Risk Factors for COVID-19 Complications: An Israeli Viewpoint

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KI Research Institute

OHDSI Community Call
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The Israeli Institute for Applied Research in Computational Health

KI Research Institute

- A newly established Israeli institute for applied research in computational health; an independent, self-funded, not-for-profit organization
- Goal: **develop** and **apply** innovative computational **methodologies** to **explore medical databases**, **advance** a better understanding of **human health**, **promote actionable steps** to improve it.

Pregnancy, birth, early childhood

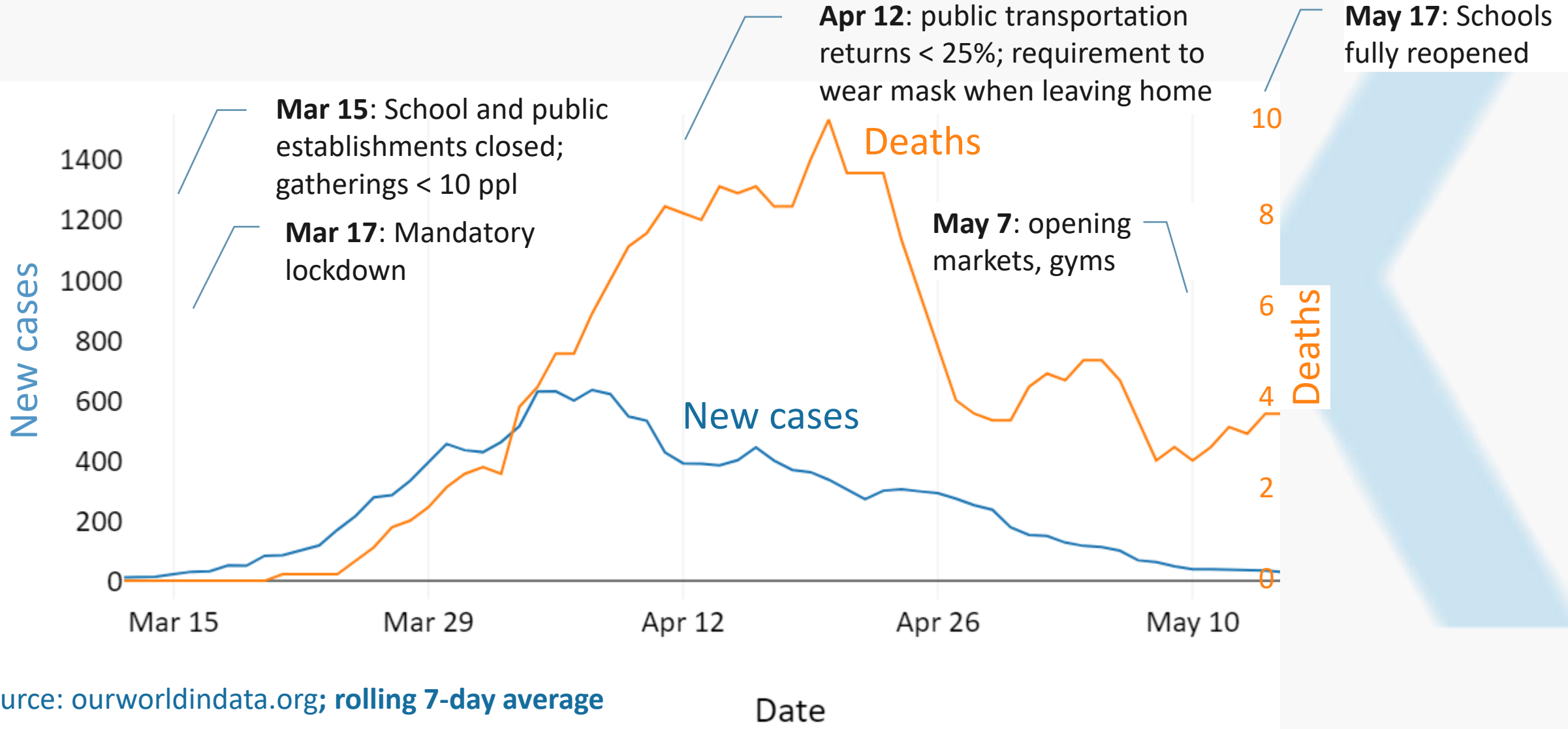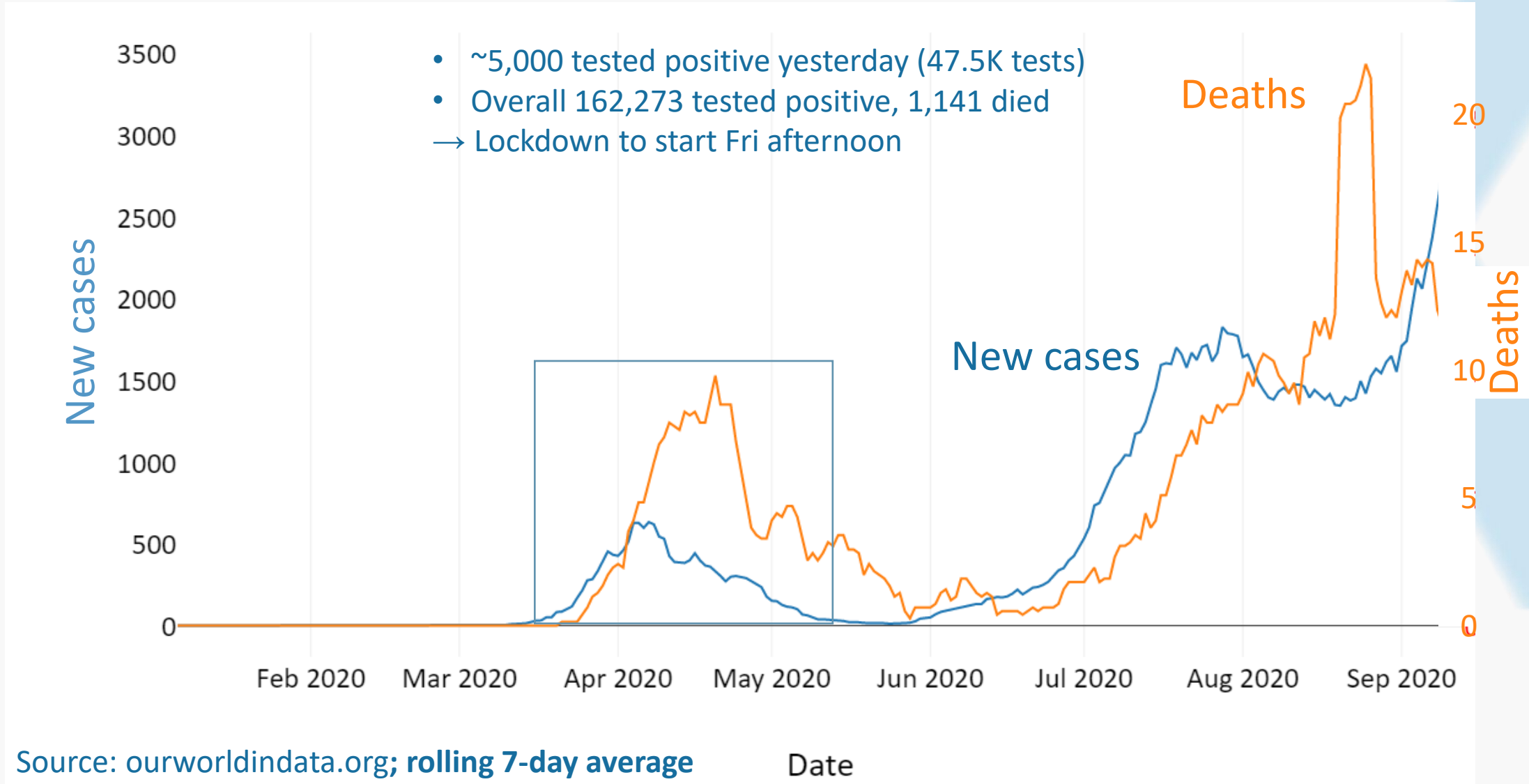Drug treatment effects

Lifestyle effects on health

COVID-19

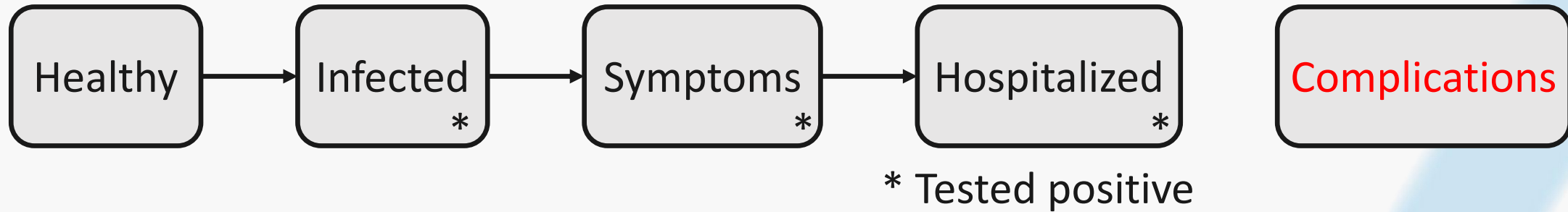Other: IBD, AD

SARS-CoV-2 in Israel: 1ˢᵗ Wave

Apr 12: public transportation returns < 25%; requirement to wear mask when leaving home

May 17: Schools fully reopened

Mar 15: School and public establishments closed; gatherings < 10 ppl

Mar 17: Mandatory lockdown

Deaths

May 7: opening markets, gyms

New cases

Source: ourworldindata.org; **rolling 7-day average**

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SARS-CoV-2 in Israel: 2ⁿᵈ Wave

- ~5,000 tested positive yesterday (47.5K tests)
- Overall 162,273 tested positive, 1,141 died
→ Lockdown to start Fri afternoon

Risk factors: It's Complicated

Healthy → Infected* → Symptoms* → Hospitalized*   Complications

*Tested positive

Reference population	Research Q	Potential biases
All (healthy)	Who's at risk to (get infected then) have complications?	Exposure, infection differ between populations (elderly, health professionals)
Tested positive	Who's at risk for complications, if tested positive?	Testing policy changes over time (far from random; asymptomatic tested less)
Symptomatic	Who's at risk for complications, if symptomatic?	Symptomatic population has distinct characteristics (compared to asymptomatic)
Hospitalized	Who's at risk for (severe) complications, if hospitalized?	Hospitalized population has distinct characteristics

Data

- Maccabi Health Services, a nationwide health plan (payer-provider), representing 2.3M individuals ($\frac{1}{4}$ of Israeli population, $< 1\%$ attrition)

- Lab data (a single central lab), full pharmacy prescription and purchase data, extensive demographic information

- Registries based on validated criteria (coded diagnoses, treatments, labs, and imaging, as applicable); continuously and retrospectively (since 1998) updated based on each patient's central medical record

Study Design

- Positive SARS-CoV-2 PCR testing (nasopharyngeal and saliva samples) until Apr 22, 2020

- Complications: Moderate or severe status, admission to ICU, death
  - Status definition varied between hospitals but was largely based on the severity of lower respiratory tract symptoms as well as shock and system failure

- Follow-up period: Apr 30, 2020

- Patient characteristics: age, sex, various existing conditions, smoking, alcohol consumption, hospitalization (in the last 3 years), nursing home, home care

Statistical Analysis

- Comparison of condition prevalence in the complicated and non-complicated sub-cohorts

- Stratification to three age groups (18-50y, 50-65y, >65y); and four (age, sex) strata (male or female; younger or older than 65 years)
  - Multiple studies showed that age, sex most strongly associated with complications

- Controlled for FDR using Benjamini and Hochberg's method

Results

- 4353 infected individuals, 173 had complications
  - 87 (50%) deteriorated to moderate and 45 (26%) to severe condition; 66 (38%) admitted to ICU (partly overlapping with other conditions); 21 (12%) died
- Complicated patients were older, sicker, predominantly male
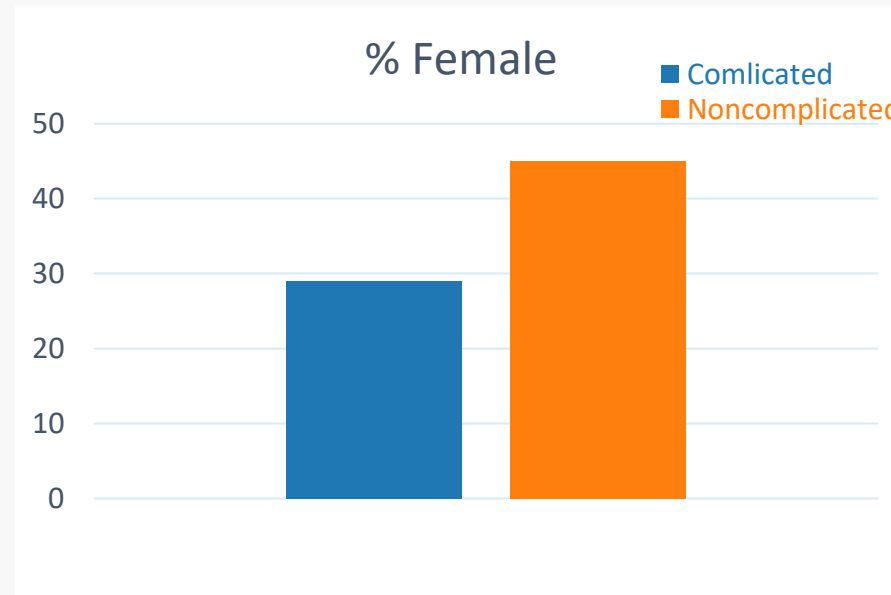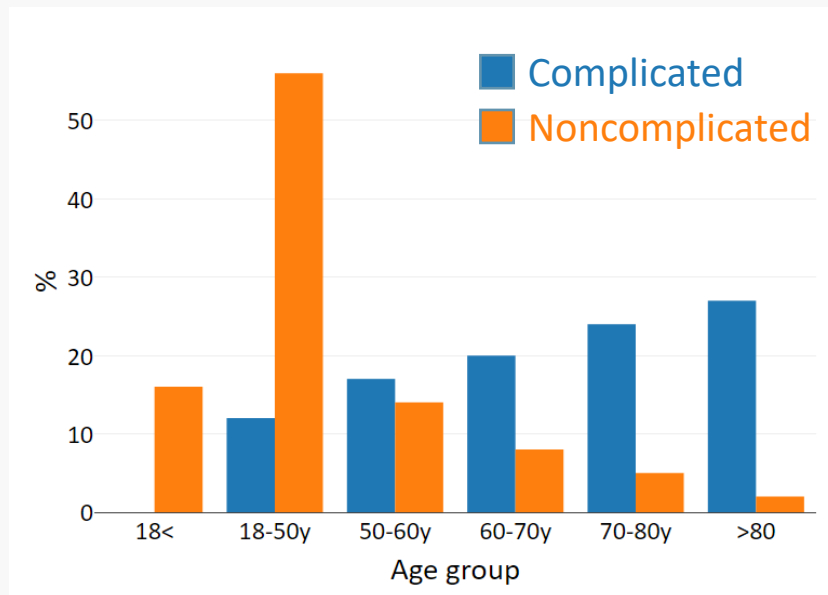
Complications vs age, sex

Prevalence of COVID-19 complications increased with age and more steeply for men than for women
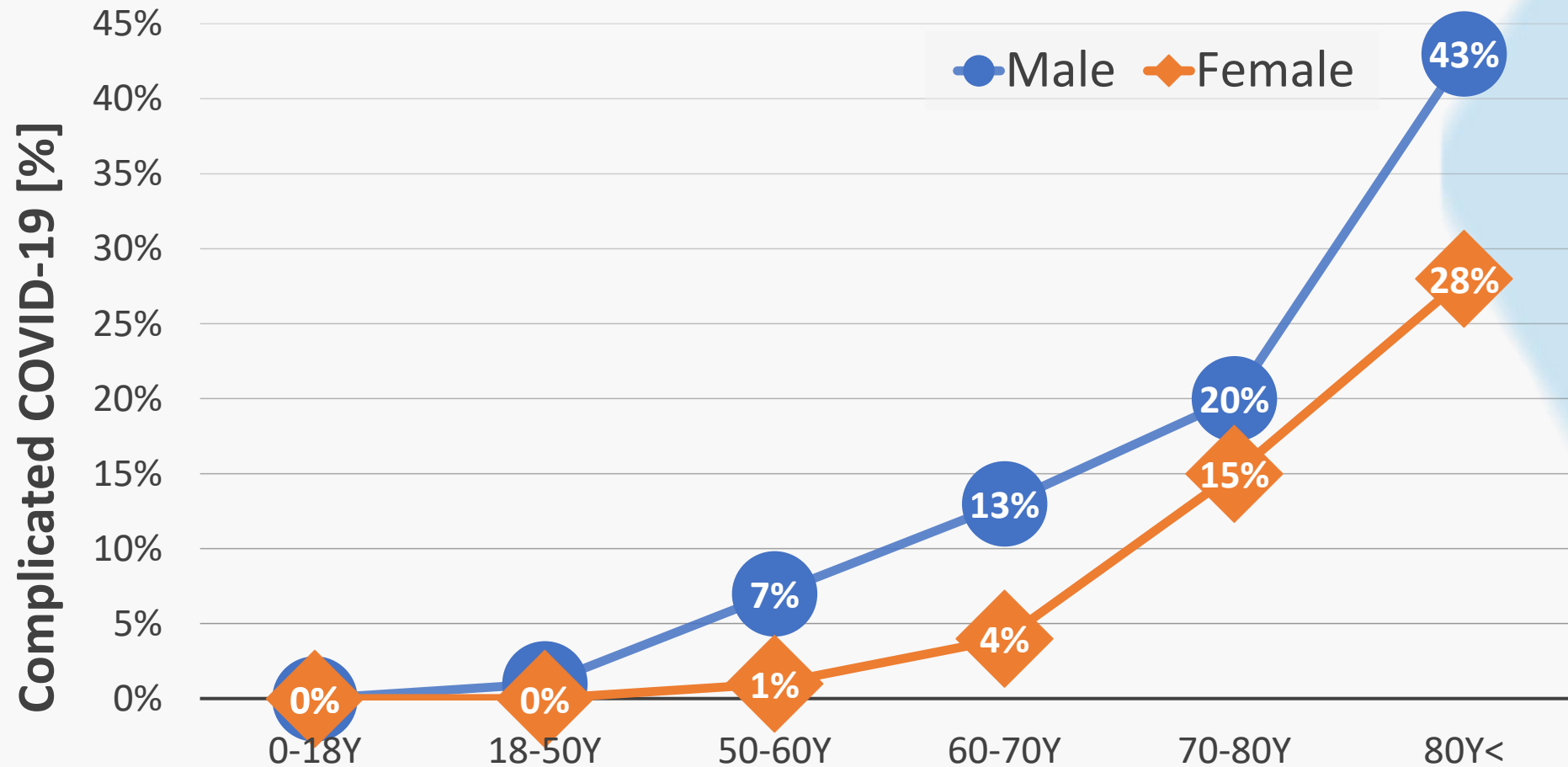
Stratification by Age

Condition	Age group	Patient counts, n				OR[a] (95% CI)	P value[b]
		With condition		Without condition			
		Complicated	Noncomplicated	Complicated	Noncomplicated		
Obesity	18-50 years	14	356	7	1977	11.09 (4.15-32.67)	<.001
Depression	18-50 years	7	229	14	2104	4.59 (1.55-12.3)	.03
Hypertension	18-50 years	4	72	17	2261	7.37 (1.76-23.41)	.04
Liver disease	18-50 years	5	125	16	2208	5.51 (1.55-16.07)	.04
Chronic kidney disease	50-65 years	14	87	27	683	4.06 (1.89-8.38)	.005
End stage renal disease	50-65 years	5	8	36	762	13.11 (3.21-48.19)	.006
Neurological disorders	≥65 years	54	113	57	317	2.65 (1.69-4.17)	<.001
Chronic kidney disease	≥65 years	70	174	41	256	2.51 (1.6-3.97)	.001
Other cardiovascular diseases	≥65 years	36	70	75	360	2.46 (1.49-4.05)	.006
Cognitive impairment	≥65 years	28	52	83	378	2.45 (1.4-4.22)	.02
Home care	≥65 years	16	22	95	408	3.12 (1.47-6.48)	.02
Hypertension	≥65 years	82	249	29	181	2.05 (1.27-3.4)	.03
Cardiovascular diseases	≥65 years	50	129	61	301	1.91 (1.22-2.99)	.03
Nursing home	≥65 years	20	35	91	395	2.48 (1.29-4.65)	.04

Stratification by (Age, Sex)

Condition	Age, sex group	OR[a]	P value[b]
End stage renal disease	<65 years; female	75.7 (6.23-570.01)	.01
Immunosuppression	<65 years; female	14.35 (2.25-69.89)	.03
Chronic kidney disease	<65 years; female	11.3 (1.78-54.41)	.04
Chronic kidney disease	<65 years; male	8.16 (3.82-16.5)	<.001
Hypertension	<65 years; male	4.56 (2.35-8.55)	<.001
Obesity	<65 years; male	3.4 (1.88-6.14)	.001
Hospitalization	<65 years; male	3.32 (1.79-6.04)	.004
End stage renal disease	<65 years; male	14.67 (2.38-66.53)	.03
Diabetes	<65 years; male	3.16 (1.32-6.79)	.04

| Condition	Age, sex group	OR[a]	P value[b]
Neurological disorders	≥65 years; female	3.55 (1.68-7.74)	.008
Chronic kidney disease	≥65 years; female	3.45 (1.57-8.06)	.02
Home care	≥65 years; female	3.72 (1.38-9.69)	.04
Other cardiovascular diseases	≥65 years; female	2.94 (1.3-6.51)	.04
Cardiovascular diseases	≥65; femal	2.76 (1.29-5.85)	.045
Cognitive impairment	≥65 years; male	4.18 (1.81-9.72)	.009
Depression	≥65 years; male	2.94 (1.55-5.58)	.01
Neurological disorders	≥65 years; male	2.56 (1.38-4.73)	.02
End stage renal disease	≥65 years; male	2.88 (1.39-5.9)	.03
Chronic kidney disease	≥65 years; male	2.24 (1.26-4.02)	.03
Fluid and electrolyte disorders	≥65 years; male	2.99 (1.39-6.38)	.03

Results Summary

- Many conditions highlighted by our analysis have been previously reported and are part of commonly used at-risk definitions (e.g., CDC's)
  - hypertension, obesity, kidney and cardiovascular diseases.
- Additional risk factors: depression, cognitive and neurological disorders
- Reduced importance of respiratory diseases and smoking

Limitations

- EHR data may be incomplete, inaccurate
- Limited number of complicated patients (<200), follow up time
- Healthcare policies (testing criteria) may introduce biases
- Univariate analysis, unable to uncover complex relations
- Risk factors in other geographies may differ

More on COVID-19

- Longitudinal symptom dynamics of COVID-19 infection
  - Analysis of EHR data including SARS-CoV-2 PCR testing, primary care visits, and longitudinal self-reported symptom surveys
  - Preprint on medRxiv
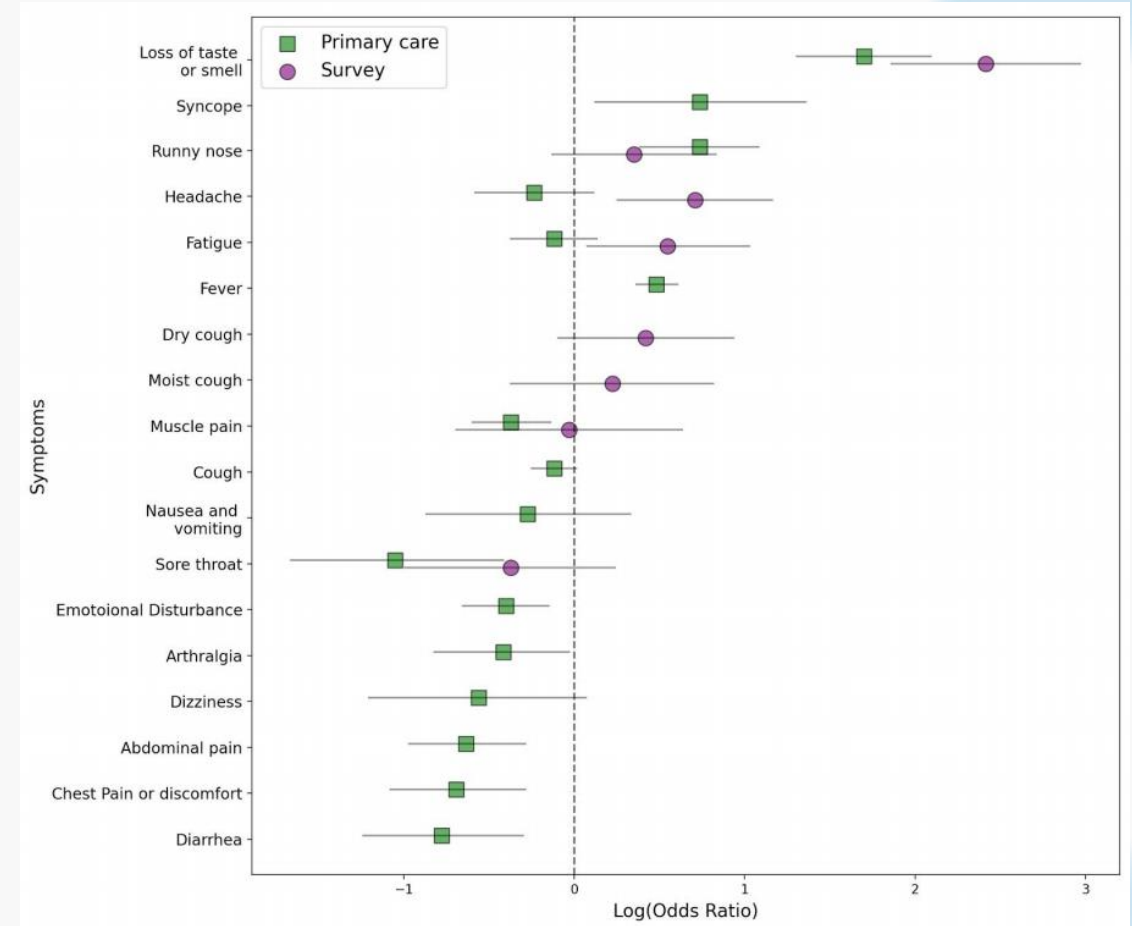
- Real-world false-negative rate of SARS-CoV-2 PCR tests

- Daily monitoring and understanding of COVID-19 morbidity in Israel

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What Factors Increase the Risk of Complications in SARS-CoV-2–Infected Patients? A Cohort Study in a Nationwide Israeli Health Organization

https://publichealth.jmir.org/2020/3/e20872/