東京大学大学院医学系研究科
公共健康医学専攻
科目名：健康医療政策学

# 大規模感染症対策の経済学的評価

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## Road Map

I) Introduction of Presenter

II) Individual behavior theory in mathematical Modeling

III) Cost-benefit analysis of PCR tests

IV) Health disparity



## Presenter's introduction

- Medical resident (orthopedic surgery) in Japan
  - → MS (Harvard Univ.) PhD (Johns Hopkins Univ.) in US (since 1995)
  - → worked for Stanford Univ. in CA, US federal agency Centers for Disease Control and Prevention (CDC) in GA, Univ. Rochester in NY., Univ. of California Davis in CA,
  - → (Since April 2020) Kanagawa University of Human Services
- Research: Preventive behavior change ((a) Infectious Disease (esp. Flu Vaccine) and (b) Chronic disease prevention (esp. Diet and Physical Activity), Tele-health, Workforce supply, Long term care (dementia), Health insurance



## 「ポストコロナ期を生きるきみたちへ」 単行本 2020/11/11


- この「歴史的転換点」以後を生きる中高生たちに向けて、5つの世代20名の識者が伝える「生き延びるための知恵」。
- 「台風とコロナ・パンデミックは同じか?」 俞炳匡



## 「ポストコロナ期を生きるきみたちへ」

**■1 Letters from around 30**
ポストコロナにやってくるのは気候危機 斎藤幸平
楽しい生活―僕らのVita Activa 青木真兵
これからの反乱ライフえらいてんちょう

**■2 Letters from over 40**
君がノートに書きつけた一編の詩が芸術であること 後藤正文
技術と社会―考えるきっかけとしての新型コロナ危機 白井聡
「タテ、ヨコ、算数」の世界の見方 岩田健太郎
支援の現場から考える、コロナ後の世界 雨宮処凛
「大学の学び」とは何か―「人生すべてがコンテンツ」を越えて 増田聡

**■3 Letters from over 50**
コロナで明らかになった日本の最も弱い部分―対話・エンパシー・HOME 平田オリザ
コロナ禍と人間―私たちはどう生きるのか 想田和弘
台風とコロナ・パンデミックは同じか? 俞炳匡
図太く、しぶとく、生きてゆけ―誰も正解を知らない問題にどう答えを出すか 山崎雅弘

**■4 Letters from over 60**
医療が無料であること 三砂ちづる
人生100年時代、ポストコロナはダブルメジャーで 仲野徹
メメント・モリ―思いがけない出会いに開かれているために 中田考
ディレンマの知性 釈徹宗

**■5 Letters from over 70**
ポストコロナ期における雇用について 内田樹
自分に固有の問題を考えること 池田清彦
コロナと価値のものさし 平川克美
マスクについて 鷲田清一



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## Basic Measures against the COVID-19

- No vaccine/preventive drug confirmed (as of Oct. 2020)
- Primary prevention (to reduce infection risk)
  - Behavior change to mitigate the negative impacts of COVID-19
    - Social distancing (*Long-term* commitment like *obesity prevention*)
    - Vaccination (*One-time* commitment; Simple??: available after spring 2021?)
- Secondary prevention (if close contact w/ infected ??)
  - Detect early enough to improve outcome
- Tertiary Prevention
  - Treatment after infected & w/ serious symptoms

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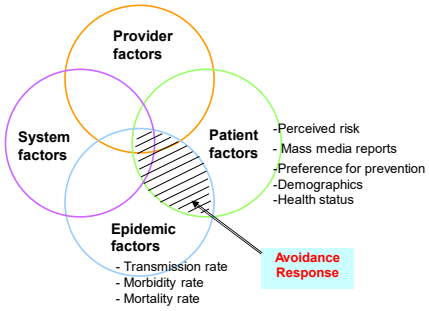
## Conceptual Framework of Preventive Behavior: Case of Infectious Disease by Yoo (2011)

Modified (CDC Task Force on Community Preventive Services, MMWR 1999)

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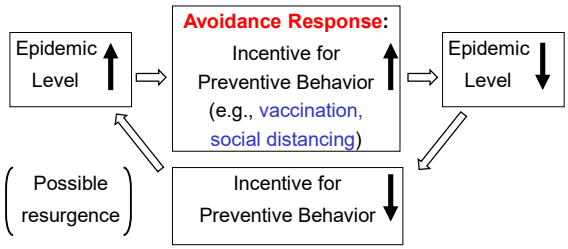
## Mutual (cyclic) Interaction between Epidemic Level and Incentive for Preventive Behavior

(Philipson 1996)

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## "Public Avoidance and the Epidemiology of novel H1N1 Influenza A"

Byung-Kwang Yoo, et al.

*National Bureau of Economic Research (NBER)* (*)

*Working Paper,* 2010, (www.nber.org/papers/w15752).

(*) *NBER* is the nation's leading nonprofit economic research organization. 16 of the 31 American Nobel Prize winners in Economics and 6 of the past Chairmen of the President's Council of Economic Advisers have been researchers at the *NBER*.

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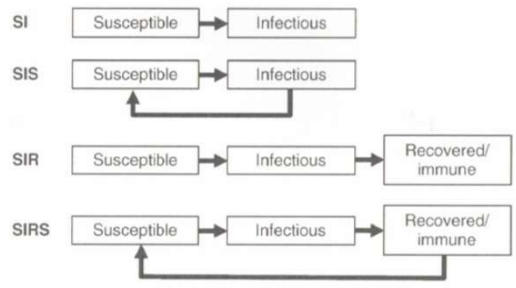
## Common structures for models used to describe the transmission of infections.

(source: Vyunncyky 2020, p.16)

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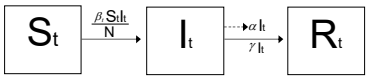
## 3 Compartment Model of Epidemic Susceptible-Infected-Recovered (SIR) Model




$S_t$: the number of susceptible people on day t
$I_t$ : the number of infected people on day t
$R_t$: the number of recovered (immune) people on day t
N: the total state population as of July 1, 2008

| α = the case fatality rate | $\beta_t$ = the virus attack rate | γ = the recovery rate |
|---|---|---|

## 2 Components of Disease Attack Rate

Attack rate = product of 2 components

- constant baseline attack rate
  - "biological" transmission rate
  - Same as "basic reproduction number of R0"
- baseline contact frequency
  - differs among subgroups (eg, age, occupation)

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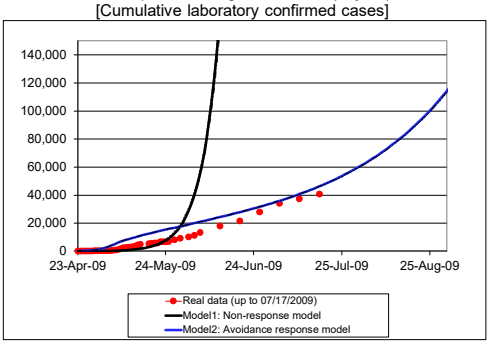
Test Validity of Avoidance Response Model:
novel H1N1 influenza epidemic path in the U.S.
from April 23 to August 31, 2009 (day 86)
[Cumulative laboratory confirmed cases]

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## 3 Components of Disease Attack Rate

Attack rate = product of 3 components

- constant baseline attack rate
  - "biological" transmission rate
- baseline contact frequency
  - differs among subgroups (eg, age, occupation)
- *avoidance response* parameters (original)
  - influenced by the disease prevalence rate [past week, in residential state]

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## How to empirically measure attack rate and avoidance response?

- Original data from CDC website
  - State level, daily "*cumulative*" confirmed cases
  - →Micro-simulation to obtain #s in S/I/R compartments in "*each day*" in each state (200 iterations)
  - →Calculate "attack rate", varying daily for each state (panel data: $\beta_{it}$, i: 50 states, t: day (from state-onset))
- Regression analysis of panel data

$$\beta_{it} = \beta_0 \exp( c_0 t - m_0 w(I_{it}))$$

$m_0$ :avoidance response, $\beta_0$ : baseline attack rate, w(I): prevalence in past week, $c_0$ : time factor

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The time-variant reproductive rate ($RR_t$) in Yoo et al (2010), changing every day
(= net reproduction number (Rn) in slides #10-20))

We calculate the time-variant reproductive rate ($RR_t$) as the product of 3 terms:

the attack rate, the proportion of susceptibles in the total population, and the duration in the infective compartment

$$\beta_t \left( \frac{S_t}{N_t(\gamma + \alpha)} \right)$$

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## Key assumptions of simulation models

- 3 simulation models in comparison
  - Model 1: Non-response model (without accounting for avoidance response)
  - Model 2: Avoidance response model
  - Model 3: same as Model 2, but assumes a second upsurge started Oct. 1, 2009
- Proportion of labo-confirmed cases among infected
  - 5% (CDC 2009)
- Pandemic influenza vaccine effectiveness
  - 50% (sensitivity analyses in NBER paper)
- Novel H1N1 flu vaccine supply (data as of early Oct. 2009)
  - Oct. 1-7: 1 million; Oct. 8-14: 6 million; Oct. 15- Dec. 2: 3 million [doses per day]
  - 196 million doses in total

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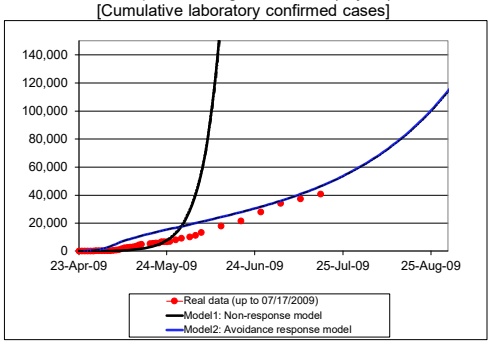
## Test Validity of Avoidance Response Model:
novel H1N1 influenza epidemic path in the U.S.
from April 23 to August 31, 2009 (day 86)
[Cumulative laboratory confirmed cases]

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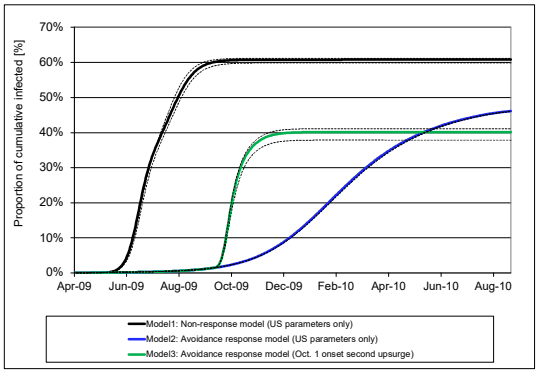
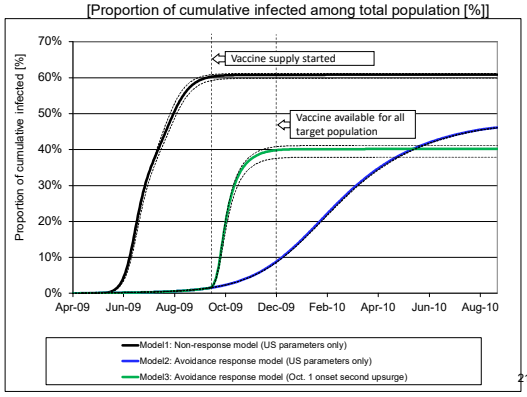
## Forecast US "baseline" pandemic path: 04/23/09-09/05/10
[ Proportion of cumulative infected among total population [%]




## Forecast US "baseline" pandemic path: 04/23/09-09/05/10
[Proportion of cumulative infected among total population [%]]

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## Estimated effectiveness of vaccination programs in 3 Models
Change in the final size [% of cumulative infected among total population]

| Model | Model assumptions | | Final size | |
|---|---|---|---|---|
| | Avoidance response | 2nd upsurge in Oct. 2009 | No vaccination | Change with vaccination |
| 1 | No | No | 61.1% | 0.0% |
| 2 | Yes | No | 46.2% | -11.6% |
| 3 | Yes | No | 40.1% | -6.2% |

- Pandemic influenza vaccine effectiveness: 50%
  - Vaccine supply (data as of early Oct. 2009): Oct. 1-7: 1 million; Oct. 8-14: 6 million; Oct. 15- Dec. 2: 3 million [doses per day]; 196 million doses in total

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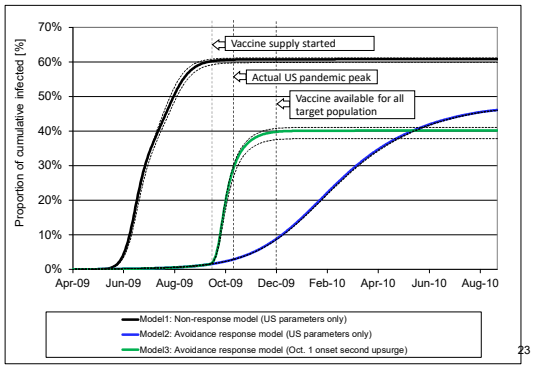
## Forecast US "baseline" pandemic path: 04/23/09-09/05/10
[ Proportion of cumulative infected among total population [%]

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## Estimated effectiveness of vaccination programs in 3 Models
Change in Peak Timing (Observed peak = end of Oct. 2009)

| model | Final size | | Timing of peak | |
|---|---|---|---|---|
| | No vaccination | Change with vaccination | No vaccination | Change with vaccination |
| | [1] | [2] | [3] | [4] |
| 1 | 61.1% | 0.0% | 7/9/2009 | 0 |
| 2 | 46.2% | -11.6% | 2/13/2010 | +30 days |
| 3 | 40.1% | -6.2% | 10/19/2009 | -1 day |

Model 1: Non-response model (without accounting for avoidance response)
Model 2: Avoidance response model
Model 3: Avoidance response model, with a second upsurge started Oct. 1, 2009

Most important principle in data analysis

*Garbage in, garbage out.*

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## 抗体保有調査結果

**概要**

■6月1日～7日にかけて、東京都・大阪府・宮城県において、各都府県により無作為抽出し、本調査への参加に同意をいただいた一般住民の方（東京都1,971名、大阪府2,970名、宮城県3,009名、計7,950名）を対象に抗体検査を実施しました。
■本調査では、陽性の判定をより正確に行うため、２種の検査試薬の両方で陽性が確認されたものを「陽性」としています。

**測定結果**

| | | アボット（+） | アボット（−） | 計 | モコバイオ（参考値） | 累積感染者数（感染率）5/31時点 |
|---|---|---|---|---|---|---|
| 東京都 | ロシュ（+） | 2 (0.10%) | 4 (0.20%) | 6 (0.30%) | 21 (1.07%) | 5,236人 (0.038%) |
| | ロシュ（−） | 2 (0.10%) | 1,963(99.59%) | 1,965(99.70%) | | |
| | 計 | 4 (0.20%) | 1,967(99.80%) | *1,971* | | |
| 大阪府 | | アボット（+） | アボット（−） | 計 | 37 (1.25%) | 1,783人 (0.02%) |
| | ロシュ（+） | 5 (0.17%) | 5(0.17%) | 10 (0.34%) | | |
| | ロシュ（−） | 11(0.37%) | 2949(99.29%) | 2960(99.66%) | | |
| | 計 | 16 (0.54%) | 2954(99.46%) | *2,970* | | |
| 宮城県 | | アボット（+） | アボット（−） | 計 | 36 (1.20%) | 88人 (0.004%) |
| | ロシュ（+） | 1(0.03%) | 6(0.20%) | 7 (0.23%) | | |
| | ロシュ（−） | 2(0.07%) | 3000(99.7%) | 3002(99.77%) | | |
| | 計 | 3 (0.10%) | 3006 (99.9%) | *3,009* | | |

■ 各自治体の抗体保有率は、**東京都0.10%、大阪府0.17%**、**宮城県は0.03%**でした。
■ 各自治体の抗体保有者は、累積感染者数と比較すると多いものの、依然として**大半の人が抗体を保有していない**という結果でした。
■ 本事業は国全体として過去に新型コロナウイルスに感染した人の割合を推定するものであり、**個別に現在の感染を診断するための調査ではありません。**
■ 現時点でこれらの**抗体の性質（体内での持続期間や、2回目の感染から守る機能があるかどうか）は確定していません。**

Yoo BK（兪炳匡）. 日本に於ける新型コロナウイルス・パンデミックの抗体検査結果の比較と分析. ***参議院予算委員会資料補足資料（3）***. 2020年. https://www.ric.u-tokyo.ac.jp/topics/2020/ig-20200716_all.pdf;

- 過去のPCR検査が著しく抑制されていたことを、今回の検査結果に基づく筆者の分析が示唆している（図表３と６）。
- 「抗体保有率に基づく推定感染率（分子）」と「PCR検査に基づく累積感染率（分母）」の比率を計算した（図表３と６）。この比率は最大（95%CIの上限値）で、東京都（54倍）、大阪府（44倍）、宮城県（120倍）にもなる。
- 東京都の入院治療の必要だった陽性患者の約7（=54倍x20%x70%）分の１だけが、PCR検査を受けて陽性結果を得られたと推定。
- 今後、PCR検査機能・キャパシティ（ないし検査へのアクセス）の大幅な向上が必要とされる。

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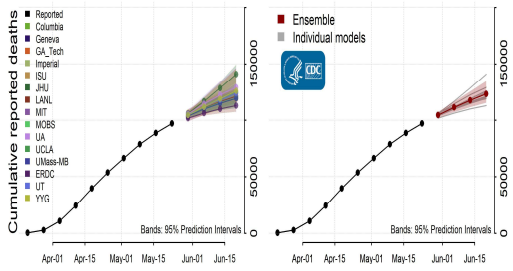
CDC's forecast: Deaths of COVID-19 (as of May 27, 2020)
https://www.cdc.gov/coronavirus/2019-ncov/covid-data/forecasting-us.html

**National Forecast**

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# Questions for Students

- What are the big differences b/w the estimates in CDC (previous slide) and those in Japan (that you have seen somewhere before)?
- You might want to simulate (# of infected, # of ICU beds needed) by yourself?

→ CDC provides FREE software "COVID-19 Surge" (https://www.cdc.gov/coronavirus/2019-ncov/hcp/COVIDSurge.html)

- You might want to simulate (# of Tracers needed) by yourself?

→ CDC provides FREE software "COVID-19 Tracer" https://www.cdc.gov/coronavirus/2019-ncov/downloads/php/COVID_TracerManual-508.pdf

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## Discussion Points
## (Note: (?) indicates limited evidence as of today)

How applicable is the basic SIR model for the COVID19?

- Infection w/out symptoms → Spread speed↑, Hard to trace infected (under-count "S" in the SIR model?)
- Multiple infections (?, how much % of infected?)
  - → Herd Immunity more difficult, i.e., longer time to reach herd immunity ?
  - → Not SIR model but SIRI or the mix of these models? (See next slide)
- Poor antibody response (?, how much % of infected?)
  - → Vaccine effectiveness↓ or the vaccine development would be difficult ?
  - → Herd Immunity more difficult, i.e., longer time to reach herd immunity ?
  - → Not SIR model but the mix of SIS, SIR and SIRS models?

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# References


- Vynnycky E, An Introduction to Infectious Disease Modelling 1st Edition, Oxford University Press, USA; 1 edition (July 15, 2010), ISBN-10: 0198565763
- Yoo BK, "How to improve influenza vaccination rates in the U.S.," ***Journal of Preventive Medicine & Public Health,*** 2011 Jul;44(4):141-8
- Yoo BK, Kasajima M, Bhattacharya J, "Public Avoidance and the Epidemiology of Novel H1N1 Influenza A," ***National Bureau of Economic Research Working Paper***, w15752, 2010, www.nber.org/papers/w15752




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## 新型コロナウイルスの無症状者に対するPCR検査の費用対便益分析

Yoo BK (兪炳匡), 高木俊, 野口晴子.

**早稲田大学現代政治経済研究所 WINPEC Working Paper Series No. J2002**, 2020年10月;

https://www.waseda.jp/fpse/winpec/assets/uploads/2020/10/J2002-1_version_p6_corrected.pdf,



## 目的：

**無症状者対象の大規模PCR検査を経済的に正当化できる、計量的な条件を「仮想例」として提示する。**

Only Japan doubts "**無症状者対象の大規模PCR検査**"

Recent papers (Paltier et al.; Neilan et al), outside Japan, focus on the frequency (once or 3 times per week) of the PCR and the combination of PCR (nasal or saliva) &other-tests (like lung-CT, antibody, antigen)



## 方法：費用対便益分析

2つの選択肢：

（選択肢１）感染リスクが低い・ないし不明な、無症状者を対象とするPCR検査を一度のみ実施する；

（選択肢２）１次スクリーニングとしてのPCR検査が陽性であれば、直ちに２次スクリーニングとして再度PCR検査を行う。

各選択肢の比較対象:

現状どおり（有症状者と濃厚接触者のみがPCR検査を受診可能）

-- "Do-Nothing" (Status quo) = Conventional name in cost-benefit analysis literature in economics field

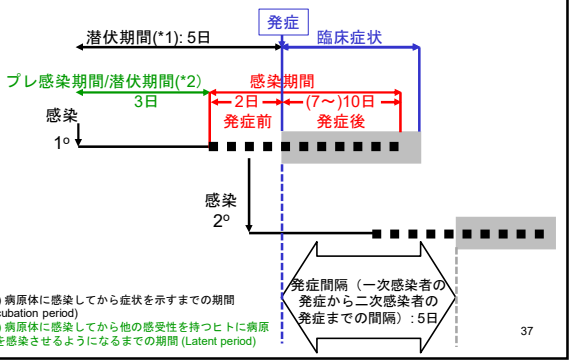


## 方法：費用対便益分析

（Do-nothing）に比較して、（選択肢１と２）

- 追加的費用:（a) PCR検査と(b) 隔離の費用, (c) 無症状1次感染者の発見に伴う『社会費用1』（経済外部性）
- 追加的便益：（a）発症前の早期発見と（b）無症状者の発見による、2次感染者発見に伴う『社会費用２』（経済外部性）の減少。
- 『社会費用1』『社会費用２』
  - これらのパラメーターは、集団・組織ごとに異なり、会社・医療機関を閉鎖する損失額を含む。
  - 『社会費用２』は、3次（４次）感染までの費用を含むので、『社会費用１』よりも大きいと仮定
  - 正確な推定は困難であるため、複数のシナリオ（感度分析）を示す。

COVID-19症状の時間経過: 感染期間と潜伏期間(*1)、プレ感染期間 (潜伏期間*2).
点線は感染期間を、**影付きの長方形は臨床症状を呈している期間**を示す.
(Vynnycky 2010, p.3を改変)




(*1) 病原体に感染してから症状を示すまでの期間 (Incubation period)
(*2) 病原体に感染してから他の感受性を持つヒトに病原体を感染させるようになるまでの期間 (Latent period)

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# Decision Tree

- 費用便益分析の標準的なモデル
- 起こり得る全事象の確率、最終結果の便益・費用は事前に予想できると仮定
- 仮想的な個人１人（検査対象を代表）が経験する事象を示す。
- 時間は左から右に経過

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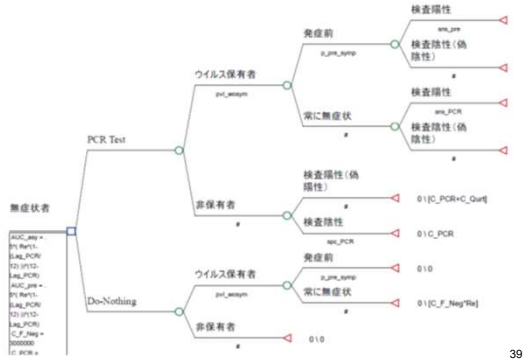
## Decision Tree

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## Result 1:便益費用比

1つの仮想例:
ある集団・組織における有症状者を含めた感染症の有病率が3%、
「社会費用1」を100万円、「社会費用2」を500万円とする。
この集団・組織に属する「無」症状者全員を対象とするPCR検査（選択肢1）を実施すると、費用節約が可能になり、
便益費用比（営利企業の投資回収率や純益率と同じ）は、1.4になると推定された。

- すなわち、100万円の費用を支出して（選択肢1）を実施すると、140万円の費用減少が可能になる。換言すると、40万円（＝140万円―100万円）の費用節約（ないし純益）を生むことが可能。
- 自治体レベルなら、1億円の費用を支出して、4000万円の費用節約が可能。
- 有病率が高くなる程、便益費用比は高くなる。

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表２．新型コロナウイルスの無症状者に対する
スクリーニングPCR検査の費用対便益分析

| スクリーニング方法 | PCR検査の費用 1回当り | 便益費用比 |
|---|---|---|
| （選択肢1）PCR検査を一度のみ実施する。 | 1万円 | 1.39 |
| | 5千円 | 2.03 |
| （選択肢2）１次スクリーニングとしてPCR検査を行い、検査陽性であれば、直ちに２次スクリーニングとして再度PCR検査を行う | 1万円 | 1.48 |
| | 5千円 | 2.31 |

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表3(part) 有病率が高くなる程、便益費用比は高くなる

| 有病率 | 便益費用比（選択肢１） |
|---|---|
| 20% | 4.79 |
| 15% | 4.59 |
| 10% | 4.24 |
| 5% | 3.45 |
| 4% | 3.16 |
| 3% | 2.77 |
| 2% | 2.22 |
| **1%** | **1.39** |
| 0.8% | 1.17 |
| 0.6% | 0.93 |
| 0.4% | 0.65 |
| 0.2% | 0.35 |
| 0.1% | 0.18 |

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**表4. 新型コロナウイルスの無症状者に対するPCR検査の損益分岐点分析：「便益費用比が１」になるために必要な「2次感染者１人当たりの『社会費用2』の閾値」の推定**

| (1) | (2) | | (3) |
|---|---|---|---|
| **有病率** | **2次感染者１人当たりの『社会費用2』の閾値§** | | **便益費用比** |
| | **選択肢1** | **選択肢2** | |
| 10% | ¥1,180,000 | ¥1,170,000 | 1 |
| 5% | ¥1,450,000 | ¥1,410,000 | 1 |
| **1%†** | **¥3,610,000** | **¥3,370,000** | **1** |
| 0.1% | ¥27,900,000 | ¥25,300,000 | 1 |
| 0.01% | ¥271,000,000 | ¥244,000,000 | 1 |

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**図表5. 新型コロナウイルスの無症状者に対するスクリーニングPCR検査（選択肢２：２次スクリーニングを行う）の、1次元感度分析における損益分岐点（閾値）と、「便益費用比が１以上（純便益）」を実現するための条件**

| (1) | (2) | (3) |
|---|---|---|
| **変数（「決定モデル」内のパラメーターの名称）** | **損益分岐点（閾値）§** | **基本モデルの値** |
| **有病率関連** | | |
| 有症状者を含む有病率 (pvl) | ≥ 0.60% | 1 % |
| ウイルス保有者に占める「常に無症状者」の割合 (p_asy) | （なし） | 45% |
| **費用** | | |
| 無症状1次感染者１人当りの『社会費用1』(C_Soc_1) | ≤ 314万円 | 100万円 |
| 2次感染者１人当りの『社会費用2』(C_Soc_2) | ≥ 337万円 | 500万円 |
| PCR検査費用 (C_PCR) | ≤ 16,800円 | 1万円 |
| 無症状者対１人1回当りの隔離費用 (C_Qurt) | ≤ 222万円 | 189,500円 |

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図4. 2次元感度分析：無症状者対象のPCR検査
「行う（図中の赤色部分）」 vs「しない （青色部分）」
横軸（X軸）： 有病率（0.1%-1%）
縦軸（Y軸）：1次感染者1人当たりの『社会費用1』（0円-400万円）
解釈：有病率と『社会費用1』の組み合わせ点（例、X= 0.7%, Y=100万円）が赤色部分の内部なら「PCR検査を行うべき」

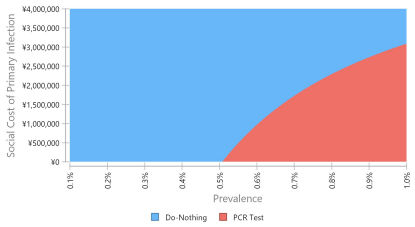


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図5. 2次元感度分析：無症状者対象のPCR検査
「行う（図中の赤色部分）」 vs「しない （青色部分）」
横軸（X軸）： 有病率（0.1%-1%）
縦軸（Y軸）：2次感染者1人当たりの『社会費用2』（0円-1千万円）
解釈：有病率と『社会費用2』の組み合わせ点（例、X= 0.5%, Y=1,000万円）が赤色部分の内部なら「PCR検査を行うべき」

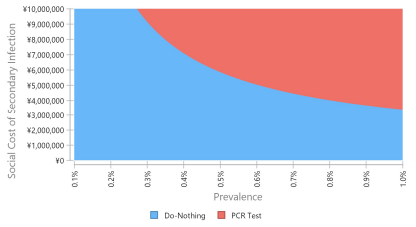


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図6. 2次元感度分析：無症状者対象のPCR検査
「行う（図中の赤色部分）」 vs「しない （青色部分）」
横軸（X軸）：1次スクリーニングPCR検査の感度（50%-100%）
縦軸（Y軸）：1人1回の PCR検査費用（0円-2.5万円）
解釈：感度と検査費用の組み合わせ点（例、 X=50%, Y= 5,000円）が赤色部分の内部なら「PCR検査を行うべき」

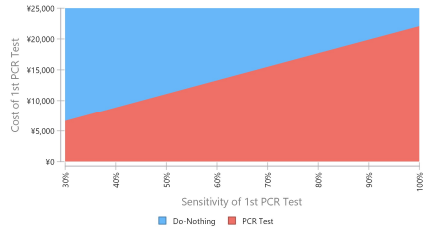


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図10. 2次元感度分析：無症状者対象のPCR検査
「行う（図中の赤色部分）」 vs「しない （青色部分）」
横軸（X軸）：1次スクリーニングPCR検査の感度（30%-100%）
縦軸（Y軸）：1次スクリーニングPCR検査の特異度(30%-100%）
PCR検査費用： ￥5,000
解釈：感度と特異度の組み合わせ点（例、 X = 70%, Y= 90%）が赤色部分の内部なら「PCR検査を行うべき」

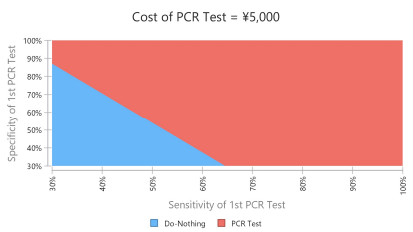


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図11．2次元感度分析：無症状者対象のPCR検査
「行う（図中の赤色部分）」 vs「しない （青色部分）」
横軸（X軸）：1次スクリーニングPCR検査の感度（30%-100%）
縦軸（Y軸）：1次スクリーニングPCR検査の特異度(30%-100%）
PCR検査費用： ￥10,000
解釈：感度と特異度の組み合わせ点（例、 X = 70%,
Y= 90%）が赤色部分の内部なら「PCR検査を行うべき」

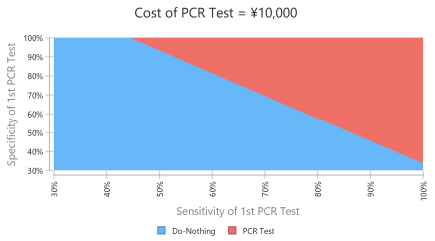


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図13．2次元感度分析：無症状者対象のPCR検査
「行う（図中の赤色部分）」 vs「しない （青色部分）」
横軸（X軸）：1次スクリーニングPCR検査の感度（30%-100%）
縦軸（Y軸）：2次スクリーニングPCR検査の感度(30%-100%）
解釈：1次感度と2次感度の組み合わせ点（例、 X = 70%,
Y= 90%）が赤色部分の内部なら「PCR検査を行うべき」

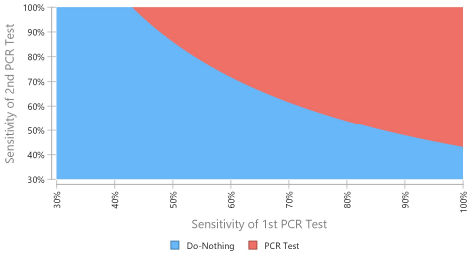


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図14．2次元感度分析：無症状者対象のPCR検査
「行う（図中の赤色部分）」 vs「しない （青色部分）」
横軸（X軸）：1次スクリーニングPCR検査の特異度（50%-100%）
縦軸（Y軸）：2次スクリーニングPCR検査の特異度(50%-100%）
解釈：1次特異度と2次特異度の組み合わせ点（例、 X = 90%,
Y= 90%）が赤色部分の内部なら「PCR検査を行うべき」

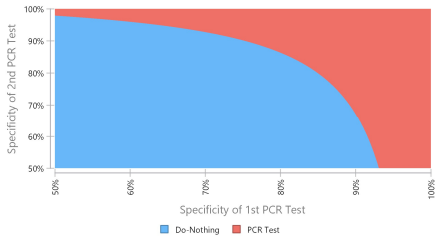


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図15．2次元感度分析：無症状者対象のPCR検査
「行う（図中の赤色部分）」 vs「しない （青色部分）」
横軸（X軸）： 検体採取後、隔離までの日数（0-4）
縦軸（Y軸）：1次スクリーニングPCR検査の感度（30%-100%）
解釈：特異度と検査費用の組み合わせ点（例、 X = 2,
Y = 70%）が赤色部分の内部なら「PCR検査を行うべき」

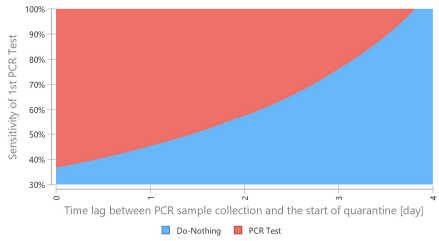


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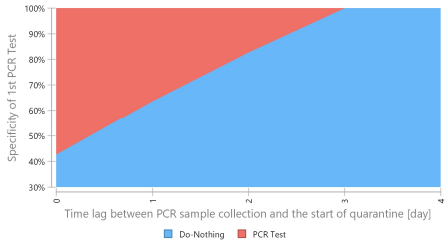
図16．2次元感度分析：無症状者対象のPCR検査
「行う（図中の赤色部分）」 vs「しない （青色部分）」
横軸（X軸）： 検体採取後、隔離までの日数（0-5）
縦軸（Y軸): 1次スクリーニングPCR検査の特異度（95%-100%）
解釈：特異度と検査費用の組み合わせ点（例、 X = 1日,
Y = 80%）が赤色部分の内部なら「PCR検査を行うべき」

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## Road Map

I) Introduction of Presenter

II) Individual behavior theory in mathematical Modeling

III) Cost-benefit analysis of PCR tests

IV) Health disparity

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## Definition by US CDC (2018) 1

Health disparities are

preventable differences in the burden of disease, injury, violence, or opportunities to achieve optimal health that are experienced by socially disadvantaged populations.

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## Definition by US CDC (2018) 2

Populations can be defined by factors such as
race or ethnicity, gender, education or income, disability, geographic location (e.g., rural or urban), or sexual orientation.

Cf. Socio-economic status (SES) often includes education, income (& asset) etc. – social class (why not used in US?)

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## Definition by US CDC (2018) 3

Health disparities result from multiple factors, including

- Poverty
- Environmental threats
- Inadequate access to health care
- Individual and behavioral factors
- Educational inequalities

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## What are the criteria to compare in the health care fields?

How to compare/rank?

- Hospital A vs. Hospital B
- Health maintenance organization (HMO) A vs. HMO B
- Public health program in City A vs. City B

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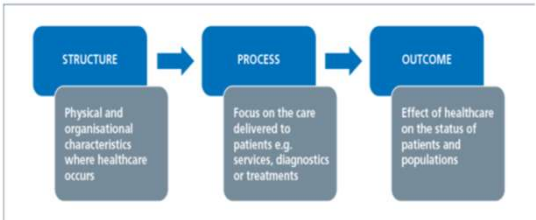
## Donabedian's model for measuring quality care (Donabedian 2005)

Table source: UK NHS: https://improvement.nhs.uk/documents/2135/measuring-quality-care-model.pdf

Figure 1: The Donabedian model for quality of care

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## Donabedian's model for measuring quality care (Donabedian 2005): summary source: UK NHS: https://improvement.nhs.uk/documents/2135/measuring-quality-care-model.pdf

**Structure** measures: these reflect the attributes of the service/provider

- such as staff to patient ratios and operating times of the service.
- These are otherwise known as input measures.
- Other Examples: # of MDs, Hospital beds per population
- Easy to measure/improve (but roughest measure)

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Donabedian's model for measuring quality care (Donabedian 2005): summary source: UK NHS: https://improvement.nhs.uk/documents/2135/measuring-quality-care-model.pdf

**Process** measures: these reflect the way your systems and processes work to deliver the desired outcome.

- For example, the length of time a patient waits for a senior clinical review, if a patient receives certain standards of care or not, if staff wash their hands, recording of incidents and acting on the findings and whether patients are kept informed of the delays when waiting for an appointment.

- Other Examples: Quantity of H care utilization, Timing (delayed or not) of H care utilization
- Relatively easy to measure (but not the final goal, except primary/secondary prevention)

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Donabedian's model for measuring quality care (Donabedian 2005): summary source: UK NHS: https://improvement.nhs.uk/documents/2135/measuring-quality-care-model.pdf

**Outcome measures**: these reflect the impact on the patient and demonstrate the end result of your improvement work and whether it has ultimately achieved the aim(s) set.

- Examples of outcome measures are reduced mortality, reduced length of stay, reduced hospital acquired infections, adverse incidents or harm, reduced emergency admissions and improved patient experience.

- Best measures (among 3 model categories) but still needs careful risk-adjustment (i.e., controlling for baseline health status and other SES factors)

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Question for All students
RE the following examples

Q1) Under Donabedian's model, which type of quality is measured?

- Structure, Process or Outcome

Q2) To prevent the observed disparity, what type of prevention is needed?

- Primary, Secondary or Tertiary

Q3) To improve the internal/external validity of a study, what will you recommend as a peer reviewer?

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Disparity example 1 under COVID
Cited in Khunti et al, BMJ. 2020 Apr 20

"Concerns about a possible association between ethnicity and outcome were raised after

the first 10 doctors in the UK to die from covid-19 were identified as being from ethnic minorities."

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Disparity example 2 under COVID
Cited in Khunti et al, BMJ. 2020 Apr 20

- "Of 2249 patients admitted to 201 critical care units in England, 64.8% were white, 13.8% were Asian, 13.6% were black, and 7.8% were from other or mixed ethnic groups."
- "The ethnic minority population of the UK was around 13% at the time of the last census in 2011."

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Disparity example 3 under COVID
Cited in Khunti et al, BMJ. 2020 Apr 20

"An analysis by the *Washington Post* reports that counties with black majorities have three times the rate of covid-19 cases, and almost six times the rate of deaths, compared with counties where white residents are in the majority."

66

Disparity example 4 under COVID
Azar et al. Health Aff. 2020 May 21

- Analyzed 1,052 confirmed cases of COVID-19 from January 1–April 8, 2020 in Northern California, US
  - Enrolled in a large health care system (Sutter)
- Compared with non-Hispanic white patients, African Americans (AA) had 2.7 times the odds of hospitalization, after adjusting for age, sex, comorbidities, and income.
  - No difference in testing
  - *"Disparity may not be in who is tested, but when"*
  - Delayed care (more advanced stage at time of a test)
  - Because patients view delaying care as sensible option

  → Patients may lose $ or a job, if test (+)

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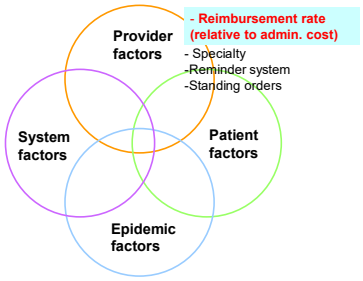
Conceptual Framework of Preventive Behavior:
Case of Vaccination
(Task Force on Community Preventive Services, MMWR 1999)

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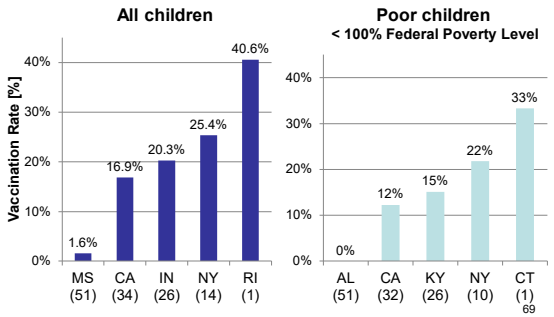
## Child Full Vaccination Rate (6-23mo) 2005-06 season (state ranking)

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1) Medicaid reimbursement to administer vaccination

**Background**

- Medicaid reimbursement for administering vaccination
  - Min: $2.00 (NH etc); Max: $17.86 (NY) in 2005
  - Median: $8.40
- Provider cost: $20 to adm. one flu shot at pediatric clinic
  [2006 dollar value] (Yoo et al., *Pediatrics*, 2009)
  - *Physicians are losing money by giving flu shots*
  - Financial loss for VFC vaccination in all private pediatric practices [2006 dollars]
    2006-07 season
    - 20% vaccinated: Financial loss = $40 million
    - If 90% vaccinated: Financial loss = $208 million

    (Yoo et al. *Pediatrics* 2009)

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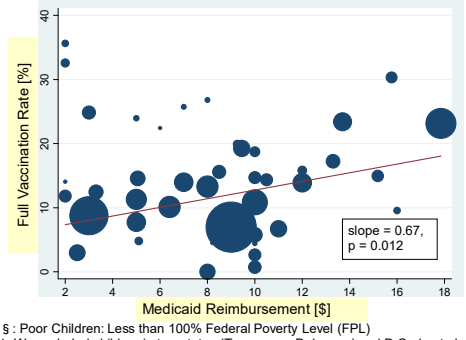
State-level Reimbursement Rate and Full-Vaccination Rate among Poor Children§ in 48 States† (adj. with 15 factors) (Yoo et al., *Pediatrics 2010*)




§ : Poor Children: Less than 100% Federal Poverty Level (FPL)
†: We excluded children in two states (Tennessee, Delaware) and D.C. due to lack of data.
Size of circles weighted with state poor child population size)

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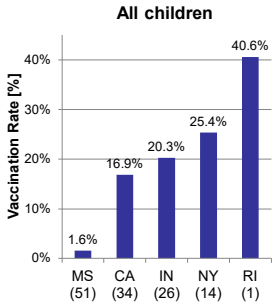
## Child Full Vaccination Rate (6-23mo) 2005-06 season (state ranking)




- Geographic health disparity example
- After you control for individual factors (maternal education attainment) and aggregated factors (# of MDs per population), no difference in flu shot rate across states among all children/non-poor children. → No disparity?

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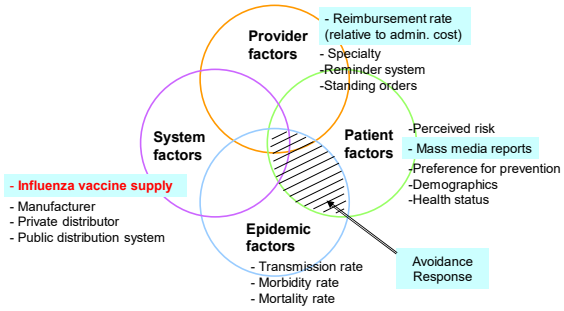
## Conceptual Framework of Preventive Behavior: Case of Vaccination

(Task Force on Community Preventive Services, MMWR 1999)

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## Does influenza vaccine supply delay/shortage affect racial/ethnic disparities?

(Yoo et al., *American J of Preventive Medicine*, 2011)

**Background**

Link et al did not find any change in racial/ethnic disparities during seasons with vaccine supply delay/shortage

- Comparing *different subjects* across consecutive seasons

→ Hard to judge if the cause is the changes in patients or those in system (or both)?

**Methods:** Very difficult general question

How to control *individual patient preference?*

e.g.1, I do not like any injection (i.e., fear of needle)

e.g.2, I do not like physicians/clinics

e.g.3, I believe that a vaccine causes autism or other very serious side effects

→ (If you are a reviewer) killing critique(?)

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## Does influenza vaccine supply delay/shortage affect racial/ethnic disparities?

(Yoo et al., *American J of Preventive Medicine*, 2011)

**Methods** (to control *individual preference*)

How about comparing the *same subjects* across seasons?

- Assuming individual preference is stable for 2 years
- (period 1) 2000-2001 and 2001-2002 seasons through (period 4) 2003-2004 and 2004-2005 seasons.
- Medicare Current Beneficiary Survey (MCBS) community-dwelling elderly (un-wt N =2,306–2,504, weighted N = 8.23-8.99 million).
- Multivariable logistic regression analyses
  - Outcome = flu shot receipt
  - Covariates = 15 individual level factors

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## Results

- Improved vaccine supply assoc. with ↓ racial/ethnic disparities in flu shot rates among nationally-representative Medicare elderly
  - 2%-11% compared with non-Hispanic White
- Worse supply assoc. with ↑ disparities
  - 2%-7% compared with non-Hispanic White
- "Dose-response" relationship b/w supply-change and disparity-change
  - "Largest disparity ↑" follows "largest supply↓"
  - "Smallest disparity ↑" follows "smallest supply↓"

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## Policy Implications

- Stabilizing the vaccine supply
  - Public buy-back plan: Buy un-used vaccines from manufactures and healthcare providers (public subsidy)
- The creation of an adult program similar to the Vaccines-for-Children (VFC) program
  - To sustain delivery of vaccines to safety-net providers with limited vaccine investment resources
  - Federally Qualified Health Centers and practices - serving large proportions of African-American and Hispanic patients
- Active provider and patient reminder/recall systems
- Targeted communication campaigns

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"Cost-effectiveness analysis of a television campaign to promote seasonal influenza vaccination among the elderly,"
***Value in Health***,
2015 Jul;18(5):622-630, (PMID: 26297090)
Kim M, **Yoo BK** (corresponding author)

Mentored as the first author's post-doctoral fellow training.

**Journal Ranking**

- **2018 Impact Factor: 5.037**
- **6th of 353 in Economics**
- **3rd of 79 in Health Policy & Services**
- **3rd of 94 in Health Care Sciences & Services**

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## Research Objectives

- To determine the cost-effectiveness of "a hypothetical national TV flu shot campaign" targeting US Medicare elderly
  - Comparator: No "national TV flu shot campaign" (status quo)
- Key parameters in decision model:
  - Cost (2012 USD):TV campaign
  - Effectiveness: # of vaccinated Medicare elderly

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## Study Design 1

- Time horizon: 4 months (Sep. 1~ Dec. 31, 2012)
- Societal perspective
- Race-ethnicity specific cost-effectiveness:
  - Non-Hispanic White (W)
  - Non-Hispanic African American (AA)
  - English-speaking Hispanic (EH)
  - Spanish-speaking Hispanic (SH) (used Spanish in MCBS survey)

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## Study Design 2

- Intervention details:
  - 30-sec TV campaign for flu shot at prime time
  - Once a week during Sep. – Dec. (17 weeks)
  - Aired in 3 nationwide TV networks (ABC, CBS, NBC)
- Intervention cost (2012 USD):
  - Production cost (P): one-time cost
  - Broadcasting cost (B): 30-sec prime time cost
  - Total cost= P+[B*(17 weeks)*(3 networks)]

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## Table 1 (continued): Model Inputs

| Medicare elderly population | Estimate | Range | Source |
|---|---|---|---|
| Total (2012) | 39 million | | 3 |
| Non-Hispanic White | 83.3% | | 3 |
| Non-Hispanic African American | 9% | | 3 |
| Hispanic (English) | 4.2% | | 3, 4 |
| Hispanic (Spanish) | 3.5% | | 3, 4 |
| **Baseline vaccination coverage rate¶** | **Estimate** | **Range** | **Source** |
| Non-Hispanic White | 68% | 63%~71% | 5 |
| Non-Hispanic African American | 50% | 40%~56% | 5 |
| Hispanic (English) | 66% | 58%~71% | 4, 5 |
| Hispanic (Spanish) | 42% | 31%~53% | 4, 5 |

¶Average and range of 14 seasons (1999 ~ 2012)
3: Centers for Medicare & Medicaid Services (CMS)
4: Yoo et. al. (2011) "Influenza Vaccine Supply and Racial/Ethnic Disparities in Vaccination Among the Elderly"
5: Centers for Disease Control and Prevention (CDC)

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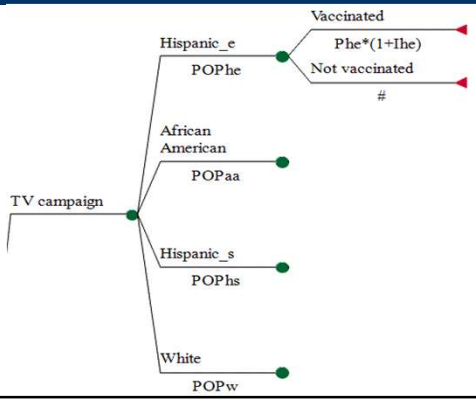
## Figure 1: Decision Tree Model

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## Table 2: Cost Effectiveness Analysis

| Model | Incremental Cost [$ million] | Incremental Effect [persons] | ICER [$ per vaccinated] |
|---|---|---|---|
| Deterministic model | 6.0 million | 335,000 | **$18** |
| Probabilistic model (95% CI) | 6.7 million (4.7 m- 9.2 m) | 300,000 (184,000, 378,000) | **$24 ($14- $40)¶** |

All costs in US 2012 Dollars, ICER = Incremental Cost Effectiveness Ratio, #: Rounded at 1,000, 95% CI = 95% confidence interval, ¶: ICER<$38.47: 96.9% of 10,000 iterations

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## Table 3: Subpopulations: *Disparity in?*

| Race/Ethnicity | Deterministic model | Probabilistic model |
|---|---|---|
| | ICER | ICER (95% confidence interval) |
| Non-Hispanic White | $16 | $23 ($13-$40)¶ |
| Non-Hispanic African American | $39 | $31 ($15-$53)¶ |
| Hispanic (English speaking) | $17 | $22 ($13-$40)¶ |
| Hispanic (Spanish speaking)* | Dominated | Dominated |

All costs in US 2012 Dollars, ICER = Incremental Cost Effectiveness Ratio, #: Rounded at 1,000. * "TV campaign" was dominated by "without the TV campaign" ¶: ICER<$38.47: 96.9% (W), 78.9% (AA), and 97% (EH) of 10,000 iterations

Most groups: Cost effective (ICER < threshold of $38.47)

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## Result 2: *Disparity in?*

- Effect on Racial/Ethnic Disparity
  - W-AA groups: 0.6 pp ↑ in vaccination disparity
  - W-EH groups: 0.1 pp ↑ in vaccination disparity
  - W-SH groups: 1.5 pp ↑ in vaccination disparity

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## Discussion 1

- Reasons for disparity increase in vaccination rate among racial/ethnic groups
  - (i) English as a language barrier (SH group)
    → less likely to be exposed to English TV campaign
  - (ii) Limited vaccine supply (AA and SH group)
    → more likely to be delayed in vaccination

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## Conclusions

- Nationwide TV campaign is reasonably cost effective.
- Nationwide TV campaign may increase the racial/ethnic disparity.
- Nationwide TV campaign justifiable to implement, accompanying Spanish-language campaign

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## References


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## Take home messages

- Systematic analyses of health disparity
  - 1/2/3 prevention
  - Donabedian's model for quality care
- "Paradox in disparity"
  Disparity could be worsened by
  - Technological advancement
  - New information on disease/prevention/treatment
  - Insurance (and other?)

  → Because highest SES can gain the full benefits

  → How to mitigate/prevent the potential exacerbation of disparity?

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# Question?

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PPT slides of
- Today's lecture (Full slides)
- 4 series-lectures on pandemic

are available in my personal blog:
https://www.bkyoo.org/

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# Appendix

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**レポート提出先：**
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## 「超過死亡の推定」の問題点


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2020年10月12日（改訂3版）

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## 推定方法論の概要

- ❑ 季節性インフルエンザに比べると、推定方法論は未確定
- ❑ 日本の厚生労働省・国立感染症研究所は、米国CDCと欧州CDCがそれぞれ開発した２つ方法論を採用(*)
- ❑ 基本計算方法：
- 「超過死亡数」 ＝ 「実際の死亡数」－「予想数」
- 「予想数」は、過去の同時期と同じと仮定して、重回帰分析で推定・計算可能。
- 推定値の不確実性：計算方法の仮定次第で、理論上「予想数と超過死亡数」は100以上の推定値が得られる。
- 正確さの比較：これらの100以上の「予想数と超過死亡数」の推定値の正確さについて、数学的理由のみで優劣をつけるのは、ほぼ不可能かつ無意味。

(*)文献： https://www.niid.go.jp/niid/ja/from-idsc/493-guidelines/9748-excess-mortality-20jul.html
https://www.niid.go.jp/niid/ja/from-idsc/493-guidelines/9887-excess-mortality-20sep.html

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## 不確実な推定値の妥当性を高める為に必要な分析・議論

（重要な順にリストした。１が最重要。）

**１）関連する感染指標との地域・時期における整合性が高い超過死亡数は妥当性が高い**
- 検査指標：PCR検査・抗体検査で人口当たりの検査陽性率が高い地域・時期では、超過死亡数が多いと予想される
- 臨床指標：入院（ICU）・外来受診データでCOVID-19の診断名が人口当たり多い地域・時期では、超過死亡数が多いと予想される

**２）地域・時期・疾患分類ごとに詳細な超過死亡数を推定して、妥当性を検討すべき**
- 時期：少なくとも毎月ごとに推定すべき。（米国CDCは毎週毎に発表：スライド4）
- 疾患分類：少なくとも呼吸器系・循環器系・Alzheimer病/認知症（施設入所者は高リスク）を独立して推定すべき。（米国CDCは更に詳細な分類も推定：スライド4）
- 地域：少なくとも都道府県。昼間人口の変動が多い場合、隣接する県を含めた推定値も追加すべき。

**３） 過去のデータを分析する際に、少なくと年齢・性別は、2020年の人口構成データと同じになるように調整すべき。**

**４） 重回帰分析の仮定について、感度分析を行い頑健性を確認。**
- 「（死亡）予想数」の計算に用いる過去データの期間（例、8年または5年）や過去データの集積期間（例、特定の週に前後5週または7週を平均）の複数の結果を比較

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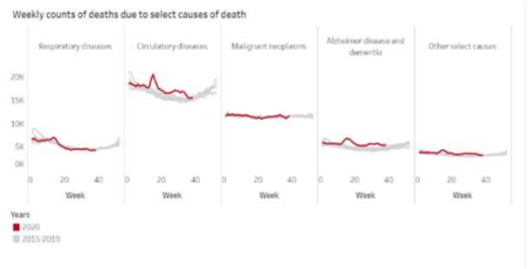
米国CDCのCOVID-19による超過死亡数の報告例

週ごと、5診断分類ごと（呼吸器系、循環器系、悪性新生物、認知症、その他）に報告

図中の赤色の折れ線が2020年のデータ、灰色の折れ線が過去の5年間のデータ

図の解釈：赤色の折れ線が灰色の折れ線を上回る（超過死亡を認める）時期は、他の指標（PCR検査の検査陽性数の上昇の時期）と一致するので、妥当性は高い

source: https://www.cdc.gov/nchs/nvss/vsrr/covid19/excess_deaths.htm#dashboard

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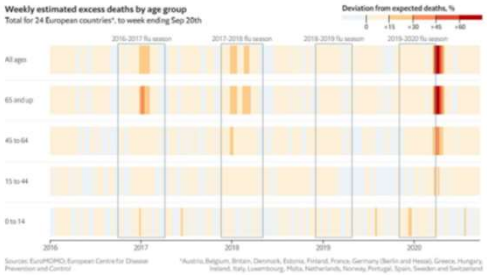
欧州諸国のCOVID-19による超過死亡の報告例

超過死亡の単位は、比較が容易な[予想数に対する%増加率]

解釈：過去4年間のデータと比較し、季節性インフルエンザの影響（Boxで囲まれた時期）を除外すると、COVID-19による超過死亡の明らかな増加（図中の濃色部分）があり、4年齢階級中、65歳以上の超過死亡が特に多い。

https://www.economist.com/graphic-detail/2020/07/15/tracking-covid-19-excess-deaths-across-countries

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## 日本の国立感染症研究所による超過死亡推定

source: https://www.niid.go.jp/niid/ja/from-idsc/493-guidelines/9887-excess-mortality-20sep.html
https://www.niid.go.jp/niid/ja/from-idsc/493-guidelines/9748-excess-mortality-20jul.html

| | 2020 | | 2019 | | 2018 | | 2017 | |
|---|---|---|---|---|---|---|---|---|
| 都道府県 | Farrington | Euro-MOMO | Farrington | Euro-MOMO | Farrington | Euro-MOMO | Farrington | Euro-MOMO |
| 東京 | 30-291 | 77-647 | 237-1427 | 182-1855 | 446-2084 | 135-1514 | 254-2253 | 0-980 |
| 神奈川 | 0-83 | 0-210 | 96-826 | 130-1316 | 153-1054 | 82-1141 | 253-1768 | 3-1008 |
| 全国 | 191-4577 | 319-7467 | 1317-14779 | 1023-19836 | 3373-23095 | 1108-20862 | 2940-26890 | 299-17316 |

（注）表中のFarringtonとEuroMOMOは、それぞれ米国CDCと欧州CDCの推定方法

日本の推定方法・発表の問題点

- 分析期間が長期過ぎる（上記表は2020年1月から6月まで、まとめて分析）。
- 毎月ごと、死亡原因の疾患分類ごとの詳細な分析・発表が無い。
- 関連する感染指標との地域・時期における整合性、すなわち超過死亡推定値に妥当性についての議論・分析が不十分。
- スライド5の例に倣い、超過死亡は絶対数だけでなく、比較・解釈が容易な「増加率」でも表示すべき。
- スライド5の例に倣い、季節性インフルエンザの時期（影響）も表示すべき。

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