Transient sensitivity analysis for developing pandemic disease prevention strategies

Zamana Bağlı Duyarlılık Analizi ile Pandeminin Yol Açtığı Hastalıktan Korunma Stratejileri geliştirilmesi

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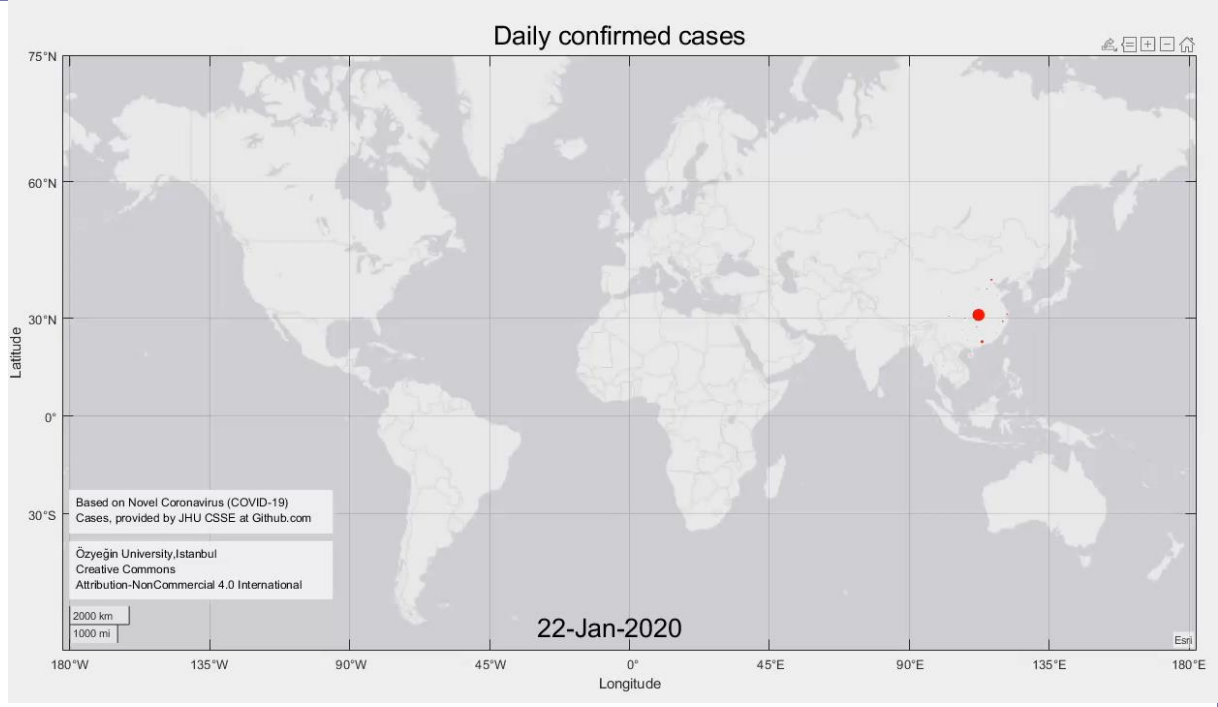
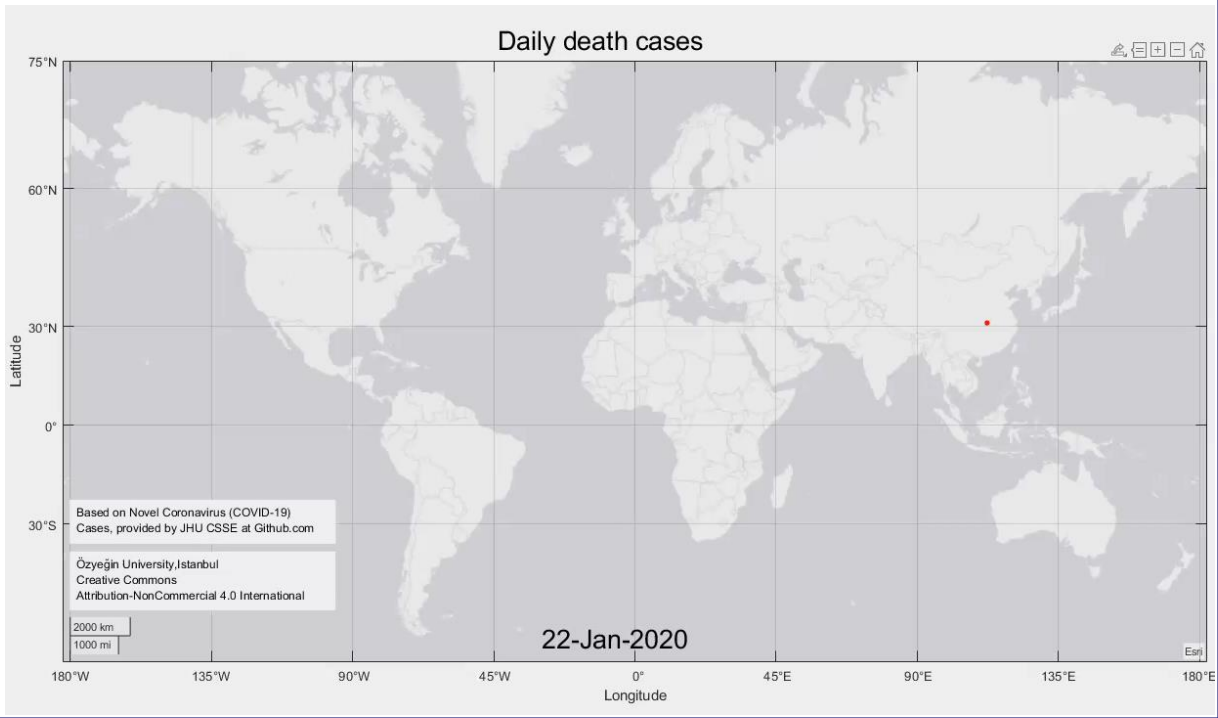
Dikkat!

Bu raporda sunulan hesaplar kesin değildir. Verilecek kararlara yardımcı olması için hazırlanmıştır. Kullanılan hesap yöntemi ve model katsayıları, literatürdeki araştırmalara göre tutucu bir şekilde seçilmiştir.

World is shaking

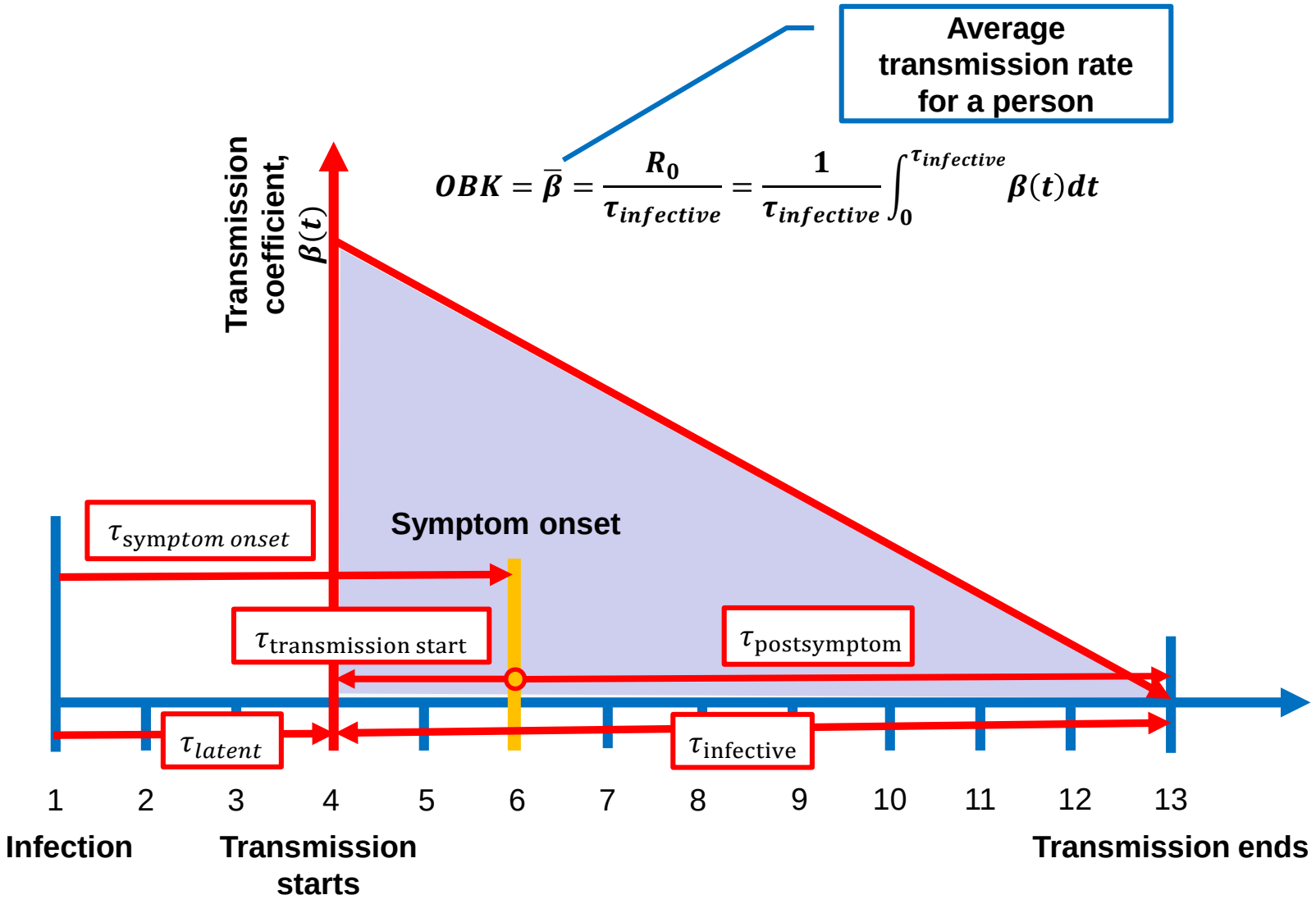
- Infected and death patients will increase continuously.
- Health system will collapse or collapsing in many countries.
- Lock-down measures are back and economy experiences the second shock.
- Pandemic will continue to exists until most of the people become immune.



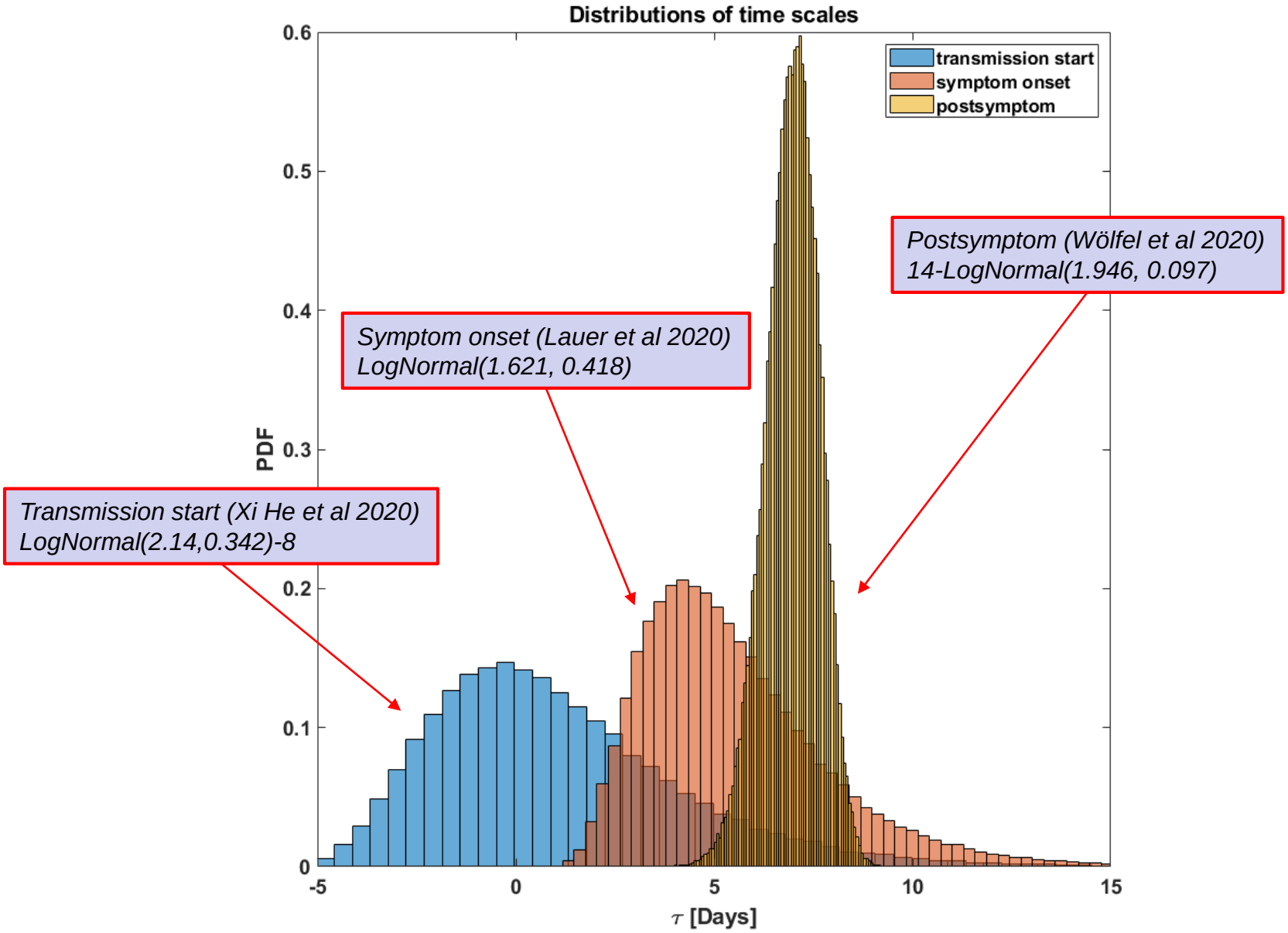


ÖZYEĞİN ÜNİVERSİTESİ

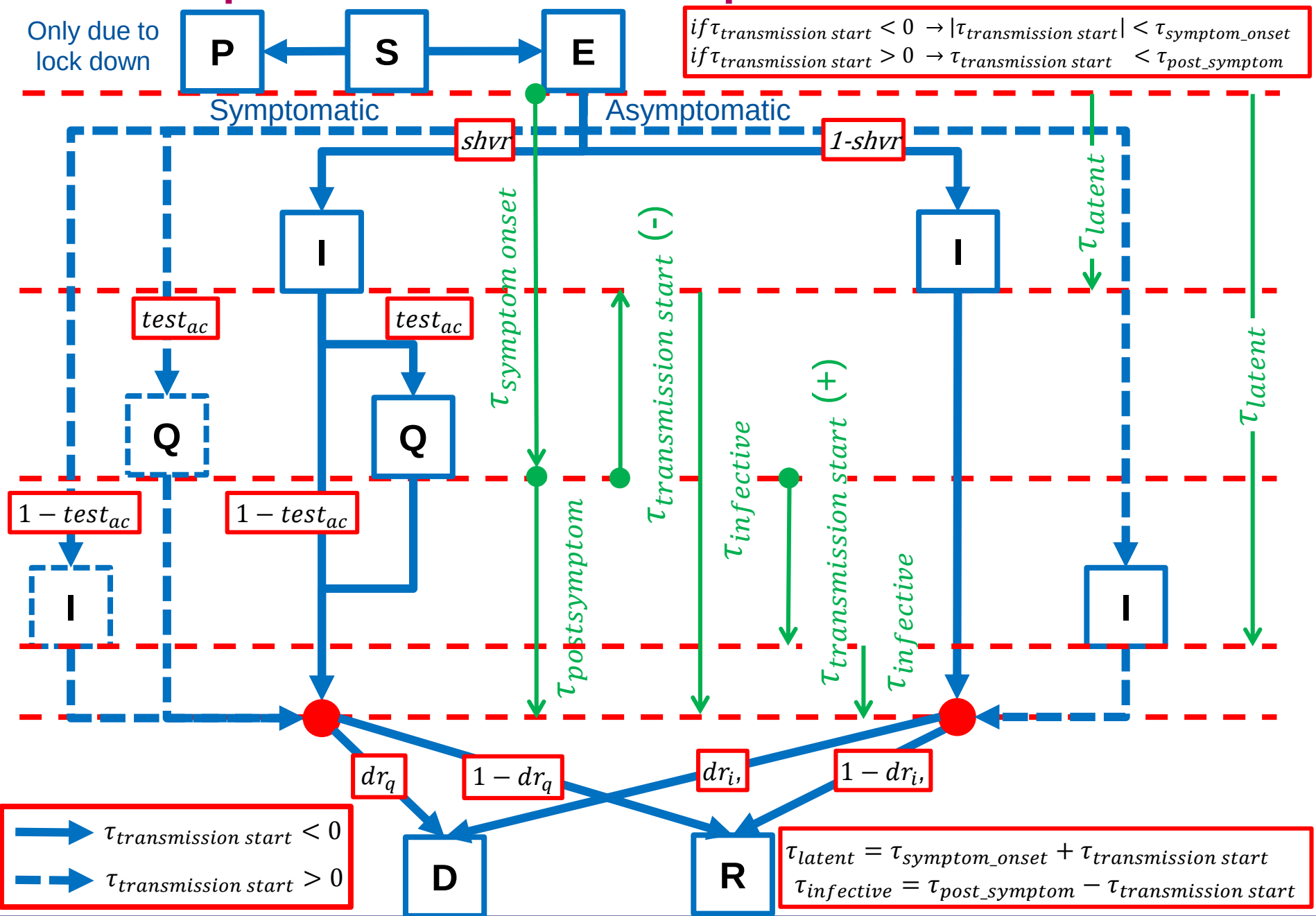
Time-scales of the disease



Probabiliy distributions of time scales



Possible paths of disease development



Susceptible Exposed Infective Removed Equation System (pre-symptomatic transmission $\tau_{transmission\ start} < 0$)

$$\frac{dS}{dt} = -\bar{\beta}(t)\frac{SI}{N} + \alpha(t)S$$

$$\frac{dE}{dt} = \bar{\beta}(t)\frac{SI}{N} - \frac{1}{\tau_{latent}}E$$

Calculated from lock down rules

N: initial population

$$\frac{dI}{dt} = \frac{1}{\tau_{latent}}E - \frac{(1 - shvr\ )}{\tau_{infective}}I + \frac{shvr\ test_{ac}}{\tau_{transmission\ start}}I - \frac{shvr\ (1 - test_{ac})}{\tau_{infective}}I$$

$$\frac{dQ}{dt} = -\frac{shvr\ test_{ac}}{\tau_{transmission\_start}}I - \frac{1}{\tau_{postsymptom}}Q$$

$$\frac{dR}{dt} = \frac{(1 - dr_q)}{\tau_{postsymptom}}Q + \frac{(1 - dr_q)\ shvr\ (1 - test_{ac})}{\tau_{infective}}I + \frac{(1 - dr_i)(1 - shvr)}{\tau_{infective}}I$$

$$\frac{dD}{dt} = \frac{dr_q}{\tau_{postsymptom}}Q + \frac{dr_q\ shvr\ (1 - test_{ac})}{\tau_{infective}}I + \frac{dr_i(1 - shvr\ )}{\tau_{infective}}I$$

$$\frac{dP}{dt} = -\alpha S$$

Instantaneous population

$$N = S + P + E + I + R - D$$

Katsayı	Anlamı
$\bar{\beta}(t)$	Birim zamanda ortalama bulaşan insan
α(t)	Birim zamanda korumaya alınma katsayısı
SHVR	Semptom göstermeye başlayanların hastaneye gitme oranı.
$test_{ac}$	Yapılan testlerin doğruluk oranı.
dr_q	Ağır semptom gösterip, hastanade yatan ve karantinaya alınan hastaların ölüm oranı.
dr_i	Karantinaya girmeden bulaşıcılığı geçmiş hastaların ölüm oranı, normal ölüm oranı olrak alınmıştır.

ÖZYEĞİN ÜNİVERSİTESİ

Susceptible Exposed Infective Removed Equation System (post-symptomatic transmission $\tau_{transmission\ start} > 0$)

$$\frac{dS}{dt} = -\bar{\beta}(t)\frac{SI}{N} + \alpha(t)S$$

$$\frac{dE}{dt} = \bar{\beta}(t)\frac{SI}{N} - \frac{shvr\ test_{ac}}{\tau_{sypmtom\ onset}}E - \frac{shvr(1-test_{ac})}{\tau_{latent}}E - \frac{(1-shvr)}{\tau_{latent}}E$$

$$\frac{dI}{dt} = \frac{shvr(1-test_{ac})}{\tau_{latent}}E + \frac{(1-shvr)}{\tau_{latent}}E - \frac{shvr(1-\ test_{ac})}{\tau_{infective}}I - \frac{(1-shvr)}{\tau_{infective}}I$$

$$\frac{dQ}{dt} = \frac{shvr\ test_{ac}}{\tau_{sypmtom\ onset}}E - \frac{1}{\tau_{postsymptom}}Q$$

$$\frac{dR}{dt} = \frac{(1-dr_q)}{\tau_{postsymptom}}Q + \frac{(1-dr_q)\ shvr\ (1-test_{ac})}{\tau_{infective}}I + \frac{(1-dr_i)(1-shvr)}{\tau_{infective}}I$$

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ÖZYEĞİN ÜNİVERSİTESİ

Unknown model parameters

$$\frac{dS}{dt} = -\bar{\beta}(t)\frac{SI}{N} + \alpha(t)S$$

$$\bar{\beta}(t) = \frac{\bar{\beta}_{end} - \bar{\beta}_{start}}{(1 + e^{t-initday})^{1/\nu}} + \bar{\beta}_{start}$$

$$\frac{dE}{dt} = \bar{\beta}(t)\frac{SI}{N} - \frac{1}{\tau_{latent}}E$$

$$E(0) = I(0) = \frac{Infected\ (0)}{2}$$

$$\frac{dI}{dt} = \frac{1}{\tau_{latent}}E - \frac{(1 - shvr\ )}{\tau_{infective}}I + \frac{shvr\ test_{ac}}{\tau_{transmission\ start}}I - \frac{shvr\ (1 - test_{ac})}{\tau_{infective}}I$$

$$\frac{dQ}{dt} = -\frac{shvr\ test_{ac}}{\tau_{transmission\_start}}I - \frac{1}{\tau_{postsymptom}}Q$$

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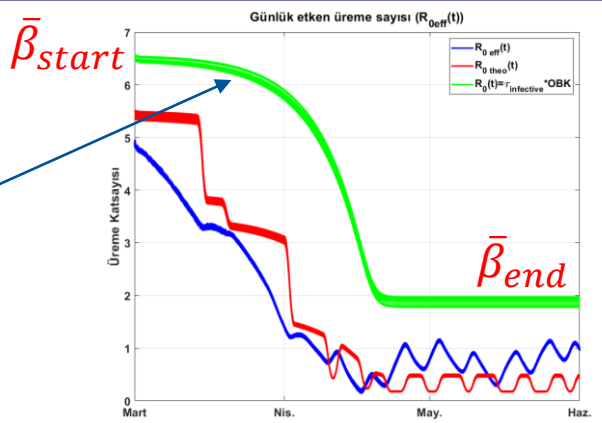
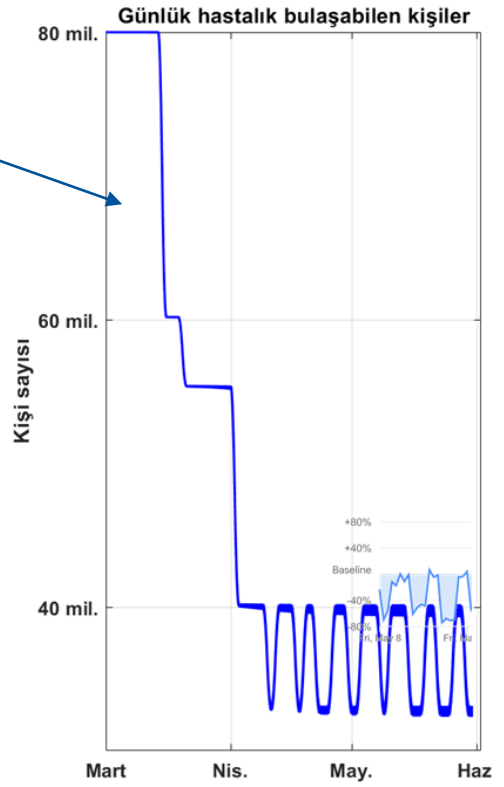
$$\frac{dP}{dt} = -\alpha S$$

$$Model\ parameters = \begin{bmatrix} Infected(0) \\ shvr \\ \bar{\beta}_{start} \\ \bar{\beta}_{end} \\ \nu \end{bmatrix}$$





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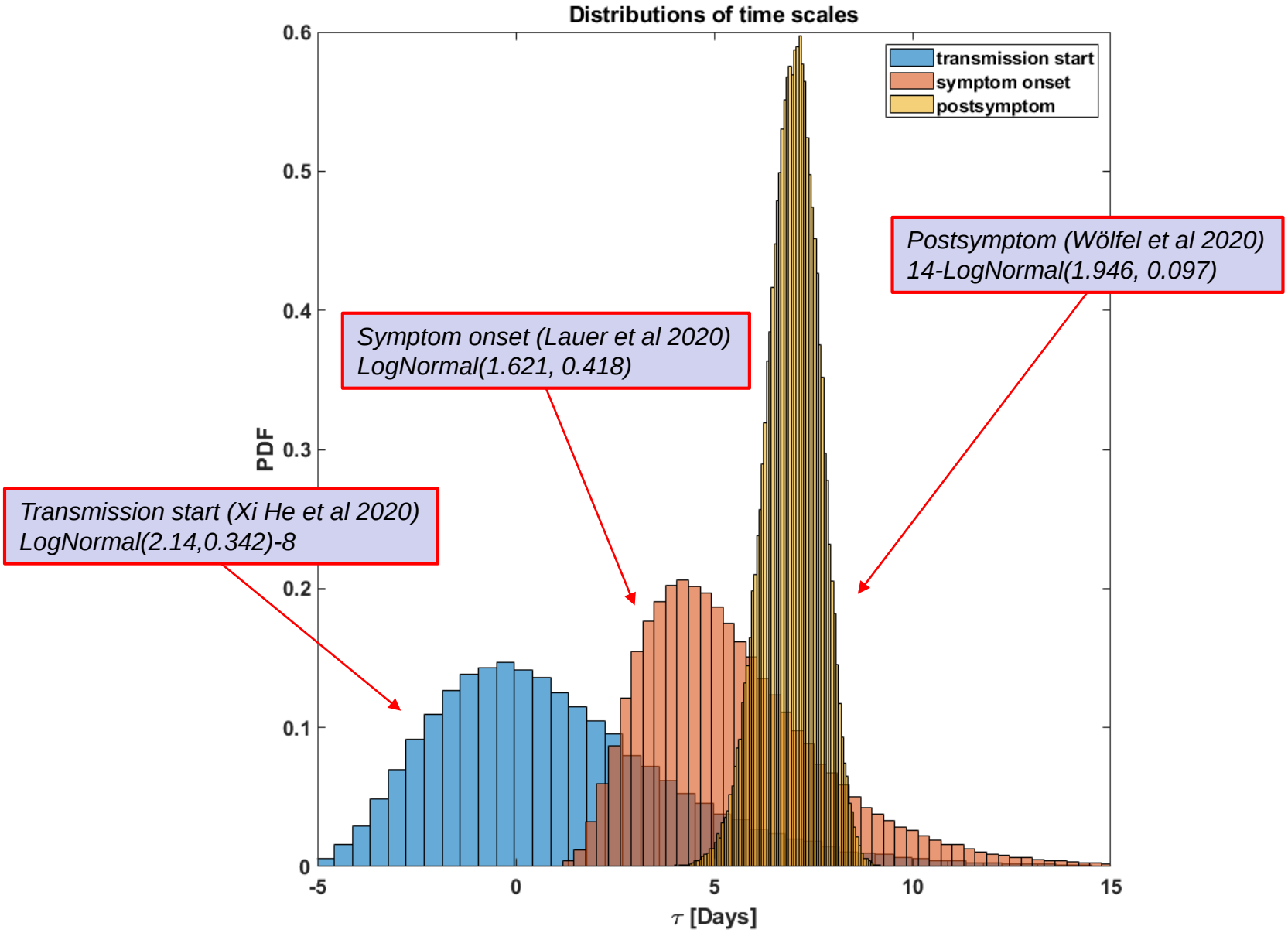
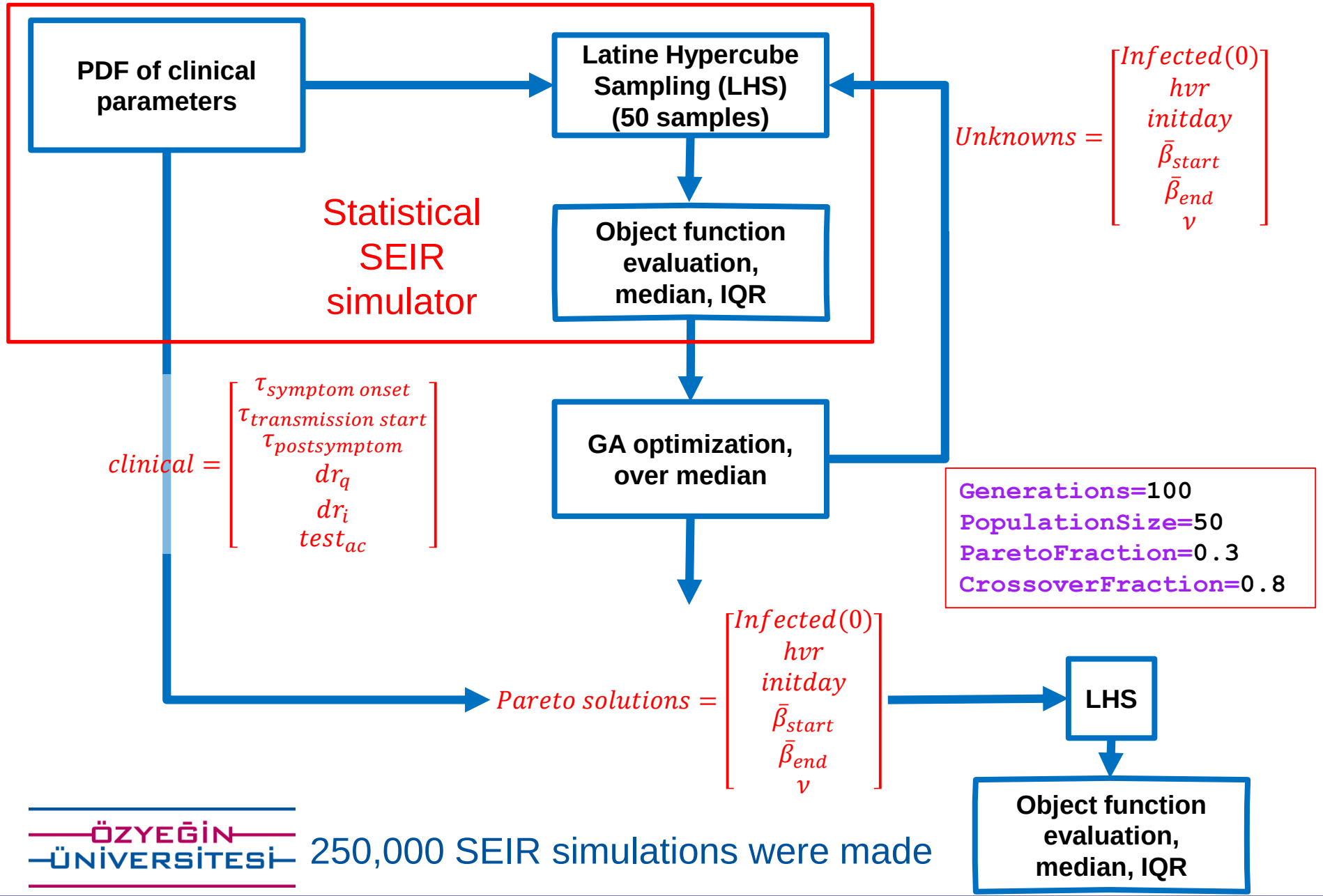
Unknown model parameters are found by using GA optimization algorithms.

Distributions of time scales



Robust optimization algorithm under uncertain conditions



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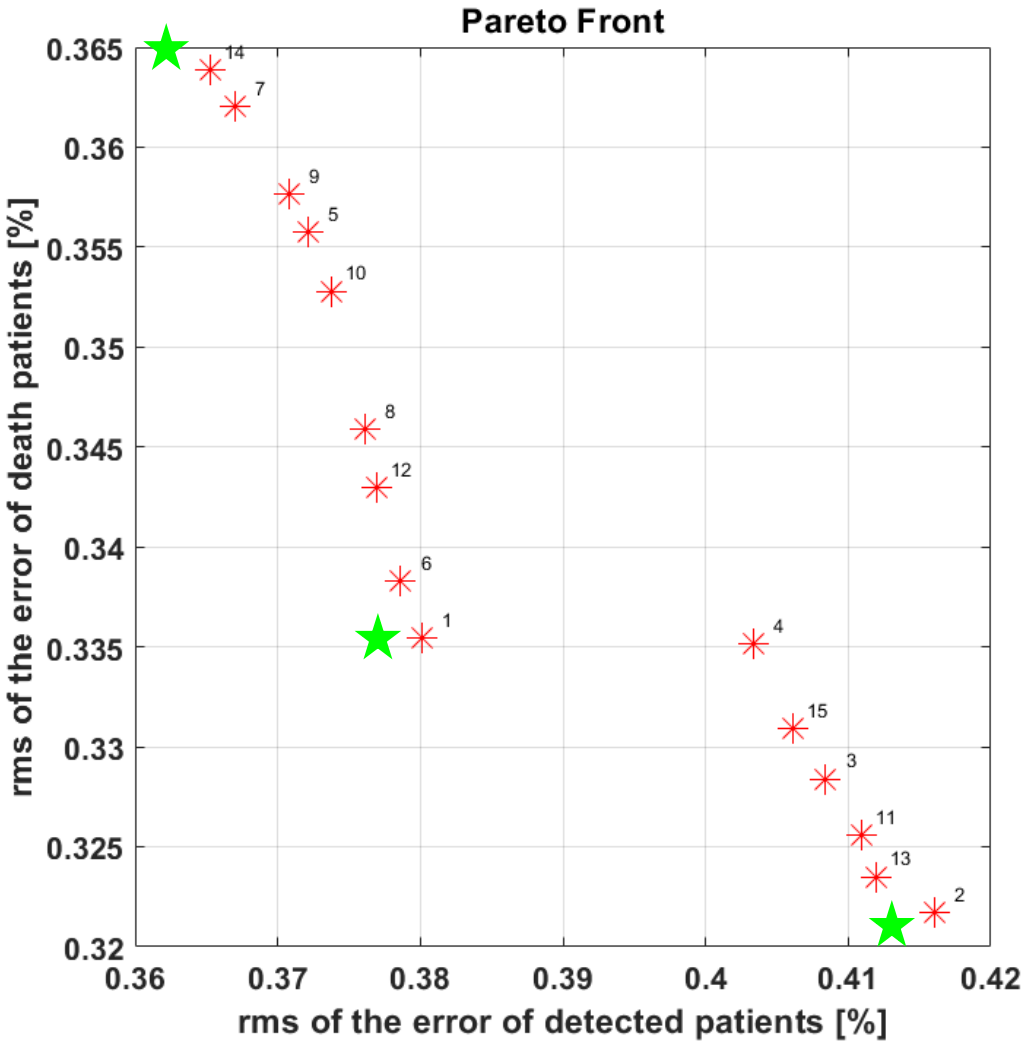
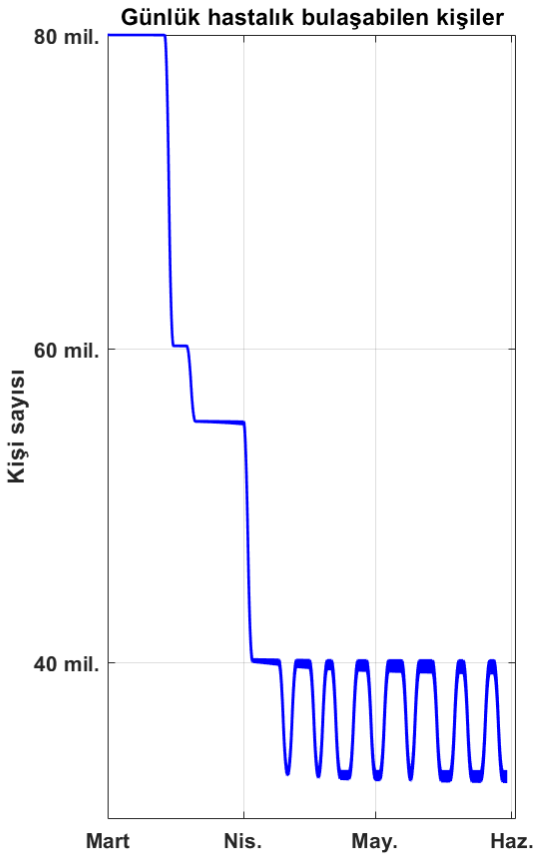
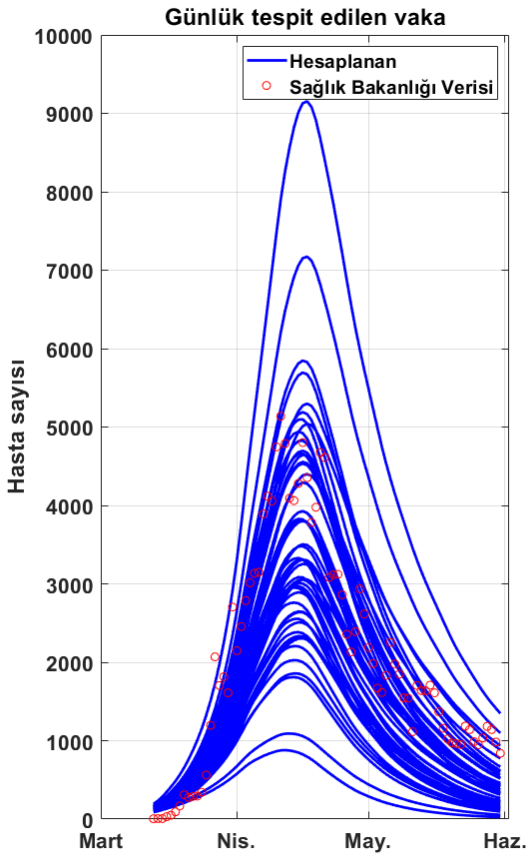
250,000 SEIR simulations were made

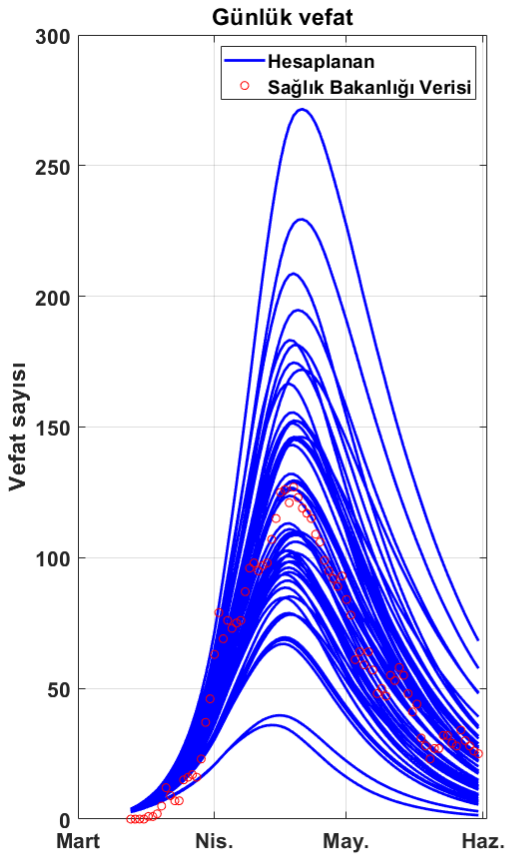
Robust optimization algorithm under uncertain conditions



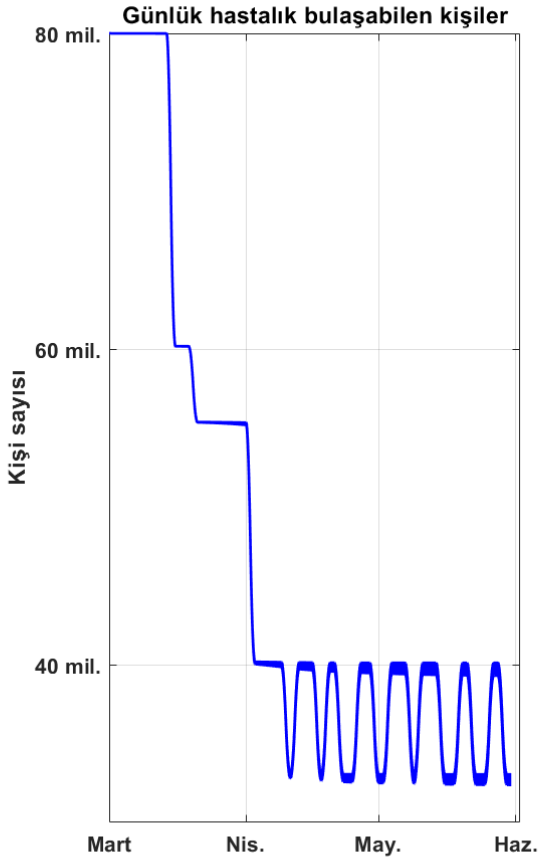
Robust optimization algorithm under uncertain conditions
Solution 14

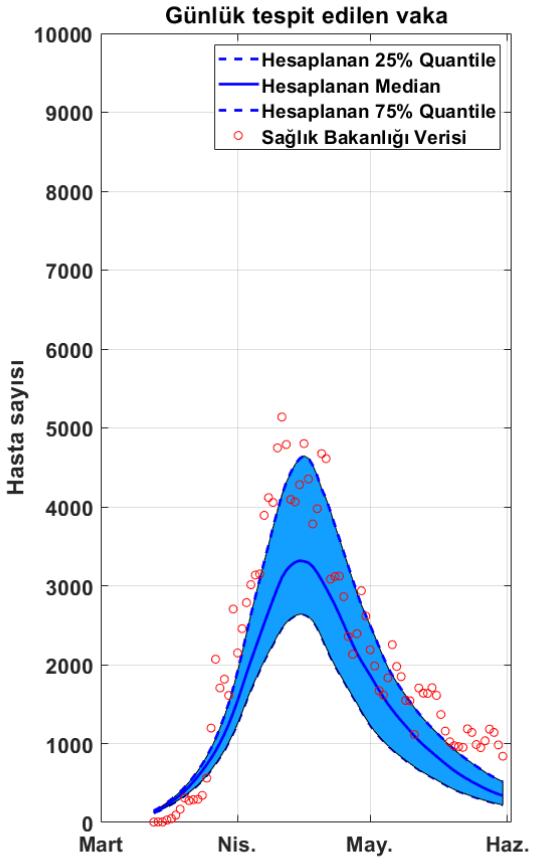


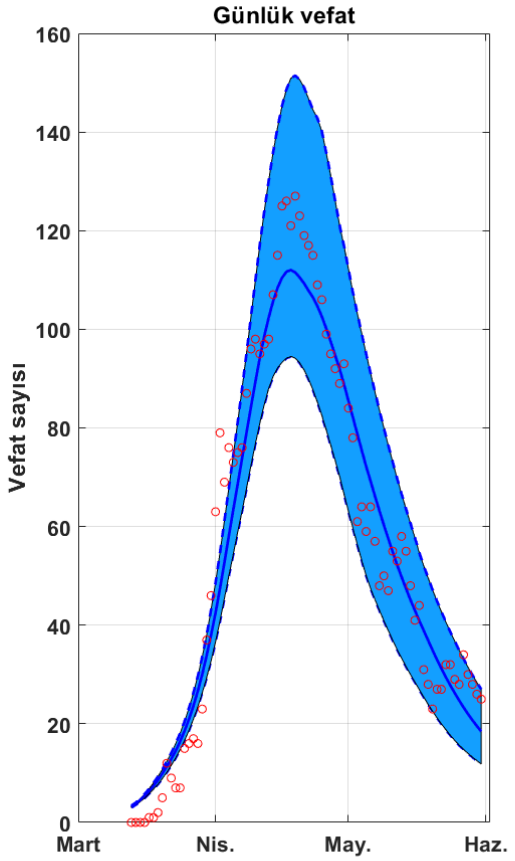




Robust optimization algorithm under uncertain conditions: Solution 14 (min rms error of detected patients)







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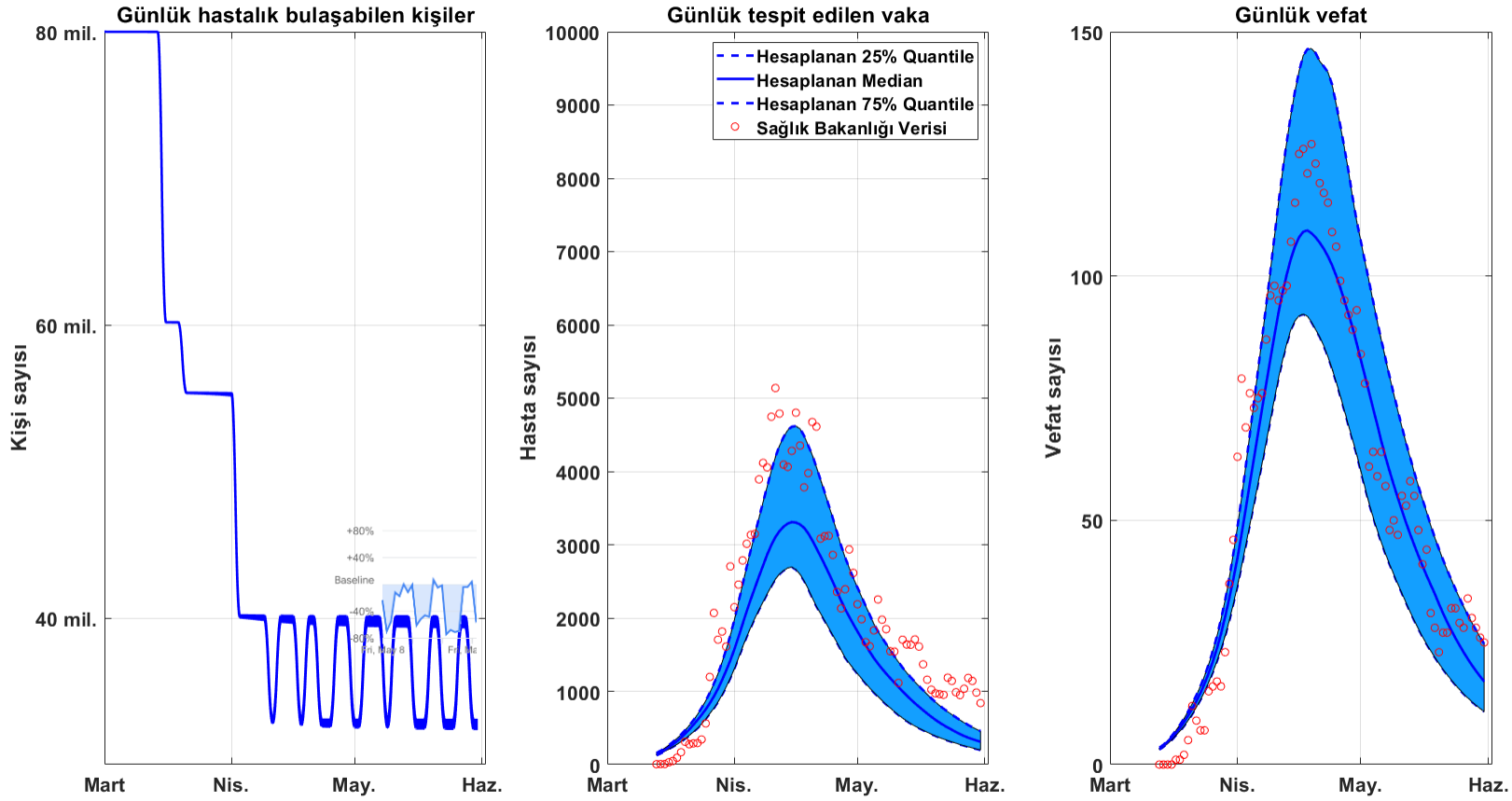
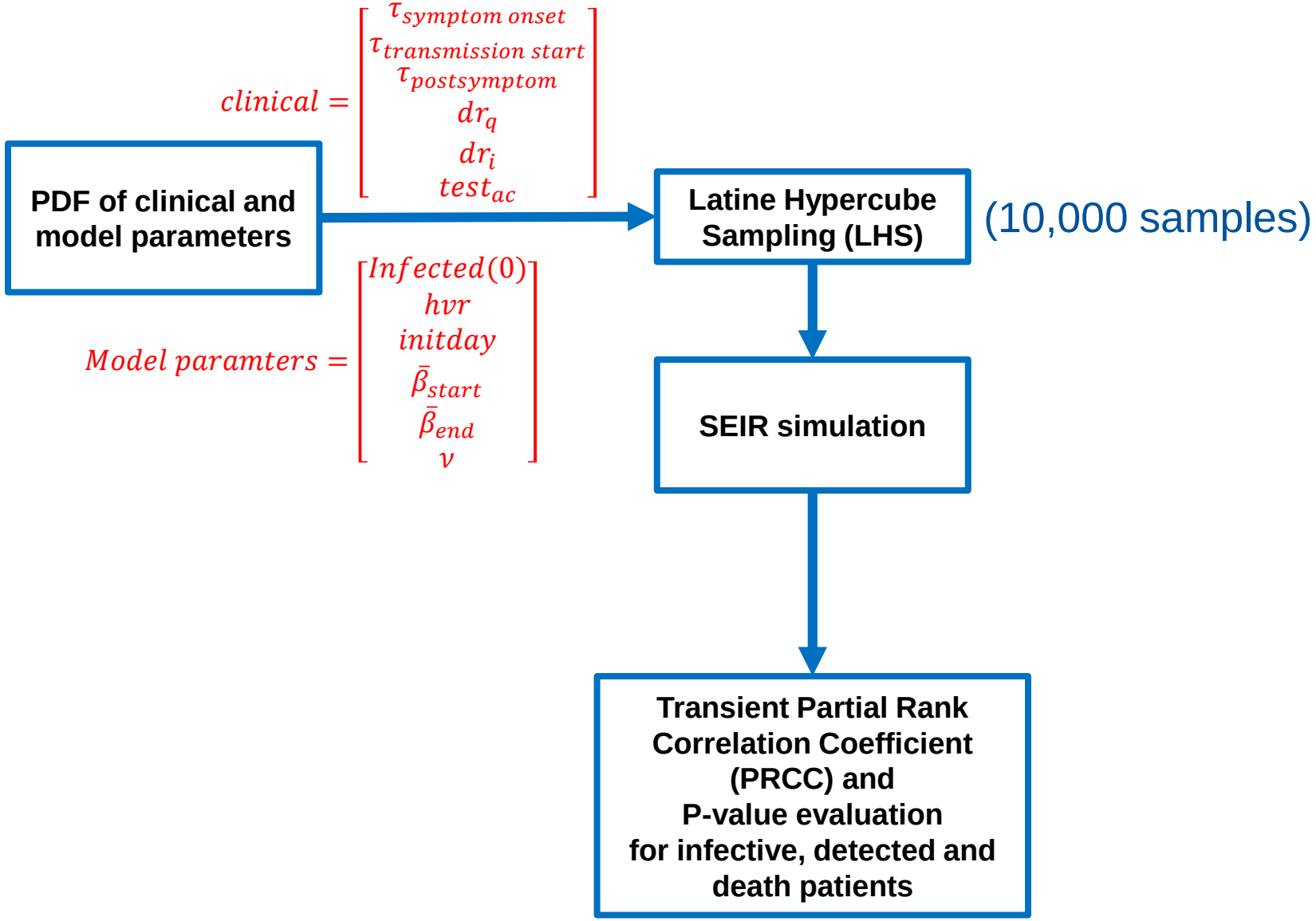
Robust optimization algorithm under uncertain conditions: Solution 1 (mid error for detected and death patients)



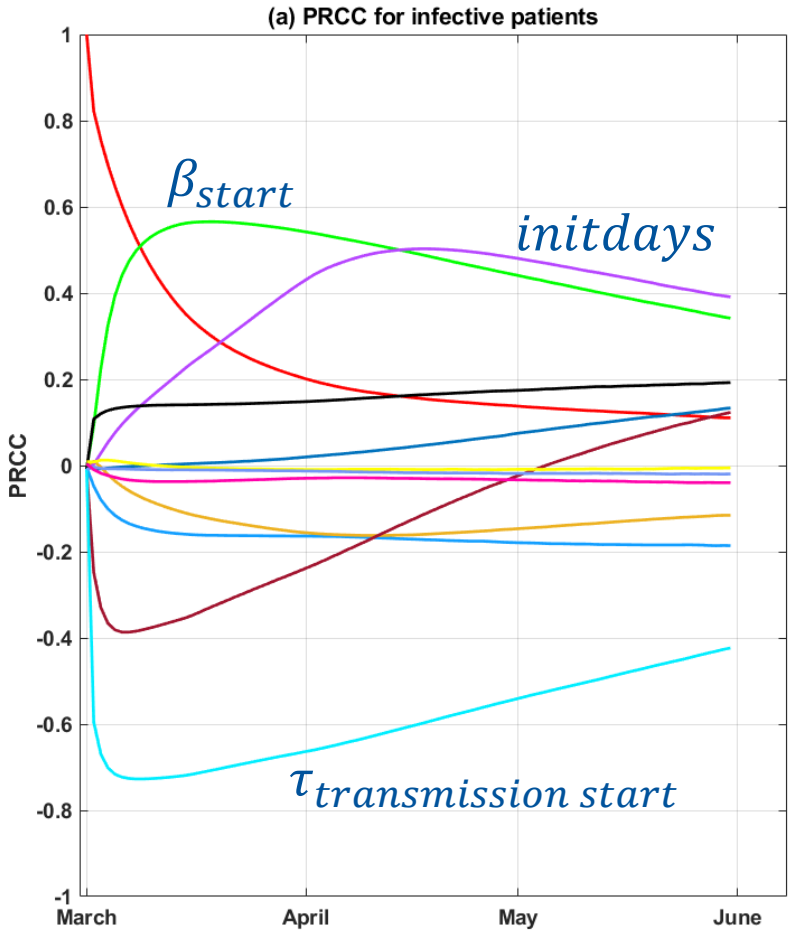
Transient sensitivity analysis algorithm

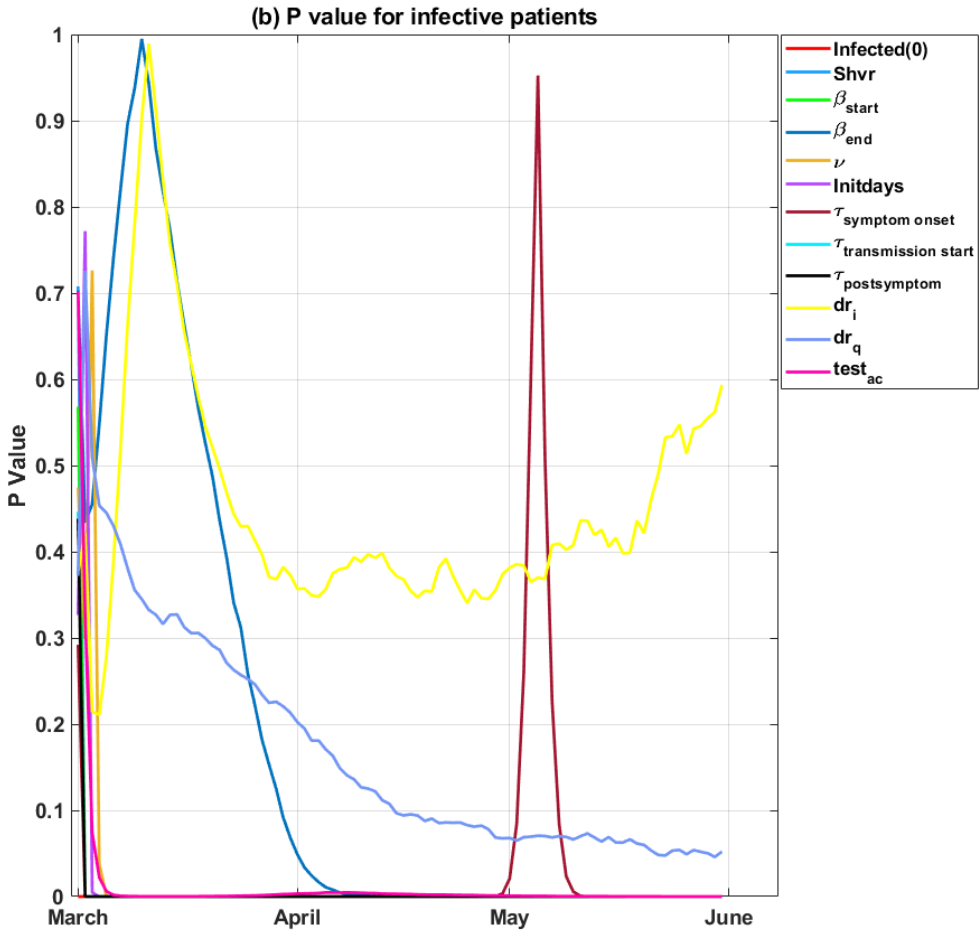


ÖZYEĞİN ÜNİVERSİTESİ

Marino, S., Hogue, I. B., Ray, C. J., & Kirschner, D. E. (2008). A methodology for performing global uncertainty and sensitivity analysis in systems biology. Journal of Theoretical Biology, 254(1), 178–196. https://doi.org/10.1016/j.jtbi.2008.04.011

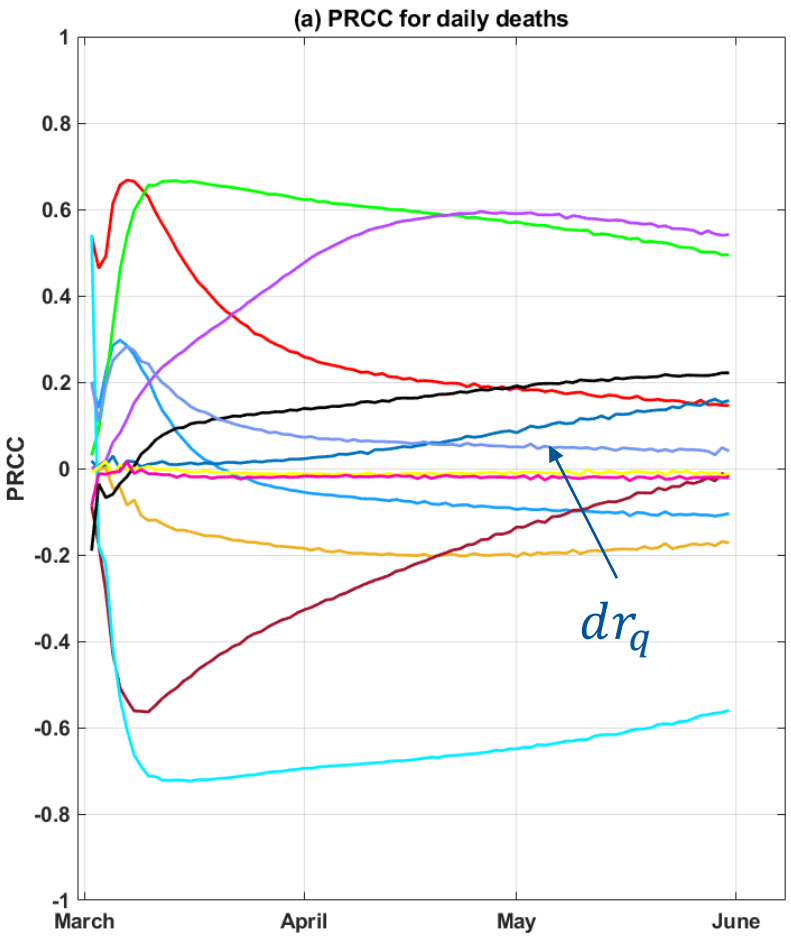
PRCC and P value for infective patients (new)

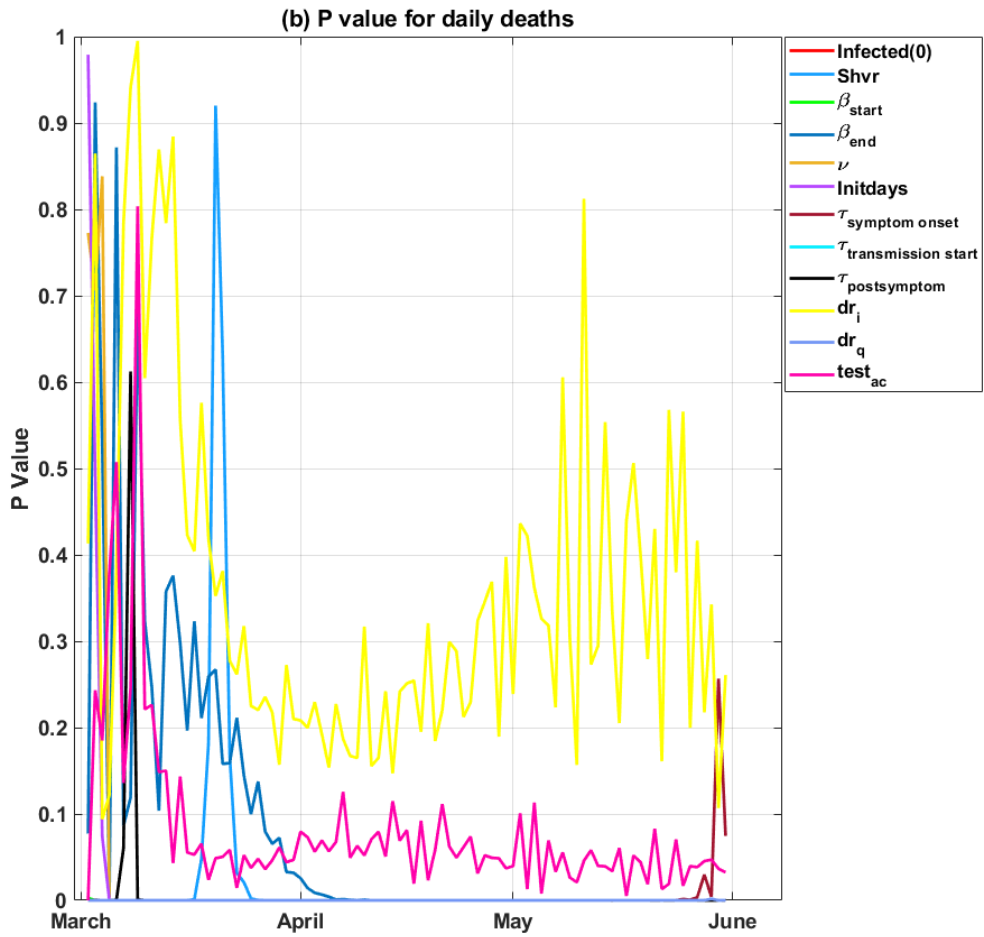




- Parameters related to clinical parameters show always significant correlation.
- Since the number of susceptible are still too large, parameters related to death, as expected, appear to be insignificant.
- Sypmtom onset time scale takes very high P-value, when the PRCC for the same variable takes zero value.
- An interesting observation is that the –correlation of the symptom onset time-scale becomes + at the post peak phase.

PRCC and P value for daily died patients





- Even if the health system works as desired, clinical success is not the most influential parameter on the # of deaths.
- In other words, prevention is the most influential strategy to decrease to number of death patients.
- If there were no patient, there would be no death.

Conclusions

- In order to cease the pandemic nationally, it is shown quantitatively that transmission process has to be broken.
- Transmission can be broken now by
  - Lock down
  - Contact tracing and effective quarantine measures (works best when exposed patients are low). This will reduce new transmissions at pre and post symptomatic phase.
  - Personal measures
    - Mask, hygiene, social distance
    - Less social activity
    - Avoiding closed and crowded environments
  - Institutional measures
    - Regulations for public transport
    - Regulations for closed room usage, esp. regarding airborne transmission.
  - Vaccine (When will it resolve the pandemic?)
- Even if the health system works as desired, clinical success is not the most influential parameter on the # of deaths.

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