

# Obesity and COVID-19

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# Disclosure

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I have no conflict of interest  
in relation to this presentation

# Content

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- Obesity and obesity-related complications are major risk factors for COVID-19.
- Why are people living with obesity at increased risk of COVID-19 infection and worse outcomes?
- Importance of more detailed phenotyping, weight gain prevention and continuous management of obesity and related complications during the COVID-19 pandemic.

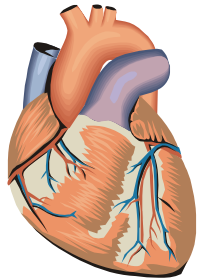
# Obesity: a gateway to many NCDs

## Prevalence

Overweight: >50%

Obesity: ~ 13%

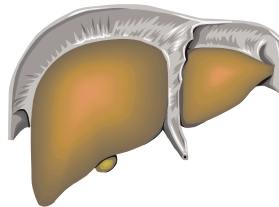
# OBESITY



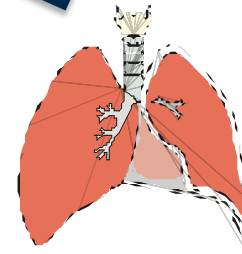
Cardiovascular disease



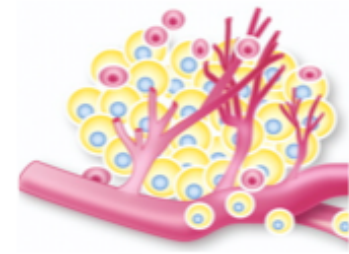
Type 2 diabetes



NAFLD



Respiratory diseases



Cancer

# Obesity and COVID-19

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- Obesity may also impact communicable diseases (i.e. independent risk factor for 2009 H1N1 influenza A virus <sup>1,2</sup>).
- Obesity-related complications are major risk factors for COVID-19. <sup>3,4</sup>

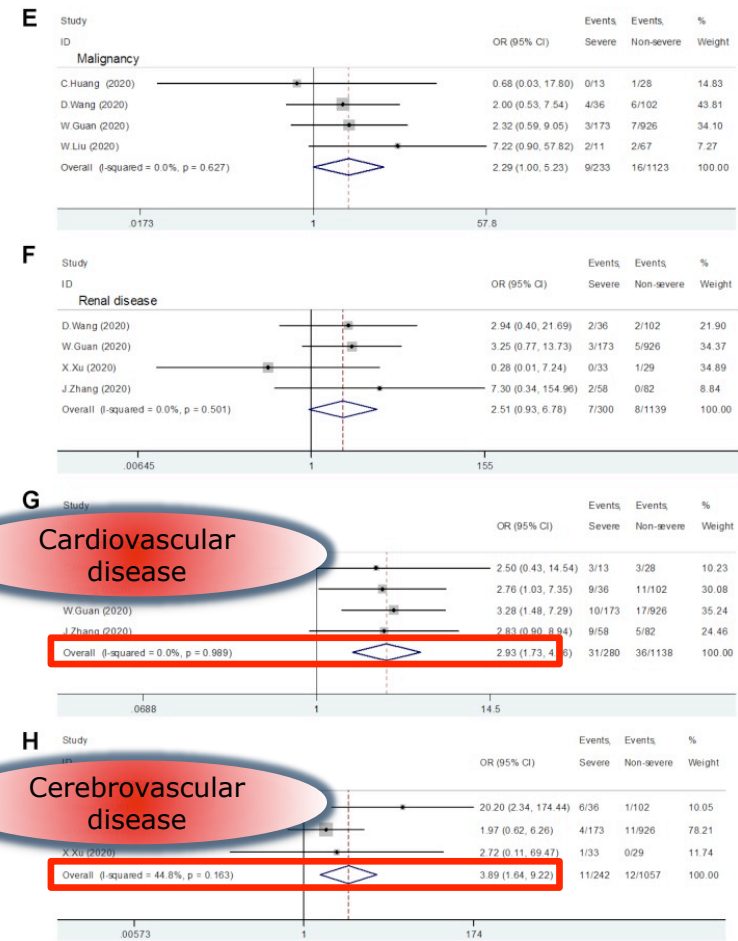
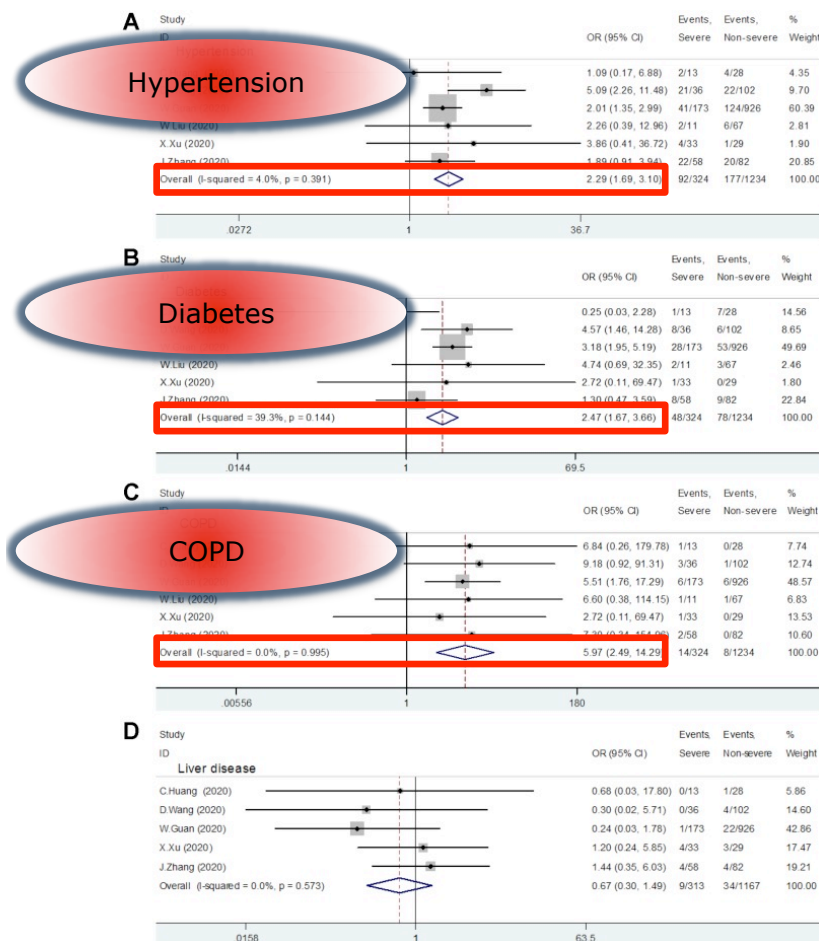
<sup>1</sup> Van Kerkhove et al., *PloS Med*, 2011

<sup>2</sup> Sun et al., *Infect Dis*, 2016

<sup>3</sup> Wang et al., *Aging*, 2020

<sup>4</sup> Goossens et al., *Obes Facts*, 2020

# Obesity-related complications and risk of COVID-19 exacerbation: a meta-analysis



(6 studies, ~1500 patients, ~20% 'severe' cases) Wang et al., Aging, 2020

# Obesity and COVID-19

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- Obesity may also impact communicable diseases (i.e. independent risk factor for 2009 H1N1 influenza A virus <sup>1,2</sup>).
- Obesity-related complications are major risk factors for COVID-19. <sup>3,4</sup>
- Obesity is an independent determinant of COVID-19 severity and outcomes. <sup>4,5</sup>

<sup>1</sup> Van Kerkhove et al., *PloS Med*, 2011

<sup>2</sup> Sun et al., *Infect Dis*, 2016

<sup>3</sup> Wang et al., *Aging*, 2020

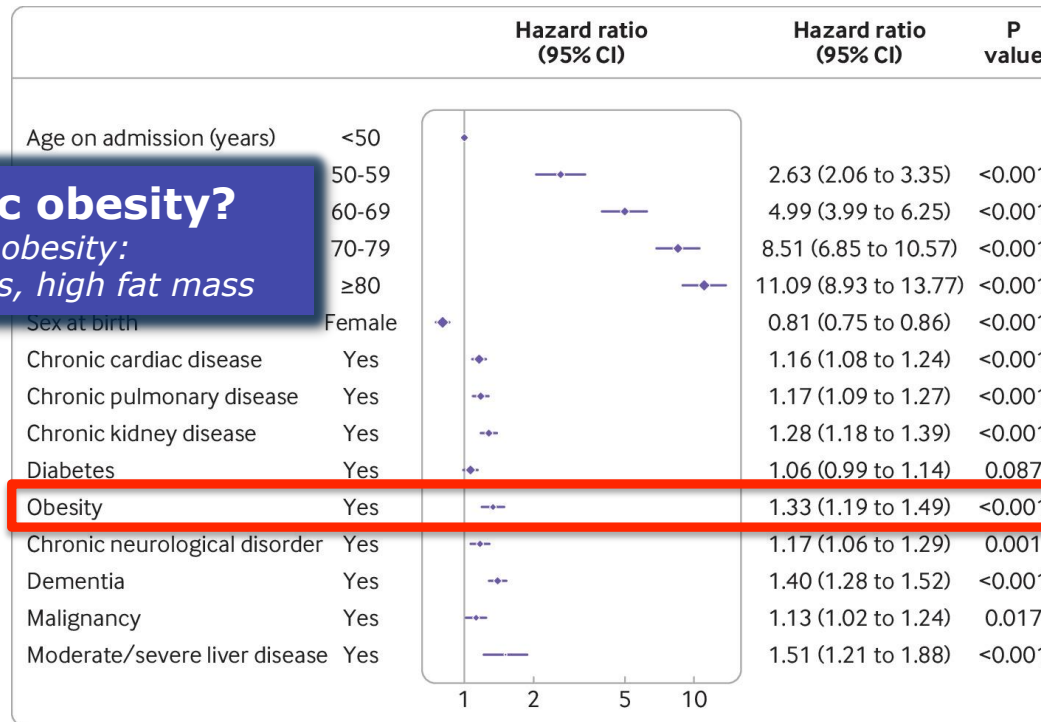
<sup>4</sup> Goossens et al., *Obes Facts*, 2020

<sup>5</sup> Docherty et al., *BMJ*, 2020

# Obesity: An independent determinant of mortality in COVID-19 patients

Prospective observational cohort study >20,000 hospital inpatients with COVID-19 (UK)

**Sarcopenic obesity?**  
*'hidden' obesity:*  
*low muscle mass, high fat mass*

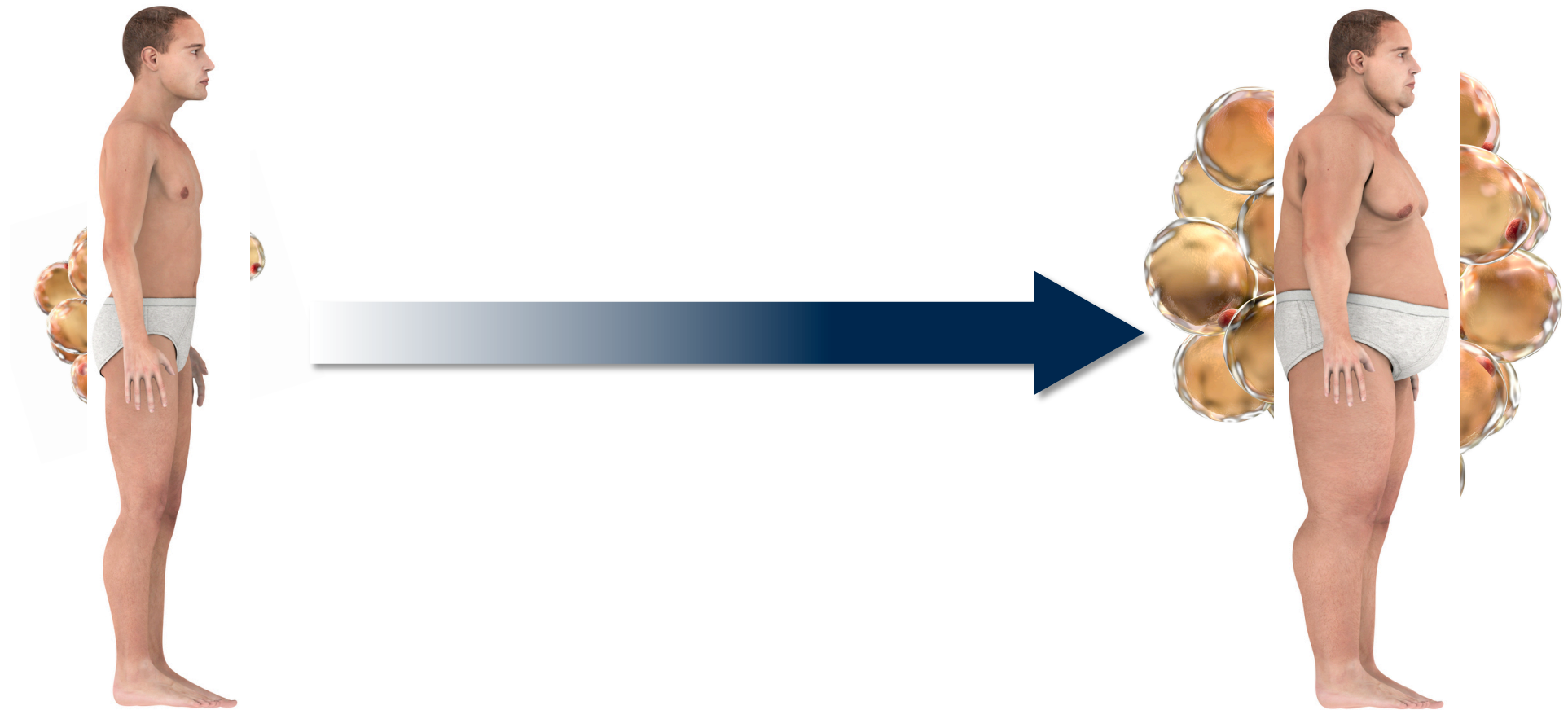


**Increasing age, male sex, and chronic comorbidity, including obesity, were independent risk factors for mortality**



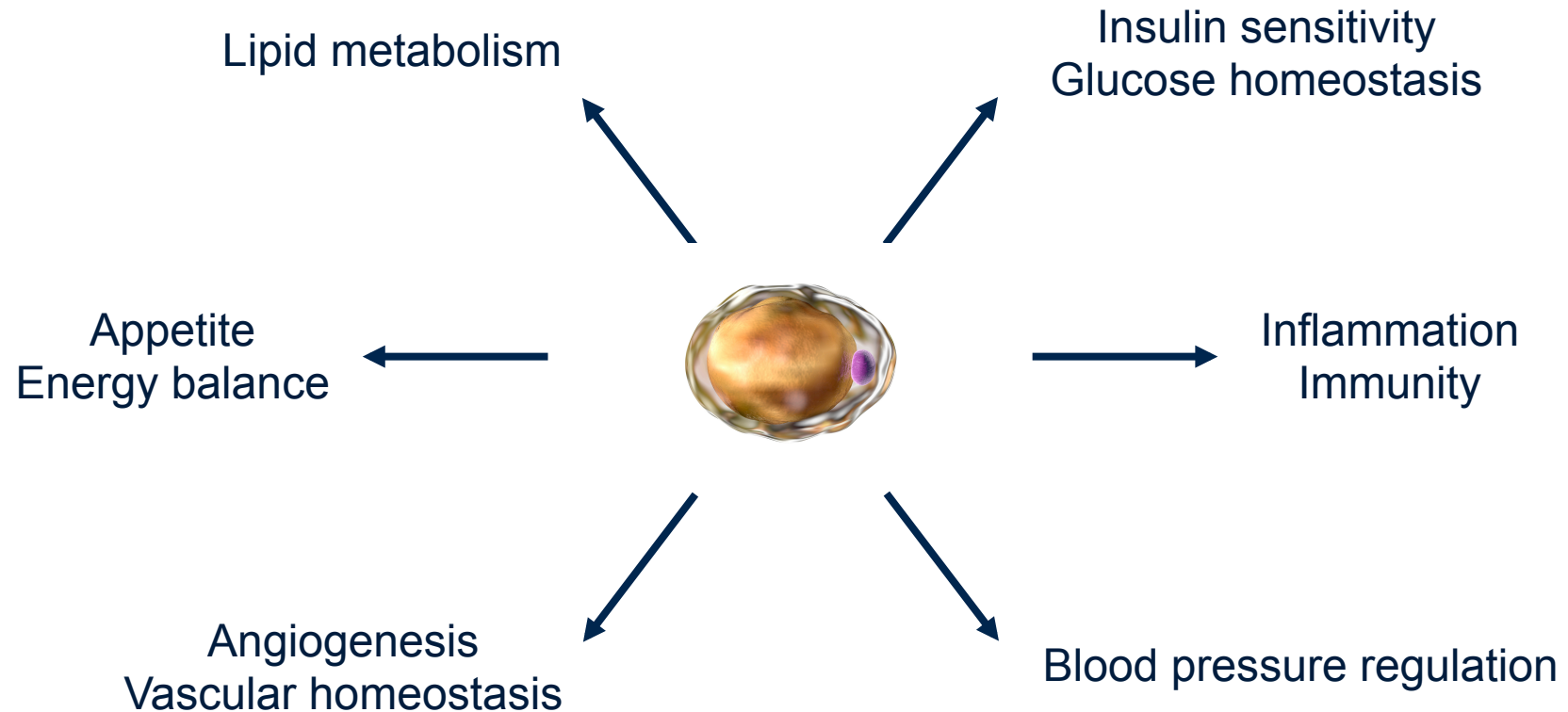
Why are people living with obesity at increased risk of COVID-19 infection and worse outcomes?

# Fat cell enlargement in obesity



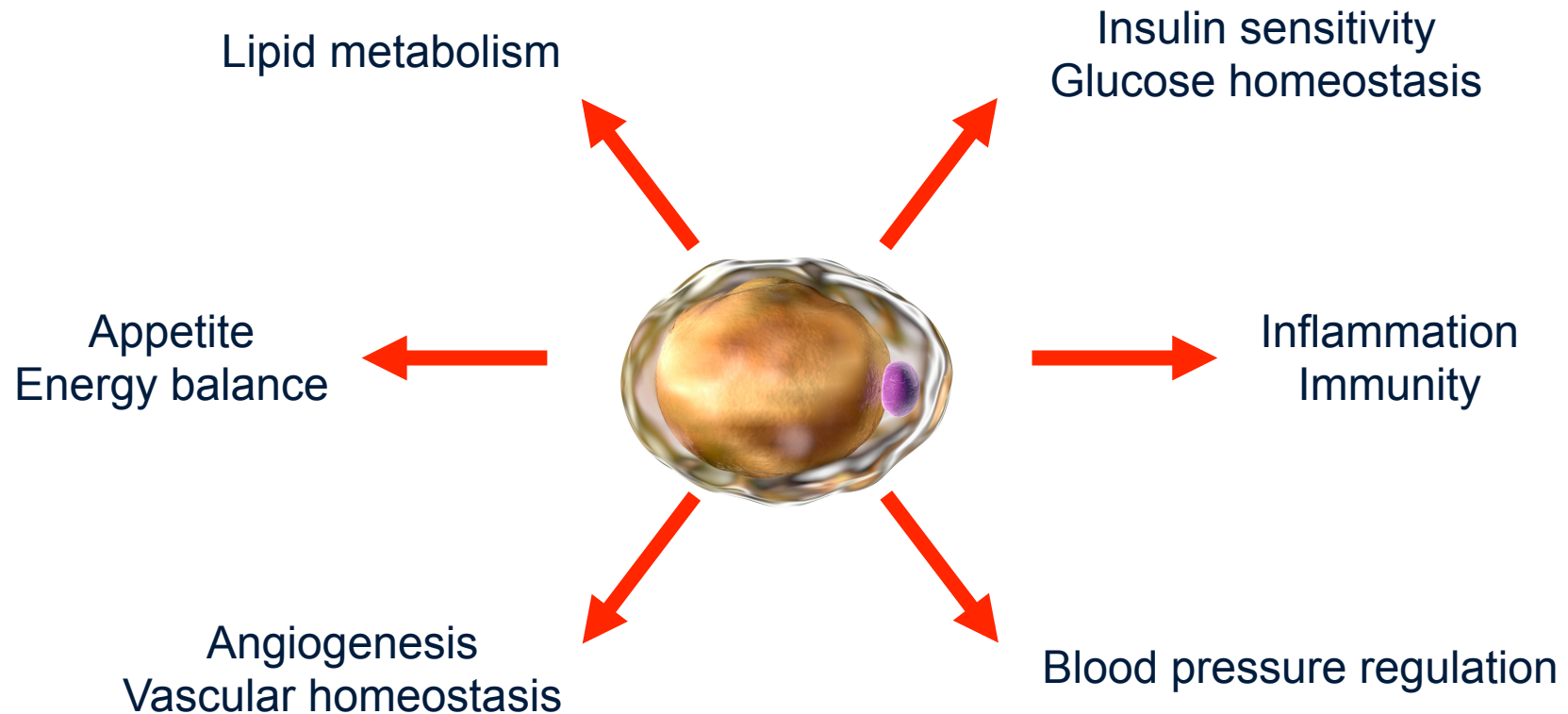
# Adipose tissue is a highly dynamic, metabolically active, endocrine organ

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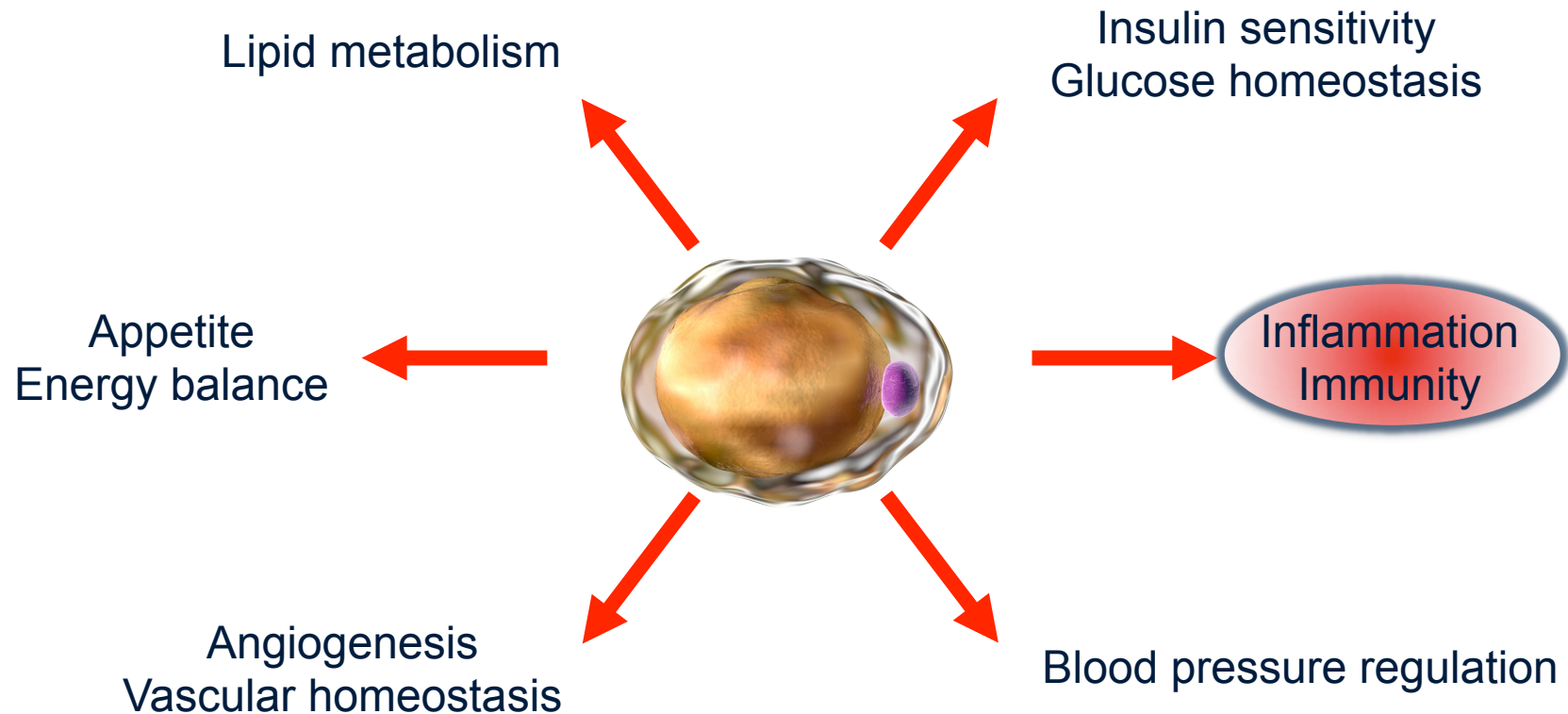
# Impaired endocrine function of adipose tissue in people living with obesity

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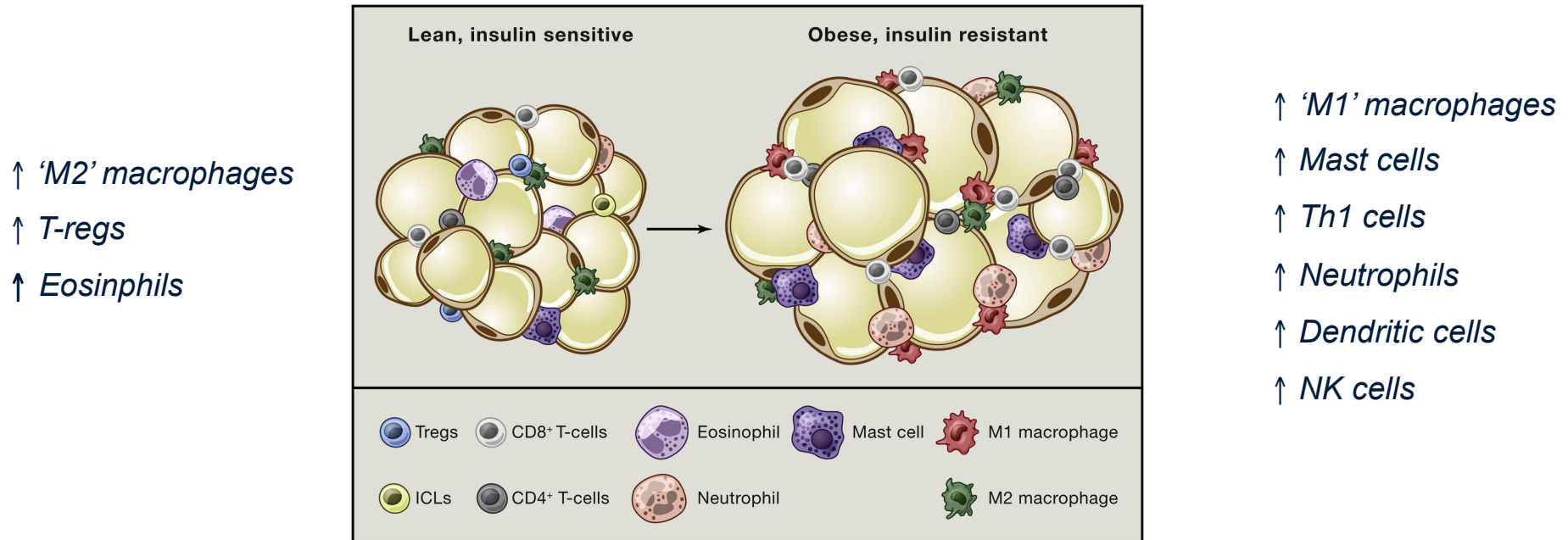


# Impaired endocrine function of adipose tissue in people living with obesity

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# Dynamic changes in immune cell populations in WAT during the development of obesity



**A proinflammatory adipose tissue phenotype in obesity is closely related to sustained low-grade systemic inflammation, obesity-related complications, and NCDs**

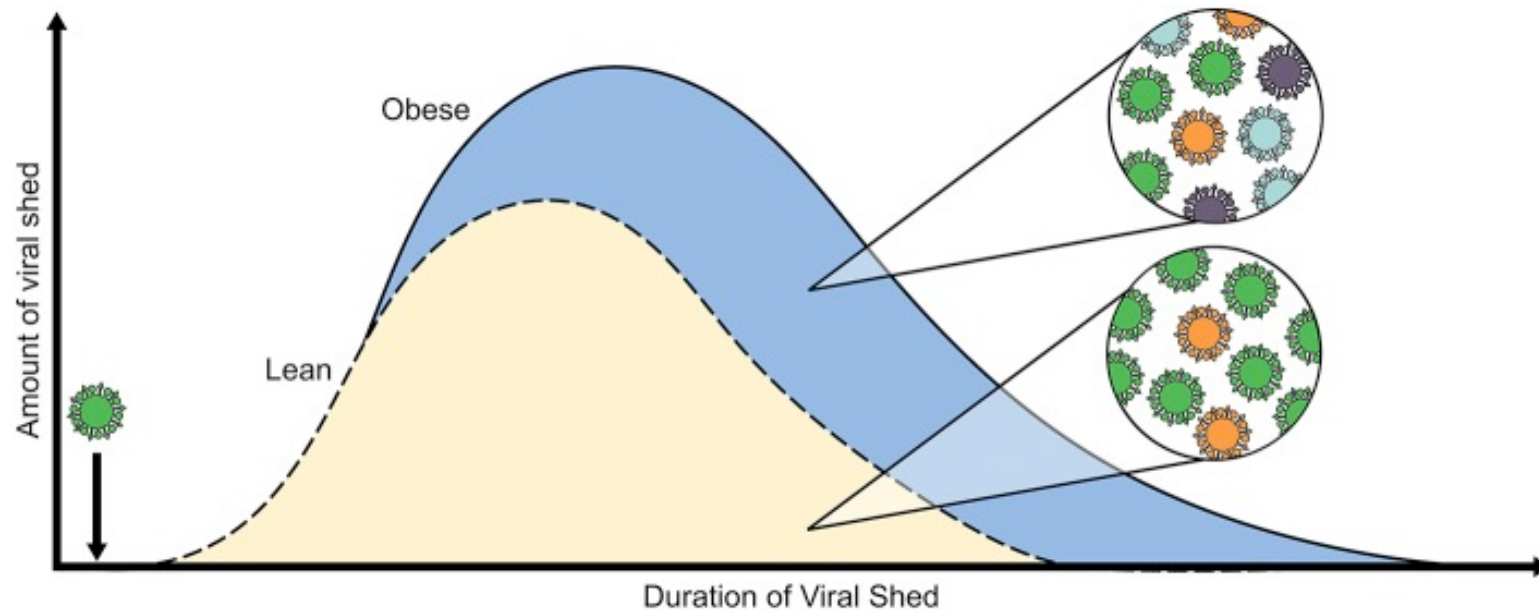
# Immunological perturbations in obesity impact the response to infection

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- T cells exert a key role in the response to infection by supporting the function and regulating activation of other immune cells to produce pro-/anti-inflammatory factors.
- **Obesity**
  - Dampened and delayed antiviral responses to infection (i.e. reduced efficacy of T and B cell responses).
  - Reduced effectiveness of antivirals and vaccination.
  - Increased viral load and life cycle.

*Green & Beck, Curr Opin Immunol, 2017*  
*Dhurandhar et al., Obes Rev, 2015*  
*Honce et al., Front Immunol, 2019*  
*Goossens GH, Obes Facts, 2020*

# Increased viral load and extended infections in the obese host



**Poorer outcomes and recovery from infections in obesity**



# Obesity and COVID-19: Shared immunological perturbations

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- SARS-CoV-2 invasion → host immune response.
- A robust and persistent antiviral immune response might induce massive production of inflammatory cytokines  
→ 'Inflammatory cytokine storm' → **organ damage.**
- **COVID-19 patients**  
Increased proinflammatory cytokines (i.e. IL-6, TNF $\alpha$ ) and lower CD4+ and/or CD8+ T cell and total T lymphocyte count in more severe cases (i.e. severe pneumonia / ICU)  
→ '**Cytokine storms**' related to **COVID-19 severity.**

*Perlman & Dandekar, Nat Rev Immunol, 2005*

*Xu et al., Lancet Resp Med, 2020*

*Chen et al., J Clin Invest, 2020*

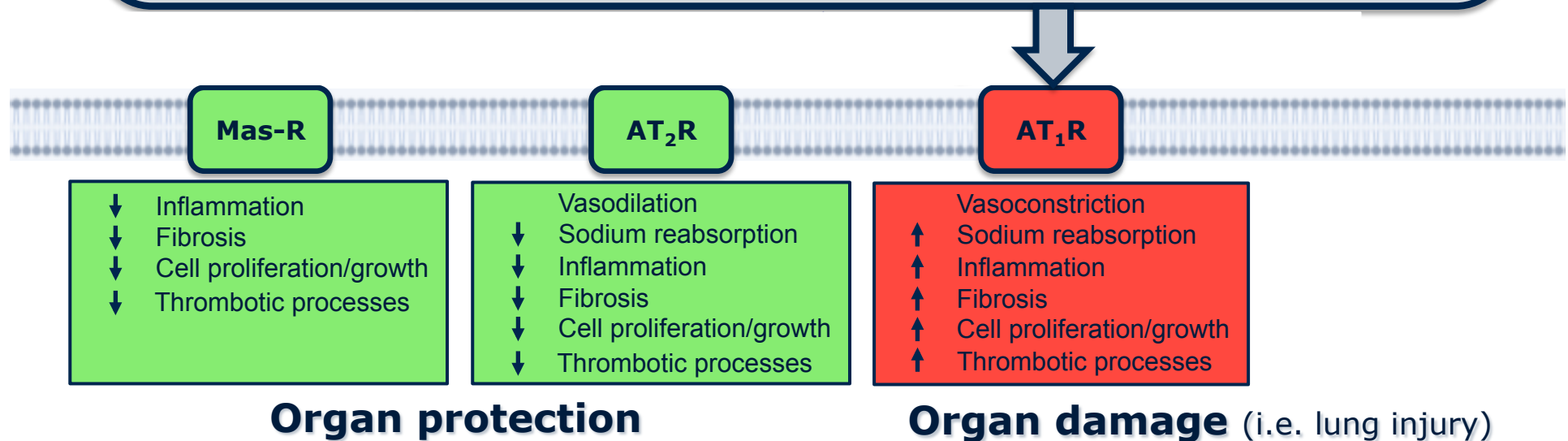
*Huang et al., Cytokine Part A, 2020*

*Goossens GH, Obes Facts, 2020*

# Obesity – inflammation – COVID-19: A key role for the renin-angiotensin system?

## Increased RAS activity in obesity and many NCDs

(i.e. cardiovascular diseases, diabetes, kidney disease, pulmonary disease)



# Obesity – inflammation – COVID-19: A key role for the renin-angiotensin system?

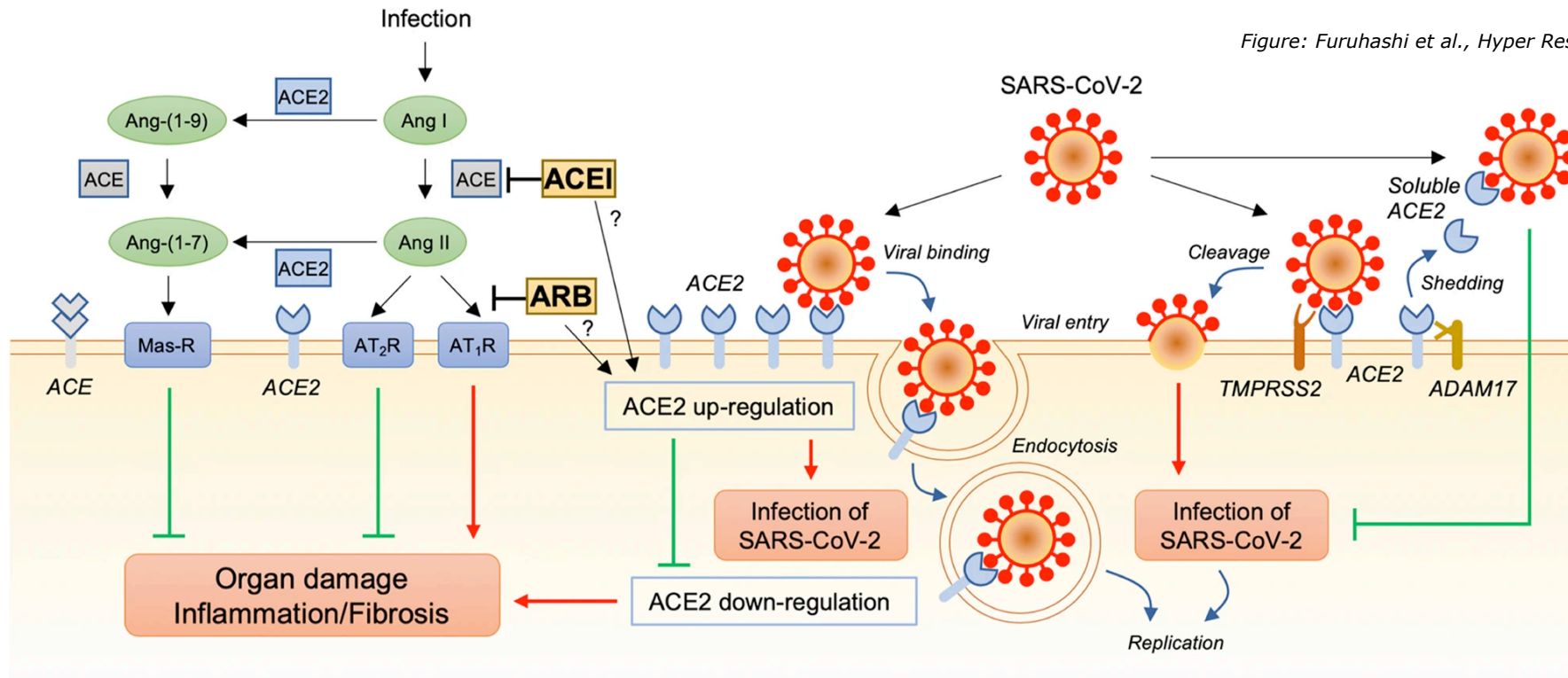
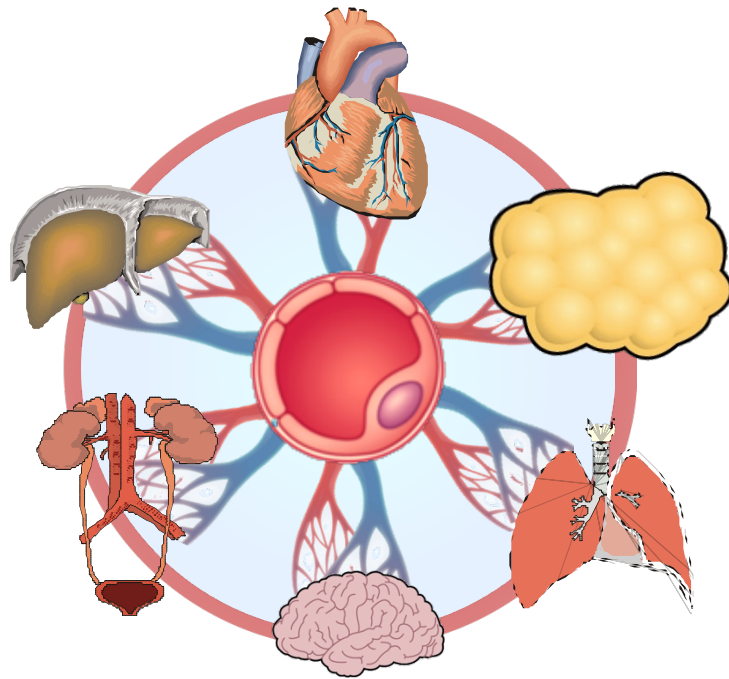


Figure: Furuhashi et al., *Hyper Res*, 2020

**Elevated plasma Ang II concentrations in patients with COVID-19, associated with increased viral load and degree of lung injury**

# Increased RAS activity in obesity may impact COVID-19 susceptibility and outcomes

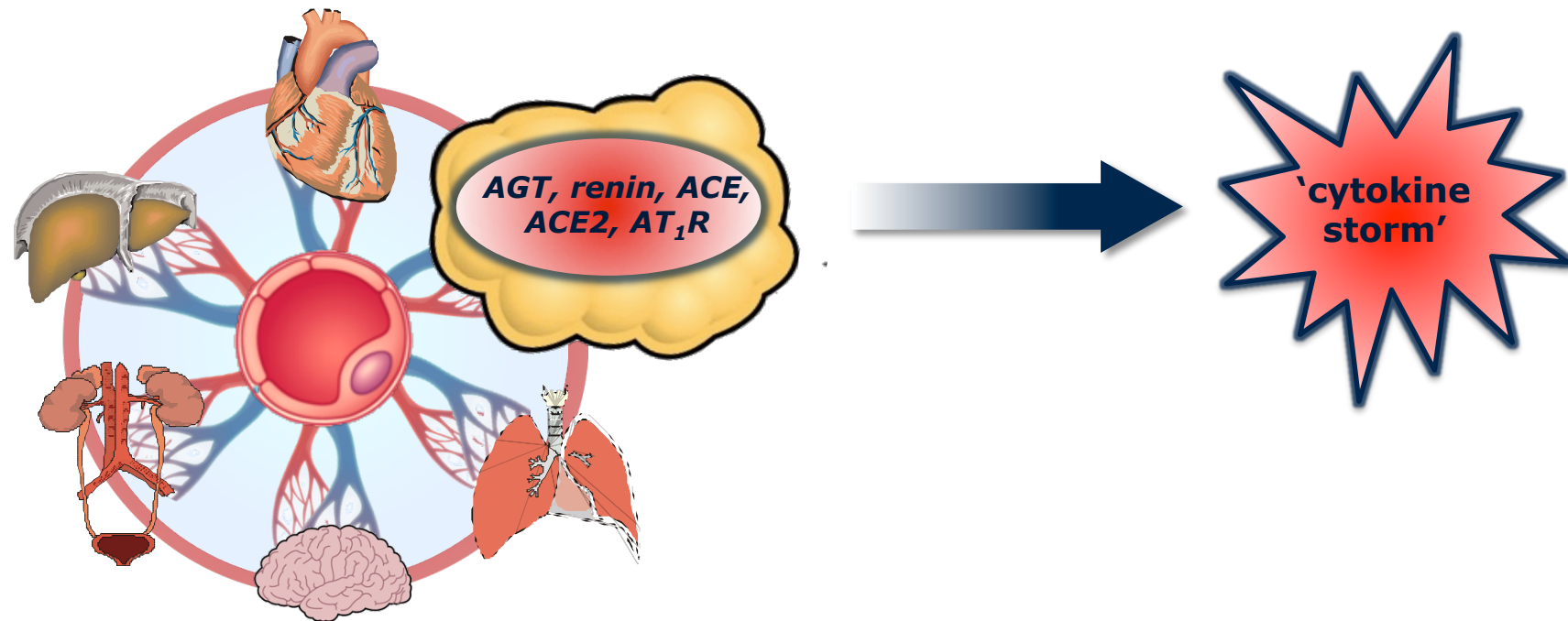
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*Goossens GH, Obes Rev, 2003*

# Increased RAS activity in obesity may impact COVID-19 susceptibility and outcomes

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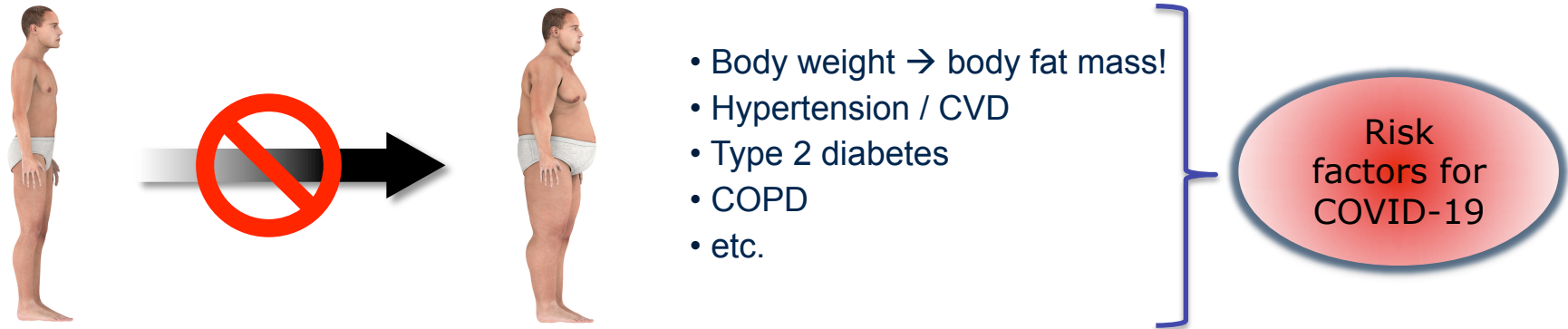
**The increased fat mass in obesity, characterized by a pro-inflammatory phenotype and increased RAS activity, may impact COVID-19 initiation, progression and outcomes**

# Future directions

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- Careful interpretation of early studies!  
(i.e. retrospective, uncontrolled, confounders, limited statistical power)
- RCTs investigating the effects of immunosuppressants and ACEi/ARBs (vs. usual care or placebo) → many ongoing.
- A better understanding of COVID-19 pathogenesis and treatment responses is needed to develop/optimize strategies to combat COVID-19 in population subgroups.
- Better phenotyping of patients: Beyond BMI  
→ *fat mass, body fat distribution (W/H ratio).*
- Impact RAS blockade on tissue ACE2 (i.e. adipose tissue).

# Prevention and clinical management of obesity during the COVID-19 pandemic



**Weight gain prevention and continuous management of obesity and related complications is crucial!**



# Take home messages

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- Obesity is a major risk factor for the initiation, progression and outcomes of COVID-19.
- Link between immunological perturbations, increased activity of the renin-angiotensin system and COVID-19 susceptibility and clinical outcomes in people with obesity.
- More detailed phenotyping of COVID-19 patients is needed to better understand disease pathogenesis and treatment responses in different populations → Beyond BMI!
- Weight gain prevention and continuous management of obesity and related complications is crucial to lower the risk of SARS-CoV-2 infection and poor outcomes in COVID-19 patients.



### Position Statement

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# Obesity and COVID-19: A Perspective from the European Association for the Study of Obesity on Immunological Perturbations, Therapeutic Challenges, and Opportunities in Obesity

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Gema Frühbeck<sup>a, e</sup> Dana Mullerova<sup>a, f</sup> Euan Woodward<sup>a, g</sup>  
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<https://www.karger.com/Article/FullText/510719>

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European Association for the Study of Obesity

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# Therapeutic strategies to combat COVID-19

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- **Immune-modulating drugs**

- *(Hydroxy)chloroquine*

- (to lower viral invasion)

- *Selective JAK1/JAK2 blockade*

- (to lower viral invasion and induce immune suppression)

- *Blockade of cytokine receptors*

- (i.e. IL-6, IL-1 antibodies; to lower cytokine storm)

- *Corticosteroids and other immunosuppressants*

- **RAAS- modulating drugs**

- *Renin-angiotensin system inhibitors/blockers (ACEi/ARBs)*

- *Recombinant ACE2*