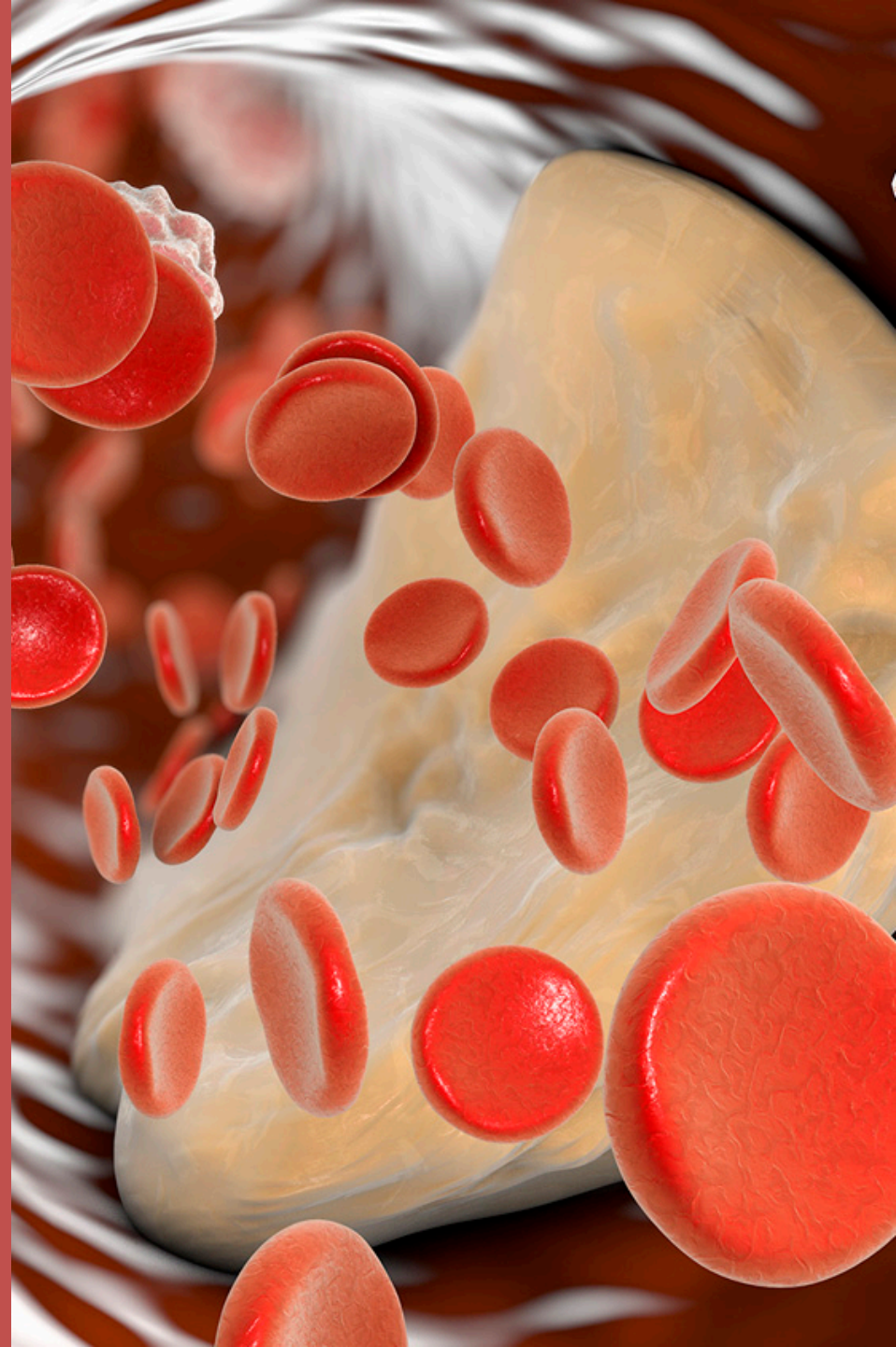
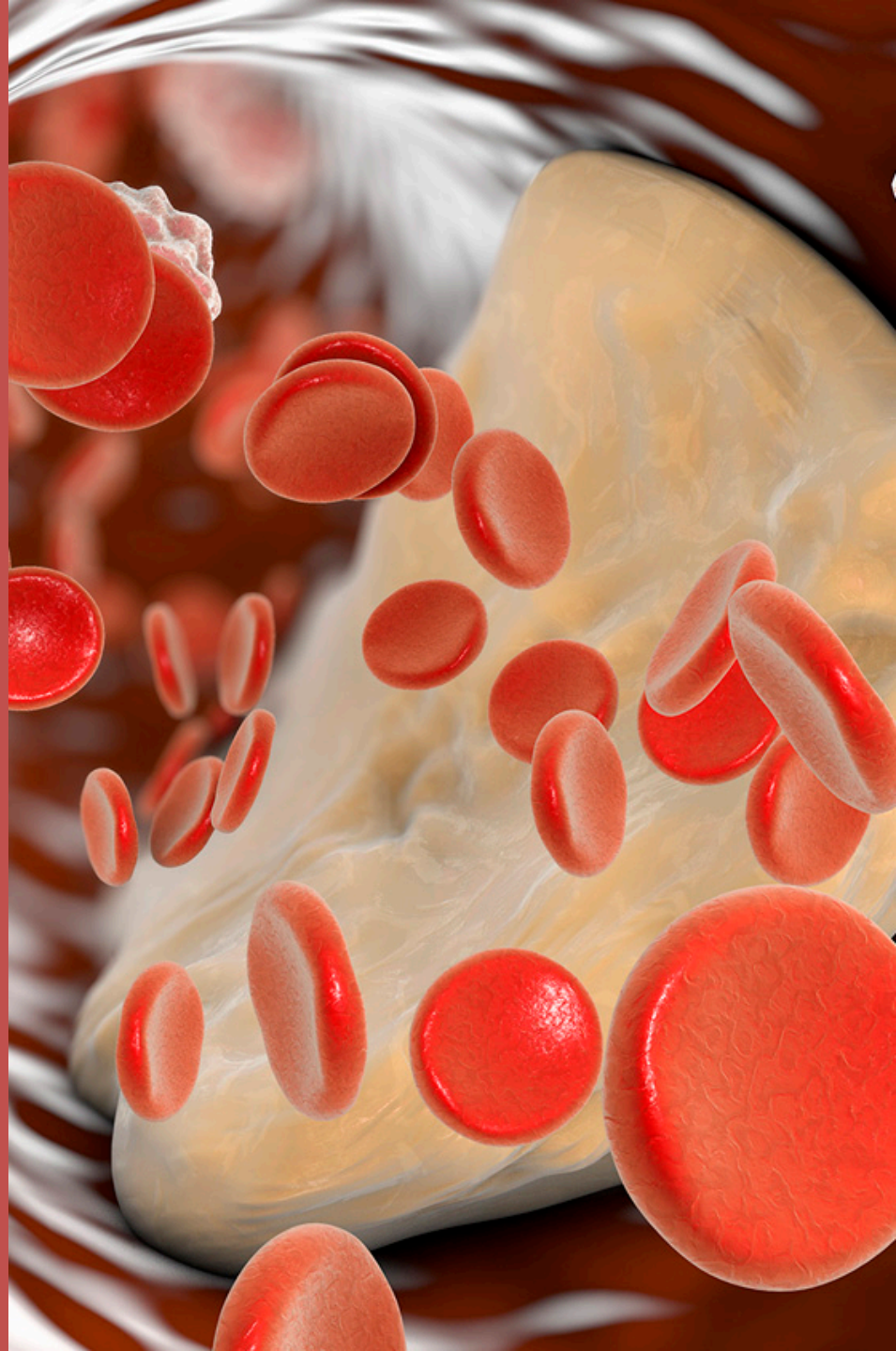
# Lipid Management Guidelines – 2020 Focus on Icosapent Ethyl (IPE)

Yehuda Handelsman, MD, FACP, FNLA, FASPC, MACE
*Chair*



# These Guidelines Focus Primarily on ASCVD Prevention and Not Necessarily on Triglyceride Management



# Japan Atherosclerosis Society (JAS) Guidelines for Prevention of Atherosclerotic Cardiovascular Diseases 2017

CQ28. *For patients with dyslipidemia complicated by hypertriglyceridemia or low HDL-C, would fibrate, nicotinic acid derivative or n-3 PUFA possess beneficial effect in suppressing ASCVD incidence when used in combination with statin?*

Combination therapy using
or fibrate with statin is effective in suppressing ASCVD incidence. (Evidence level 2, recommendation

# ADA Standards of Care: Update
## March 2019/January 2020

In patients with ASCVD or other cardiac risk factors on a statin with controlled LDL-C, but elevated triglycerides (135-499), the addition of icosapent ethyl should be considered to reduce cardiovascular risk.

# Update to ADA Standards of Medical Care in Diabetes – 2019

March 27, 2019/January 2020

**Section 10** – Cardiovascular Disease and Risk Management: Lipid Management

Treatment of Other Lipoprotein Fractions or Targets:

In patients with ASCVD or other cardiac risk factors on a statin with controlled LDL-C, but elevated triglycerides (135-499), the addition of icosapent ethyl should be considered to reduce cardiovascular risk.

*"It should be noted that data are lacking with other omega-3 fatty acids, and results of the REDUCE-IT trial should not be extrapolated to other products."*

**Other Combination Therapy**

Combination therapy **(statin/fibrate) has not been shown to improve atherosclerotic cardiovascular disease outcomes** and is generally not recommended.

Combination therapy **(statin/niacin) has not been shown to provide additional cardiovascular benefit** above statin therapy alone, may increase the risk of stroke with additional side effects, and is generally not recommended.

American Diabetes Association. 10. Cardiovascular disease and risk management: Standards of Medical Care in Diabetes—2019 [web annotation]. Diabetes Care 2019;42(Suppl. 1):S103–S123. Retrieved from https://hyp.is/JHhz_lCrEembFJ9LIVBZIw; Diabetes Care Volume 43, Supplement 1, January 2020.

# Omega-3 Fatty Acids for the Management of Hypertriglyceridemia

## A Science Advisory From the American Heart Association



The use of n-3 FAs (4 g/d) in patients is supported by a 25% reduction in major adverse cardiovascular end points in REDUCE-IT, a randomized placebo-controlled trial of in high-risk patients on statin therapy.

We conclude that prescription n-3 FAs, whether EPA+DHA or EPA-only, at a dose of 4 g/d, are clinically useful for reducing triglycerides, after any underlying causes are addressed and diet and lifestyle strategies are implemented, either as monotherapy

The ACC published the AHA advisory and reported on it. (The ACC *did not develop or adjusted their own Guidelines.)*

## Recommendations for drug treatment of patients with hypertriglyceridaemia

| Recommendations | Class[a] | Level[b] |
|---|---|---|
| Statin treatment is recommended as the first drug of choice to reduce CVD risk in high-risk individuals with hypertriglyceridaemia [TG levels >2.3 mmol/L (>200 mg/dL)].[355] | I | B |
| In high-risk (or above) patients with TG levels between 1.5–5.6 mmol/L (135–499 mg/dL) despite statin treatment, n-3 PUFAs (icosapent ethyl 2×2 g/day) should be considered in combination with a statin.[194] | IIa | B |
| In primary prevention patients who are at LDL-C goal with TG levels >2.3 mmol/L (>200 mg/dL), fenofibrate or bezafibrate may be considered in combination with statins.[305–307,356] | IIb | B |
| In high-risk patients who are at LDL-C goal with TG levels >2.3 mmol/L (>200 mg/dL), fenofibrate or bezafibrate may be considered in combination with statins.[305–307,356] | IIb | C |

# 2019 ESC/EAS Guidelines for the Management of Dyslipidaemias: Lipid Modification to Reduce Cardiovascular Risk

| | | |
|---|---|---|
| In high-risk (or above) patients with TG levels between 1.5–5.6 mmol/L (135–499 mg/dL) despite statin treatment, n-3 PUFAs (icosapent ethyl 2×2 g/day) should be considered in combination with a statin.[194] | **IIa** | **B** |

# NLA Position Statement on the Use of Icosapent Ethyl in High- or Very-High-Risk Patients 10/2019

## *Proposed* NLA Position on the Use of Icosapent Ethyl in High and Very-high-risk Patients

- For patients 45 years of age or older with clinical ASCVD, or 50 years of age or older with type 2 diabetes requiring medication and ≥1 additional risk factor*, and fasting triglycerides 135-499 mg/dL on maximally tolerated statin, with or without ezetimibe, treatment with icosapent ethyl is recommended for ASCVD risk reduction. (I B-R)

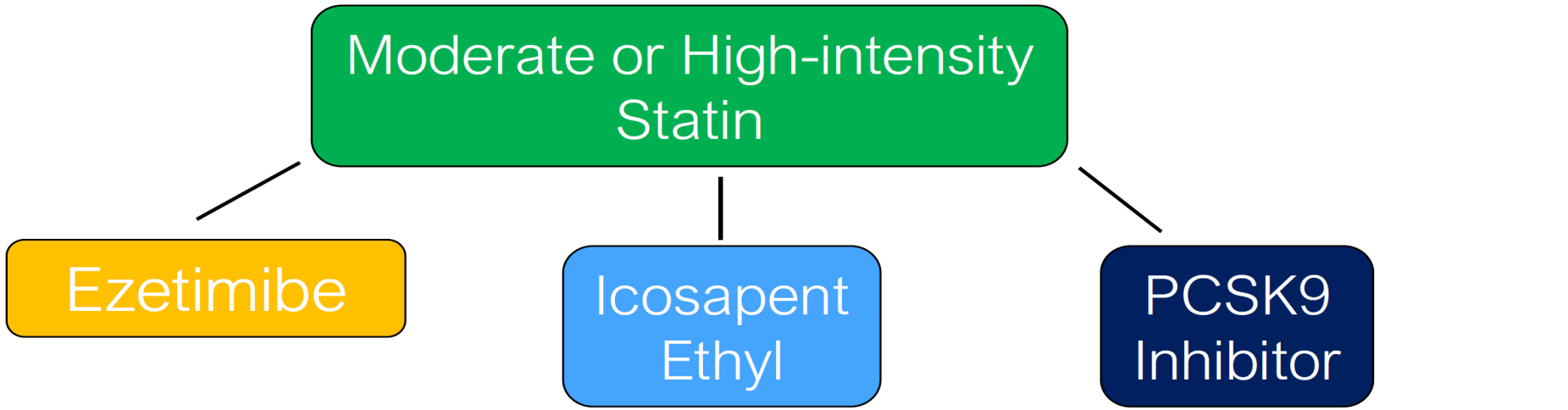
| CLASS I (STRONG) | Benefit >>> Risk |
|---|---|
| Suggested phrases for writing recommendations:<br>▪ Is recommended<br>▪ Is indicated/useful/effective/beneficial | |

| LEVEL B-R | (Randomized) |
|---|---|
| ▪ Moderate-quality evidence‡ from 1 or more RCTs<br>▪ Meta-analyses of moderate-quality RCTs | |

* 
- Age: men ≥55 years and women ≥65 years
- Cigarette smoker or stopped smoking within 3 months
- Hypertension (≥140 mmHg systolic OR ≥90 mmHg diastolic) or on antihypertensive medication
- HDL-C ≤40 mg/dL for men or ≤50 mg/dL for women
- hs-CRP >3.0 mg/L
- Renal dysfunction: Creatinine clearance >30 and <60 mL/min
- Retinopathy
- Micro- or macro-albuminuria
- ABI <0.9 without symptoms of intermittent claudication

# NLA Position Statement on the Use of Icosapent Ethyl in High- or Very-High-Risk Patients

## Adjunctive Therapies for ASCVD Risk Reduction in High- or Very-high-risk Statin-treated Patients Supported by RCT Evidence




Acute coronary syndrome within 10 days (IMPROVE-IT)

Cannon, CP et al.. N Engl J Med 2015;372:2387-97

Stable ASCVD; or Diabetes + ≥1 additional risk factor + TG 135-499 mg/dL (REDUCE-IT)

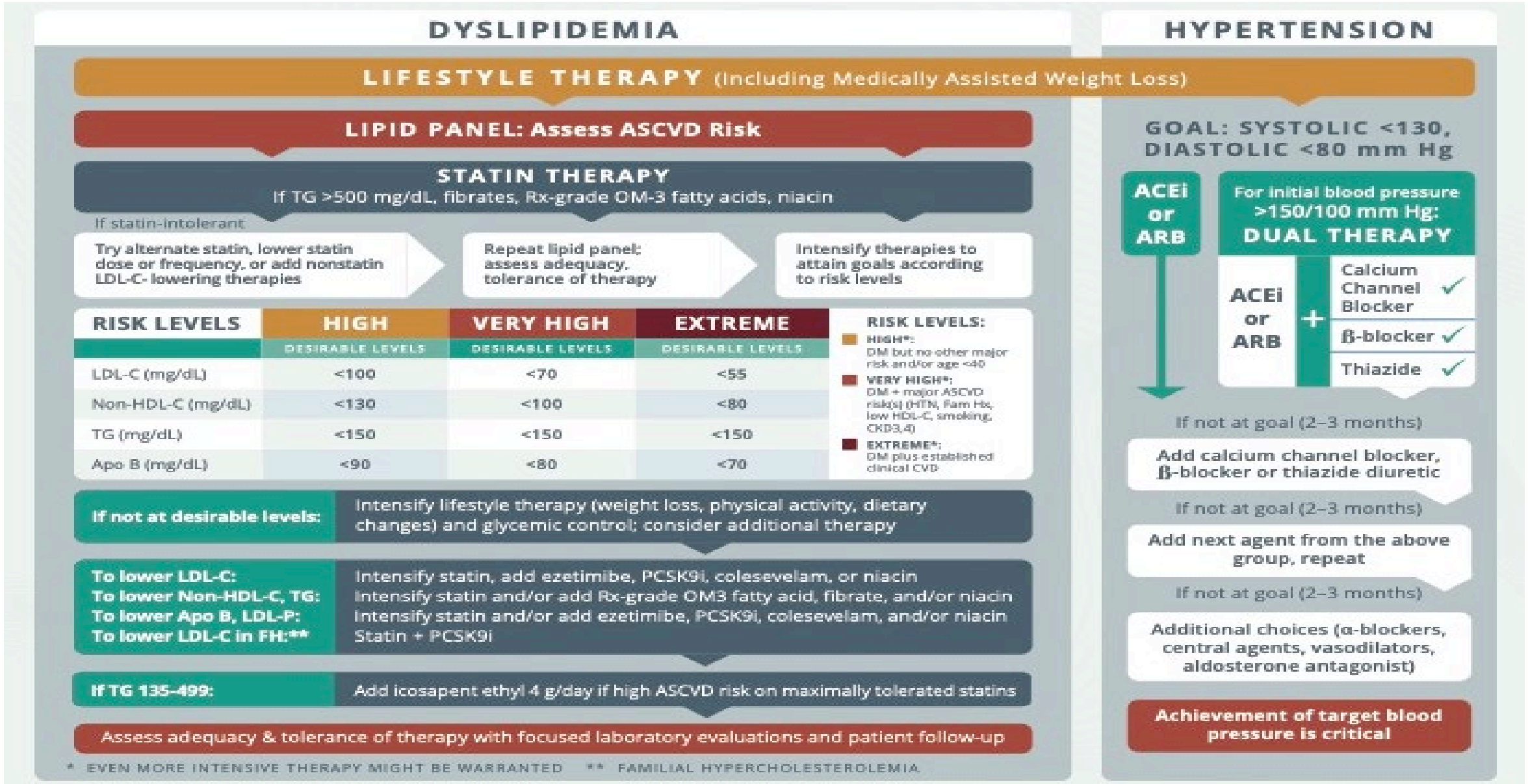
Bhatt, DL et al. N Engl J Med 2019;380:11-22

Stable ASCVD + additional risk factors; or ACS within 1-12 months (FOURIER, ODYSSEY-Outcomes)

Sabatine MS et al. N Engl J Med 2017;376:1713-1722

Schwartz GG et al. N Engl J Med 2018; 379:2097-2107

# AACE: ASCVD Risk Factor Modifications Algorithm



# Clinical Management of Stable Coronary Artery Disease in Patients With Type 2 Diabetes Mellitus

## A Scientific Statement From the American Heart Association

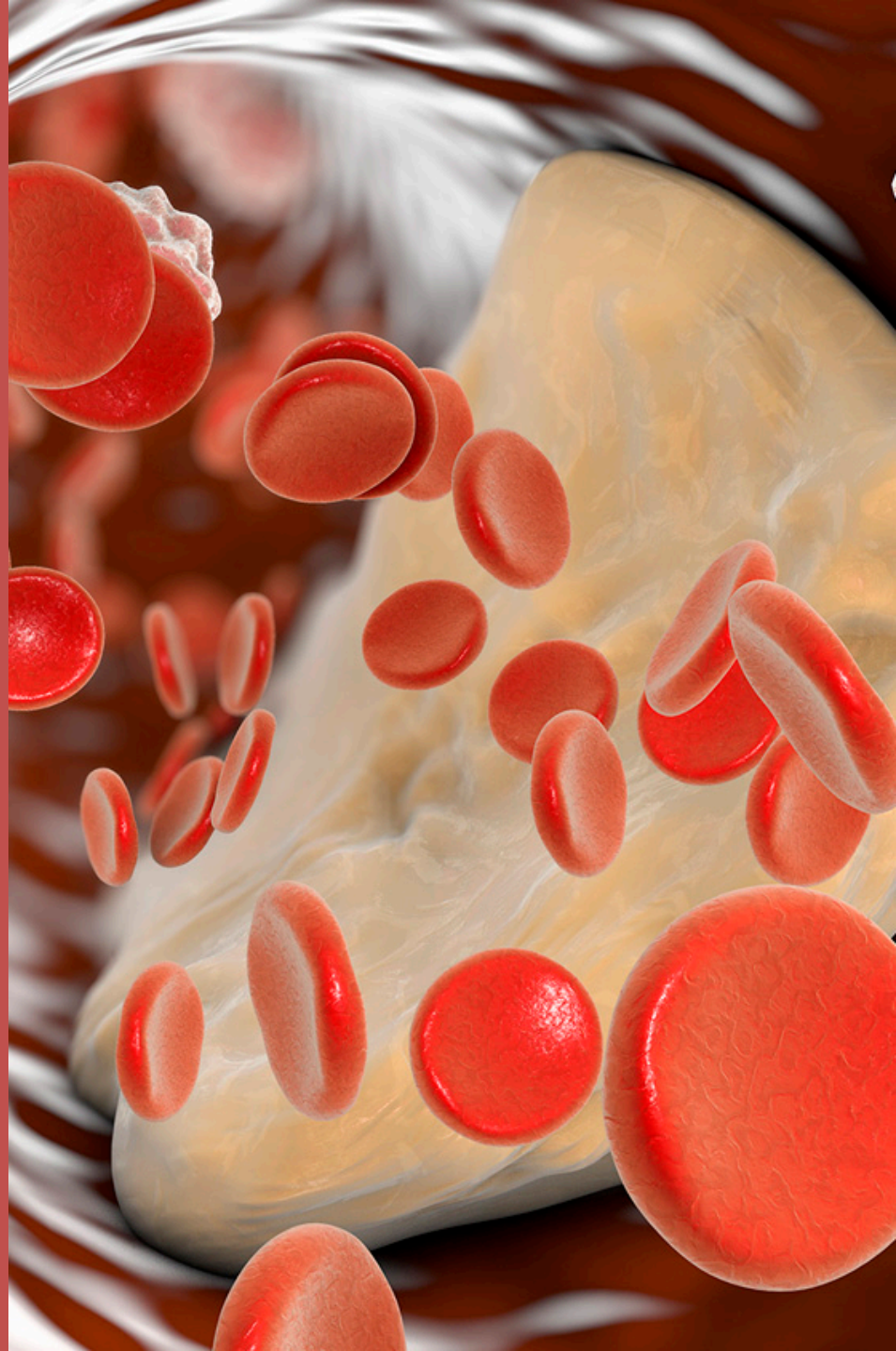
**Underlying Issue: Atherogenic lipid anomalies include hypertriglyceridemia, low HDL-C, and small, dense LDL particles**

| | |
|---|---|
| **High-intensity statins** | Cornerstone of lipid therapy and secondary prevention |
| **Ezetimibe and PCSK9 inhibitors** | Additional cardiovascular risk reduction when LDL is >70 mg/dL despite maximally tolerated statins |
| **Niacin** | Not recommended |
| **Fibrates** | Recommended when triglycerides are very high (e.g., >500 mg/dL) to reduce the risk of pancreatitis |

*Circulation*. 2020;141:e779–e806. DOI: 10.1161/CIR.0000000000000766 **May 12, 2020**

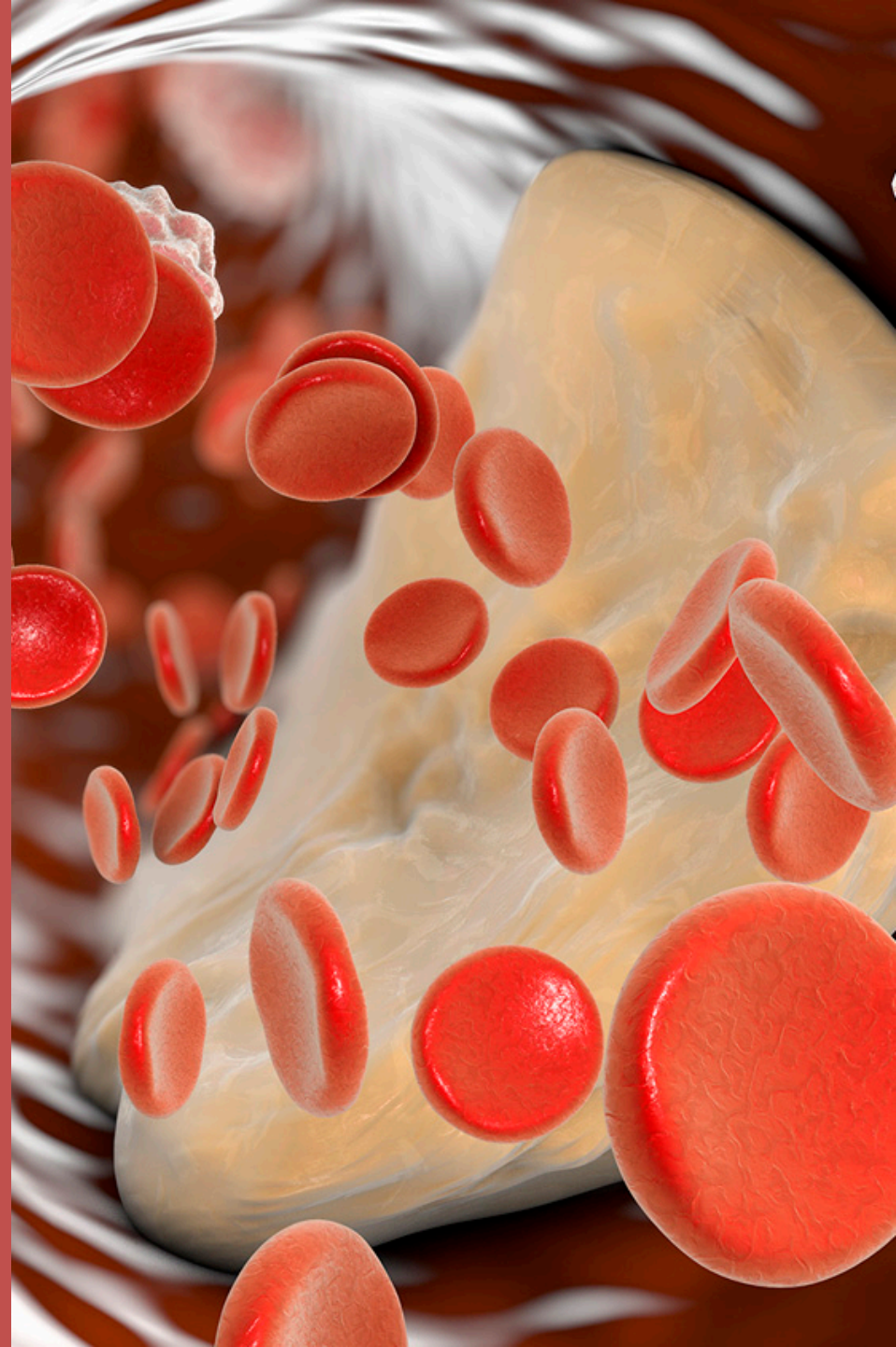
# EPA – Icosapent Ethyl Role in Clinical Practice

## The Future: IPE Should Be Considered STANDARD OF CARE (*yh*)



# EPA – Icosapent Ethyl Role in Clinical Practice

## Thank You  Questions



# Life and Medicine in the Era of COVID-19

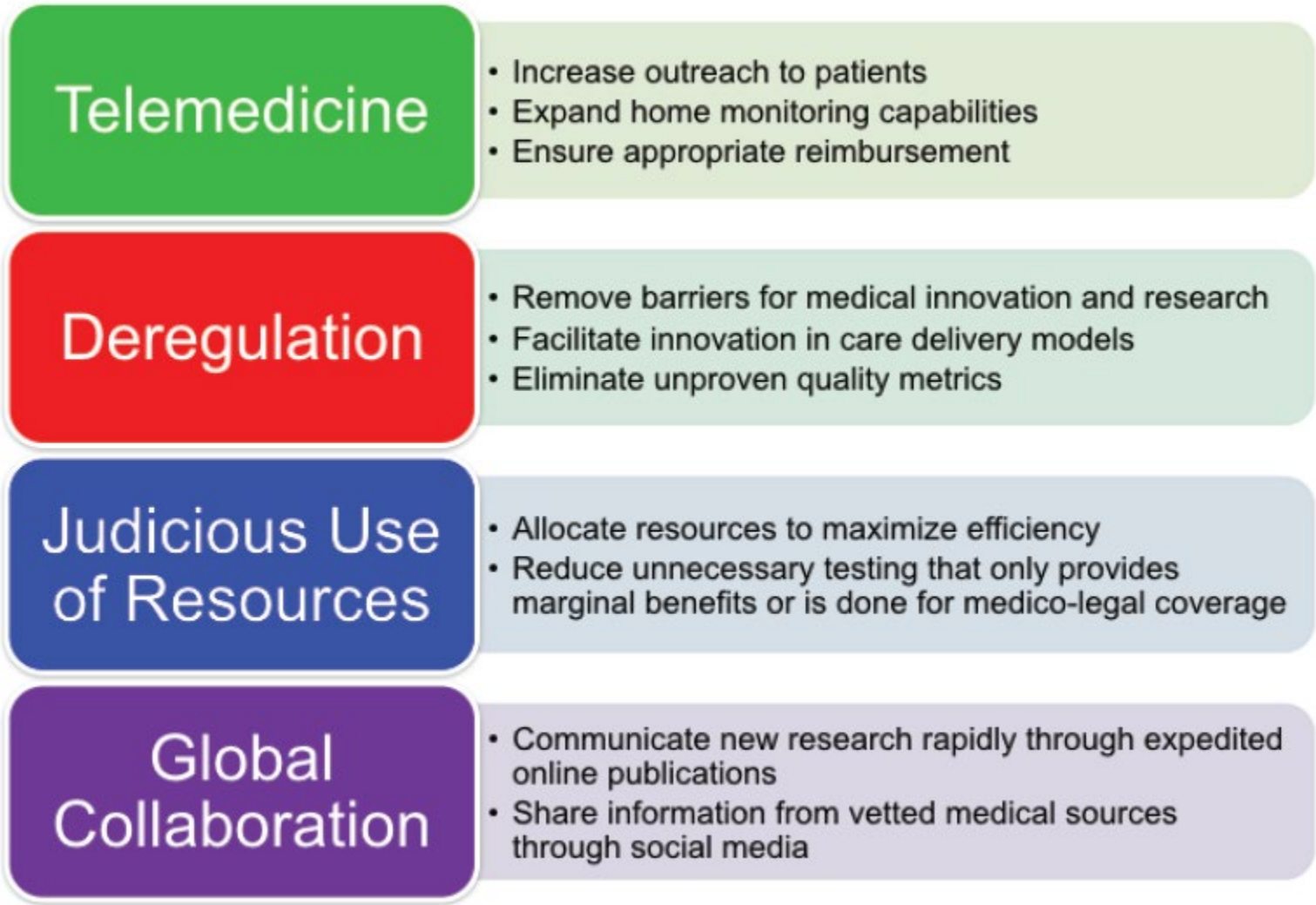
**Deepak L. Bhatt, MD, MPH**

***Executive Director of Interventional Cardiovascular Programs,***
***Brigham and Women's Hospital Heart and Vascular Center***
***Professor of Medicine, Harvard Medical School***

BWH BRIGHAM AND WOMEN'S HOSPITAL
| Heart & Vascular Center |

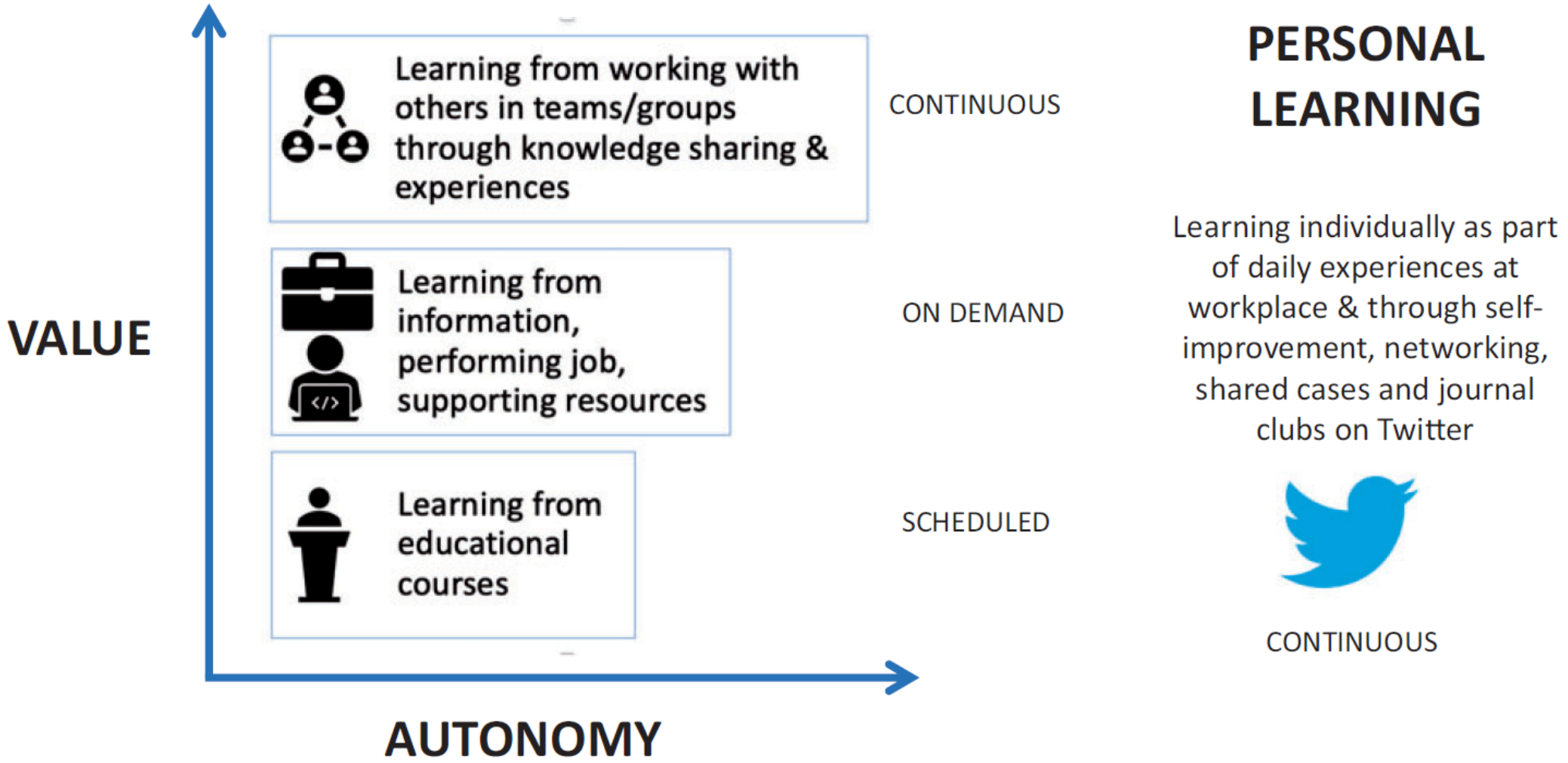
HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL

# COVID-19
# An Unintended Force for Medical Revolution?




**Wang X, Bhatt DL. *J Invasive Cardiol* 2020;32(4):E81-E82.**

# Twitter-based Learning for Continuing Medical Education?




Thamman R, Gulati M, Narang A, Utengen A, Mamas MA, Bhatt DL. *European Heart Journal* 2020;0, 1-3.

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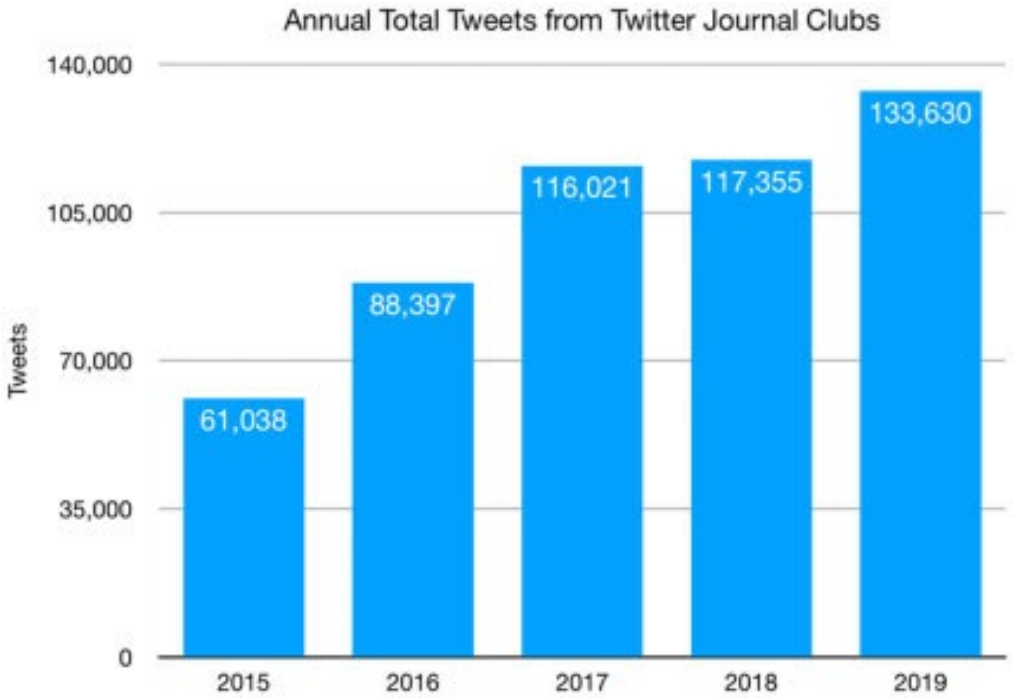



Twitter data from all identified Twitter Journal Club hashtags in the time period from January 1, 2015 to December 31, 2019, as analyzed in Symplur Signals.

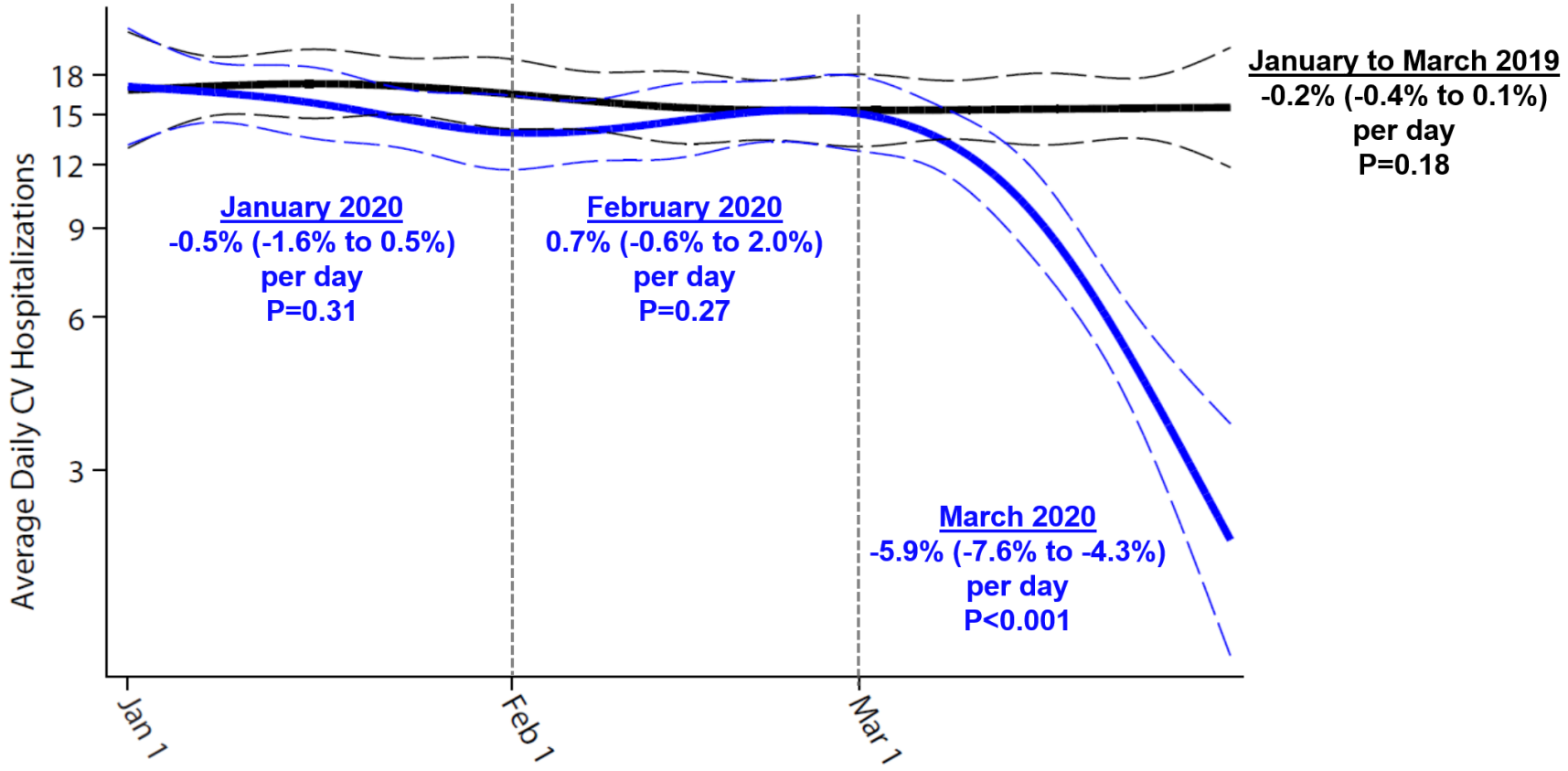
**Thamman R, Gulati M, Narang A, Utengen A, Mamas MA, Bhatt DL. *European Heart Journal* 2020;0, 1-3.**

# The Consequences of the COVID-19 Pandemic on non-COVID-19 Clinical Trials

- Hurricane Katrina, 9/11, Ukrainian War, etc.
  - Horrible, though disruption to research was local, not global
- Non-COVID research initiation suspended or de-prioritized
- Event rates affected, morbidity and mortality increased
- Follow-up visits more challenging, data less complete
- Termination of several ongoing trials

**Bagiella E, Bhatt DL, Gaudino M. *JACC* 2020. doi: https://doi.org/10.1016/j.jacc.2020.05.041.**

# Declines in Hospitalizations for CV Conditions During COVID-19: Mass General Brigham




Bhatt AS, Moscone A, McElrath EE, Varshney AS, Claggett BL, Bhatt DL, Januzzi JL, Butler J, Adler DS, Solomon SD, Vaduganathan M. *JACC* 2020. doi: https://doi.org/10.1016/j.jacc.2020.05.038.

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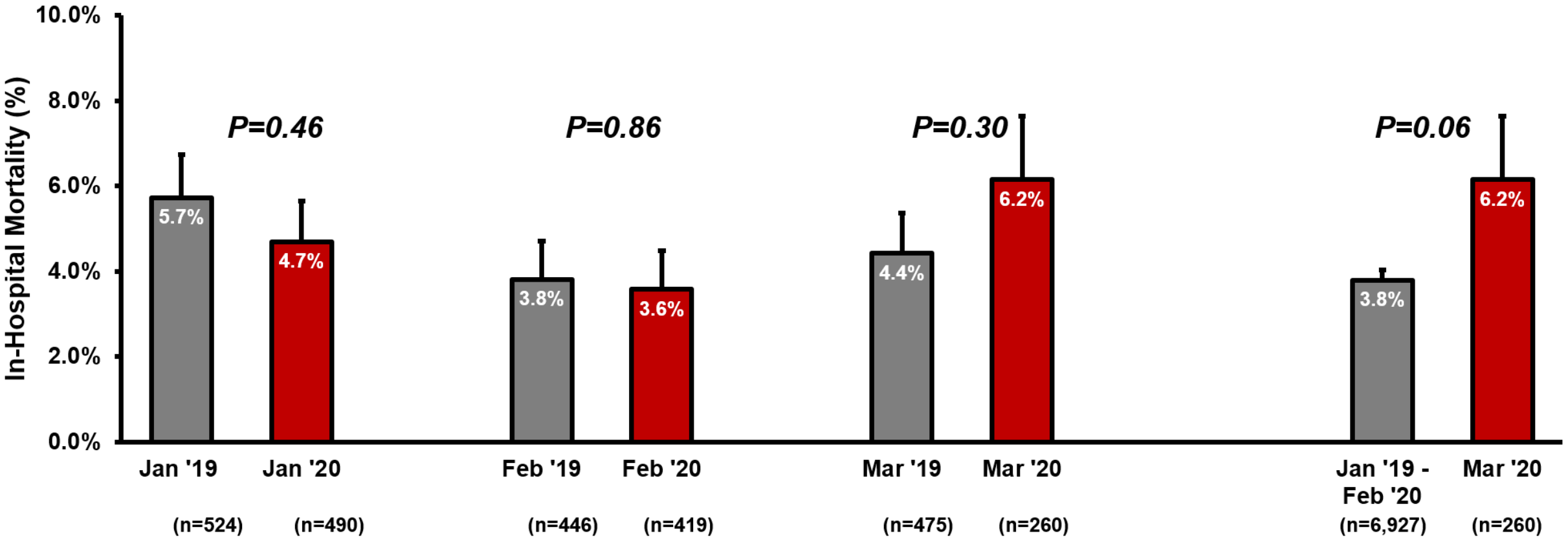


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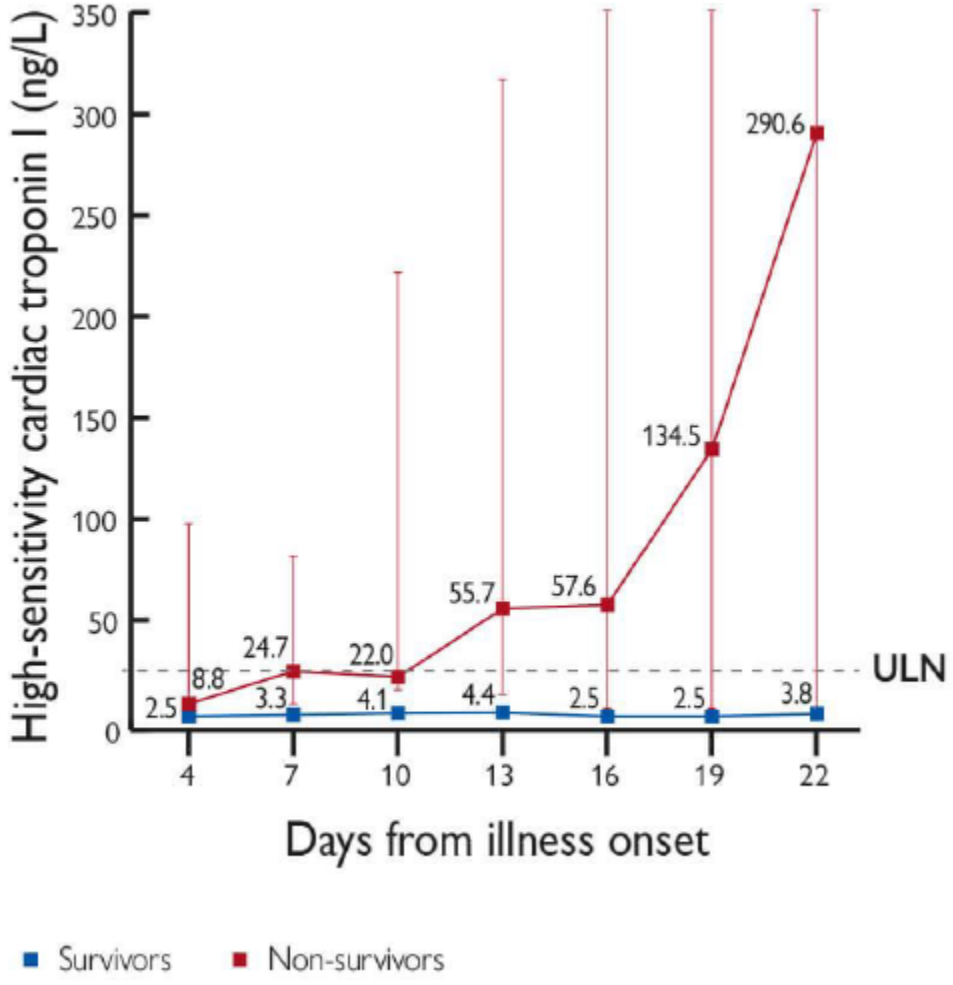
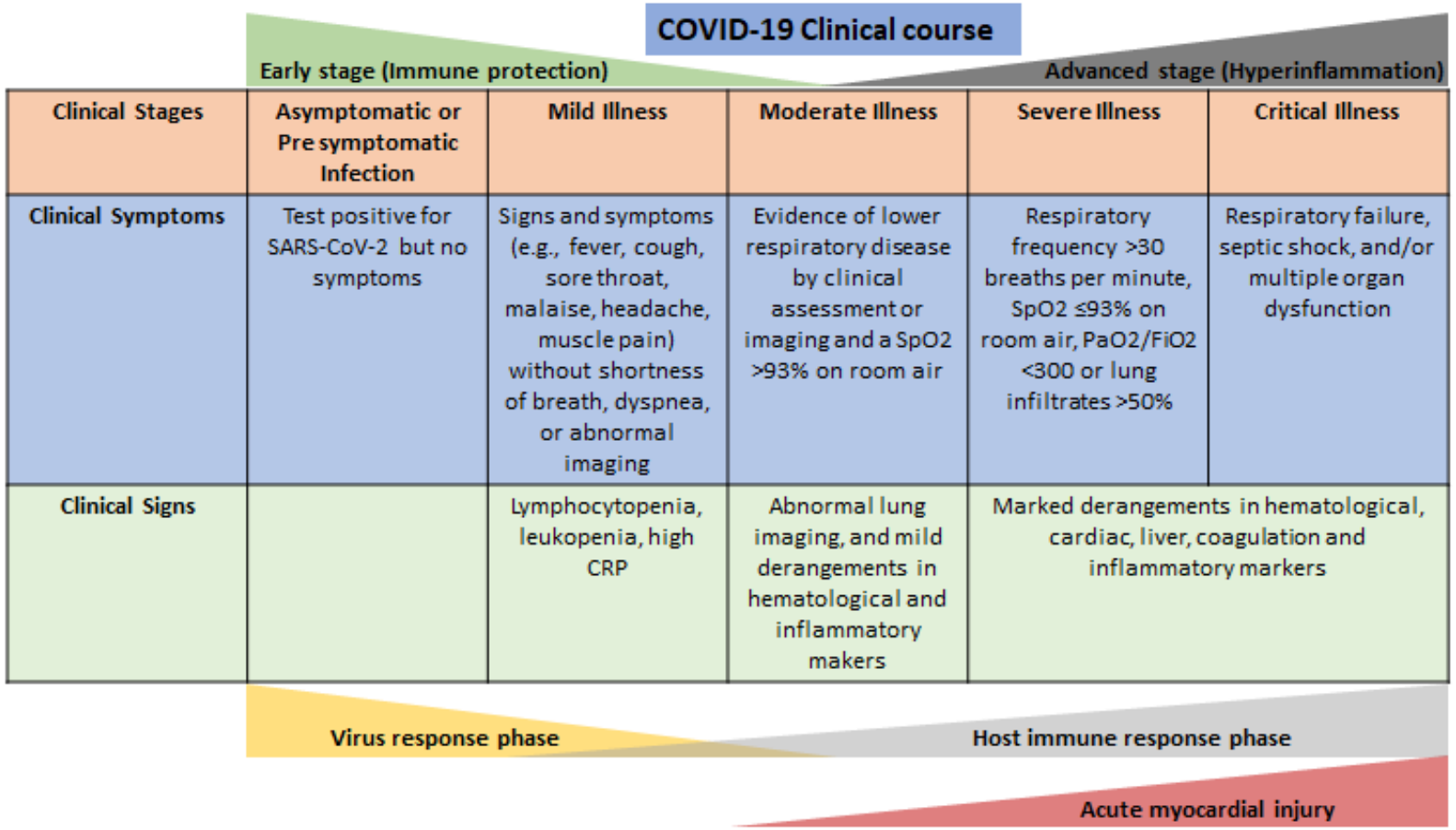
# Biomarker Elevation Suggesting Cardiovascular Conditions in Patients with COVID-19 Infection

- In non-survivors, troponin levels progressively increased in parallel with the severity of COVID-19 and the development of ARDS
- BNP/NT-proBNP are frequently elevated among patients with severe inflammatory and/or respiratory illnesses




Zhou F, et al. *Lancet* 2020. Shi S, *JAMA Cardiol* 2020.

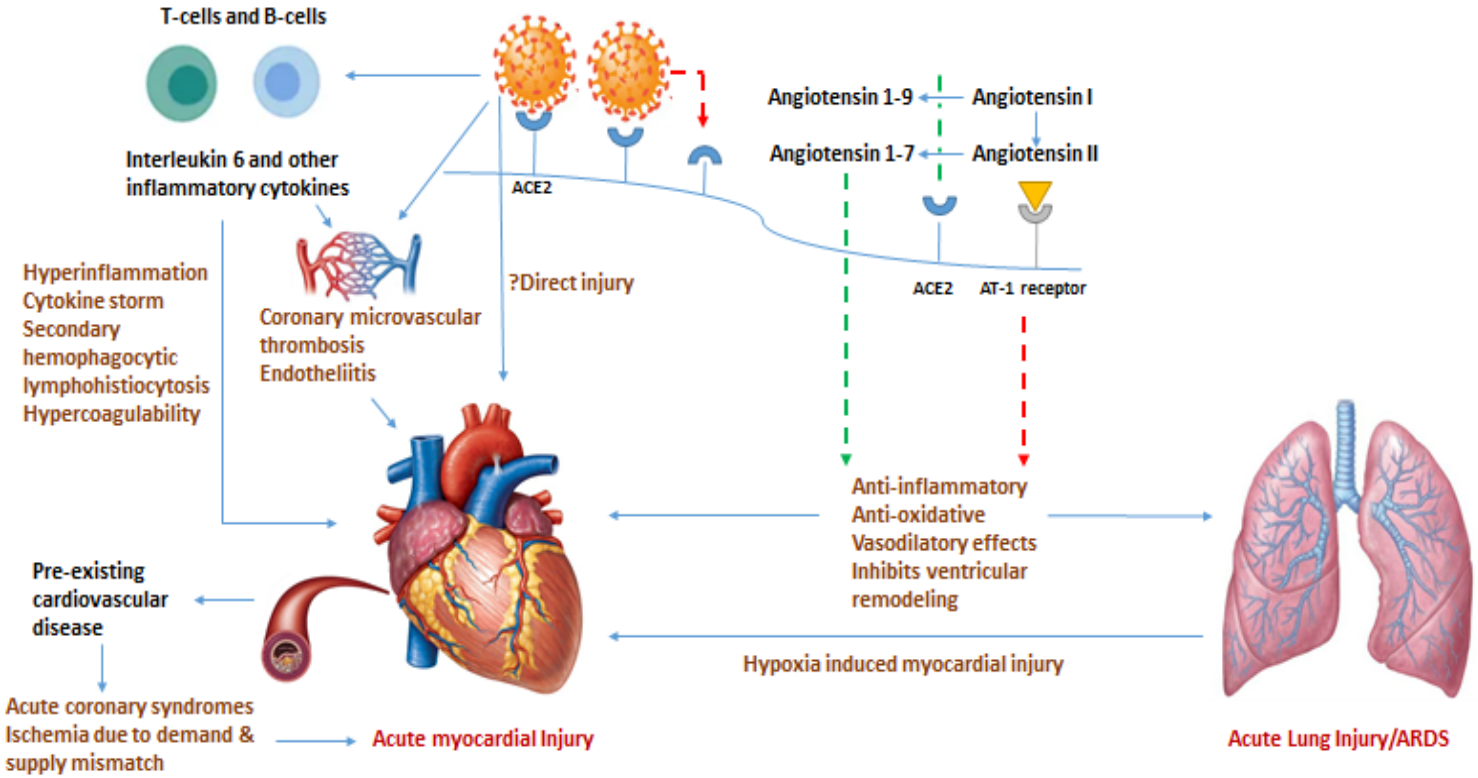
# Acute Myocardial Injury in Patients Hospitalized with COVID-19 Infection




| Clinical Stages | Asymptomatic or Pre symptomatic Infection | Mild Illness | Moderate Illness | Severe Illness | Critical Illness |
|---|---|---|---|---|---|
| Clinical Symptoms | Test positive for SARS-CoV-2 but no symptoms | Signs and symptoms (e.g., fever, cough, sore throat, malaise, headache, muscle pain) without shortness of breath, dyspnea, or abnormal imaging | Evidence of lower respiratory disease by clinical assessment or imaging and a SpO2 >93% on room air | Respiratory frequency >30 breaths per minute, SpO2 ≤93% on room air, PaO2/FiO2 <300 or lung infiltrates >50% | Respiratory failure, septic shock, and/or multiple organ dysfunction |
| Clinical Signs | | Lymphocytopenia, leukopenia, high CRP | Abnormal lung imaging, and mild derangements in hematological and inflammatory makers | Marked derangements in hematological, cardiac, liver, coagulation and inflammatory markers | |

Bavishi C, Bonow RO, Trivedi V, Abbott JD, Messerli FH, Bhatt DL. *Progress in Cardiovascular Diseases* 2020. In press.

# Acute Myocardial Injury in Patients Hospitalized with COVID-19 Infection

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BRIGHAM AND WOMEN'S HOSPITAL

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## *Thank You!*

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