Management of T2DM patients with Covid-19

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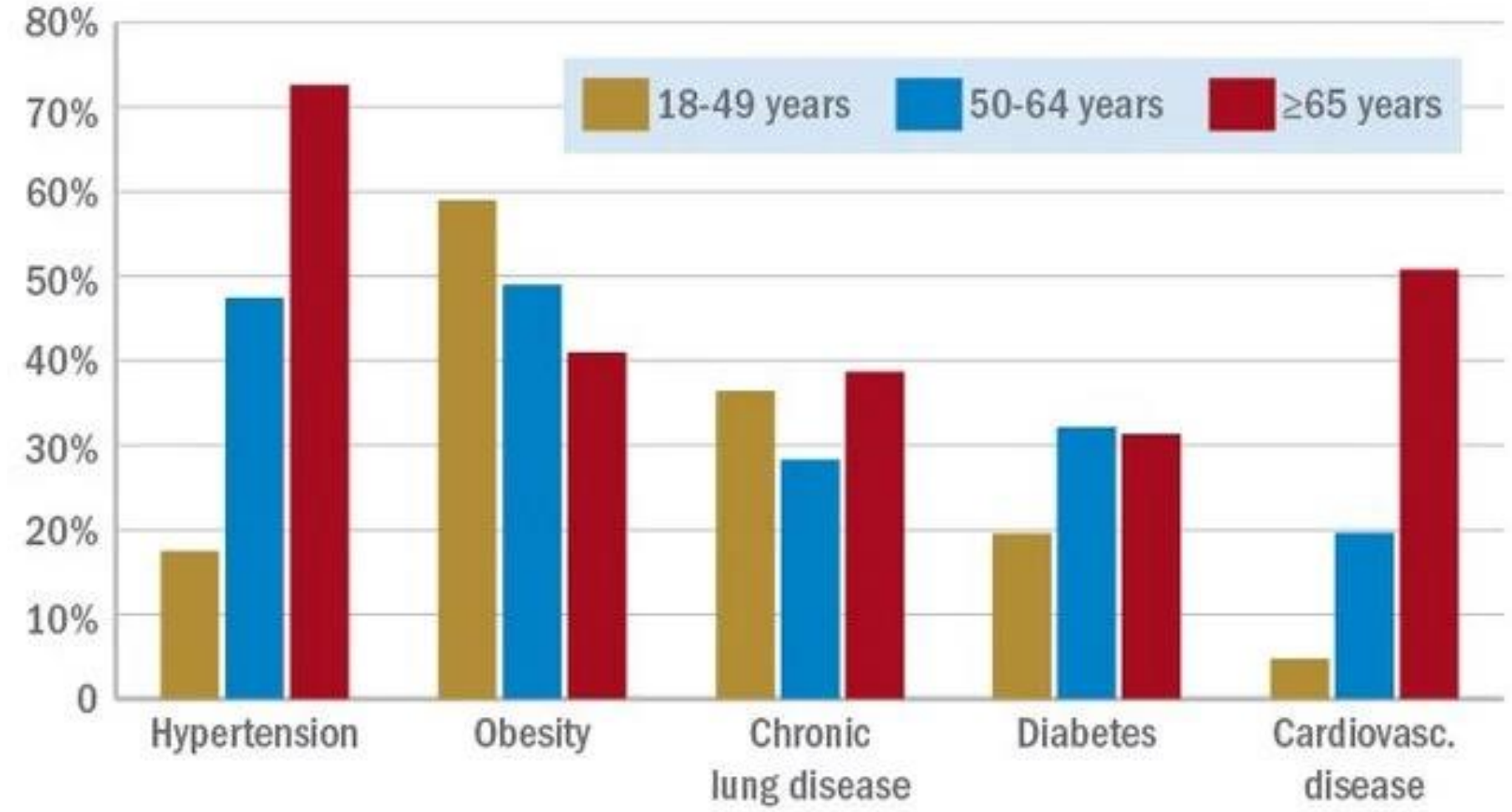
Underlying conditions among adults hospitalized with COVID-19

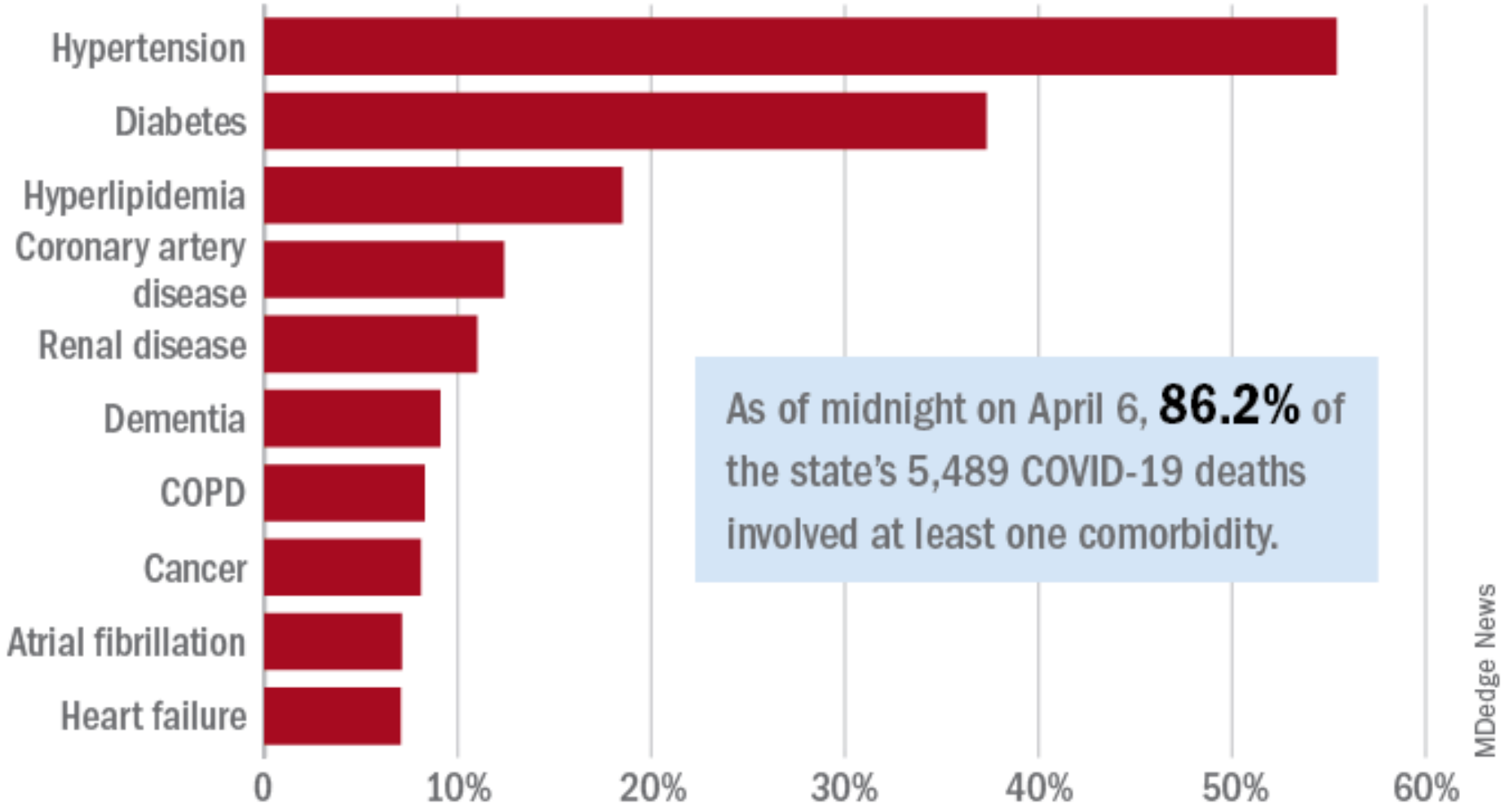


Note: Based on data from the COVID-19–Associated Hospitalization Surveillance Network for patients hospitalized in 99 counties in 14 states from March 1-30, 2020.

Source: MMWR. 2020 Apr 8:69(early release):1-7

https://www.medscape.com/viewarticle/928531

Leading comorbidities among COVID-19 deaths in New York



Note: Data reported on a daily basis by hospitals, nursing homes, and other health care facilities.

Source: New York State Department of Health

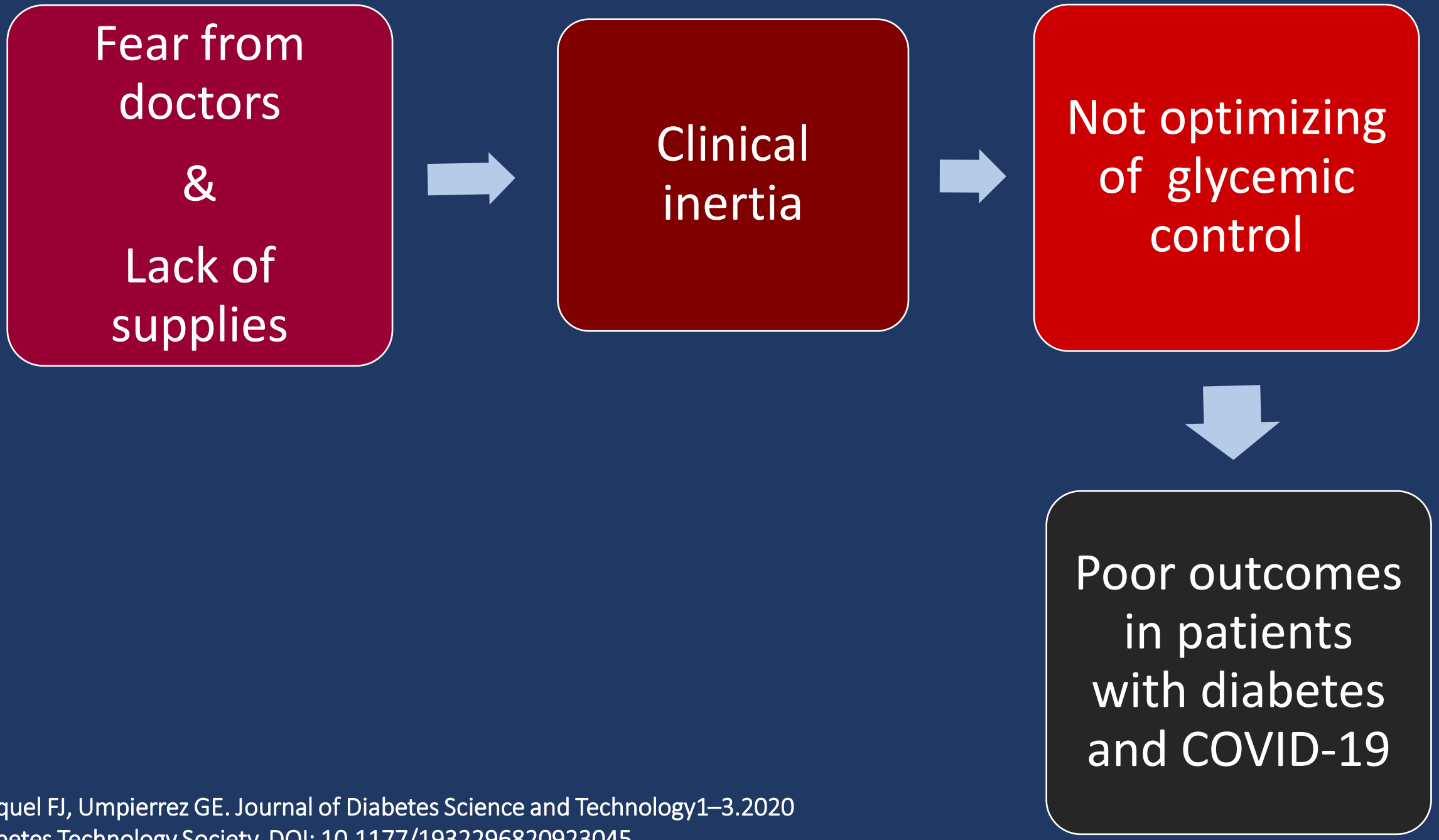
https://www.the-hospitalist.org/hospitalist/article/220457/coronavirus-updates/comorbidities-rule-new-yorks-covid-19-deaths

Guan W-jie, Liang W-hua, Zhao Y, et al. Comorbidity and its impact on 1590 patients with Covid-19 in China: A Nationwide Analysis. Eur Respir J 2020

	COPD		Diabetes		Hypertension	
	No (n=1566)	Yes (n=24)	No n=1460	Yes n=130	No (n=1321)	Yes (n=269)
Abnormal Chest Image						
Radiograph	236/1566 (15.1)	7/24 (29.2)	218/1460 (14.9)	25/130 (19.2)	178/1321 (13.5)	65/269 (24.2)
CT	1113/1566 (71.1)	17/24 (70.8)	1034/1460 (70.8)	96/130 (73.8)	926/1321 (70.1)	204/269 (75.8)

Guan W-jie, Liang W-hua, Zhao Y, et al. Comorbidity and its impact on 1590 patients with Covid-19 in China: A Nationwide Analysis. Eur Respir J 2020

	COPD		Diabetes		Hypertension	
	No (n=1566)	Yes (n=24)	No n=1460	Yes n=130	No (n=1321)	Yes (n=269)
Severity	239/1566 (15.3)	15/24 (62.5)	209/1460 (14.3)	45/130 (34.6)	166/1321 (12.6)	88/269 (32.7)
Composite end point	119/1566 (7.6)	12/24 (50.0)	100/1460 (6.8)	31/130 (23.8)	78/1321 (5.9)	53/269 (19.7)
Death	44/1566 (2.8)	6/24 (25.0)	37/1460 (2.5)	13/130 (10.0)	22/1321 (1.7)	28/269 (10.4)
Admission of ICU	92/1566 (5.9)	7/24 (29.2)	80/1460 (5.5)	19/130 (14.6)	61/1321 (4.6)	38/269 (14.1)
Invasive ventilation	45/1566 (2.9)	5/24 (20.8)	39/1460 (2.7)	11/130 (8.5)	28/1321 (2.1)	22/269 (8.2)



Pasquel FJ, Umpierrez GE. Journal of Diabetes Science and Technology1–3.2020
Diabetes Technology Society. DOI: 10.1177/1932296820923045

Management of T2DM patients with Covid-19

- Out patients
- In hospital patients :
  - Non critically ill
  - Critically ill

T2DM out-patients with Covid-19

- Reducing the risk of COVID-19
  - Social distancing and hand washing.
  - Good glycaemic control to reducing the risk of infection and severity.
    - More frequent blood glucose self monitoring
    - Influenza and pneumonia vaccinations
    - Special care to stabilize their cardiac/renal status.
  - Adequate control of blood pressure and lipids.

https://www.cebm.net/covid-19/managing-diabetes-during-the-covid-19-pandemic/

Lancet Diabetes Endocrinol 2020Published Online April 23, 2020 https://doi.org/10.1016/ S2213-8587(20)30152-2

Management of health anxiety and diabetes-related distress during the COVID-19 pandemic

Distancing but still social – Therapeutic Recreation during COVID-19

https://www.sinaihealth.ca/news/distancing-but-still-social-therapeutic-recreation-during-covid-19/

Management of patients with COVID-19

Out-patient care

Prevention of infection in diabetes

- Sensitisation of patients with diabetes for the importance of optimal metabolic control
- Optimisation of current therapy if appropriate
- Caution with premature discontinuation of established therapy
- Utilisation of Telemedicine and Connected Health models if possible to maintain maximal self containment

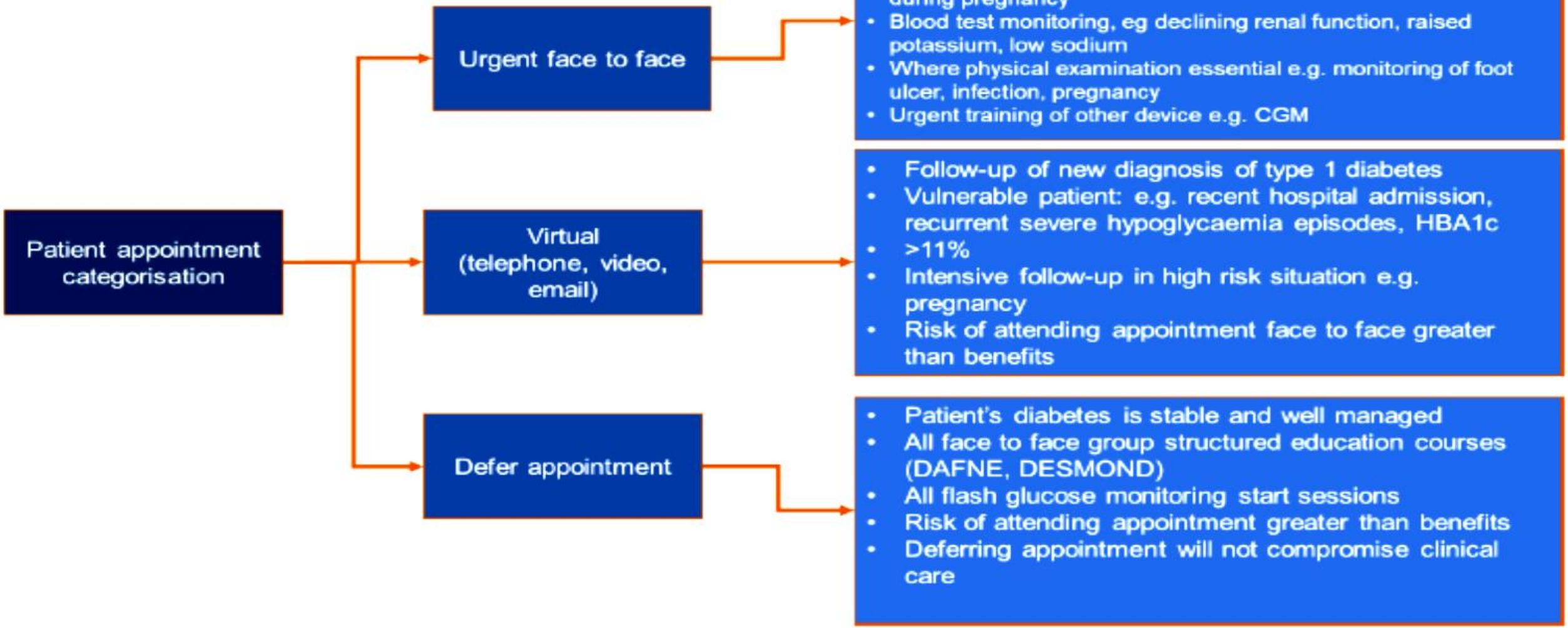
Modif. From. The Lancet Diabetes & Endocrinology DOI: (10.1016/S2213-8587(20)30152-2)

Anti Diabetic Medications during Pandemic Covid-19

- SU, metformin and SGLT2 inhibitors should not be discontinued prophylactically in outpatients who don't have evidence of COVID-19.
- GLP-1 RA and DPP-4 inhibitors, continued. Patients taking GLP-1 RA should be carefully monitored for dehydration. Adequate fluid intake and regular meals encouraged.
- Insulin therapy should never be stopped, may need to be started in new-onset patients or those with hyperglycemia after being taken off other agents

NHS London Clinical Networks

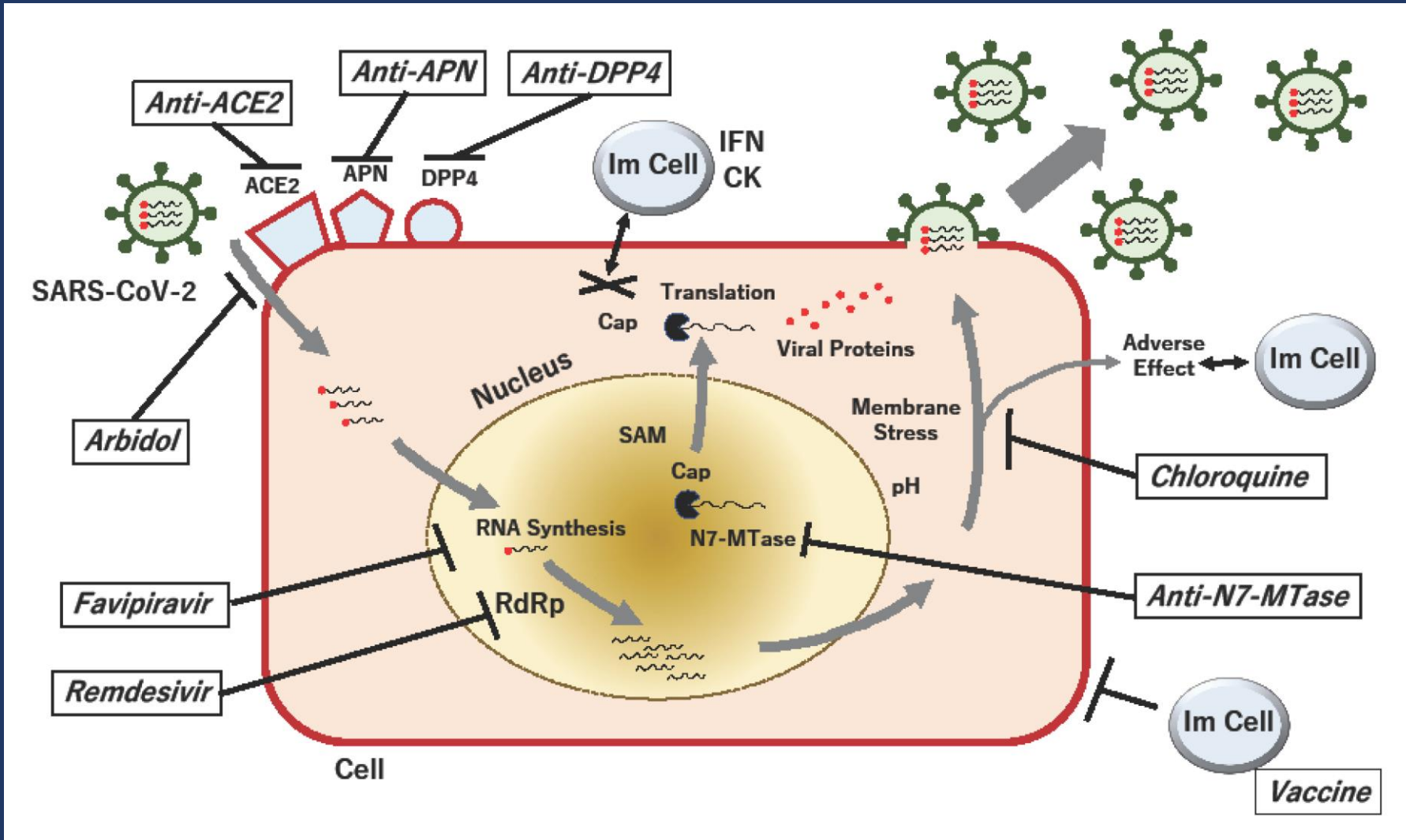
Outpatient Appointment Prioritisation for Specialist Diabetes Departments during the Coronavirus pandemic



Are some diabetes medicines better than others at fighting the virus?

- At this time, there is no rigorous scientific data from studies in people that highlights either a special benefit or a risk of a different outcome with COVID-19 for any of the common glucose-lowering medicines used to treat Type 2 diabetes.

https://www.sinaihealth.ca/news/managing-diabetes-in-the-time-of-covid-19/


Anti-ACE2
Anti-APN
Anti-DPP4
ACE2
APN
DPP4
Im Cell
IFN
CK
SARS-CoV-2
Translation
Cap
Viral Proteins
Nucleus
Adverse
Effect
Im Cell
Membrane
Stress
SAM
Cap
pH
Arbidol
Chloroquine
RNA Synthesis
N7-MTase
Favipiravir
RdRp
Anti-N7-MTase
Remdesivir
Im Cell
Cell
Vaccine

Metformin

- Exerts anti-inflammatory actions in preclinical studies, ↓ circulating biomarkers of inflammation in people with T2D.
- Been used successfully in nonhospitalized subjects with stable hepatitis or HIV infections

however,

- Scant information about the immunomodulatory actions of metformin in the context of coronavirus infection.

Drucker DJ. Coronavirus Infections and Type 2 Diabetes. Endocrine Reviews, June 2020, 41(3):1–13

Metformin

- Caution in unstable hospitalized patients.
- Discontinued in people with concomitant sepsis or severe impairment of hepatic and renal function.

Drucker DJ. Coronavirus Infections and Type 2 Diabetes. Endocrine Reviews, June 2020, 41(3):1–13

Dipeptidyl peptidase-4 inhibitors

- Insufficient evidence to determine the impact of partial reduction of DPP4 activity, on clinical outcomes in humans with active coronavirus infection.
- DPP-4 inhibitors, or in combination with basal insulin, effectively control glucose in patients with mild to moderate hyperglycemia.
- In active SARSCoV-2 infection , **clinically significant** volume depletion or systemic sepsis, ↓ renal function needed adjustment of the dose of some DPP4 inhibitors.

Pasquel FJ, Fayfman M, Umpierrez GE.Curr Diab Rep. 2019 Jul 29;19(9):65.
Drucker DJ. Coronavirus Infections and Type 2 Diabetes. Endocrine Reviews, June 2020, 41(3):1–13

SGLT2 inhibitors

- SARS-CoV-2 infection associated with anorexia, dehydration, and rapid deterioration in clinical status.
- T2D with active SARS-CoV-2 infection, heightened risk for volume depletion and euglycemic ketoacidosis.
- Re-evaluation of or discontinuation of these agents in very unwell ambulatory individuals.
- Routinely discontinued in unstable patients with severe SARS-CoV-2 infection upon admission to hospital

Drucker DJ. Coronavirus Infections and Type 2 Diabetes. Endocrine Reviews, June 2020, 41(3):1–13

GLP-1R agonists

- Although GLP-1 safely lowers blood glucose in short-term studies of perioperative period and in the ICU ventilated patients with critical illness, there is insufficient experience with the safety and use of GLP-1R agonists in critically ill subjects to make therapeutic recommendations for use of these agents in the context of coronavirus infection.

Crit Care. 2018; 22: 299

Drucker DJ. Coronavirus Infections and Type 2 Diabetes. Endocrine Reviews, June 2020, 41(3):1–13

The current approach to manage inpatient diabetes with COVID-19/suspects

- Urgent need to implement **effective glycemic control treatment approaches aiming at conserving the supply of PPE and reducing HCW exposure**.
  - The use of noninsulin agents in selected groups of patients
  - Novel algorithms for hyperglycemic crises management
  - The use of diabetes technology.

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Management of diabetic in-patient or ICU with COVID-19

In-patient or intensive care unit

Monitor for new onset diabetes in infected patients (in-patient care)

Management of infected patients with diabetes (intensive care unit)

- Plasma glucose monitoring, electrolytes, pH, blood ketones, or β-hydroxybutyrate
- Liberal indication for early intravenous insulin therapy in severe courses (ARDS, hyperinflammation) for exact titration, avoiding variable subcutaneous resorption, and management of commonly seen very high insulin consumption

Modif. From. The Lancet Diabetes & Endocrinology DOI: (10.1016/S2213-8587(20)30152-2)

Terjemahan dari: Pasquel FJ, Umpierrez GE. Journal of Diabetes Science and Technology1–3.2020 Diabetes Technology Society. DOI: 10.1177/1932296820923045

Tatalaksana DMT2 pada Pasien Non-Kritis di Rumah Sakit dengan COVID-19 atau ODP

Hiperglikemia ringan atau pasien yang lemah

<200 mg/dl

≤ 2 Obat antidiabetes, Insulin naif

Lansia, Gagal Ginjal

Basal insulin dosis rendah +/- DPP4-i

Insulin: 0.1 u/kg/hari atau 10U Detemir atau Glargine (sesuaikan jika perlu)

DPP4-i : mulai dengan dosis renal sitagliptin atau linagliptin

Koreksi : insulin regular/rapid
A) Jumlah APD memadai: setiap 12 jam
B) Kekurangan APD: sebelum makan pagi saja

Hiperglikemia sedang

201-300 mg/dl

Obat antidiabetes multiple

Insulin dengan TDH < 0.6 U/kg

Basal insulin +/- DPP4-i

Insulin: 0.2-0.3 u/kg/hari Detemir atau Glargine (sesuaikan jika perlu)

DPP4-i : mulai dengan dosis renal sitagliptin atau linagliptin

Koreksi : insulin regular/rapid
A) Jumlah APD memadai: setiap 12 jam
B) Kekurangan APD: sebelum makan pagi saja

Hiperglikemia berat

>300 mg/dl

Obat antidiabetes multiple

Insulin dengan TDH > 0.6 U/kg

Basal-bolus Insulin

Insulin: turunkan TDH di rumah sebesar 20% atau mulai dengan 0.5 u/kg/hari TDH ½ basal, ½ bolus (sesuaikan jika perlu)

Tunda pemberian insulin prandial apabila asupan makan buruk

Koreksi : insulin regular/rapid
A) Jumlah APD memadai: setelah makan atau setiap 8 jam
B) Kekurangan APD: sebelum makan pagi/siang atau setiap 12 jam

Intensifikasi Terapi Apabila Target Glikemik Tidak Tercapai : Gula Darah 100-180mg/dl

APD, alat pelindung diri; DMT2, diabetes melitus tipe 2; DPP-4i, dipeptidyl peptidase-4 inhibitor; ODP, orang dalam pengawasan; TDH, total dosis harian

Insulin therapy has been the considered regimen of choice in the hospital

- **Standardized basal-bolus regimen for most non critically ill patients.**
  - Complex
    - Multiple injections, frequent point-of-care (POC) glucose testing.
  - Associated with iatrogenic hypoglycemia.
- **In the intensive care unit (ICU), insulin therapy is even less convenient.**
  - Continuous insulin infusion (CII)→ needing hourly POC testing

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Critically Ill Patients

- Glycemic target range for ICU patients: 140 - 180 mg/dL.
- Patients with mild to moderate DKA:
    - Subcutaneous insulin / 2-4 hours
- Severe DKA, HHS, or combined DKA-HHS:
    - CII is recommended.

Critically Ill Patients (cont.)

- This current approach with hourly POC glucose testing is clearly impractical.
- **→ urgent need to systematically learn novel approaches utilizing diabetes technology (ie, continuous glucose monitoring [CGM] and artificial pancreas).**

Diabetes and COVID-19

- Higher case-fatality
- Prolonged length of stay
- Higher resource utilization

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To reduce the barriers of optimizing glycemic control

- Individualized care strategies
- Novel therapeutic regimens
- Use of diabetes technology :
  Prevent healthcare workers' exposures
  Reduce the waste of invaluable PPE

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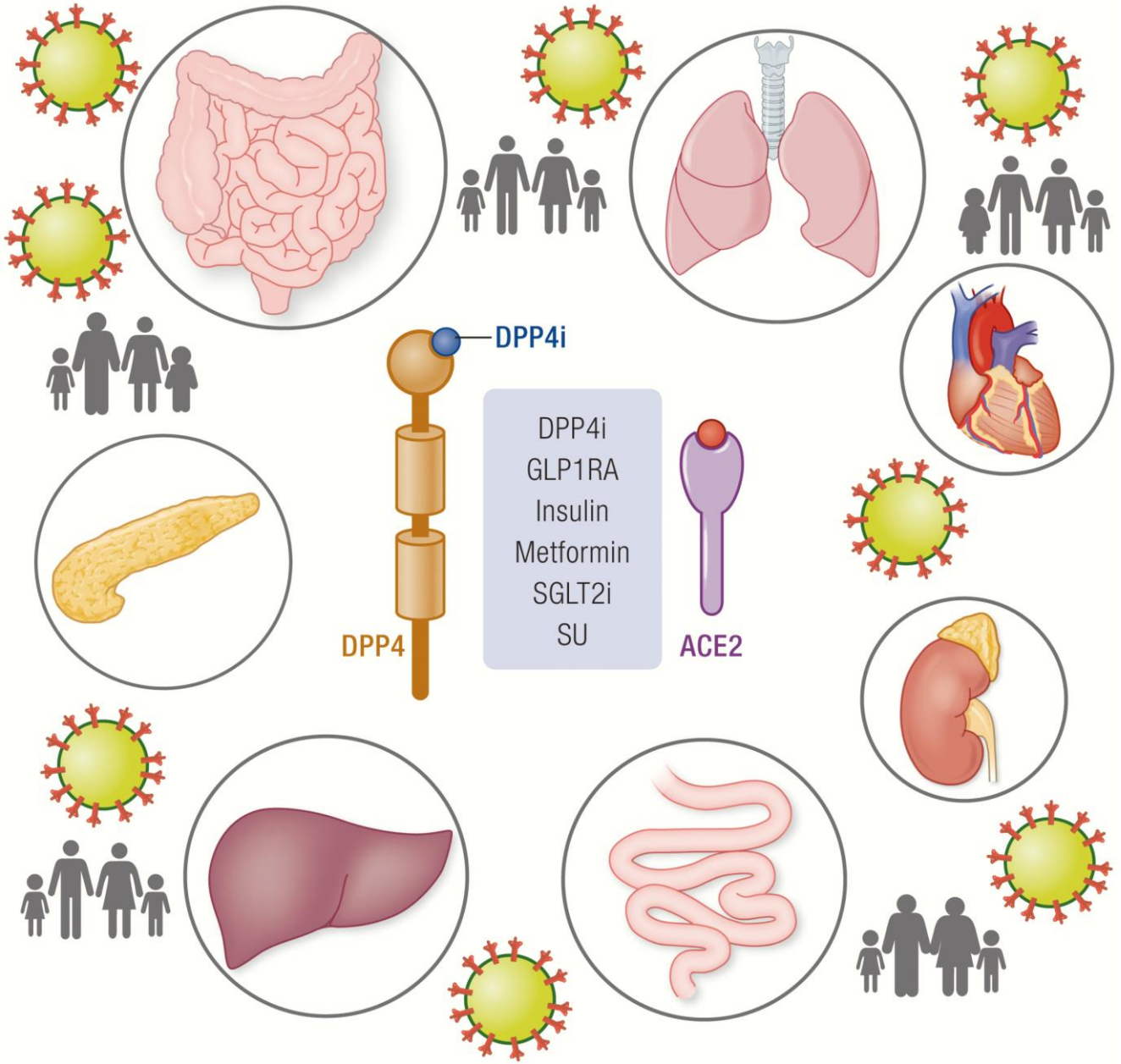
Graphical Abstract



Endocr Rev, Volume 41, Issue 3, June 2020, bnaa011, https://doi.org/10.1210/endrev/bnaa011

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