



# Pathophysiology and Management of the Obesity Metabolic Syndrome

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# Conflicts of Interest

- In the last 12 months I have received honoraria, travel or fees for speaking or advisory boards from
  - Abbott Diabetes
  - AstraZeneca
  - Boehringer-Ingelheim
  - Eli Lilly
  - Menarini
  - Novo Nordisk
  - Roche
  - Sanofi Diabetes

# Practical Advice – October 2023



Google  
“CPOC” and “diabetes”

Guideline for  
Perioperative Care  
for People with  
Diabetes Mellitus  
Undergoing Elective  
and Emergency  
Surgery

Updated October 2023

# Non-Insulin Agents

Google  
“CPOC” and “diabetes”

Diabetes medication	Day prior to admission	Timing of surgery	
		Patient for am surgery	Patient for pm surgery
<b>Acarbose</b>	Take as normal	Omit morning dose if not eating	Give morning dose if eating
<b>Meglitinide</b> (repaglinide or nateglinide)	Take as normal	Omit morning dose if not eating	Give morning dose if eating
<b>Metformin</b> (AND eGFR >60 ml/min/1.73m <sup>2</sup> OR procedure not requiring use of contrast media <sup>1,2</sup> )	Take as normal	If taken once or twice a day – take as normal If taken three times per day, omit lunchtime dose	If taken once or twice a day – take as normal If taken three times per day, do not take lunchtime dose
<b>Sulphonylurea</b> (eg glibenclamide, gliclazide, glipizide, glimiperide)	Take as normal	Omit on morning of surgery If taken twice daily, take evening dose if eating	Do not take on day of surgery
<b>Pioglitazone</b>	Take as normal	Take as normal	Take as normal
<b>DPP4 inhibitor</b> (eg sitagliptin, vildagliptin, saxagliptin, alogliptin, linagliptin)	Take as normal	Take as normal	Take as normal
<b>GLP-1 Receptor Agonist</b> (eg exenatide, liraglutide, lixisenatide, dulaglutide, semaglutide) Daily/Weekly administration	Take as normal	Take as normal	Take as normal
<b>SGLT-2 inhibitors</b> (eg dapagliflozin, canagliflozin, empagliflozin, ertugliflozin)	Omit on day before surgery	Omit on day of surgery	Omit on day of surgery

# GLP-1 and SGLT2i – Differences



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## NEWS

June 29, 2023

### American Society of Anesthesiologists Consensus-Based Guidance on Preoperative Management of Patients (Adults and Children) on Glucagon-Like Peptide-1 (GLP-1) Receptor Agonists

Girish P. Joshi, M.B.B.S., M.D., Basem B. Abdelmalak, M.D., Wade A. Weigel, M.D., Sulpicio G. Soriano, M.D., Monica W. Harbell, M.D., Catherine I. Kuo, M.D., Paul A. Stricker, M.D., Karen B. Domino, M.D., M.P.H., American Society of Anesthesiologists (ASA) Task Force on Preoperative Fasting

Glucagon-like peptide-1 (GLP-1) receptor agonists are approved by the Food and Drug Administration for treatment of type 2 diabetes mellitus and cardiovascular risk reduction in this cohort (see table).<sup>1</sup> In addition, GLP-1 receptor agonists are also used for weight loss. Several entities have recommended to hold these drugs either the day before or day of the procedure.<sup>2-7</sup> For patients on weekly dosing, it is recommended to hold the dose for a week.<sup>8</sup>

BJA

British Journal of Anaesthesia, 132 (4): 639–643 (2024)

doi: 10.1016/j.bja.2023.12.015

Advance Access Publication Date: 29 January 2024

Editorial

## EDITORIAL

### Perioperative use of glucagon-like peptide-1 receptor agonists and sodium-glucose cotransporter 2 inhibitors for diabetes mellitus

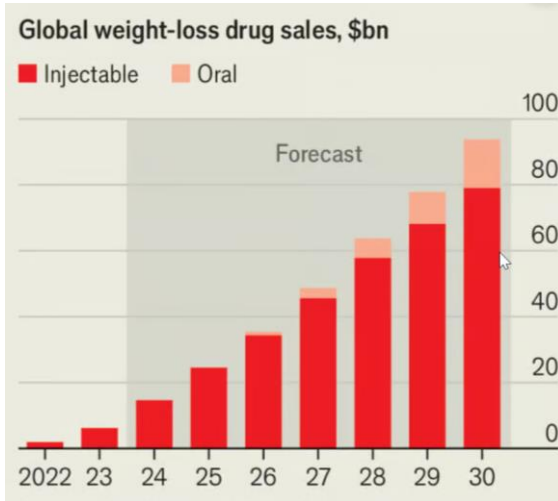
Ketan Dhatariya<sup>1,2,\*</sup>, Nicholas Levy<sup>3</sup>, Kim Russon<sup>4</sup>, Anil Patel<sup>5</sup>, Claire Frank<sup>6</sup>, Omar Mustafa<sup>7,8</sup>, Philip Newland-Jones<sup>9</sup>, Gerry Rayman<sup>10</sup>, Sarah Tinsley<sup>11</sup> and Jugdeep Dhesi<sup>12</sup>



# Wonder Drugs?



# A \$100Bn Market



**United States, estimated launch dates of selected weight-loss drug candidates**

● Injectables ● Oral

Year	Manufacturer	Drug	Type
2026	Eli Lilly	orforglipron	Oral
	Novo Nordisk	cagrisema	Injectable
	Novo Nordisk	semaglutide	Oral
2027	Boehringer Ingelheim/ Zealand Pharma	servodutide	Injectable
	Eli Lilly	retatrutide	Injectable
2028	Altimune	pemvidutide	Injectable
	Amgen	maritide	Injectable
	Pfizer	danuglipron	Oral
	Viking Therapeutics	VK2735	Injectable
	2029	Eli Lilly	mazdutide
2029 onwards	Structure Therapeutics	GSBR-1290	Oral
	Zealand Pharma	dapigliptide	Injectable
	Novo Nordisk	amycretin	Oral
2030 onwards	Roche	CT-388	Injectable
	Zealand Pharma	petrelintide	Injectable

	On the market	Clinical trial status	Route of administration	Receptor target
Exenatide	Yes	Finished	Injection	GLP-1
Liraglutide	Yes	Finished	Injection	GLP-1
Semaglutide	Yes	Finished	Injection or oral	GLP-1
Tirzepatide	Yes	Finished	Injection	GLP-1, GIP
Dulaglutide	Yes	Finished	Injection	GLP-1
Albiglutide	Yes	Finished	Injection	GLP-1
Lixisenatide	Yes	Finished	Injection	GLP-1
Cagrisema	No	Phase 3	Injection	GLP1, amylin
Survodutide	No	Phase 3	Injection	GLP-1, glucagon
Retatrutide	No	Phase 2	Injection	GLP-1, GIP, and glucagon
NNC0165-1875 + semaglutide	No	Phase 2	Injection	GLP-1, PPY
Efinopegdutide	No	Phase 2	Injection	GLP-1, glucagon
Danuglipron	No	Phase 2b	Oral	GLP-1
Orforglipron	No	Phase 1b	Oral	GLP-1
Amycretin	No	Phase 1	Oral	GLP-1, amylin

GIP=glucose-dependent insulinotropic polypeptide. PPY=pancreatic polypeptide.

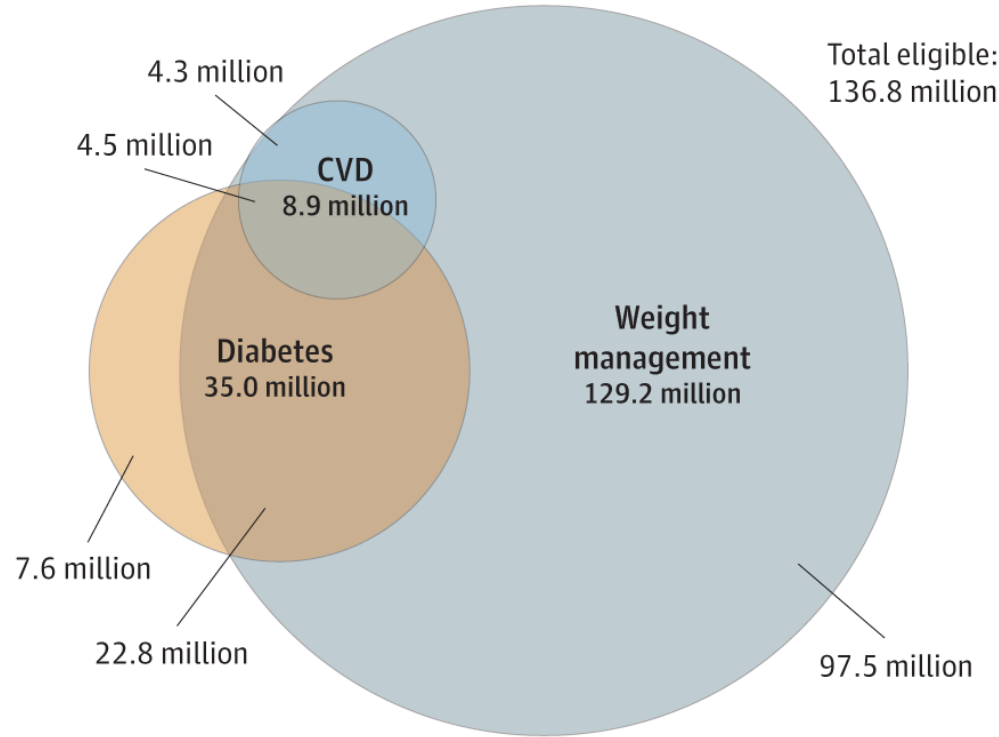
**Table:** List of selected currently available and future GLP-1 receptor agonists and their targets

The Economist 26<sup>th</sup> October 2024

Zushin P-J et al Lancet [https://doi.org/10.1016/S0140-6736\(24\)02255-4](https://doi.org/10.1016/S0140-6736(24)02255-4)

# Eligibility?

Half of ALL US adults are eligible to be on a GLP-1





# BMJ 26<sup>th</sup> October 2024

NEWS



The BMJ

Cite this as: *BMJ* 2024;387:q2281<http://dx.doi.org/10.1136/bmj.q2281>

Published: 17 October 2024

## Weight loss drugs for the unemployed—how will the government's new trial work?

Ministers want to examine the impact of the weight loss drug tirzepatide on people's health outcomes and employment status. **Elisabeth Mahase** looks at how the study will work

Elisabeth Mahase

### What has been announced?

A new partnership between the government and the pharmaceutical company Eli Lilly<sup>1</sup> will trial “innovative approaches to treating obesity as part of

NHSE has asked for an initial six month implementation period, after which 220 000 patients would become eligible to receive the drug—based on their health needs and clinical benefit—over a three

# BMJ 26<sup>th</sup> October 2024



## CONCLUSIONS

In this comparative cohort study, no increased risk of pulmonary aspiration during upper gastrointestinal endoscopy was observed among adults with type 2 diabetes using GLP-1 receptor agonists compared with SGLT-2 inhibitors within 30 days of the procedure; however, GLP-1 receptor agonists were associated with a higher risk of discontinuation of endoscopy, possibly owing to a higher risk of retained gastric content. In the absence of evidence from randomized trials, these findings could inform future practice recommendations on the preprocedural protocol for patients requiring endoscopy.



OPEN A



Check for up

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## RESEARCH

ation or

abetta Paterno<sup>1</sup>

8 years; 63.7%  
receptor agonists  
risk per 1000  
0.26 for pulmonary  
discontinuation  
of inhibitor use,  
associated with



# Delphi Consensus – GLP-1

- The risk of pulmonary aspiration and mitigation strategies should be discussed with the patient using a shared decision-making approach.
- People should continue to take GLP-1 RAs throughout the peri-operative period.
- Adhere to routine fasting guidelines.

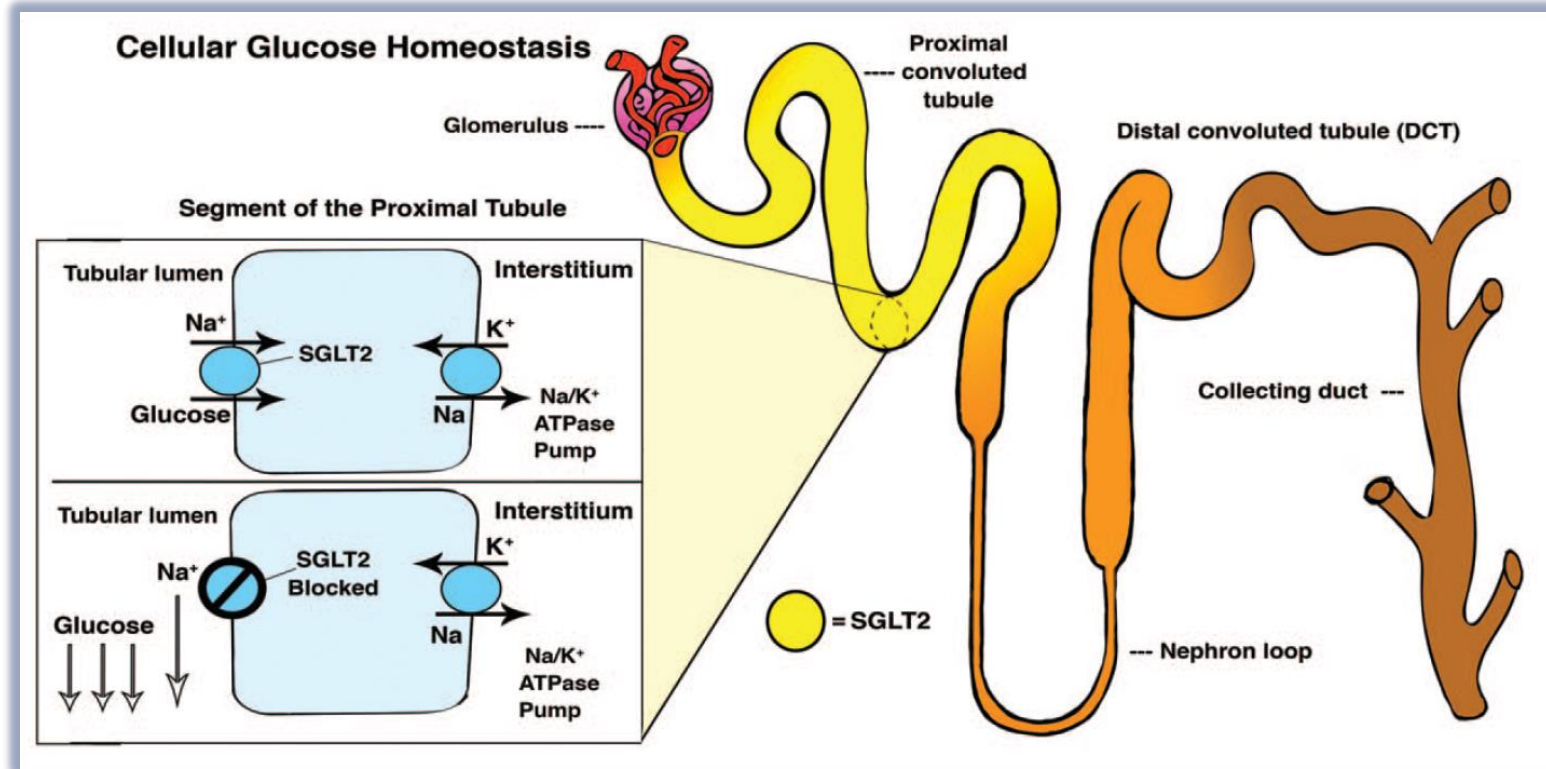
# Delphi Consensus – GLP-1

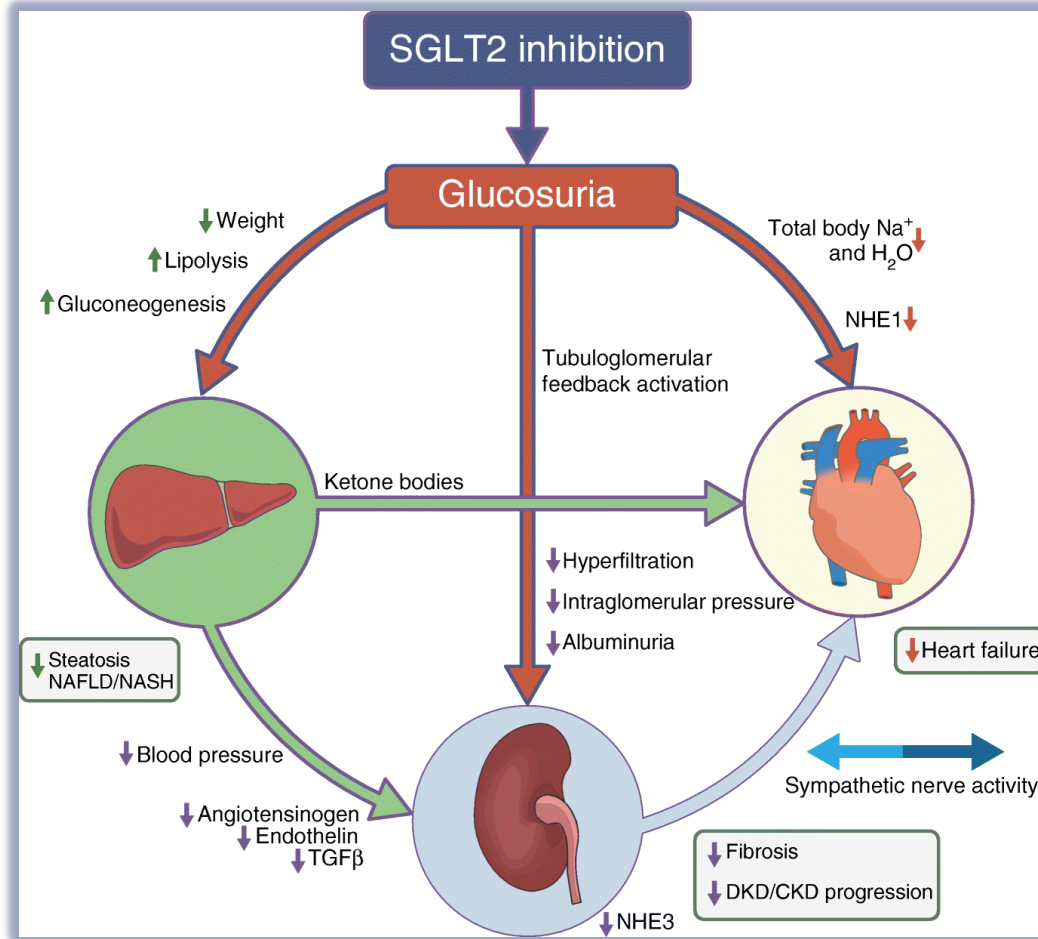
- Upper gastrointestinal symptoms alone should not be used to determine gastric content.
- Consider regional anaesthesia as the primary anaesthetic technique, if appropriate.
- Individualised pulmonary aspiration risk assessment should be completed, accounting for drug, patient and procedural factors.

# Delphi Consensus – GLP-1

- Consider point-of-care gastric ultrasound before induction of anaesthesia.
- Anaesthesia and airway management should aim to reduce the risk of pulmonary aspiration.

# How do SGLT2i Work?





# Delphi Consensus – SGLT2i

- The risk of peri-operative ketoacidosis and mitigation strategies should be discussed with the patient using a shared decision-making approach.
- SGLT2is should be omitted the day before and on the day of a procedure.
- Adhere to recommended fasting guidelines and avoid prolonged starvation times.



# Delphi Consensus – SGLT2i

- For patients discharged from hospital on the day of surgery, SGLT2is should be restarted when eating and drinking normally (usually 24-48 hours after surgery).
- For patients admitted to hospital after surgery, SGLT2is should be restarted when eating and drinking normally and capillary ketones are  $< 0.6$  mmol/l.

# Delphi Consensus – SGLT2i

- For people on a very low calorie/liver shrinkage diet for the purposes of surgery, SGLT2is should be withheld from commencement of the diet, with consideration if alternative diabetes treatment is needed during this time.
- Written sick day rules should be provided to patients.

# A New Guideline

- Is being developed jointly by the JBDS, BOMMS, CPOC on the specialist needs of those undergoing bariatric surgery – watch this space!

# In Summary

- Obesity is a disease – a product of genes and environment
- It is NOT the fault of the individual
- Newer agents will help hugely



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