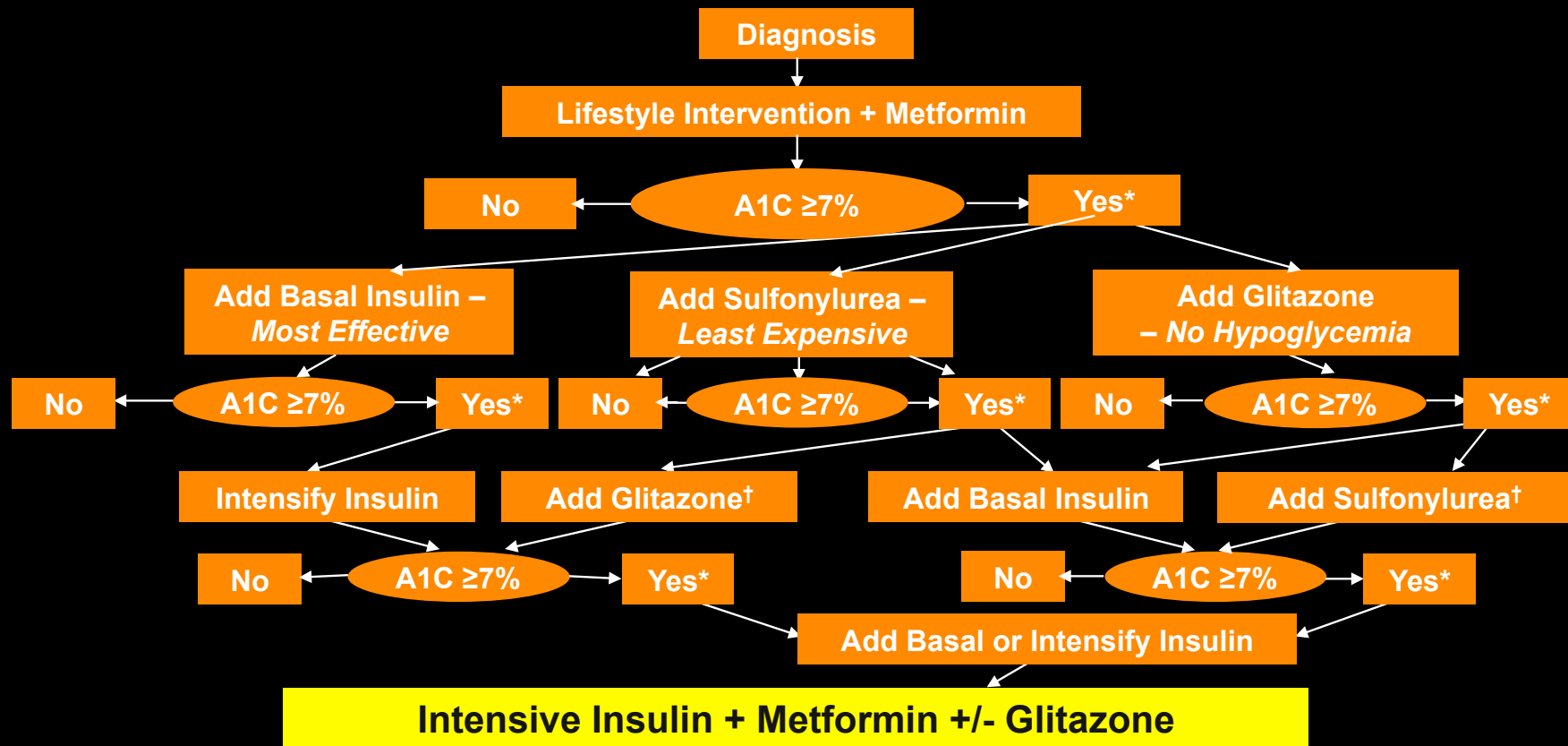


Antihyperglycemic Agents in Type 2 Diabetes

Class	A1C Reduction	Fasting vs PPG	Hypo-glycemia	Weight Change	Dosing (times/day)	Outcome Studies
Metformin	1.5	Fasting	No	Neutral	2	UKPDS
Insulin, Long-acting	1.5 - 2.5	Fasting	Yes	Gain	1, Injected	DIGAMI, UKPDS, (DCCT)
Insulin, Rapid-acting	1.5 - 2.5	PPG	Yes	Gain	1-4, Injected	DIGAMI, UKPDS, (DCCT)
Sulfonylureas	1.5	Fasting	Yes	Gain	1	UKPDS
"Glitazones"	0.5 - 1.4	Fasting	No	Gain	1	PROactive

Adapted from: Nathan DM, et al. *Diabetes Care*. 2007;30:753-759; Nathan DM, et al. *Diabetes Care*. 2006; 29:1963-1972; Nathan DM, et al. *Diabetes Care*. 2008;31:173-175. ADA. *Diabetes Care*. 2008;31:S12-S54.

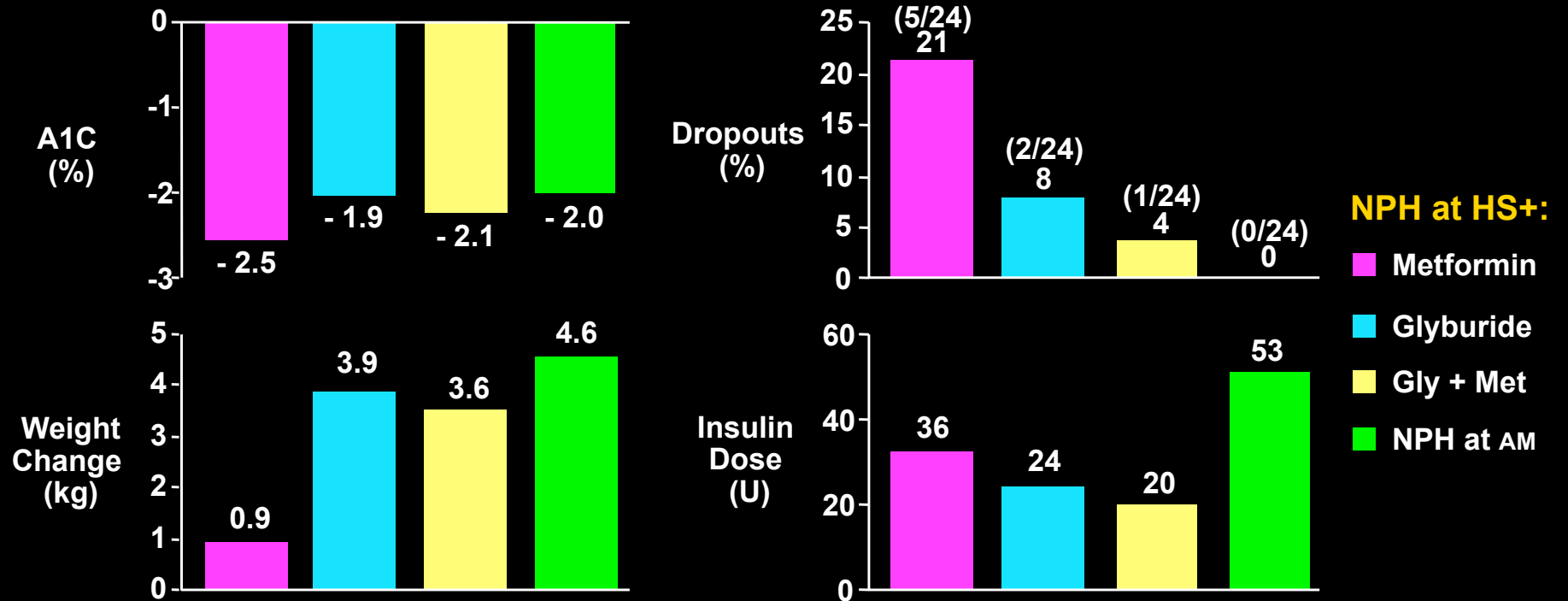
ADA/EASD Consensus: Treatment Algorithm



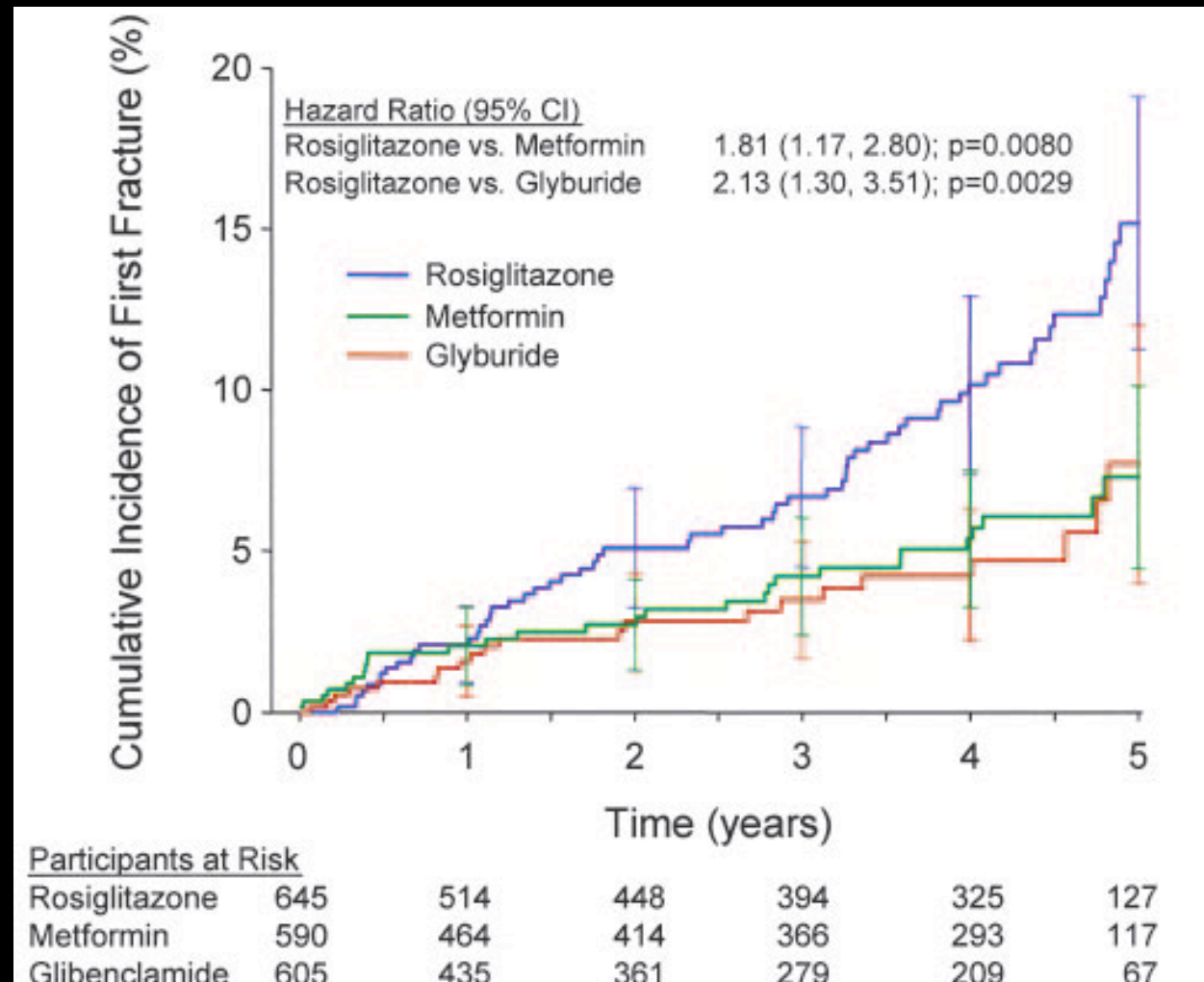
*Check A1C every 3 months until $<7\%$ and then at least every 6 months. †Although 3 oral agents can be used, initiation and intensification of insulin therapy is preferred based on effectiveness and expense.

ADA/EASD. *Diabetes Care*. 2006;29:1963-1972.

FINFAT Study: Bedtime NPH + Various Oral Agents



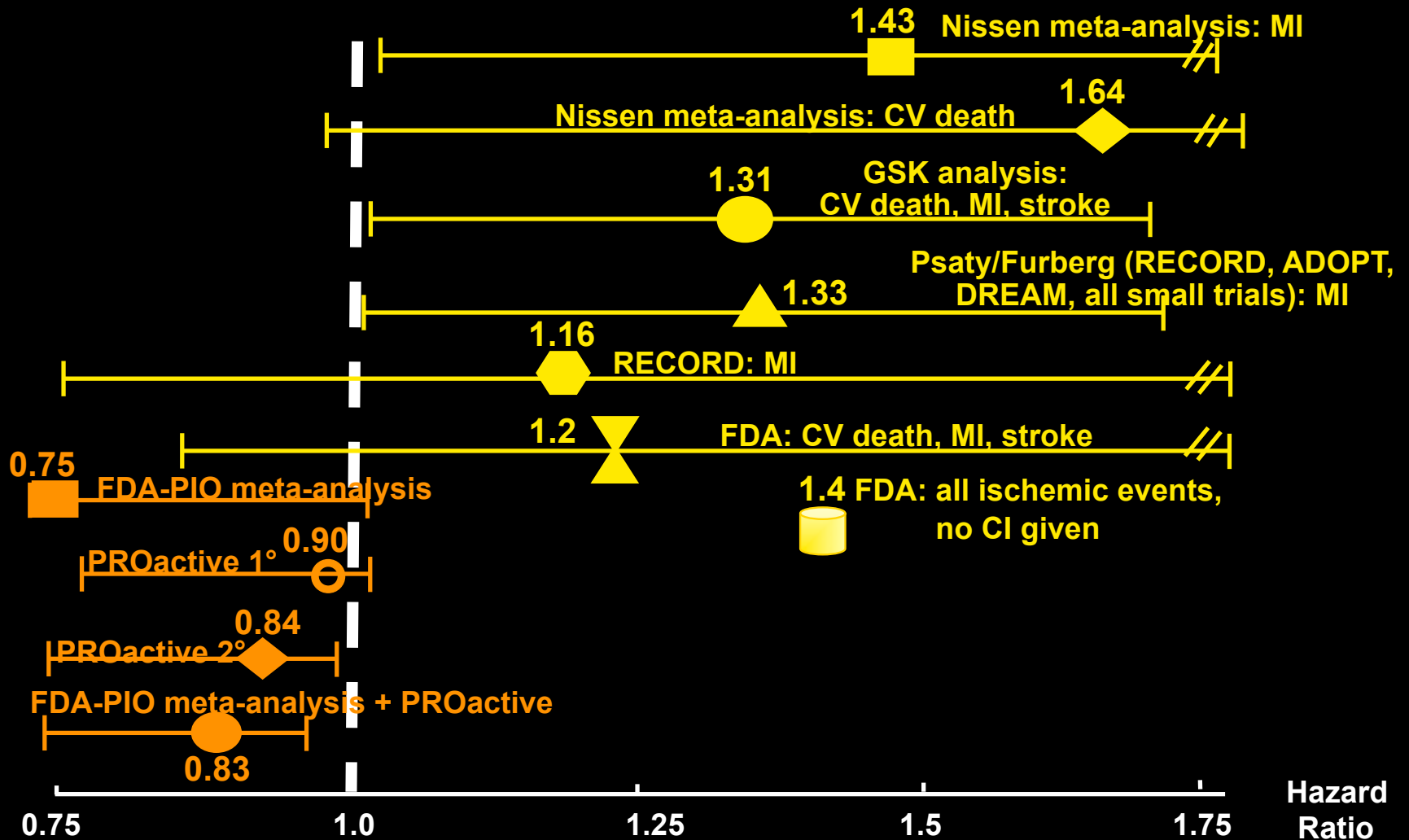
Fractures in Women Treated With Glitazones



Kahn SE, et al. *Diabetes Care*. 2008;31:845-851.

Hazard Ratio for Cardiovascular Events

Rosiglitazone vs Pioglitazone



Adapted from: Lincoff AM, et al. *JAMA*. 2007;298:1180-1188; Singh S, et al. *JAMA*. 2007;298:1189-1195.

Antihyperglycemic Agents in Type 2 Diabetes

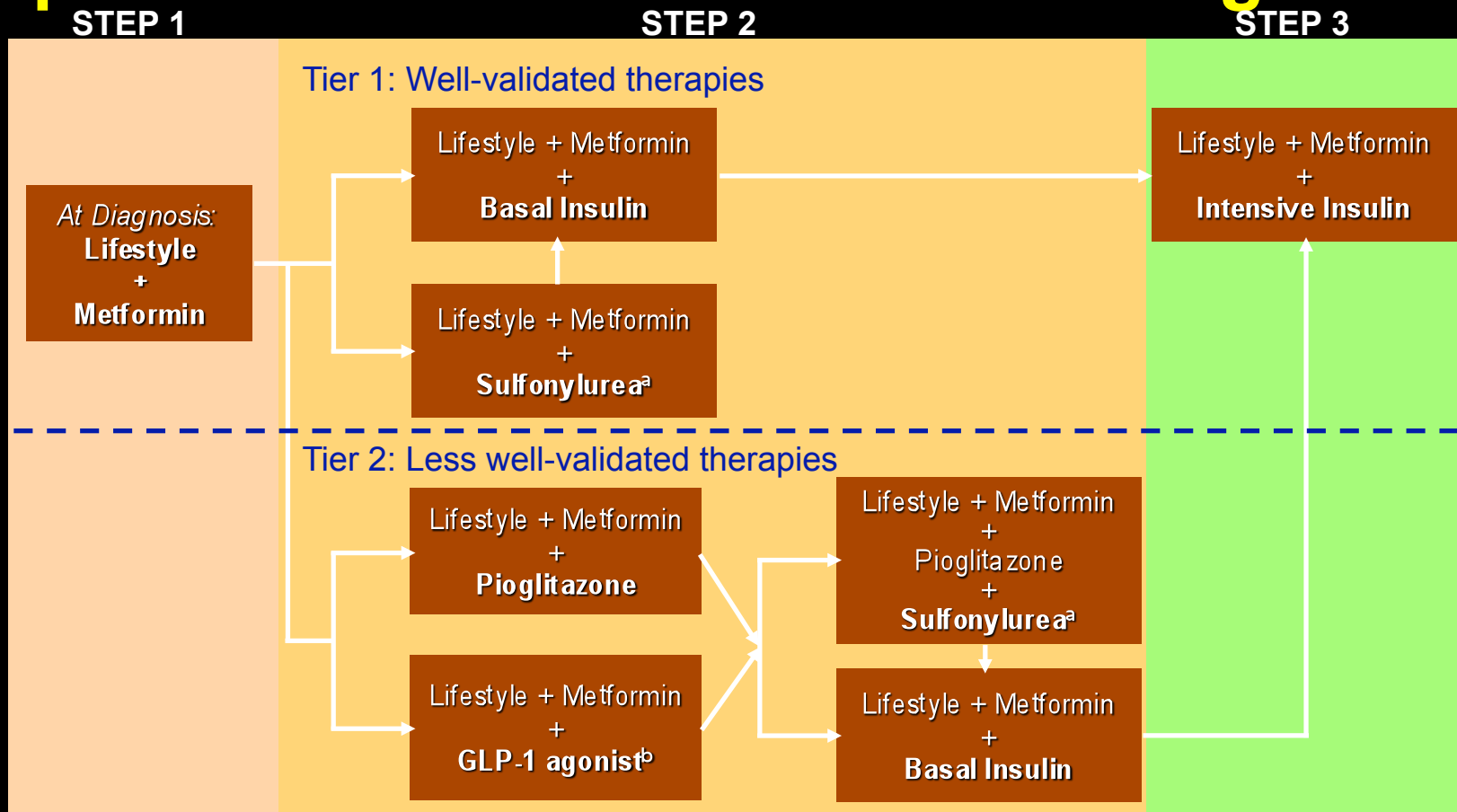
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Sulfonylureas	1.5	Fasting	Yes	Gain	1	UKPDS
"Glitazones"	0.5 - 1.4	Fasting	No	Gain	1	PROactive
Repaglinide	1 - 1.5	Both	Yes	Gain	3	None
Nateglinide	0.5 - 0.8	PPG	Rare	Gain	3	Navigator Pending
Alpha-glucosidase Inhibitors	0.5 - 0.8	PPG	No	Neutral	3	None
Amylin-mimetics (pramlintide)	0.5 - 1.0	PPG	No	Loss	3, Injected	None
Incretin Agonists (exenatide)	0.5 - 1.0	PPG	No	Loss	2, Injected	None
DPP-IV Inhibitor (sitagliptin)	0.6 - 0.8	Both	No	Neutral	1	TECOS pending
Bile acid sequestrant (colesevelam)	0.5	Fasting	No	Neutral	1-2	None

Adapted from: Nathan DM, et al. *Diabetes Care*. 2007;30:753-759; Nathan DM, et al. *Diabetes Care*. 2006; 29:1963-1972; Nathan DM, et al. *Diabetes Care*. 2008;31:173-175. ADA. *Diabetes Care*. 2008;31:S12-S54. WeiChol PI. 1/2008

Incretin Mimetics and DPP-4 Inhibitors:

Properties/Effect	Exenatide	DPP-4 Inhibitors	Investigational >24 hr agonists
Glucose-dependent stimulation of insulin secretion	Yes	Yes	Yes
Glucose-dependent reduction of increased glucagon	Yes	Yes	Yes
Slows gastric emptying	Yes	No	Little or no
Effect on body weight	Weight loss	Weight neutral	Weight loss
Effect on A1C	~1%	<1%	>1%
Effect on fasting glucose	Modest	Modest	Good
Effect on postprandial glucose	Good	Modest	Modest
Effect on CVD risk factors	Improve with weight loss	No consistent change	Improve
Side effects	Nausea	~ None observed	Less nausea, skin
Administration	Subcutaneous Twice-daily	Oral Once-daily	Subcutaneous Daily or weekly

Updated ADA/EASD Consensus Algorithm



Reinforce lifestyle interventions at every visit and check A1C every three months until A1C < 7.0 %, then at least every 6 months thereafter. Change interventions whenever A1C ≥ 7.0 %.

Rosiglitazone is no longer recommended.

^aSulfonylureas other than glyburide or chlorpropamide.

^bInsufficient clinical use to be confident regarding safety.

Nathan DM, et al., *Diabetes Care* published online on December 17, 2008 as dc08-9025