The Mathematics and Statistics of Infectious Disease Outbreaks

Michael Höhle[1]

[1]Department of Mathematics
Stockholm University, Sweden

L12: Digital Contact Tracing[1]

Stockholm University

[1]LaMo: 2020-09-17 @ 11:39:52

Overview

Outline

Contact tracing (1)

- From the $R_0 = \beta/\gamma$ expression in the SIR model we infer that two non-pharmaceutical components of controlling an infectious disease are:
  - reduce β for infectious individuals (early detection, change of behaviour in infectious, social distancing)
  - (sometimes forgotten) reduce the time period where infectious individuals spread the disease $\rightarrow$ increase γ
- Contact tracing is the process of identifying persons who had contact with an infected person in order to test, isolate and trace onwards

Contact tracing (2)

Goals of contact tracing (Source: Wikipedia):

- To offer diagnosis, counseling and treatment to already infected individuals
- To alert contacts to the possibility of infection and offer preventive services or prophylactic care
- To interrupt transmission chains and, hence, reduce the spread of an infection
- To learn about the epidemiology of a disease in a particular population, e.g., in which settings does transmissions occur

Contact tracing (2)

- In an influential paper, Ferretti et al. (2020) argued that a digital contact tracing app could speed up contact tracing s.t. $R(t) < 1$ would be possible
- The conclusions are based on simulations including rather positive assumptions about the effectiveness of such an digitial effort
- However, some experience from, e.g., South Korea existed which used GPS location for contact tracing

Outline

German Corona-Warn-App

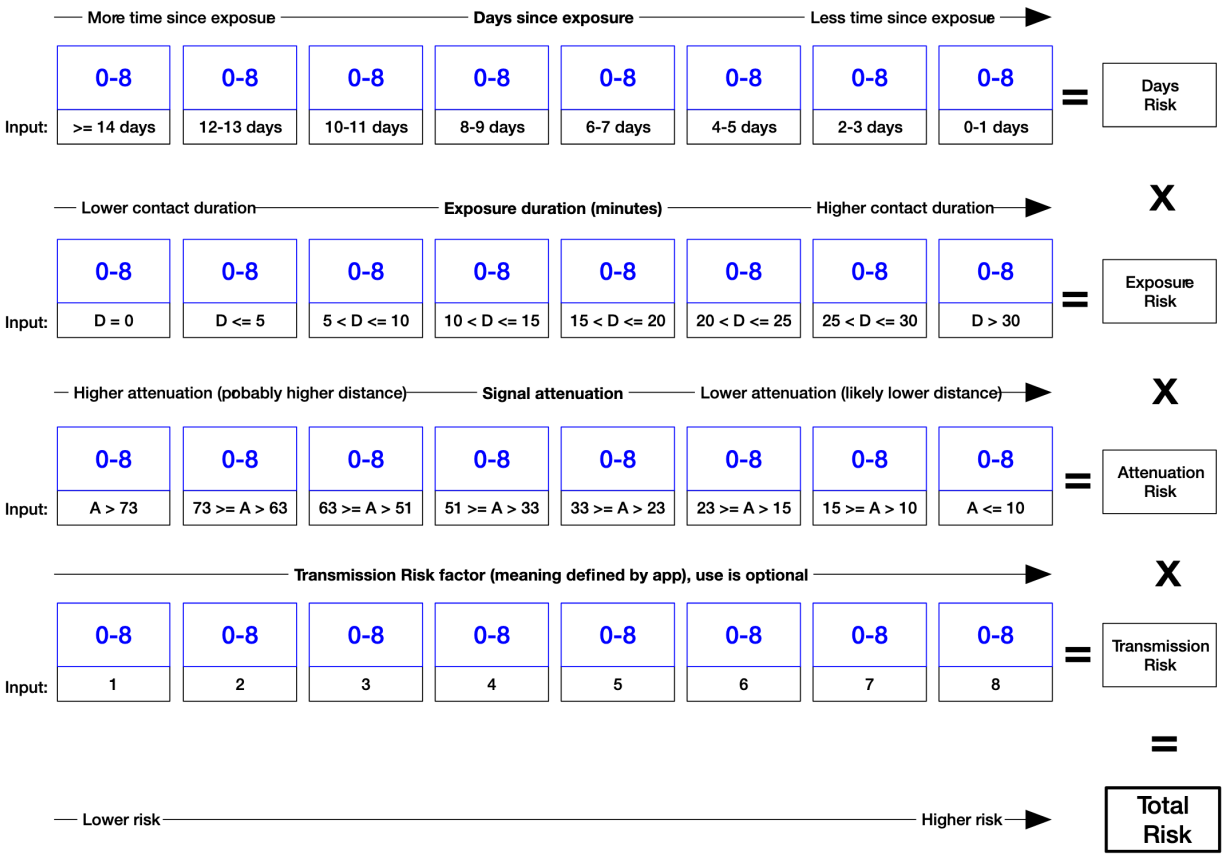
- The Corona-Warn-App is a decentral DP-3T inspired open-source contact tracing app based on the Apple/Google Exposure Notification system enabling privacy-preserving contact tracing

- 16.9 mio downloads as of 2020-08-11
- Probability that for a random pair both are CWA users: $\frac{16}{83} \cdot \frac{16}{83} = 3.7\%$ (assuming random distribution in population)

Inference Problem

- On the current day you get the information about all individuals who reported a positive test result during the past 14 days (aka. diagnosis keys)
- Given our history of all contacts during the last 14 days, we can determine if any of our contacts were with such a reported diagnosis key
- Given a contact with the diagnosis key A how likely is it that this lead to a transmission?
  - it depends on duration and closeness of the contact
  - it depends on infectiousness of the infected at the time of contact

Risk Calculation per Exposure Key

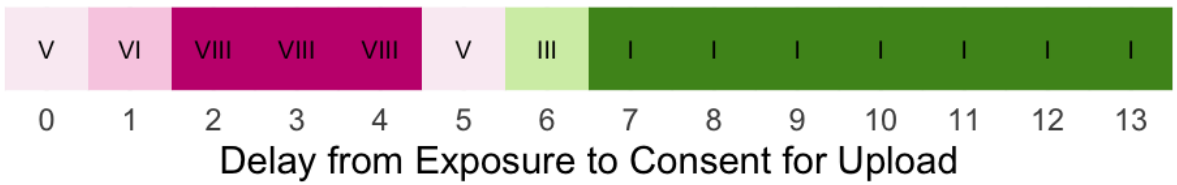


Source: Corona Warn App, Solution Architecture, Fig. 12 (Apache License 2.0)

Outline

Transmission Risk Level

- The transmission risk level can be used to enhance the classification with epidemiological information



- The following treatment is closely following the document *Epidemiological Motivation of the Transmission Risk Level* (CWA Team, 2020) written as part of the CWA development

Sequence of events for an infected person

- $T_E = T_{\text{infection}}$: transmission of SARS-CoV-2 to an exposed person A from some unknown source
- $T_I = T_{\text{infectious}}$: start of the infectious period in person A, i.e. A is able to infect others
- $T_S = T_{\text{symptoms}}$: onset of symptoms in person A (also referred to as DSO, day of symptom onset)
- $T_P = T_{\text{sampling}}$: time of sampling of person A
- $T_R = T_{\text{result}}$: time of A obtaining the positive test result
- $T_U = T_{\text{upload}}$: time where person A uploads the positive test result to the system (aka. DU, day of upload)

Information about Symptoms in A at DU

Four cases:

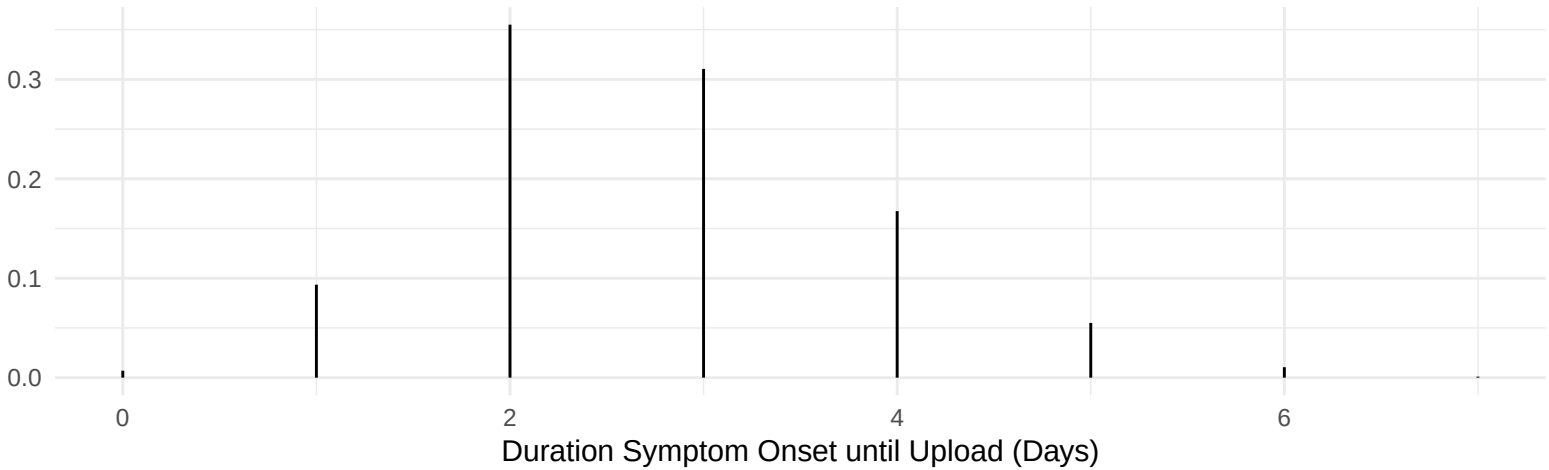
- Knowledge of DSO in A
- Knowledge that A was symptomatic, but not DSO not available, only DU
- Knowledge that A was not symptomatic at or before DU (completely asymptomatic or pre-symptomatic)
- Unknown symptom status at DU

Case 1: Duration between DSO and DU

- Consider the durations $T_U - T_R$, $T_R - T_P$ and $T_P - T_S$ and let T_C be the time of contact between A and B
- We find the distribution of

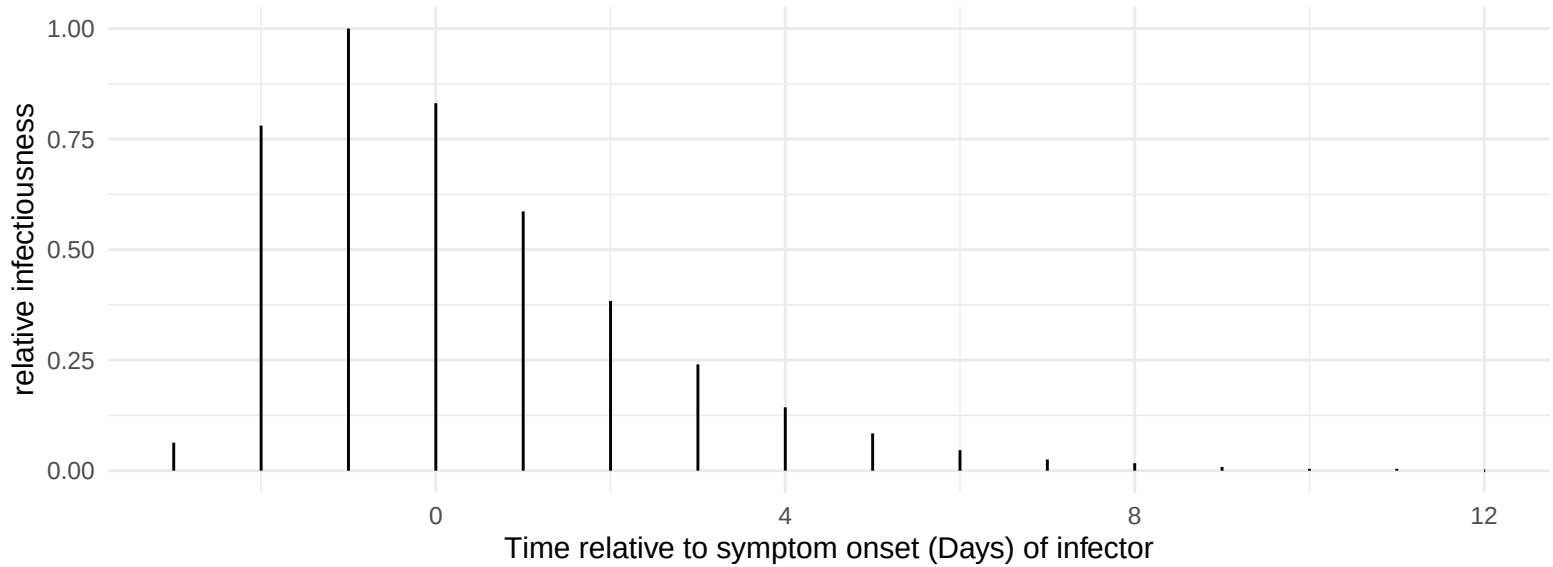
$$T_U - T_S = (T_U - T_R) + (T_R - T_P) + (T_P - T_S)$$

  by a convolution of the 3 durations
- Given informed assumptions we obtain the following PMF



Infectiousness (1)

- He et al. (2020b) provides a distribution for time of exposure in B relative to symptom onset in A
- Distribution is used as proxy for the infectiousness of A, $v_A(d)$



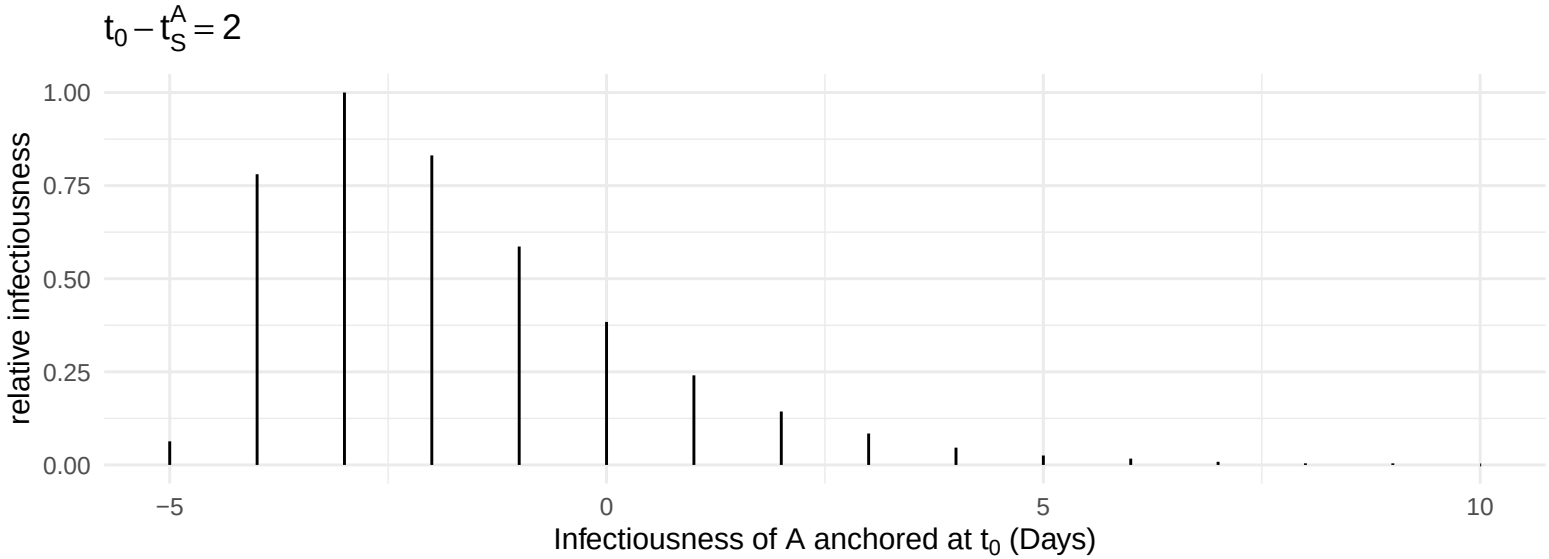
- Recently, a correction appeared moving the graph further to the left (He et al., 2020a).

Infectiousness (2)

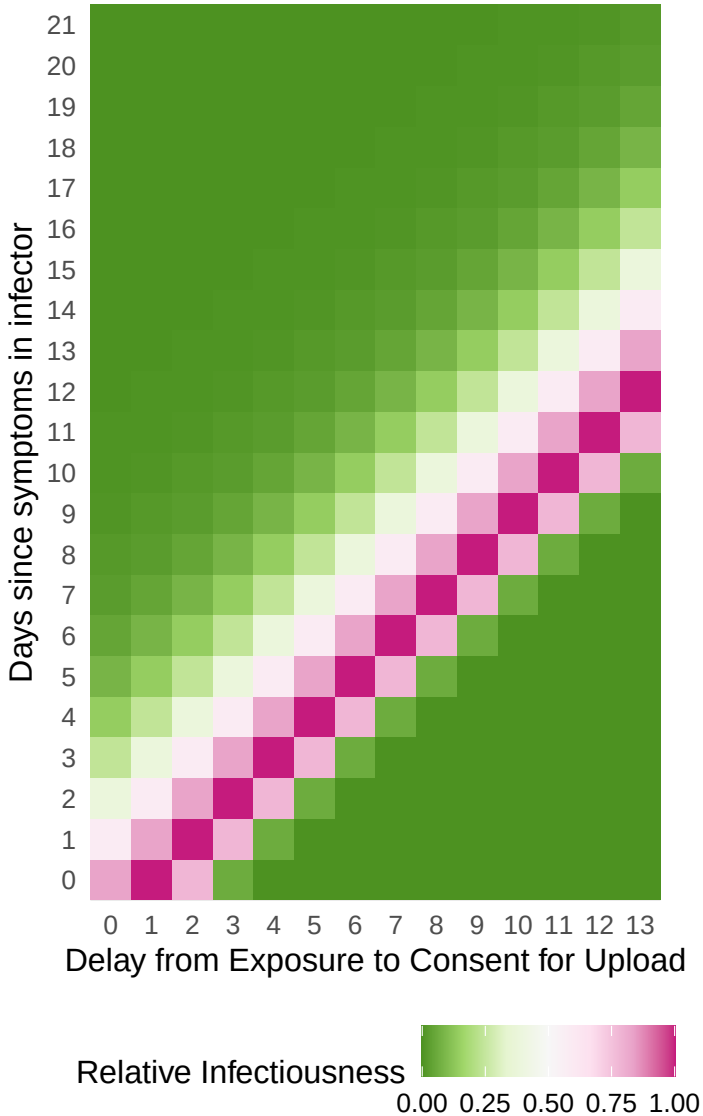
- At time now t_0, the onset of symptoms in the primary case A happened $t_0 - t_S^A \geq 0$ days ago.
- Relative infectiousness of A anchored s.t. time zero is at t_0 and a function of how many days d ago the contact was :

$$\lambda_A(d) = v_A(-d + (t_0 - t_S^A))$$

- Example: Plot of the infectiousness profile, if DSO happened 2 days before upload.



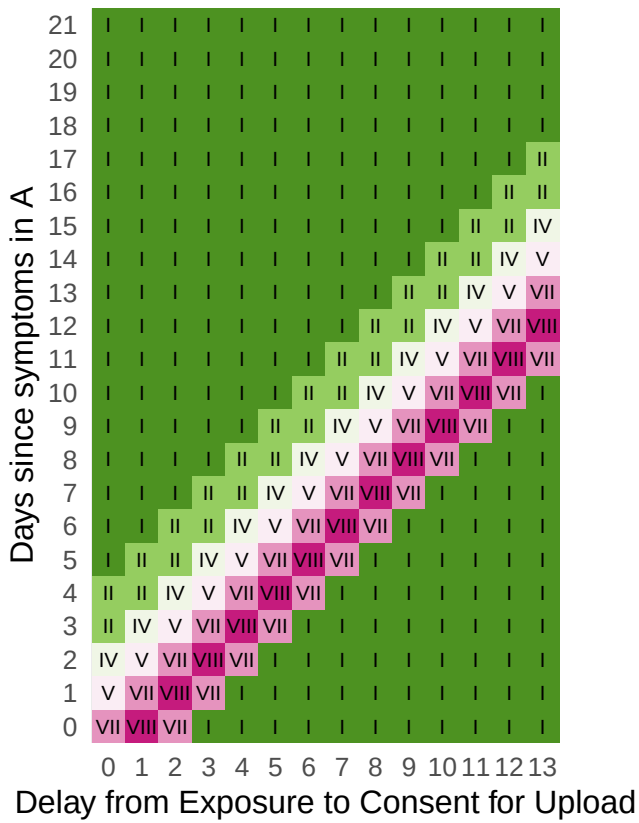
Infectiousness (3)



Infectiousness (4) - Transmission risk level

Discretization of the $[0, 1]$-scale into 8 equal-sized intervals:

$$\lambda_A(d) = l \quad \Leftrightarrow \quad \frac{l-1}{8} \leq \lambda_A^{(*)}(d) < \frac{l}{8}, \quad \text{where } l \in \{1, \ldots, 8\}.$$



Case 2 (1)

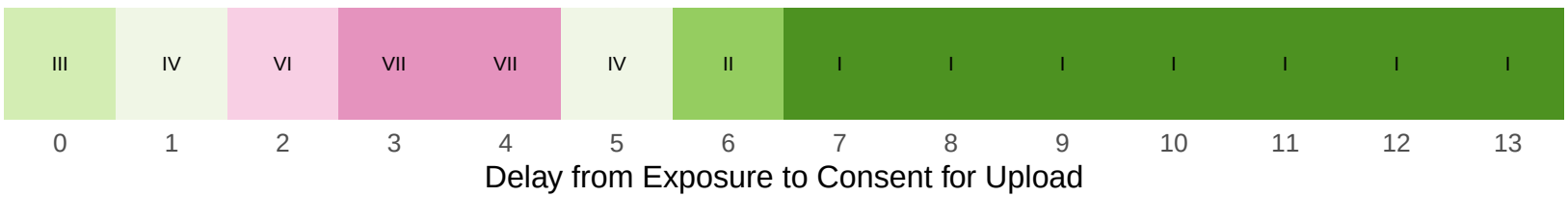
- We know that A is symptomatic at time of upload, but do not know the exact DSO
- We can infer a probability distribution for the DSO T_S^A from knowledge about the duration between DSO and upload given by and knowing the date of upload t_0
- Marginalizing over the DSO

$$\lambda_A^{(*)}(d,\ T_S^A \leq t_0) = \mathbb{E}_{T_S^A}\left[\lambda_A^{(*)}(d, T_S^A = t_S^A) \,\middle|\, T_S^A \leq t_0\right]$$

$$= \sum_{t_S^A = t_0 - 13}^{t_0} \lambda_A^{(*)}(d, T_S^A = t_S^A) \cdot f_{T_U - T_S}(t_0 - t_S^A)$$

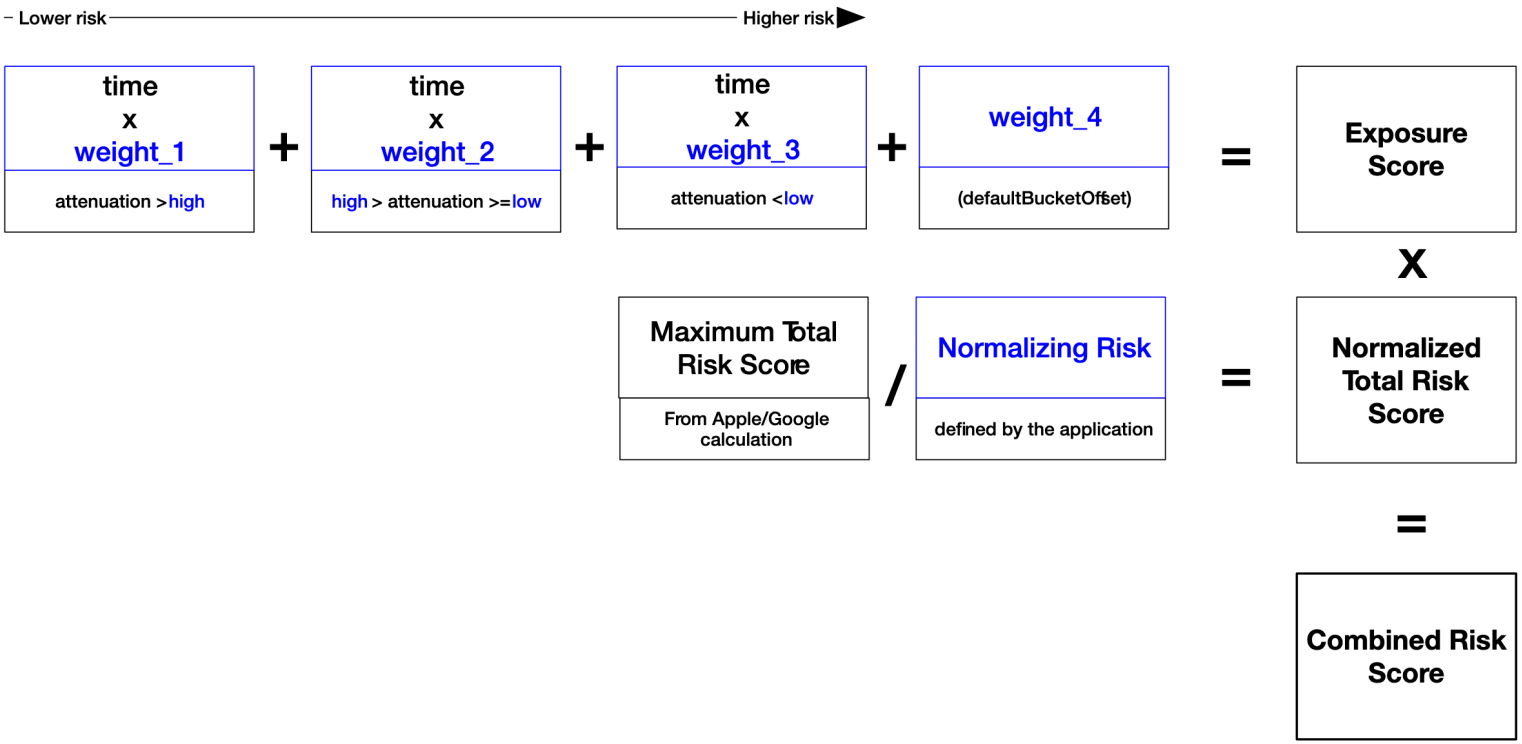
Case 2 (2)

Resulting risk levels:



Overall Risk

Summing over all exposures and days:



Source: Corona Warn App, Solution Architecture, Fig. 13 (Apache License 2.0)

Outline

Discussion

- Application of statistical modelling in an App run by $\sim$ 16 mio users
- It has become clear that contact tracing apps are not the silver bullet for COVID-19 control. Some press voices:
  - Contact-tracing apps have been a disaster, but could they still save us?, DigitalTrend
  - Europe Proves Contact-Tracing Apps Aren't A Coronavirus Cure-All, Huffpost
- However, they provide an important supplement to manual contact tracing and speed up the digitialization of testing processe leading to quicker turn-around for test results

Outline

Outline

Convolution of Discrete Random Variables (1)

Let X and Y be two independent integer random variables PMFs f_X and f_Y, respectively. Then their sum $Z = X + Y$, aka. as the convolution of X and Y, has the PMF

$$f_Z(z) = \sum_x f_X(x) f_Y(z - x).$$

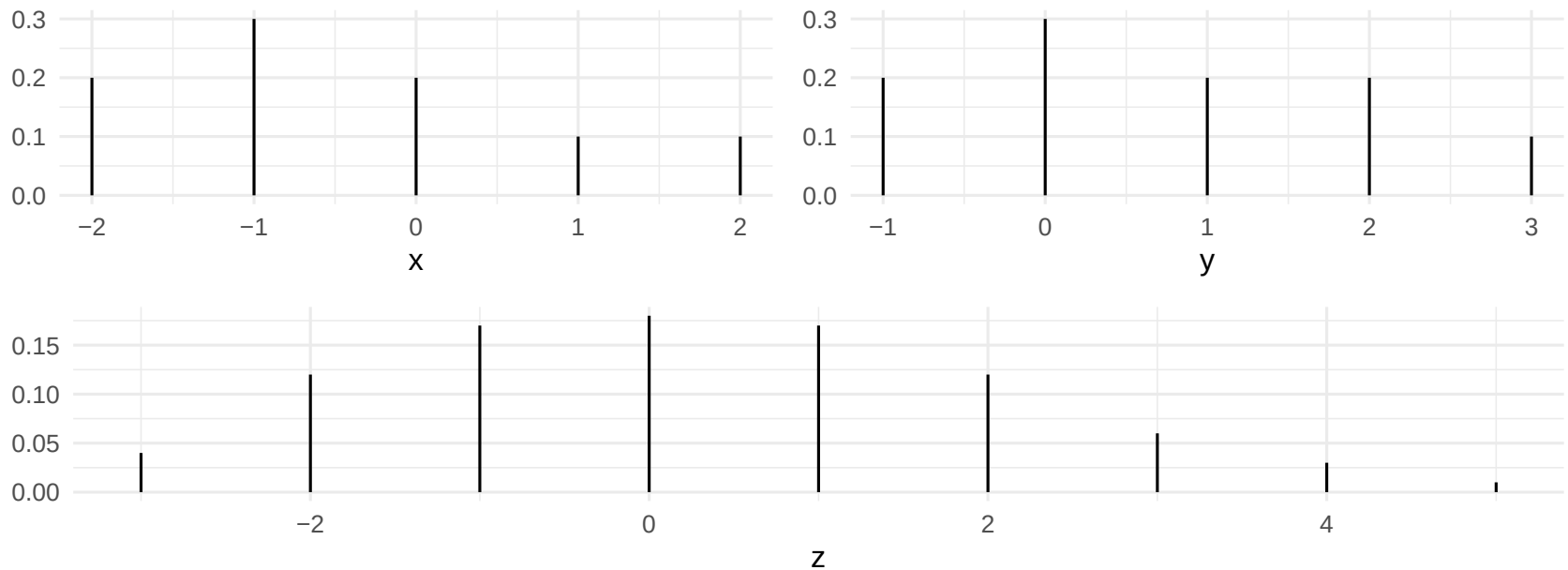
Convolution of Discrete Random Variables (2)

```r
#' Function to convolute two discrete probability distributions with
#' support on 0, 1, ... I.e. we compute the PMF of Z = X + Y.
#'
#' @param fX - the PMF of X given as a named vector, where the names
#'             represent the support X_min, ..., 0, 1, ..., X_max
#' @param fY - the PMF of Y given as a named vector, where the names
#'             represent the support Y_min, ..., 0, 1, ..., Y_max
#' @return A names vector containing the PMF of Z = X+Y.
#'

convolute <- function(fX, fY) {
  fZ <- rep(0, 1 + (length(fX) - 1) + (length(fY) - 1))
  names(fZ) <- as.character(seq(
    min(as.numeric(names(fX))) + min(as.numeric(names(fY))),
    max(as.numeric(names(fX))) + max(as.numeric(names(fY)))
  ))

  for (i in names(fX)) {
    for (k in names(fY)) {
      j <- as.numeric(i) + as.numeric(k)
      fZ[as.character(j)] <- fZ[as.character(j)] + fX[i] * fY[k]
    }
  }

  fZ
}
```

Convolution of Discrete Random Variables (3)

Example:

```
pdf_z <- convolute(
  pdf_x <- c(`-2` = .2, `-1` = .3, `0` = .2, `1` = .1, `2` = .1),
  pdf_y <- c(`-1` = .2, `0`  = .3,  `1` = .2, `2` = .2, `3`= .1)
)
```



Literature I


CWA Team (2020). *Epidemiological Motivation of the Transmission Risk Level*. Corona-Warn-App. URL: https://github.com/corona-warn-app/cwa-documentation/blob/master/transmission_risk.pdf.


Ferretti, Luca, Chris Wymant, Michelle Kendall, Lele Zhao, Anel Nurtay, Lucie Abeler-Dörner, Michael Parker, David Bonsall, and Christophe Fraser (May 2020). "Quantifying SARS-CoV-2 transmission suggests epidemic control with digital contact tracing". In: *Science* 368.6491, eabb6936.


He, Xi et al. (2020a). "Author Correction: Temporal dynamics in viral shedding and transmissibility of COVID-19". In: *Nature Medicine*.

Literature II

He, Xi et al. (2020b). "Temporal dynamics in viral shedding and transmissibility of COVID-19". In: *Nature Medicine* 26.5, pp. 672–675. DOI: 10.1038/s41591-020-0869-5. URL: https://doi.org/10.1038/s41591-020-0869-5.