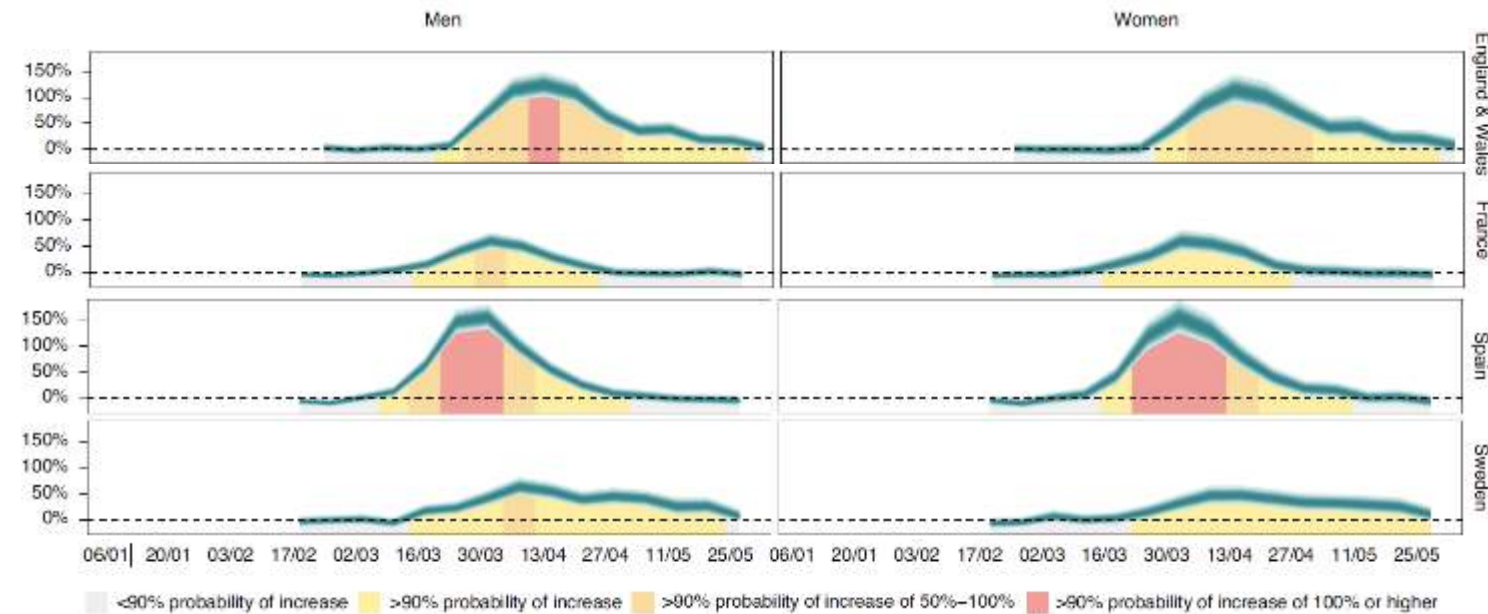
Kontis V et *al. Nature Med. Oct* 2020

Effect of the first wave on all-cause mortality

Death returned to levels that would expected without the pandemic in April (e.g. France & Spain).

But remained above the levels expected in others (e.g. UK & Sweden)

Limits:
- No data on underlying cause of death
- Not access data for several other countries
- No data on total mortality by socio-demographic status
- No explanation for the observed difference among countries

- Difference between health care system → comparaison ?

Weekly percent increase in mortality from any cause as a result of the COVID-19 pandemic by country. The turquoise shading shows the credible intervals around the median prediction.

→ The heterogeneous mortality effects of the COVID-19 pandemic reflect differences in how well countries have managed the pandemic and the resilience and preparedness of the health and social care system.

EPIDEMIOLOGY (December the 21ᵗʰ 2020)

1. What is the situation in the World?

- More than 30 millions of confirmed cases in the World and 1 million global deaths

2. What is the incubation period & R_0?

- The median incubation period is 5 days with an initial basic reproductive number between 2 to 6 before control measures

- Presymptomatic transmission: 44% - Infectiousness decline quickly within 7 days.

3. What is the impact of non-pharmaceutical intervention on _R_?

- Introducing and lifting NPIs were associated with reductions and increases of _R_, respectively, with no immediate effect

4. What do we know about the risk of transmission & the mode of transmission?

- Person to person transmission – transmission seems to be more effective in adolescents than in adults

- Route of transmission: droplet, direct contact, plausible aerosol

- Increased risk for SARS-CoV-2 infection among health-care workers compared with the general community.

- Most close contact exposures were to private or public gathering

5. What is the impact of the different measures taken by countries?

- Face masks reduce the transmission of respiratory viruses and probably of SARS-CoV-2

- Pandemic lockdown can have an important impact on the access to the health system in some countries

- The number of excess deaths from all-causes was 23% (7–38%) higher than the number of deaths assigned to COVID-19

- Reflect differences in the resilience and preparedness of the health and social care system

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research & action
targeting emerging infectious diseases

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