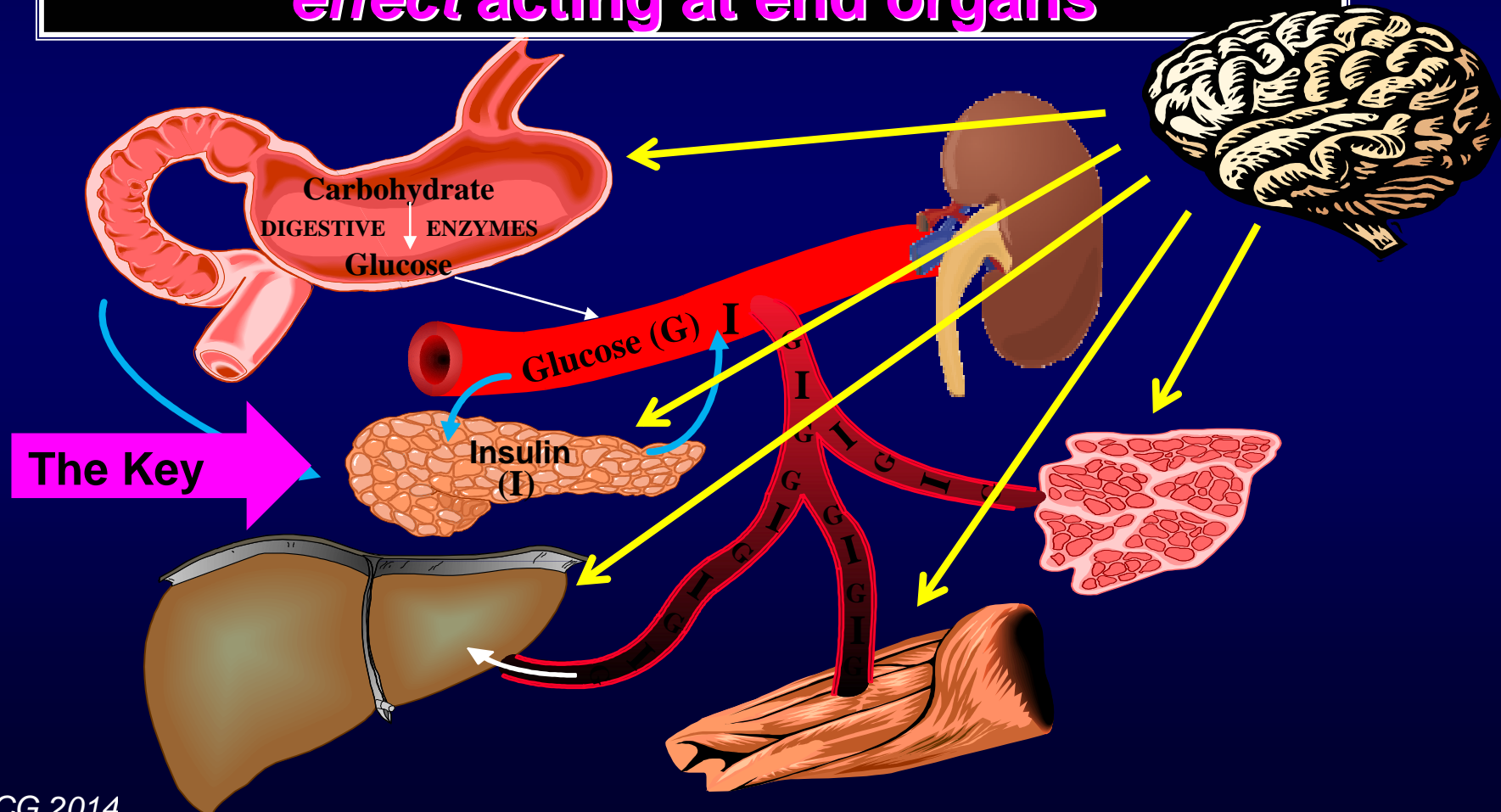


Case 1

- 45 year-old male patient seen at the clinic (Medicine).
- Workplace stress (financial analyst); occasionally goes jogging.
- Two-year duration of T2DM. No previous cardiovascular events. Coexisting mild intermittent asthma.
- BMI: 32.
- On diet + metformin, HbA1C = 7.8%.
- FPG in the morning \approx 120-130 mg/dl.
- Next step in his medical management?

Physiology of Normoglycemia

If glucose is high → *insufficient insulin effect acting at end organs*



Tools to Control G Levels

- *Increase the effect of available insulin*

Diet +/- weight loss

Activity

Metformin (liver)

TZDs (fat, muscle, liver)

- *Increase the supply of insulin (to increase effect)*

Sulfonylureas

Glinides

Insulin

Incretins (GLP-1, DPP4-I)

- *Reduce the need for insulin supply (improve the match between insulin supply & effect)*

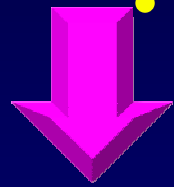
AGIs (acarbose)

SGLT2 inhibitors

Incretins (GLP-1, DPP4-I)

Pramlintide

Tools to Lower G Levels



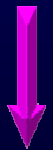
- Insulin: Long acting: *glargine, detemir, degludec, NPH*
Medium: *regular*
Rapid: *lispro, aspart, glulisine*



- Sulfonylurea: *glyburide**, *gliclazide, glimepiride, glipizide*
- Glinide: *repaglinide, nateglinide*



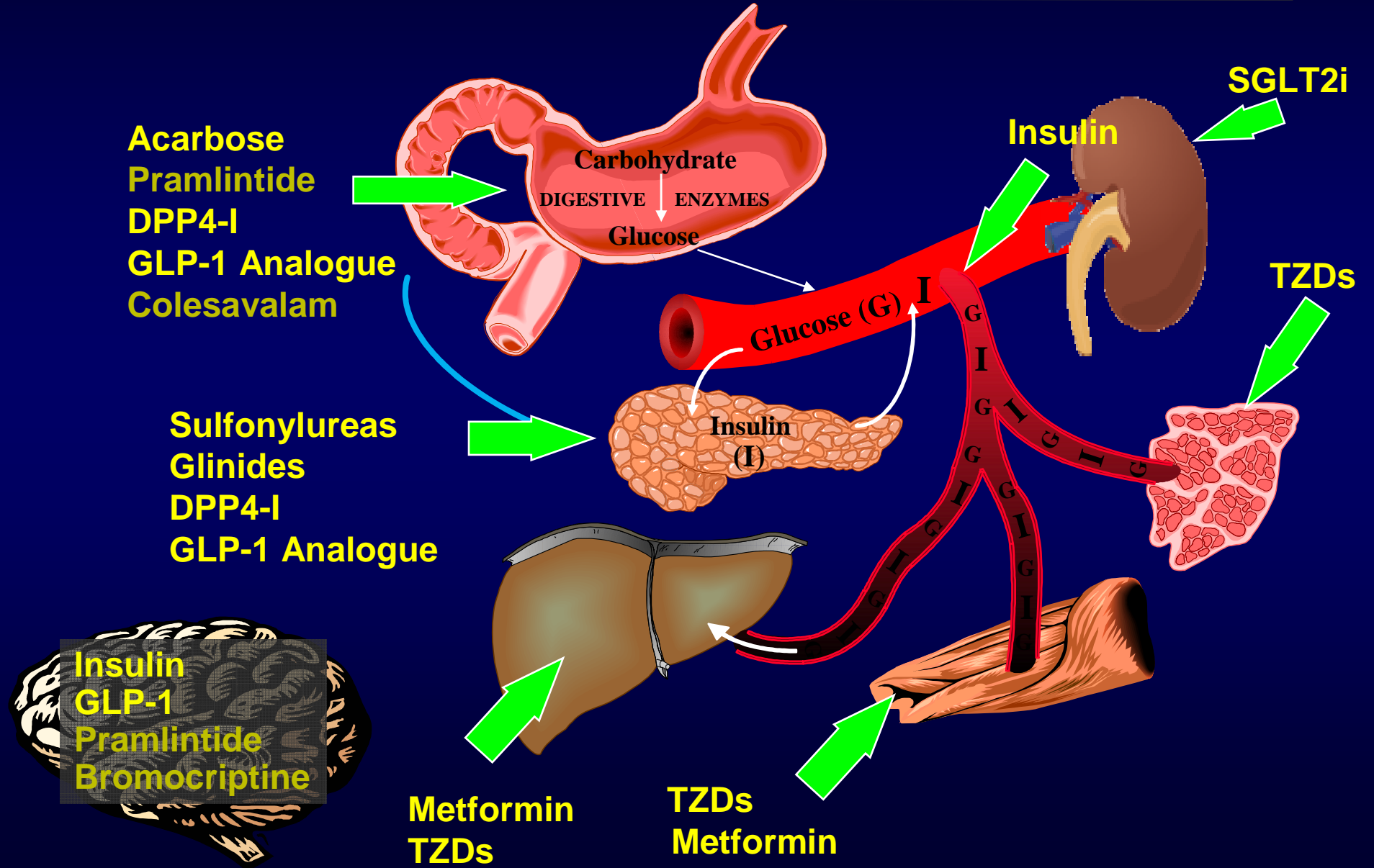
- Biguanide: *metformin*
- TZD: *pioglitazone, rosiglitazone*
- SGLT2i: *canagliflozin, dapagliflozin, empagliflozin*



- GLP -1 analog: *exenatide, liraglutide, lixisenatide*
- DPP4-I: *sitagliptin, vildagliptin, saxagliptin*

- Alpha Glucosidase Inhibitor: *acarbose, miglitol*

Tools to Lower G Levels



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- BMI: 32.
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- Next step in his medical management?

Case 2

- 60 year-old male patient, admitted for NSTEMI, treated with angioplasty.
- Roughly, 10-yr duration of T2DM. Hypertension. Hypercholesterolemia. Intermittent claudication.
- BMI: 31.
- eGFR = 70 ml/min/1.73m².
- HbA1C = 8.1%.
- Treatment before current admission: metformin, 850 mg/12 h plus sustained-release gliclazide, 90 mg/day.
- Any changes in treatment before/at discharge?

How to start insulin it: INSIGHT Trial

In people with type 2 diabetes who are treated with lifestyle alone, 1 agent or sub-maximal doses of 2 oral agents by specialists or generalists & can easily be managed without insulin....

... does the addition & titration of basal insulin to a FPG \leq 5.5 mmol/L (100 mg/dL) safely achieve an A1c \leq 6.5% faster & more frequently than increasing or adding oral agents?

Trial Design

Lifestyle alone

1 oral agent,
(SU, Metformin
Repaglinide)

2 oral agents
where at least is
at \leq half max.
dose

RAND

Current Rx + Insulin Glargine
Titrated to FPG \leq 5.5 (100)

Oral agent mono-Rx (SU,
metformin, repaglinide) OR

Dose/add a 2nd oral agent OR

Dose of 2 agents to max OR

Add a 3rd agent

-2 Wks

**Wk 0
(baseline)**

**Wk 24
(end)**

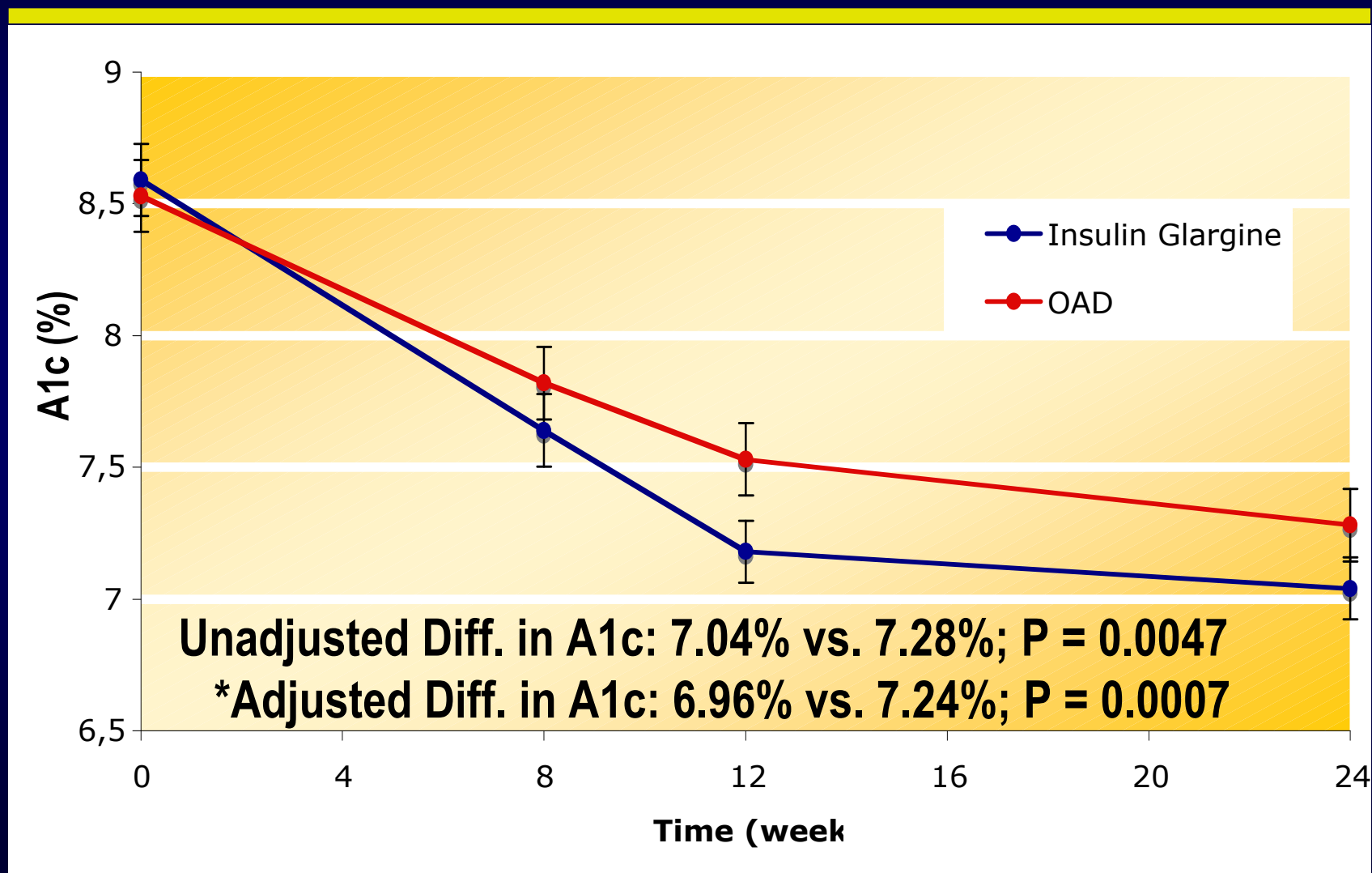
Screening phase

Treatment phase

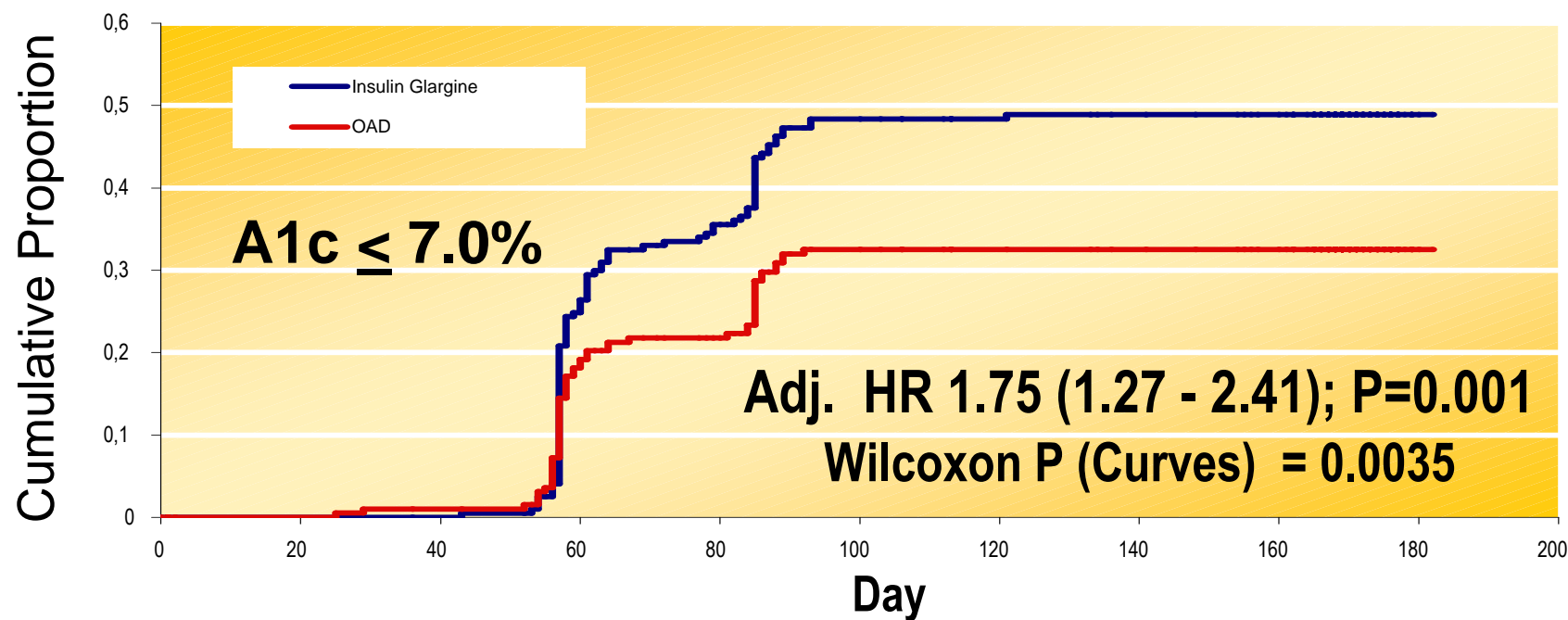
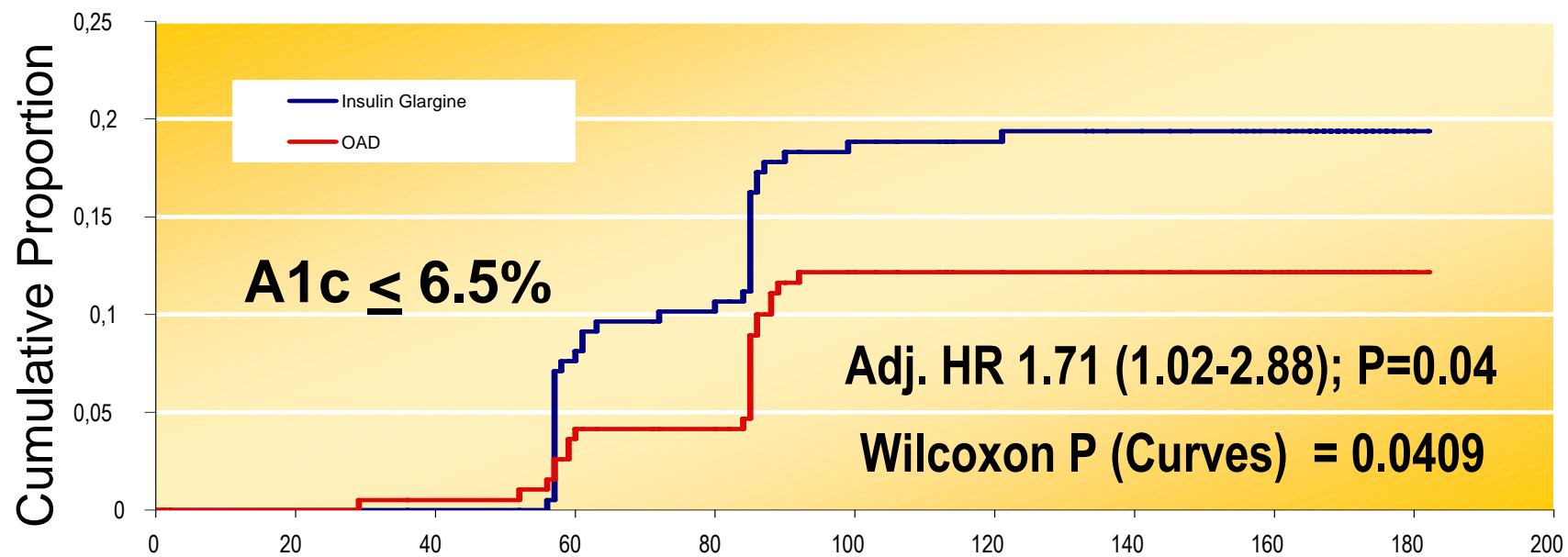
Baseline Characteristics

	Total 405	Insulin 206	OADs 199
Expert (%)	145 (35.8)	75 (36.4)	70 (35.2)
Family MD (%)	260 (64.2)	131 (63.6)	129 (64.8)
Age (yrs)	56.5 (9.8)	56.3 (9.4)	56.8 (10.1)
DM Duration (yrs)	7.9 (6.0)	7.6 (5.4)	8.2 (6.5)
BMI (kg/m ²)	31.3 (4.5)	31.1 (4.4)	31.5 (4.6)
A1c (%)	8.6 (1.0)	8.6 (1.0)	8.5 (1.0)
Drug Naïve (%)	68 (16.8)	38 (18.4)	30 (15.1)
Metformin <i>or</i> SU (%)	165 (40.7)	81 (39.3)	84 (42.2)
Metformin <i>&</i> SU (%)	172 (42.5)	87 (42.2)	85 (42.7)

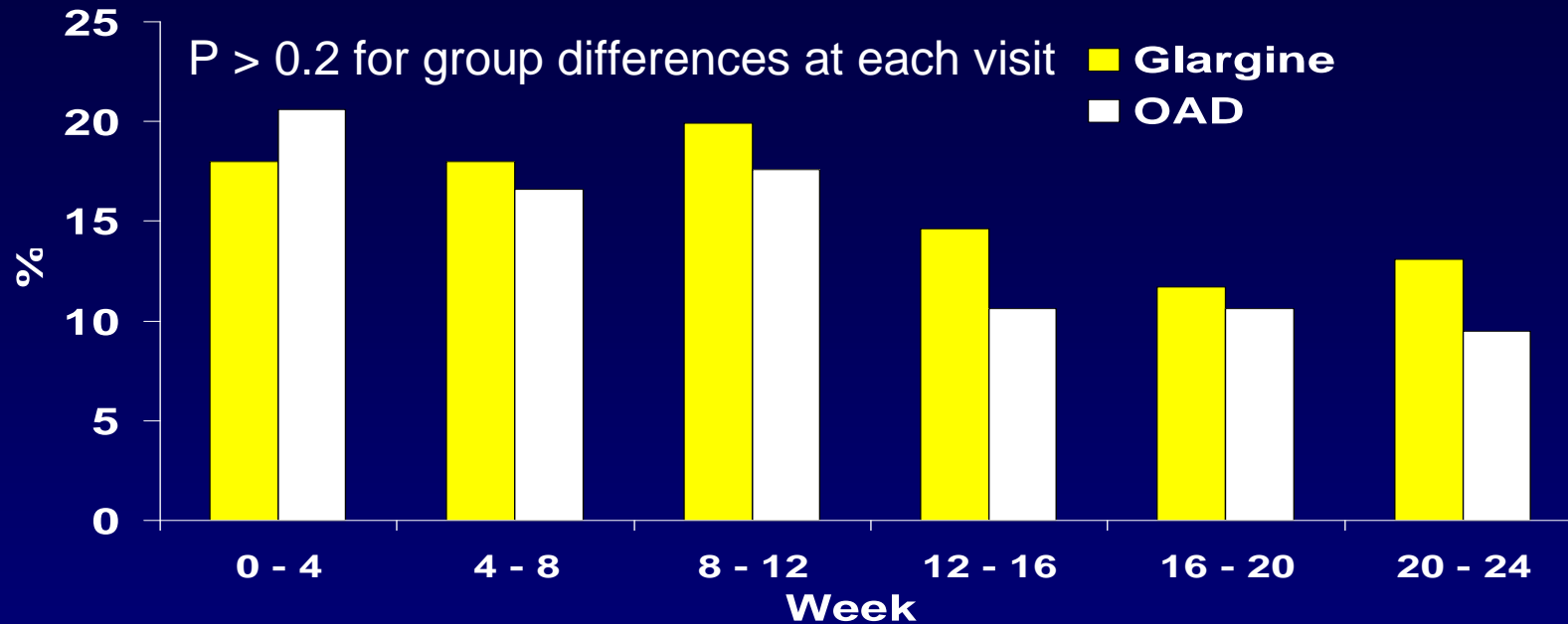
Achieved A1c (95% CI)



* Adjusted for baseline values, stratum or site



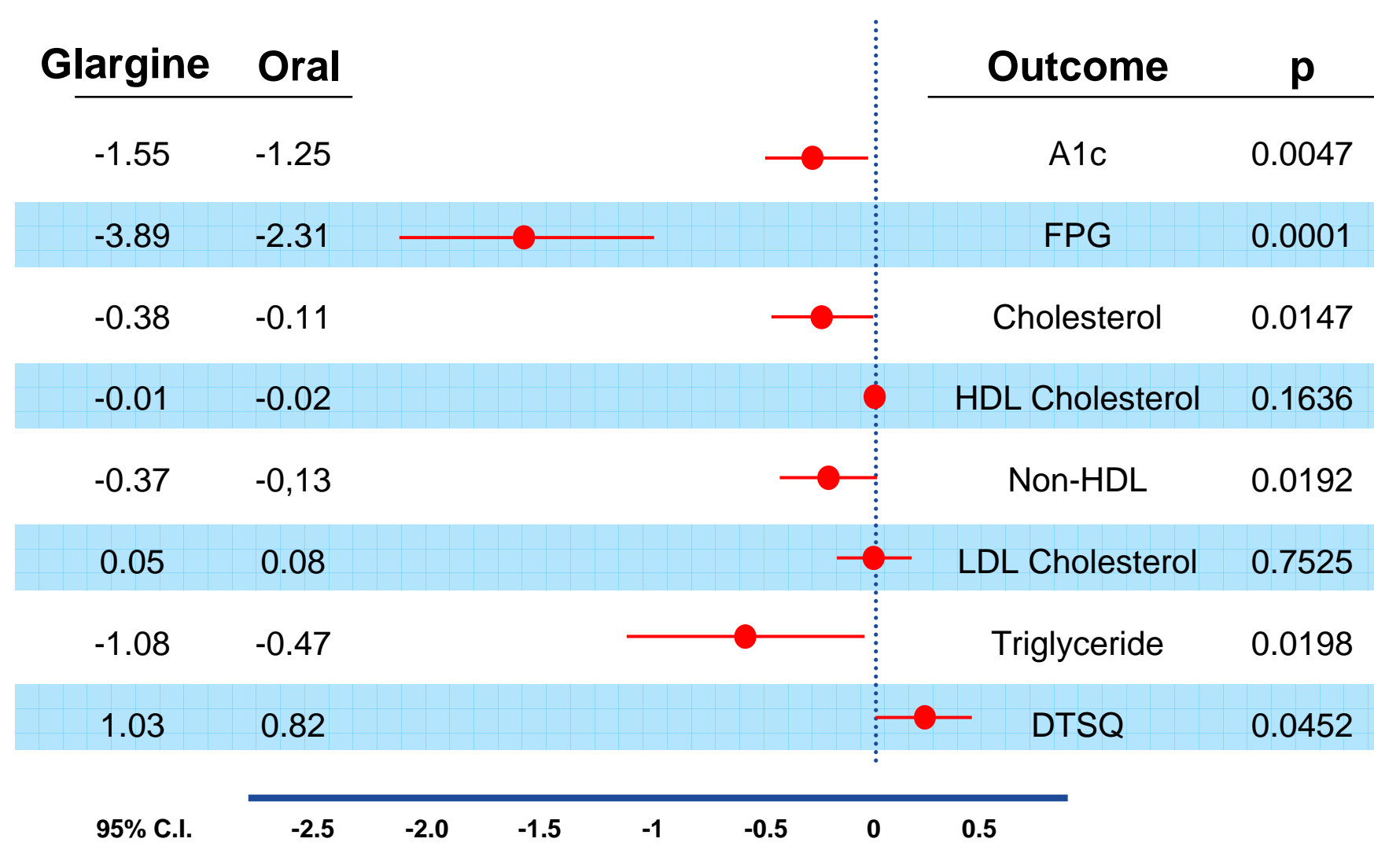
Hypoglycemia & Weight



(Adj. baseline, site stratum)

	Glargine	OAD	Diff. (95% CI)
Final – Initial Waist	1.23	-0.74	1.97 (0.96, 2.98)
Final – Initial BMI	0.72	0.06	0.65 (0.39, 0.92)
Final – Initial Weight	2.11	0.16	1.94 (1.16, 2.73)

Other Endpoints



Case 2

- 60 year-old male patient, admitted for NSTEMI, treated with angioplasty.
- Roughly, 10-yr duration of T2DM. Hypertension. Hypercholesterolemia. Intermittent claudication.
- BMI: 31.
- eGFR = 70 ml/min/1.73m².
- HbA1C = 8.1%.
- Treatment before current admission: metformin, 850 mg/12 h plus sustained-release gliclazide, 90 mg/day.
- ***Any changes in treatment before/at discharge?***

Case 3

- 38 year-old man; formerly unknown diabetes; admits having recently experienced polyuria and polydipsia.
- Admitted to the ICU for pneumonia and shock, needing steroids and mechanical ventilation.
- BMI at admission: 40 (weight: 130 kg). At discharge: 36.
- HbA1c = 9%.
- At the Medicine ward he is treated with metformin 850 mg/12h plus basal-boluses insulin.
- After spending 19 days in the hospital, he is close to be discharged in good condition. Gone off steroids now.
- Basal glargine dose has been gradually reduced to 14 IU at night, needing additional glulisine 5 IU for lunch.
- Would you keep this treatment at discharge?

Potential Approaches

- Consider the big picture!!!
- What type of diabetes does he have???
- Intensive medical therapy
 - *Lifestyle*
 - *Drugs*
- Metabolic surgery

Features of Basal Insulin Therapy

The G level tells you when the dose is right

There is no maximum or minimum dose

Easily titrated & virtually painless

No contraindication & no true drug interactions

Easy-to-use insulin preparations & delivery devices

Often only need 1 dose/day

Medicine has more experience with insulin therapy
than almost any other agent (i.e. 91 years)

Case 4

- 75 year-old female patient seen at the clinic.
- 25 year-duration T2DM. Long-standing stable angina due to small vessels obstruction, not amenable to PCI. LVEF: 55%.
- CKD with confirmed microalbuminuria (180 mg/g) and eGFR = 58 ml/min/1.73m².
- Recent weight gain; BMI: 30.5.
- HbA1C = 8%.
- Current treatment: metformin 850 mg/12h plus linagliptin 5 mg/day.
- Next step?