MODELLING SARS-COV-2 TRANSMISSION IN THE FRENCH COMMUNITY AND HOSPITALS

LULLA OPATOWSKI, SIMON CAUCHEMEZ, LAURA TEMIME
HOSPITALS, at the heart of the outbreak

- Non controlled importation in the hospital
  - Admission of Covid+ patient
  - Covid+ health care worker
  - Especially in hospitals not dedicated to host covid patients

Virus circulation in the community

- Important flow of patients from the community
- Saturation
- Disorganisation – ward closure etc

Risk of nosocomial transmission
A series of investigations

**Community**
1. Estimating the burden of SARS-Cov2 in the French community
2. Contact survey on contacts during lockdown in France

**Hospital**
1. Hospital transmission, how to define $R_0$
2. Strategies of tests in long term care hospitals
3. Perspectives : Nods-cov2
1. ESTIMATING THE BURDEN OF SARS-COV-2 IN FRANCE: Integrating multiple data types

Simon Cauchemez, Mathematical Modelling of Infectious Diseases Unit, Institut Pasteur

Science, Salje et al, 2020
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Key questions and challenges

• Questions:
  ➢ What has been the impact of the French lockdown on SARS-CoV-2 transmission?
  ➢ What is the proportion of the French population that has been infected by SARS-CoV-2? At a national and regional level?
  ➢ Can we anticipate ICU admissions and bed occupancy to support planning?

• Challenges:
  ➢ Hospital surveillance provides a good picture of severe covid19 cases across France but only shows the tip of the epidemic
    ➢ Joint analysis of hospital surveillance data and other data that can be used to ascertain the missing part of the epidemic
  ➢ Epidemics have non linear dynamics
    ✓ Use of mathematical models to capture these dynamics
Integrating multiple types of data

Passive hospital surveillance in France

As of May 7th
95,210 hospitalisations
16,386 hospital deaths

Active surveillance Princess Diamond

- 3711 passengers,
- 712 tested positive,
- 14 deaths,
- 4 still in ICU after >2 months (assume they will die)

Limitations:
- More healthy?
- Some infections missed?

Serosurveys and studies in specific locations
Progressively integrated to the framework
Approach

What we observe from the French hospital data
Approach
Estimates of risks by age group and sex

A. Probability of hospitalization | infected

- Male
- Female

B. Probability of ICU | hospitalized

- Male
- Female

C. Probability of death | hospitalized

- Male
- Female

D. Infection fatality ratio (IFR)

- Male
- Female

- 3.6%
- 19%
- 18%
- 0.7%
Age-structured deterministic compartmental model

Fit on SI-VIC data corrected for reported delays

$g$: negative binomial distribution

MCMC with Metropolis Hasting
Impact of lockdown and national dynamics

Reproduction numbers
- Before lockdown: 2.9 (2.8, 2.99)
- Lockdown: 0.67 (0.65, 0.68)
- 77% reduction

Nationally: 4.4% (2.8%-7.2%)
Ile de France: 9.9% (6.6-15.7%)
Grand Est: 9.1% (6.0-14.6%)
Sensitivity analysis

Assess the impact of hypotheses, such as children infectiousness or delays to hospitalizations
Discussion

• Only looking at hospital deaths.
  • Excluded population living in homes for elderly people (EHPAD).
  • Possibility of other non-hospital deaths.

• Limits of Diamond Princess cruise ship data
  • Small. Healthier population? Missed infections?
  • Progressively adding more data as they become available.

• Next steps:
  • Integration of serological data when available.
  • Integration of confirmed cases reporting
  • Models to monitor changes in transmission after the lockdown.
2. CONTACTS DURING LOCKDOWN IN FRANCE: Preliminary results from the SocialCov survey

Paolo Bossetti, Lulla Opatowski, Bich Tram Huynh, Marie Sanchez, Armiya Youssouf Abdou
SocialCov, a survey in the general population

- Lockdown has drastically modified contacts within the community
  - Existing contact matrices not relevant

- Build specific contact matrices

- SocialCov, questionnaire
  - Targeting participants >18 yo
  - Designed to spread on social networks (mail, What’s app, FB, twitter etc)
Characteristics of the participants

>42,000 participants >18 yo between April 10 and April 28
Lockdown associated organization

C

Professional situation

- Work from home
- Work outside home
- Unemployed/Retired

After Lockdown
Before Lockdown

percentage

0 20 40 60 80 100

a

Child care outside the household (5.1%)

- Other
- External person >60 y-o
- External person <60 y-o
- Provided service of child care

percentage

0 20 40 60 80 100
Lockdown associated behaviour
Lock-down age contact matrices

(a) Contacts Home (N=42036)

(b) Contacts Work (N=4567)

(c) Contacts shops (N=12987)

(d) Contacts other types (N=12325)

(e) Contacts transport (N=203)

(f) Contacts total (N=42036)
Discussion

• Strong impact of Lock-down on contact patterns (expected)

• Survey in the general population => not a representative population
  • 2/3 women => not so many differences
  • Comparison statistics regarding the French population
    • household size, activity rate etc
    • INSEE data

Next steps:
  • Re-launch the survey post Lock-down to build new matrices
  • Launch versions for other countries
    • Collaborations with Institut Pasteur in Asia or Africa
    • looking for translations/adaptations
A series of investigations

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Especially in hospitals not dedicated to host Covid patients

Risk of nosocomial transmission
Result of fruitful discussions with the « Modelling COVID-19 in hospitals » REACTinG AVIESAN working group:

3. DISCUSS ABOUT $R_0$ IN HEALTHCARE SETTINGS
Comments regarding the reproductive number

• The reproductive number depends on the population in which the virus circulates
  ◦ density of contacts

• In hospitals, density of contacts strongly differs from the one in the community
  ◦ Patients / health care workers
  ◦ frequency and specificity of contacts

=> we don’t expect R to be similar to the one estimated in the community

• Objective, get insight into what would be R in a hospital

Comments regarding the reproductive number in a health care settings

• Under simplifying assumptions:

\[ R_0 = p \times d_{Ctc} \times n_{Ctc} \times d_{Inf} \]

- Average contact duration in min.
- Average duration of infectivity ~10 days
- Proba per min. of contact
- Average # of contacts per ind. per day

\[ R_0^H = R_0^C \times \frac{d_{Ctc}^H \times n_{Ctc}^H}{d_{Ctc}^C \times n_{Ctc}^C} \]

Possible ranges of $R^H$ depending in $R^C$ and $n_{Ctc}$

\[
R_0^H = R_0^C \times \frac{d_{Ctc}^H \times n_{Ctc}^H}{d_{Ctc}^C \times n_{Ctc}^C}
\]

Values computed for $d_{Ctc}^H$ ranging 10-40 minutes

<table>
<thead>
<tr>
<th>Assumed value for basic reproduction number in the community ($R_0^C$)</th>
<th>5</th>
<th>10</th>
<th>15</th>
<th>18</th>
<th>20</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>0.4-1.7</td>
<td>0.8-3.3</td>
<td>1.3-5</td>
<td>1.5-6</td>
<td>1.7-6.7</td>
</tr>
<tr>
<td>2.5</td>
<td>0.5-2.1</td>
<td>1.4-2</td>
<td>1.6-6.3</td>
<td>1.9-7.5</td>
<td>2.1-8.3</td>
</tr>
<tr>
<td>3</td>
<td>0.6-2.5</td>
<td>1.3-5</td>
<td>1.9-7.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.5</td>
<td>0.7-2.9</td>
<td>1.5-5.8</td>
<td>2.2-8.8</td>
<td>2.6-10.5</td>
<td>2.9-11.7</td>
</tr>
<tr>
<td>4</td>
<td>0.8-3.3</td>
<td>1.7-6.7</td>
<td>2.5-10</td>
<td>3-12</td>
<td>3.3-13.3</td>
</tr>
</tbody>
</table>

Rehabilitation hospital 170 beds
iBird study, 34 min
\[=> R \sim 7.6\]

R values range 0.4 – 13.3

MedRxiv, Temime et al, 2020
Discussion

• Very simplified formalization
  • Does not take into account heterogeneities in contacts
  • Does not take into account differences in infectivity of patients, HCWs and individuals from the community
  • Does not take into account isolation, barrier measures and hygiene

• Illustrates the high risk for transmissions in health care settings
  • Strongly depend on the type of health care settings and contact patterns
  • Justification for implemented measures, eg. limitations of group activities etc
4. Improving COVID-19 surveillance in long-term care

A simulation study

David Smith, Audrey Duval, Laura Témime, Lulla Opatowki
Long term care facilities (LTCF)

**Importation** of the virus in hospitals non dedicated to COVID-19 patients
- Via patients on admission (transfers...)
- Via health care workers (HCWs)

Rehabilitation hospitals or nursing homes worldwide **have reported outbreaks**
- high rates of infection and mortality among patients and healthcare workers

**Surveillance level has been low in these settings**
- In France: tests limited to individuals presenting with characteristic COVID-19 symptoms or signs of severity
  => tip of the iceberg
- Timely detection of nosocomial COVID-19 outbreaks is essential
- Difficulty: **LIMITED testing resources**

Long term care facilities (LTCF)

**Objective:** investigate strategies to improve COVID-19 surveillance, taking into account limited testing resources
Outbreak simulation

- Simulator of SARS-Cov-2 transmission over a detailed contact network (patients and HCWs)
  - (adapted from Duval, ICCS, 2019)
  - Detailed contact data from the iBird study, collected over 4 months in a LTCF (170 beds)

- Epidemiological characteristics of SARS-Cov-2:

  - Incubation: 2-5 days
  - Infectious, presymptomatic: 1-3 days
  - Infectious, asymptomatic: 7 days
  - Infectious, symptomatic: 7-10 days

- Estimation of a reproduction number for the hospital by extrapolation from the community estimate
High risk of transmission, strong stochasticity

No measure

High stochasticity

Delay before observation of symptomatic or severe cases

MedRxiv, Smith et al, 2020
Outbreak risk after Covid introduction

No measure implemented, LTCF

Outbreak risk:
⇒ Index patient => 98%
⇒ Index HCW => 64 %

• Highy specific to the LTCF, where high frequency of patient-patient contacts
• Highlights interest of control measures aiming at limiting between-patients interactions
### Simple strategies for surveillance implementation

**Hypothesis:** the total number of daily available tests for the hospital is limited

<table>
<thead>
<tr>
<th>Surveillance strategy</th>
<th>Description</th>
<th>Indications evaluated</th>
<th>Daily testing capacity always reached?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline indication-based testing</td>
<td>Administer RT-PCR tests to any individuals indicated for testing, up to the daily testing capacity</td>
<td>Symptoms (severe) [reference strategy]</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Symptoms (any)</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Admission</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Random (patients)</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Random (healthcare workers)</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Random (all)</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Probability of detection for the different importation scenarios

Probability of detecting the outbreak over time, 4 tests per day

=> Test only severe symptoms is not optimal

MedRxiv, Smith et al, 2020
More sophisticated strategies

Hypothesis: the total number of daily available tests for the hospital is limited

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<td>Testing cascades</td>
<td>Administer RT-PCR tests to individuals according to cascades of priority, until daily testing capacity is reached. First priority is always given to individuals presenting with severe COVID-like symptoms.</td>
<td>Symptoms (severe) $\rightarrow$ Symptoms (mild) $\rightarrow$ Random (patients)</td>
<td>Yes</td>
</tr>
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<td></td>
<td></td>
<td>Symptoms (severe) $\rightarrow$ Symptoms (mild) $\rightarrow$ Admission $\rightarrow$ Random (patients)</td>
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Minimizing detection delay

Median delay of detection when combined importation, depending on the number of available tests
Minimizing detection delay

Median delay of detection when combined importation, depending on the number of available tests

Suggests that focusing on individuals with severe symptoms = not optimal:
- Cascade strategies reduce detection delay
- Extend to patients and HCWs with mild symptoms
- Use everyday testing capacity
More sophisticated strategies

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<td></td>
<td>Symptoms (severe) → Admission → Symptoms (mild) → Random (patients)</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Group testing</strong></td>
<td>First administer individual RT-PCR tests to anyone presenting with severe COVID-like symptoms. Subsequently, if any tests remain, pool clinical specimens together up to a maximum of 2, 4, 8 or 16 specimens, and run one RT-PCR test across all specimens</td>
<td>Symptoms (any)</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Admission</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Random (patients) (always maximizes number of specimens per group test)</td>
<td>No</td>
</tr>
</tbody>
</table>
Cascade or group testing?

Detection lag (in days)

Daily testing capacity

MedRxiv, Smith et al, 2020
Cascade or group testing?

- Low capacity => group testing dominates
- High capacity => cascades reduce delays

MedRxiv, Smith et al, 2020
Discussion

• No control measure considered
  • Hospitals have reduced patients activities or visits and increased barrier protections
  • Next step: Evaluate impact of control strategies once virus is detected in the hospital

• Results suggest that reference standard-of-care is a comparatively poor strategy.

• Specific to LTCF
  • Typical contact network
  • Not clear generalisation to other types of wards
Extension and perspective: Nods-Cov2

Epidemiological study aims at collecting dynamic of contacts through wireless « LogSensors » in different types of wards :

- Emergency
- Wards dedicated to paediatric care
- ICU
- Covid+/Covid-
- etc

PI Didier Guillemot, Study partners :

Hospices Civils de Lyon, les Hôpitaux Universitaires de Bordeaux, l'Assistance Publique-Hôpitaux de Paris, l’Inserm, l’Université de Versailles Saint Quentin-Université Paris Saclay, l’Institut Pasteur, l’Université de Bordeaux, Université de Lyon/CIRI et l’Inria.
Merci !