ULB UNIVERSITÉ LIBRE DE BRUXELLES

FSM Faculté des Sciences de la Motricité

REKI Connects

"Emerging populations in rehabilitation in internal diseases"

Physical exercise as preventive and therapeutic tool in different types of diabetes mellitus

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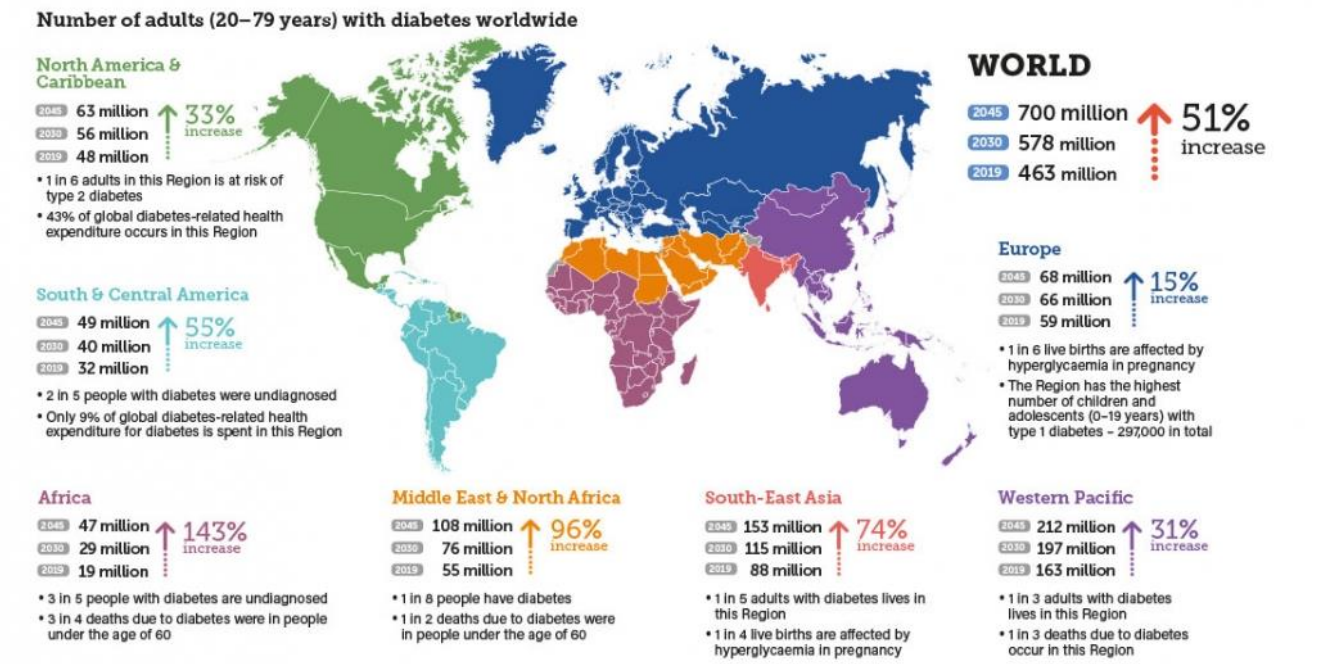
Faculty of Motor Sciences

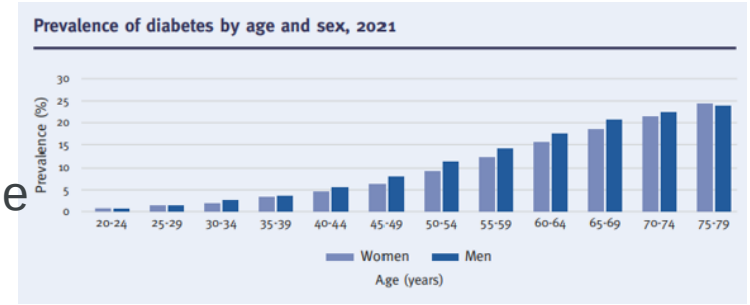
- Introduction
- Subjects With Type 1 Diabetes
- Subjects With Type 2 Diabetes
- Diabetes in pregnancy
- Other specific types

Alarming rate worldwide

Prevalence and incidence have increased this last decade



36% of people living with diabetes are undiagnosed



7% of the population
5% of national health costs

Atlas of the International Fédération of Diabète, Edition 2017

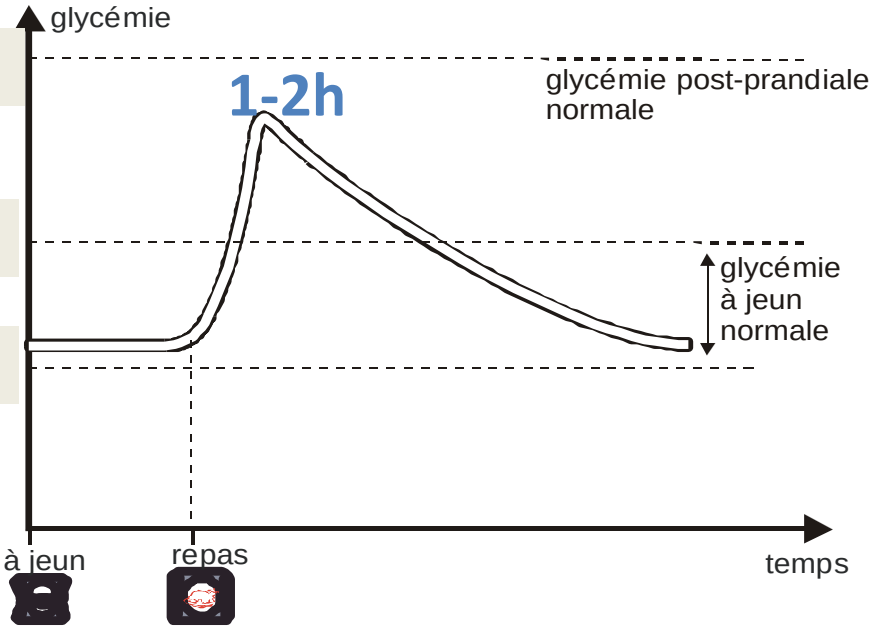
summary of the Cost of Diabetes in Europe-Type II study (CODE-2) and analysis of the situation in Belgium

Definition

Diabetes is a chronic, metabolic disease characterized by elevated levels of blood glucose (or blood sugar), which leads over time to serious health organic damage

** Two test, if no symptoms

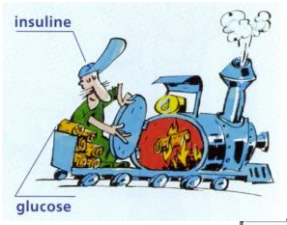


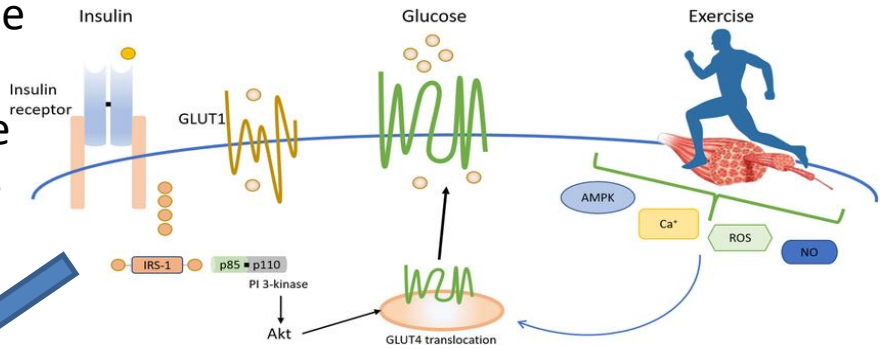



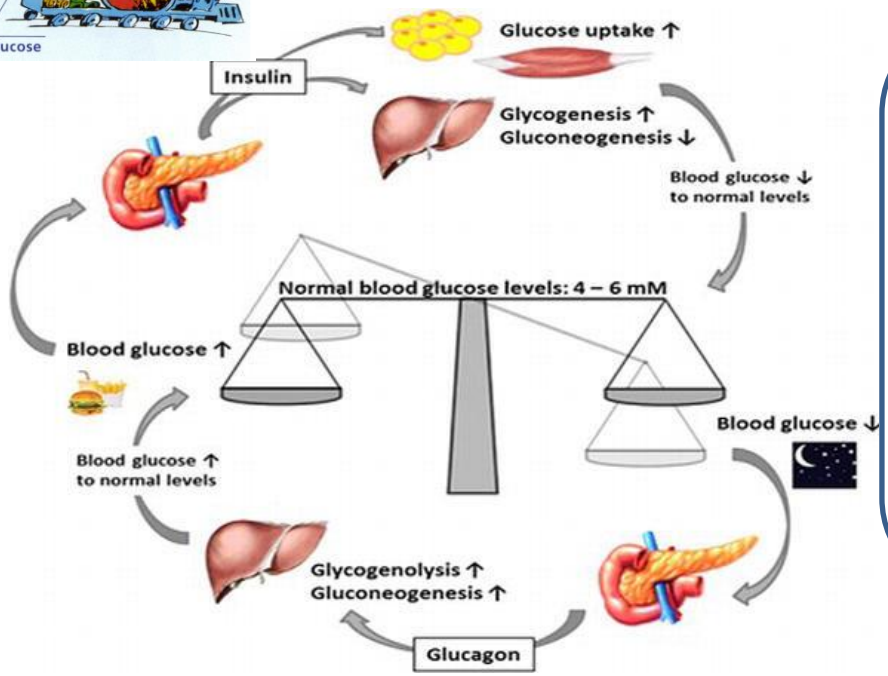
GLUCOSE HOMEOSTASIS	NORMAL	IMPAIRED*	DIABETIC**
Fasting Plasma Glucose (mg/dl)	**< 100**	**100 - 125**	**≥ 126**
2-h PG (mg/dl) post 75 glucose	**< 140**	**140 - 199**	**≥ 200**
HbA1c (%) (depuis 2010)	**≤ 5.6**	**5.7 - 6.4**	**≥ 6.5**

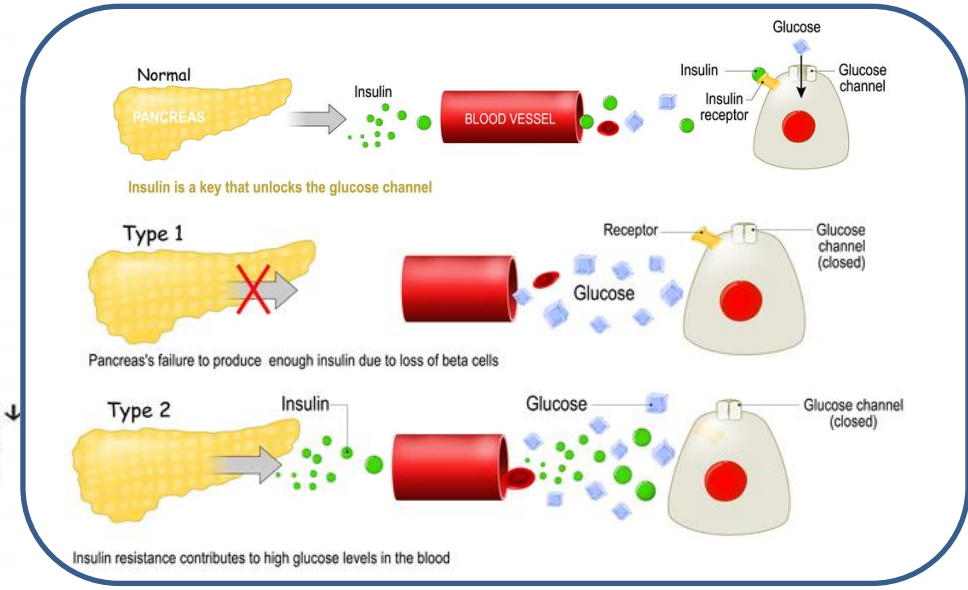
Physiology

Exercise: skeletal muscle increases glucose uptake during exercise by 10x or more, compared with rest, and does not require insulin for glucose uptake during exercise



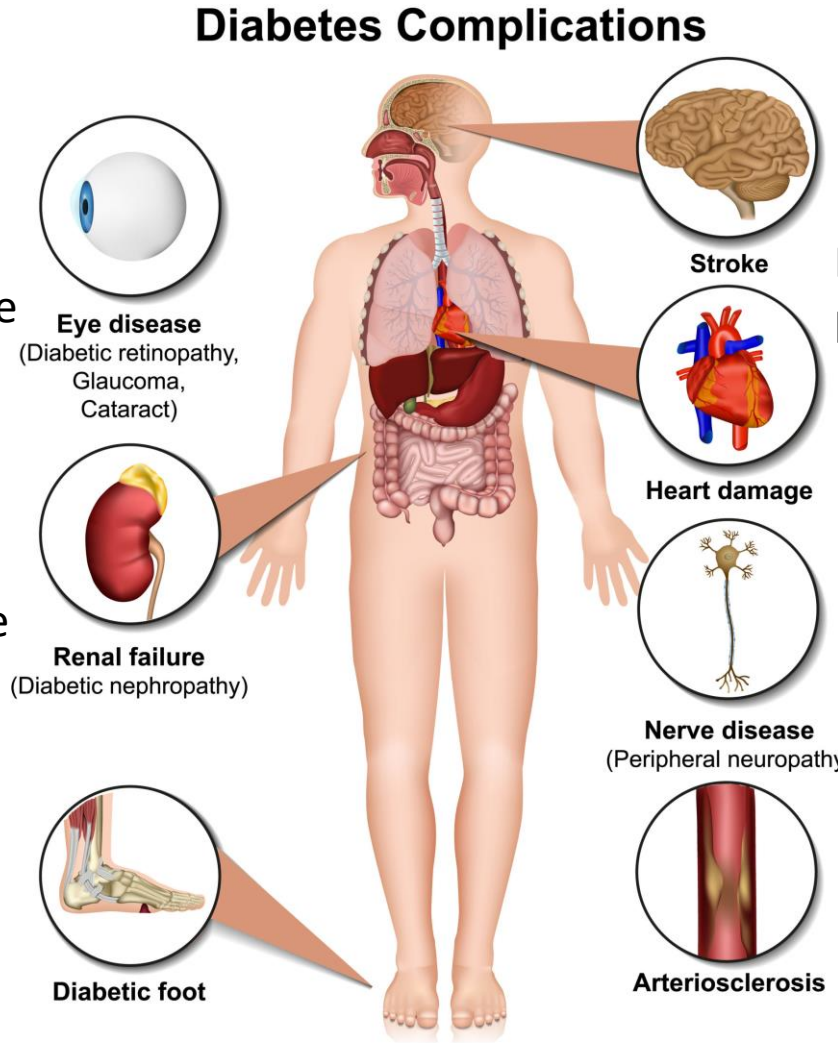






Ploug, T., et al. 1984

Complications consequences



No high intensity exercise

Rule out coronary and/or peripheral vacular disease

Avoid high blood pressure

Be alert to wounds and sensation disturbances

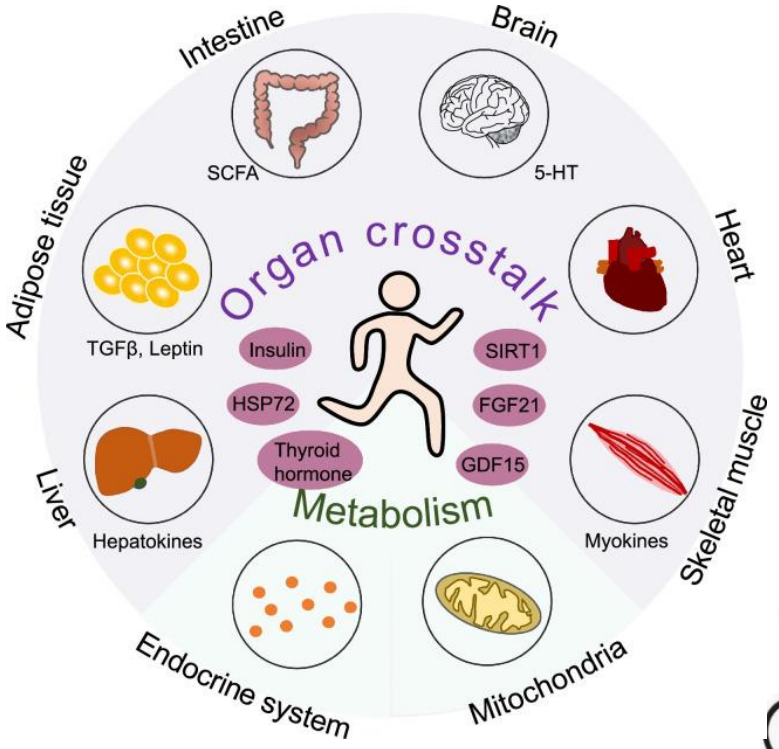
Be alert to deregulated BP

Check feet/shoe before exercise

Early diagnostic (and healthy life style) is the starting point for prevention

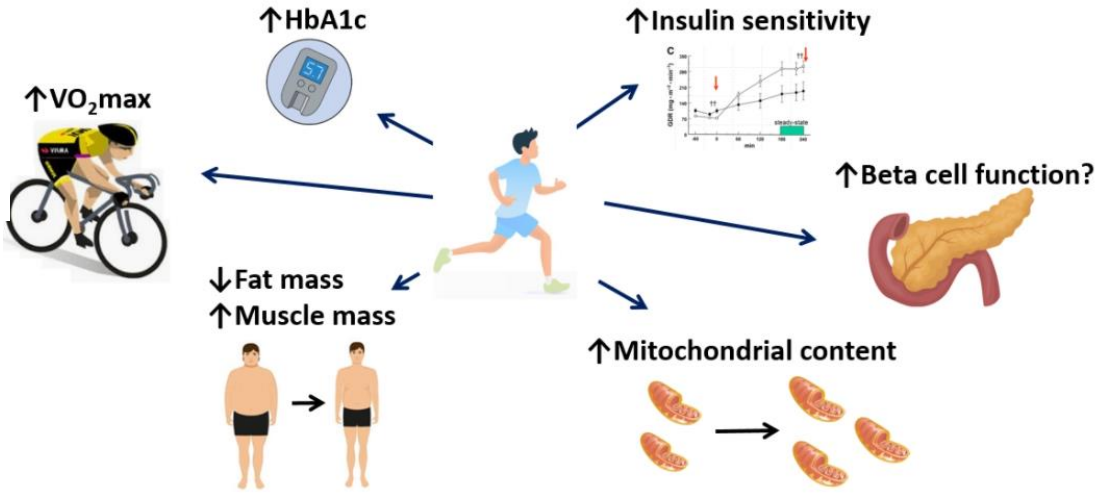
ACSM ADA Guidelines 2022

Exercise Therapy



Exercise leads to systemic effects by evoking the coordinated and integrated adaptation of multiple organ systems.

This multiple organ system also specifically acts on Diabetes management targets



Qiu Y, et al. J Sport Health Sci. 2023

Kirwan JP, Cleve Clin J Med. 2017.

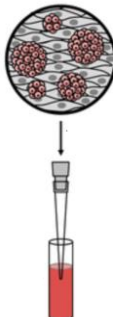
Exercise and β-cell protection

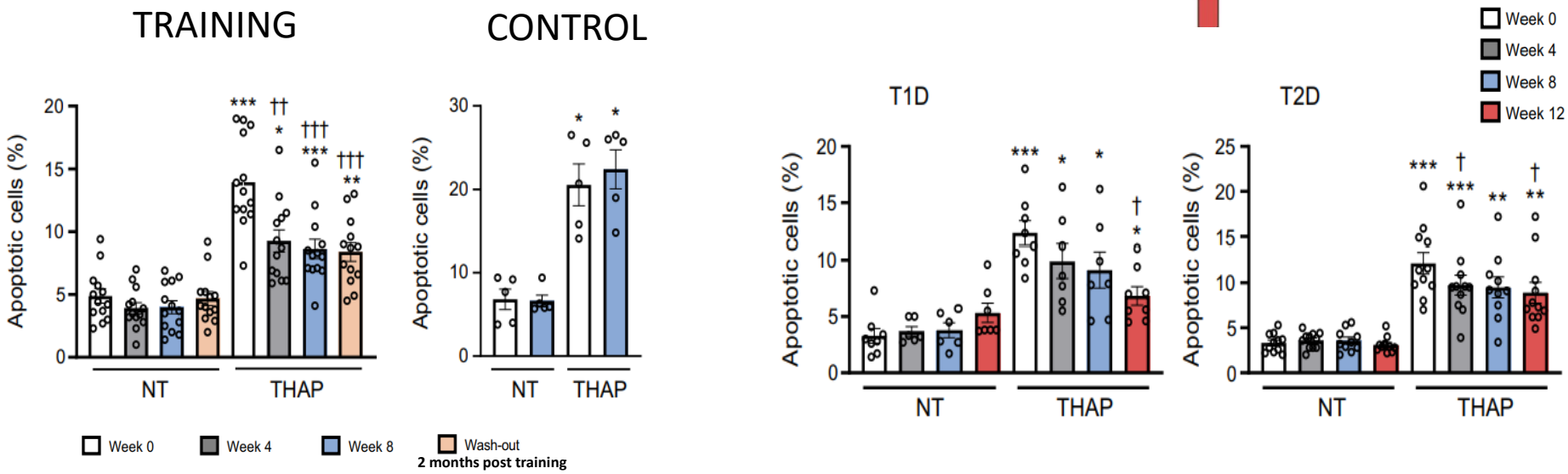
Exercise as a non-pharmacological intervention to protect pancreatic beta cells in individuals with type 1 and type 2 diabetes.

Coomans de Brachène A, Scoubeau C, Musuaya AE, Costa-Junior JM, Castela A, Carpentier J, **Faoro V**, Klass M, Cnop M, Eizirik DL.

- Serum (N=82) + thapsigargin
- pre-& post 8-12wk training

Human beta cell *EndoC-βH1*



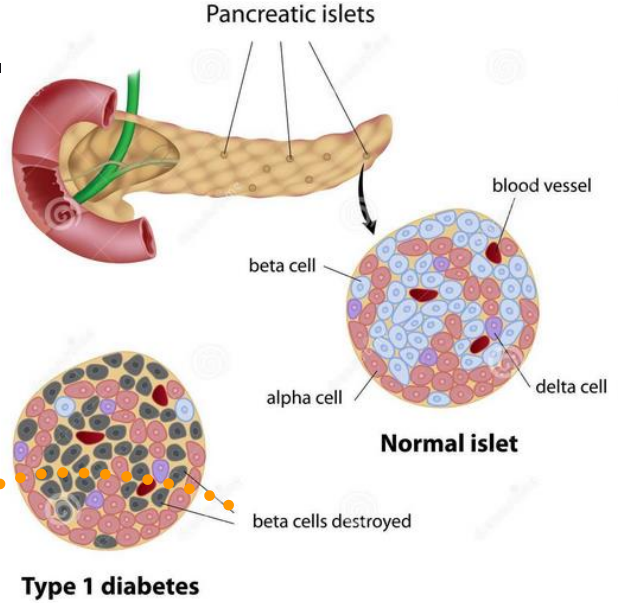


// type of exercise training or participant age, sex, BMI or ethical ancestry
// with Clusterin: clearance of cellular debris and apoptosis

Coomans de Brachène A et al. Diabetologia. 2023

Patients with Types 1 diabetes mellitus

Type 1 Diabetes (T1D)



↑ LIPOLYSIS

Adipocytes

Insulin

Glucose

Glycemia ↑

↓ GLYCOGEN
↑ PROTEOLYSIS

Myocytes

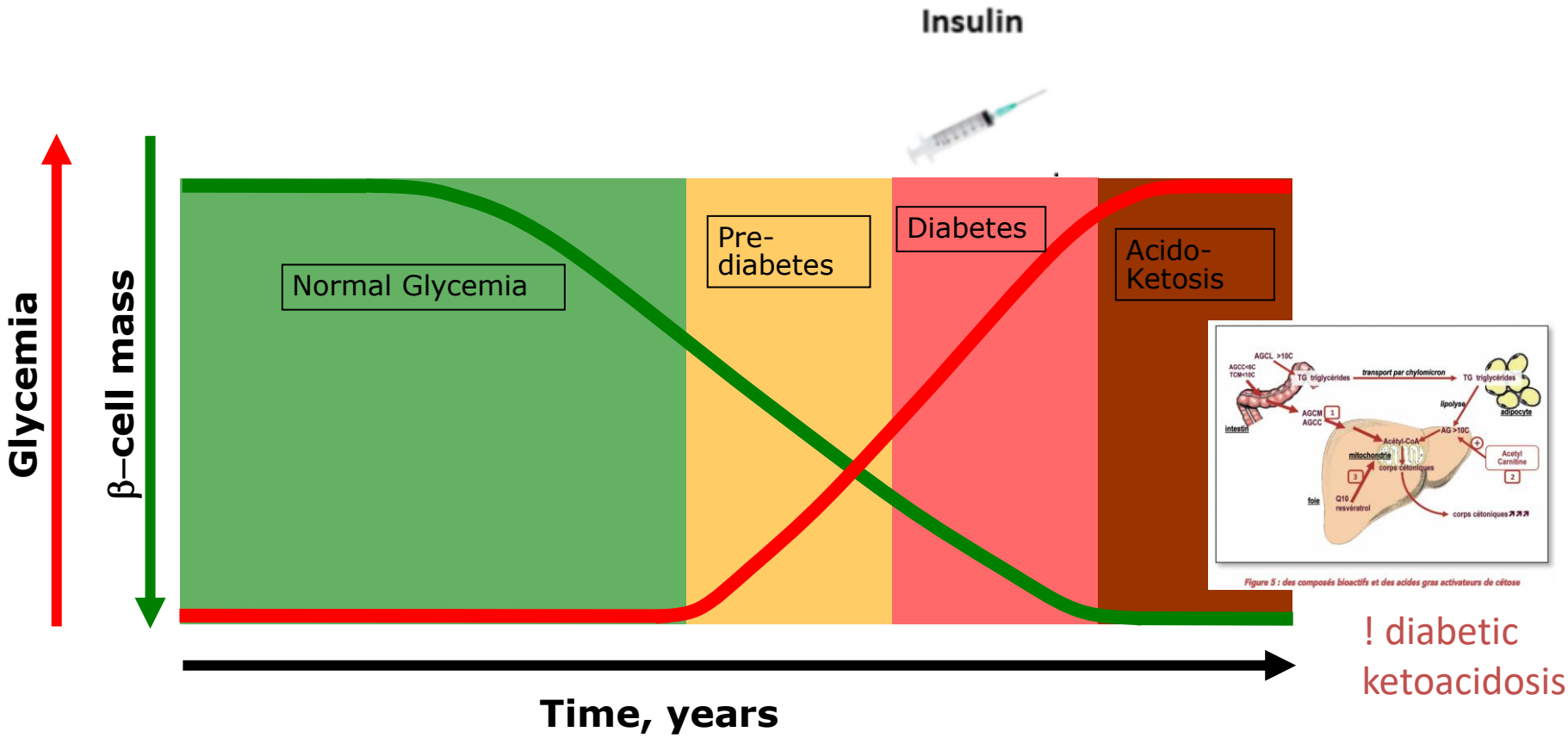
↑ NEOGLUCOGENESIS
↓ GLYCOGEN

Foie

Insulitis autoantibodies to β-cells

Autoimmune disease

Residual β-cell function is present at the time of diagnosis with Type 1 diabetes.
Preserving this β-cell function reduces complications.



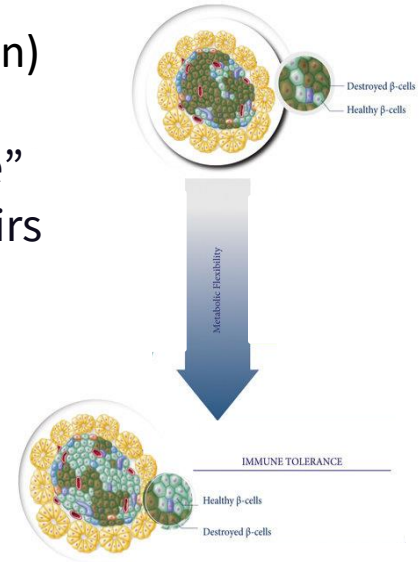
! diabetic ketoacidosis

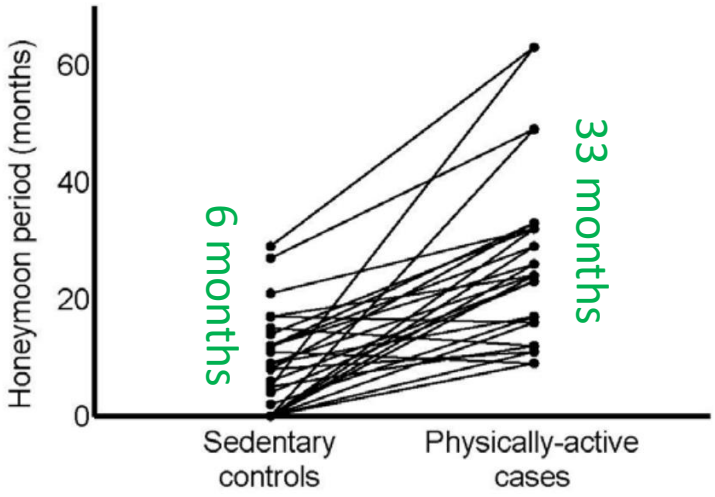
'Honeymoon' period

T1D 'honeymoon period' five times longer in men who exercise: a case-control study

Retrospective analyses of IDAA1c (correlates with endogenous insulin)
- 17 recently diagnosed T1D, with "significant levels of exercise"
- 34 matched with sedentary pairs for age, sex and weight

Prospective?
Minimal exercise?
Women/children?
Training protocol?

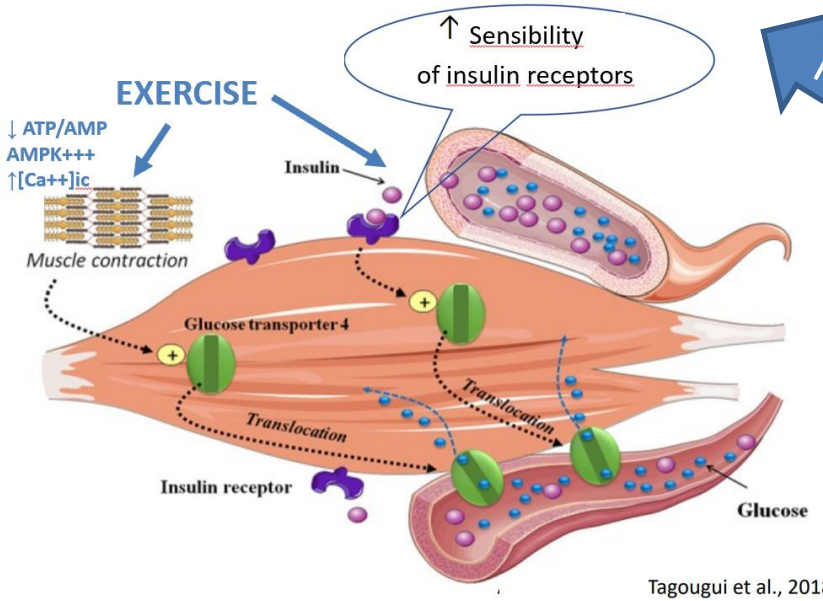




CCl: Exercise during first few months of diagnosis may in the long term improve blood glucose levels, reduce hypoglycemic attacks and the risk of long-term complications (such as retinopathy and neuropathy, …).

Chetan MR, et al. Diabet Med. 2019.

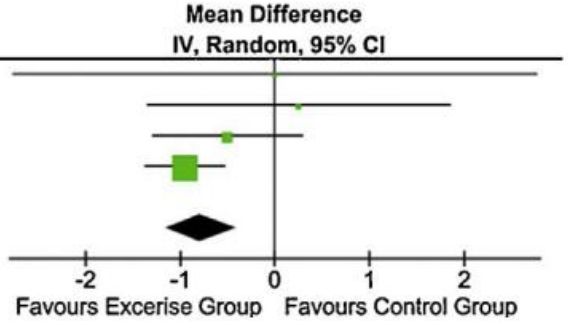
Exercise & Glucose intake



Tagougui et al., 2018

Study or Subgroup	Excerise group Mean	SD	Total	Control group Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Year
Landt 1985	12	3	9	12	2.45	6	1.7%	0.00 [-2.77, 2.77]	1985
Wallberg-Henriksson 1986	10.83	1.42	6	10.58	1.53	7	5.2%	0.25 [-1.35, 1.85]	1986
Laaksonen 2000	8	1	20	8.5	1.6	22	21.0%	-0.50 [-1.30, 0.30]	2000
Salem 2010	7.95	1.06	148	8.9	1.4	48	72.1%	-0.95 [-1.38, -0.52]	2010
Total (95% CI)			183			83	100.0%	**-0.78 [-1.14, -0.41]**	

Heterogeneity: Tau² = 0.00; Chi² = 2.95, df = 3 (P = 0.40); I² = 0%
Test for overall effect: Z = 4.16 (P < 0.0001)



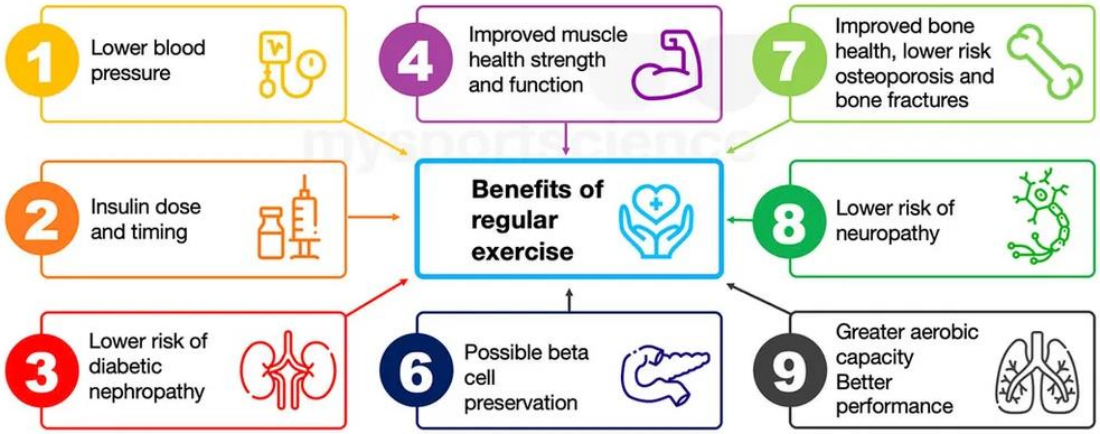
Post-treatment glycated hemoglobin (HbA_{1C})*.

Yardley JE et al. Diabetes Res Clin Pract. 2014

Benefits

Improved insulin sensitivity

Improved glycaemic control



Cardiac and endothelial function (+ lipid profile)

↑ social and mental health, self-image

Functional capacity including balance & flexibility

↓all-cause and disease-related mortality and diabetes-related co-morbidities

! Hypoglycaemia !

- **Hyperglycaemia**
- **Musculoskeletal soreness, injury**
- **Acute myocardial infarctus risk**
- **Feet Damage**

(! If neuropathy and foot ulcers)

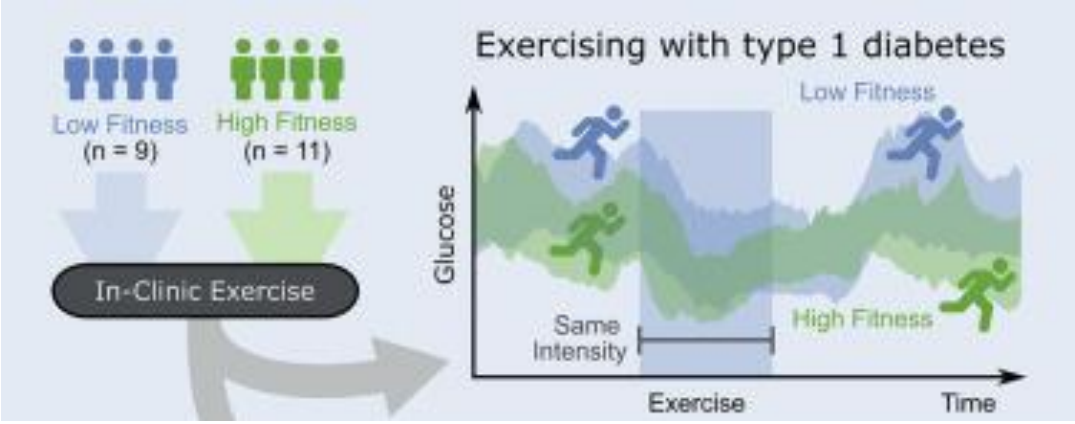
- **Retinopathy** (! BP↑)

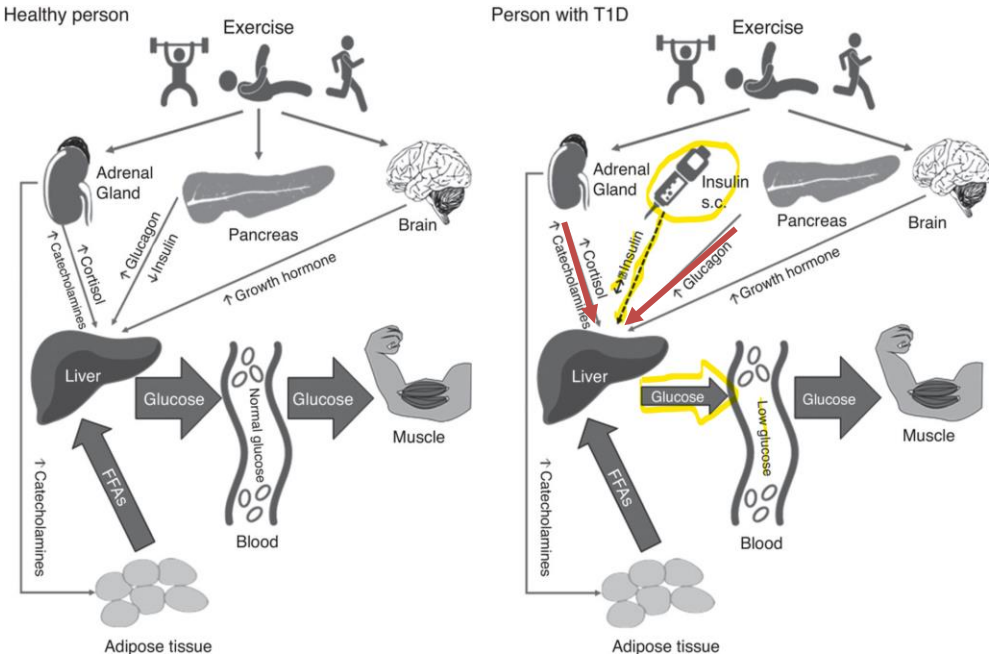
Riddle Peters Nature rev 2023

Hypoglycemia

Hypoglycaemia: difficult to predict

- ↑ risk : 1–3 h after meal (if usual insulin)
- risk : 45 min of starting anaerobic exercise until 24h post-exo
- Inter- and intra-subject variability



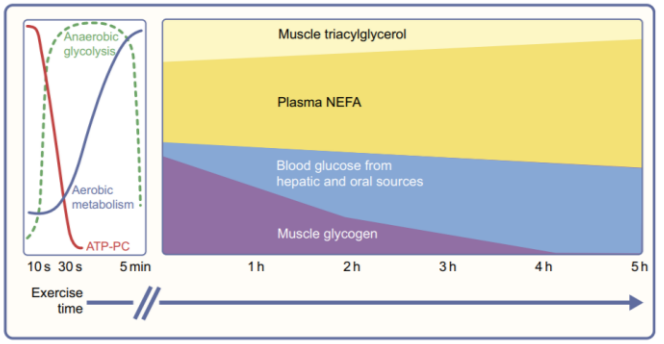


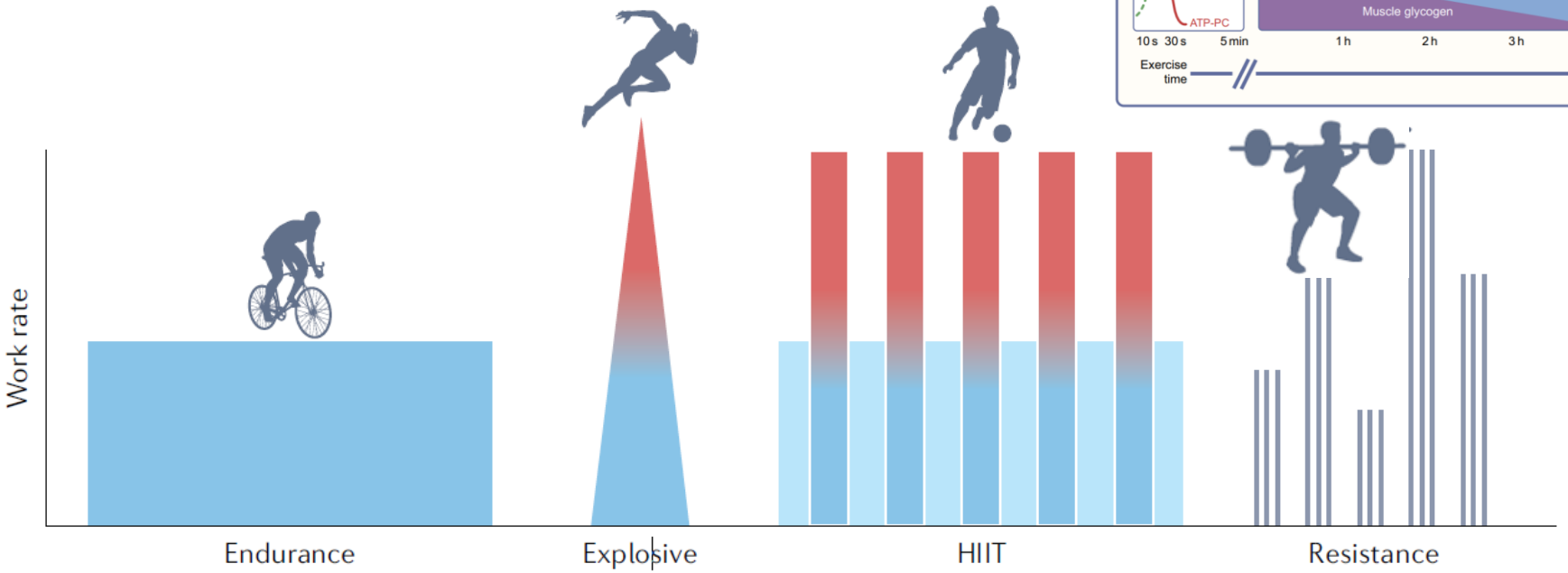
Altered barriers to hypoglycemia

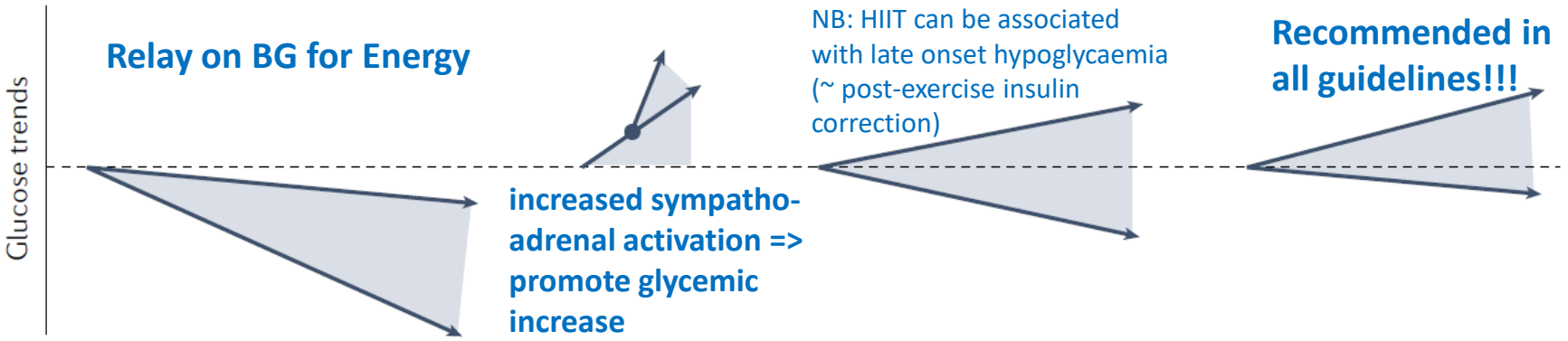
The normal protective hormonal response (i.e. increase in glucagon and catecholamines) is diminished or absent

Riddell, M.C., et al. Diabetologia 2020
Cockcroft JE et al. Exp Physiol, 2020

Glycemic response







GLYCEMIA Safe range: 90-200 mg/dl Best performance : 108 -144 mg/dl

~145 mg/dl

< 125 : ~15 g sugar

<70: suspend

~90 mg/dl

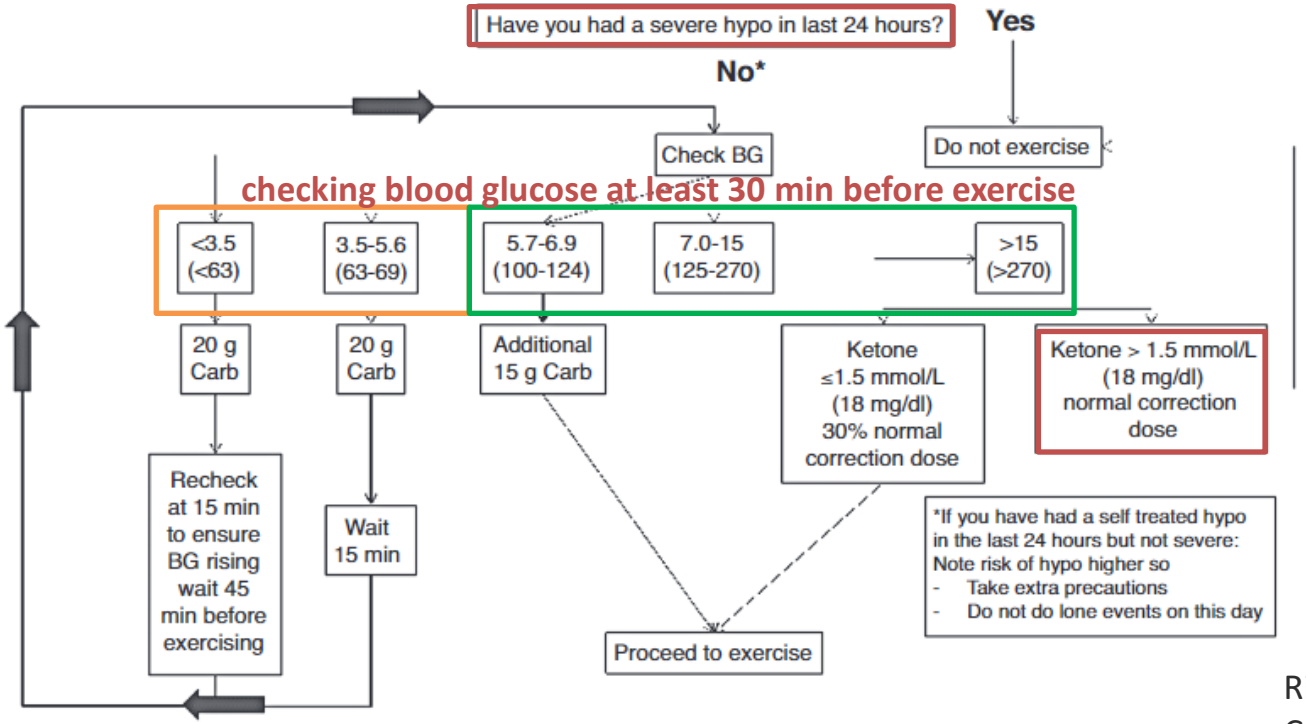
Kelly, Hamilton, & Riddell, 2010

Riddle & Peters. Nature Rev 2023

Before Training

Inadequate preparation for exercise-associated hypoglycaemia is an exercise contraindication

	Meal before exercise		
	Activities lasting 30-45 minutes	Activities lasting >45 minutes	Meal after exercise
Continuous, moderate to vigorous intensity aerobic activities (eg, jogging/running, moderate intensity swimming, bicycling, cross country, aerobic play)	25%-50% bolus reduction	50%-75% bolus reduction	Up to 50% bolus reduction
Mixed aerobic and anaerobic burst activities (eg, hopping, skipping, dance, gymnastics, tag, dodgeball, field and team sports, individual racquet sports, etc.)	~25% bolus reduction	~50% bolus reduction	Up to 50% bolus reduction



If have know direction of glucose from > two blood glucose readings, flash monitor, or continuous glucose monitor.

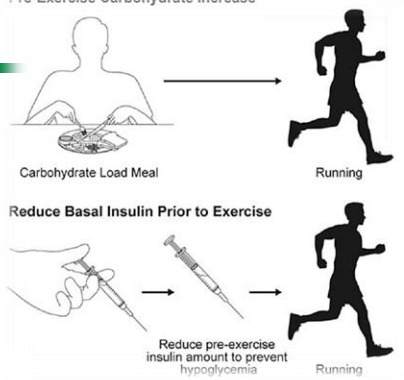
If ↑ and glucose 100-124 (5.7-6.9): no need for extra carbs, proceed to exercise. Stick to advice if in any other range.

If ↓ and glucose 100-124 (5.7-6.9): take twice as much carbs at 20 and 40 minutes into exercise

If ↓ and glucose 125-162 (7.0-9.0): take 15 grams of carbs at start of exercise

Riddle et al. The Lancet 2016
Cockcroft JE et al. Exp Physiol, 2020

Endurance exercise



Related to : type of exercise, time of day and type of insulin therapy

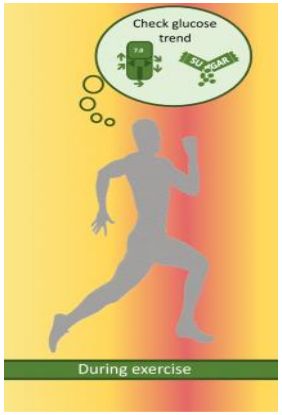
	Endurance exercise performance in athletes with and without diabetes	Hypoglycaemia prevention under low insulin conditions	Hypoglycaemia prevention under high insulin conditions
Meal (low fat, low glycaemic index) consumed before exercise	A minimum of 1 g carbohydrate per kg bodyweight according to exercise intensity and type	A minimum of 1 g carbohydrate per kg bodyweight according to exercise intensity and type	A minimum of 1 g carbohydrate per kg bodyweight according to exercise intensity and type
Meal or snack consumed immediately before exercise (high glycaemic index)	No carbohydrate required for performance	If blood glucose concentration is less than 5 mmol/L (<90 mg/dL), ingest 10–20 g carbohydrate	If blood glucose concentration is less than 5 mmol/L (<90 mg/dL), ingest 20–30 g carbohydrate
Meal consumed after exercise	1·0–1·2 g carbohydrate per kg bodyweight	Follow sports nutrition guidelines to maximise recovery with appropriate insulin adjustment for glycaemic management	Follow sports nutrition guidelines to maximise recovery with appropriate insulin adjustment for glycaemic management
Exercise (up to 30 min duration)	No carbohydrate required for performance	If blood glucose concentration is less than 5 mmol/L (<90 mg/dL), ingest 10–20 g carbohydrate	Might require 15–30 g carbohydrate to prevent or treat hypoglycaemia
Exercise (30–60 min duration)	Small amounts of carbohydrate (10–15 g/h) could enhance performance	Low to moderate intensity exercise (aerobic): small amounts of carbohydrate (10–15 g/h) depending on exercise intensity and blood glucose concentration measured during the activity High intensity exercise (anaerobic): no carbohydrate required during exercise unless blood glucose concentration measured during the activity is less than 5 mmol/L (<90 mg/dL); if so, ingest 10–20 g carbohydrate; replace carbohydrate needs after exercise	Might require up to 15–30 g carbohydrate every 30 min to prevent hypoglycaemia
Exercise (60–150 min duration)	30–60 g carbohydrate per h	30–60 g carbohydrate per h to prevent hypoglycaemia and enhance performance	Up to 75 g carbohydrate per h to prevent hypoglycaemia and enhance performance*
Exercise (>150 min duration); mixture of carbohydrate sources	60–90 g carbohydrate per h spread across the activity (e.g. 20–30 g carbohydrate every 20 min) Use carbohydrate sources that use different gut transporters (eg, glucose and fructose)	Follow sports nutrition guidelines (60–90 g/h) with appropriate insulin adjustment for glycaemic management	Follow sports nutrition guidelines (60–90 g/h) with appropriate insulin adjustment for glycaemic management

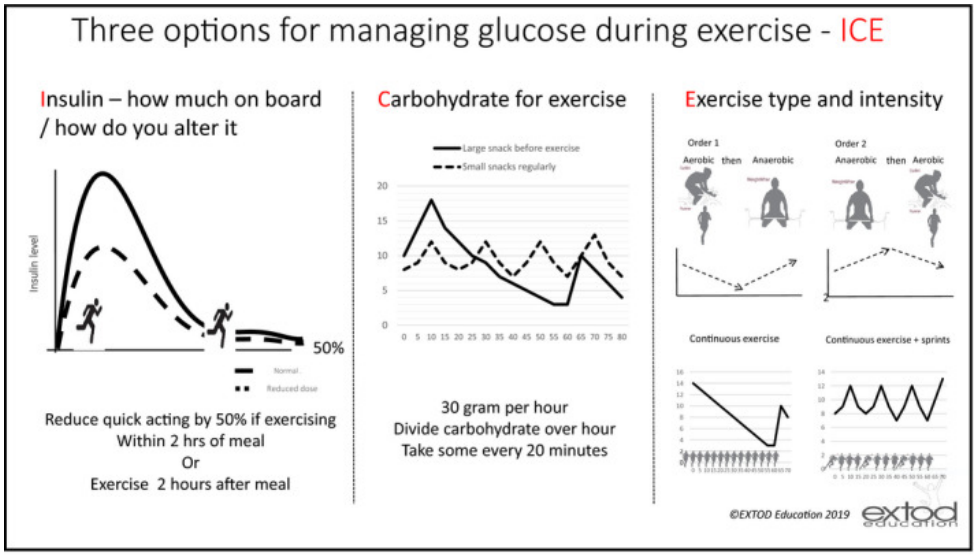
These guidelines are based on published studies,[59-61] and on our own expert opinion. *Carbohydrate consumption at a high rate might cause gastric upset in some individuals and might contribute to hyperglycaemia during and after the activity. To increase the rate of carbohydrate absorption during exercise, and maintain hydration status, sports beverages containing glucose and fructose might be preferable.

***Table 1*: Carbohydrate requirements for endurance (aerobic) exercise performance and hypoglycaemia prevention**

Riddle et al. The Lancet 2017

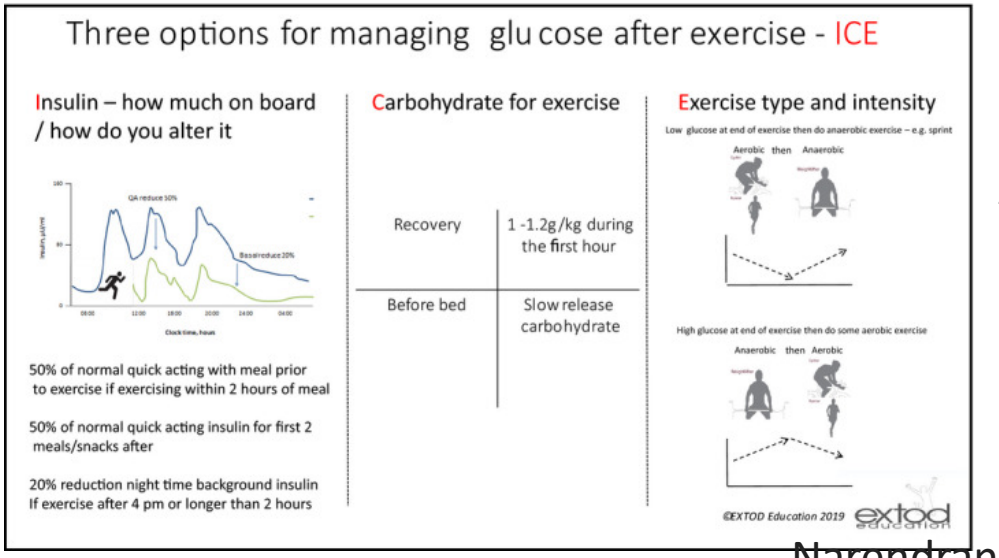
During and After Exercise





During exercise;
↑glycose consumption
=> risk hypoglycemia

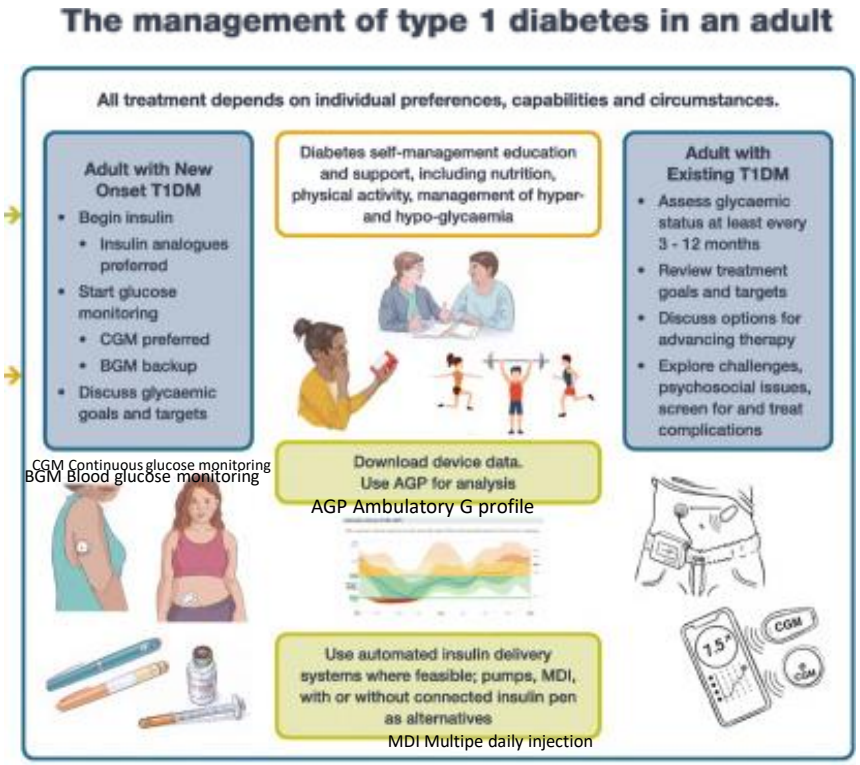
CHECK ARROW



After exercise; ↑glycogen synthesis in muscle and liver => risk hypoglycemia

Narendran P et al. Diabet Med. 2020

Management T1D Adults



American Diabetes Association Standards of Medical Care in Diabetes:

Adults with T1DM should engage > 150 min of moderate-to-vigorous-intensity aerobic physical activity/week, (**fit individuals:** > 75 min/week of vigorous-intensity or HIIT)

- spread over at least 3 days/week,
- with no more than 2 consecutive days without activity

- Resistance activity: 2–3 sess/week (non-consecutive days
- Flexibility exercise: > 2/week (yoga, tai chi or other stretching activities, …)

☺ respond to changes in insulin sensitivity (stress, exercise, diurnal rhythms, hormones, …)

☺ improve glucose control around exercise

☹ set device in "exercise mode" long (90min) before (to↓ insulin)

☹ returne to routine setting fater exercise

☹ delay of measure/response

Riddle et al. The Lancet 2016

Holt RIG et al. ADA/EADA. Diabetologia. 2021

American Diabetes Association Professional Practice Committee et al. *Diabetes Care* 2022

Children

American Diabetes Association (ADA) Standards of Medical Care in Diabetes and Office of Disease Prevention and Health Promotion (ODPHP):

Children/adolescents with T1D, T2D, or prediabetes should participate in moderate to vigorous-intensity aerobic activity for at least 60 min/day, with vigorous muscle-strengthening and bone-strengthening activities at least 3 days/week.

- Toddlers : > 30 min PA/day and < 60 min sitting at a time
(promote motor skills and muscular development)

- Children and adolescents: >60 min PA /day

- Aerobic activities such as running, swimming, biking, ...
- Anaerobic exercises: jumping, sprinting,...
- Strength training: yoga, weights, …

! 5–15 grams of carbohydrates for every 30 minutes of activity

☹ Not met in 2/3

☹ Difficult because mainly unplanned and spontaneous PA

American Diabetes Association. Diabetes Care. 2019
Physical Activity Guidelines. Health.gov. 2019.

Aerobic Exercise

Skeletal muscle releases numerous signalling myokines during exercise that have critical roles in improving cardiovascular, metabolic, immune and neurological health

Endurance exercise training: with or without resistance exercise, for 12 weeks or more in T1DM improves several important cardiometabolic status markers;
Including triglyceride levels, LDL levels, waist circumference and body weight

Post-exercise insulin sensitivity in the recovering muscles remains elevated for up to 48 h to help restore muscle glycogen reserves.

HIIT: Safe in T1D.

Reduces HbA1c, total daily insulin requirements and cardiometabolic risk profile

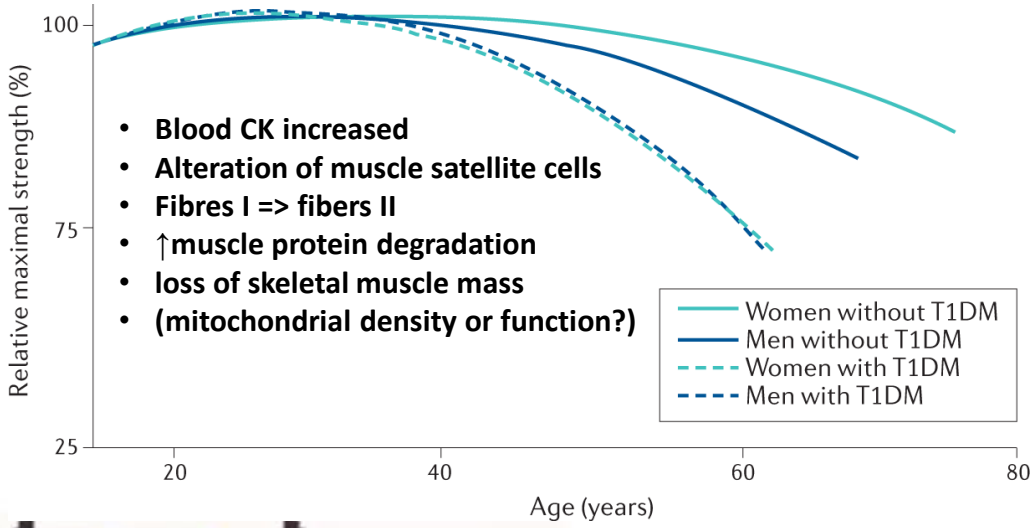
Hyperglycemia + [lactate]↑ inhibiting GH et Cortisol => ! Late onset HYPOGLYCEMIA

Riddle et al. The Lancet 2017
Riddle & Peters. Nature Rev 2023
Ostman, C.et al. *Diabetes Res. Clin. Pract.* 2018

Resistance Exercise

Fight against « **Diabetic myopathy** »
Insufficient insulin levels (anabolic) for muscle growth and repair
Elevations of glucocorticoids and glucagon,
=> catabolism and excessive ketone

Regular exercise: reverse this process - ↑ muscle mass, function, capillarization, oxidative capacity and insulin sensitivity



- Build muscle mass
  - Increases metabolism!
- Develop and maintain muscle strength, muscle power, and muscle endurance
- Benefits for prevention of chronic diseases
- Maximizes and maintains bone mass
- Improves posture & reduces risk of back injury

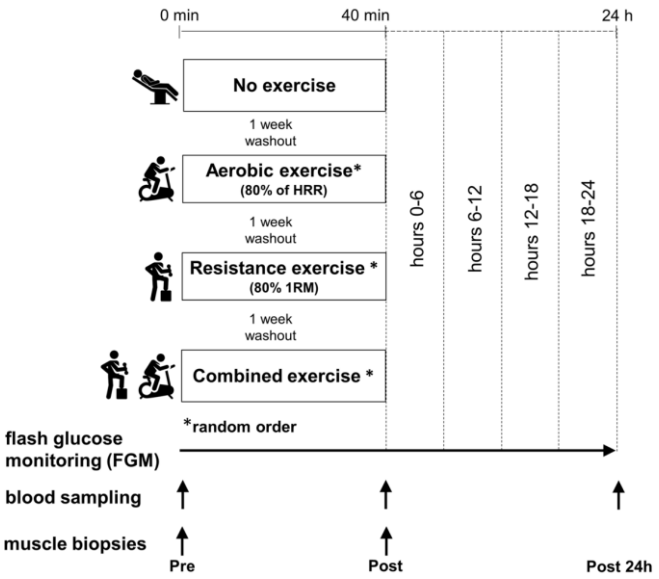
Duration – each training session at minimum of 5-10 exercises involving major muscle groups (upper body, lower body, and core)

involve completion of 10–15 repetitions to near fatigue per set early in training, progressing over time to heavier weights (or resistance) that can be lifted only 8–10 times.

Riddle et al. The Lancet 2016
Momeni, Z., L Int. J. Environ. Res. PublicHealth 18, 8716 (2021).
McCarthy, O. et al. Front. Endocrinol. 2019

Concurrent Training

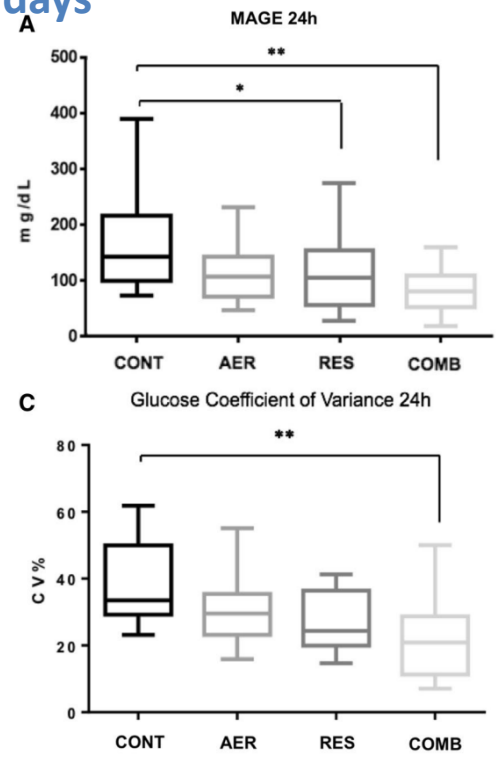
"People with type 1 diabetes should be encouraged to engage in a combination of aerobic and resistance exercise on most days"



BIOPSY

-RES: ↑ muscle signalling related to muscular growth/ remodelling, ↑ glucose homeostasis.

-AER:↑ muscle signalling related to muscular oxidative metabolism, ↑ glucose homeostasis.



COMB: more effective in reducing IG fluctuations compared to AER or RES.

COMB: simultaneously activates muscle signalling pathways involved in substrate metabolism and anabolic adaptations, which can help to improve glycaemic control and maintain muscle health in T1D.

Minnock, D. et al. *Eur. J. Appl. Physiol.* 2020

Conclusion

- T1D is associated with marginal impairments in skeletal muscle health and cardiorespiratory fitness; however, these impairments can be offset with good glycaemic control and exercise training.
- In general, endurance exercise activities reduce glycaemia and explosive activities raise glycaemia, while high-intensity interval training and resistance training activities can have a moderating effect.
- Reductions in basal and/or bolus insulin delivery are typically required for endurance activities, along with supplemental carbohydrate feeding for performance reasons or if glucose level falls below **126 mg/dl** during the activity.
- Increases in insulin delivery after explosive exercise, resistance exercise and/or high-intensity interval training might be required if hyperglycaemia develops; however, **the risk of post-exercise hypoglycaemia is heightened in the 12–24 h** after exercise so frequent glucose monitoring is required.
- Automated insulin delivery systems and continuous glucose monitoring technologies have the potential to improve glucose control around most forms of exercise. However, minimize insulin on board and maintain glycaemia on target (90–180 mg/dl) during the activity when using automated insulin delivery and continuous glucose monitoring.

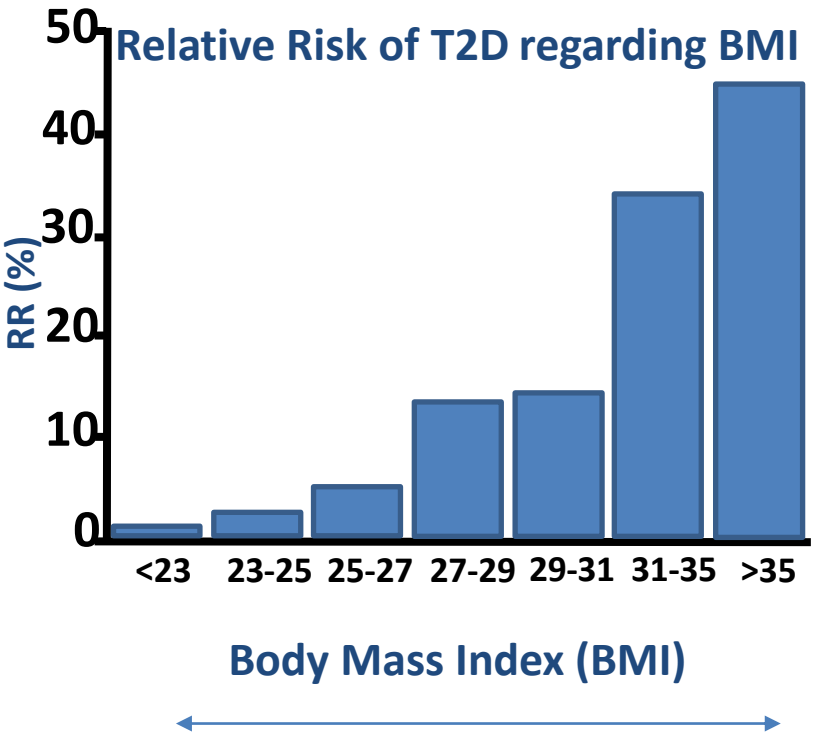
Riddell & Peters A.L. *Nat Rev Endocrinol* 2023

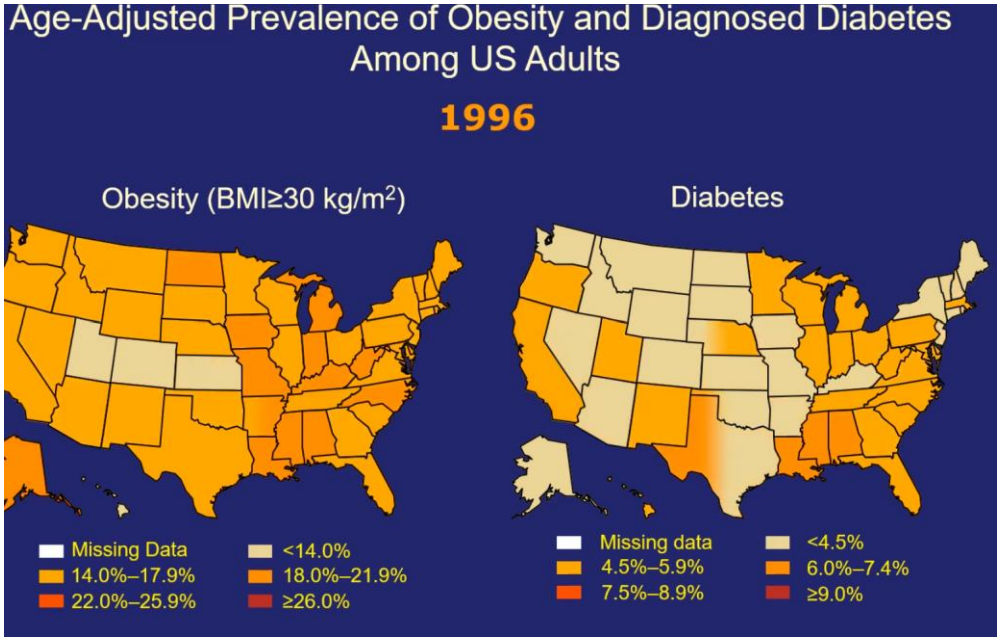
Patients with Types 2 diabetes mellitus

Type 2 Diabetes (T2D)

Most common type of diabetes (90% of all diabetes worldwide) and is most prevalent in elderly.

Combination of genetic and environmental factors + varying degrees of abnormalities of insulin secretion and action



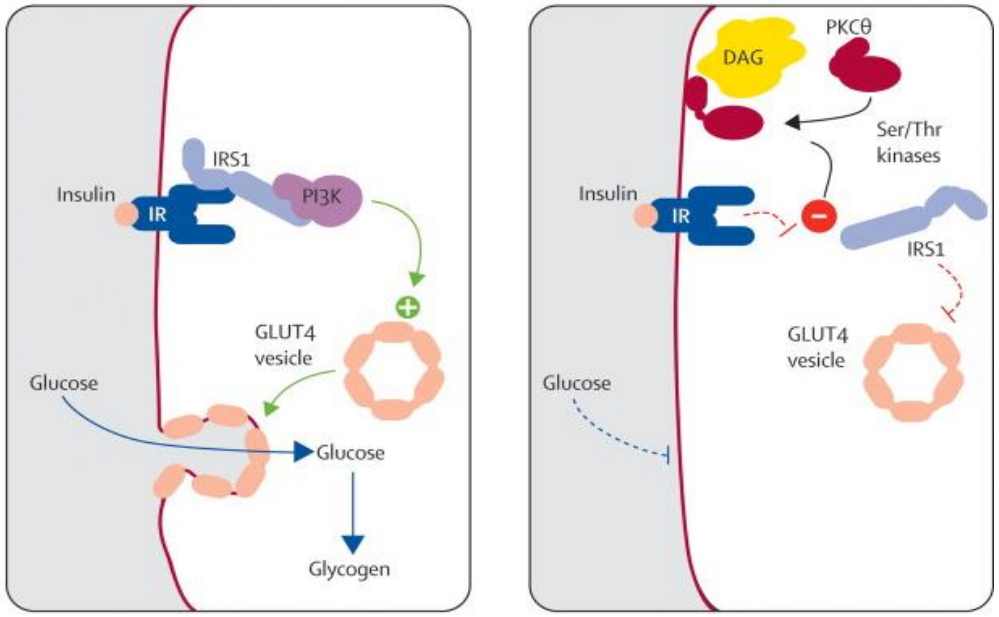


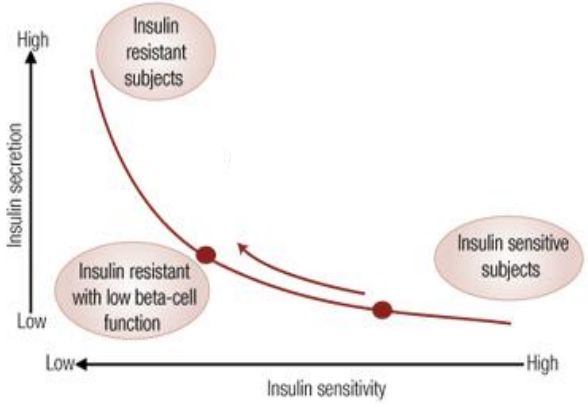
Chan et al. Diabetes Care 1994;17: 961-969

Crandall JP et al. Nat Clin Pract Endocrinol Metab. 2008

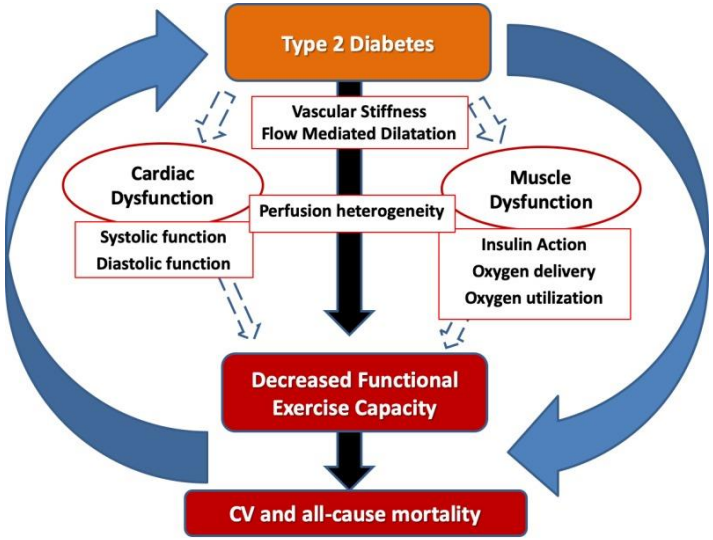
Insuline Resistance

Impaired Insulin signaling with reduced GLUT4 translocation, resulting in decreased cellular glucose uptake.





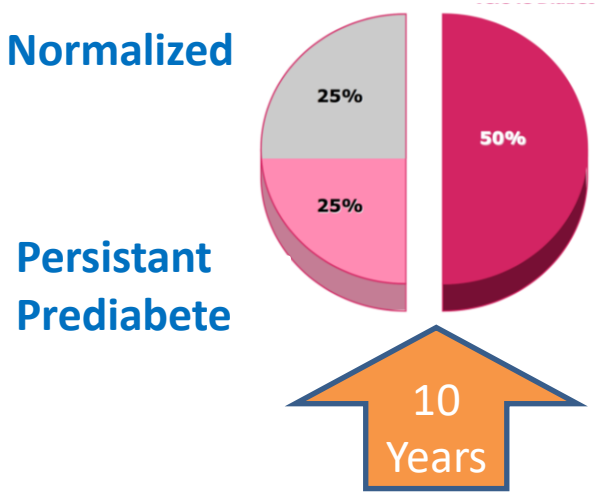
1.Lipid Accumulation: formation of toxic metabolites that interfere with insulin signaling.
2.Inflammation: Inflammatory cytokines (TNF-α and IL-6) activate pathways that inhibit insulin signaling
3.Mitochondrial Dysfunction: leads to reduced ATP production, impaired glucose oxidation, ROS production => oxidative stress



The Lancet, 2010

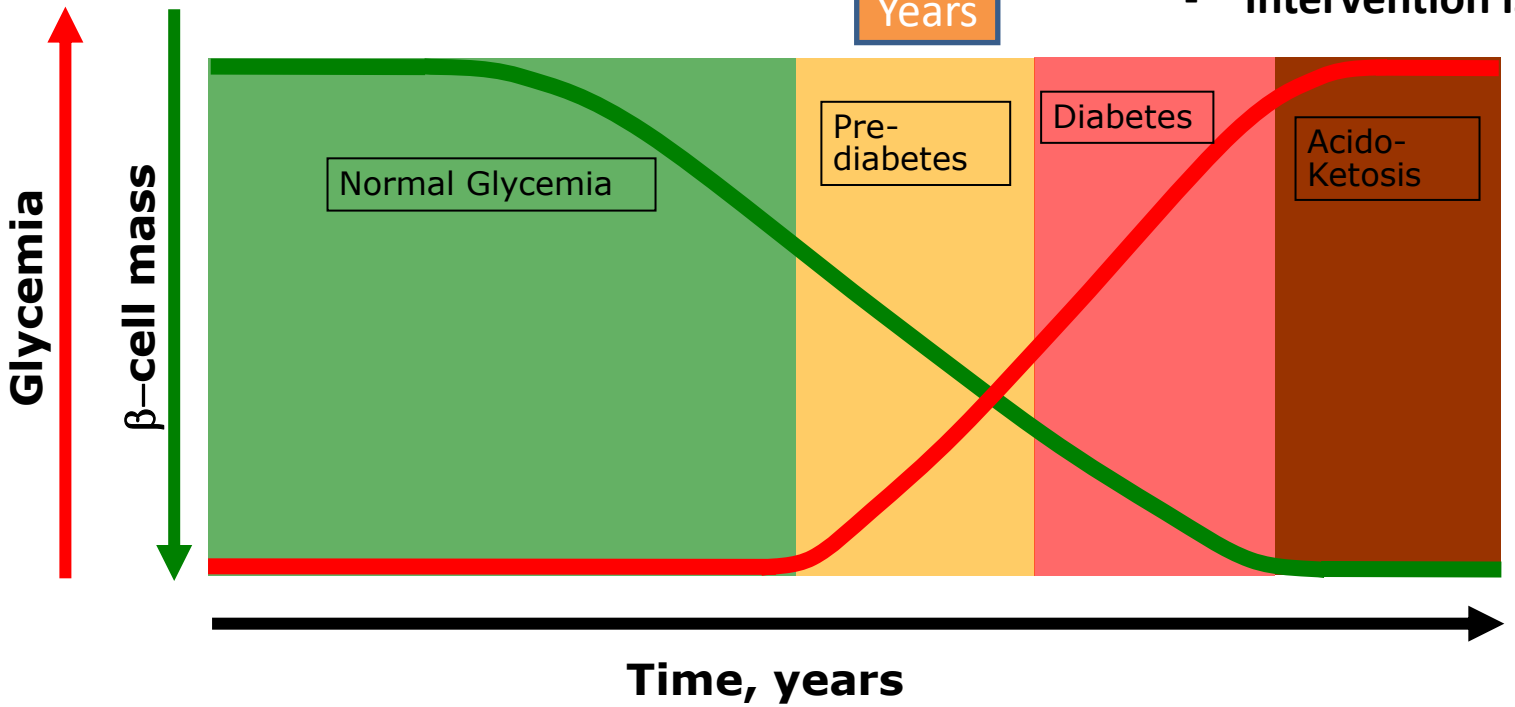
Salwa et al, 2023

Natural Drift



T2D

- **Risk development of T2D**
- **(linked to severity of hyperglycemia,weight/age**
- **heightened risk of CVD;**
- **Intervention is urgent!**



IDF Atlas 2020

Prevention with Life style intervention

Major randomised primary prevention trials in type 2 diabetes using lifestyle modification

Study (year); country; no. of participants	Intervention	Duration; main outcome (relative risk reduction %)
Da Qing Diabetes Prevention Study (CDQDPS);[27] (1997); China; n = 577 Da Qing Diabetes Prevention Extended Study (CDQDPS);[29] (2008) Da Qing Diabetes Prevention Extended Study (CDQDPS);[28] (2014)	Lifestyle modification	6.0 years; Diet: (31.0) Exercise: (46.0) Diet + exercise: (42.0) 20.0 years; (43.0) 23.0 years; (45.0)
Diabetes Prevention Study;[34] (2001); Finland; n =522 Diabetes Prevention Extended Study;[31] (2013)	Lifestyle modification	3.2 years; Intervention: (58.0) 13.0 years; Intervention: (38.0)
Diabetes Prevention Program;[35] (2002); United States; n= 3234 Diabetes Prevention Program Outcome Study;[30] (2009)	Lifestyle modification, metformin	2.8 years; Intervention: (58.0) 10.0 years; Intervention: (34.0)
Indian Diabetes Prevention Programme-1;[36] (2006); India; n =531	Lifestyle modification, metformin	2.6 years; Intervention: (28.5)
Indian Diabetes Prevention Programme-2;[37] (2009); India; n= 407	Lifestyle modification, pioglitazone	3.0 years; No benefit by adding pioglitazone
Indian SMS Study;[38] (2013); India; n=537	Lifestyle modification, SMS	2.0 years; Intervention: (36.0)
Indian SMS Study Extended Follow-Up;[32] (2018); n=346	Lifestyle modification	3.0 years; Intervention: (30.0)
Diabetes Community Lifestyle Improvement Programme (D-CLIP);[39] (2016)	Lifestyle modification, Metformin	3.0 years; Intervention: (32.0)
Pakistan Diabetes Prevention Study; [40] (2012); Pakistan; n= 317	Lifestyle modification, Metformin	1.5 years; Intervention: (71.0)
Prevention of type 2 diabetes by lifestyle intervention;[41] (2005); Japan; n = 458	Lifestyle modification	4.0 years; Intervention: (67.4)
Zensharen Study for Prevention of Lifestyle Diseases;[42] (2011); Japan; n=641	Lifestyle modification	3.0 years; (44.0)

Type 2 diabetes prevention (or, at least, delay) is possible with lifestyle modification

IDF Atlas 2019

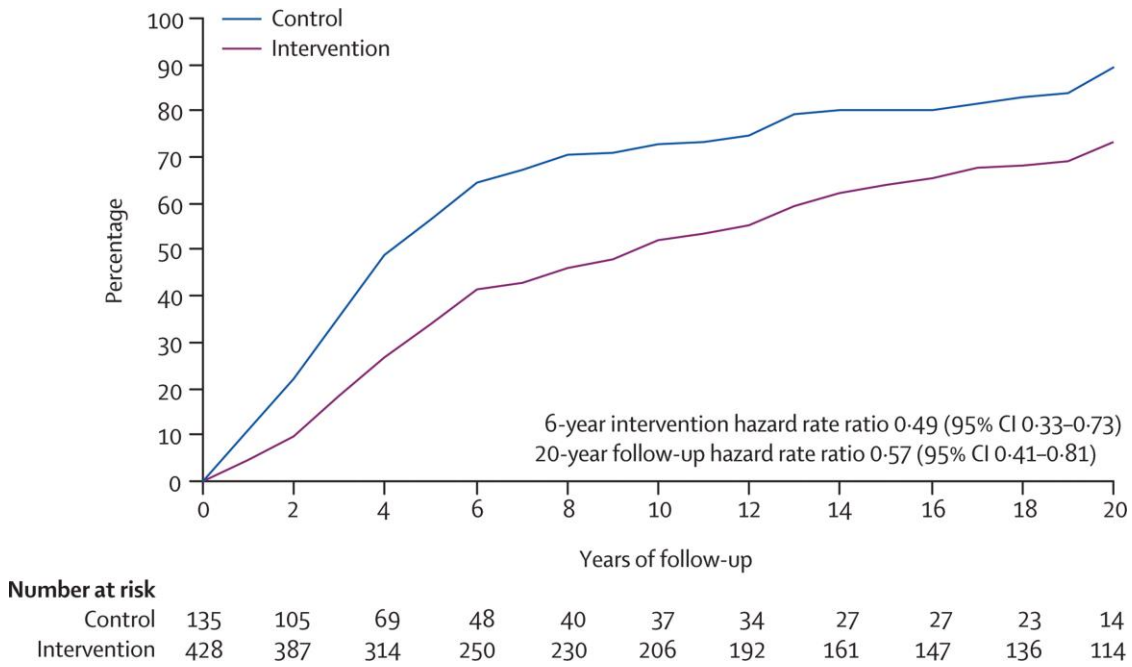
First Preventive longitudinal trial

- DaQing, 577 adults with pre-diabetes

Reduction risk for T2D

- -Diet only: -31%
- -Exercise only: -42%
- Diet+exercise : -46%

Lower risk at 23 year follow up; - 45%



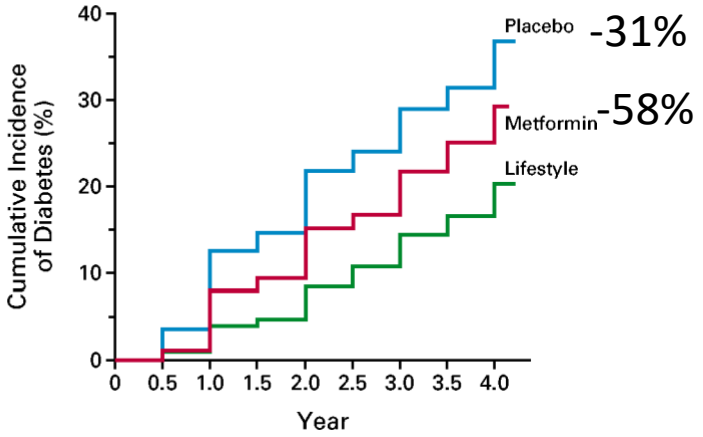
Chen Y et al. Diabetologia 2021

36

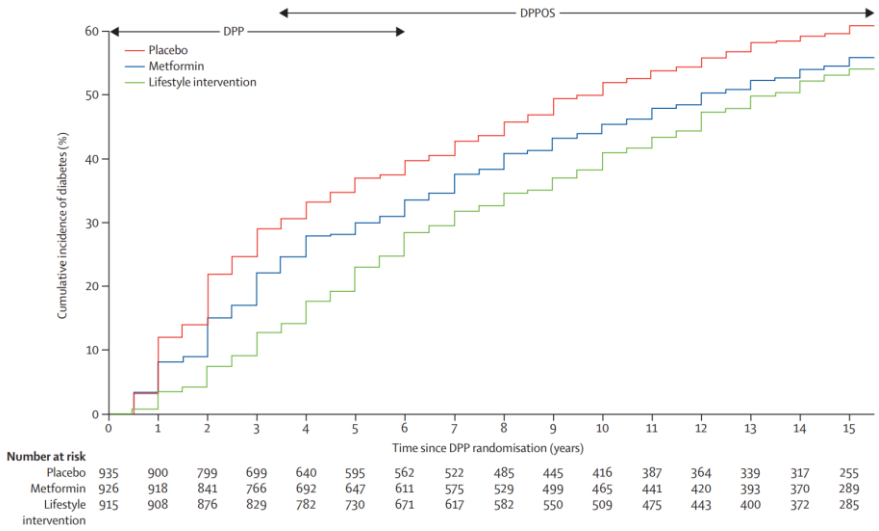
US Diabetes Prevention Program

N=3234 pre- diabetes
3 groups, follow-up 4 y
Lifestyle: weight reduction (7%) + moderate PA (150min/w)

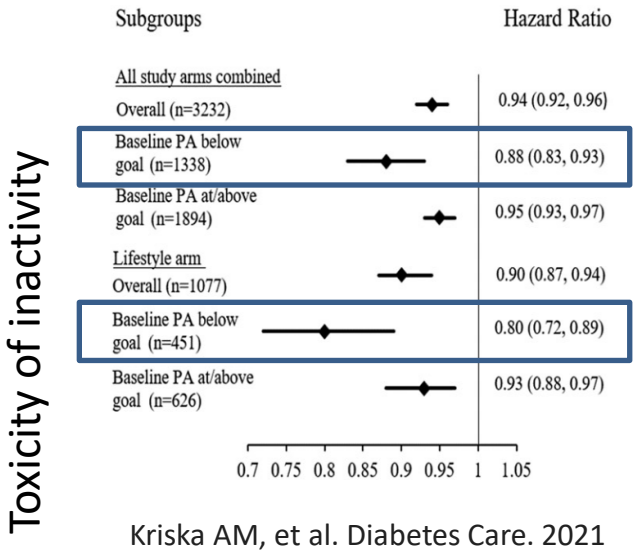
CCL: Lifestyle changes > Metformin reduced the incidence of diabetes in persons at high risk.



Knowler WC, et al. N Engl J Med. 2002



Diabetes Prevention Program Research Group. Diabetes Care. 2012



Kriska AM, et al. Diabetes Care. 2021

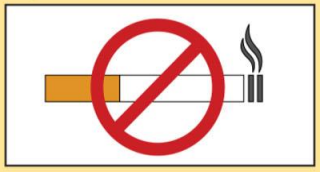
Integrative care

Healthy Lifestyle Behaviors & Psychological Well-being

Healthy Diet

Regular Physical Activity

Stop Tobacco Product Use



Adequate Sleep

Psychological Well-being

Assess	Advise	Agree	Assist	Arrange
Assess patient's relevant lifestyle behavior, beliefs and motivation for change using the OARS* approach	Advise on the health risks and benefits of lifestyle behavior and personalized recommendations using the Ask-Tell-Ask Approach	Agree on SMART (specific, measurable, achievable, realistic, and timed) goals for behavior change through shared decision-making	Assist with identifying solutions and action steps to address barriers to behavior change using problem-solving techniques	Arrange follow-up on progress to goals, referrals, and access to resources, as needed, using the Tell-back/Teach-back approach

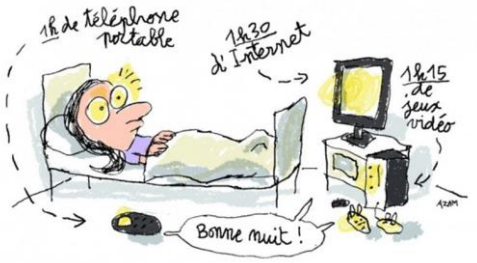
Aim for Ideal Cardiovascular Health

Patient-Centered Counseling
Shared Decision Making

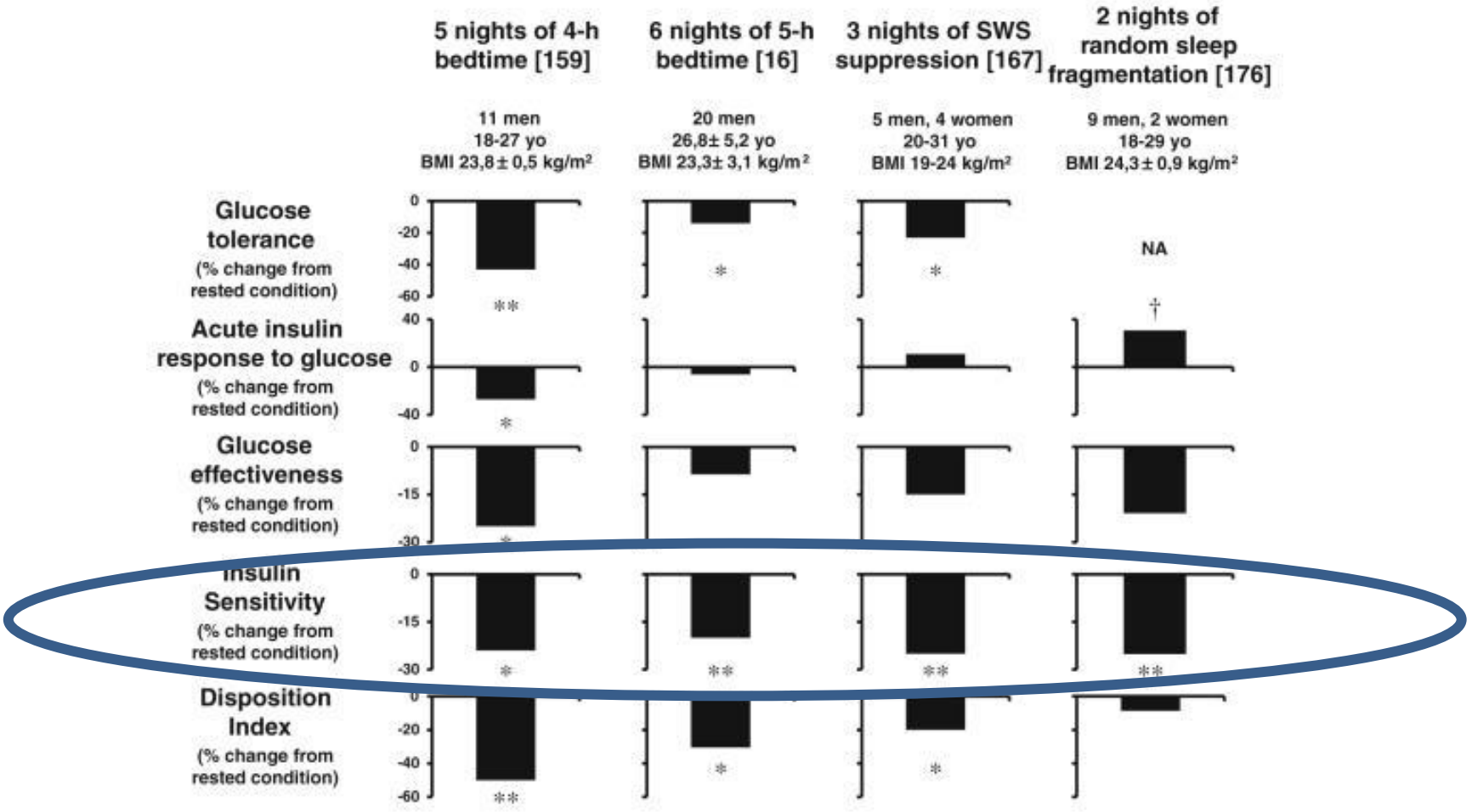
Micro-challenge

Kris-Etherton PM et al. AHA Journal 2021,

Sleep deprivation

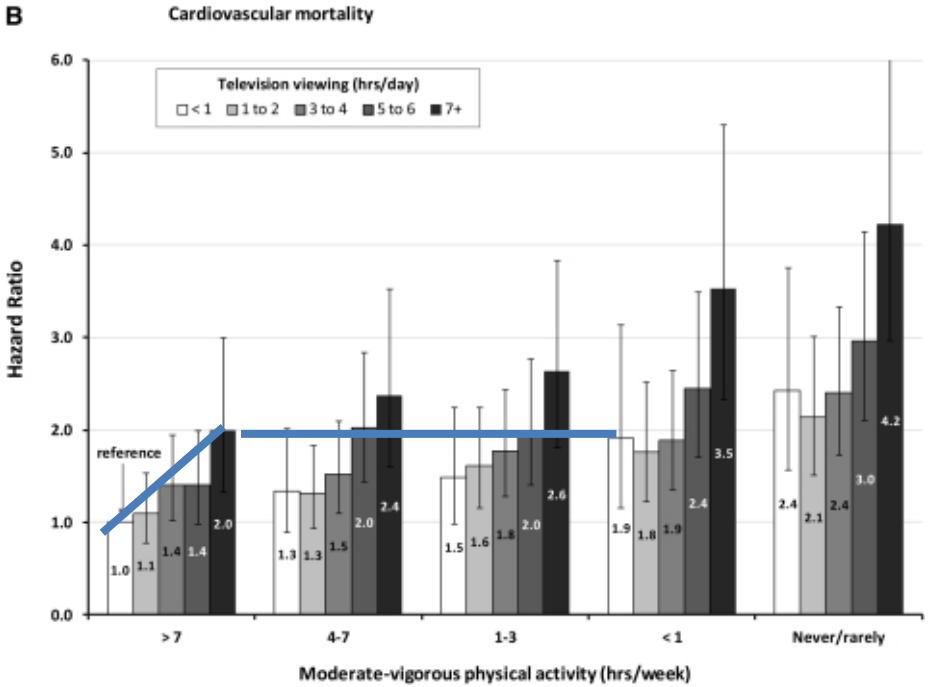


Qualitative and quantitative lack of sleep, influences the hormono-metabolic context by increasing the ghrelin/leptin ratio and reducing insulin sensitivity

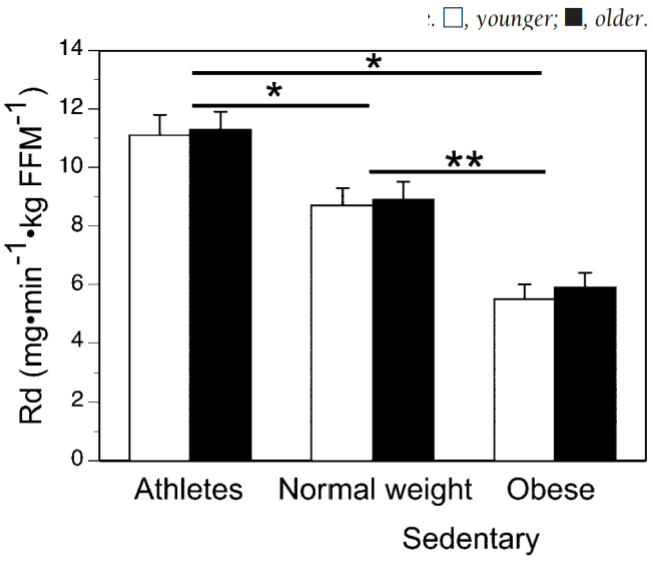


Spiegel et al. Lancet. 1999 Buxton et al. Diabetes. 2010 Stamatakis Chest. 2010 Tasali et al. 2008

Sedentarity



N=240819 participants



Sendetarity kills, independently of physical activity

Sendetarity reduces insulin senstivity, independently of age (but BMI effect)

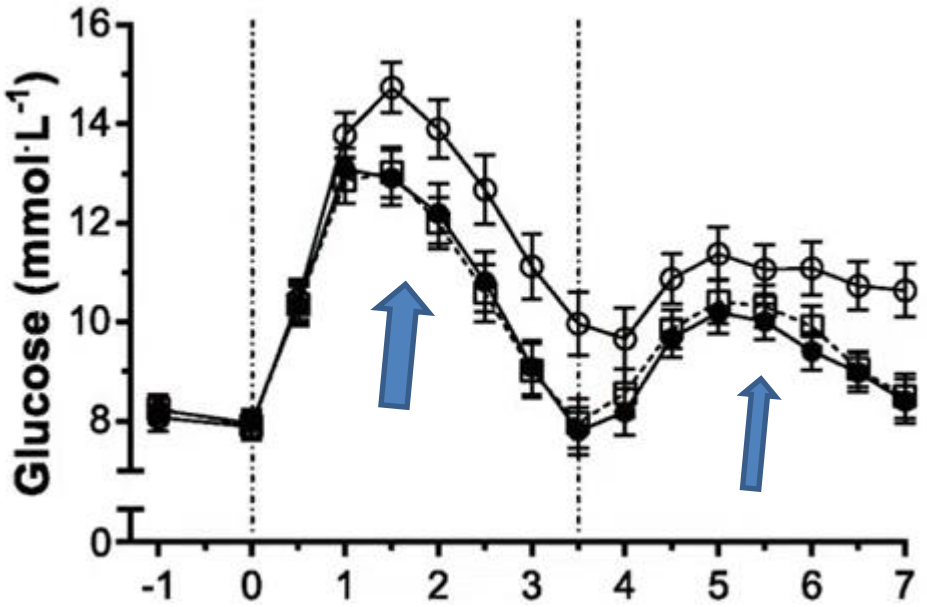
Matthews et al. Am J Clin Nutr 2012

Amati F et al. Diabetes Care 2009

Sedentarity en blood sugar

- N= 24 with T2D (62y)
- Trials;
  - Sitting only
  - 3min light walking every 30min
  - 3min simple resistance activities every 30min

Interrupted sitting lowered postprandial glucose and insulin levels over 7h



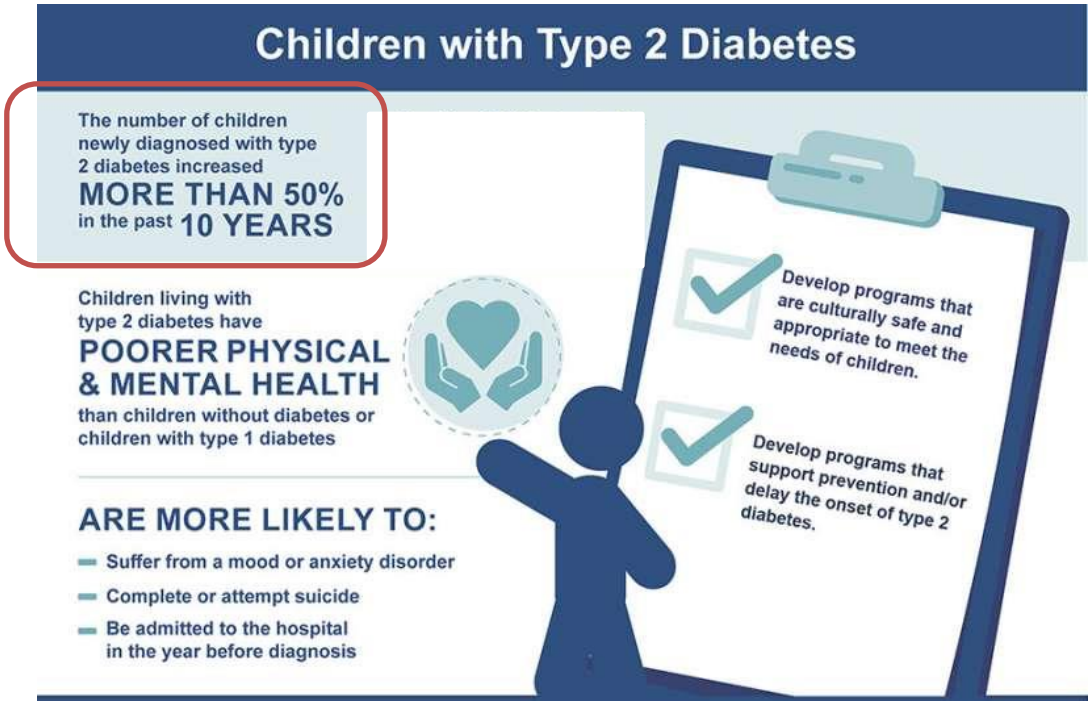
ADA: Too much screen time is associated with higher blood sugar levels
Recommendation breaking up time sitting by walking, leg extensions, or overhead arm stretches every 30 minutes.

Promote spontaneous PA (sometimes easyer than « sport »)
Fitness gains less, but still beneficial to health (particularly if IR and a higher BMI)

Post-prandial energy expenditure reduces glucose level (regardless of exericse type/intensity)
Min 45 min for best effect.

Dempsey PC et al. Diab Care. 2016
Kanaley J. et al. MSSE 2022

Adolescents with T2D



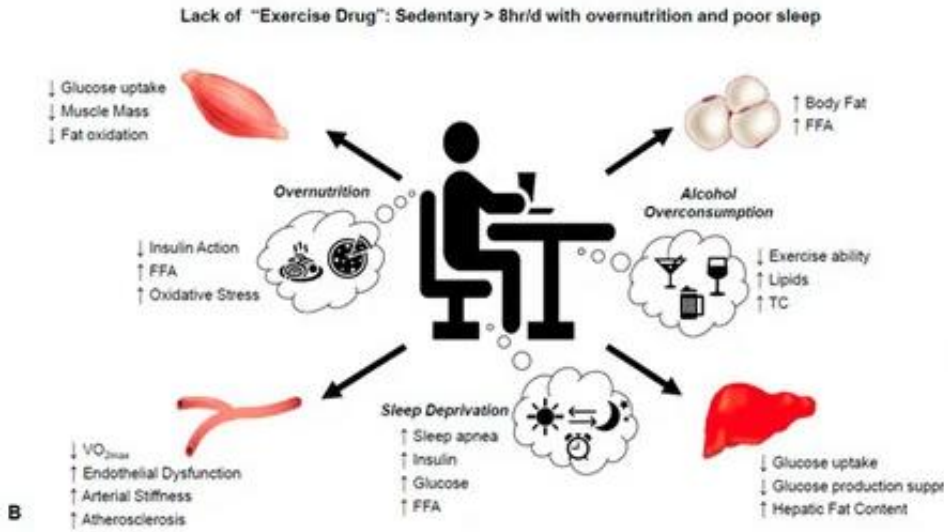
Family members of T2D adolescents have minimal physical activity and fitness lifestyle

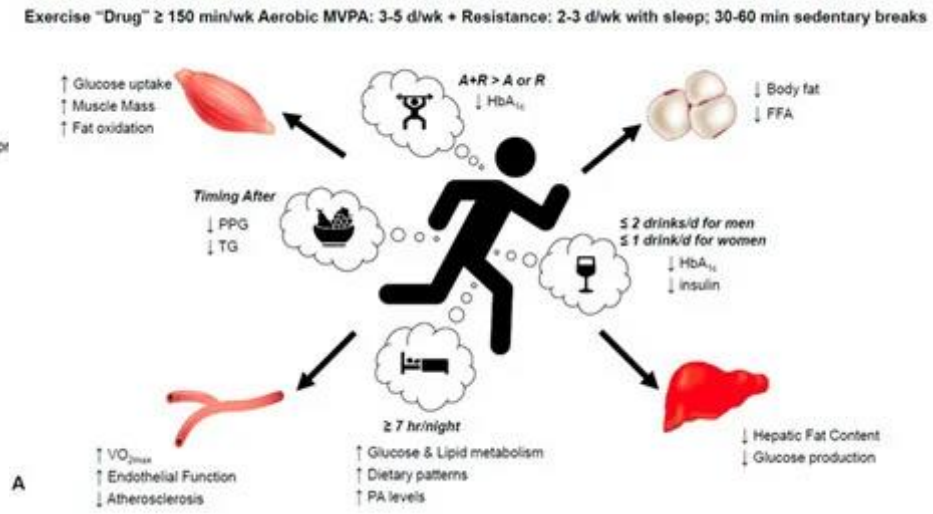
Most studies T2D have been done in adults… reasonable to believe that the results are applicable to adolescents (?)

☹ Young T2D, intensive lifestyle interventions + metformin have not been superior to metformin alone in managing glycemia (?)

Kanaley J. et al. MSSE 2022
Pinhas-Hamiel O et al. Arch Pediatr Adolesc Med. 1
Faulkner MS. Journal for specialists in pediatric nursing. 2010
ISPAD Clinical Practice Consensus Guidelines 2018

Maximizing the Exercise "Drug" to Combat Insulin Resistance





Remchak MM et al. **Maximizing the Exercise "Drug"** Nutrients 2021

Exercise « Prescription »

AIM:

- **Glucose management and insuline level reduction**
- Cardio-vascular risk reduction
- Body composition
- Secondary Prevention

Aerobic

Resistance

Balance

Flexibility

TABLE 3. Indications for preparticipation exercise stress testing.

In general, maximal graded exercise stress testing may be indicated for adults matching one or more of these criteria:

- Age >40 yr, with or without CVD risk factors other than diabetes
- Age >30 yr and
  - Type 1 or T2D >10 yr duration
  - Hypertension
  - Cigarette smoking
  - Dyslipidemia
  - Proliferative or preproliferative retinopathy
  - Nephropathy including microalbuminuria
- Any of the following, regardless of age
  - Known of suspected cardiovascular, coronary artery, or peripheral artery disease
  - Autonomic neuropathy
  - Advanced nephropathy with renal failure

Safety First!

Medical clearance prior to start harder exercise particularly if sedentary

Kanaley J. et al. MSSE 2022

Structured Exercise in T2D: meta-analysis

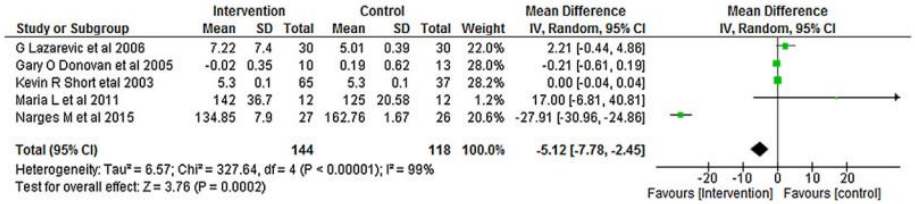


Fig. 4. Forest plot for analysis of fasting blood sugar.

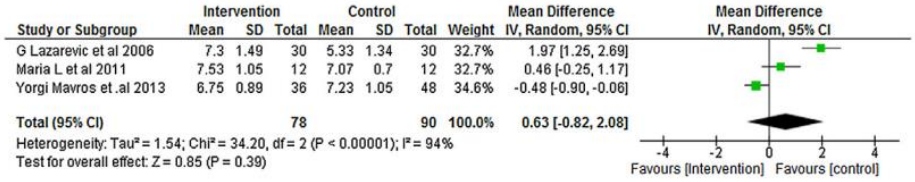


Fig. 5. Forest plot for analysis of glycated hemoglobin.

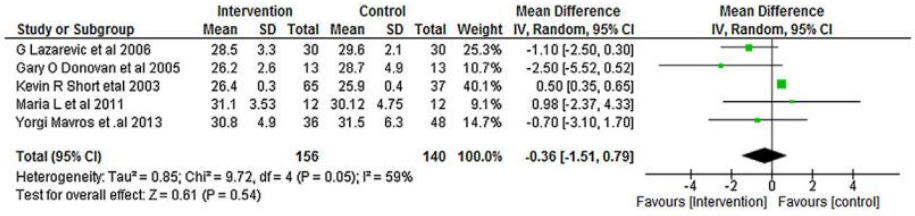


Fig. 6. Forest plot for analysis of body mass index.

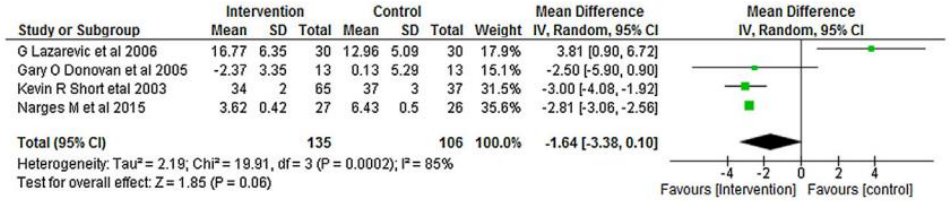


Fig. 2. Forest plot for analysis of fasting insulin level.

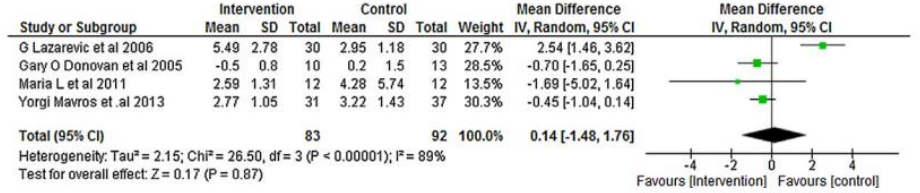


Fig. 3. Forest plot for analysis of homeostatic model assessment for insulin resistance.

Exercise represents an effective interventional strategy to improve glycaemic control in T2DM.

Sampath KA et al. Ann Phys Rehabil Med. 2019

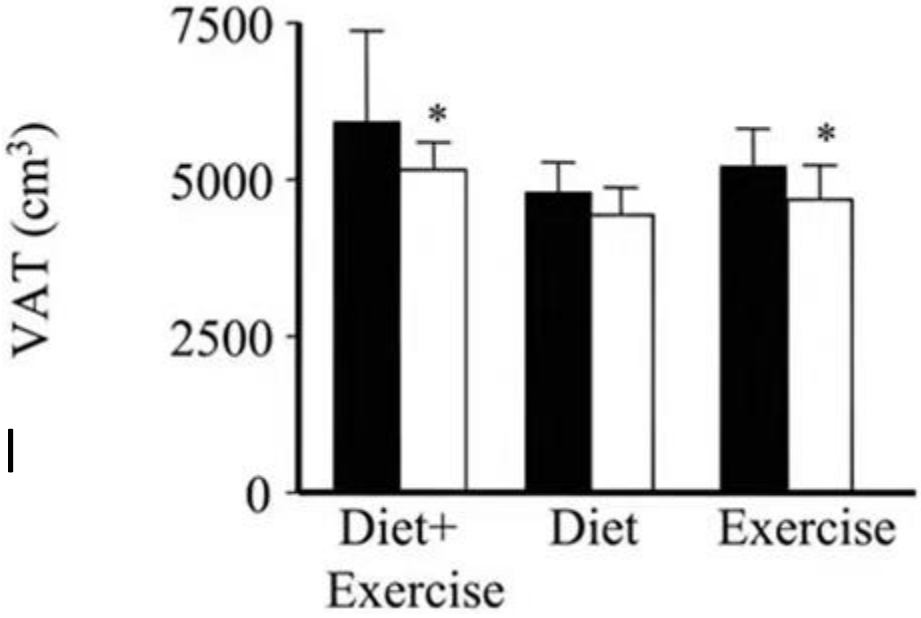
Adapted FITT

Type of Training	Type	Intensity	Frequency	Duration	Progression
Aerobic 	Walking, jogging, cycling, swimming, aquatic activities, rowing, dancing, interval training	40%–59% of $\dot{V}O_2R$ or HRR (moderate), RPE 11–12; or 60%–89% of $\dot{V}O_2R$ or HRR (vigorous), RPE 14–17	3–7 $d \cdot wk^{-1}$, with no more than 2 consecutive days between bouts of activity	Minimum of 150–300 $min \cdot wk^{-1}$ of moderate activity or 75–150 min of vigorous activity, or an equivalent combination thereof	Rate of progression depends on baseline fitness, age, weight, health status, and individual goals; gradual progression of both intensity and volume is recommended
Resistance 	Free weights, machines, elastic bands, or body weight as resistance; undertake 8–10 exercises involving the major muscle groups	Moderate at 50%–69% of 1RM, or vigorous at 70%–85% of 1RM	2–3 $d \cdot wk^{-1}$, but never on consecutive days	10–15 repetitions per set, 1–3 sets per type of specific exercise	As tolerated; increase resistance first, followed by a greater number of sets, and then increased training frequency
Flexibility 	Static, dynamic, or PNF stretching; balance exercises; yoga and tai chi increase range of motion	Stretch to the point of tightness or slight discomfort	≥2–3 $d \cdot wk^{-1}$ or more; usually done with when muscles and joints are warmed up	10–30 s per stretch (static or dynamic)group; 2–4 repetitions of each	As tolerated; may increase range of stretch as long as not painful
Balance 	Balance exercises: lower body and core resistance exercises, yoga, and tai chi also improve balance	No set intensity	≥2–3 $d \cdot wk^{-1}$ or more	No set duration	As tolerated; balance training should be done carefully to minimize the risk of falls

Kanaley J. et al. MSSE 2022

Aerobic training

- N= 33 postmonoposal women with T2D
- 14 weeks of intervention;
  - Diet
  - Aerobic exercise
  - Both



Decrease in subcutaneous and total FM in all interventions BUT… VAT decreased only with exercise, regardless of calorie restriction

VAT reduction in T2D: moderately high volume of exercise (~500 kcal) done 4–5 d/wk

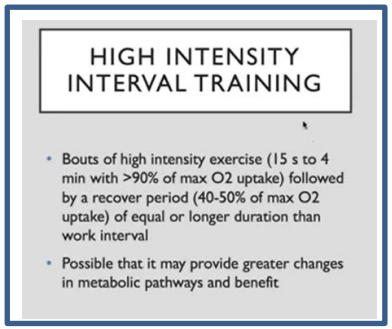
Regular aerobic exercise training: ↑glycemic management, ↓time in hyperglycemia and ↓ 0.5%–0.7% HbA1c

Giannopoulou et al. J Clin Endocrionol Metab. 2005
Kanaley J. et al. MSSE 2022

Adapted FITT

Regular aerobic exercise training:
↑glycemic management, ↓time in hyperglycemia and ↓ 0.5%–0.7% HbA1c
insulin sens., lipids, BP, VO2max, VT1 (even without weight loss)

Type of Training	Type	Intensity	Frequency	Duration	Progression
Aerobic 	Walking, jogging, cycling, swimming, aquatic activities, rowing, dancing, interval training HIIT if possible	40%–59% of $\dot{V}O_2R$ or HRR (moderate), RPE 11–12; or 60%–89% of $\dot{V}O_2R$ or HRR (vigorous), RPE 14–17	3–7 d·wk^{-1}, with no more than 2 consecutive days between bouts of activity	Minimum of 150–300 min·wk^{-1} of moderate activity or 75–150 min of vigorous activity, or an equivalent combination thereof	Rate of progression depends on baseline fitness, age, weight, health status, and individual goals; gradual progression of both intensity and volume is recommended
Resistance 	Free weights, machines, elastic bands, or body weight as resistance; undertake 8–10 exercises involving the major muscle groups	Moderate at 50%–69% of 1RM, or vigorous at 70%–85% of 1RM	2–3 d·wk^{-1}, but never on consecutive days	10–15 repetitions per set, 1–3 sets per type of specific exercise	Bouts of <10min for very deconditionned
Flexibility 	Static, dynamic, or PNF stretching; balance exercises; yoga and tai chi increase range of motion	Stretch to the point of tightness or slight discomfort	≥2–3 d·wk^{-1} or more; usually done with when muscles and joints are warmed up	10–30 s per stretch (static or dynamic)group; 2–4 repetitions of each	As tolerated; may increase range of stretch as long as not painful
Balance 	Balance exercises: lower body and core resistance exercises, yoga, and tai chi also improve balance	No set intensity	≥2–3 d·wk^{-1} or more	No set duration	As tolerated; balance training should be done carefully to minimize the risk of falls

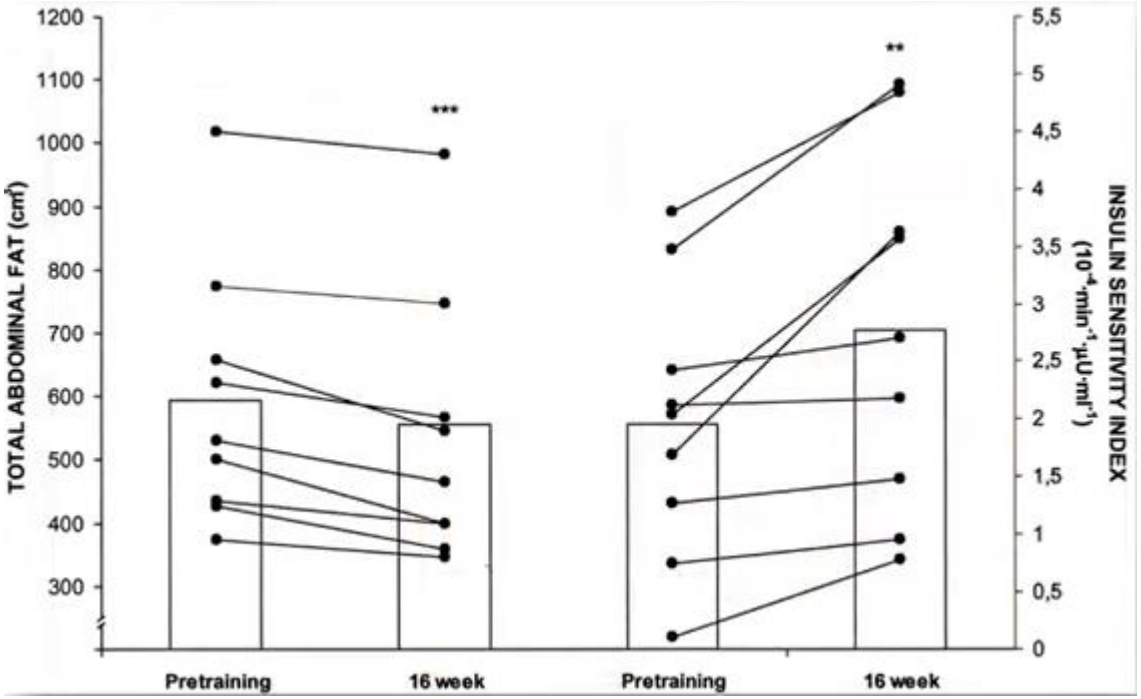


NB: Greater energy expenditure postprandially reduces glucose levels regardless of exercise intensity or type, and durations ≥45 min provide the most consistent benefits.

Kanaley J. et al. MSSE 2022

Resistance

- N= 9 men with T2D
- 16 weeks of intervention;
  - Resistance training 2x/week (supervised and progressive)



Unchanged body mass but subcutaneous and VAT decreased by 10%

Insulin sensitivity increased by 46%, fasting glucose decreased (despite +15% energy intake)

Ibanez et al. Diab Care. 2005
Colberg S. Diabetes Care, 2016

Adapted FITT

Resistance: +10%–15% strength, muscle mass, bone density, BP, lipid, insulin sensitivity

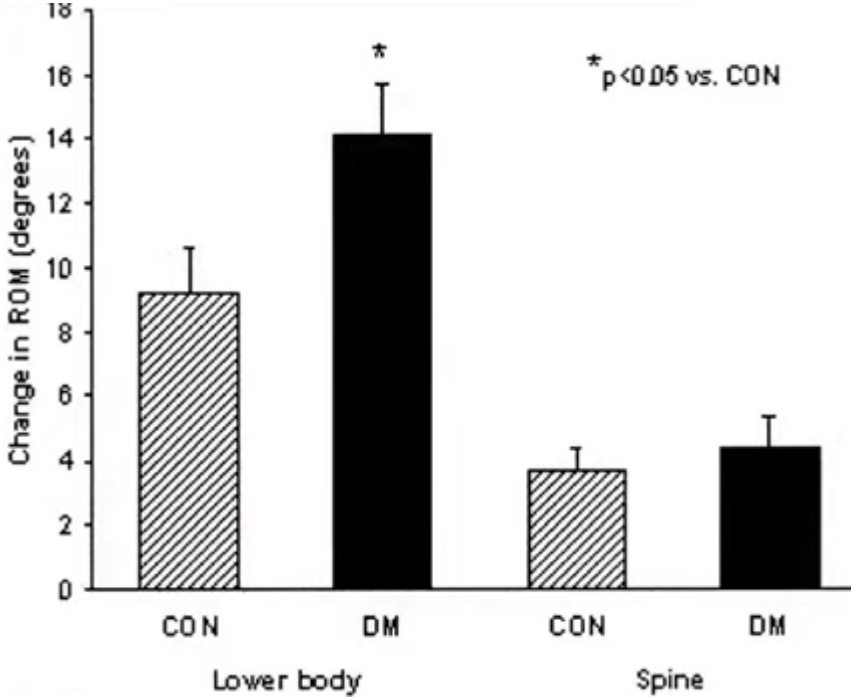
High Intensity Resistance : Best for overall for glucose management and↓ insulin levels

Type of Training	Type	Intensity	Frequency	Duration	Progression
Aerobic 	Walking, jogging, cycling, swimming, aquatic activities, rowing, dancing, interval training	40%–59% of $\dot{V}O_2R$ or HRR (moderate), RPE 11–12; or 60%–89% of $\dot{V}O_2R$ or HRR (vigorous), RPE 14–17	3–7 d·wk^{-1}, with no more than 2 consecutive days between bouts of activity	Minimum of 150–300 min·wk^{-1} of moderate activity or 75–150 min of vigorous activity, or an equivalent combination thereof	Rate of progression depends on baseline fitness, age, weight, health status, and individual goals; gradual progression of both intensity and volume is recommended
Resistance 	Free weights, machines, elastic bands, or body weight as resistance; undertake 8–10 exercises involving the major muscle groups	Moderate at 50%–69% of 1RM, or vigorous at 70%–85% of 1RM	2–3 d·wk^{-1}, but never on consecutive days	10–15 repetitions per set, 1–3 sets per type of specific exercise	As tolerated; increase resistance first, followed by a greater number of sets, and then increased training frequency ↑R => ↑ sets => ↑ Freq
Flexibility 	Static, dynamic, or PNF stretching; balance exercises; yoga and tai chi increase range of motion	Stretch to the point of tightness or slight discomfort	≥2–3 d·wk^{-1} or more, usually done with when muscles and joints are warmed up	10–30 s per stretch (static or dynamic)group; 2–4 repetitions of each	As tolerated, may increase range of stretch as long as not painful
Balance 	Balance exercises: lower body and core resistance exercises, yoga, and tai chi also improve balance	No set intensity	≥2–3 d·wk^{-1} or more	No set duration	As tolerated; balance training should be done carefully to minimize the risk of falls

Kanaley J. et al. MSSE 2022

Flexibility

- N= 9 men with T2D vs C
- 8 weeks of intervention;
  - Flexibility/Resistance training 3x/week (supervised and progressive)



Hypergycemia increases joint structure stiffness (glucose+collagen)

Improved strenght, Rage of motion around certain joints (more in T2D)

Herriott et al. Diab Care. 2004

Adapted FITT

Critical with aging and diabetes (glycation of joint structures)

Type of Training	Type	Intensity	Frequency	Duration	Progression
Aerobic 	Walking, jogging, cycling, swimming, aquatic activities, rowing, dancing, interval training	40%–59% of $\dot{V}O_2R$ or HRR (moderate), RPE 11–12; or 60%–89% of $\dot{V}O_2R$ or HRR (vigorous), RPE 14–17	3–7 $d \cdot wk^{-1}$, with no more than 2 consecutive days between bouts of activity	Minimum of 150–300 $min \cdot wk^{-1}$ of moderate activity or 75–150 min of vigorous activity, or an equivalent combination thereof	Rate of progression depends on baseline fitness, age, weight, health status, and individual goals; gradual progression of both intensity and volume is recommended
Resistance 	Free weights, machines, elastic bands, or body weight as resistance; undertake 8–10 exercises involving the major muscle groups	Moderate at 50%–69% of 1RM, or vigorous at 70%–85% of 1RM	2–3 $d \cdot wk^{-1}$, but never on consecutive days	10–15 repetitions per set, 1–3 sets per type of specific exercise	As tolerated; increase resistance first, followed by a greater number of sets, and then increased training frequency
Flexibility 	Static, dynamic, or PNF stretching; balance exercises; yoga and tai chi increase range of motion	Stretch to the point of tightness or slight discomfort	≥2–3 $d \cdot wk^{-1}$ or more; usually done with when muscles and joints are warmed up	10–30 s per stretch (static or dynamic)group; 2–4 repetitions of each	As tolerated; may increase range of stretch as long as not painful
Balance 	Balance exercises: lower body and core resistance exercises, yoga, and tai chi also improve balance	No set intensity	≥2–3 $d \cdot wk^{-1}$ or more	No set duration	As tolerated; balance training should be done carefully to minimize the risk of falls

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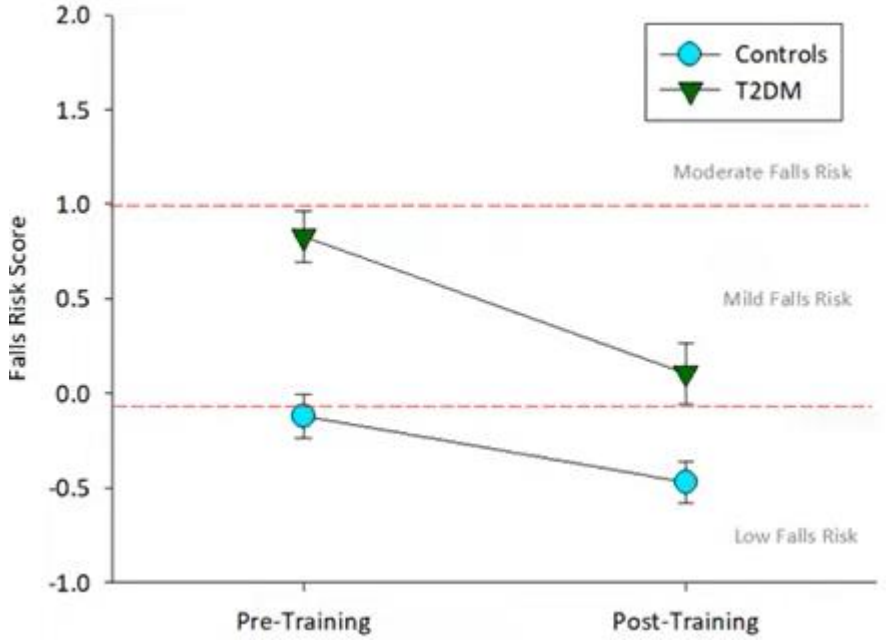
Balance

- N= 26 with T2D vs C (>50y)
- T2D with mild-to-moderate neuropathy, slower reaction time and increased postural sway
- 6 weeks of intervention;
  - Balance/Resistance training 3x/week (supervised and progressive)



Improved reaction time and reduced falls risk (more in T2D)

Important preventively with age (>40y) and overweight

HELP prevent falls (! Peripheral neuropathy)

Morrison et al. Diab Care. 2010

Adapted FITT

Critical with aging, diabetes (glycation of joint structures), neuropathy

Type of Training	Type	Intensity	Frequency	Duration	Progression
Aerobic 	Walking, jogging, cycling, swimming, aquatic activities, rowing, dancing, interval training	40%–59% of $\dot{V}O_2R$ or HRR (moderate), RPE 11–12; or 60%–89% of $\dot{V}O_2R$ or HRR (vigorous), RPE 14–17	3–7 d·wk^{-1}, with no more than 2 consecutive days between bouts of activity	Minimum of 150–300 min·wk^{-1} of moderate activity or 75–150 min of vigorous activity, or an equivalent combination thereof	Rate of progression depends on baseline fitness, age, weight, health status, and individual goals; gradual progression of both intensity and volume is recommended
Resistance 	Free weights, machines, elastic bands, or body weight as resistance; undertake 8–10 exercises involving the major muscle groups	Moderate at 50%–69% of 1RM, or vigorous at 70%–85% of 1RM	2–3 d·wk^{-1}, but never on consecutive days	10–15 repetitions per set, 1–3 sets per type of specific exercise	As tolerated; increase resistance first, followed by a greater number of sets, and then increased training frequency
Flexibility 	Static, dynamic, or PNF stretching; balance exercises; yoga and tai chi increase range of motion	Stretch to the point of tightness or slight discomfort	≥2–3 d·wk^{-1} or more; usually done with when muscles and joints are warmed up	10–30 s per stretch (static or dynamic)group; 2–4 repetitions of each	As tolerated; may increase range of stretch as long as not painful
Balance 	Balance exercises: lower body and core resistance exercises, yoga, and tai chi also improve balance	No set intensity	≥2–3 d·wk^{-1} or more	No set duration	As tolerated; balance training should be done carefully to minimize the risk of falls

preferably daily

Older adults; > 60min/wk

Balance exercise equipement, uneven surfaces, pillow stand, qigong, …

Simple balance exercises: Heel-to-toe walk, backward walk, sit-to- stand, change position, one leg stading, side leg raises, eyes closed, …

Kanaley J. et al. MSSE 2022

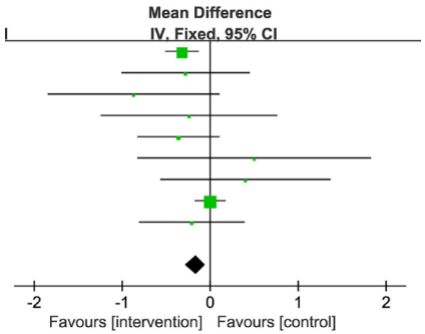
ACSM's Guidelines, 11th Ed. 2021

ULB UNIVERSITÉ LIBRE DE BRUXELLES

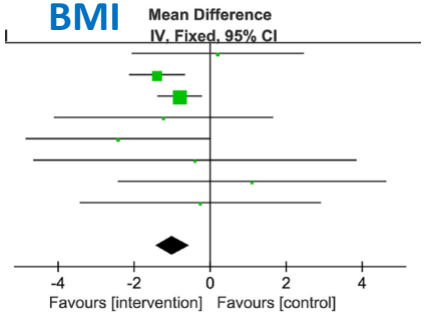
Combined Training

- Combined training (aerobic+ resistance) for optimal health and glucose management
- On the same or different days

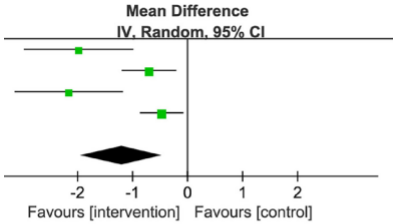
HbA1c



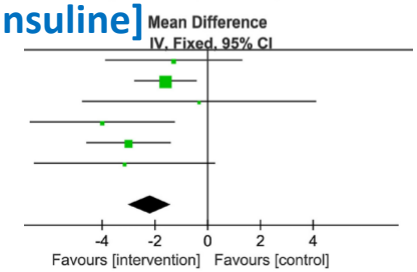
BMI



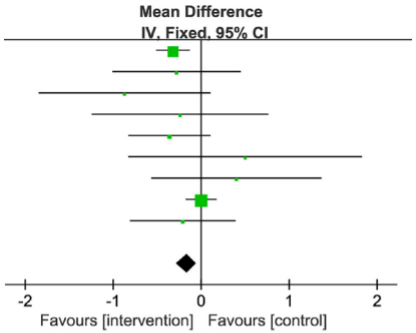
IR



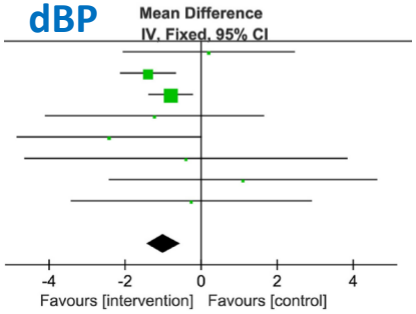
[insuline]



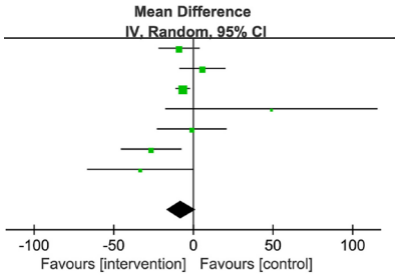
sBP



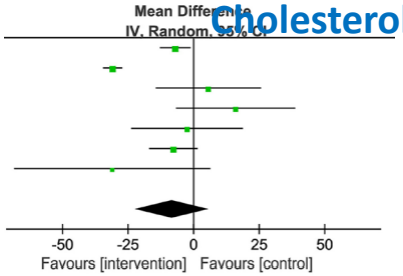
dBP



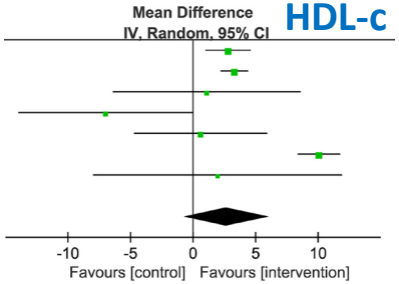
Triglyceride



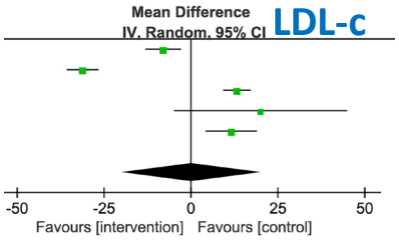
Cholesterol



HDL-c



LDL-c



> 5% weight-loss is necessary for benefits on HbA1c, BP, lipids

Combined exercise exerted significant effects in improving glycaemic control, weight-loss and insulin sensitivity among patients with T2D with overweight/obesity

Zhao X et al. BMJ. 2021

Kanaley J. et al. MSSE 2022

Table 3—Exercise training recommendations: types of exercise, intensity, duration, frequency, and progression

	Aerobic	Resistance	Flexibility and Balance
Type of exercise	• Prolonged, rhythmic activities using large muscle groups (e.g., walking, cycling, and swimming) • May be done continuously or as HIIT	• Resistance machines, free weights, resistance bands, and/or body weight as resistance exercises	• Stretching: static, dynamic, and other stretching; yoga • Balance (for older adults): practice standing on one leg, exercises using balance equipment, lower-body and core resistance exercises, tai chi
Intensity	• Moderate to vigorous (subjectively experienced as "moderate" to "very hard")	• Moderate (e.g., 15 repetitions of an exercise that can be repeated no more than 15 times) to vigorous (e.g., 6–8 repetitions of an exercise that can be repeated no more than 6–8 times)	• Stretch to the point of tightness or slight discomfort • Balance exercises of light to moderate intensity
Duration	• At least 150 min/week at moderate to vigorous intensity for most adults with diabetes • For adults able to run steadily at 6 miles per h (9.7 km/h) for 25 min, 75 min/week of vigorous activity may provide similar cardioprotective and metabolic benefits	• At least 8–10 exercises with completion of 1–3 sets of 10–15 repetitions to near fatigue per set on every exercise early in training	• Hold static or do dynamic stretch for 10−30 s; 2−4 repetitions of each exercise • Balance training can be any duration
Frequency	• 3–7 days/week, with no more than 2 consecutive days without exercise	• A minimum of 2 nonconsecutive days/week, but preferably 3	• Flexibility: ≥2−3 days/week • Balance: ≥2−3 days/week
Progression	• A greater emphasis should be placed on vigorous intensity aerobic exercise if fitness is a primary goal of exercise and not contraindicated by complications • Both HIIT and continuous exercise training are appropriate activities for most individuals with diabetes	• Beginning training intensity should be moderate, involving 10−15 repetitions per set, with increases in weight or resistance undertaken with a lower number of repetitions (8−10) only after the target number of repetitions per set can consistently be exceeded • Increase in resistance can be followed by a greater number of sets and finally by increased training frequency	• Continue to work on flexibility and balance training, increasing duration and/or frequency to progress over time

Colberg et al., 2016

Barriers

- Perceived lack of time…
- Motivation
- Accessibility
- Convenience
- Injuries and co-morbidities

"Welcome to the Diabetic Hotline! If you need a new excuse for cheating on your diet, press 1. If you need a new excuse for skipping your workout, press 2..."

Adress these and make SMART goals for participation

Digital Health Apps for training
-Supervision
-Motivation
-Monitoring
-BG associated

Progression for fragile patients: Start lowly, progress slowly (?)
Preventing injuries and enhance compliance

- Fear of hypoglycemia

Most T2D medication have no impact on BG response to PA

!!! with **exogeneous insulin or insulin-secretagogues**

- Sulfonylureas
- Meglitinides/glinides

supplement carbohydrate or reduce insulin during and after exercise

Kanaley J. et al. MSSE 2022

Safety

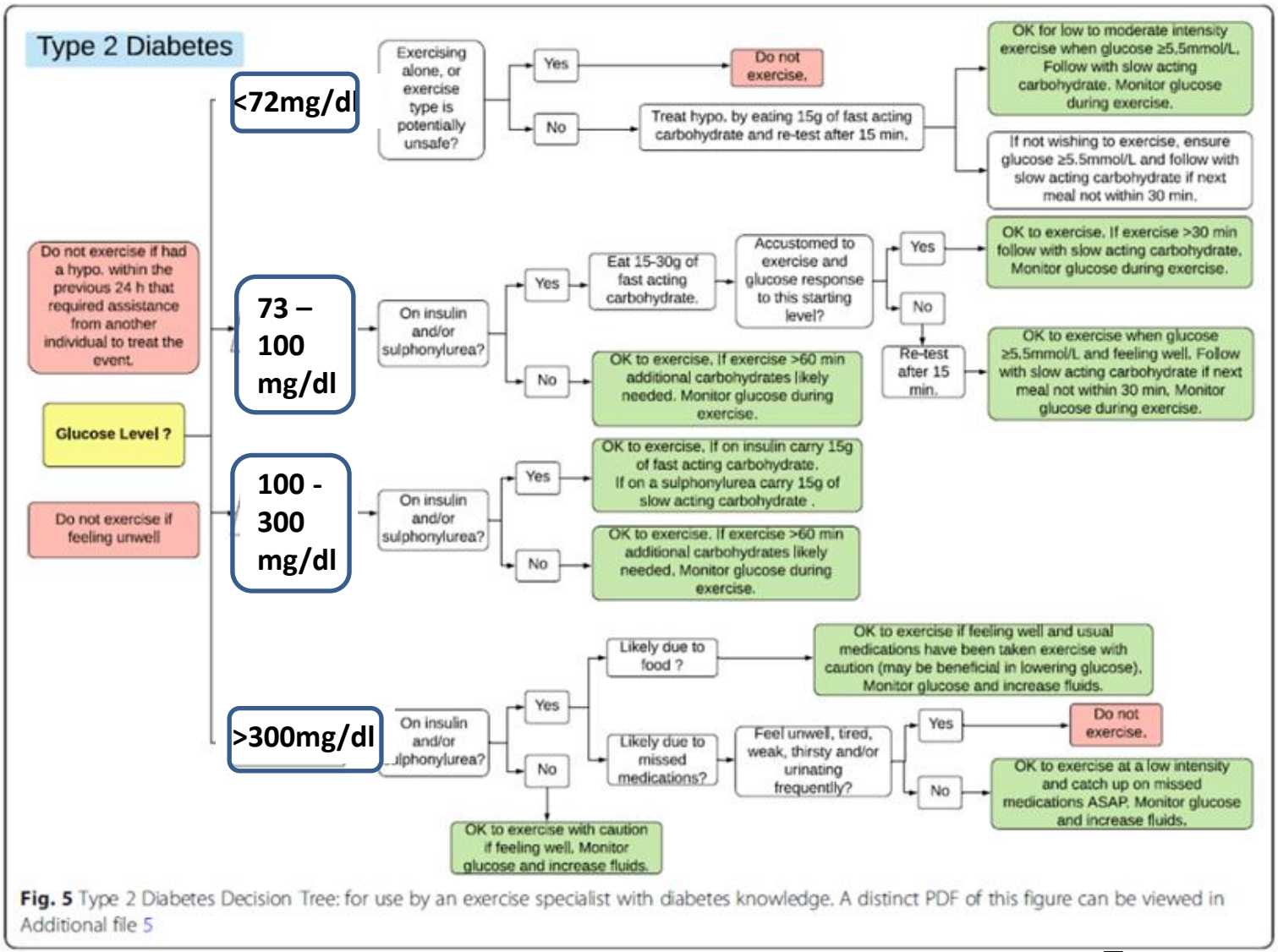


Fig. 5 Type 2 Diabetes Decision Tree: for use by an exercise specialist with diabetes knowledge. A distinct PDF of this figure can be viewed in Additional file 5

Sugar intake

Follow closely for Hypo

OK

! Keto No HI

Turner et al. 2019

Conclusion

- T2D and pre-diabetes are characterized by insulin resistance that can be lowered with lifestyle changes, including PA
- Both T2D and PD car be prevented/delayed with intensive lifestyle management
- Although lifestyle changes can lead to weightloss, PA is critical for weight maintenance after loss and improved insulin action
- Those with lowest baseline activity levels have the most to gain from being active
- Include regular PA of any type when dieting to lose visceral fat and retain muscle mass
- Recommended activities include aerobic, resistance, flexibility and balance training along with more daily movement and activity breaks

Diabetes in pregnancy

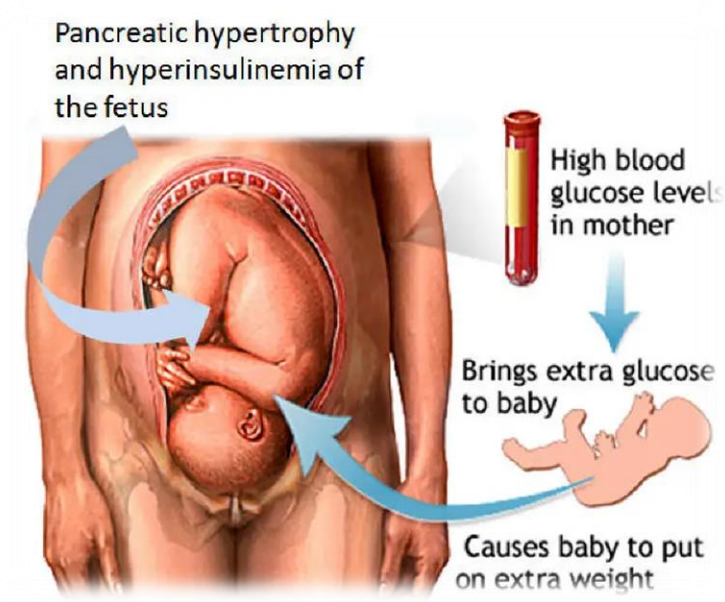
Definition

WHO and International Federation of Gynaecology and Obstetrics (FIGO):

Diabetes in pregnancy (DIP): Condition in which the body is unable to produce or use enough insulin effectively to regulate blood sugar levels during pregnancy => **hyperglycemia**

INCLUDING:

- Gestational diabetes (80% DIP)
- T1D pregnant women
- T2D pregnant women



From 2011 to 2019:

The rate of gestational diabetes in the U.S. rose from **47.6** to **63.5** per 1,000 live births.

Short-term complications

Maternal
- Pre-eclampsia/eclampsia

Neonatal
- Macrosomia
- Large for gestational age
- Shoulder dystocia
- Higher body fat

Delivery
- Prolonged labor
- Caesarean birth
- Surgical complications
- Longer hospital stay
- Maternal hemorrhage
- Infection

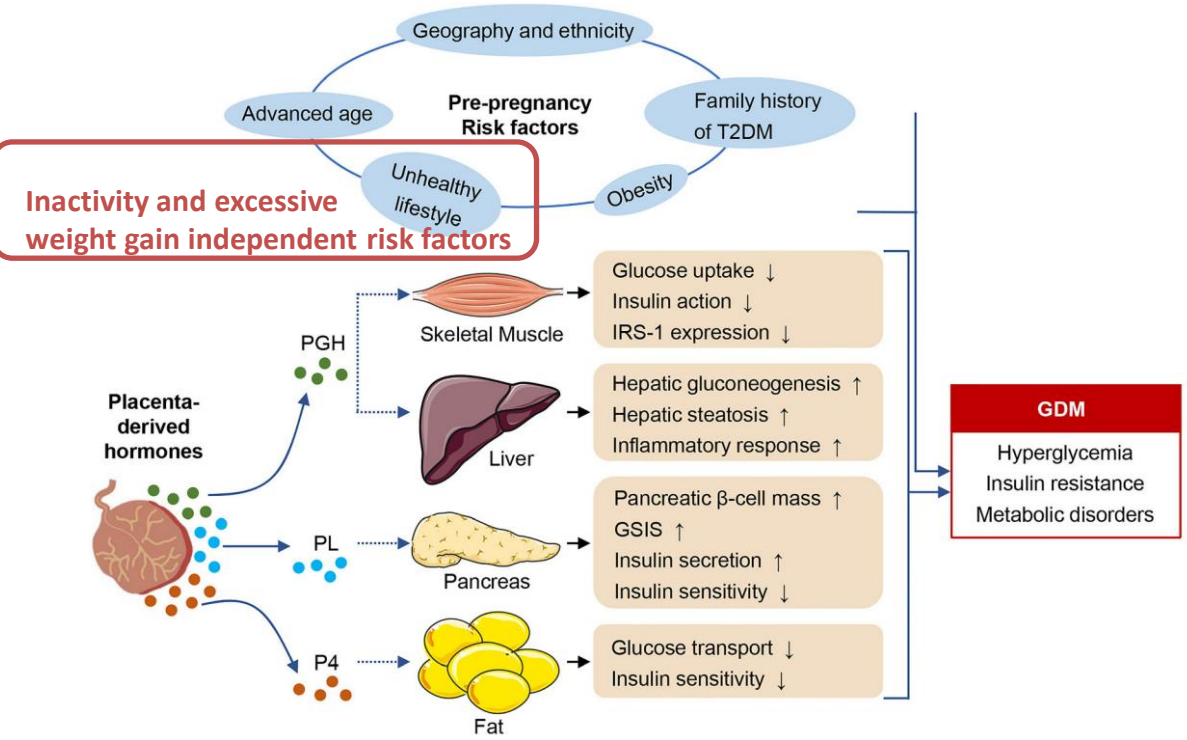
Long-term complications

Maternal and Child
- Type 2 diabetes mellitus
- Cardiovascular disease
- Metabolic syndrome
- Obesity

American Diabetes Association. Diabetes Care 2020
International Association of Diabetes and Pregnancy Study Groups (IADPSG). Diabetes Care. 2010

GDM Pathogenesis

During pregnancy, placenta hormones can interfere with insulin's ability to regulate blood sugar. More insulin is then required. In GDM, the pancreas is unable to produce enough insulin to meet this increased demand.



Most likely 24 week

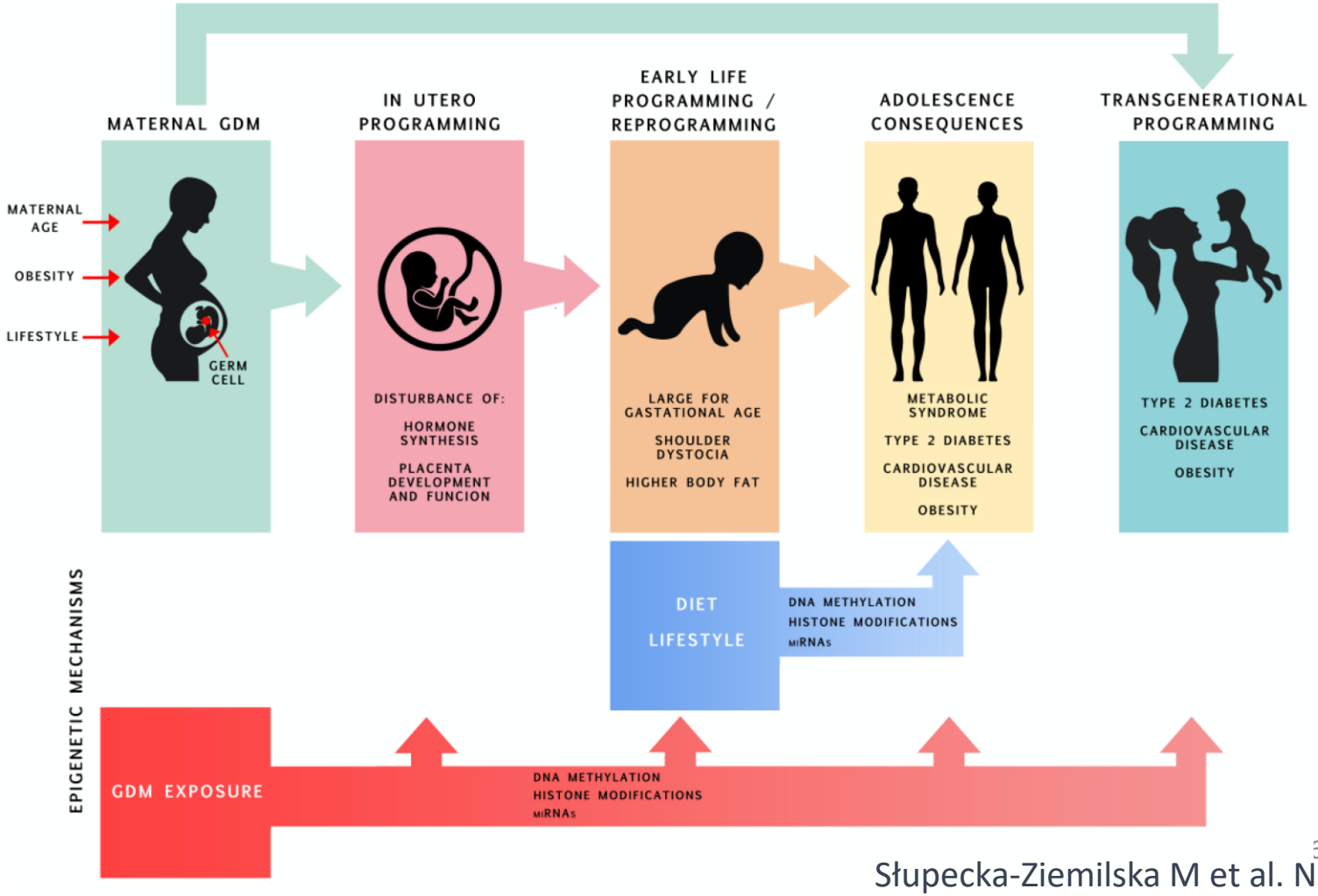
Routine prenatal screening
Oral Glucose Tolerance Test

Fasting	**92 mg/dl**
1 hour	**180 mg/dl**
2 hours	**153 mg/dl**
3 hours	**140 mg/dl**

Gao, X *et al. Rev Endocr Metab Disord* 2021

Diabetic vicious cycle

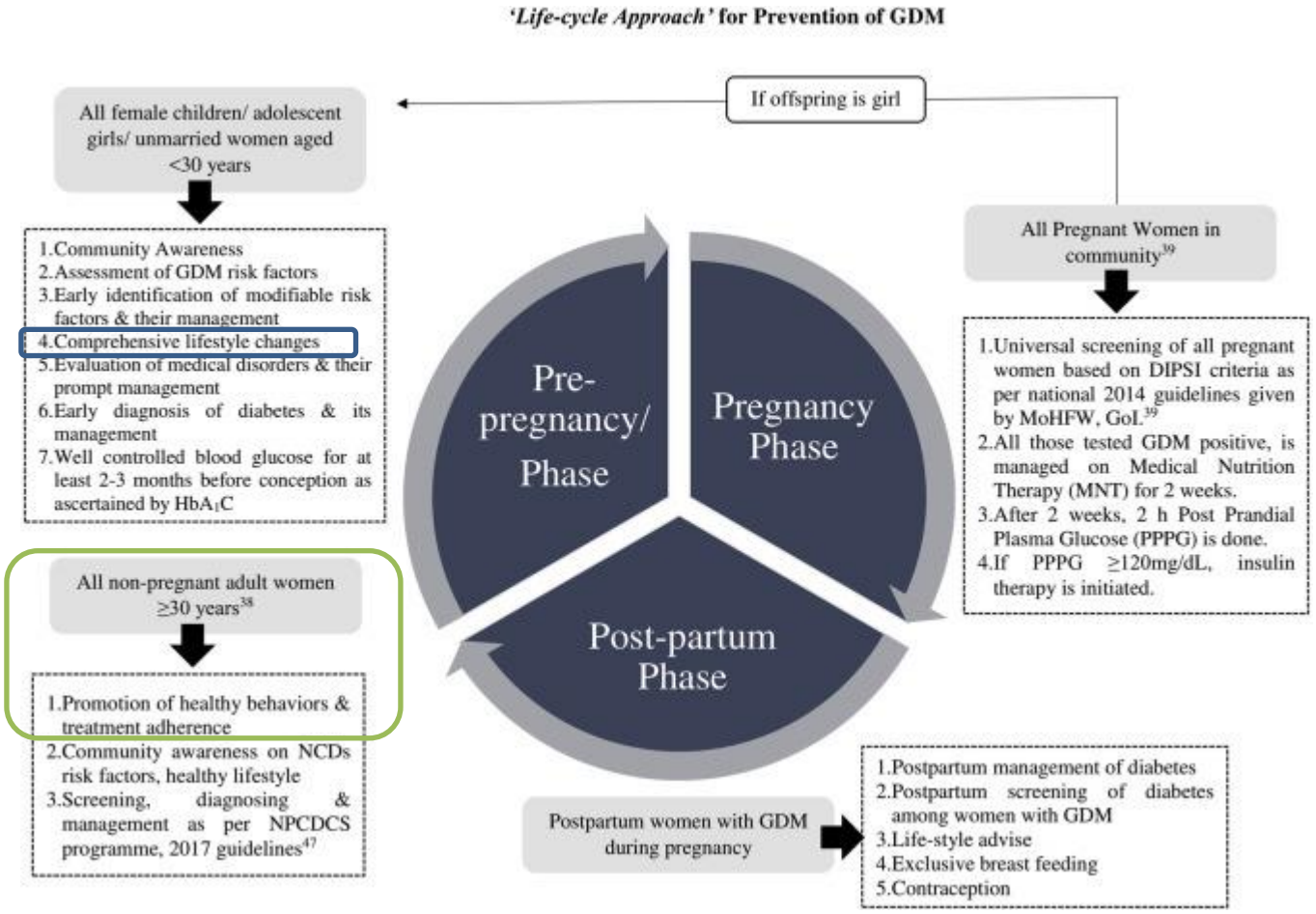
Female offspring of women with diabetes during pregnancy become more likely to develop obesity and T2D by the of childbearing age… perpetuating the cycle.



Słupecka-Ziemilska M et al. Nutrients. 2020

Life-circle approach

Preventive approach consisting of **raising awareness and life-style management** of the young girl **born to a mother with Diabetes in pregnancy AND all women > 30 years**, in addition to care **during** and **after** pregnancies.

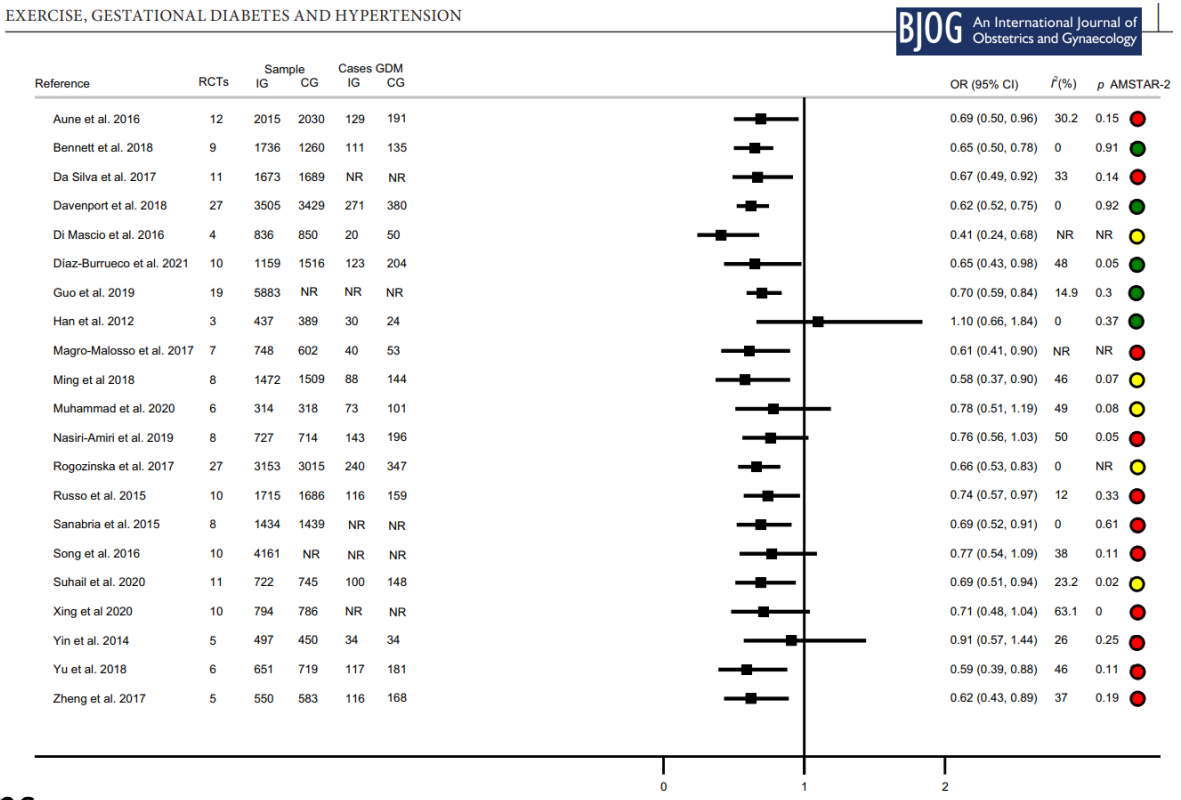


How?
Prescription?
Therapist?

Surabhi M et al. Clinical Epidemiology and Global Health 2019

Preventing gestational diabetes

Exercise has a beneficial effect on the incidence of GDM and GH in pregnant women:



Greater benefits:

- Supervised exercise interventions
- Initiating during the first semester
- Lasting more than 45minutes per session
- Low to moderate Intensity

Obesity?

Higher intensity?

Martínez-Vizcaíno V etal. BJOG. 2023.

Pre-gestational medical conditions

T1D, T2D and hypertension

☺ **Systematic review and meta-analysis:**

Prenatal exercise reduced the odds of cesarean birth by 55% and did not increase the risk of adverse maternal and neonatal outcomes (OR 0.45; 95% CI, 0.22–0.95)

☹ **Limited evidence**

Suggesting a need for high-quality investigations on exercise in this specific population of women

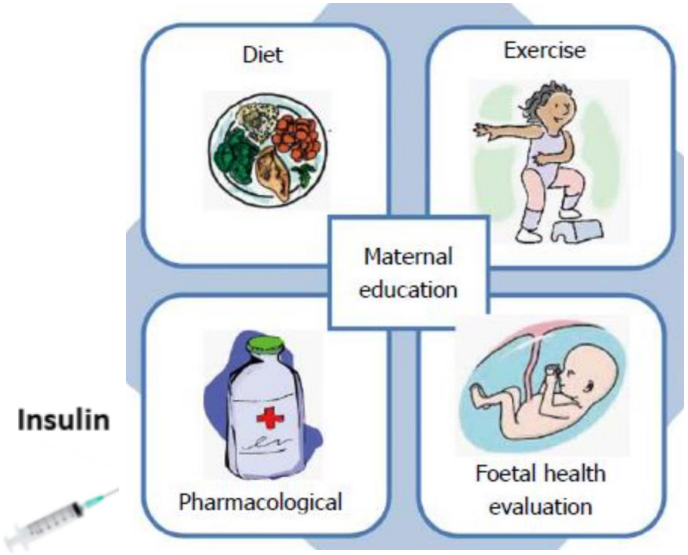
Adesegun D, J Obstet Gynaecol Can 2022

Management

AIM: **Blood glucose homeostasis**

Close monitoring of BS for management and complications preventions.

Combination of dietary changes, exercise, and insulin therapy if needed.

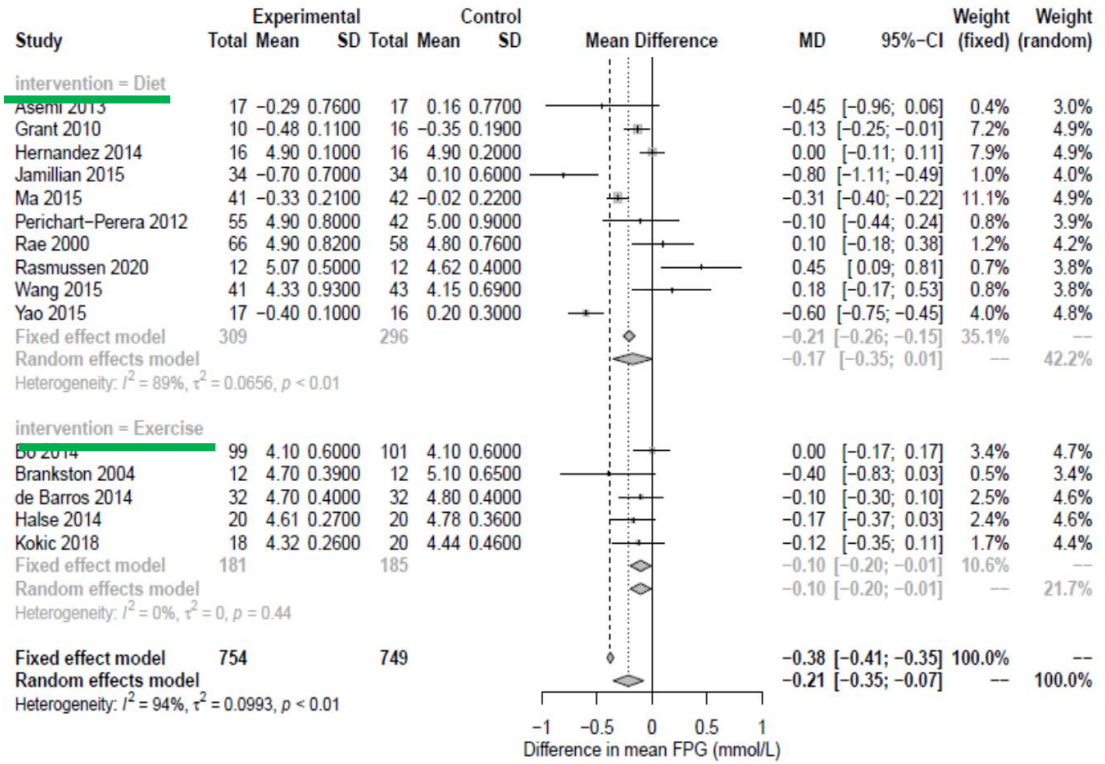


Guidelines strongly support pregnant women with diabetes to exercise regularly.

American Diabetes Association (ADA) ADA 2021
American College of Obstetricians and Gynecologists (ACOG)

Key Role

Key role of diet and exercise in the management of GDM with promising advantageous effects on measures of glycemia



=> Need to develop more suitable lifestyle recommendations for women with DIP.

- Need for large, well-designed RCTs that clarify the most effective lifestyle intervention across a range of outcomes in women with all diabetes types during pregnancy
- Ideally incorporate longer-term outcomes in mothers and offspring

Dingena CF et al. Nutrients. 2023

Adapted FITT

! Individual assessment to suit abilities/ clinical circumstances

N guidelines from 15
USA, UK, Australia, N-Z, Iran, Sri Lanka, China, Turkey, Int.Fed.Gyn.Obstr.

Frequency: min 5 days/wk –> Everyday	<2 days without?	6	2
Intensity: Moderate intensity	maintain previous PA level? High intensity? Measurement?	8	1
Time: - 30min/session	min 10? Min 140-150min/wk? 55min/sess 3day/wk	12	3
- after meal	1h?	5	1
Type: - safe activities	Flexibility ?	15	2
- Aerobic exercise	Exact type? Machines? swimming	11	3
- Resistance training	2-3 x 10-15rep (2-3/wk)?	8	1
- walking		7	
! Advise to engage regular PA after birth	If fasting G > 104 mg/dl?	7	1

Yang X, et al. Int J Nurs Pract. 2023
Kanaley J, et al. MSSE 2022

Contraindications

Absolute Contraindications	Relative Contraindications
Ruptured membranes	Recurrent pregnancy loss
Premature labour	Gestational hypertension
Unexplained persistent vaginal bleeding	A history of spontaneous preterm birth
Placenta praevia after 28 weeks gestation	Mild/moderate cardiovascular or respiratory disease
Pre-eclampsia	Symptomatic anaemia
Incompetent cervix	Malnutrition
Intrauterine Growth restriction	Eating disorder
Higher-order multiple pregnancies (e.g. triplets)	Twin pregnancy after the 28th week
Uncontrolled Type 1 diabetes	Other significant medical conditions
Uncontrolled thyroid disease	
Uncontrolled hypertension	
Other serious cardiovascular, respiratory or systemic disorder	

Obesity

History of extremely sedentary lifestyle

Chinese Medical Association Perinatal Medicine Branch 2013

ACOG, American College of Obstetricians and Gynecologists
Sports Medicine Australia

- Clear tendency for ketosis or ketoacidosis,
- Blood glucose > 132 mg/dl

- Severe diabetic complications: nephropathy, diabetic foot, fundus lesions or retinopathy

Professional Committee of Gestational Diabetes Mellitus, 2021
Canadian Society for Exercise Physiology
Society of Obstetricians and Gynaecologists of Canada

Meah VL et al. Br J Sports Med. 2020

Warning signs during exercise

TABLE 5 Warning signs to discontinue exercise for pregnant women with GDM.

Topic	Number of recommended guidelines	Recommended guidelines
High heart rate	1	QCG, 2021
Dyspnoea prior to or during exertion	2	Professional Committee of Gestational Diabetes Mellitus, 2021; QCG, 2021
Dizziness, faintness, nausea	2	Professional Committee of Gestational Diabetes Mellitus, 2021; QCG, 2021
Headache	2	Professional Committee of Gestational Diabetes Mellitus, 2021; QCG, 2021
Decreased fetal movements	2	CSPM, 2013; QCG, 2021
Overfrequent fetal movement	1	CSPM, 2013
Uterine contractions, vaginal bleeding, amniotic fluid leakage	3	CSPM, 2013; Professional Committee of Gestational Diabetes Mellitus, 2021; QCG, 2021
Back or pelvic pain	1	QCG, 2021
Chest pain	2	Professional Committee of Gestational Diabetes Mellitus, 2021; QCG, 2021
Hypogastralgia	1	CSPM, 2013
Muscle weakness	2	Professional Committee of Gestational Diabetes Mellitus, 2021; QCG, 2021
Calf pain or swelling or sudden swelling of ankles, hands and/or face	1	QCG, 2021

Abbreviations: CSPM, Chinese Medical Association Perinatal Medicine Branch; QCG, Queensland Clinical Guidelines.

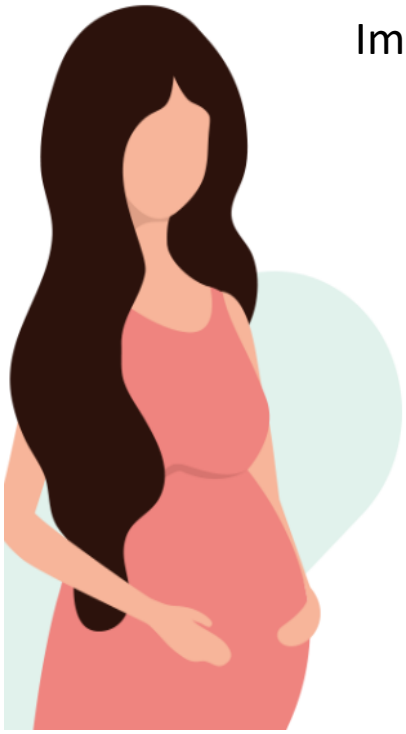
- Monitor blood sugar levels before, during, and after exercise
- Staying hydrated
- Eating a balanced diet
- ! Insulin: Pay attention to glucopenia or delayed hypoglycaemia

Chinese Medical Association Perinatal Medicine Branch

Women with using insulin should pay attention to:
• Avoid the peak period of insulin action
• Avoid the moving limbs on insulin injection site
• Monitor blood glucose before exercise:
BG < 99 mg/dl, advanced food before the exercise;
BG > 250 mg/dl, uridone needs to be detected,
if the uridone was positive, women needs to cease exercise
• Bring some candy or cookies during exercise and eat immediately once you have hypoglycaemia
• Carry cards with your name, illness, home address and contact information for accidental fainting or coma

Padayachee C & Coombes JS. World J Diabetes. 2015
Yang X, et al. Int J Nurs Pract. 2023

Post-partum



Immediately postpartum GDM, insulin resistance decreases dramatically

Only **around 5-10% of women** face issues with diabetes post their delivery

=> important to monitor blood sugar levels and insulin requirements need to be evaluated

⇒ lifestyle intervention should be started ASAP (<3 years) after the pregnancy

Mothers diagnosed with diabetes during their pregnancy have a **50% risk of developing type 2 diabetes** in the next 10 years

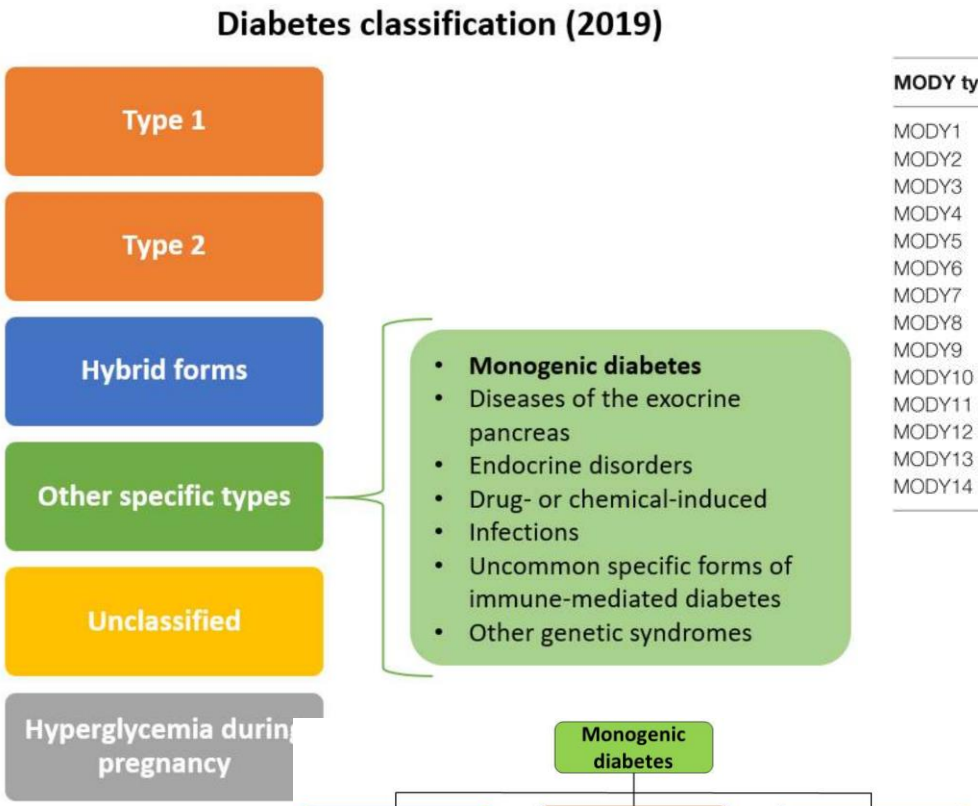
NB: Babies born to mothers with GDM also have a higher lifetime risk of obesity and T2D

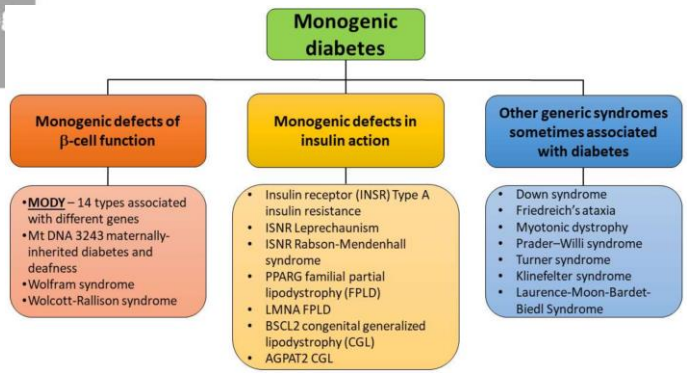
Women with history of GDM found to have prediabetes should receive INTENSIVE lifestyle interventions and/or metformin to prevent T2D

International Association of Diabetes and Pregnancy Study Groups (IADPSG). Diabetes Care. 2010

Other specific types of diabetes

Classification of types of diabetes





MODY type	Gene	Chromosomal locus	Frequency (%)
MODY1	HNF4α	20q13	5
MODY2	GCK	7p13	15–25
MODY3	HNF1α	12q24	30–50
MODY4	PDX/IPF1	13q12.2	<1
MODY5	HNF-1β	17q12	5
MODY6	NEUROD1	2q31	<1
MODY7	KLF11	2p25	<1
MODY8	CEL	9q34	<1
MODY9	PAX4	7q32	<1
MODY10	INS	11p15	<1
MODY11	BLK	8p23.1	<1
MODY12	ABCC8	11p15	<1
MODY13	KCNJ11	11p15.1	<1
MODY14	APPL1	3p14.3	<1

☺ Exercise interventions can be beneficial for people with all types of diabetes, including MODY. Help improve overall health and well-being.

☹ However, it's important to note that lifestyle interventions alone are not sufficient to manage most forms of diabetes, including MODY.

Sperling Ma et al. National Institute of Diabetes and Digestive and Kidney Diseases (US); 2018

WHO, 2019

MODY 2, mutation in the GCK gene (slightly elevated blood sugar levels and do not require insulin or other medications to manage their diabetes), is often mild and can sometimes be managed with lifestyle interventions alone.

Precision Therapy for a Chinese Family With Maturity-Onset Diabetes of the Young

Juyi Li[1†], Meng Shu[2†], Xiufang Wang[3], Aiping Deng[1], Chong Wen[4], Juanjuan Wang[5], Si Jin[2] and Hongmei Zhang[5*]*

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Objective: To determine the pathogenic gene and explore the clinical characteristics of maturity-onset diabetes of the young type 2 (MODY2) pedigree caused by a mutation in the glucokinase (*GCK*) gene.

Methods: Using whole-exome sequencing (WES), the pathogenic gene was detected in the proband—a 20-year-old young man who was accidentally found with hyperglycemia, no ketosis tendency, and a family history of diabetes. The family members of the proband were examined. In addition, relevant clinical data were obtained and genomic DNA from peripheral blood was obtained. Pathologic variants of the candidate were verified by Sanger sequencing technology, and cosegregation tests were conducted among other family members and non-related healthy controls. After adjusting the treatment plan based on the results of genetic testing, changes in biochemical parameters, such as blood glucose levels and HAblc levels were determined.

Results: In the *GCK* gene (NM_000162) in exon 9, a heterozygous missense mutation c.1160C > T (p.Ala387Val) was found in the proband, his father, uncle, and grandmother. Thus mutation, which was found to co-segregate with diabetes, was the first discovery of such a mutation in the Asian population. After stopping hypoglycemic drug treatment, good glycemic control was achieved with diet and exercise therapy.

Conclusion: *GCK* gene mutation c.1160C > T (p.Ala387Val) is the pathogenic gene in the *GCK-MODY* pedigree. Formulating an optimized and personalized treatment strategy can reduce unnecessary excessive medical treatment and adverse drug reactions, and maintain a good HbA1c compliance rate

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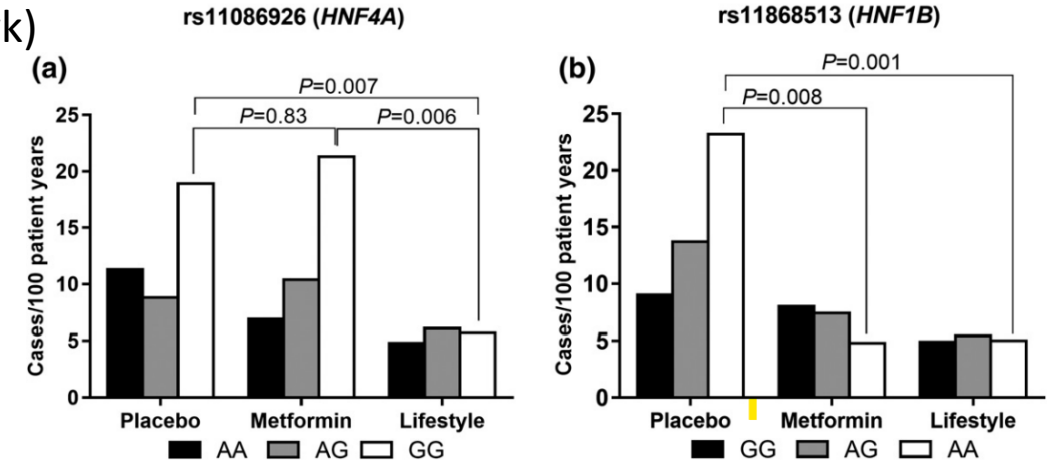
US Prevention program

2806 genotyped DPP participants
- intensive lifestyle intervention (n = 935)

(weight loss of 7% and 150 min PA/wk)
- metformin (n = 927)
- placebo (n = 944)



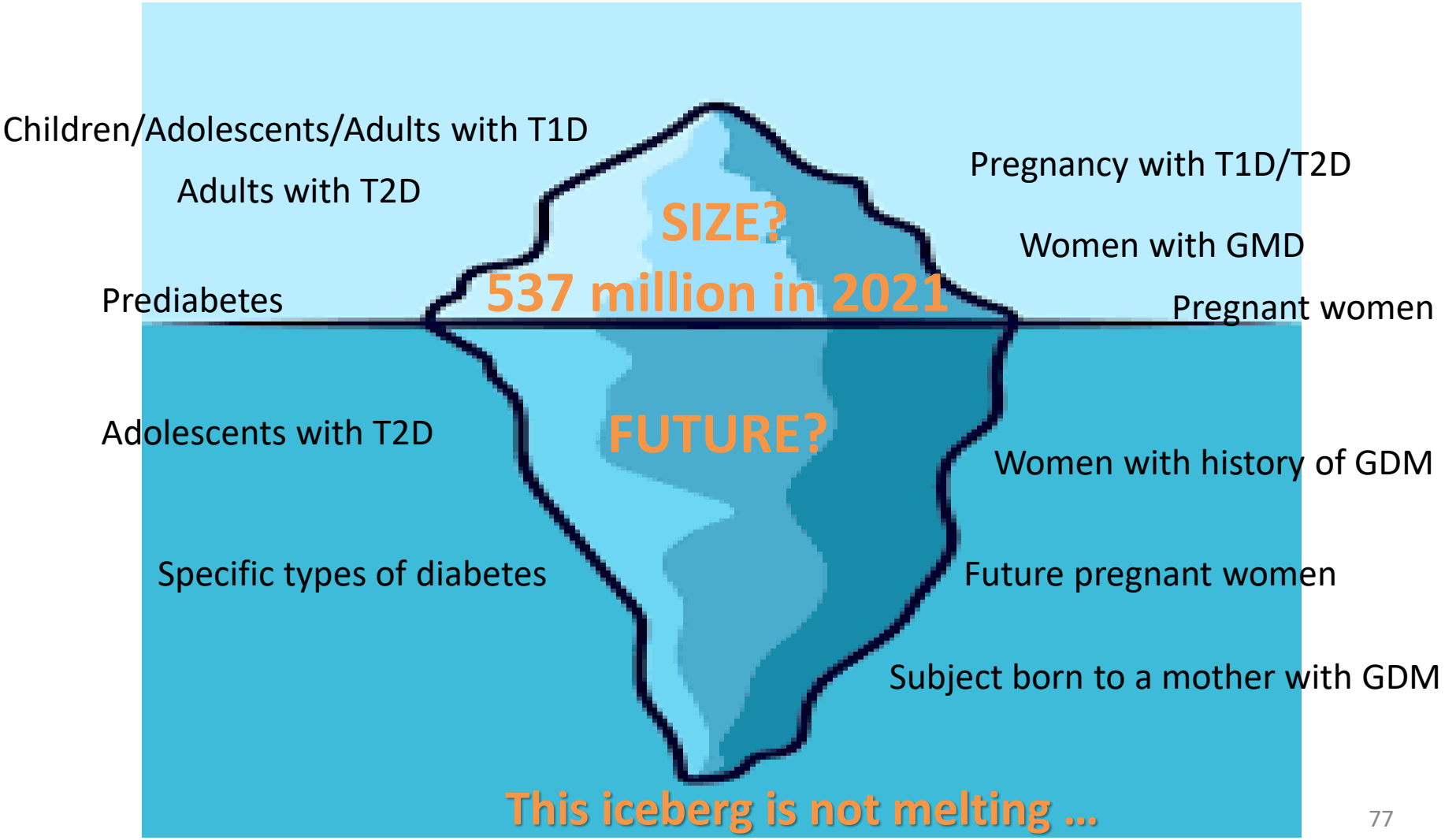
Results after 1 year:
- HNF4A: ↑ β-cell function with metformin and lifestyle but not placebo
- NEUROD1: ↑ insulin secretion with metformin but not with placebo and lifestyle changes

Conclusions: Genetic variation among MODY may influence response to insulin-sensitizing interventions.

Billings L et al. Diabetes Prevention Program Research Group. J Clin Endocrinol Metab. 2017

Conclusions

Emerging populations in « Exercise Therapy »



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Thank you!

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