



# Asymptomatic transmission of SARS-CoV-2

TOM BECKER

NORTHWEST PORTLAND AREA INDIAN HEALTH BOARD



# Game plan

- ▶ Review a recent mathematical modelling article on asymptomatic transmission and highlight some supportive manuscripts/data (the article seemed to be quoted a lot in national news this past week as 'gospel')

# Objectives



- ▶ Cite evidence related to the asymptomatic transmission potential for SARS-CoV-2 from pre-symptomatic and never symptomatic infected persons
- ▶ (Keep in mind that we are not talking today about % of asymptomatics in a population or in a group of people who are infected with SARS CoV-2....but transmission potential of asymptomatics)

# Take home messages

- ▶ This study is a modelling study based on certain assumptions and may not reflect reality (which is harder to study)
- ▶ Assuming 30% of all infected persons never develop symptoms and that asymptomatic persons' infectivity is 75% that of symptomatic persons, then analyses indicate:
- ▶ Asymptomatic people with SARS-CoV-2 infection account for about 50% of all transmission
- ▶ Effective control of infection spread will require reducing risk of transmission from asymptomatic, as well as symptomatic, Covid-19 patients

# Reminder about strengths of study designs re: causal inference

- ▶ RCT's
- ▶ Other clinical trials (like randomized community trials)
- ▶ Cohort studies
- ▶ Case-control studies
- ▶ Cross-sectional studies (surveys—literature reflects these)
- ▶ Case series (mostly we have these for COVID-19)
- ▶ Case studies (also a lot of these reports)
- ▶ Ecologic studies (also some new designs)



# Additional designs

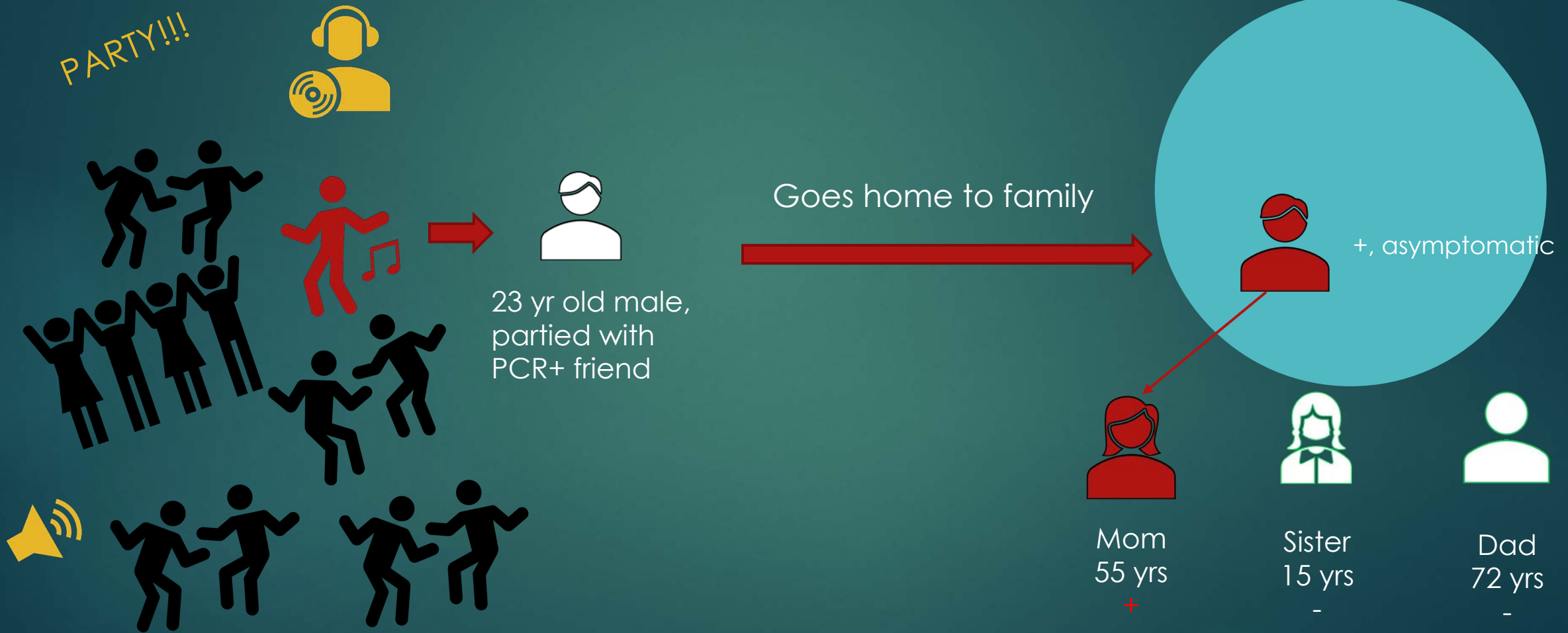
- ▶ Meta-analyses of articles that track same outcome/s
- ▶ Mathematical modelling studies



# Case presentation—asymptomatic transmission in California

- ▶ Family of four living in Southern California
- ▶ 23 year old son, h/o liking to party, contacted by a friend who was symptomatic and tested SARS-CoV-2 positive on PCR
- ▶ 23 year old family index case, who was completely asymptomatic, tested positive by PCR
- ▶ 55 year old mom, no significant med hx, soon tested positive after a day of cough, fever, malaise
- ▶ 72 year old high-risk dad and 15 year old daughter tested multiple times and remained negative

# Transmission





# Outcomes of family

- ▶ Son remained asymptomatic since first test, quarantined (but did not isolate) at home
- ▶ Mom had 8 days of fever, malaise, cough; quarantined at home (did not isolate). No shortness of breath.
- ▶ Dad tested 4 times over 10 days, remained negative on PCR and no signs or symptoms of Covid-19 disease
- ▶ Daughter tested 4 times over same period, also negative on all tests and no signs or symptoms of disease

# Background



- ▶ Lab studies confirm that levels of viral RNA in respiratory secretions are already high at the time symptoms/signs of Covid-19 appear
- ▶ Lab and epi data suggest that never symptomatic Covid-19 patients may be as likely as symptomatic persons to transmit SARS CoV-2 infection
- ▶ Estimates of never symptomatic cases range from 0 to 50%, depending on the population and study reported

# Important definition for the Johansson study (JAMA 2021)

Asymptomatic transmission includes both:

- ▶ Pre-symptomatic transmission from people who later develop Covid-19 signs and symptoms
- ▶ Never symptomatic transmission

# Methods, Johansson et al

- ▶ Authors evaluated articles (mostly from China) that addressed symptomatic, pre-symptomatic, and never symptomatic transmission re: multiple parameters, such as day of maximum infectivity, length of infectious period
- ▶ Articles in meta-analysis had to meet pre-determined criteria to be included for estimates of parameters relevant to transmission
- ▶ Using R software for analysis and employing best estimates of infectivity, day of illness when infection risk is highest, and other parameters...the authors varied the parameters and re-did all analyses with the different parameters (sensitivity analysis)
- ▶ Presented data in graphic form (in part)

**Table. Key Assumptions and Evidence Informing Those Assumptions**

Source	Evidence base	Estimate or assumption
<b>Assumptions for presymptomatic transmission</b>		
Peak infectiousness relative to onset, d		
Casey et al, 2020 <sup>18</sup>	Range, 17 studies	-3 to 1.2 d
Assumed baseline	NA	0 d
Assumed range	NA	-2 to 2 d

## Assumptions for never symptomatic transmission

### Proportion never symptomatic

Oran et al, 2020 <sup>12</sup>	Inferred range, 16 studies	30% to 45%
Buitrago-Garcia et al, 2020 <sup>14</sup>	Meta-estimate, 7 studies	26% to 37%
Davies et al, 2020 <sup>20</sup>	Age-dependent estimate, 6 studies	20% to 70%
Assumed baseline	NA	30%

### Relative infectiousness of individuals who never have symptoms



Lee et al, 2020 <sup>9</sup>	303 patients, assessment of viral shedding	Approximately 100%
Chaw et al, 2020 <sup>15</sup>	1701 secondary contacts	40% to 140%
Mc Evoy et al, 2020 <sup>16</sup>	Inferred range, 6 studies	40% to 70%
Assumed baseline		75%

### Overall proportion of individuals who never have symptoms transmission

Assumed range	NA	0% to 70%
---------------	----	-----------

# Under most reasonable set of assumptions, based on meta-analysis-derived assumptions:

- ▶ 59% of all transmission is from asymptomatic persons, both categories of asymptomatic combined
- ▶ From patients who never develop symptoms: account for 24%
- ▶ From patients who eventually develop symptoms: account for 35%



Next, the authors present 6 graphs with varying assumptions affecting transmission....one example follows



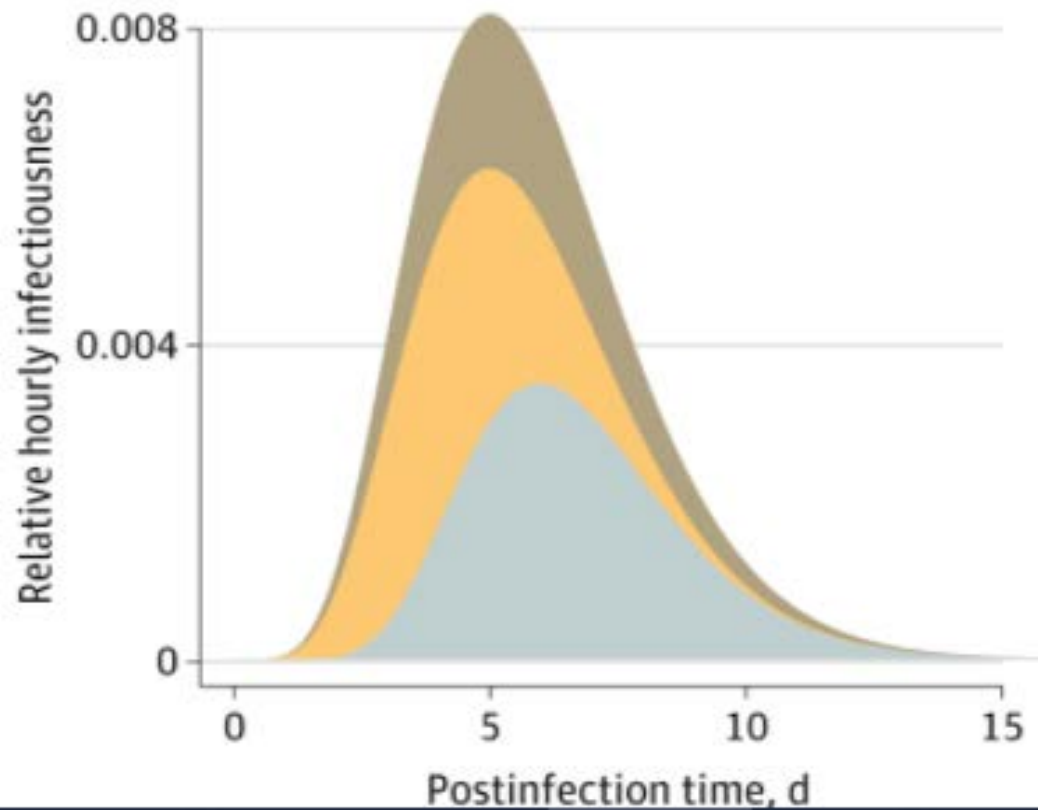
Peak infectiousness: day 5

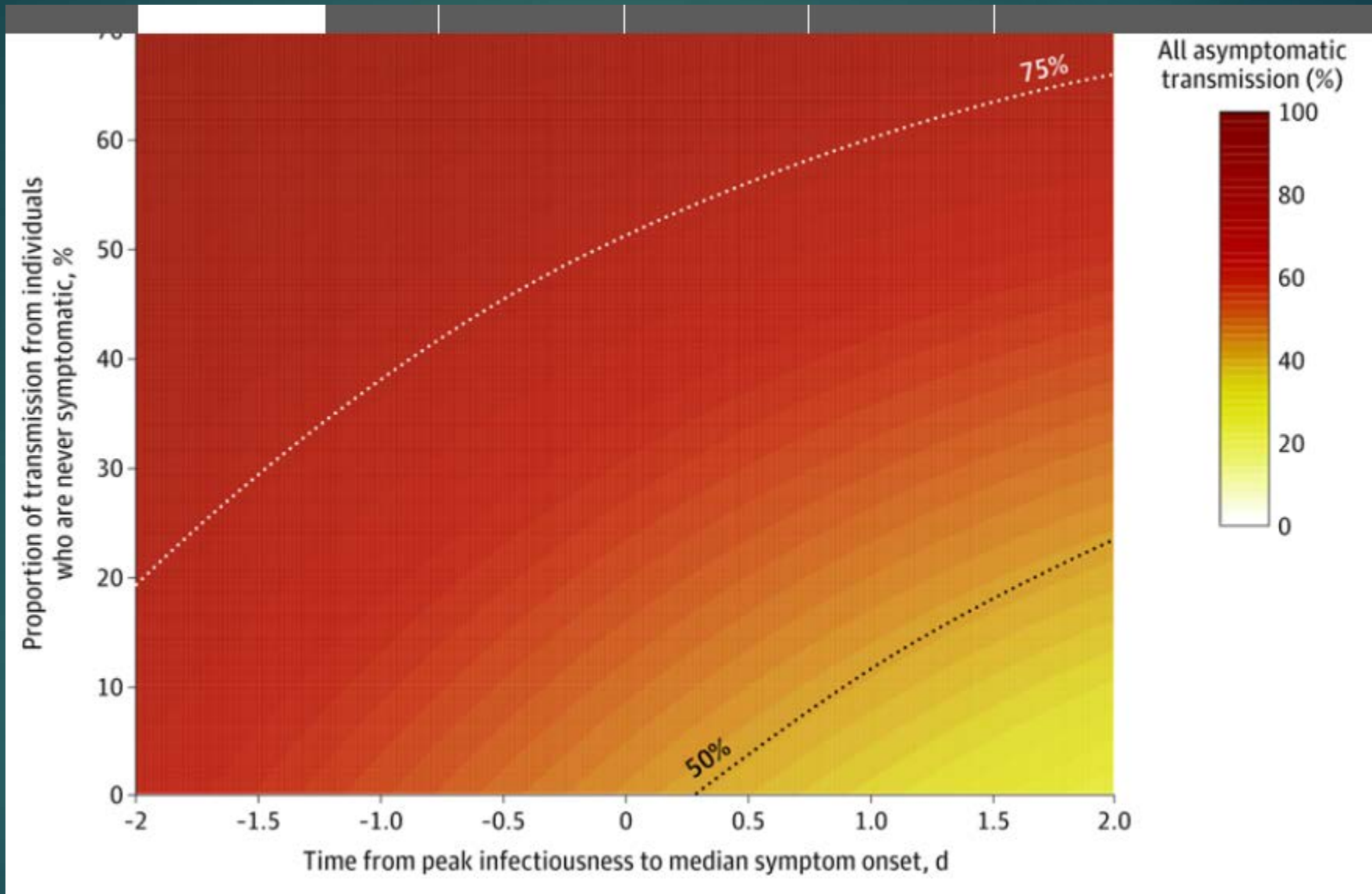
Presymptomatic: 35%

Never symptomatic: 24%

Symptomatic: 41%

**E** Transmission from individuals who are never symptomatic (24%)





# Theory/ies for less severe illness in younger people that may be relevant to the case report

- ▶ ACE2 receptors appear to be a docking station for SARS-CoV2
- ▶ Nasal biopsy study of 305 people aged 1-60 showed that ACE2 enzyme expression went up with increasing age
- ▶ Fewer receptors seems to track with less severe disease
  
- ▶ Another expert noted that adults have more ACE2 receptors in pulmonary tree than do children and young people...thus more lung disease

# Summary points

- ▶ Mathematical modelling, with parameters based on data derived from meta-analyses, may offer some new insights into disease transmission/transmission potential
- ▶ If the models are valid, we public health-oriented workers need to be concerned more about asymptomatic spread (and act accordingly)
- ▶ From a 'real world' standpoint, designing and implementing experimental studies on asymptomatic SARS-CoV-2 transmission are hard to accomplish

# Take home test

- ▶ How would you design an actual study (not theoretical) to evaluate asymptomatic transmission of SARS-CoV-2?



# References

- ▶ Johansson Michael, et al. SARS-CoV-2 transmission from people without symptoms. *JAMA Network Open* 2021; 4(1): e2035057
- ▶ Once again, thanks to Grazia Ori Cunningham, MPH