HAUX

Perspectivas para a

Remissão do Diabetes:

Mudança de estilo de vida

DR. CLAYTON MACEDO
ENDOCRINOLOGIA E MEDICINA DO ESPORTE

ENDOCRINOLOGIA DO EXERCÍCIO – CETE

MEDICINA ESPORTIVA UNIFESP

UNIFESP UNIVERSIDADE FEDERAL DE SÃO PAULO 1933

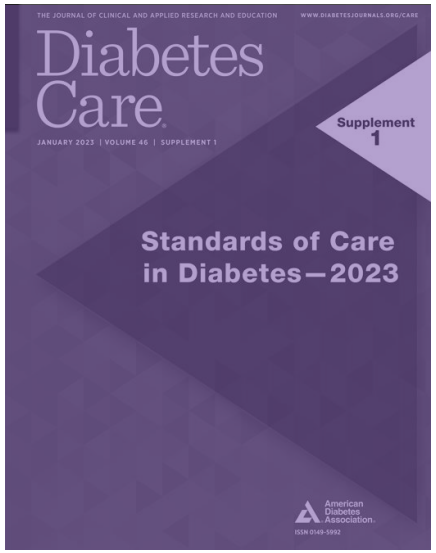
Declaração de Conflito de Interesse

Clayton Luiz Dornelles Macedo
CREMERS 14857
CREMESP 68901 RS

De acordo com a Norma 1595/2000 do Conselho Federal de Medicina e a Resolução RDC 96/2008 da Agência de Vigilância Sanitária declaro que:

Participei de estudos clínicos subvencionados por Sanofi aventis, Takeda e Lilly
Fui/sou conferencista da Merck, AstraZeneca, Abbott, Lilly, BMS, MSD, Sanofi aventis, Servier e Novo Nordisk
Sócio fundador da Haux Company
Coordenador do Programa #BombaTôFora

8. Obesity and Weight Management for the Prevention and Treatment of Type 2 Diabetes: *Standards of Care in Diabetes—2023*



Recomendação 8.5

- Indivíduos com diabetes e com excesso de peso ou obesidade podem se beneficiar de perdas de peso modestas ou maiores. Uma perda de peso relativamente pequena (aproximadamente 3–7% do peso basal) melhora a glicemia e outros fatores de risco cardiovasculares intermediários.

A

- Perdas de peso maiores e sustentadas (>10%) geralmente conferem maiores benefícios, incluindo efeitos modificadores da doença e possível remissão do diabetes tipo 2, e podem melhorar os resultados cardiovasculares e a mortalidade a longo prazo.

B

Diabetes Care. 2023 Jan 1;46(Suppl 1):S128-S139. doi: 10.2337/dc23-S008.

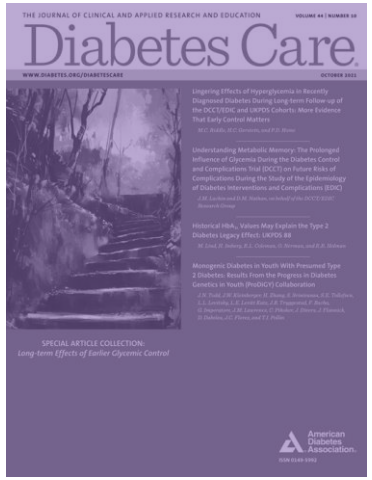
Consensus Report: Definition and Interpretation of Remission in Type 2 Diabetes

Matthew C. Riddle,[1] William T. Cefalu,[2] Philip H. Evans,[3] Hertzel C. Gerstein,[4] Michael A. Nauck,[5] William K. Oh,[6] Amy E. Rothberg,[7] Carel W. le Roux,[8] Francesco Rubino,[9] Philip Schauer,[10] Roy Taylor,[11] and Douglas Twenefour[12]

Diabetes Care 2021;44:2438–2444 | https://doi.org/10.2337/dci21-0034

Table 1—Interventions and temporal factors in determining remission of T2D

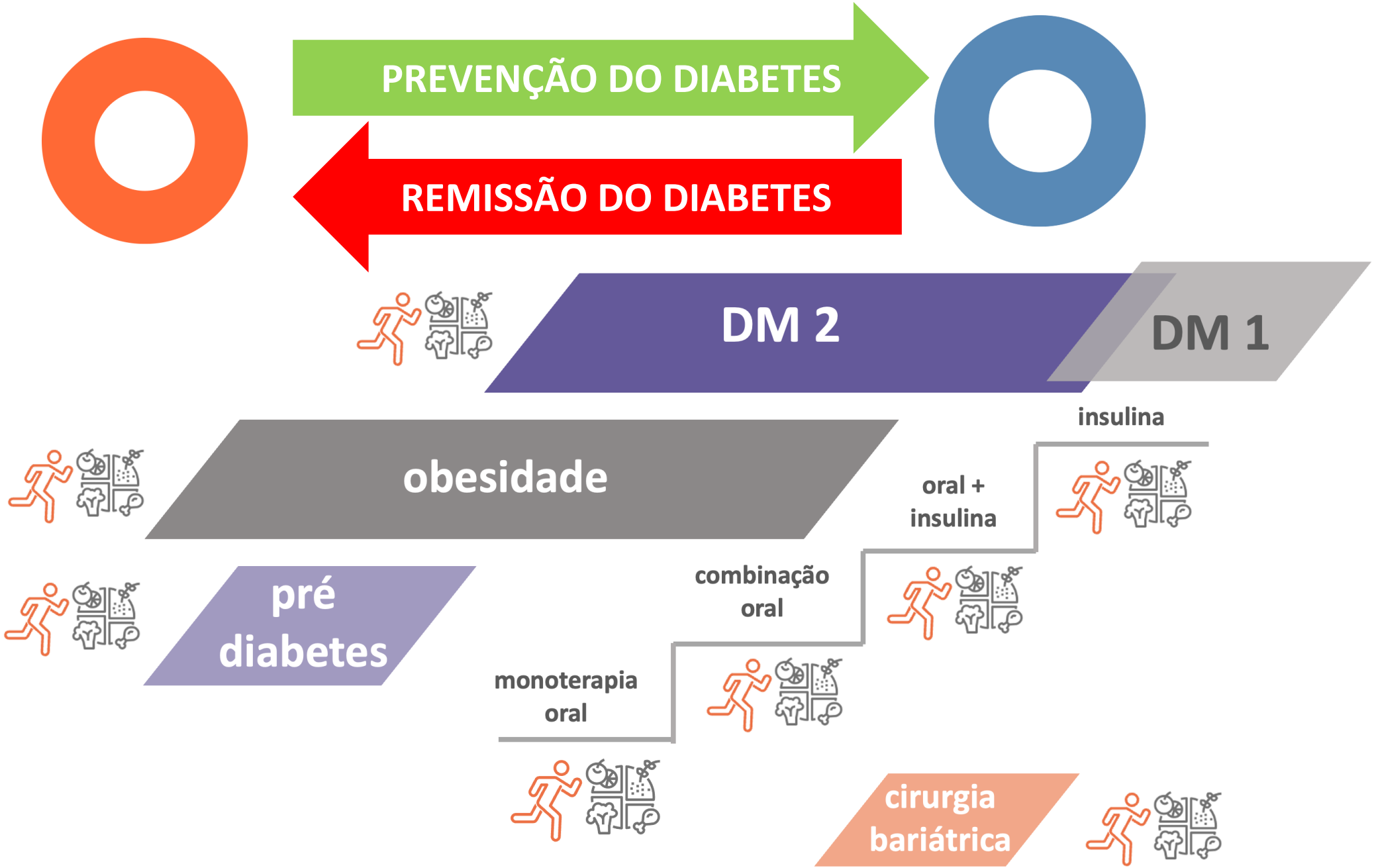
Intervention *Note: Documentation of remission should include a measurement of HbA_{1c} just prior to intervention*	Interval before testing of HbA_{1c} can reliably evaluate the response	Subsequent measurements of HbA_{1c} to document continuation of a remission
Pharmacotherapy	At least 3 months after cessation of this intervention	Not more often than every 3 months nor less frequent than yearly
Surgery	At least 3 months after the procedure *and* 3 months after cessation of any pharmacotherapy	
Lifestyle	At least 6 months after beginning this intervention *and* 3 months after cessation of any pharmacotherapy	



ADA

REMISSÃO = manutenção dos níveis de hemoglobina glicada (HbA1c) abaixo de 6,5% por pelo menos três meses na ausência de intervenção farmacológica.[3]

Diabetes Care. 2021 Aug 30;44(10):2438–44. doi: 10.2337/dci21-0034.


PREVENÇÃO DO DIABETES
REMISSÃO DO DIABETES
DM 2
DM 1
obesidade
pré diabetes
monoterapia oral
combinação oral
oral + insulina
insulina
cirurgia bariátrica

The Miracle Drug: Exercise is Medicine®

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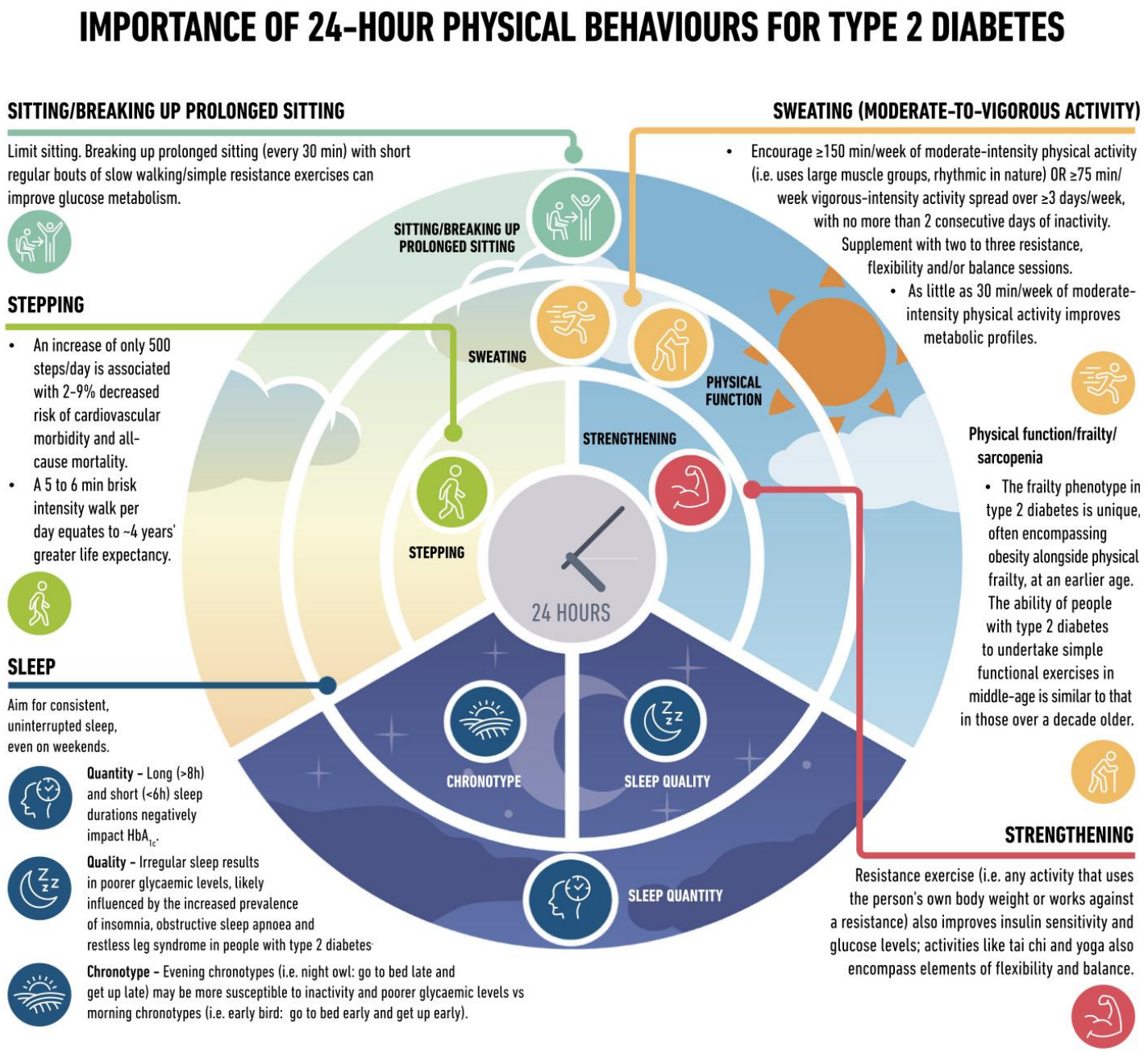
https://www.exerciseismedicine.org

> While other determinants of health (genetics, environment, and medical care) influence health outcomes, by far the most important factor contributing to health outcomes is individual lifestyle and behavior.

Am J Lifestyle Med. 2020;14(5):511-523. doi: 10.1177/1559827620912192.

Management of hyperglycaemia in type 2 diabetes, 2022.
A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)

5. Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes: *Standards of Care in Diabetes—2023*



Diabetologia. 2022 Dec;65(12):1925-1966. doi: 10.1007/s00125-022-05787-2.
Diabetes Care. 2023 Jan 1;46(Suppl 1):S68-S96. doi: 10.2337/dc23-S005.

Management of hyperglycaemia in type 2 diabetes, 2022. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)

5. Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes: *Standards of Care in Diabetes—2023*

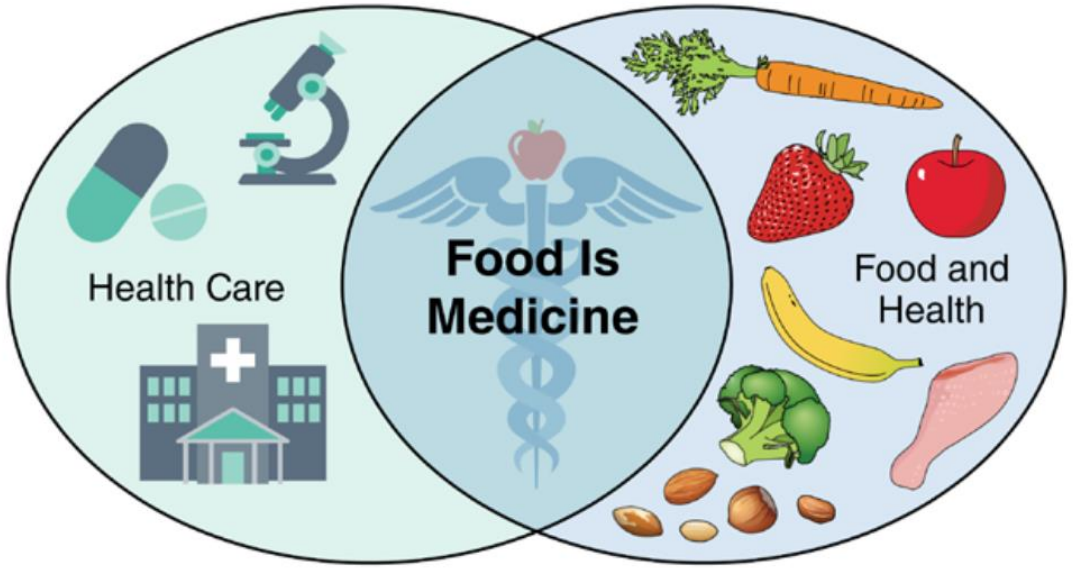
	Glucose/insulin	Blood pressure	HbA_{1c}	Lipids	Physical function	Depression	Quality of life
SITTING/BREAKING UP PROLONGED SITTING	↓	↓	↓	↓	↑	↓	↑
STEPPING	↓	↓	↓	↓	↑	↓	↑
SWEATING (MODERATE-TO-VIGOROUS ACTIVITY)	↓	↓	↓	↓	↑	↓	↑
STRENGTHENING	↓	↓	↓	↓	↑	↓	↑
ADEQUATE SLEEP DURATION	↓	↓	↓	↓	?	↓	↑
GOOD SLEEP QUALITY	↓	↓	↓	↓	?	↓	↑
CHRONOTYPE/CONSISTENT TIMING	↓	?	↓	?	?	↓	?

Diabetologia. 2022 Dec;65(12):1925-1966. doi: 10.1007/s00125-022-05787-2.
Diabetes Care. 2023 Jan 1;46(Suppl 1):S68-S96. doi: 10.2337/dc23-S005.

AHA PRESIDENTIAL ADVISORY

Food Is Medicine: A Presidential Advisory From the American Heart Association

Kevin G. Volpp, MD, PhD, FAHA, Chair; Seth A. Berkowitz, MD, MPH, Co–Vice Chair; Shreela V. Sharma, PhD, RD, MA, Co–Vice Chair; Cheryl A.M. Anderson, PhD, MPH, MS, FAHA; LaPrincess C. Brewer, MD, MPH, FAHA; Mitchell S.V. Elkind, MD, MS, MPhil, FAHA; Christopher D. Gardner, PhD, FAHA; Julie E. Gervis, PhD; Robert A. Harrington, MD, FAHA; Mario Herrero, PhD, MSc; Alice H. Lichtenstein, DSc, MS, FAHA; Mark McClellan, MD, PhD; Jen Muse, MS, RD; Christina A. Roberto, PhD; Justin P.V. Zachariah MD, MPH, FAHA; on behalf of the American Heart Association



Circulation. 2023;148:00–00. DOI: 10.1161/CIR.0000000000001182

Editorial

Food as medicine: translating the evidence

Dietary interventions have the potential to treat a wide variety of chronic conditions and diseases, but generating strong evidence and a framework for their integration into health systems will be critical for their success.

nature

Nat Med. 2023 Apr;29(4):753-754. doi: 10.1038/s41591-023-02330-7.

Management of hyperglycaemia in type 2 diabetes, 2022.
A consensus report by the American Diabetes Association (ADA)
and the European Association for the Study of Diabetes (EASD)

4. Comprehensive Medical Evaluation and Assessment of Comorbidities: *Standards of Care in Diabetes—2023*

Redução do peso
Remissão do DM2

Diabetes Care. December 2022, Vol.46, s49-s67.2. doi::10.2337/dc23-S004

Traduzindo grandes estudos de estilo de vida:

PREVENÇÃO E REMISSÃO DO DM2

Medicina Baseada em Evidências

Intensificação de mudança de Estilo de vida x Prevenção do DM2

The New England
Journal of Medicine

VOLUME 346 FEBRUARY 7, 2002 NUMBER 6

REDUCTION IN THE INCIDENCE OF TYPE 2 DIABETES WITH LIFESTYLE INTERVENTION OR METFORMIN

DIABETES PREVENTION PROGRAM RESEARCH GROUP*

- intervenção no estilo de vida, reduziu o risco de desenvolvimento de DM2 em **58%**
- tratamento com metformina em **31%**

(em comparação com o placebo, após uma média de três anos)

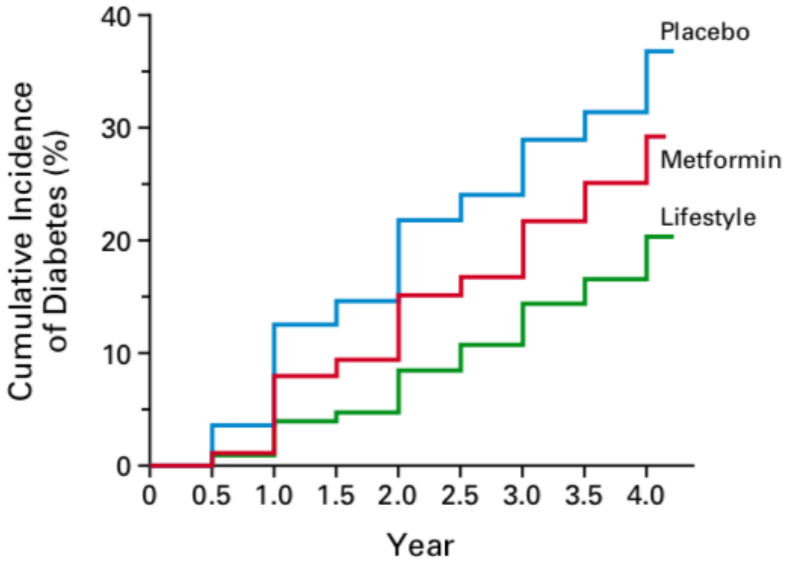


Figure 2. Cumulative Incidence of Diabetes According to Study Group.

N Engl J Med. 2002;346(6):393-403. doi:10.1056/NEJMoa012512

Diabetes Prevention Program Outcomes Study - DPPOS

- O **DPPOS** procurou avaliar os efeitos de longo prazo das intervenções DPP no desenvolvimento posterior de DM2 e suas complicações, incluindo retinopatia, nefropatia e doença cardiovascular.

10-year follow-up of diabetes incidence and weight loss in the Diabetes Prevention Program Outcomes Study

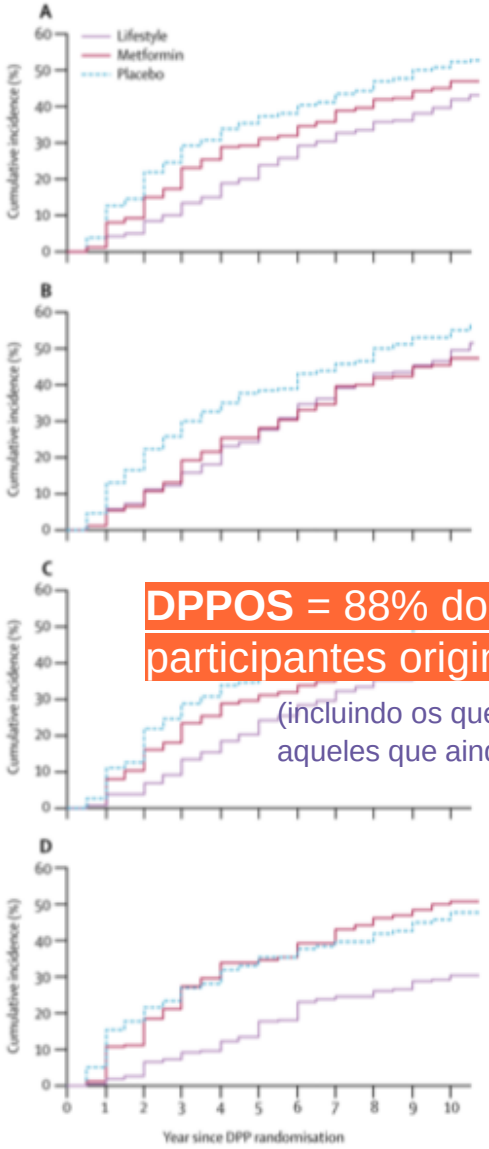
Incidência de DM2

incidência de diabetes nos 10 anos desde a randomização do DPP foi reduzida em

34% no grupo de estilo de vida
(no DPP 58%)

18% no grupo de metformina
(no DPP 31%)

em comparação com o placebo.



DPPOS = 88% dos 3.234 participantes originais do DPP

(incluindo os que desenvolveram DM2 e aqueles que ainda não desenvolveram DM).

Lancet. 2009 Nov;374(9702):1677-86. doi: 10.1016/S0140-6736(09)61457-4.

Regression From Prediabetes to Normal Glucose Regulation and Prevalence of Microvascular Disease in the Diabetes Prevention Program Outcomes Study (DPPOS)

11 anos de seguimento

Regressão para normoglicemia:

reduziu risco de doença microvascular em 22% (OR 0,78)

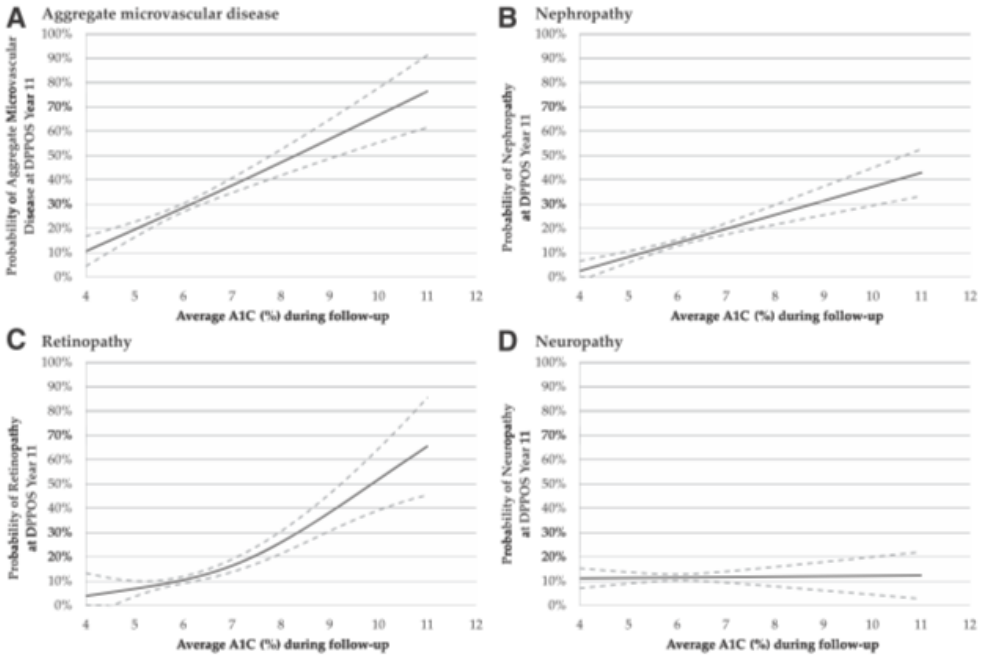


Figure 1—Predicted, unadjusted prevalence of aggregate MVD (retinopathy, nephropathy, and/or neuropathy) (*A*), nephropathy (*B*), retinopathy (*C*), and neuropathy (*D*) as a function of A1C levels during DPPOS follow-up. Solid lines represent a smoothed, fitted relationship, whereas the dotted lines represent the pointwise 95% CI.

Diabetes Care. 2019;42(9):1809-1815. doi:10.2337/dc19-0244

Medicina Baseada em Evidências

Intensificação de mudança de Estilo de vida x Remissão do DM2

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Cardiovascular Effects of Intensive Lifestyle Intervention in Type 2 Diabetes

The Look AHEAD Research Group*

Look AHEAD Action for Health in Diabetes

- intervenção intensiva no estilo de vida perda de peso de pelo menos 7%
- sessões de aconselhamento em grupo e individuais, ocorrendo semanalmente durante os primeiros 6 meses, com frequência decrescente ao longo do estudo
- meta calórica de 1.200 a 1.800 kcal por dia
- uso de produtos substitutos de refeição
- pelo menos 175 minutos de atividade física de intensidade moderada
- ferramentas de estratégias para pacientes com dificuldade em atingir as metas de perda de peso

N Engl J Med. 2013 Jul 11;369(2):145-54. doi: 10.1056/NEJMoa1212914.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Cardiovascular Effects of Intensive Lifestyle Intervention in Type 2 Diabetes

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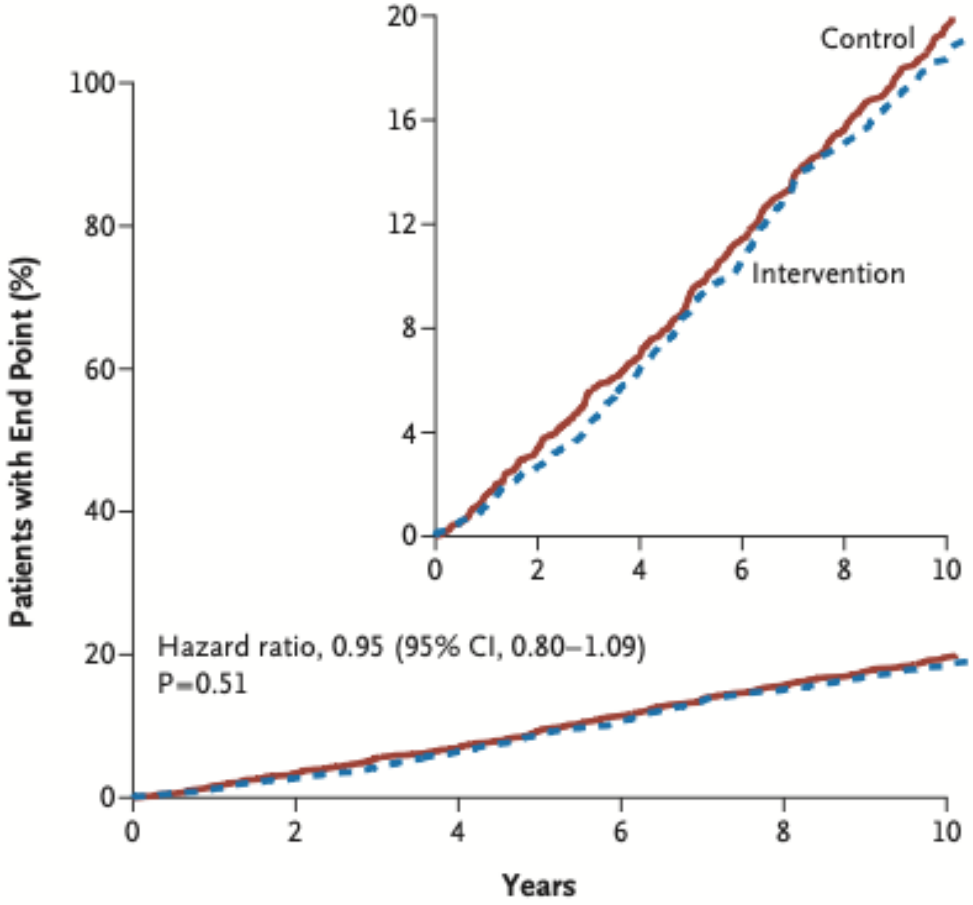
Look AHEAD Action for Health in Diabetes



N Engl J Med. 2013 Jul 11;369(2):145-54. doi: 10.1056/NEJMoa1212914.

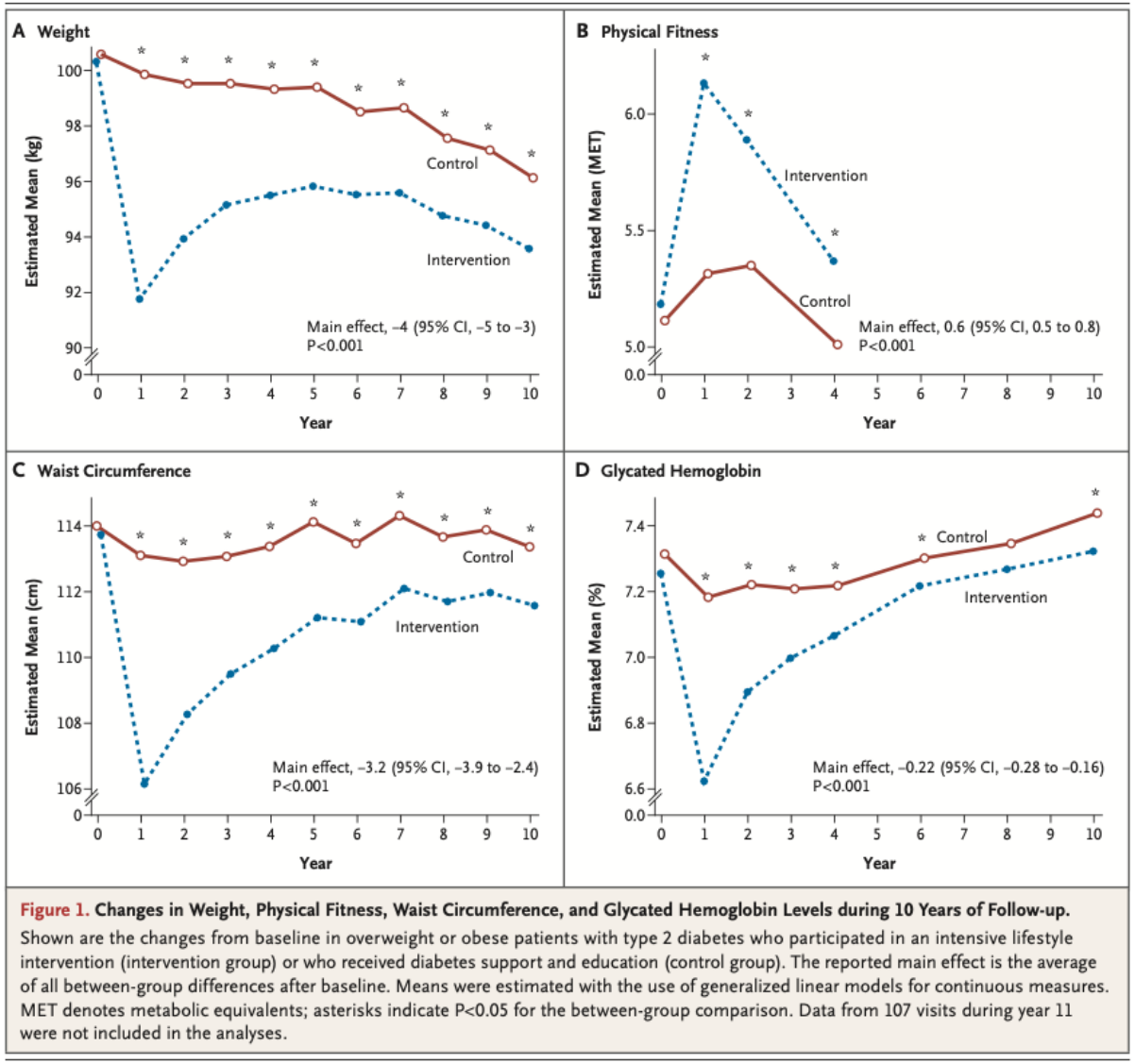


Figure 1. Changes in Weight, Physical Fitness, Waist Circumference, and Glycated Hemoglobin Levels during 10 Years of Follow-up.
Shown are the changes from baseline in overweight or obese patients with type 2 diabetes who participated in an intensive lifestyle intervention (intervention group) or who received diabetes support and education (control group). The reported main effect is the average of all between-group differences after baseline. Means were estimated with the use of generalized linear models for continuous measures. MET denotes metabolic equivalents; asterisks indicate P<0.05 for the between-group comparison. Data from 107 visits during year 11 were not included in the analyses.

Look AHEAD Action for Health in Diabetes

N Engl J Med. 2013 Jul 11;369(2):145-54. doi: 10.1056/NEJMoa1212914.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Cardiovascular Effects of Intensive Lifestyle Intervention in Type 2 Diabetes

The Look AHEAD Research Group*

Look AHEAD Action for Health in Diabetes

Benefícios significativos:

HbA1c

Condicionamento CV

Circunferência abdominal

Perfil lipídico e pressão arterial

N Engl J Med. 2013;11,369(2):145-54

Nefropatia Lancet Diabetes Endocrinol. 2014;2(10):801-9

Neuropatia Diabetologia 2017, 60:980–8

Gordura visceral Endocr Res 2017;42(2):86-95

Depressão Diabetes Care 2014;37:1544-53

Qualidade de vida Diabetes Care 2014;37:1544-53

Número e dose de medicamentos

N Engl J Med. 2013;11,369(2):145-5

Association of the magnitude of weight loss and changes in physical fitness with long-term cardiovascular disease outcomes in overweight or obese people with type 2 diabetes: a post-hoc analysis of the Look AHEAD randomised clinical trial

*The Look AHEAD Research Group**

Look AHEAD Action for Health in Diabetes

Pessoas que perderam **10% do peso corporal** no primeiro ano tiveram **risco 21% menor do desfecho primário** (HR = 0,79).

	Weight-change categories (percentage weight loss in first year; n=4834)					Fitness-change categories (change in metabolic equivalents in first year; n=4406)				
	Gain or stable (<2% loss)	Small loss (≥2–<5%)	Medium loss (≥5–<10%)	Large loss (≥10%)	p value	Loss or stable (<0·5 loss)	Small gain (≥0·5–<1·0)	Medium gain (≥1·0–<2·0)	Large gain (≥2·0)	p value
Primary outcome										
Events per person-years	289/17 075	141/7870	154/8570	128/8942	..	347/19 997	95/6091	102/7183	72/5312	..
Crude rate per 100 person-years	1·69	1·79	1·80	1·43	..	1·74	1·56	1·42	1·36	..
Unadjusted hazard ratio (95% CI)	1·00	1·07 (0·88–1·31)	1·07 (0·88–1·31)	0·83 (0·67–1·02)	0·21	1·00	0·88 (0·70–1·10)	0·80 (0·64–1·00)	0·76 (0·59–0·98), p=0·032*	0·009
Adjusted hazard ratio† (95% CI)	1·00	1·08 (0·88–1·33)	1·16 (0·95–1·42)	0·79 (0·64–0·98), p=0·034*	0·17	1·00	0·87 (0·68–1·10)	0·83 (0·66–1·05)	0·78 (0·60–1·03), p=0·079*	0·03
Secondary outcome										
Events per person-years	422/16 699	206/7657	203/8411	186/8792	..	504/19 596	131/5996	145/7056	100/5220	..
Crude rate per 100 person-years	2·53	2·69	2·41	2·12	..	2·57	2·18	2·05	1·92	..
Unadjusted hazard ratio (95% CI)	1·00	1·08 (0·91–1·27)	0·96 (0·81–1·13)	0·83 (0·70–0·99), p=0·035*	0·04	1·00	0·83 (0·69–1·01)	0·79 (0·65–0·95), p=0·012*	0·73 (0·59–0·91), p=0·005*	0·0005
Adjusted hazard ratio† (95% CI)	1·00	1·05 (0·88–1·25)	0·97 (0·82–1·16)	0·76 (0·63–0·91), p=0·003*	0·006	1·00	0·84 (0·69–1·02)	0·79 (0·65–0·96), p=0·019*	0·77 (0·61–0·96), p=0·023*	0·0031

Data are for the overall study population (intensive lifestyle intervention and diabetes support and education [control] groups combined). *p value refers to pairwise comparison with referent group (gain or stable weight loss in weight-change analyses and loss or stable fitness gain in fitness change analyses). †Adjusted for sex, age, baseline weight (from weight-change models), baseline fitness (from fitness-change models), history of cardiovascular disease, insulin use, diabetes duration, smoking status, LDL cholesterol, systolic blood pressure, and diastolic blood pressure.

Table 2: **Primary and secondary outcomes associated with changes in weight and fitness (overall study population)**

Lancet Diabetes Endocrinol. 2016 Nov;4(11):913-921. doi: 10.1016/S2213-8587(16)30162-0.

Eight-Year Weight Losses with an Intensive Lifestyle Intervention: The Look AHEAD Study

Look AHEAD Action for Health in Diabetes

- **Atividade física (kcal/semana)**
- **Redução calórica**
- **Redução de gordura**
- **Aumento do exercício (semanas/ano)**
- **Monitoramento de peso**

TABLE 4 Weight control behaviors at Year 8 for ILI participants who maintained (N = 324) versus regained (N = 117) their ≥10% weight loss, achieved at Year 1

	Year 8 weight change		
Year 8 behaviors	Maintained ≥10% Loss	Gained above baseline weight	P value
Physical activity (kcal/wk)	1471.9 ± 121.2	799.9 ± 100.9	0.001
Reduced Kcal (no. wk/yr)	20.4 ± 1.4	11.9 ± 2.1	<0.001
Reduced fat (no. wk/yr)	24.2 ± 1.5	15.6 ± 2.2	<0.001
Increased exercise (no. wk/yr)	12.9 ± 1.3	8.2 ± 1.8	0.013
Meal replacements (no. wk/yr)	22.8 ± 2.0	17.3 ± 2.9	0.072
Monitored weight			
≥Weekly, N (%)	262 (82.4)	81 (69.8)	0.001
≥Daily, N (%)	152 (47.8)	33 (28.4)	<0.001

Values shown are LS means (raw means for Paffenbarger) ± standard error or frequency count (percentage).
P values are adjusted for clinical site and baseline value.

Obesity .2014;22, 5–13. doi:10.1002/oby.20662

Association of an Intensive Lifestyle Intervention With Remission of Type 2 Diabetes

Look AHEAD Action for Health in Diabetes

Remissão	2	3	4 anos
parcial	9,2%,	6,4%	3,5%
intervenção intensiva no estilo de vida (n = 2.262)			
	1,7%	1,3%	0,5%
grupo de apoio e educação (n=2.241)			
completa	1,3%	0,7% em 1 e 4 anos.	

Figure 2. Prevalence of Any Remission (Partial or Complete) by Intervention Condition and Year

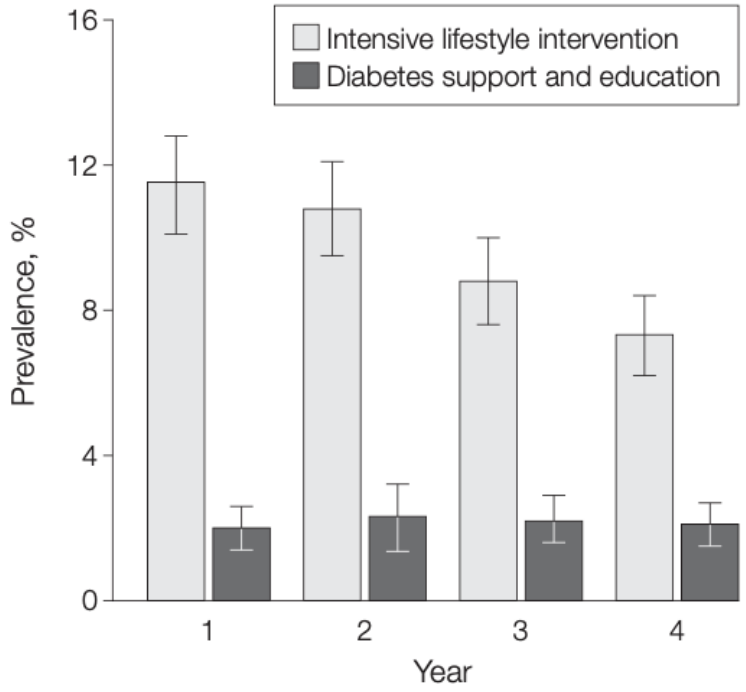
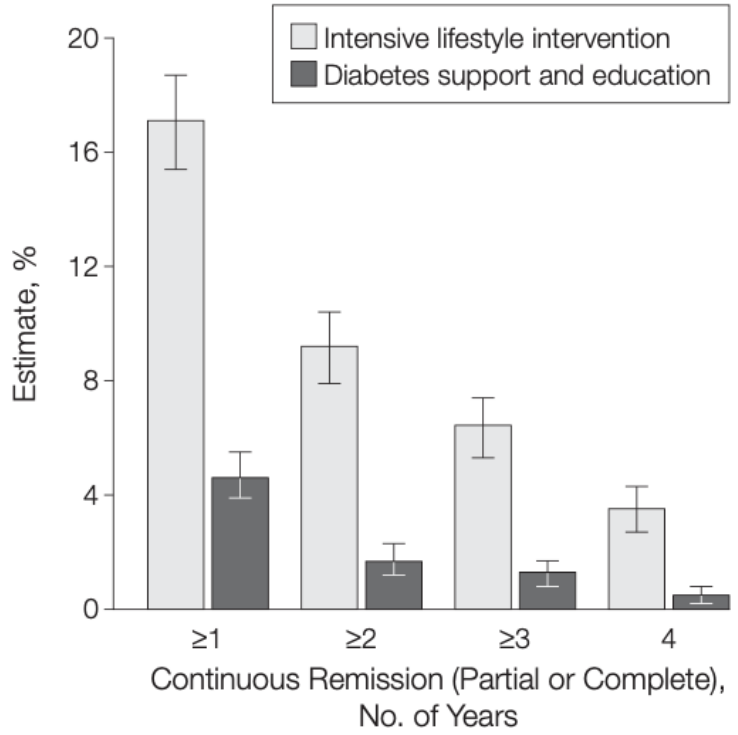


Figure 3. Duration of Any Remission (Partial or Complete) by Intervention Group and Duration of Sustained Remission



JAMA. 2012 Dec 19;308(23):2489-96. doi: 10.1001/jama.2012.67929.

Association of an Intensive Lifestyle Intervention With Remission of Type 2 Diabetes

Look AHEAD Action for Health in Diabetes

PREDITORES DE REMISSÃO:

- menor duração do diabetes
- menor HbA1c
- não uso de insulina
- não uso de medicação anti-hipertensiva
- ausência de DCV
- maior perda de peso no primeiro ano
- melhor “fitness”

Table 2. Odds Ratios and Probability of Any Remission Associated With Key Demographic and Health Status Predictors for the Overall Sample and by Intervention Group[a]

		Year 1 Remission in Overall Sample, Odds Ratio (95% CI)				Unadjusted Probability of Year 1 Remission, % (95% CI)		
	No. (%) of Sample	Univariate	*P* Value	Multivariate	*P* Value	Overall	DSE	ILI
Diabetes duration tertile, y								
Low: 0 to <2	1168 (26.1)	1 [Reference]		1 [Reference]		13.5 (11.6-15.6)	5.1 (3.5-7.3)	21.2 (18.0-24.7)
Middle: 2 to <7	1707 (38.2)	0.42 (0.32-0.54)	<.001	0.43 (0.32-0.58)	<.001	6.1 (5.0-7.4)	1.4 (0.8-2.5)	11.1 (9.1-13.4)
High: ≥7	1597 (35.7)	0.15 (0.10-0.22)	<.001	0.21 (0.14-0.33)	<.001	2.2 (1.6-3.1)	0.5 (0.2-1.4)	4.1 (2.9-5.7)
Body mass index tertile								
Low: <32.5	1501 (33.3)	1 [Reference]		1 [Reference]		7.0 (6.3-8.7)	2.0 (1.2-3.3)	12.4 (10.2-15.0)
Middle: 32.5-37.7	1501 (33.3)	1.02 (0.77-1.35)	.89	0.92 (0.66-1.28)	.62	7.4 (6.2-8.9)	1.8 (1.0-3.0)	13.2 (10.9-15.8)
High: >37.7	1501 (33.3)	0.73 (0.54-0.99)	.04	0.75 (0.53-1.07)	.11	5.4 (4.3-6.7)	2.2 (1.4-3.6)	8.8 (6.9-11.1)
Hemoglobin A_{1c} tertile, %								
Low: <6.7	1300 (28.9)	1 [Reference]		1 [Reference]		10.4 (8.9-12.3)	3.6 (2.4-5.4)	17.1 (14.4-20.3)
Middle: 6.7-7.6	1634 (38.2)	0.70 (0.54-0.90)	<.001	0.76 (0.56-1.03)	.07	7.5 (6.3-9.0)	2.0 (1.3-3.3)	13.0 (10.8-15.5)
High: >7.6	1569 (35.7)	0.24 (0.17-0.34)	<.001	0.40 (0.27-0.60)	<.001	2.7 (2.0-3.6)	0.7 (0.3-1.5)	4.9 (3.6-6.7)
No insulin use	2251 (80.7)	1 [Reference]		1 [Reference]		8.1 (7.2-9.0)	2.3 (1.7-3.1)	13.8 (12.3-15.6)
Insulin use	864 (19.3)	0.10 (0.05-0.21)	<.001	0.23 (0.11-0.51)	<.001	0.8 (0.4-1.8)	0.5 (0.1-1.9)	1.2 (0.5-2.9)
No hypertension medications	571 (25.25)	1 [Reference]		1 [Reference]		8.3 (6.8-10.1)	2.0 (1.1-3.6)	15.2 (12.3-18.6)
Hypertension medications	3398 (75.5)	0.73 (0.56-0.94)	.02	0.77 (0.57-1.06)	.11	6.2 (5.4-7.1)	2.0 (1.4-2.8)	10.3 (8.9-11.9)
No cardiovascular disease history	1949 (86.2)	1 [Reference]		1 [Reference]		7.1 (6.3-8.0)	2.2 (1.6-3.0)	12.1 (10.7-13.6)
Cardiovascular disease history	639 (14.2)	0.60 (0.40-0.90)	.01	0.91 (0.57-1.46)	.69	4.4 (3.0-6.3)	0.7 (0.2-2.6)	7.9 (5.4-11.4)
1-y Weight loss tertile, %								
Low: <1 (including weight gain)	1464 (33.3)	0.08 (0.05-0.12)	<.001	0.15 (0.08-0.27)	<.001	1.4 (0.9-2.1)	1.1 (0.7-1.9)	2.7 (1.2-5.9)
Middle: 1 to 6.5	1465 (33.4)	0.21 (0.16-0.29)	<.001	0.37 (0.26-0.53)	<.001	3.7 (2.8-4.8)	2.1 (1.3-3.4)	5.4 (3.9-7.3)
High: >6.5	1464 (33.3)	1 [Reference]		1 [Reference]		15.2 (13.4-17.2)	7.1 (4.9-11.1)	16.4 (14.5-18.6)
1-y Fitness change tertile, %								
Low: <−2.3	925 (24.4)	1 [Reference]		1 [Reference]		3.1 (2.1-4.4)	1.1 (0.5-2.4)	7.1 (4.7-10.6)
Middle: 2.3 to <17.9	1593 (42.0)	1.83 (0.77-1.96)	<.001	1.23 (0.77-1.96)	.39	5.5 (4.5-6.7)	2.0 (1.3-3.3)	9.4 (7.5-11.7)
High: ≥17.9	1274 (33.6)	4.31 (1.14-2.86)	<.001	1.80 (1.14-2.86)	.01	12.0 (10.3-13.9)	3.7 (2.2-6.2)	15.6 (13.3-18.1)

Abbreviations: DSE, diabetes support and education; ILI, intensive lifestyle intervention; NA, data not available (no cases).
[a] Category thresholds for diabetes duration, body mass index (calculated as weight in kilograms divided by height in meters squared), hemoglobin A_{1c}, weight change, and fitness change are based on tertiles of the overall sample. Multivariable analyses adjust for intervention group and all variables in the table. Available case analysis is based on sample sizes expressed in second column.

JAMA. 2012 Dec 19;308(23):2489-96. doi: 10.1001/jama.2012.67929.

DIRECT : Diabetes Remission Clinical Trial

Primary care-led weight management for remission of type 2 diabetes (DiRECT): an open-label, cluster-randomised trial

Lancet. 2018 Feb 10;391(10120):541-551. doi: 10.1016/S0140-6736(17)33102-1.

DiRECT Intervention: Counterweight-Plus Protocol

Total Diet Replacement - Counterweight Pro800

- Nutritionally complete (vitamins & minerals)
- 830 kcal: 61%E carbohydrate, 13% fat, 26% protein
- >2.25 litres fluid per day
- Fibre supplement

- **Maintain PA** ~30mins/ day

- **STOP** all anti-diabetes medications
- **STOP** all antihypertensive medications

Lean et al, Br J General Practice (2013),
Leslie et al, BMC Family Practice (2016)

DiRECT Diabetes Remission Clinical Trial

University of Glasgow | Newcastle University | DiABETES UK CARE. CONNECT. CAMPAIGN.

DiRECT Intervention: Counterweight-Plus Protocol

Stepped Food Reintroduction

- Add a ~400kcal meal every 2-3 weeks
  Step-counters: gradually increase PA

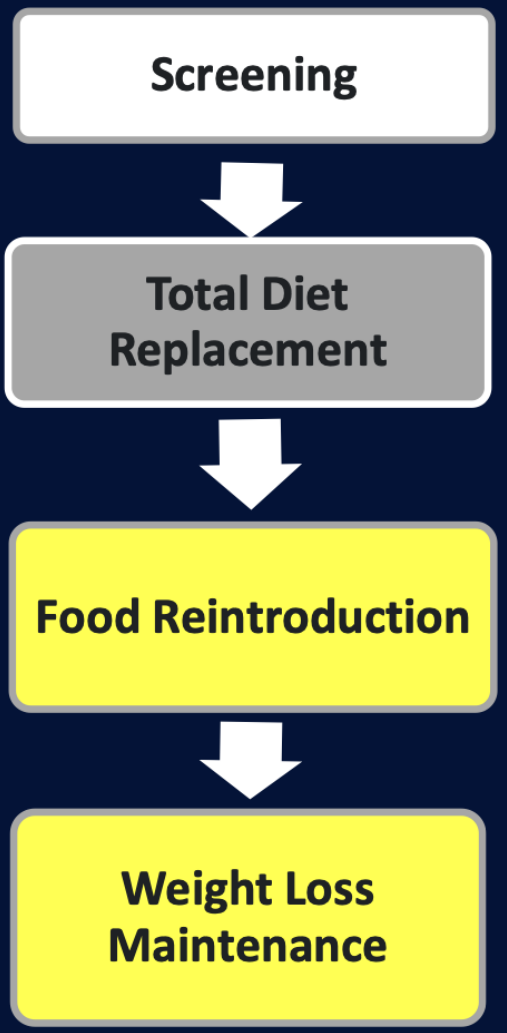
Weight Loss Maintenance

- Food-based diet
- 50%E carbohydrate, 35% fat, 15% protein
- Encourage up to 15,000 steps/day

Relapse Management

(regain >2kg, relapse of diabetes)

- Tool-kit approach: offer orlistat , meal replacement, brief TDR and FR



Lean et al, Br J General Practice (2013),

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DiRECT Diabetes Remission Clinical Trial

University of Glasgow | Newcastle University | DiABETES UK CARE. CONNECT. CAMPAIGN

DiRECT
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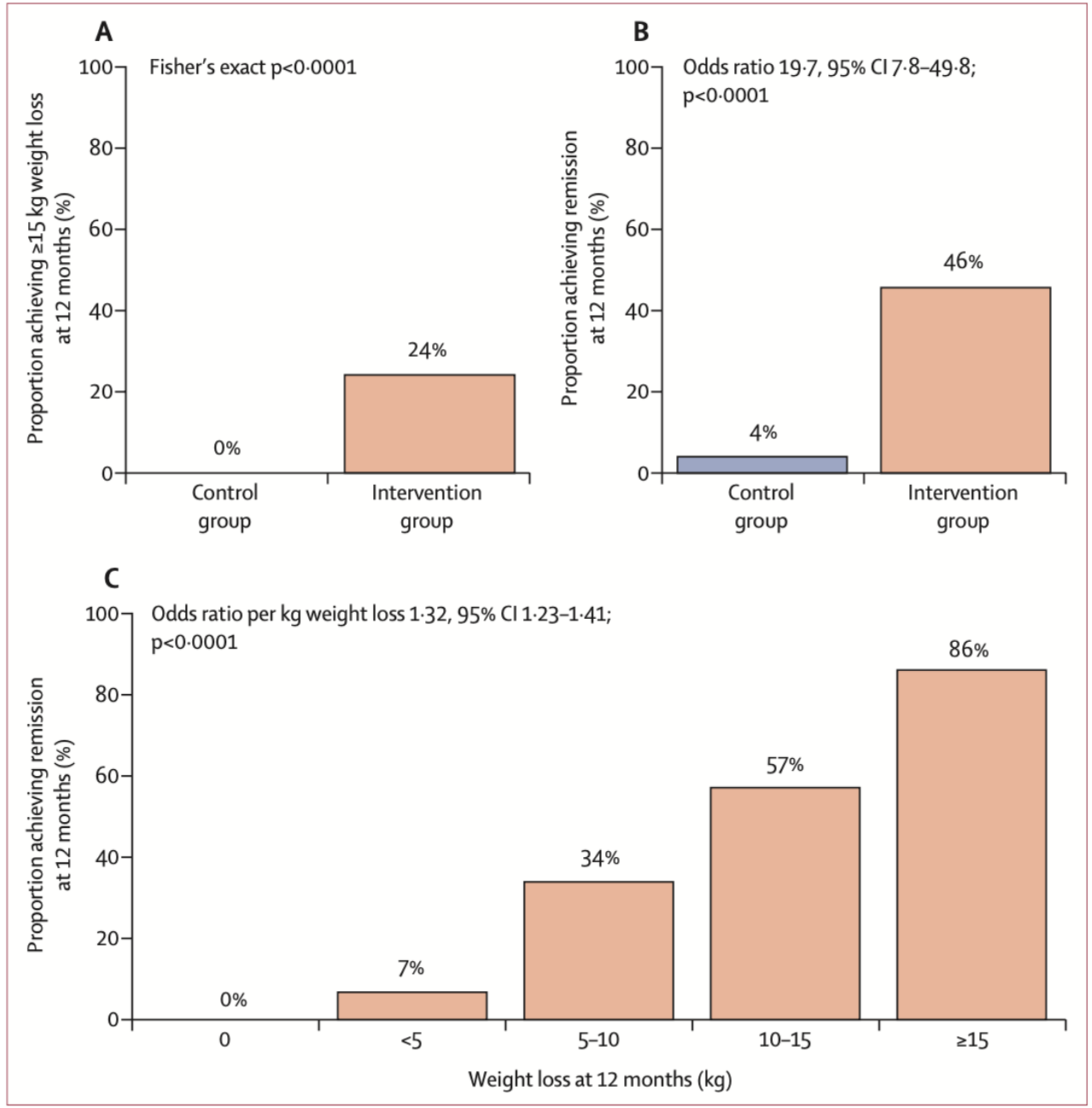
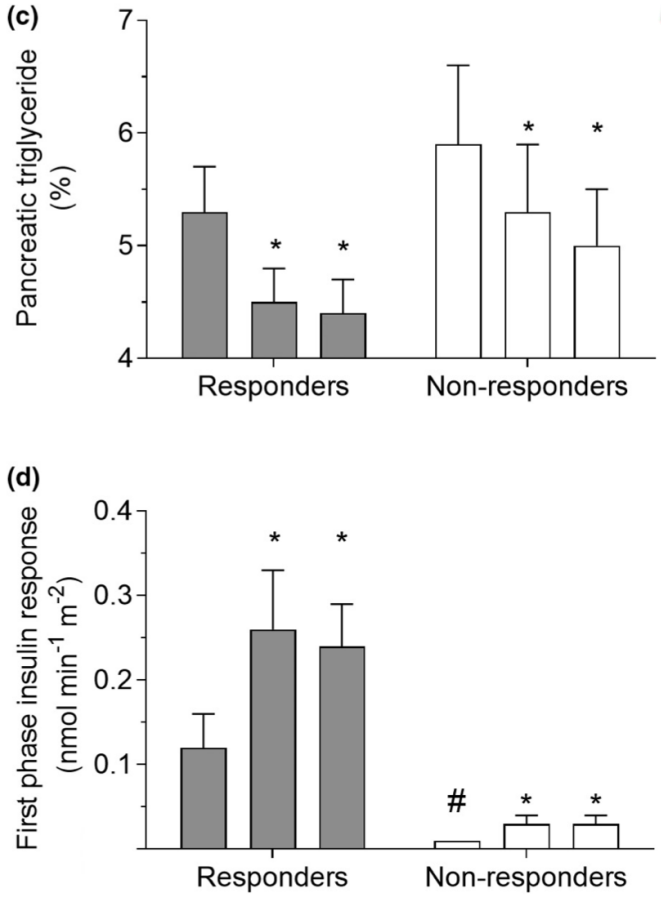
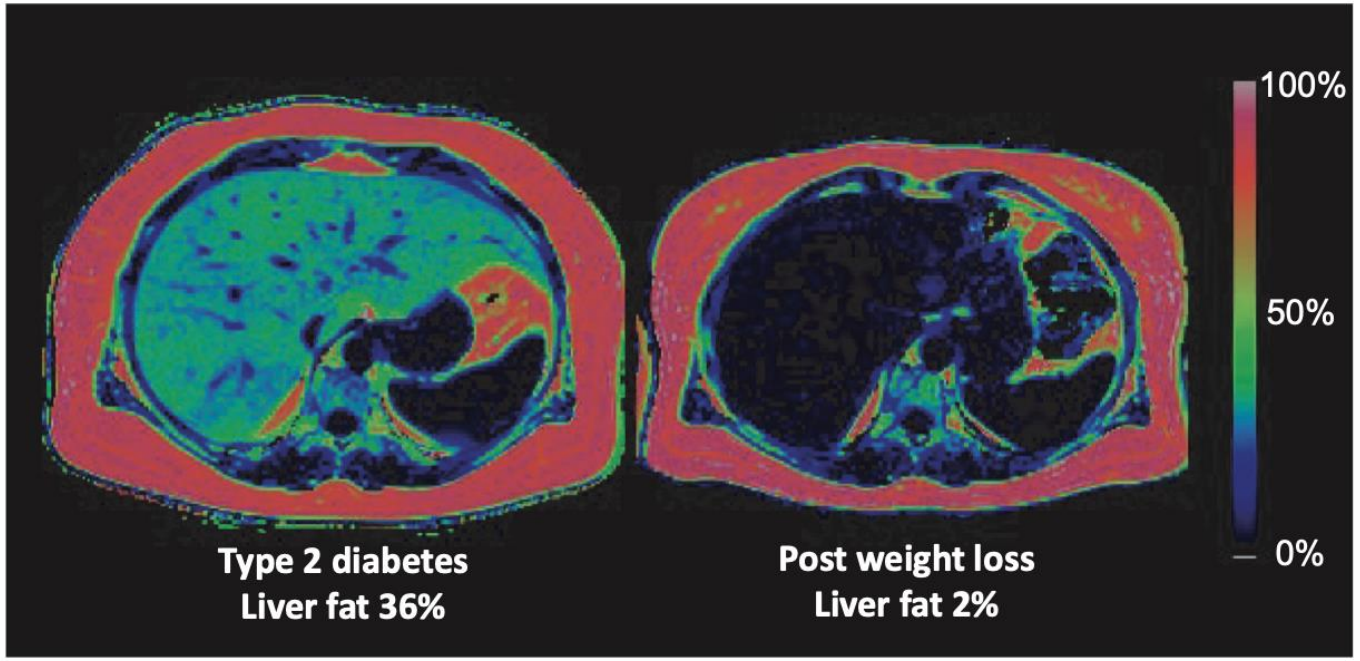


Lancet. 2018 Feb 10;391(10120):541-551. doi: 10.1016/S0140-6736(17)33102-1.

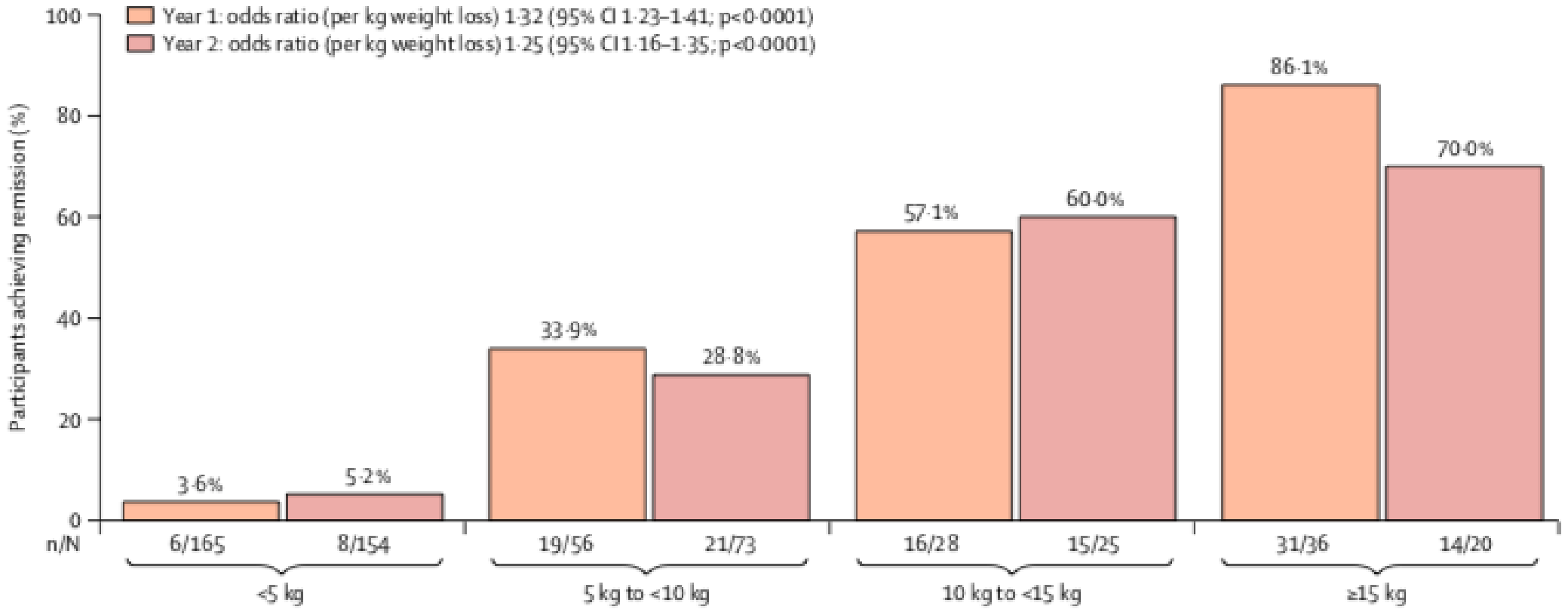
DiRECT
Diabetes Remission Clinical Trial





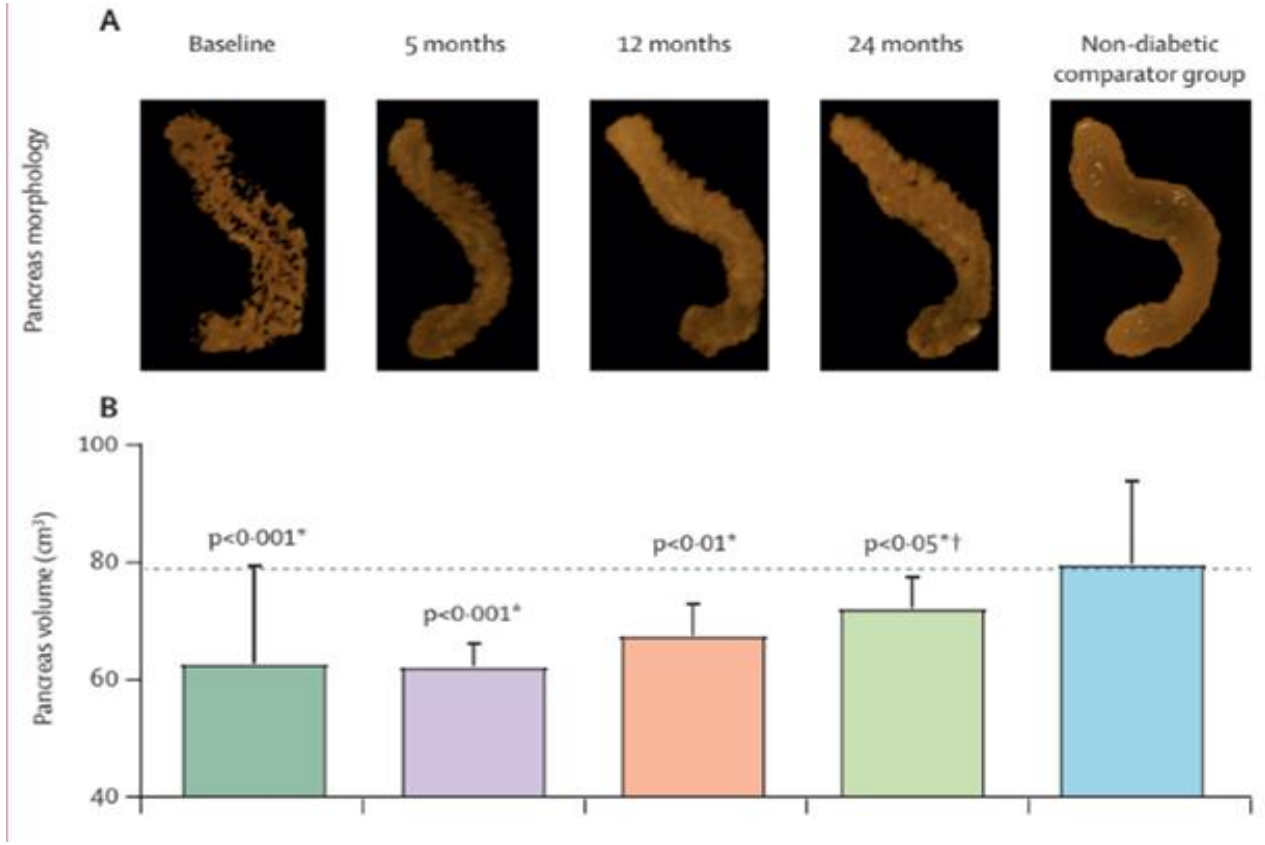
J Intern Med. 2021 Jun;289(6):754-770. doi: 10.1111/joim.13214.

Durability of a primary care-led weight-management intervention for remission of type 2 diabetes: 2-year results of the DiRECT open-label, cluster-randomised trial



Lancet Diabetes Endocrinol. 2019 May;7(5):344-355. doi: 10.1016/S2213-8587(19)30068-3.

Morfologia do pâncreas- análise post-hoc DIRECT



Lancet Diabetes Endocrinol. 2020 Dec;8(12):939-948. doi: 10.1016/S2213-8587(20)30303-X. Epub 2020 Oct 5.

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/ Reversal of Type 2 diabetes Upon Normalisation of Energy intake in the non-obese (ReTune)

Reversal of Type 2 diabetes Upon Normalisation of Energy intake in the non-obese (ReTune)

https://www.rdm.ox.ac.uk/news/retune-study-shows-remission-of-type-2-diabetes-possible-in-non-obese-people

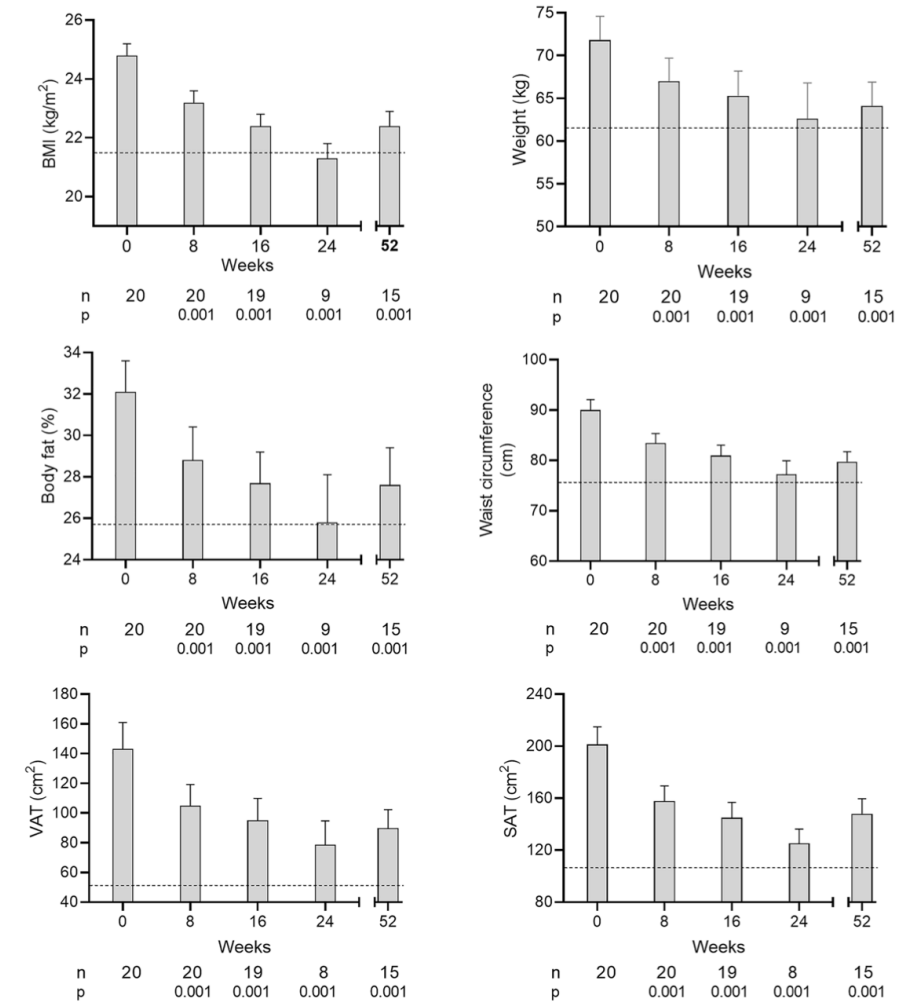

Figure 1. Time course of change in major clinical parameters after each cycle of weight loss and at 12 months

Reversal of Type 2 diabetes Upon Normalisation of Energy intake in the non-obese (ReTune)

A hipótese do **Limiar de Gordura Pessoal** postulou diferentes limiares individuais para excesso de lipídios e efeitos adversos na função das células β.

Para testar esta hipótese, pessoas com diabetes tipo 2 e índice de massa corporal <27kg/m2 (n = 20) foram submetidas a ciclos repetidos de perda de peso de 5% (12 meses).

Clin Sci (Lond). 2023 Aug 31;137(16):1333-1346. doi: 10.1042/CS20230586.

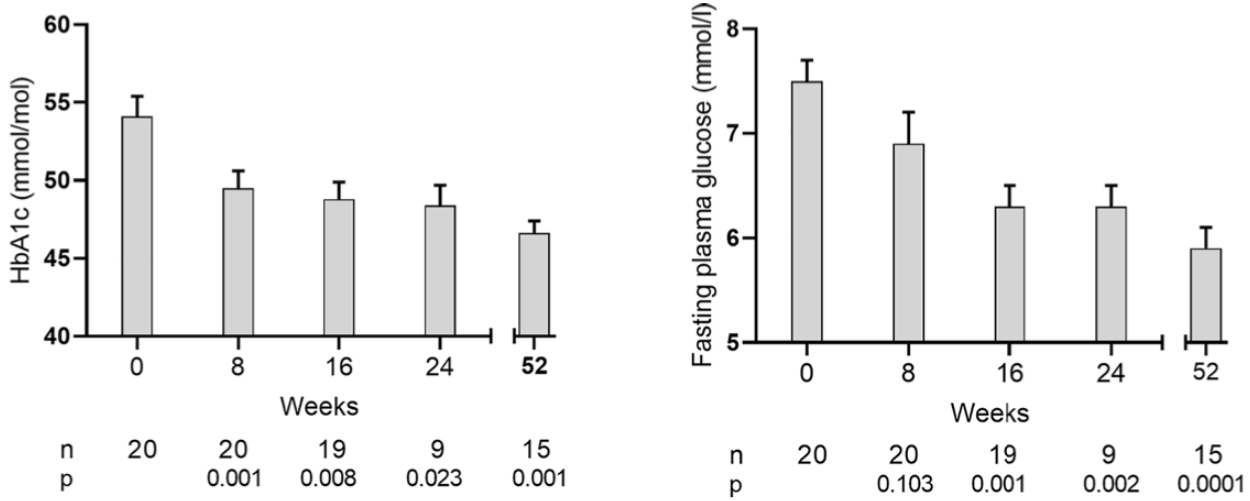

Figure 3. Time course of change in glycaemic measures after each cycle of weight loss and at 12 months

Change in mean (+SEM) HbA_{1c} and fasting plasma glucose values in the T2D group during weight stability following each weight loss cycle and also after longer term follow up at 12 months. Numbers of participants and significance level versus baseline are shown below each time point.

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Reversal of Type 2 diabetes Upon Normalisation of Energy intake in the non-obese (ReTune)

A remissão sustentada do diabetes foi alcançada em 70%, pela perda de peso inicial de 6,5%.

Clin Sci (Lond). 2023 Aug 31;137(16):1333-1346. doi: 10.1042/CS20230586.

Original research Open access

MJ Nutrition, revention & Health

What predicts drug-free type 2 diabetes remission? Insights from an 8-year general practice service evaluation of a lower carbohydrate diet with weight loss

- Dieta com baixo teor de carboidratos e perda de peso
- 9.800 pacientes.
- Consultas convencionais “individuais”
- Consultas em grupo e telefonemas pessoais, conforme necessário.
- 33 meses
- Perda de peso de 10 kg.
    - **A remissão do diabetes foi alcançada em 77% com duração de DM2 inferior a 1 ano, caindo para 20% com duração superior a 15 anos.**

Duração <1 ano representa uma importante janela de oportunidade para alcançar a remissão do diabetes sem medicamentos.

- DM2 mal controlado que pode não atingir a remissão: maiores melhorias no controle do diabetes.

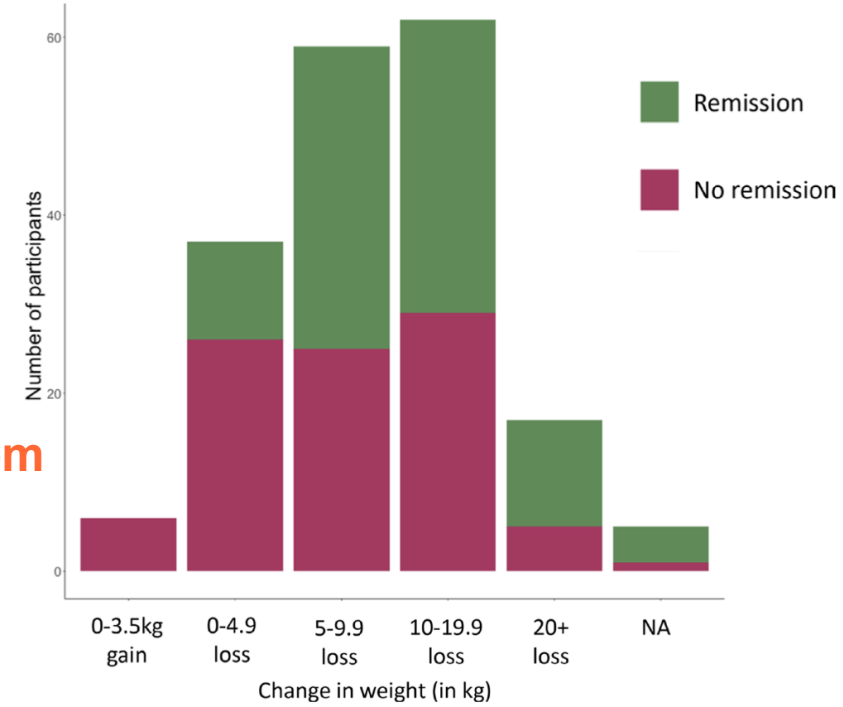
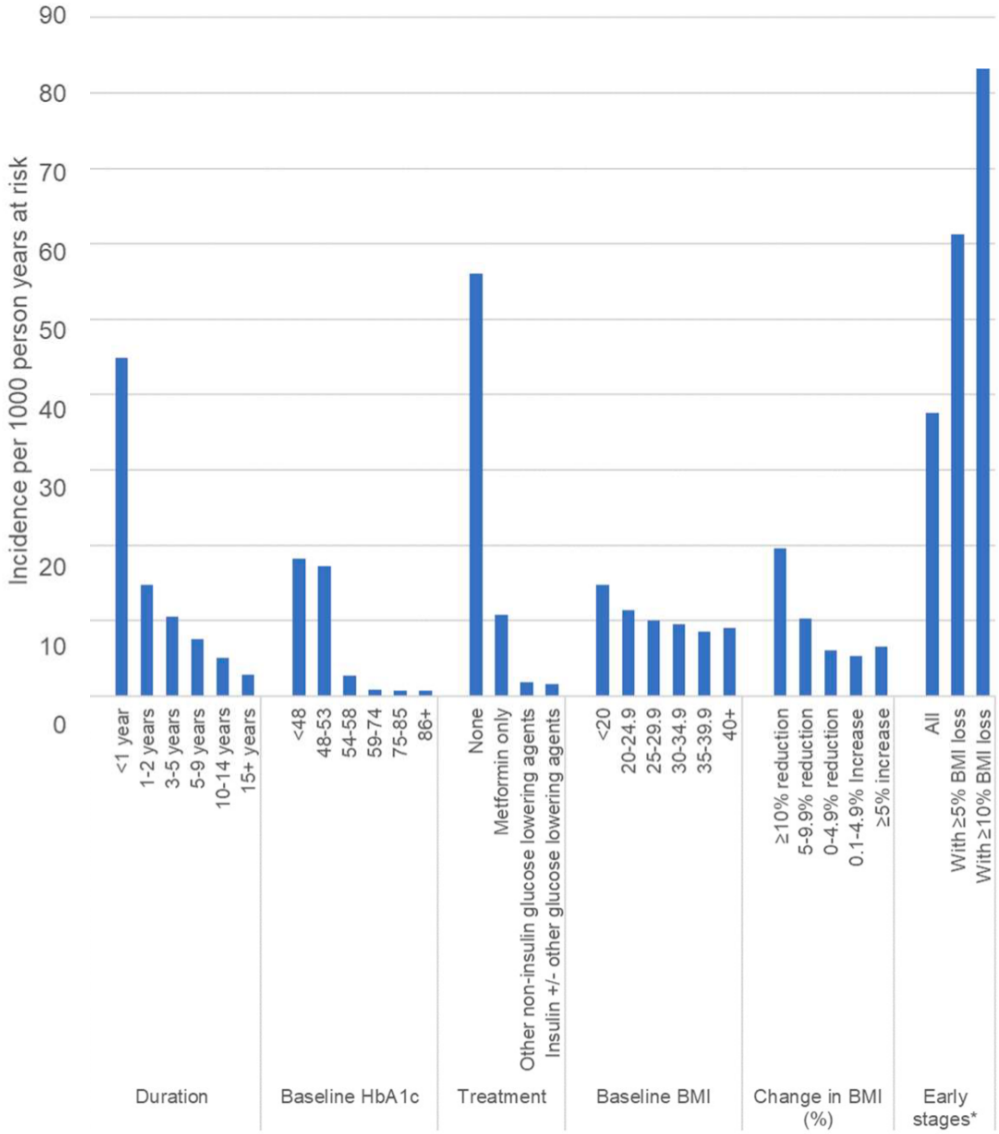


Figure 2 Number of patients divided into those who achieve remission and those who do not plotted against change in weight (in kg). NA, not applicable.

BMJ Nutr Prev Health. 2023 Jan 2;6(1):46-55. doi: 10.1136/bmjnph-2022-000544.

Incidence and Characteristics of Remission of Type 2 Diabetes in England: A Cohort Study Using the National Diabetes Audit

- 2.297.700 pessoas com diabetes tipo 2
  - incidência geral de remissão: 9,7%
  - diagnóstico <1 ano: 44,9%

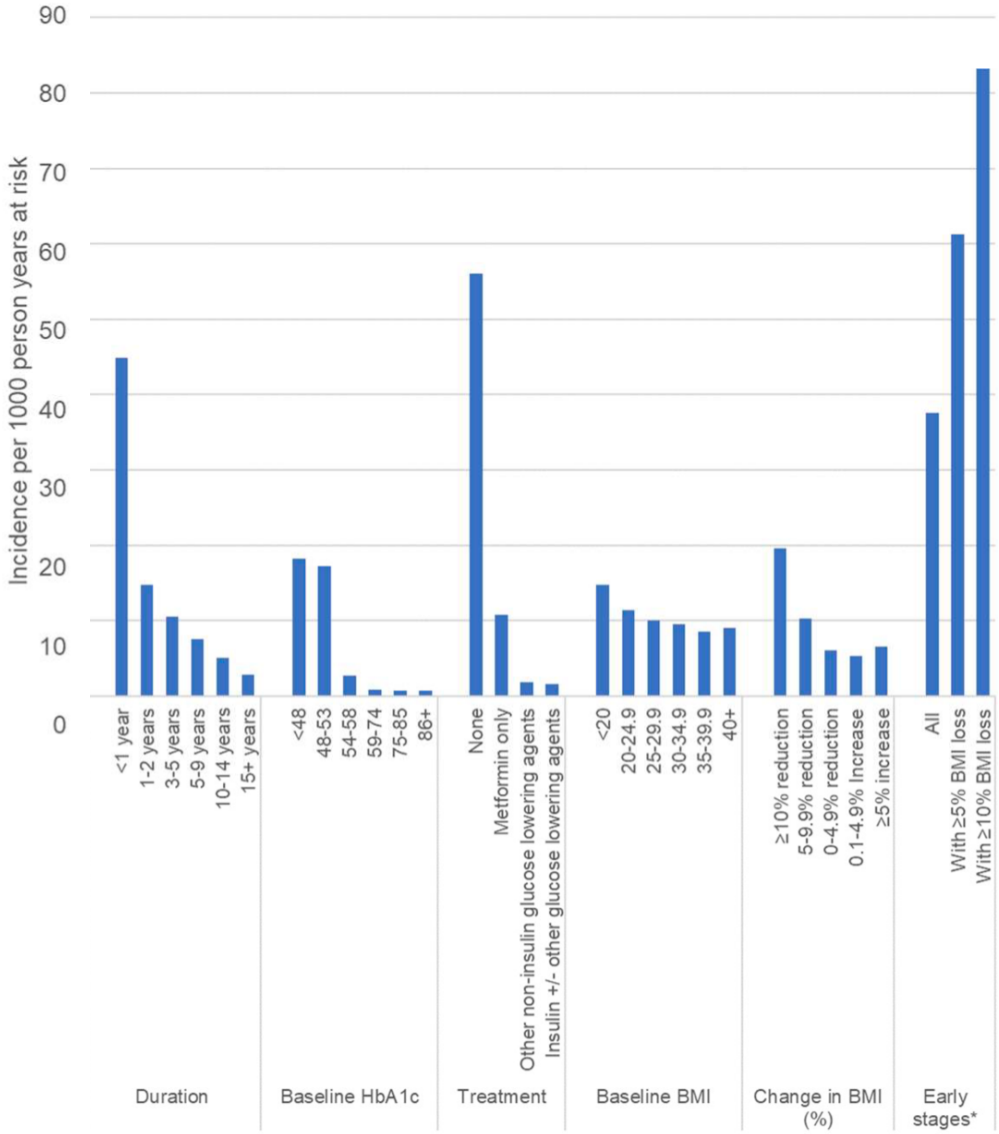


Diabetes Care. 2022 May 1;45(5):1151-1161. doi: 10.2337/dc21-2136.

Incidence and Characteristics of Remission of Type 2 Diabetes in England: A Cohort Study Using the National Diabetes Audit

Outros fatores basais associados a maiores chances de remissão:

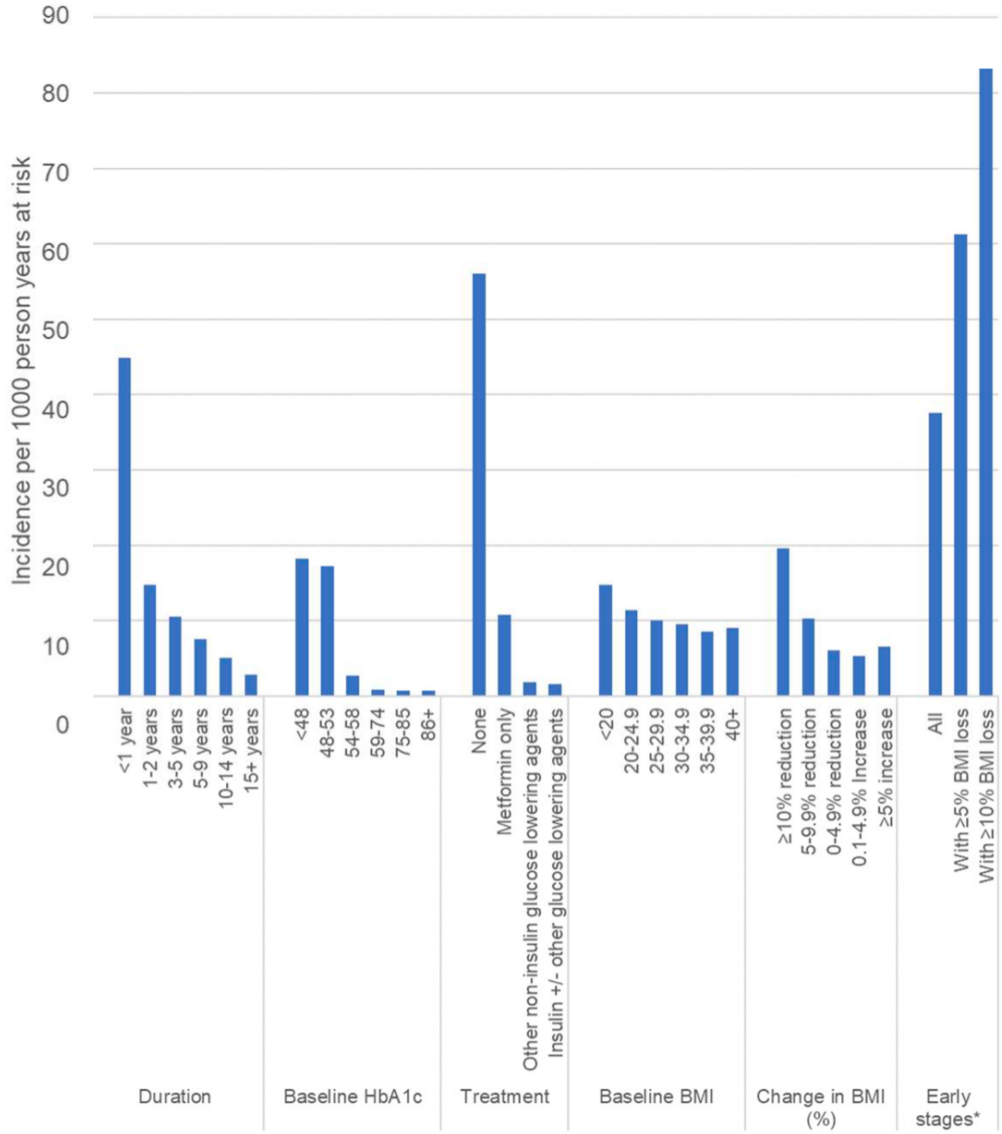
- ausência de prescrição de medicamentos para redução da glicose,
- menores níveis de HbA1c e IMC,
- redução do IMC,
- etnia branca,
- sexo feminino,
- menor privação socioeconômica.



Diabetes Care. 2022 May 1;45(5):1151-1161. doi: 10.2337/dc21-2136.

Incidence and Characteristics of Remission of Type 2 Diabetes in England: A Cohort Study Using the National Diabetes Audit

- prescrição de metformina isoladamente ou nenhum medicamento para redução da glicose, redução do IMC de ‡10%):
  - incidência de remissão por 1.000 pessoas-ano foi de 83,2%



Diabetes Care. 2022 May 1;45(5):1151-1161. doi: 10.2337/dc21-2136.

Estamos praticando inércia clínica quando não investimos em mudança de estilo de vida...

Estamos praticando inércia clínica quando ficamos somente no discurso “coma menos” e “mexa-se mais”

REMISSÃO DO DM2

- Tratamento proativo para hiperglicemia
- Perda significativa de peso

ANTES DE ALTERAÇÕES IRREVERSÍVEIS NAS CÉLULAS B

Diabetes Metab J. 2022 Mar;46(2):165-180. doi: 10.4093/dmj.2021.0377

- O DM2 não é um diagnóstico que indivíduos vulneráveis e nós, profissionais da saúde, devemos aceitar impotentes.
- A remissão do DM2 pode ser alcançada através de uma abordagem personalizada.
- A redução de peso deve ser priorizada (> 10%).
- Mudar o conceito de DM2 para o de uma condição urgente que requer intervenção rápida, em vez de basicamente uma doença crônica e progressiva.
- Devemos incluir esta mudança de paradigma na nossa compreensão do DM2 e no nosso discurso educativo como endocrinologistas para o benefício dos nossos pacientes.

Clayton Macedo, adaptado de Diabetes Metab J. 2022 Mar;46(2):165-180. doi: 10.4093/dmj.2021.0377

Vamos combater o diabetes tipo 2 até a remissão?

BMJ. 2017 Sep 13;358:j4030. doi: 10.1136/bmj.j4030.

Obrigado!!!

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Clayton Luiz Dornelles Macedo

drclaytonendocrino

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