



Limitations of A1c



**Some slides from talks
at ADA, June 2023**



HbA1c is not Perfect

HbA1c has a number of weaknesses

- ▶ Several factors affect accuracy
- ▶ **Delays in therapy escalations**
- ▶ Does not address effects of daily life activities on glucose

HbA1c does not measure

- ▶ Hypoglycemia
- ▶ Glycemic variability (GV)

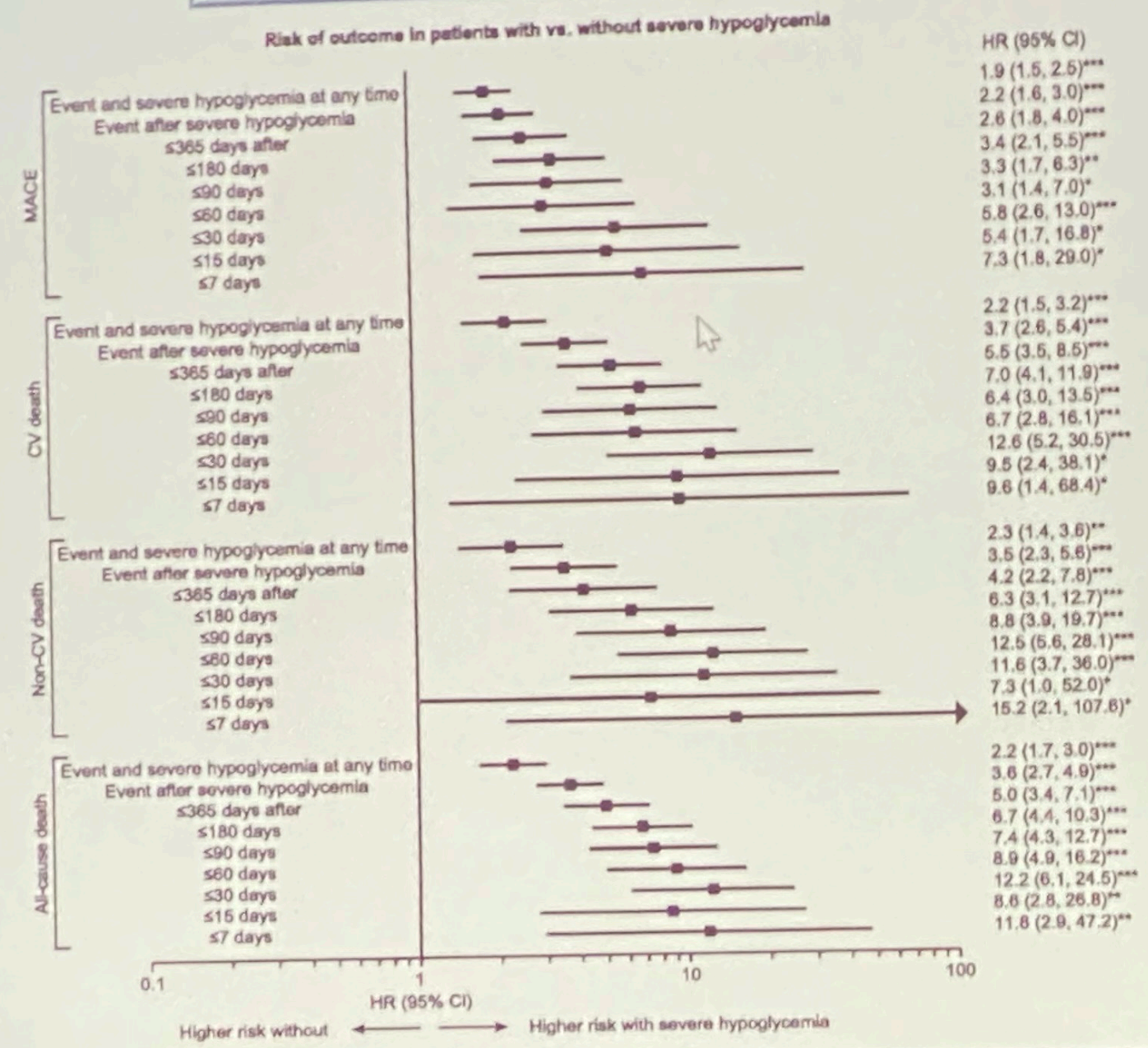
Severe hypoglycemia and CV events/death LEADER trial; n=9,304

A1c cannot provide evidence of episodes of hypoglycemia.

This slide shows the associations between an episode of severe hypoglycemia and 'major adverse cardiovascular events', and death.

The more recent the hypoglycemia, the greater the risk.

This risk is one of the major reasons for the growing emphasis on CGM rather than A1c to control glycemia.



A1c can be affected by factors shown on this slide.

Several of these may be common among patients needing surgery, e.g. chronic hemorrhage, anemia, underlying kidney or liver disease.



Some of the Factors Modulating Accuracy of HbA_{1c}

	Erythropoiesis	Hemolysis (erythrocytes lifespan)	Altered hemoglobin
<p>↓ Falsely low HbA_{1c}</p>	<p>Increased erythropoiesis</p> <ul style="list-style-type: none"> • Hemorrhage • Administration of erythropoietin • Pregnancy • High altitude 	<p>Decreased erythrocytes lifespan</p> <ul style="list-style-type: none"> • Chronic liver / kidney disease • Hemolytic anemia • Hemoglobinopathies • Antiretroviral treatment 	<ul style="list-style-type: none"> • Hemoglobinopathies • Methemoglobin
<p>↑ Falsely high HbA_{1c}</p>	<p>Decreased erythropoiesis</p> <ul style="list-style-type: none"> • Different anemia (iron deficiency, infections, tumor) 	<p>Increased erythrocytes lifespan</p> <ul style="list-style-type: none"> • Splenectomy • Different anemia • Hemoglobinopathies 	<ul style="list-style-type: none"> • Hemoglobinopathies

Gallagher et al., J Diabetes. 2009;1(1):9-17
<https://www.consultant360.com/articles/when-a1c-unreliable>
 Campbell L. et al., J Clin Pathol. 2019;72:12-19



Conclusions

HbA1c has served us well but it has limitations related to:

- Inaccuracy in reflecting average glucose in some individuals
- Slow assessment of response to glycemic lowering therapies
- Inability to address hypoglycemia and glycemic variability, which are associated with adverse clinical outcome

We should use additional CGM-derived glycemic markers to optimise glucose management in all individuals with diabetes (this is not limited to T1D):

- Time in range (TIR)
- Time below range (TBR) or hypoglycemia
- Glycemic variability