PROJECTIONS OF ICU OCCUPATION AND HOSPITAL MORTALITY DURING THE COVID-19 EPIDEMIC IN THE CANTON OF VD

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Mandate

In march 2020, DGS (Direction Générale de la Santé) contacted us to develop a software tool to follow COVID-19 epidemic in the Canton of VD and project the following quantities under different scenarios:

1. Global bed occupation in intensive care units (ICU) in VD hospitals (initial request)
2. Hospital mortality (additional request)

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Goals:

- Assess whether and when ICUs could be overflooded by COVID-19 patients ($\sim$ 200 ICUs beds for COVID-patients available in VD)
- Assess whether ice skating rinks would be needed to store deceased patients before funerals

In the event of ICUs overflooding, patients admission to ICU would be restricted and granted only to those patients with the best chances of survival. A patient in need of IC and whose access to ICU is refused is virtually condemned to die.

Data

DGS initially provided **aggregated data** with daily information on

- cumulative counts of COVID-19 hospitalized patients
- number of ICU beds occupied by COVID-19 patients
- number of COVID-19 related deaths

and later provided anonymized **individual patient data** with

- age, sex
- dates of hospital admission/discharge and ICU transfer/discharge (if applicable)
- health status (alive/dead) on hospital discharge

Data (Excel file) was updated every day or couple of days. Last available update on April 17, 2020.

Projections for ICU beds occupation

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Based on daily **cumulative number of hospitalizations** (more precise than cumulative counts of detected cases which depend on screening policy)

Projections based on 5 potentially time-varying parameters:

1. **EGP** = Exponential Growth Parameter for cumulative number of hospitalizations
2. **ICP** = Intensive Care Proportion (% hospitalized patients that will require IC at some point)
3. **LAG** = Time interval between hospital admission and ICU transfer
4. **ADP** = Admission probability (% patient requiring IC that will be admitted in ICUs)
5. **LOS** = Length of Stay in ICU

Each parameter drawn from a distribution with potentially time-varying mean/median and variance. User input crucial for EGP and ADP!

1. EGP: Exponential Growth Parameter

Defines how the **cumulative number of hospitalized patients** grows from day j to day $j+1$

Let N_j denote the cumulative number of hospitalized patients up to day j. The cumulative number of hospitalized patient on day $j+1$ is given by

$$N_{j+1} = \mathrm{EGP}_{j+1} \cdot N_j$$

with $\mathrm{EGP}_j \geq 1$ and $\mathrm{EGP}_j = 1$ defining the end of the epidemic.

Distribution:

$$\log(\mathrm{EGP}_j - 1) \sim \mathcal{N}\left(\log(\mathrm{megp}_j - 1), \mathrm{vegp}_j\right)$$

Projected cumulative counts of hospitalizations were used to derive daily new hospitalizations (i.e. incident cases).

2. ICP: Intensive Care Proportion

Defines proportion of hospitalized patients that will require IC at some point. DGS estimated that 1 hospitalized patient out of 5 would require IC (verified on individual patient data).

Distribution:

$$\text{logit}(\text{ICP}_j) \sim \mathcal{N}\left(\text{logit}(\text{micp}_j), \text{vicp}_j\right)$$

Simulation of IC requirement for a patient: Let g_{ij} denote the indicator variable for IC requirement for patient i among patients who were admitted to hospital on day j, such that

- $g_{ij} = 1$: patient i will require IC at some point (during hospitalization)
- $g_{ij} = 0$: patient i will not require IC

Then g_{ij} is simulated according to

$$g_{ij} \sim \text{Bernoulli}\left(\text{ICP}_j\right)$$

3. LAG: Time to (theoretical) ICU transfer

Defines number of days between hospital admission and ICU transfer (only applies to patients requiring IC (i.e. $g_{ij} = 1$)

Distribution:

$$\mathrm{LAG}_{ij} \sim \mathrm{NegBin}\left(\mathrm{mlag}_j, \mathrm{vlag}_j\right)$$

Estimates based on available data: mlag=2 and vlag=9 days ($q_{95\%} = 8, q_{99\%} = 14$)

4. ADP: (ICU) Admission Probability

Defines proportion of patients with $g_{ij} = 1$ that will be effectively admitted in ICU on day $k = j + \text{LAG}_{ij}$. Ideally $\text{ADP}_j = 1$ (no restriction).

Distribution (if $\text{ADP}_j < 1$):

$$\text{logit}(\text{ADP}_j) \sim \mathcal{N}\left(\text{logit}(\text{madp}_j), \text{vadp}_j\right)$$

Ideal situation:

Simulation of admittance of patient i on day k: Let a_{ij} denote the indicator variable for ICU admission for patient i (with $g_{ij} = 1$) on day $k = j + \text{LAG}_{ij}$, such that

- $a_{ij} = 1$: patient i is admitted in ICU on day k
- $a_{ij} = 0$: patient i is not admitted in ICU on day k (=death)

Then a_{ij} is simulated according to

$$a_{ij} \sim \text{Bernoulli}\left(\text{ADP}_j\right)$$

5. LOS: Length of Stay in ICU

Defines length of stay (nb days) in ICU (only applies to patients requiring IC)

Distribution:

$$\mathrm{LOS}_{ij} \sim \mathrm{NegBin}\left(\mathrm{mlos}_j, \mathrm{vlos}_j\right)$$

Estimates based on available data: mlos=13 and vlos=154 days
$(q_{95\%} = 38, q_{99\%} = 57)$

Simulation steps

1. Draw parameters EGP_j, ICP_j and ADP_j from their distribution for each day j
2. Project cumulative counts of hospitalizations using EGP and derive incident hospitalized cases based on observed/projected cumulative counts
3. Generate binary indicator $g_{ij} \sim \text{Bernoulli}(\text{ICP}_j)$ for fake patient i hospitalized on day j
4. Restrict attention to those patients with simulated $g_{ij} = 1$ and generate $\text{LAG}_{ij} \sim \text{NegBin}(\text{mlag}_j, \text{vlag}_j)$
5. Decide whether patient i will be admitted in ICU on day $k = j + \text{LAG}_{ij}$ by generating $a_{ij} \sim \text{Bernoulli}(\text{ADP}_j)$
6. For patients with $a_{ij} = 1$, generate $\text{LOS}_{ij} \sim \text{NegBin}(\text{mlos}_j, \text{vlos}_j)$
7. Build bed occupancy matrix and sum-up nb of beds occupied each day

Simulations repeated 1000 times (could be increased...) $\rightarrow$ construct **predictive distribution of the number of occupied ICU beds on each day** (from start of the epidemic until X days in the future). Predictive distribution summarized using median and e.g. quantiles 5% and 95%

Projections for hospital mortality

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Uses daily number of new hospitalizations (as observed or projected using EGP)

We wanted mortality to be adjusted for age (strong predictor) and possibly sex/IC requirements. The following age groups were defined:

Age group	Global proportion	Proportion of females
< 70 y	50%	37%
70-85 y	33%	41%
≥ 85 y	17%	53%

Simple broad age categories enables investigation of scenarios were the structure of the population of hospitalized patients changes with time (e.g. future arrival of old patients from nursing homes etc)

For this reason, ICP (disease severity), LAG and total hospital LOS were derived using statistical models and were not allowed to vary over time anymore!

Probability to require IC and lag

The probability p_i that patient i did require IC at some point during hospitalization was modeled as a function of age and sex in a logistic regression model:

$$\text{logit}(p_i) = f(\text{age}_i + \text{sex}_i)$$

IC indicator variable for new patients simulated as $g_i \sim \text{Bernoulli}(p_i)$

For existing patients without IC information (i.e. those still in hospital but not yet admitted in ICU), the indicator g_i was imputed using this model ($M = 50$ imputations).

Lag was generated according to $\text{LAG}_i \sim \text{Weibull}(\mu, \sigma)$

Survival models for competitive risks

Time to death

Event: death

Censoring: patient still in hospital + patient who left hospital alive (i.e. cured)

$$T_{1i} \sim \text{Weibull}(\mu_{1i}, \sigma_1)$$
$$\log(\mu_{1i}) = f_1(\text{age}_i + \text{sex}_i + g_i)$$
$$h_{1i} = \text{instant hazard}$$

Time to hospital release (dead or alive)

Event: hospital release (dead or alive)

Censoring: patient still in hospital

$$T_{2i} \sim \text{Weibull}(\mu_{2i}, \sigma_2)$$
$$\log(\mu_{2i}) = f_2(\text{age}_i * g_i + \text{sex}_i)$$
$$h_{2i} = \text{instant hazard}$$

Probability of dying at the end of hospital given by h_{1i}/h_{2i}

Simulating patient death (in hospital)

Let n_j define the number of existing/projected new hospitalizations on day j:

1. Draw age/sex from defined distribution (i.e. age categories)
2. Generate IC status g_i according to logistic regression model for $i = 1, ..., n_j$
3. Generate total hospital LOS T_{2i} using Weibull model for time to hospital release (adjusted for age, sex and g_i)
4. If $g_i = 1$, generate a lag time according to lag model (conditionned on $\text{LAG}_i <= \text{LOS}_i$)
5. Calculate hazard of death $h_{1i} = h_1(T_{2i})$ and hazard of exiting hospital either alive or dead $h_{2i} = h_2(T_{2i})$
6. Draw death indicator $\delta_i \sim \text{Bernoulli}(h_{1i}/h_{2i})$

1000 simulations: allows to construct predictive distribution of the cumulative number of deaths occurring every day. Predictive distribution summarized using median and e.g. quantiles 5% and 95%

Three types of mortality projections

Type 3 Require aggregated data on hospitalizations (mortality data optional). Uses observed cumulative counts of hospitalized patients and generate new patients/deaths from the start of the epidemic

- Prediction intervals for past. Can be compared to observed cumulative death counts (when available) for "goodness of fit"
- Mimics what could have happened in a similar epidemic with same cumulative number of hospitalizations but with different patients

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- Only an approximation!

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Type 1 Require individual patient data. Uses all individual patient data (i.e. observed age, sex, IC and death status)

- No prediction intervals for past (as for type 2)
- Coherent deaths counts (i.e. accounts for all available information)

Software links

R Shiny application available on dedicated server (at least up to June 5, 2020):

https://stat-cmb.ddns.net/COVID19/

Source code:

https://github.com/kilou/COVID19