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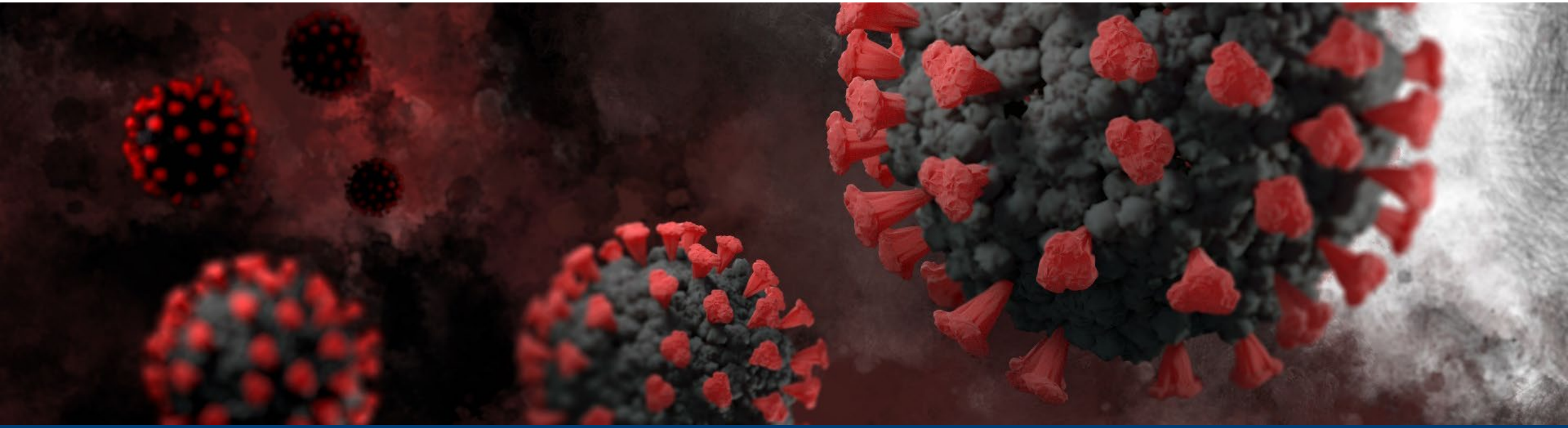


The intersection of two pandemics: Obesity & COVID-19

Winter 2022

Learning Objectives

- At the end of this educational activity, participants should be able to:
  - Describe the role of obesity as a significant and potentially modifiable risk factor for increased COVID-19 infection severity and the development of more severe disease sequelae after infection.
  - Provide an overview of the correlations between obesity and the risk of developing post-COVID-19 syndrome.
  - Discuss the reciprocal relationship between obesity and the COVID-19 pandemic.
  - Identify how health disparities contribute to both obesity and COVID-19 infection risks and outcomes.
  - Recognize the long-term impact of COVID-19 on obesity rates in adults and children.

Risk for COVID-19 mortality

- The two factors most strongly associated with COVID-19 death were:
  - Obesity
  - Hypertension

Obesity as a negative prognostic indicator

- People with obesity are at a:
  - Higher risk of being SARS-CoV-2-positive (OR 1.46, 95% CI 1.30–1.65)
    - Higher risk of complications in the COVID-19 disease course Hospitalization—OR 2.13 (95% CI 1.74–2.60)
    - ICU admission— OR 1.74 (95% CI 1.46–2.08)
    - In-hospital death—OR 1.48 (95% CI 1.22–1.80)
- ***Odds of severe disease increase with increasing severity of obesity***

Why are people with obesity at greater risk for more severe disease with COVID-19?

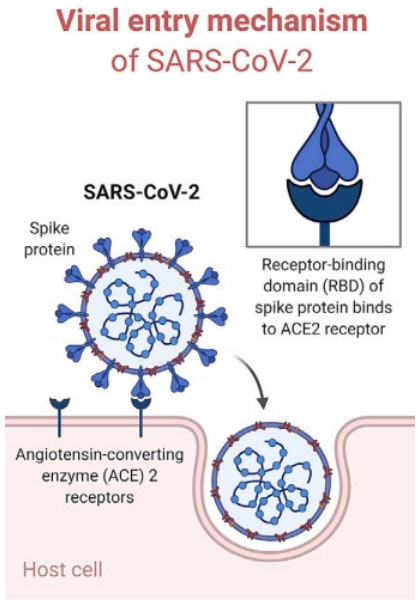
- Obesity is associated with:
  - A chronic low grade pro-inflammatory state
    - Impaired immune function
  - Altered ventilatory mechanics
  - Greater adipose tissue → ↑ opportunity for viral entry and viral replication
  - Other chronic conditions that predispose to greater risk
  - Social determinants of health (SDoH) that are associated with poorer overall health and quality of life

Obesity is a Pro-Inflammatory State

- Obesity is characterized by metabolic impairments and chronic low-grade systemic inflammation → pro-inflammatory microenvironment
  - Infection with Sars-Cov2 triggers an immune reaction that further aggravates cytokine production and ↑ the risk of cytokine storm
  - The metabolic dysregulations seen in people with obesity are closely related to an impaired immune system (both innate & adaptive) → altered response to viral infection, which leads to:
    - Greater susceptibility to infections
    - Longer viral shedding
    - Greater duration of illness and severity of the disease
- Excess adipose tissue can promote this pro-inflammatory microenvironment by altering the adipokines → favorable pro-inflammatory state:
  - ↑ leptin
  - ↓ adiponectin (anti-inflammatory) characterized by the production of adipokines (adipose-tissue derived cytokines)
    - → + macrophage production of IL-6 & TNF-α → Cytokine storm if infected with COVID-19
    - → Greater risk for septic shock, severe sepsis and death

Excess adipose tissue in COVID severity

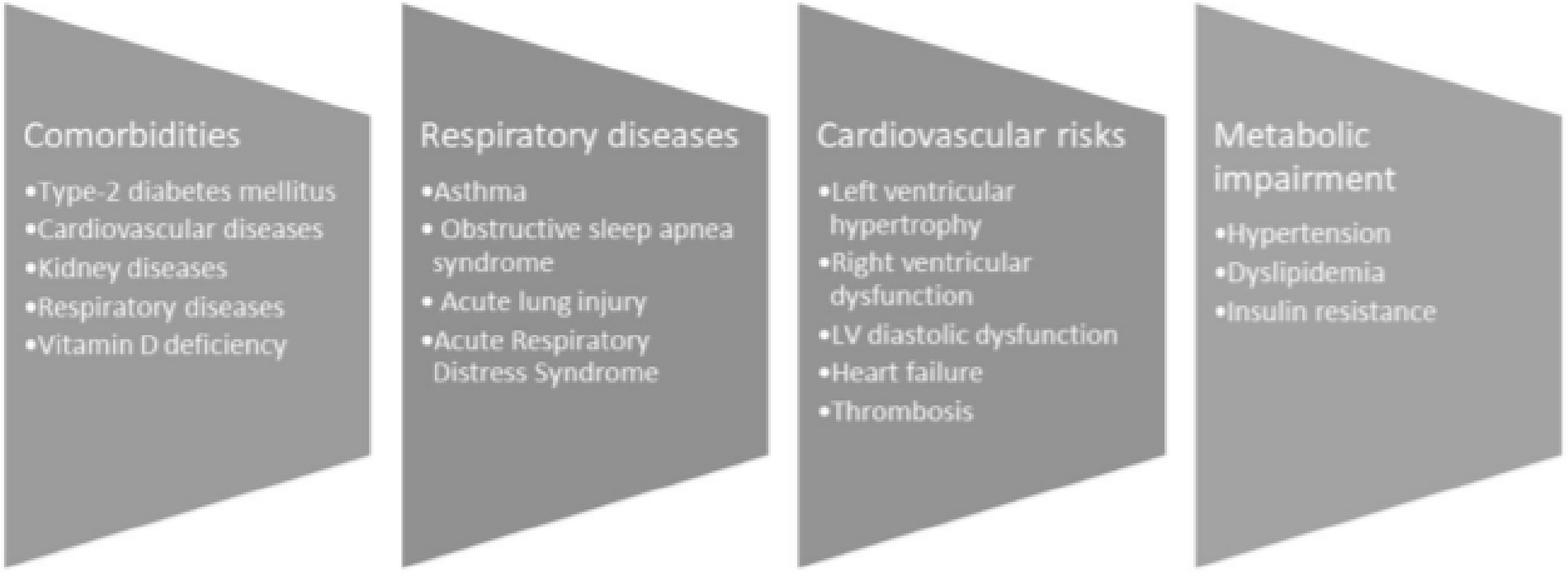
- People with obesity often develop insulin resistance and overactivity of the renin angiotensin- aldosterone system (RAAS)
  - Angiotensin Converting Enzyme-2 (ACE2): modulates blood pressure and maintains blood pressure homeostasis via negative regulation of the renin-angiotensin system (RAS)
- The ACE2 receptor is the portal of entry for COVID-19 into the body
  - People with obesity have an excess of adipose tissue
  - Adipose tissue overexpresses the ACE2 receptor → ↑ opportunity for viral replication and shedding
  - Viral shedding is also prolonged in patients with obesity due to impaired immune response
    - ↓ macrophage activation and impaired B- and T-cell responses



The role of excess adipose tissue & compromised pulmonary function

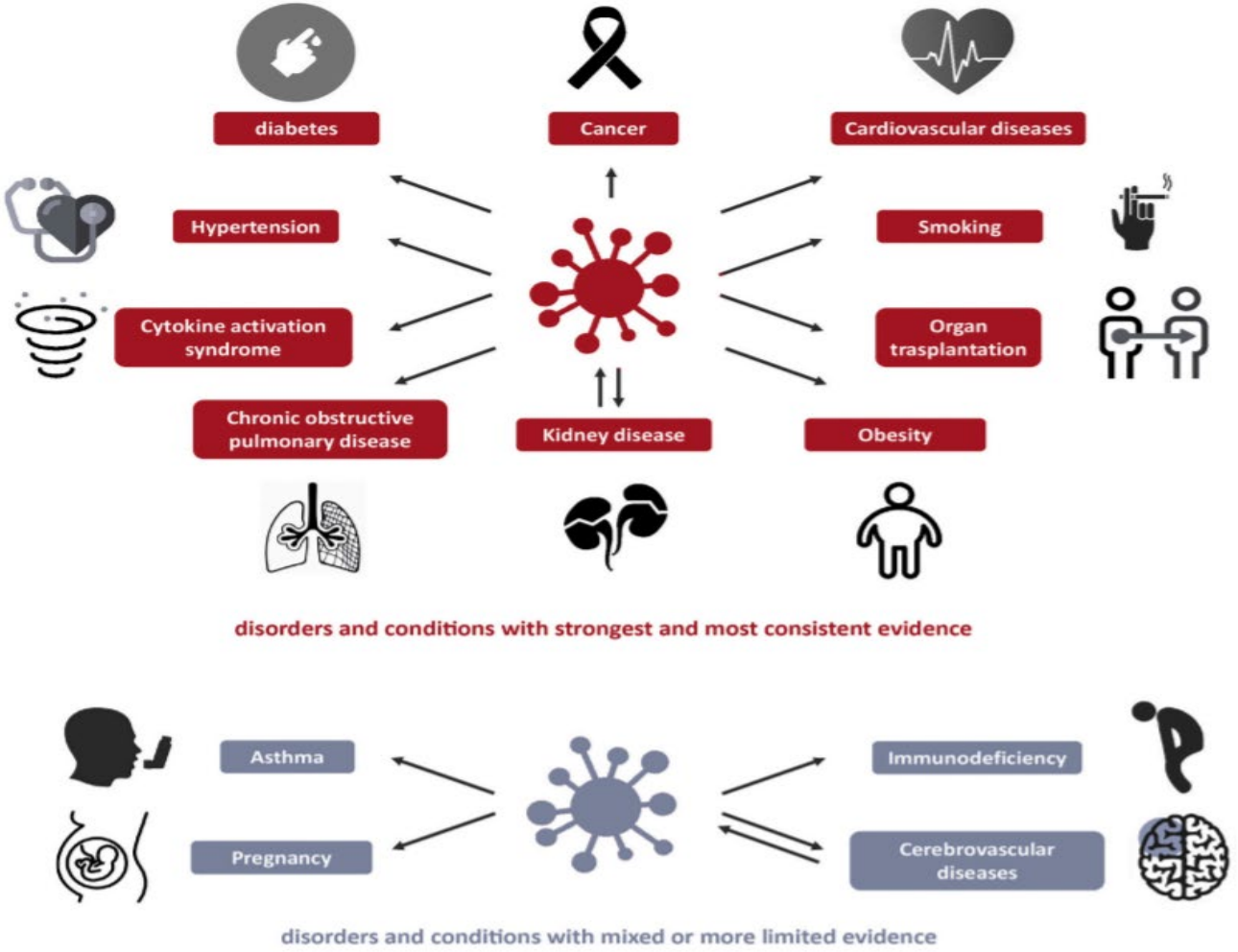
- People who have ↑ abdominal obesity may have compromised pulmonary function due to:
  - ↓ diaphragmatic excursion
  - Impaired ventilation at the bases of the lung → ↓ oxygen saturated blood levels.
- Chronic low-grade inflammation is due to ↑ levels of circulating proinflammatory cytokines, e.g. leptin, TNF-α, IL-6, may impair immune response and affect the lung parenchyma and bronchi
- Obesity is **also** associated with impaired pulmonary function due to ↓ expiratory reserve volume, functional capacity, and respiratory system compliance.
- **Obesity can lead to ↑ risk of respiratory failure, need for ICU stay and need for invasive ventilation:**
  - The degree of oxygen impairment and markers of inflammation are the strongest predictors of poor outcomes during COVID-19 hospitalization.
  - Overexpression of ACE2 receptors in the lung **and** adipose tissue → better understanding of why people with obesity have an ↑ risk for ventilation, ICU stay, and complicaion in people with obesity

Obesity is closely related other conditions that increase risk for poor outcomes after COVID-19



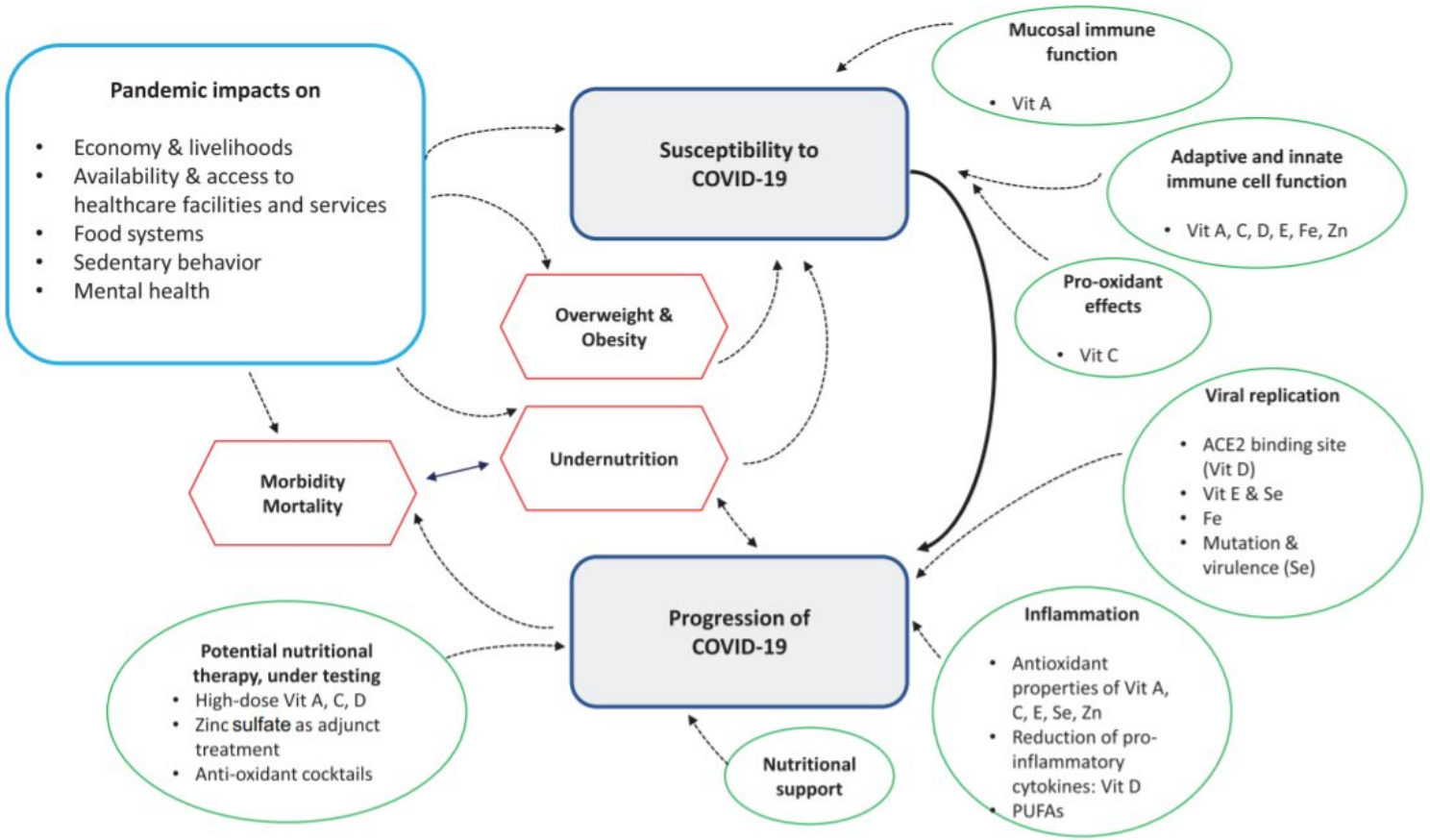
Source: Aghili et al. *Int J Obes (Lond)*. 2021 May;45(5):998-1016

Interrelations and other conditions in obesity



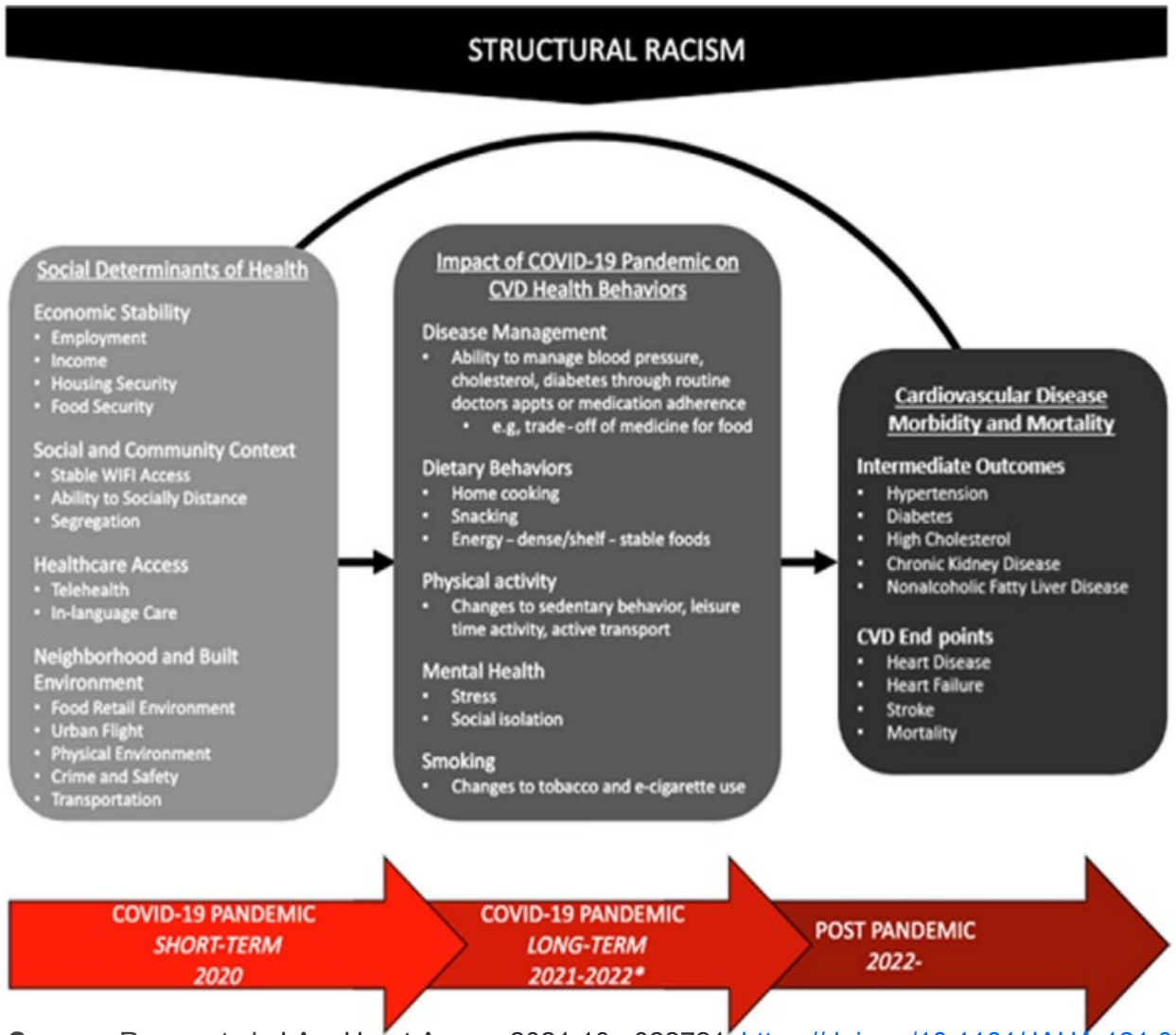
Source: Gasmi A, et al. *Clin Immunol.* 2021

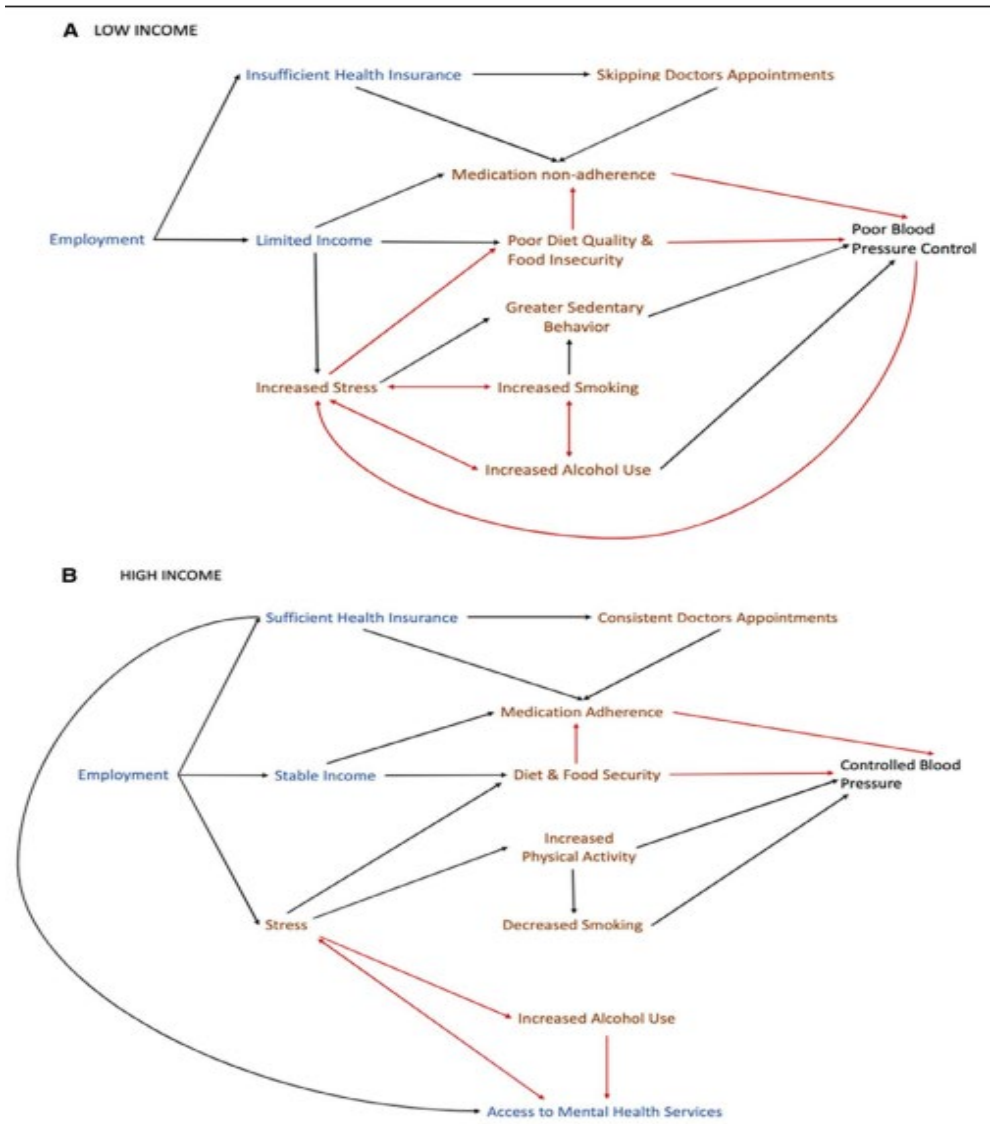
Nutrition, Obesity and COVID-19



Source: James, et al. J Nutr. 2021

Social Determinants of Health and COVID-19





Source: Russo et al. J Am Heart Assoc. 2021;10:e022721. https://doi.org/10.1161/JAHA.121.022721

COVID, Obesity and Structural Racism

- Discrimination → chronic and toxic stress
  - ↑ cravings for unhealthy foods → ↑ risk of developing obesity
  - Distrust of healthcare systems
  - Delay in care
  - ↓ uptake of vaccines

COVID-19 may have worsened the pediatric obesity pandemic

Food Insecurity and Pediatric Obesity: a Double Whammy in the Era of COVID-19

June M. Tester[1,2] · Lisa G. Rosas[3] · Cindy W. Leung[4]

Accepted: 7 October 2020

The COVID-19 pandemic: an unprecedented tragedy in the battle against childhood obesity

Maximilian Andreas Storz, MD
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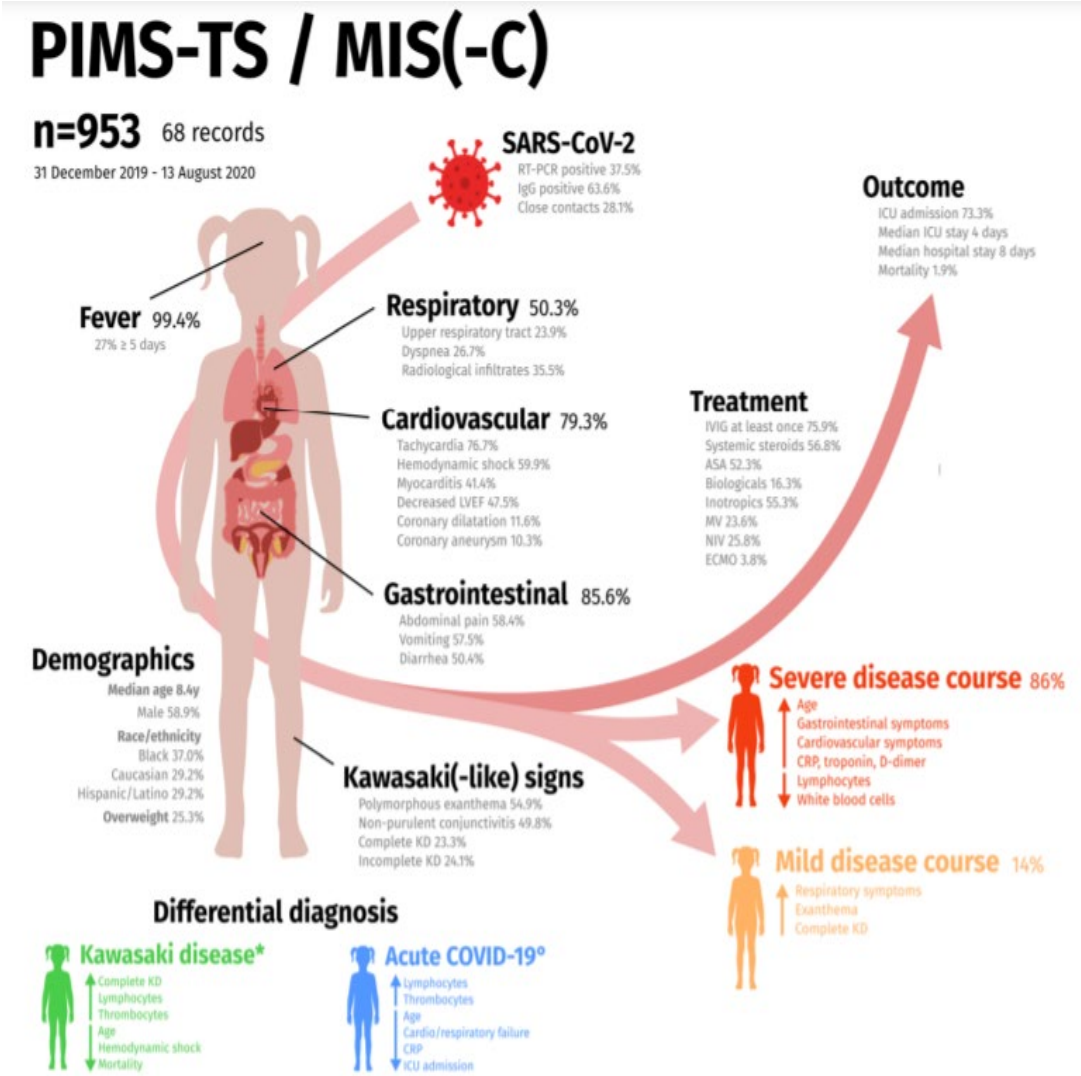
The Pediatric Face of COVID-19

- Overall, children with COVID-19 exhibit mild or asymptomatic disease
- Children with pre-existing conditions are at a ↑ risk of severe COVID-19 & associated mortality
- Childhood obesity is likely positively correlated with COVID-19 severity
- Although rare, the pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 infection (PIMS-TS) is condition of public health concern



Source: Hoste, et al. Eur J Pediatr 2021

Health disparities & COVID-19

- African-American populations experience disproportionately higher COVID-19 infection rates and excess mortality due to COVID-19,
- Hispanic populations experience disproportionately higher infection rates and excess mortality due to COVID-19, but not higher case-fatality rates, but lower than African-Americans
- African-American and Hispanic populations have an ↑ risk for hospitalization due to COVID-19
- Asian populations appear to have similar rates of infections, hospitalizations, and deaths as White populations
- American Indian, Alaska Native, and Pacific Islander populations experience excess mortality due to COVID-19, but further studies are required

- **Disparities are more likely to be due to exposure-related factors than biologic susceptibility**

What are driving the health disparities?

- Disparities in health and socioeconomic status are the primary drivers of the disproportionate burden of COVID-19 in communities of color
- These inequities make these communities more prone to chronic conditions, e.g. type-2 diabetes, obesity, and cardiovascular diseases →
  - Greater prevalence and severity of disease after COVID-19 infection
- ***The correlation between obesity, type 2 diabetes and COVID-19 infection is most pronounced in African-Americans***

Obesity increases risk for long-haul COVID

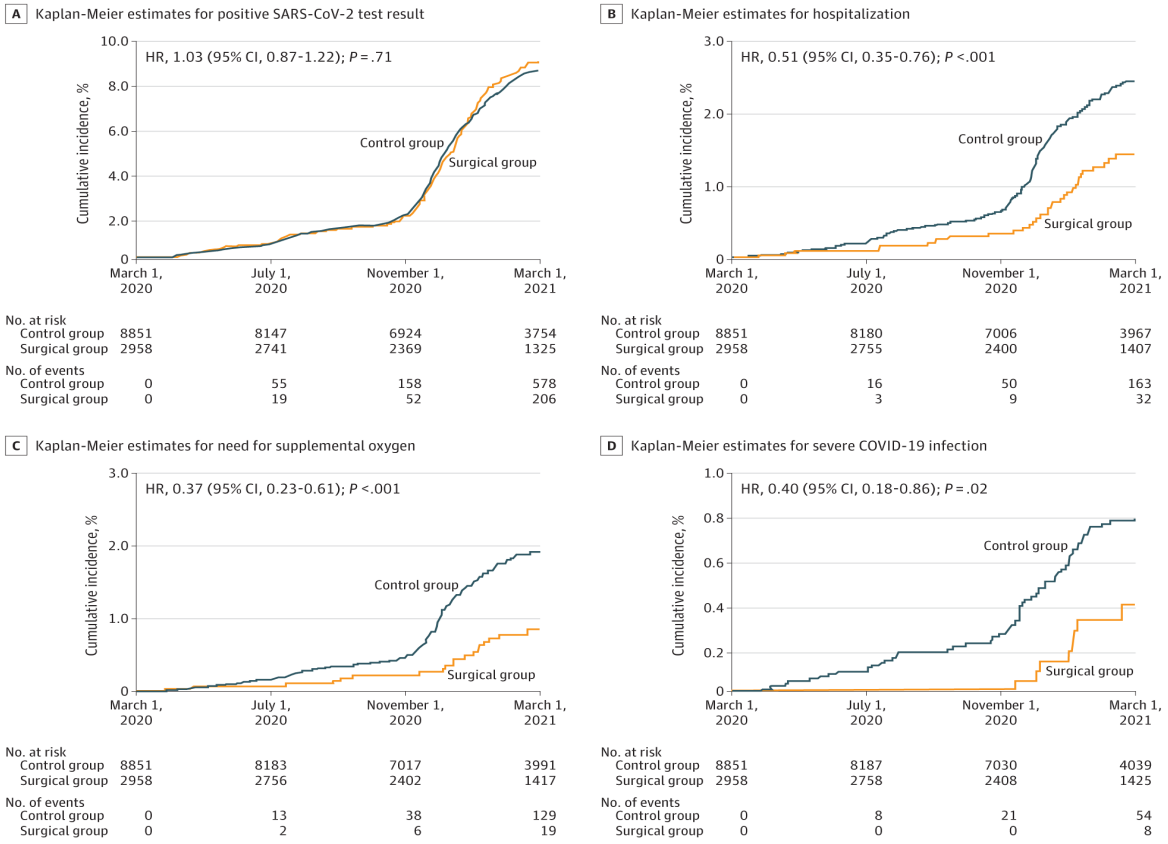
- Chronic/Post–COVID-19: Sequela of disease lasting ≥3 months
- May lead to an ↑ in:
  - Chronic medical conditions:
    - Depression
    - Stroke
    - Cardiac Injury
    - Chronic renal disease
    - Type 2 diabetes

Long term effects of COVID-19 and obesity

- A study that looked at people with a history of obesity and past-infection with COVID-19 found:
  - Persistently higher levels of inflammatory cytokines → oxidative stress
  - Impaired innate and acquired immune function, can lead to long-term metabolic disorders
  - Greater degree of lung function impairment compared to patients without obesity
  - A greater number of post-COVID symptoms
    - Most notably: poor sleep quality
    - No statistically significant differences in specific post-COVID symptoms and limitations of daily living activities
- Fatigue and dyspnea were the most prevalent long-term post-COVID symptoms
- ***The greater number of post-COVID symptoms seen in people with obesity may be due to the multifactorial and multi-system nature of the disease***

Weight loss may mitigate the impact of COVID-19 in people with obesity

- Even in those whose BMI still falls within the obese range, there is evidence that surgically induced weight loss prior to COVID-19 infection ↓ the severity of disease
  - 49% lower risk for hospitalization
  - 63% lower risk of need for supplemental oxygen
  - 60% lower risk of severe COVID-19 infection
- ***No such studies have looked at the impact of non-surgical weight loss on severity of COVID-19***



Source: Aminian et al. *JAMA Surg.* Published online December 29, 2021.

Conclusions

- Obesity is an important and modifiable risk factor that can be targeted for COVID-19 disease management
- COVID-19 presents an opportunity to activate and engage people from underserved populations in the healthcare system
- Obesity may be a modifiable risk factor in the treatment of post-COVID-19 syndrome
- The COVID-19 pandemic has exacerbated both the adult and pediatric obesity pandemics in the US and globally

Thank you.
Questions??

Appendix