

Type 2 Diabetes: Yesterday, Today, Tomorrow

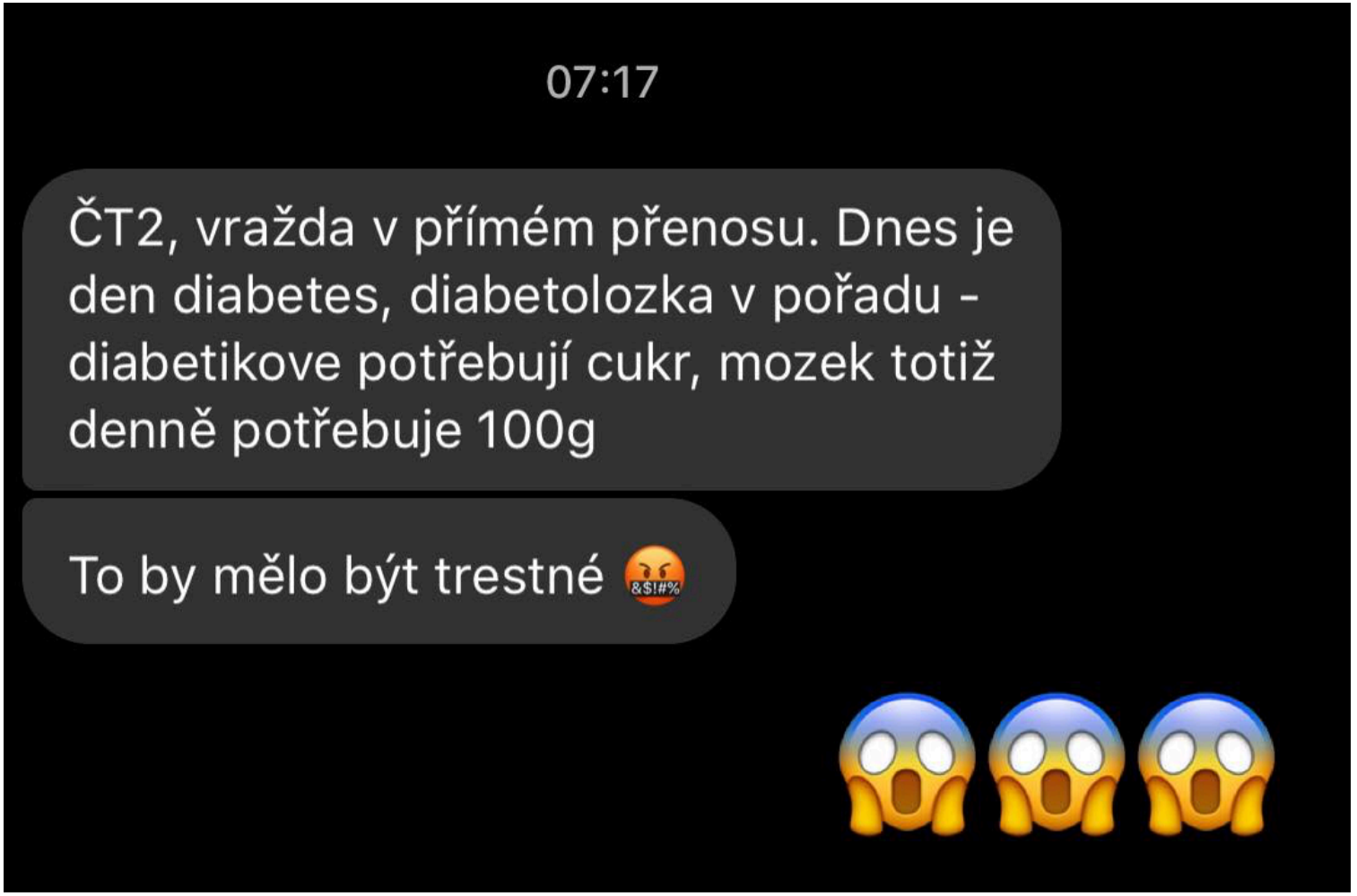
The Low Carb Universe – LCU19 – Mallorca, Spain

Jan Vyjídák
14 November 2019




International
Diabetes
Federation
world diabetes day
14 November

On the morning of the World Diabetes Day, a Czech diabetologist live on TV suggested that patients with diabetes need sugar, because brain needs 100 g per day. “Should be criminal”, a former T2D patient says.



Jakub asks about glucose from protein via liver and kidney gluconeogenesis, the diabetologist responds that gluconeogenesis is not sufficient for survival, and that balanced 120 – 200 g CHO/day is acceptable.

Jakub Heglas: „Dobrý den paní doktorko, proč říkáte, že diabetik potřebuje cukr, když si glukózu dokáže tělo vytvořit z bílkovin pomocí glukoneogeneze v játrech a ledvinách ?“

MUDr. [redacted] „Glukogeneza běží, to je pravda, ale samotná i přežití nestačí. I v ketodietách je minim. 40-50g sacharidů. Myslím, že je důležitá rovnováha, 120-200g sach. denně je přijatelné, 500g opravdu škodlivé.“

The next question – what does the diabetologist think about the recent trials showing T2D remission on a diet with less than 30 g CHO/day? ”Tested in T1D long time ago, we don’t go below 50g...”

Honza - Neslazeno.cz: „Jak hodnotite nedavne studie prokazujici, ze pacienti s diabetem 2. typu mohou na strave s mene nez 30 gramy sacharidu denne snadno a rychle dosahnout remise onemocneni?“

MUDr. [redacted] „Myslím, že podobné studie byly kdysi zkoušeny u diabetiků 1. typu do objevu inzulínu, tam samozřejmě metabolicky jde o něco jiného, každopádně, obvykle se svými pacienty neklesáme pod 50g sacharidů při nízkosach. dietách podle doporučení naší odborné společnosti:-)“

Minireview

The effects of laughter on post-prandial glucose levels and gene expression in type 2 diabetic patients

Takashi Hayashi *, Kazuo Murakami

Foundation for Advancement of International Science, Bio-Laboratory, 586-9 Akatsuka-Ushigafuchi, Tsukuba, Ibaraki 305-0062, Japan

ARTICLE INFO

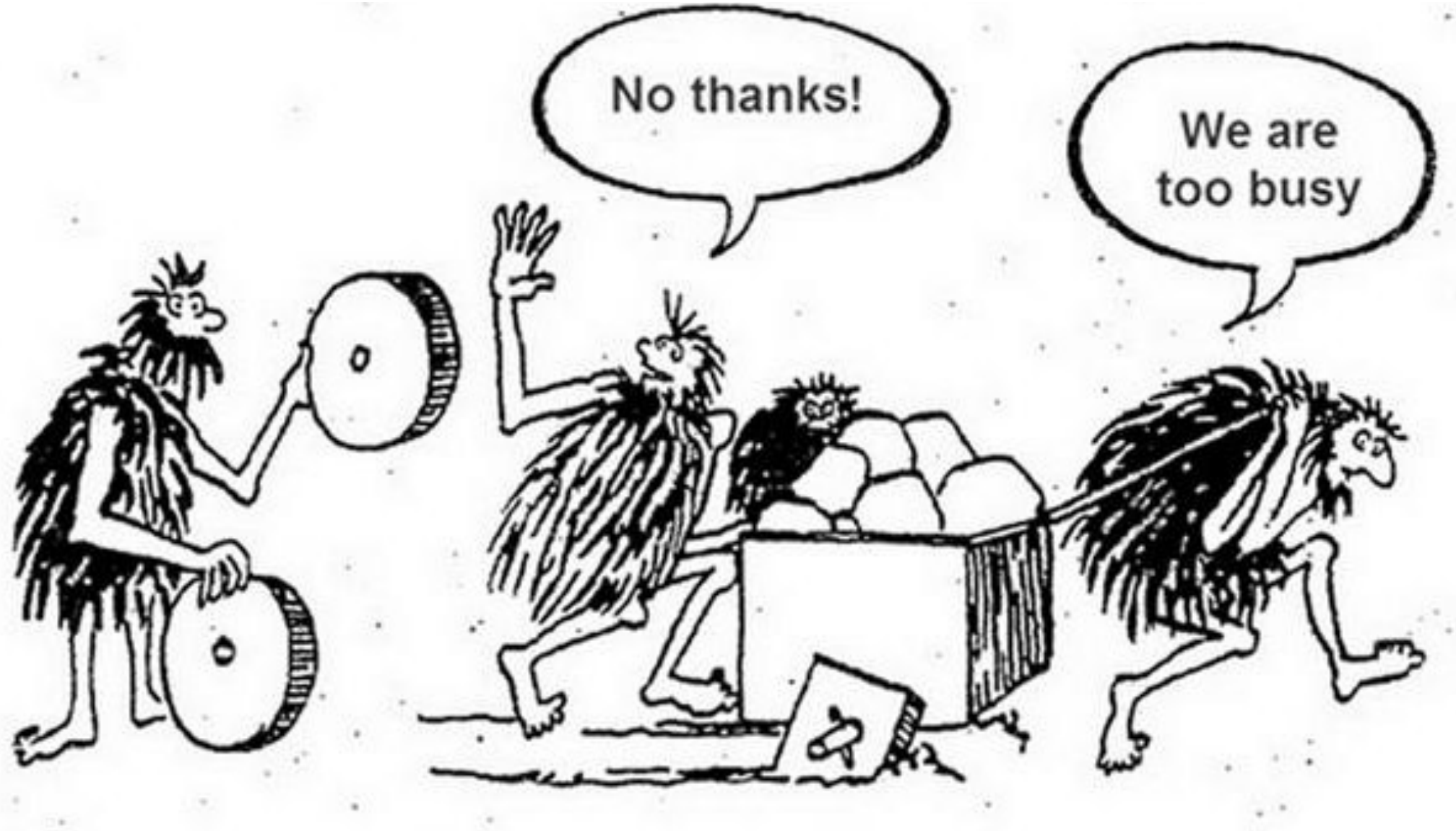
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Emotion
Type 2 diabetes

ABSTRACT

This report mainly summarizes the results of our study in which the physiological effects of laughter—as a positive emotional expression—were analyzed with respect to gene expression changes to demonstrate the hypothesis that the mind and genes mutually influence each other. We observed that laughter suppressed 2-h postprandial blood glucose level increase in patients with type 2 diabetes and analyzed gene expression changes. Some genes showed specific changes in their expression. In addition, we revealed that laughter decreased the levels of prorenin in blood; prorenin is involved in the onset of diabetic complications. Further, laughter normalized the expression of the prorenin receptor gene on peripheral blood leukocytes, which had been reduced in diabetic patients; this demonstrated that the inhibitory effects of laughter on the onset/deterioration of diabetic complications at the gene-expression level. In a subsequent study, we demonstrated the effects of laughter by discriminating 14 genes, related to natural killer (NK) cell activity, to exhibit continuous increases in expression as a result of laughter. Our results supported NK cell-mediated improvement in glucose tolerance at the gene-expression level. In this report, we also review other previous studies on laughter.

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No thanks!
We are too busy

1 Short introduction

2 T2D: Where are we now?

3 Current clinical guidelines

4 Early cures

5 Pre-insulin era

6 Discovery of insulin and the era of drugs

7 Bariatric surgery as the solution?

8 The Newcastle/Glasgow way

9 Ketogenic diets - back to Rollo?

10 Prevention

1 Short introduction

From law and legal science via international health management to healthcare consulting, healthcare quality, and evidence based medicine (and nutrition).









Over the past decade, I have worked as a management consultant on healthcare projects in the United Kingdom, Central and Eastern Europe and Asia, most recently in the Czech Republic and Slovakia.



















For some therapeutic areas – notably epilepsy, obesity and diabetes, there are several longer term RCTs for efficacy and safety, in other areas only non-randomised or pilot studies are available.

References

NESLAZENO

created 14 June 2017 (JV), edited 9 September 2019

(Czech version)

This page provides an overview of medical papers and other publications relevant to human physiology in the context of carbohydrate restriction, and to the role of carbohydrate-restricted diets in physical activity and in the treatment and/or prevention of chronic diseases. Although best efforts are taken to keep this overview updated regularly, it is not exhaustive and items are being added on an ongoing basis. For ease of reference, there are separate sections as follows:

1. Systematic Reviews/Meta-analyses (22 publications, by date)
2. Randomised Controlled Trials (45 publications by date)
3. Other Trials (17 publications, by date)
4. Review papers (16 publications, by date)
5. Monographies and other books (16 items, by author)
6. Disease-oriented overview (31 items, by disease)
7. Extended list of resources (248 items, by author)

Period covered: 1797 – 2019

Total items: 248

Note: Neslazeno (2019)

In January 2019, The Guardian and The Irish Times published an article about low carbohydrate (ketogenic) diet, including also a short version of my story.

High on fat, low on evidence: the problem with the keto diet

The ultra-low-carb ketogenic diet – which forces the body to burn fat – flies in the face of conventional nutritional advice. It is hugely popular, but is it healthy or sustainable?



▲ The keto diet is predominantly fat – carbs, apart from avocado, are virtually banned. Composite: Alamy/Getty/Guardian Design

Keto diet: High in fat and popularity, but is it healthy and sustainable?

According to some critics, the ultra-low-carb ketogenic diet is a socially acceptable form of disordered eating

Tue, Jan 8, 2019, 11:52 | Updated: Tue, Jan 8, 2019, 11:55

Laura Thomas



Keto, ketogenic diet with nutrition diagram, low carb, high fat healthy weight loss meal plan

Note: Thomas (2019)

In October 2019, I completed 10 years on an elitist, restrictive and environmentally unfriendly diet, which helped me to stop all meds I had been using for several years to no great effect.

The Guardian

THE IRISH TIMES

Jan Vyjidak, 38, a management consultant who has contributed research into energy metabolism, including carbohydrate restriction, to Public Health Collaboration, a charity that promotes healthy lifestyles, **has been on the keto diet for nearly a decade. He came to it, he says, to manage his health and improve his athletic performance. "It transformed my life," he says. "It wiped out my constant hunger, and I was able to stop all medication for my asthma and psoriasis within six months."**

Note: Thomas (2019)

A diet excluding added sugars, restricting starch etc (LCHF) is now an option in the amended CZ clinical guidelines for Gestational Diabetes, used based on individual needs and tolerance of women.

GESTAČNÍ DIABETES MELLITUS

Doporučený postup screeningu, gynekologické, perinatologické, diabetologické a neonatologické péče 2017

Materiál je konsenzuálním stanoviskem České gynekologické a porodnické společnosti (ČGPS), České diabetologické společnosti (ČDS) a České neonatologické společnosti ČNS) České lékařské společnosti Jana Evangelisty Purkyně (ČLS JEP)

Strava s vyloučením přidaných cukrů, omezením škrobů, umírněnou konzumací ovoce a dostatečným příjmem kvalitních tuků, bílkovin a zeleniny vede k lepší kompenzaci GDM a zajistí adekvátní výživu pro matku i plod bez nutnosti preventivní suplementace potravinovými doplňky.

Note: ČDS (2017b) page 7

I co-authored the most comprehensive review paper on low carbohydrate diets in the treatment of diabetes mellitus ever published in CZ medical journals.

ISSN 0042-773X (print)
ISSN 1801-7592 (online)
www.vnitrnilekarstvi.eu

Vnitřní lékařství

Nízkosacharidová strava v léčbě diabetes mellitus

Hana Krejčí[1,2], Jan Vyjídák[3,4], Matej Kohutiar[5]

[1]*III. interní klinika – klinika endokrinologie a metabolismu 1. LF UK a VFN v Praze*
[2]*Gynekologicko-porodnická klinika 1. LF UK a VFN v Praze*
[3]*Berkeley Research Group (Healthcare), London, UK*
[4]*FN Olomouc*
[5]*Ústav lékařské chemie a klinické biochemie 2. LF UK a FN Motol, Praha*

Note: Krejčí (2018)

Our team also published one of the first papers in CZ on the relationship between food processing and the prevention and treatment of chronic (lifestyle) diseases.

KLASIFIKACE POTRAVIN PODLE STUPNĚ TECHNOLOGICKÉHO ZPRACOVÁNÍ A JEJÍ VYUŽITÍ V PREVENCI CIVILIZAČNÍCH ONEMOCNĚNÍ

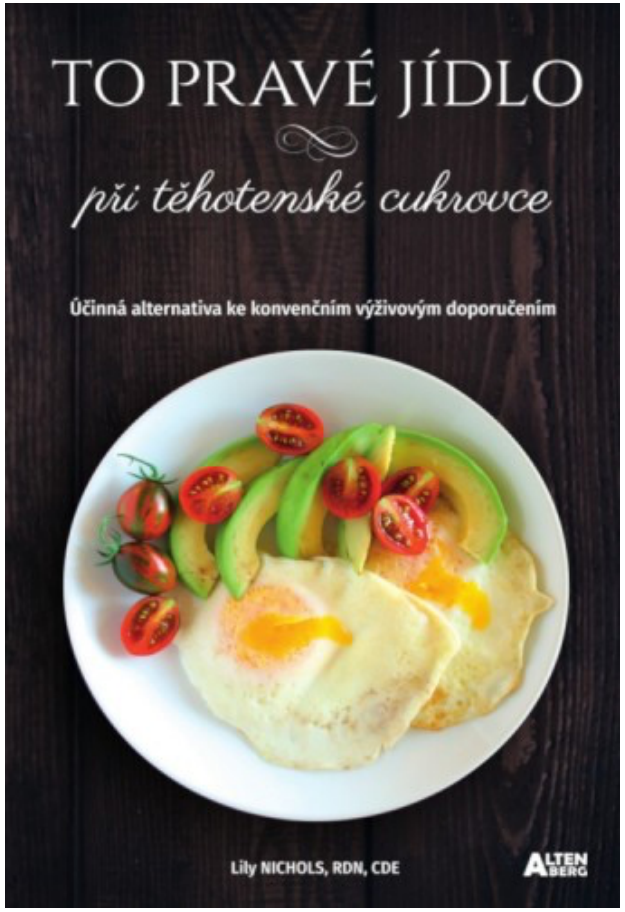
A SYSTEM OF FOOD CLASSIFICATION BASED ON DEGREE OF FOOD PROCESSING AND ITS USE IN THE PREVENTION OF LIFESTYLE DISEASES

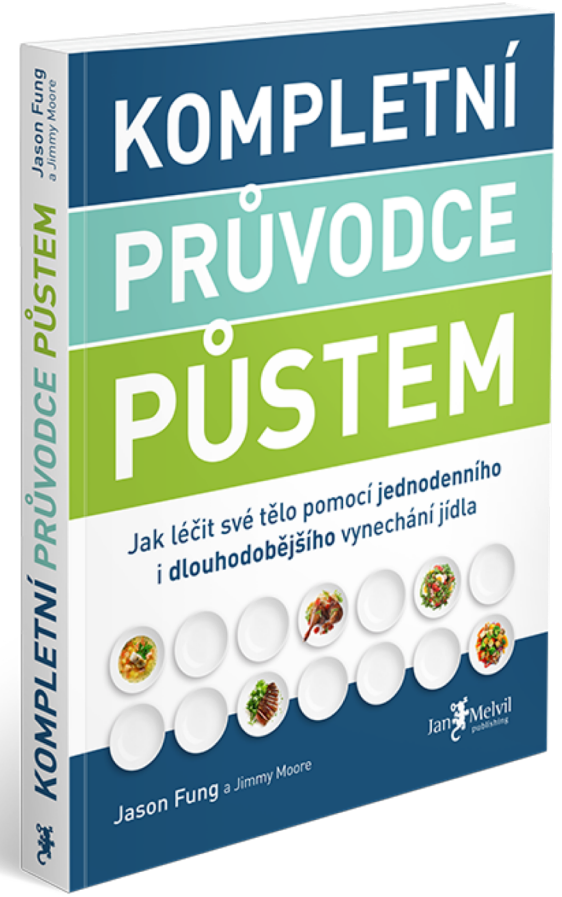
MATEJ KOHUTIAR[1], HANA KREJČÍ[2], JAN VYJÍDÁK[3]

[1]Ústav lékařské chemie a klinické biochemie 2. lékařské fakulty Univerzity Karlovy a Fakultní nemocnice v Motole
[2]3. interní klinika, Gynekologicko-porodnická klinika a Ústav patologické fyziologie 1. lékařské fakulty Univerzity Karlovy a Všeobecné fakultní nemocnice
[3]Berkeley Research Group (Healthcare), London, UK, Caja (Healthcare), Keele, UK, a Fakultní nemocnice Olomouc, Olomouc

Note: Kohutiar (2019)

Recently, a CZ edition of Lily Nichols‘ book was published, as well as Jason Fung‘s Complete Guide to Fasting. Quality information from abroad is creeping in slowly, but nothing can stop it now.





Note: Nichols (2019), Fung (2018)

2 Type 2 Diabetes – Where are we now?

In 1998, it had been estimated that the total number of people with diabetes will reach 300 million globally by 2025.

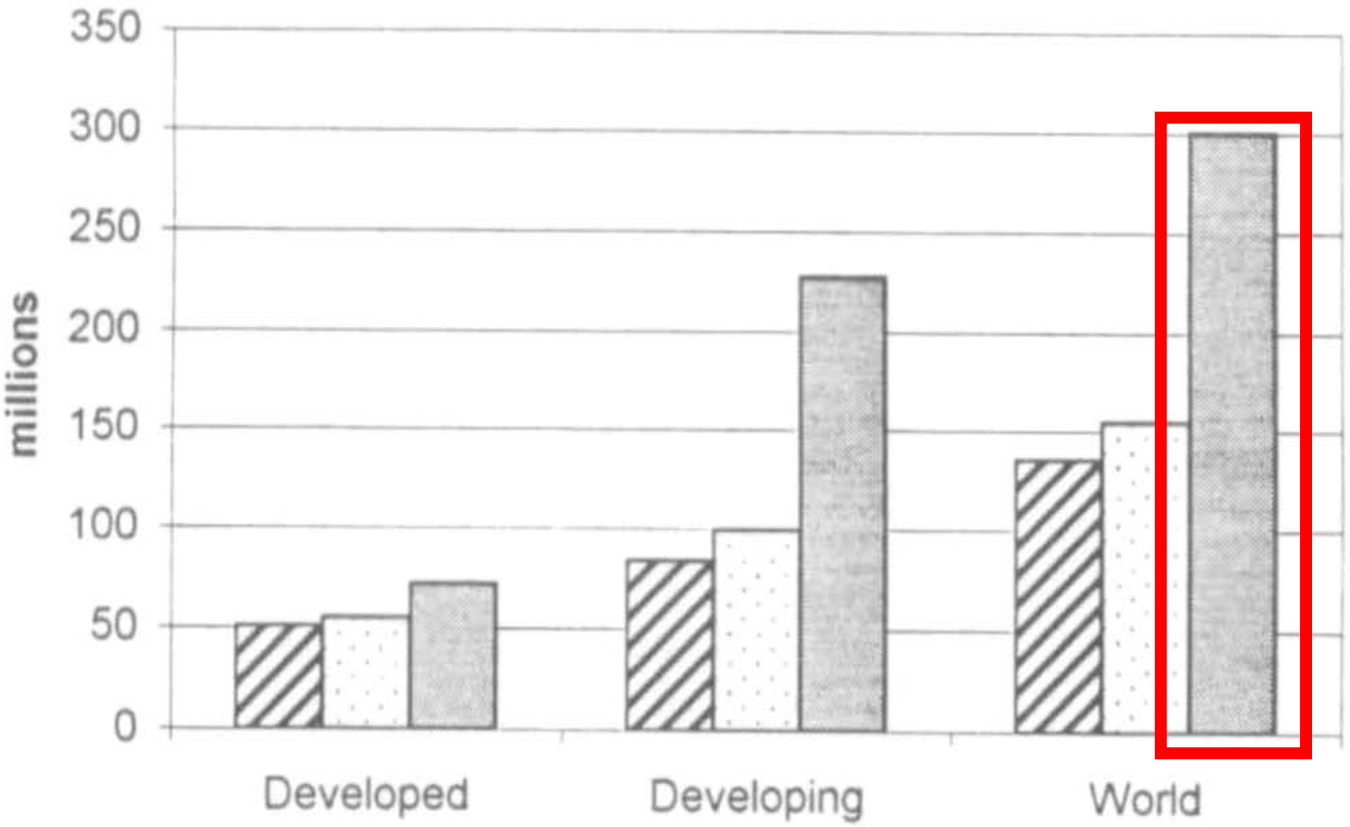
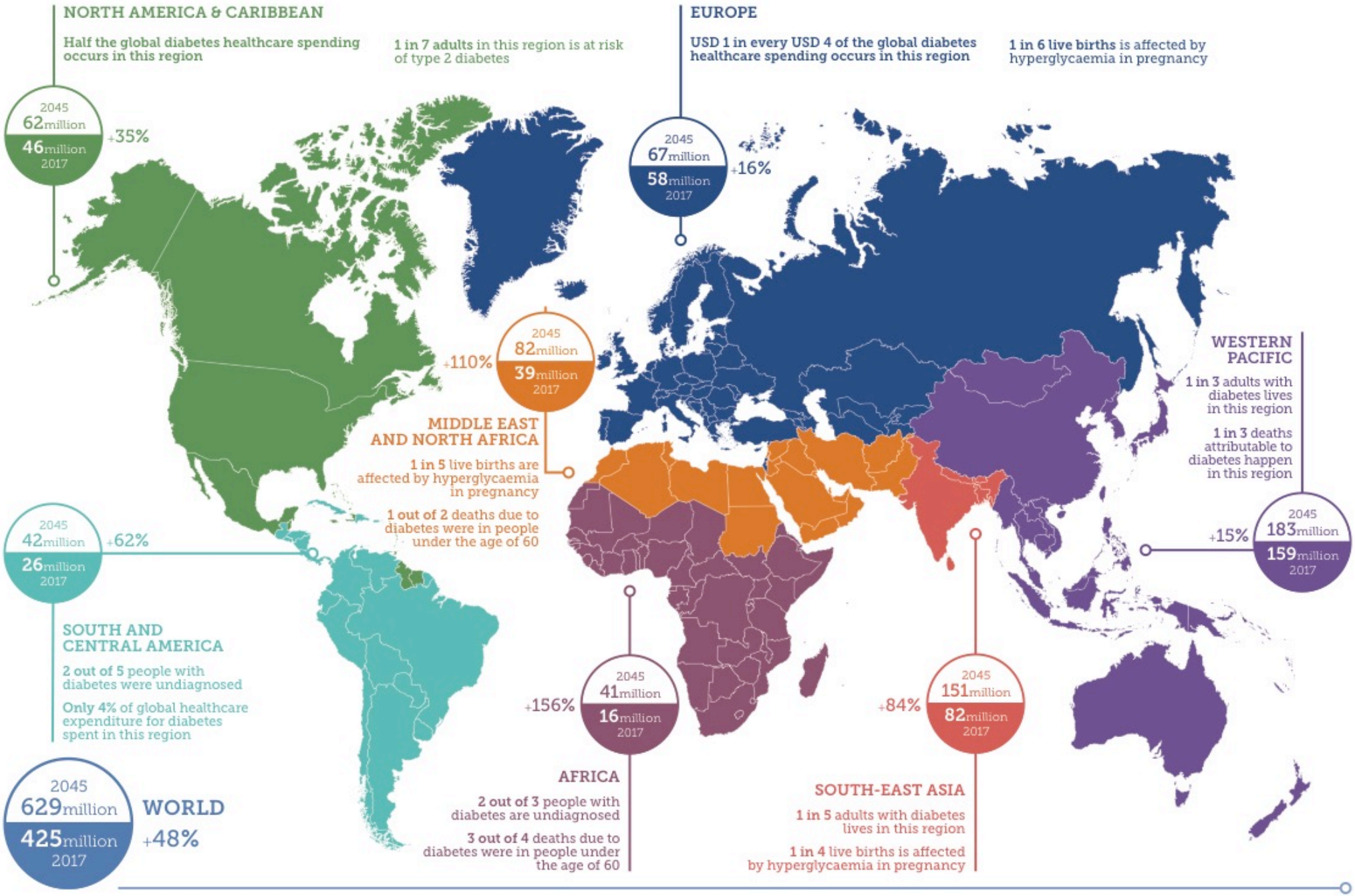
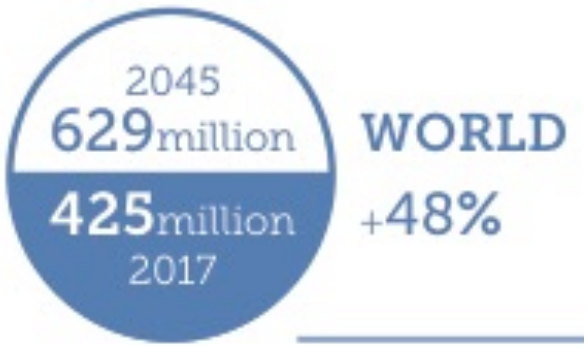


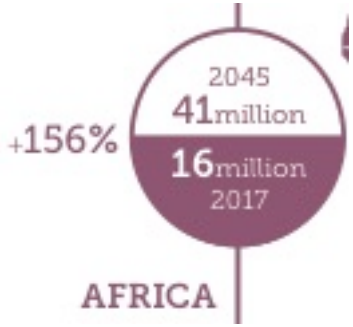
Figure 3—*Number of people with diabetes in the adult population (aged ≥20 years) by year and region. A: Developed and developing countries and world total. B: Major geographic areas. ▨, 1995; ▩, 2000; ▩, 2025.*

Note: King (1998)


NORTH AMERICA & CARIBBEAN
Half the global diabetes healthcare spending occurs in this region
1 in 7 adults in this region is at risk of type 2 diabetes
2045
62million
46million
2017
+35%
EUROPE
USD 1 in every USD 4 of the global diabetes healthcare spending occurs in this region
1 in 6 live births is affected by hyperglycaemia in pregnancy
2045
67million
58million
2017
+16%
2045
82million
39million
2017
+110%
MIDDLE EAST AND NORTH AFRICA
1 in 5 live births are affected by hyperglycaemia in pregnancy
1 out of 2 deaths due to diabetes were in people under the age of 60
WESTERN PACIFIC
1 in 3 adults with diabetes lives in this region
1 in 3 deaths attributable to diabetes happen in this region
2045
183million
159million
2017
+15%
2045
42million
26million
2017
+62%
SOUTH AND CENTRAL AMERICA
2 out of 5 people with diabetes were undiagnosed
Only 4% of global healthcare expenditure for diabetes spent in this region
2045
41million
16million
2017
+156%
AFRICA
2 out of 3 people with diabetes are undiagnosed
3 out of 4 deaths due to diabetes were in people under the age of 60
2045
151million
82million
2017
+84%
SOUTH-EAST ASIA
1 in 5 adults with diabetes lives in this region
1 in 4 live births is affected by hyperglycaemia in pregnancy
2045
629million
425million
2017
WORLD
+48%

The total number of people with diabetes is set to break 500 million in the next few years, reaching almost 630 million in 2045. Africa, Middle East and North Africa and South-East Asia hit very hard.



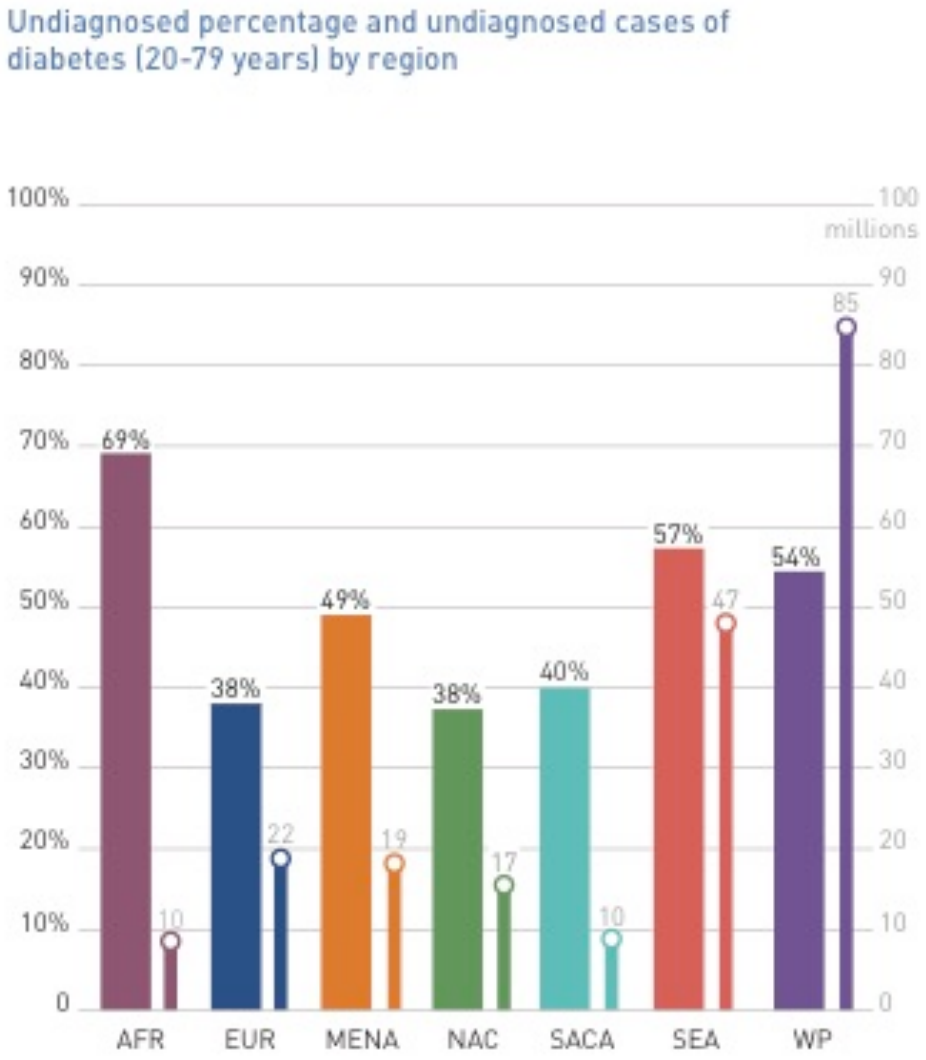






Note: IDF (2017)

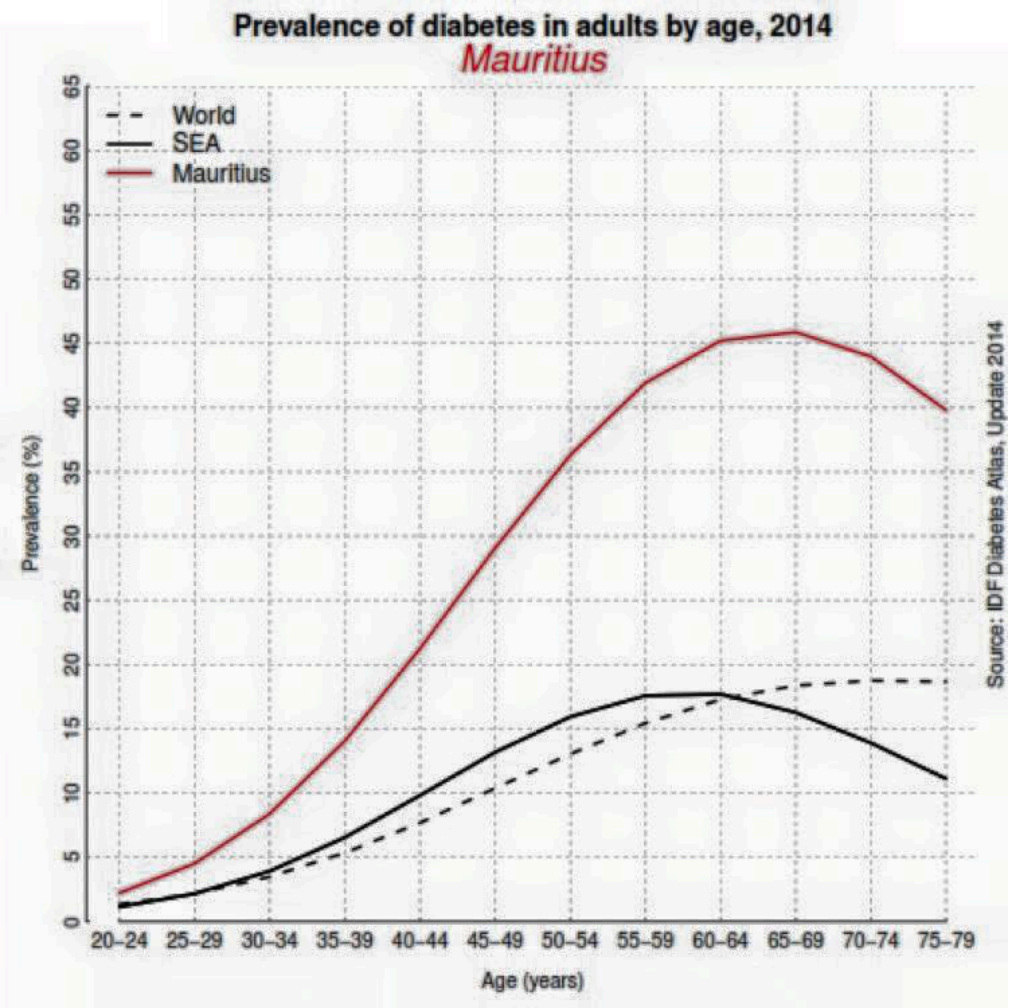
Incredibly, half of people with diabetes are not aware of their disease, including 22 million in Europe and 85 million in Western Pacific region.



Note: IDF (2017)

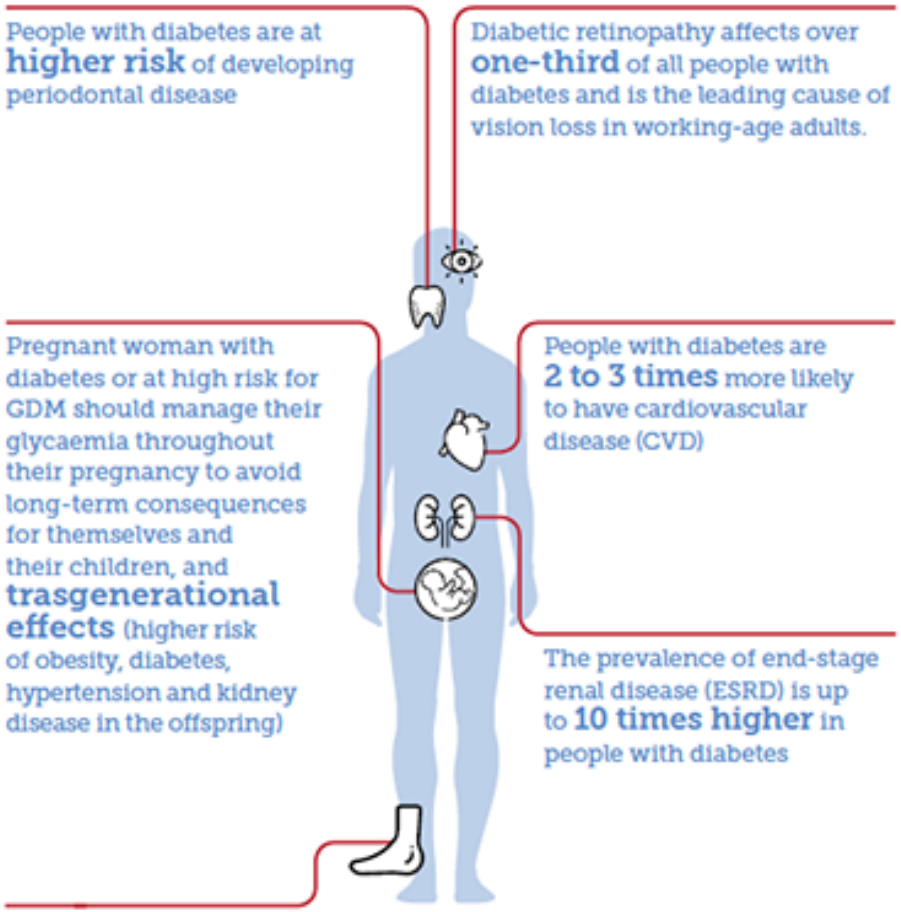


In Mauritius, almost every other adult aged 60 to 74 suffers from diabetes, according to 2014 estimates, beating the rest of the region by some margin.



Note: IDF (2014), JV archive

Diabetic complications dramatically reduce quality of life, and shorten life.



Note: IDF (2017)

Beyond health consequences, Type 2 Diabetes also has its devastating economic burden, notably in poorer countries.

"In high-income countries the burden often affects government or public health insurance budgets, while in poorer countries, a large part of the burden falls on the person with diabetes and their family due to very limited health insurance coverage," explains Seuring.

Compared with countries that have similar average income levels, people with type 2 diabetes in the US were found to have the highest lifetime health care costs related to the disease, at $283,000.

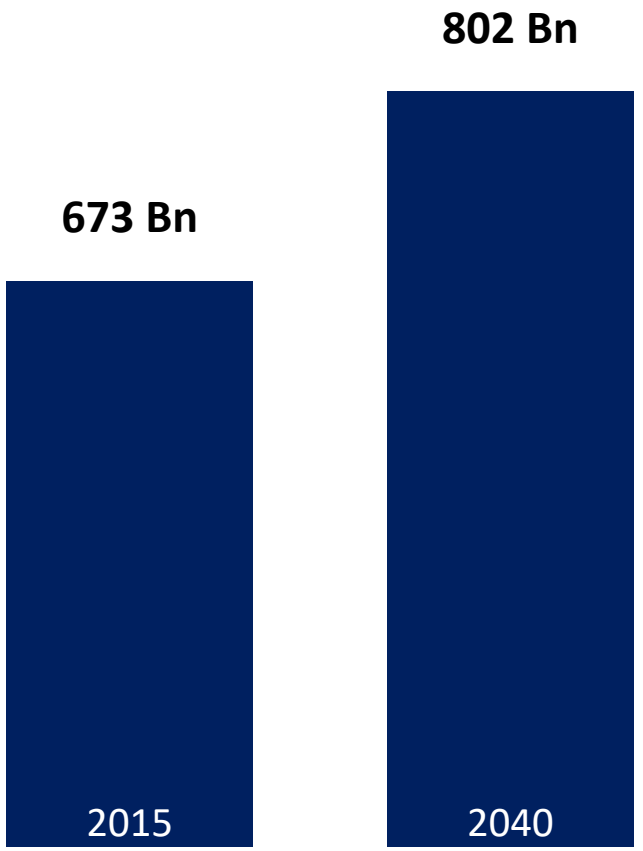
What is more, American women with type 2 diabetes were found to have the highest annual income loss worldwide, losing $21,392 per year. In the US, the condition also reduces a woman's chance of employment by 50%, the researchers found.

In all other countries, however, men with type 2 diabetes were found to have the worst employment opportunities. In Taiwan, for example, men with the condition were found to have a 19% reduced chance of employment.

Note: Seuring (2015), MedicalNewsToday (2015)

Total healthcare expenditure world wide estimated at USD 670 billion in 2015, set to increase to USD 800 billion in 20 years.

The global epidemic of type 2 diabetes has major implications for healthcare expenditures. Most countries dedicate between 5 % and 20 % of their total healthcare resources to treat diabetes and its complications [5]. In 2015, the IDF estimated that total diabetes healthcare expenditures for persons 20–79 years of age were $673 billion or 12 % of total healthcare expenditures worldwide [5]. The IDF has projected that this number will increase to $802 billion by 2040 assuming constant per capita healthcare expenditures [5].



Note: Ogurtsova (2017)

One epidemiological study after another, most recently last week, show again and again and again that the lower the dietary carbohydrate intake, the worse the health outcomes. But...

Lower carbohydrate and higher fat intakes are associated with higher hemoglobin A1c: findings from the UK National Diet and Nutrition Survey 2008–2016

Chaitong Churuangsuk[1] · Michael E.J. Lean[1] · Emilie Combet[1]

Lower carbohydrate diets and all-cause and cause-specific mortality: a population-based cohort study and pooling of prospective studies

Mohsen Mazidi[1,2]*, Niki Katsiki[3], Dimitri P. Mikhailidis[4], Naveed Sattar[5], and Maciej Banach[6,7,8]*; on behalf of the International Lipid Expert Panel (ILEP) and the Lipid and Blood Pressure Meta-analysis Collaboration (LBPMC) Group

Dietary carbohydrate intake and mortality: a prospective cohort study and meta-analysis

Sara B Seidelmann, Brian Claggett, Susan Cheng, Mir Henglin, Amil Shah, Lyn M Steffen, Aaron R Folsom, Eric B Rimm, Walter C Willett, Scott D Solomon

Note: Churuangsuk (2019), Mazidi (2019), Seidelmann (2018)

Routinely, epidemiological studies explore datasets containing almost nobody on low carbohydrate diets with <26 % of calories from CHO, and cannot differentiate between well and poorly formulated diets.

This study has limitations that must be considered when evaluating its findings. This study could not refer to very low-carbohydrate ketogenic diets, as there are no data on ketosis status for this dataset. Notably, there is no standardized definition of LCHF diets, although < 26%E CHO has been proposed as a cut-off value [44]. Only 0.24% of the study sample ($n = 8/3234$) consumed carbohydrates below this threshold, a finding comparable to data from the UK Biobank (0.34% of participants) [45]. As with all cross-

Note: Churuangsuk (2019)

... clinical trials keep showing often impressive results of carbohydrate restricted diets in diabetes and obesity, including in trials investigating complete drug-free remission of T2D.

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

Michael E J Lean, Wilma S Leslie, Alison C Barnes, Naomi Brosnahan, George Thom, Louise McCombie, Carl Peters, Sviatlana Zhyzhneuskaya, Ahmad Al-Mrabeh, Kieren G Hollingsworth, Angela M Rodrigues, Lucia Rehackova, Ashley J Adamson, Falko F Sniehotta, John C Mathers, Hazel M Ross, Yvonne McIlvenna, Paul Welsh, Sharon Kean, Ian Ford, Alex McConnachie, Claudia-Martina Messow, Naveed Sattar, Roy Taylor**

Long-Term Effects of a Novel Continuous Remote Care Intervention Including Nutritional Ketosis for the Management of Type 2 Diabetes: A 2-Year Non-randomized Clinical Trial

*Shaminie J. Athinarayanan[1], Rebecca N. Adams[1], Sarah J. Hallberg[1,2], Amy L. McKenzie[1], Nasir H. Bhanpuri[1], Wayne W. Campbell[3], Jeff S. Volek[1,4], Stephen D. Phinney[1] and James P. McCarter[5]**

Note: Lean (2019), Athinarayanan (2019)

More recent studies suggest that low carbohydrate intake, in contrast to common beliefs, does not prevent people from even strenuous and heavy exercise. Top elite athletes are in a different league.

Effects of a 4-Week Very Low-Carbohydrate Diet on High-Intensity Interval Training Responses

Lukas Cipryan [1]✉, Daniel J. Plews [2], Alessandro Ferretti [3], Phil B. Maffetone [4] and Paul B. Laursen [2]
[1] Department of Human Movement Studies & Human Motion Diagnostic Centre, Ostrava University, Czech Republic; [2] Sport Performance Research Institute New Zealand (SPRINZ), Auckland University of Technology, Auckland, New Zealand;[3] Independent researcher, Stratford Upon Avon, United Kingdom; [4] Independent researcher, Arizona, USA

Effects of a 12-week very-low carbohydrate high-fat diet on maximal aerobic capacity, high-intensity intermittent exercise, and cardiac autonomic regulation: non-randomized parallel-group study

Tomas Dostal[1], Daniel J. Plews[2], Peter Hofmann[3], Paul B. Laursen[2], Lukas Cipryan[1*]

High Rates of Fat Oxidation Induced by a Low-Carbohydrate, High-Fat Diet, Do Not Impair 5-km Running Performance in Competitive Recreational Athletes

Philip J. Prins [1]✉, Timothy D. Noakes [2], Gary L. Welton [3], Sarah J. Haley [1], Noah J. Esbenshade [1], Adam D. Atwell [1], Katie E. Scott [1], Jacqueline Abraham [1], Amy S. Raabe [4], Jeffrey D. Buxton [1] and Dana L. Ault [1]
[1] Department of Exercise Science, Grove City College, Grove City, Pennsylvania, USA; [2] The Noakes Foundation, Cape Town, South Africa; [3] Department of Psychology, Grove City College, Grove City, Pennsylvania, USA; [4] Department of Human Ecology, Youngstown State University, Youngstown, Ohio, USA.

Note: Cipryan (2018), Dostál (2019), Prins (2019)

A fairly long period of mild-to-severe fatophobia stemming from the work of Ancel Keys around 1950s still sends healthcare professionals into a meltdown when they hear ”low carbohydrate diet”.

NEWLY DIAGNOSED PATIENT WITH T2D

Patient: ”Can I eat low carbohydrate diet?”

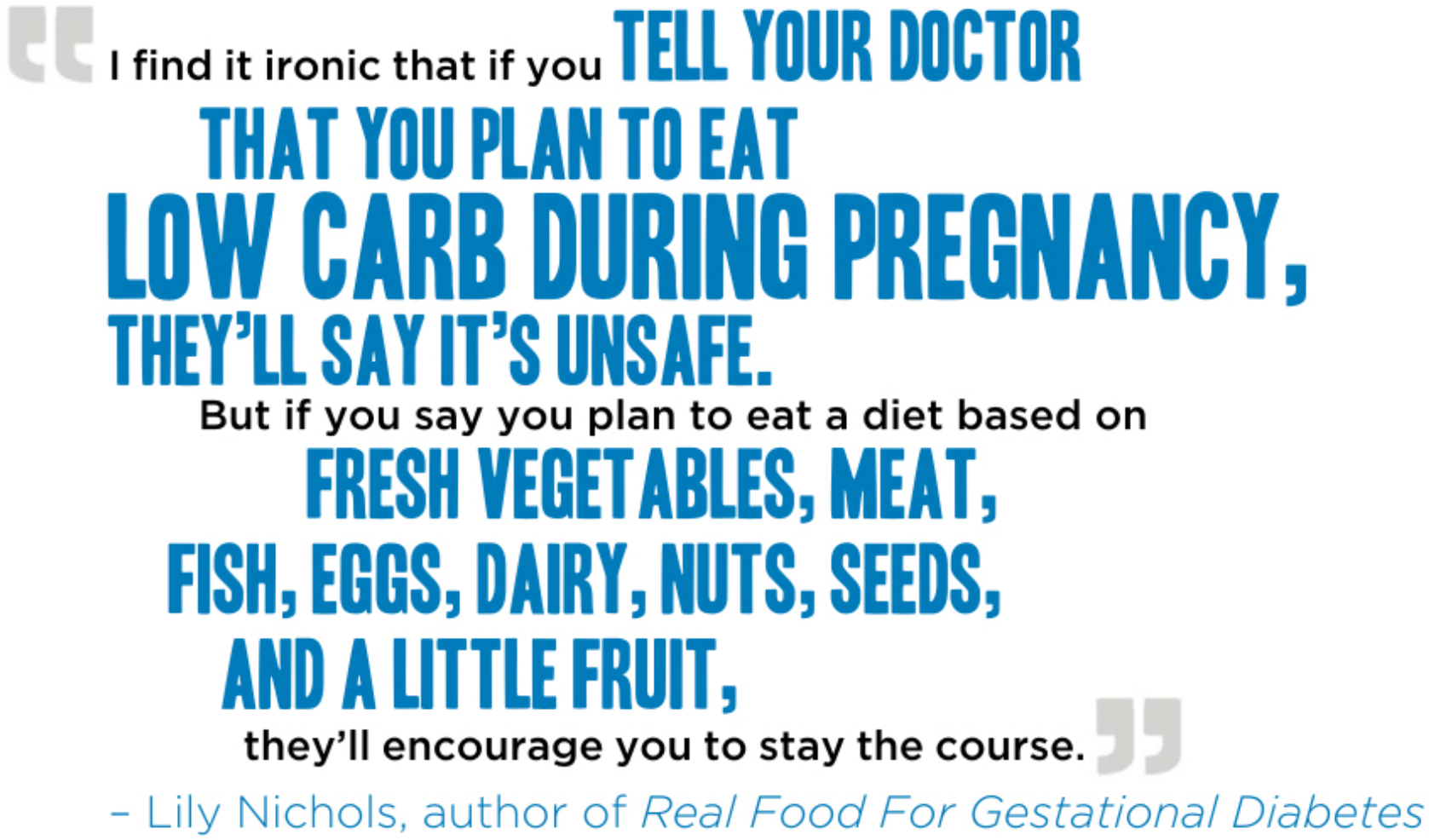
Doctor: 😱 ”Absolutely not! Bad idea.” 😱

Patient: “How about if I reduce added sugars, white flour, eat veggies with every meal, sufficient meat, fish, eggs, fermented dairy products, healthy fats and a little bit of fruit?”

Doctor: ❤️ ”Oh, sounds wonderful. Very healthy.” ❤️

Note: Krejci (2019) JV archive

A fairly long period of mild-to-severe fatophobia stemming from the work of Ancel Keys around 1950s still sends healthcare professionals into a meltdown when they hear ”low carbohydrate diet”.



Note: Noakes (2016)

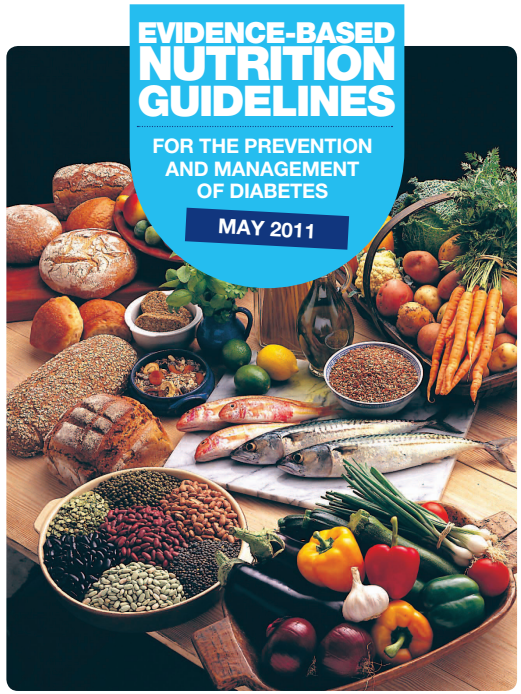
Low carbohydrate diet is subject to several legends and myths which lack biological explanation, or are based on misunderstanding of human physiology and nutrition.

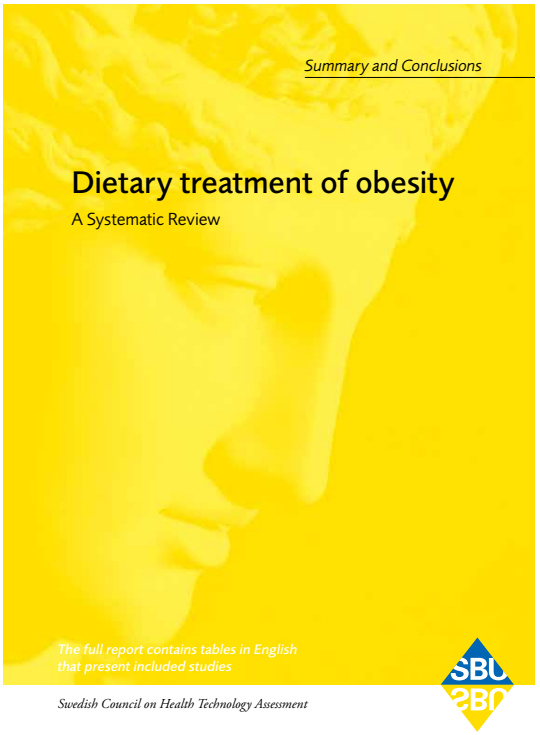
1. Dietary carbohydrate are necessary and basic source of energy for humans.
2. The brains requires glucose, and needs at least 120-130 grams of dietary carbohydrate per day.
3. Insufficient dietary carbohydrate results in ketogenesis, ketone bodies are harmful and their excess can result in ketoacidosis.
4. Low intake of carbohydrate in diabetics increases the risk of hypoglyacemia.
5. Carbohydrate restriction results in insufficient intake of nutrients, fibre, vitamins and minerals.
6. Excessive intake of dietary fat results in fat gain.
7. Excessive intake of dietary fat has deleterious effects on lipid profile and increases cardiovascular risk.
8. Excessive intake of saturated fatty acids causes cardiovascular disease.
9. Insufficient stimulation of pancreas impairs its function and results in diabetes.
10. (INSERT ANY RANDOM UNSUBSTANTIANTED OR REFUTED ARGUMENT)

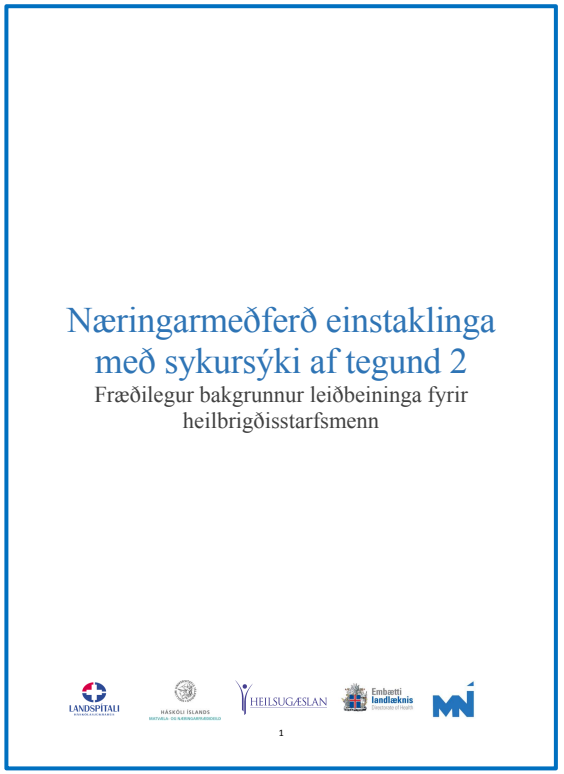
Note: JV

3 Current clinical guidelines

As of 2011, low carbohydrate diets started appearing in official clinical guidelines in the context of obesity and Type 2 Diabetes.

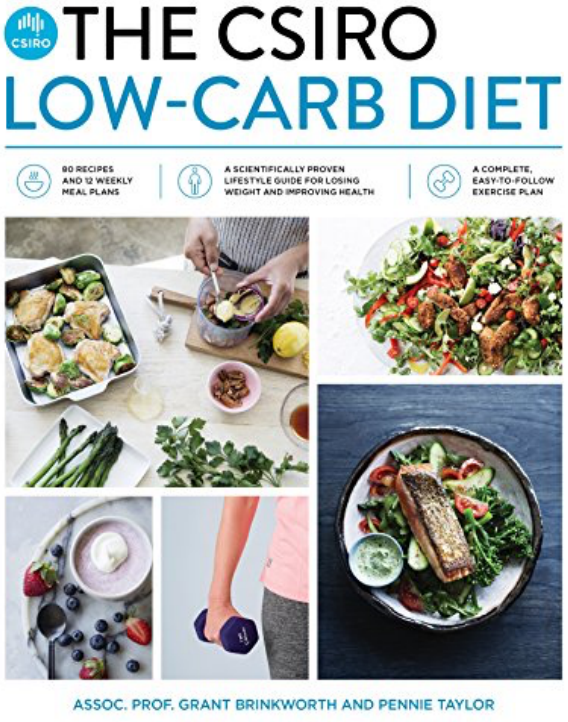


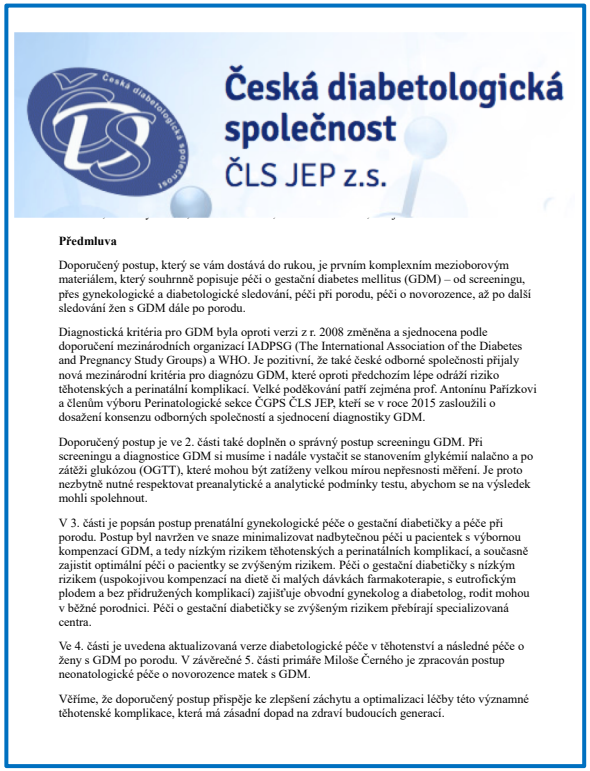




Note: Diabetes UK (2011), SBU (2013), Magnusdottir (2016)

In 2017, low carbohydrate diet was also recognized as an option for women with Gestational Diabetes.





Česká diabetologická společnost
ČLS JEP z.s.

Předmluva

Doporučený postup, který se vám dostává do rukou, je prvním komplexním mezioborovým materiálem, který souhrnně popisuje péči o gestační diabetes mellitus (GDM) – od screeningu, přes gynekologické a diabetologické sledování, péči při porodu, péči o novorozence, až po další sledování žen s GDM dále po porodu.

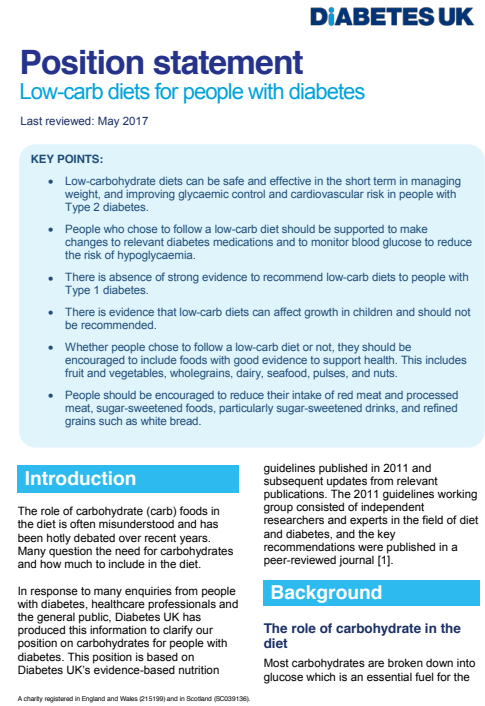
Diagnostická kritéria pro GDM byla oproti verzi z r. 2008 změněna a sjednocena podle doporučení mezinárodních organizací IADPSG (The International Association of the Diabetes and Pregnancy Study Groups) a WHO. Je pozitivní, že také české odborné společnosti přijaly nová mezinárodní kritéria pro diagnózu GDM, které oproti předchozím lépe odráží riziko těhotenských a perinatální komplikací. Velké poděkování patří zejména prof. Antonínu Pařízkovi a členům výboru Perinatologické sekce ČGPS ČLS JEP, kteří se v roce 2015 zasloužili o dosažení konsenzu odborných společností a sjednocení diagnostiky GDM.

Doporučený postup je ve 2. části také doplněn o správný postup screeningu GDM. Při screeningu a diagnostice GDM si musíme i nadále vystačit se stanovením glykémií nalačno a po zátěži glukózou (OGTT), které mohou být zatíženy velkou mírou nepřesnosti měření. Je proto nezbytně nutné respektovat preanalytické a analytické podmínky testu, abychom se na výsledek mohli spolehnout.

V 3. části je popsán postup prenatální gynekologické péče o gestační diabetičky a péče při porodu. Postup byl navržen ve snaze minimalizovat nadbytečnou péči u pacientek s výbornou kompenzací GDM, a tedy nízkým rizikem těhotenských a perinatálních komplikací, a současně zajistit optimální péči o pacientky se zvýšeným rizikem. Péči o gestační diabetičky s nízkým rizikem (uspokojivou kompenzací na dietě či malých dávkách farmakoterapie, s eutrofickým plodem a bez přidružených komplikací) zajišťuje obvodní gynekolog a diabetolog, rodit mohou v běžné porodnici. Péči o gestační diabetičky se zvýšeným rizikem přebírají specializovaná centra.

Ve 4. části je uvedena aktualizovaná verze diabetologické péče v těhotenství a následné péče o ženy s GDM po porodu. V závěrečné 5. části primáře Miloše Černého je zpracován postup neonatologické péče o novorozence matek s GDM.

Věříme, že doporučený postup přispěje ke zlepšení záchytu a optimalizaci léčby této významné těhotenské komplikace, která má zásadní dopad na zdraví budoucích generací.



DIABETES UK

Position statement

Low-carb diets for people with diabetes

Last reviewed: May 2017

KEY POINTS:

- Low-carbohydrate diets can be safe and effective in the short term in managing weight, and improving glycaemic control and cardiovascular risk in people with Type 2 diabetes.
- People who chose to follow a low-carb diet should be supported to make changes to relevant diabetes medications and to monitor blood glucose to reduce the risk of hypoglycaemia.
- There is absence of strong evidence to recommend low-carb diets to people with Type 1 diabetes.
- There is evidence that low-carb diets can affect growth in children and should not be recommended.
- Whether people chose to follow a low-carb diet or not, they should be encouraged to include foods with good evidence to support health. This includes fruit and vegetables, wholegrains, dairy, seafood, pulses, and nuts.
- People should be encouraged to reduce their intake of red meat and processed meat, sugar-sweetened foods, particularly sugar-sweetened drinks, and refined grains such as white bread.

Introduction

The role of carbohydrate (carb) foods in the diet is often misunderstood and has been hotly debated over recent years. Many question the need for carbohydrates and how much to include in the diet.

In response to many enquiries from people with diabetes, healthcare professionals and the general public, Diabetes UK has produced this information to clarify our position on carbohydrates for people with diabetes. This position is based on Diabetes UK's evidence-based nutrition guidelines published in 2011 and subsequent updates from relevant publications. The 2011 guidelines working group consisted of independent researchers and experts in the field of diet and diabetes, and the key recommendations were published in a peer-reviewed journal [1].

Background

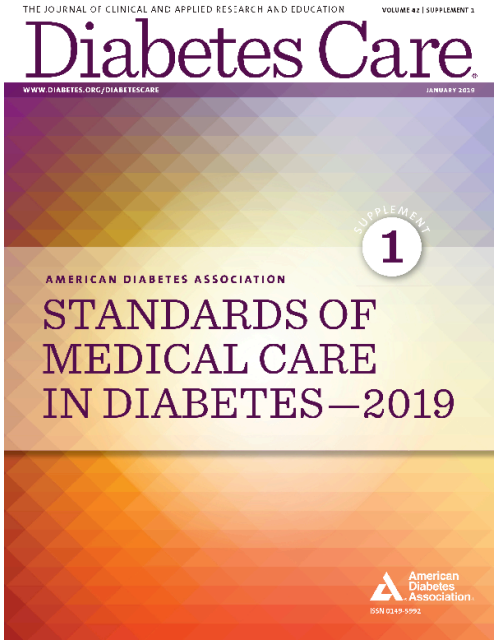
The role of carbohydrate in the diet

Most carbohydrates are broken down into glucose which is an essential fuel for the

A charity registered in England and Wales (215199) and in Scotland (SC039136).
© Diabetes UK 2017

Note: CSIRO (2016), CDS (2017), Diabetes UK (2017)

In 2018, American Diabetes Association and European Association for the Study of Diabetes included low carbohydrate diets as options in medical nutrition therapy.



Management of Hyperglycemia in Type 2 Diabetes, 2018. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)

https://doi.org/10.2337/dci18-0033

Note: ADA (2018), ADA-EASD (2018)

ADA recognized the evidence for low carbohydrate diets for glycaemic control and deprescribing.

sonal preferences, needs, and goals. In addition, research indicates that low-carbohydrate eating plans may result in improved glycemia and have the potential to reduce antihyperglycemic medications for individuals with type 2 diabetes (62–64). As research studies

Note: ADA (2018), pS48

Gradually, the prescribed range of carbohydrate intake – typically around 50% of calories – has been replaced with a variety of eating patterns and an individual approach to dietary distribution of calories.

5.10 There is no single ideal dietary distribution of calories among carbohydrates, fats, and proteins for people with diabetes; therefore, meal plans should be individualized while keeping total calorie and metabolic goals in mind.

5.11 A variety of eating patterns are acceptable for the management of type 2 diabetes and prediabetes.

Note: ADA (2018), pS49

LCHF also recognised as an effective tool for weight loss.

These diets may differ in the types of foods they restrict (such as high-fat or high-carbohydrate foods) but are effective if they create the necessary energy deficit (21,31–33). Use of meal replace-

Note: ADA (2018), pS83

While offering low carbohydrate diets as an option in Type 2 Diabetes, ADA also explicitly advises against this diet for pregnant women – in direct contrast with the Czech Diabetology Society.

in this approach. This meal plan is not recommended at this time for women who are pregnant or lactating, people with or at risk for disordered eating, or people who have renal disease, and it should be used with caution in patients taking sodium–glucose cotransporter 2 (SGLT2) inhibitors due to the potential risk of ketoacidosis (65,66). There is in-

Note: ADA (2018), pS48

A diet excluding added sugars, restricting starch etc (LCHF) is now an option in the amended CZ clinical guidelines for Gestational Diabetes, used based on individual needs and tolerance of women.

GESTAČNÍ DIABETES MELLITUS

Doporučený postup screeningu, gynekologické, perinatologické, diabetologické a neonatologické péče 2017

Materiál je konsenzuálním stanoviskem České gynekologické a porodnické společnosti (ČGPS), České diabetologické společnosti (ČDS) a České neonatologické společnosti ČNS) České lékařské společnosti Jana Evangelisty Purkyně (ČLS JEP)

Strava s vyloučením přidaných cukrů, omezením škrobů, umírněnou konzumací ovoce a dostatečným příjmem kvalitních tuků, bílkovin a zeleniny vede k lepší kompenzaci GDM a zajistí adekvátní výživu pro matku i plod bez nutnosti preventivní suplementace potravinovými doplňky.

Note: CDS (2017) page 7

While shorter term improvements in HbA1c are substantial on low carbohydrate diets, the effect diminishes at 12 and 24 months, likely due to challenges in maintaining weight loss.

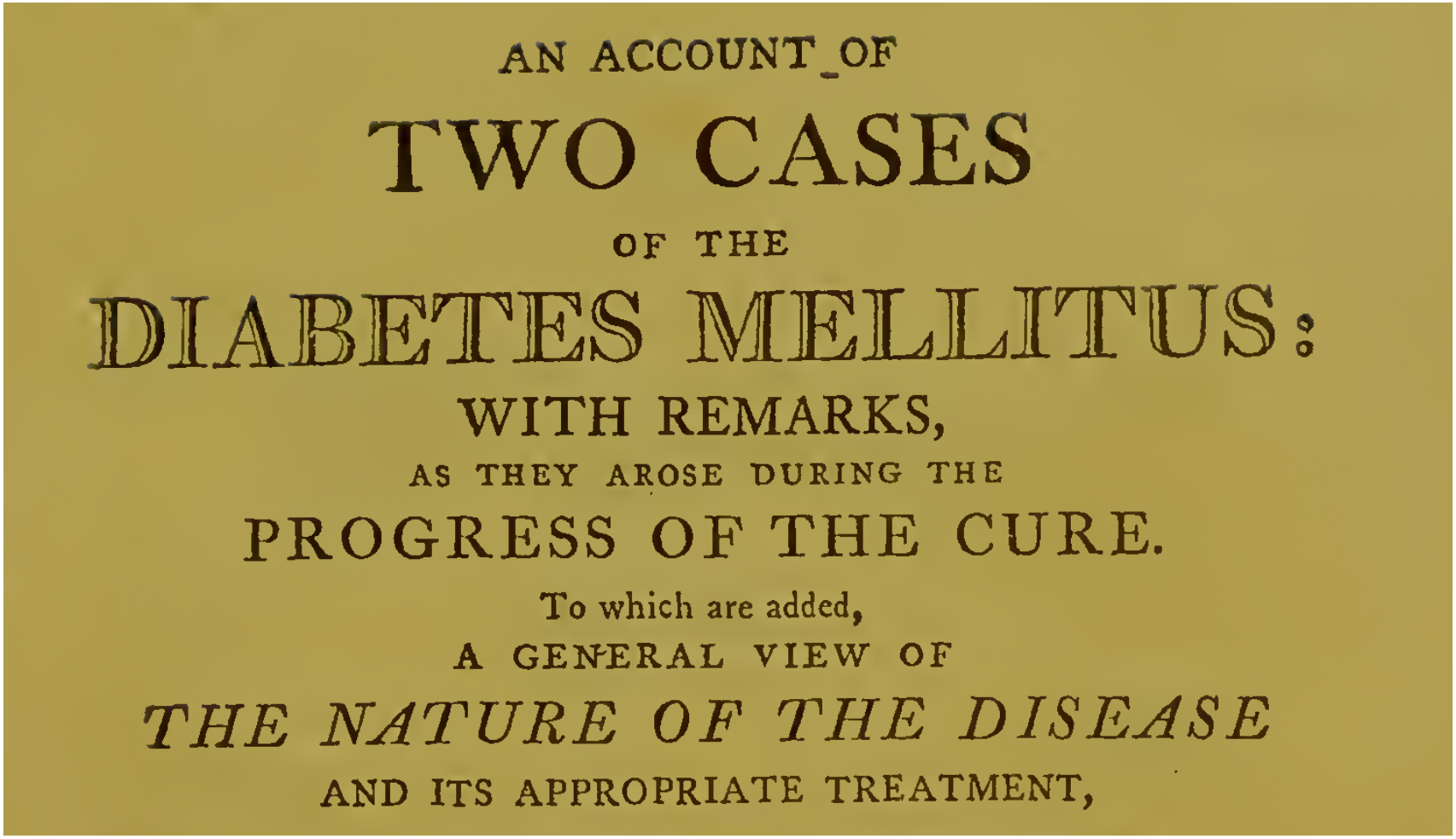
Dietary Quality and Eating Patterns. There is no single ratio of carbohydrate, proteins, and fat intake that is optimal for every person with type 2 diabetes. Instead,

−0.46%, −0.14%]) (69). Low-carbohydrate, low glycemic index, and high-protein diets, and the Dietary Approaches to Stop Hypertension (DASH) diet all improve glycemic control, but the effect of the Mediterranean eating pattern appears to be the greatest (70–72). Low-carbohydrate diets (<26% of total energy) produce substantial reductions in HbA_{1c} at 3 months (−5.2 mmol/mol, 95% CI −7.8, −2.5 mmol/mol [−0.47%, 95% CI −0.71%, −0.23%]) and 6 months (4.0 mmol/mol, 95% CI −6.8, −1.0 mmol/mol [−0.36%, 95% CI −0.62%, −0.09%]), with diminishing effects at 12 and 24 months; no benefit of moderate carbohydrate restriction (26–45%) was observed (73). Vegetarian eating pat-

Note: ADA-EASD (2018)

4 Early cures

One of the earliest references to an animal (low carbohydrate) diet comes from John Rollo, the army surgeon, from 1797, in the context of diabetes cure.



AN ACCOUNT OF

TWO CASES

OF THE

DIABETES MELLITUS:

WITH REMARKS,

AS THEY AROSE DURING THE

PROGRESS OF THE CURE.

To which are added,

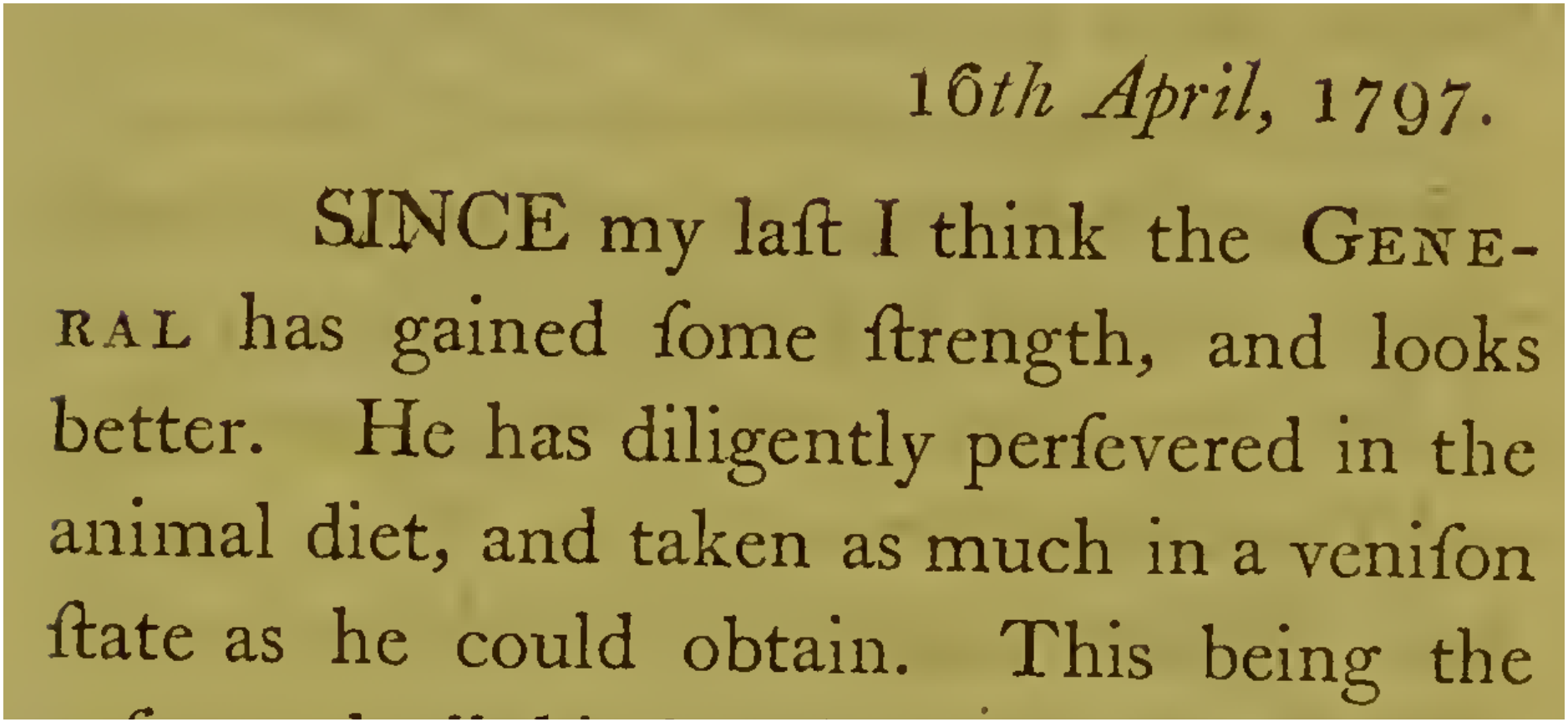
A GENERAL VIEW OF

THE NATURE OF THE DISEASE

AND ITS APPROPRIATE TREATMENT,

Note: Rollo (1797)

Animal diet was noted several times in Rollo 1797.



16th *April*, 1797.

SINCE my laſt I think the GENERAL has gained ſome ſtrength, and looks better. He has diligently perſevered in the animal diet, and taken as much in a veniſon ſtate as he could obtain. This being the

Note: p16 in Rollo (1797)

Animal diet was noted several times in Rollo 1797.

THE TWO CASES treated at GLASGOW by DOCTOR CLEGHORN, ſhew alſo the good effects of entire animal food, and of the influence of commotions in the bowels on the quantity of the urine.

THE CASE of the GENTLEMAN of 77 likewiſe ſhews the efficacy of animal food; but the MOST STRIKING CASE is that of CLARK, as related by DOCTOR GERARD.

Note: p138 in Rollo (1797)

The animal diet used by Rollo in the treatment of Captain Meredith included milk, bread, butter, blood-puddings, game, old meats, fat, pork etc.

and to diminish the appetite. Following initial blood-lettings, Rollo's treatment of Captain Meredith was as follows:

"1st. The diet to consist of animal food principally, and to be thus regulated:

Breakfast. One and a half pint of milk and half a pint of lime-water, mixed together; and bread and butter.

Noon. Plain blood-puddings, made of blood and suet only.

Dinner. Game, or old meats, which have been long kept; and as far as the stomach may bear, fat and rancid old meats, as pork. To eat in moderation.

Supper. The same as breakfast.

Note: Marble (1956)

Rollo suggested that diabetes developed due to morbid changes in stomach involving changes in the natural powers of digestion and assimilation, resulting in sugar/saccharine being developed from plants.

A view held by some at that time was that diabetes was a primary affection of the kidneys. However, Rollo developed the idea that the disease was "a primary and peculiar affection" of the stomach in which, due to some morbid changes in "the natural powers of digestion and assimilation," sugar or saccharine material was formed in that organ, chiefly from vegetable matter. It was on this basis that he advocated the use of an animal diet together with certain medication designed to quiet the overactive stomach and to diminish the appetite. Following initial blood-

Note: Marble (1956)

5 Pre-insulin era

Sugar feeding diet was based on the assumption that in order to regain strength, patients with diabetes simply need to replace the sugar lost in urine by eating it.

One diet that had a short vogue in the 1850s was sugar feeding, brainchild of the well-known but eccentric French physician Pierre Piorry (1794–1879). He thought that diabetics lost weight and felt so weak because of the amount of sugar they lost in the urine and that replacing it should restore their strength. A house surgeon to the Leicester Infirmary reported three cases in the *British Medical Journal (BMJ)* in 1858. The patients, women aged 23,

Note: Tattersall (2009)

Interestingly, physicians likely picked up on the role of semi-starvation, and recommended simple one item diets.

At the end of the nineteenth century several physicians championed 'cures' based on a specific dietary item. These included Donkin's skim-milk (1874), Mosse's potato (1902), and von Noorden's oatmeal cure (1903). They had in common periods of semi-starvation when the 'curative' item replaced food. For example,

Note: Tattersall (2009)

One version of "oatmeal cure" later picked up by William Osler was also using carbohydrate-free diet in the initial phase.

The oatmeal cure was invented by the German Carl H. von Noorden (1858–1944), one of the most respected diabetes specialists at the beginning of the twentieth century. It consisted of several days of a carbohydrate-free diet, one or two vegetable days, and then a few oat days. William Osler used it, and in the 1909 edition of his textbook included the following recipe: '250

Note: Tattersall (2009)

Fasting and saline enemas apparently made diabetics sugar free in three days.

was carried a step further by the Italian-born physician Guglielmo Guelpa (1850–1930), who worked in Paris. In 1896 he showed that fasting and saline enemas made diabetics sugar free in three days. He attributed this to the elimination of waste products and toxins and claimed equally dramatic results in asthma, epilepsy, migraine, eczema, and various eye conditions.

Note: Tattersall (2009)

Already 1860s, some physicians noted the socio-economic aspect of healthy nutrition and that poorer patients had hard time avoiding bread, potatoes, apples etc.

ther could not, or would not, follow the diet. In the *BMJ* in 1865, a physician from East Anglia lamented that dieting 'may be comparatively easy to effect in private practice; but in the case of the poor, especially the outpatient poor, who cannot be made to understand the necessity of abstaining from bread, potatoes, apples etc., it becomes a very difficult task to teach them what to eat, drink and avoid'.[11]

Note: Tattersall (2009)

Arsenic and uranium nitrate had been listed by US government among other anti-diabetic remedies...

US government publication in 1894 listed no less than forty-two anti-diabetic remedies including bromides, uranium nitrate, and arsenic. Apart from approved remedies there were the nostrums of the patent medicine men. The word 'patent' in this context is a misnomer, since to be patented the composition would have had to have been divulged. The British and American Medical Associations waged long campaigns against what they called secret remedies. In 1908 the *BMJ*

Note: Tattersall (2009)

The work of Rollo was picked up by Josef Thomayer in Prague, then part of the Austro-Hungarian Empire. In 1909, he described Rollo's diet as "a strict meat diet and a major therapy in most cases of diabetes."

„Léčení. Rollo doporučil v r. 1797 při diabetu přísnou masitou stravu. Tohoto druhu dieta je dodnes hlavním terapeutickým výkonem naším při nemoci této. Při masité stravě ve veliké většině případů množství vyloučeného cukru se zmenší, v mnohých pak případech úplně z moči vymizí. Jísti tedy smí čisté masité polévky, všeho druhu maso, máslo, slaninu (ponědvadž diabetik nemá tratiti na váze a chřadnouti, jelikož by si život ohrozil, má zejména účast másla a tuků v potravě býti pokud možno značná), vejce, sýr, čistou smetanu, rosoly, ořechy, houby, mandle, smí píti: kávu neslazenou čistou či se smetanou, podobná thé, trpká vína (např. rakouská), minerální vody, dále smí jísti takové zeleniny, které neobsahují cukry (špenát, okurky, chřest), v malém množství mrkev, jahody a maliny. Při takovéto dietě se však nemocnému obyčejně po moučné potravě zasteskne.“ [3]

Note: Rollo (1797) and Thomayer (1909) in Brož (2006)

At about the same, the founder of Czechoslovakian endocrinology, Josef Charvat, designed his slimming diet, which contained 60g CHO, 40g FAT and 70g PRO. He used it successfully in diabetes and obesity.

ní atrézií, označovaný dnes jako Bardetův-Biedlův syndrom (Biedl, 1922). Před téměř 80 lety navrhl profesor Josef Charvát redukční dietu. Charvátova dieta má energetický obsah 3700–4200 kJ a obsahuje 70 g bílkovin, 60 g sacharidů a 40 g tuků. Charvát ve své dietě doporučuje 100 g libového hovězího masa, 80 g libové šunky, 1 suchar, 2 vejce, 100 g brambor, 200 g ovoce, 300 g zeleniny, 10 g másla a 100 g mléka. Ve své době tato dieta bezpochyby představovala moderně koncipovanou dietoterapii obezity. Dnes bychom měli výhrady k vyššímu obsahu cholesterolu a nižšímu obsahu sacharidů v této dietě.

Nízkosacharidová strava není v léčbě diabetu novinkou. V předinzulinové éře byla jednou z prvních léčebných metod diabetu. Také u nás byla používána v léčbě obezity a diabetu zakladatelem české endokrinologie prof. J. Charvátem. S rozšířením farmakologických mož-

Note: Krejčí (2018), Hainer (2011)

6 Discovery of insulin and the era of drugs

The discovery of insulin marked a new era, notably for patients with Type 1 Diabetes – but insulin was soon being prescribed to patients with Type 2 Diabetes. Cost of insulin has been recently going up and up.

1923	2019
in months after diagnosis. For their discovery of insulin, Frederick Banting and John Macleod were awarded the 1923 Nobel Prize in Physiology or Medicine.[1] The members of their team sold the patent for insulin to the University of Toronto for $1 each[1]; Banting famously stated, “Insulin does not belong to me, it belongs to the world.”	costly (see table). Because of the high cost of insulin, Americans have reported rationing their medication,[3] which has resulted in worsening glycemic control and, in some cases, diabetic ketoacidosis and death.[4]

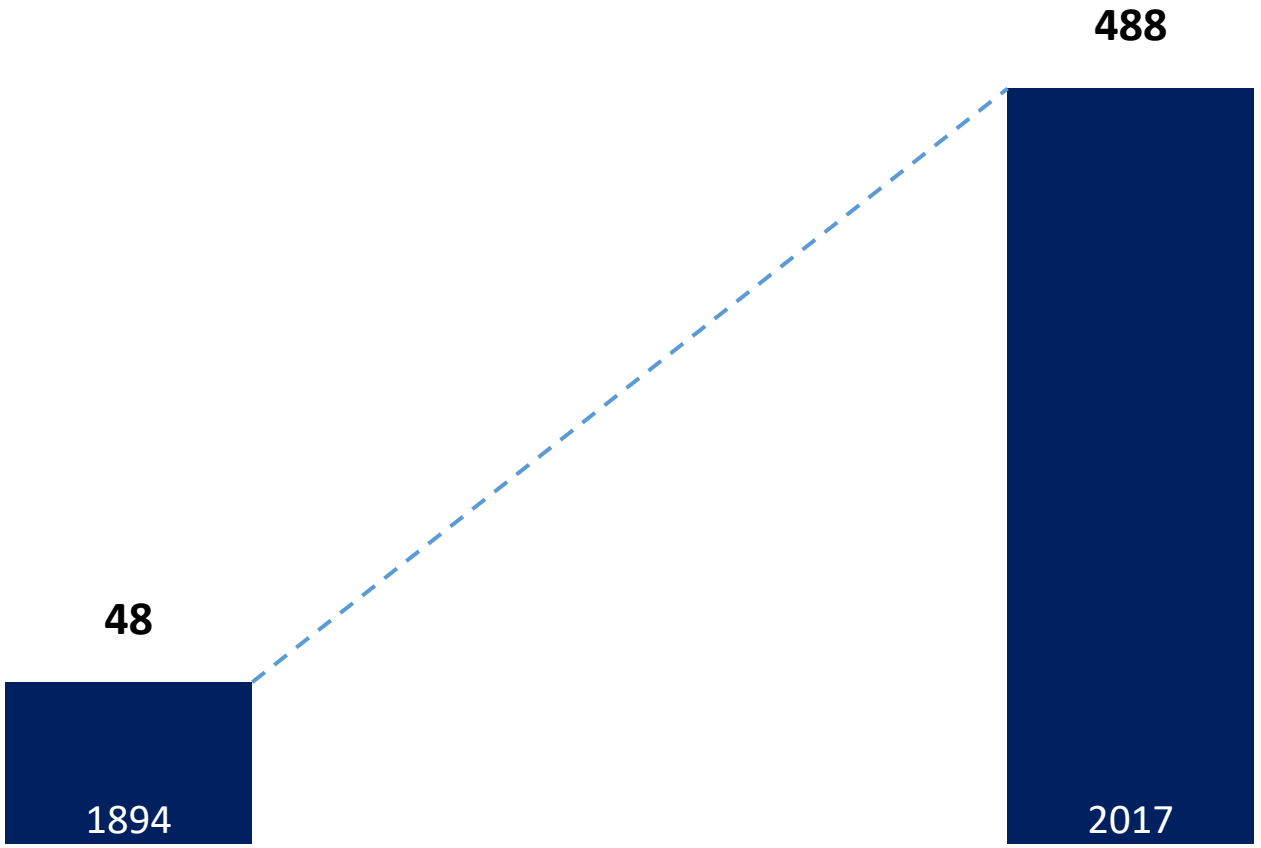
Note: Fralick (2019)

As in other therapeutic areas, notably epilepsy, diet and lifestyle had been pushed aside by new drugs coming onto the market.

Lowering blood glucose or HbA_{1c} concentrations remains the primary aim of management, as reflected in current clinical guidelines and the actions of licensed drugs. However, management and guidelines focus on use of antidiabetes drugs, with only lip service paid to diet and lifestyle advice. The scale of the market for drug therapies, and their likely inadequacy, is illustrated by the fact that 488 drugs (excluding insulins) are currently licensed worldwide to treat type 2 diabetes, with 70 generic compounds.[3] They all lower blood glucose and HbA_{1c} significantly, but no trials have yet examined drugs administered together with optimal diet and lifestyle advice for weight control.

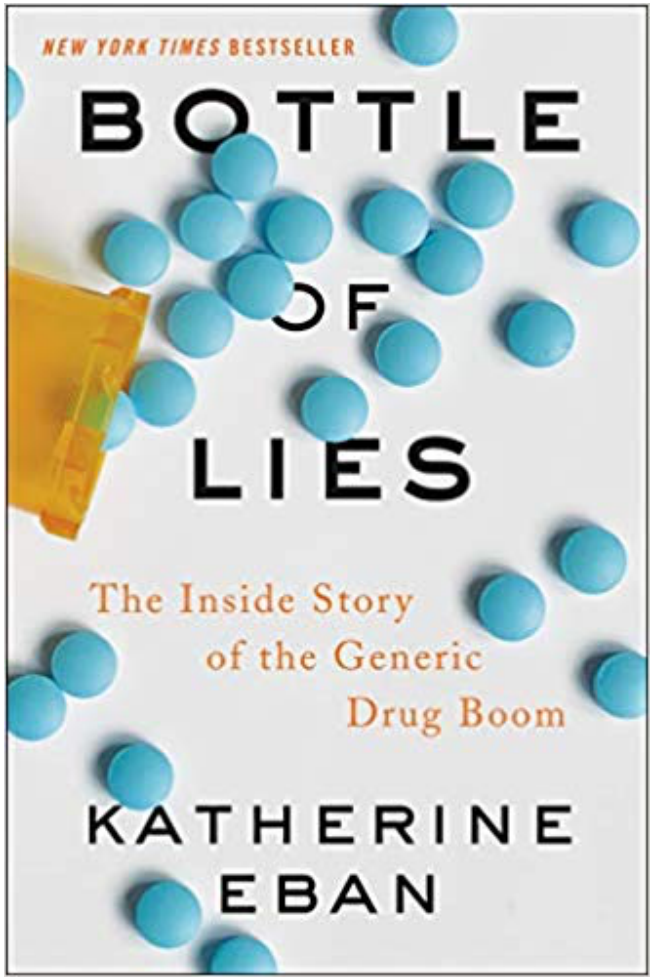
Note: McCombie (2017)

Despite almost 10x fold increase in the number of available medications in the space of 120 years (excluding insulins), the diabesity pandemic shows no signs of fatigue.



Note: Tattersall (2009), McCombie (2017)

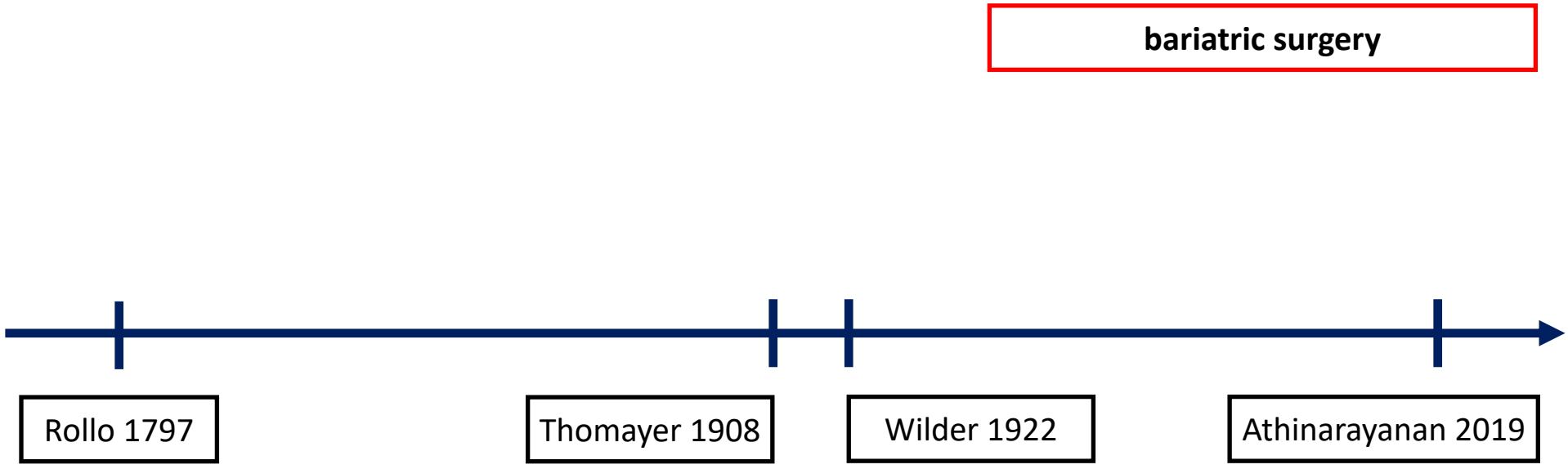
With the rapid growth of medicines and active ingredients manufacturing in less regulated markets (notably India, China), quality, efficacy and safety of some antidiabetic medications can be very poor.



Note: Eban (2019)

7 Bariatric surgery as the solution?

As of 1950s, surgeons began to notice that weight loss surgery had a positive effect on glycaemic control and T2D remission. First ”bariatric remission” RCTs came in 2000s.



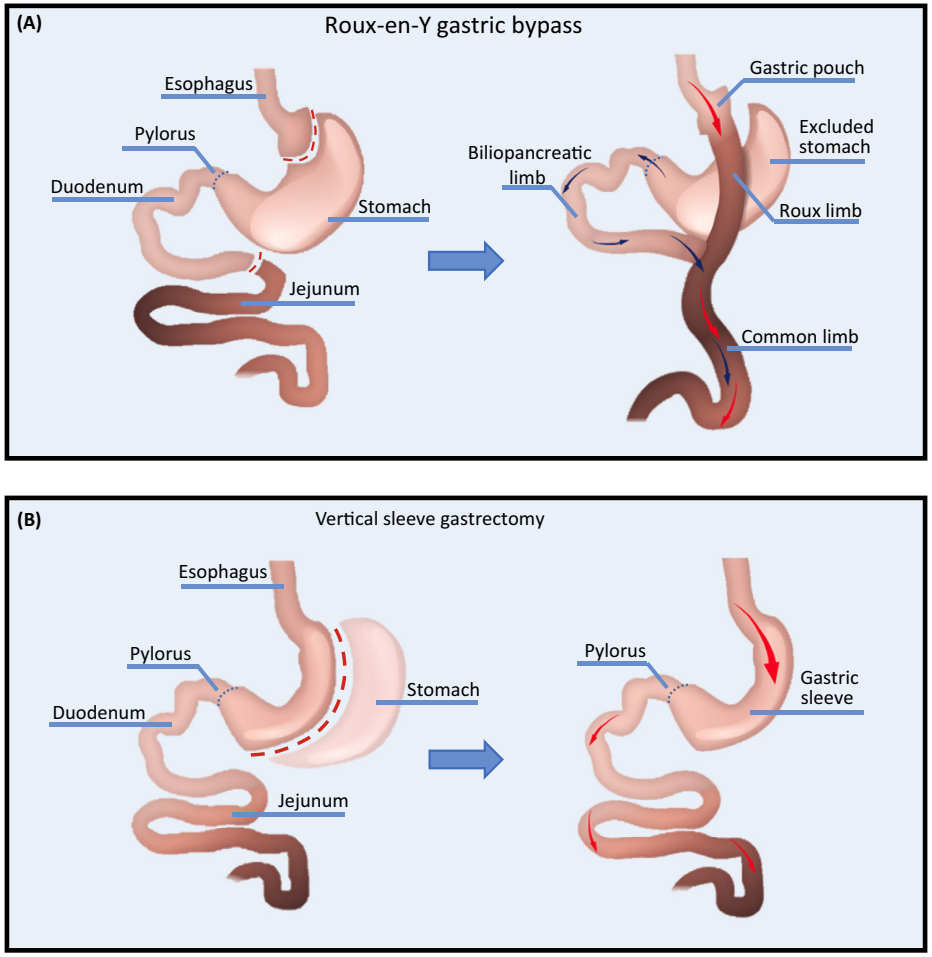
Note: Rollo (1797), Athinarayanan (2019)

For some time weight loss has been considered the primary mechanism of T2D remission due to bariatric surgery – only recently, the role of incretin hormones (GIP/GLP-1) received more attention.

Review

Intestinal Adaptations after Bariatric Surgery: Consequences on Glucose Homeostasis

Jean-Baptiste Cavin,[1] André Bado,[1] and Maude Le Gall[1,*]



Note: Cavin (2017)

Within one week of RYGB surgery, well before any significant weight loss, GLP-1 goes up and GIP plummets, as nutrients – incl. glucose – cannot be absorbed in the bypassed upper gastrointestinal tract.

Research Article

Effect of Modified Roux-en-Y Gastric Bypass Surgery on GLP-1, GIP in Patients with Type 2 Diabetes Mellitus

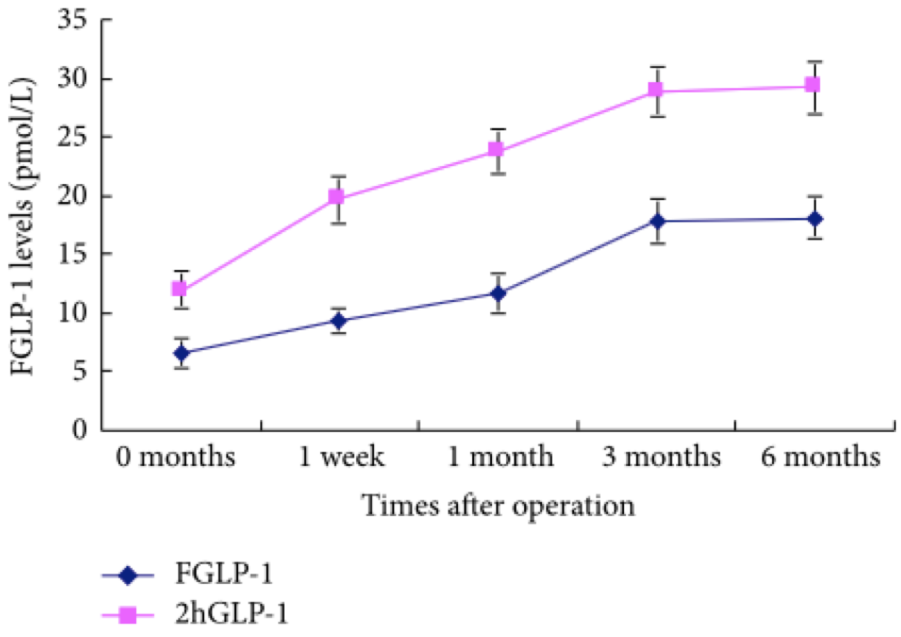


Figure 1: FGLP-1 levels before and after the surgery.

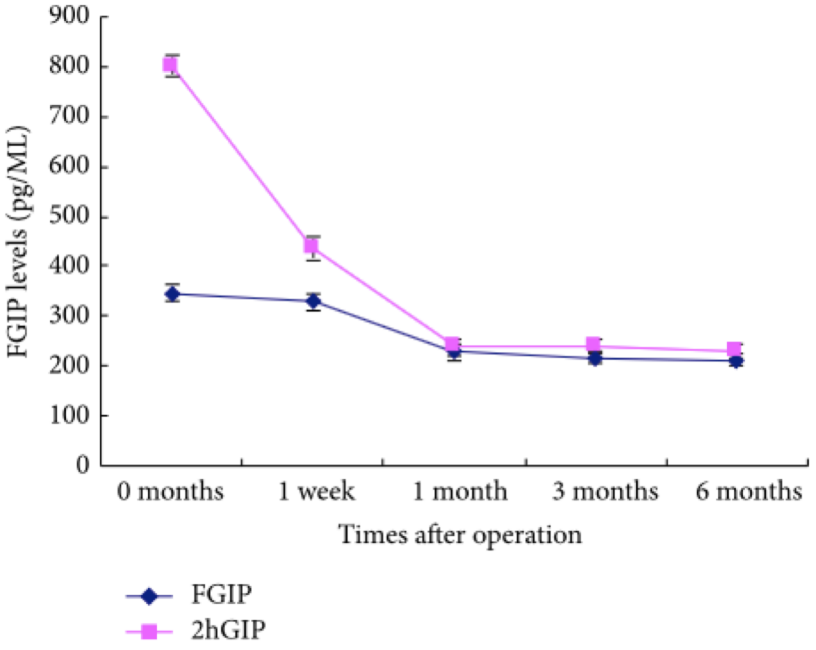
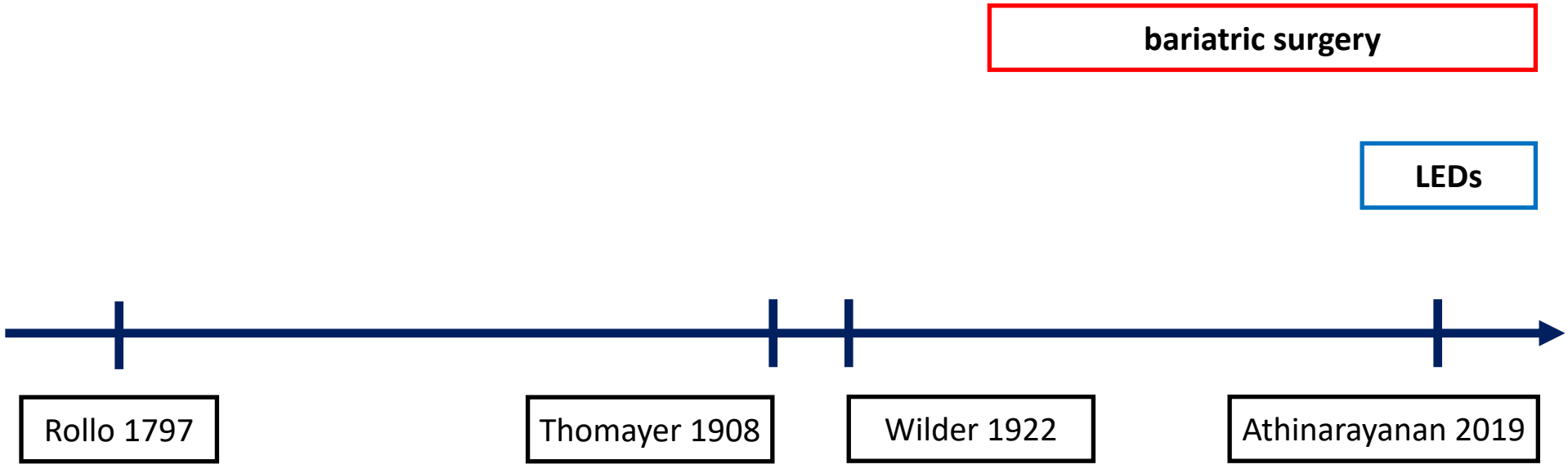


Figure 2: FGIP levels before and after the surgery.

Note: Xiong (2015)

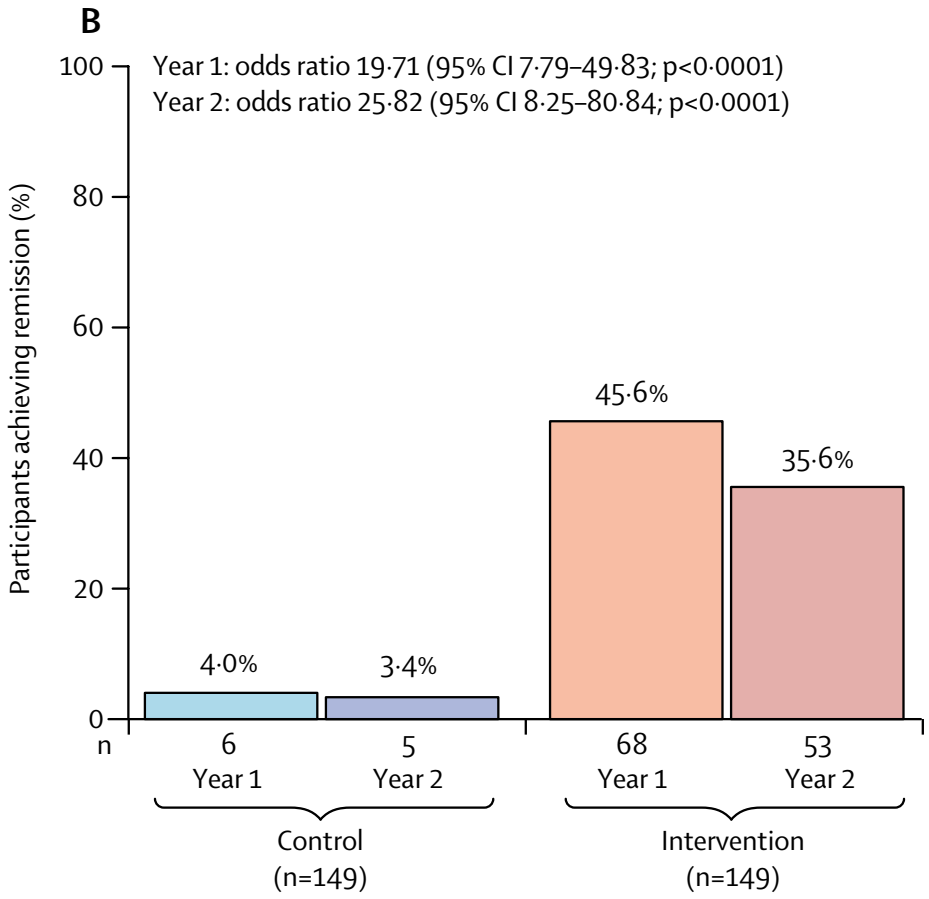
8 The Newcastle/Glasgow Way

Beginning in 2011, a series of experiments with low energy formula diets eventually led to excellent weight loss and T2D remission results in the DiRECT trial – 36% remission rate at Year 2.



Note: Rollo (1797), Athinarayanan (2019)

DiRECT trial, based on a total diet replacement for 3-5 months, followed by gradual food reintroduction and a structured support for weight loss maintenance, demonstrated excellent T2D remission results.



Procedures

The intervention programme (Counterweight-Plus), delivered entirely within a routine primary care setting by a trained NHS dietitian or nurse (as available locally), consisted of total diet replacement (825–853 kcal per day formula diet) for 3–5 months (flexible duration to allow for individual goals and circumstances), stepped food reintroduction (6–8 weeks), and then structured support for weight-loss maintenance.[12] For the maintenance phase,

Note: FIgure 2 in Lean (2019)

For weight loss maintenance, DiRECT investigators explicitly recommended low carbohydrate diet as one of the options.

Summary

1. A single cause of common type 2 diabetes can be postulated
2. Type 2 diabetes appears to be caused by reversible de-differentiation of beta cells following excess fat exposure in those susceptible
3. Heterogeneity lies in the individuals, not the basic mechanism of disease
4. Evidence-based means of achieving 15% weight loss in clinical practice are described
5. Low-carbohydrate, Mediterranean and intermittent-fasting diets have an evidence base to justify use to minimise weight regain
6. A supportive approach to these dietary strategies in routine care is required to maximise favourable long-term outcomes

Note: Taylor (2018)

9 Ketogenic diets – back to Rollo?

Virta Health has recently published two year results of their telehealth intervention including nutritional ketosis with n=262 participants on ketogenic diet and n=87 participant in usual care.

Long-Term Effects of a Novel Continuous Remote Care Intervention Including Nutritional Ketosis for the Management of Type 2 Diabetes: A 2-Year Non-randomized Clinical Trial

Shaminie J. Athinarayanan[1], Rebecca N. Adams[1], Sarah J. Hallberg[1,2], Amy L. McKenzie[1], Nasir H. Bhanpuri[1], Wayne W. Campbell[3], Jeff S. Volek[1,4], Stephen D. Phinney[1] and James P. McCarter[5]

Materials and methods: An open label, non-randomized, controlled study with 262 and 87 participants with T2D were enrolled in the CCI and usual care (UC) groups, respectively. Primary outcomes were retention, glycemic control, and weight changes at 2 years. Secondary outcomes included changes in body composition, liver, cardiovascular, kidney, thyroid and inflammatory markers, diabetes medication use and disease status.

Note: Athinarayanan (2019)

With less than 30 grams of carbohydrate and 1.5 grams of protein per kilogram of target weight per day, subjects lost significant amount of weight, supported by an online app and remote care team.

What does the Virta Treatment include?



Medical Supervision

A metabolic health specialist provides continuous medical supervision, check-ups, and safe medication reductions.



Personal Health Coach

A nutrition and behavior expert answers your questions, helps you form habits, and keeps you accountable.



Individualized Treatment Plan

Measuring blood glucose, ketones, weight, and more helps us personalize the Virta Treatment to your individual biochemistry.



A Clinic in Your Pocket

Our easy-to-use mobile and desktop app provides immediate access to care—no waiting rooms and no lines.



On-demand Resources

Learn the basics from a structured online curriculum, and access a library of recipes, guides, and meal plans for any dietary preference.



Private Virta Community

Connect with other Virta patients to find support and share tips in a positive, moderated environment.

Note: Virta Health (2019)

Unlike in DiRECT trial which excluded patients on insulin, 30% of Virta patients had been on insulin at baseline.

DIABETES MEDICATION		
Any diabetes medication, excluding metformin (%)		
CCI-all education	262	56.87 ± 3.07
Usual Care	87	66.67 ± 5.08
CCI-all vs. usual care		−9.80 ± 5.94
Sulfonylurea (%)		
CCI-all education	262	23.66 ± 2.63
Usual Care	87	24.14 ± 4.61
CCI-all vs. usual care		−0.47 ± 5.28
Insulin (%)		
CCI-all education	262	29.77 ± 2.83
Usual Care	87	45.98 ± 5.37
CCI-all vs. usual care		−16.21 ± 6.07

Note: Athinarayanan (2019)

At end of Year 2, 53% subjects reached reversal, 17% remission, and 6% complete remission. The control arm had 2 subjects in partial remission, and none in complete remission.

Diabetes Status

All within-group changes and between-group differences in diabetes status among the CCI and UC group participants appear in **Supplementary Table 4** (intent-to-treat analyses were conducted, all below ns = 262). The proportion of participants meeting the defined criteria for diabetes reversal at 2 years increased to 53.5% from baseline in the CCI group, whereas no change was observed in the UC group. Diabetes remission (partial or complete) was observed in 46 (17.6%) participants in the CCI group and two (2.4%) of the UC participants at 2 years.

Complete remission was observed in 17 (6.7%) CCI participants and none (0%) of the UC participants at 2 years.

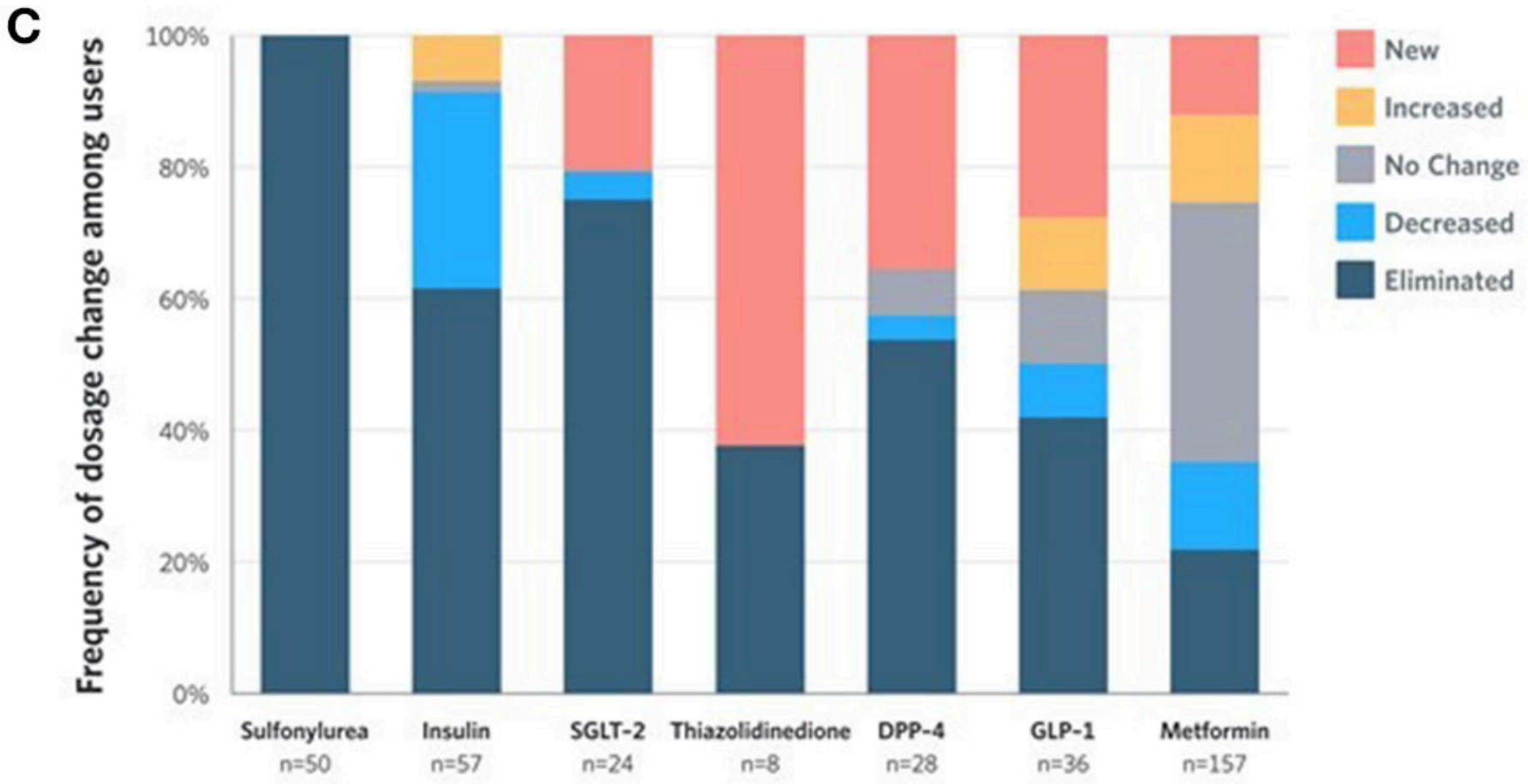
Note: Athinarayanan (2019)

Average insulin dose in the ketogenic arm (all patients on insulin at baseline) dropped by 81% from 82 to 15 IUs. In those who remained on insulin at Year 2, the average insulin dose dropped by 61% (104 to 40).

Within the CCI, reduction in glycemia occurred concurrently with reduced medication use (**Supplementary Table 3**). The proportion of CCI completers taking any diabetes medication (excluding metformin) decreased at 2 years (**Figure 3A**). The mean dose among CCI participants prescribed insulin at baseline decreased by 81% at 2 years (from 81.9 to 15.5 U/day), but not among UC participants (+13%; from 96.6 to 109.3 U/day) (**Figure 3B**). For participants who remained insulin-users at 2 years, mean dose also decreased in the CCI by 61% (from 104.3 to 40.2 U/day, $P = 9.2 \times 10^{-5}$) but not in UC participants (+19% from 103.8 to 123.5 U/day, $P = 0.29$). Among completers

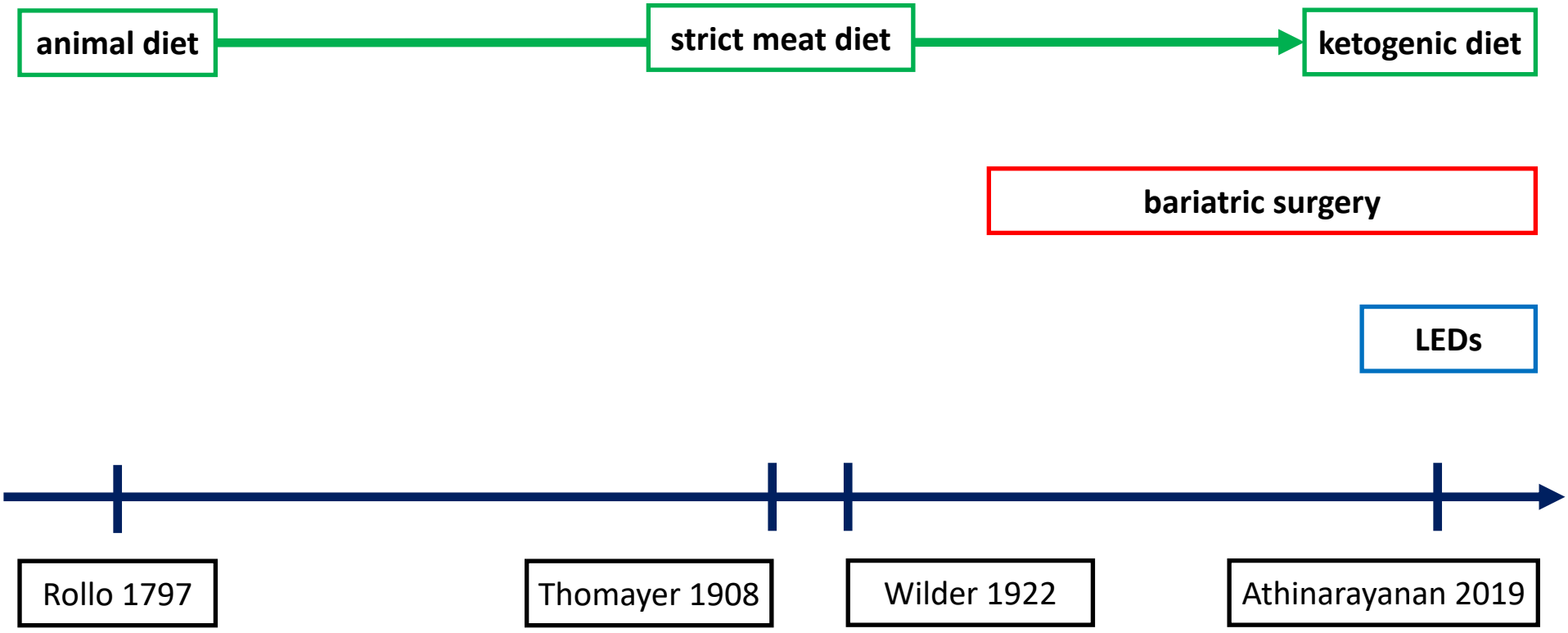
Note: Athinarayanan (2019)

60% of patients on ketogenic diet who used insulin at baseline (n=57) eliminated insulin, and further 30% reduced their insulin dose. All sulfonylureas gone.



Note: Athinarayanan (2019)

Rollo's basic concept of an animal diet made it through two centuries all the way to an animal food based ketogenic diet, picked up some non-starchy vegetables and demonstrated great results for T2D remission.



Note: Rollo (1797), Athinarayanan (2019)

10 Prevention

Low energy diets led to a remission of prediabetes in 35% of subjects within 8 weeks.

ORIGINAL ARTICLE

Men and women respond differently to rapid weight loss: Metabolic outcomes of a multi-centre intervention study after a low-energy diet in 2500 overweight, individuals with pre-diabetes (PREVIEW)

Pia Christensen PhD[1] | Thomas Meinert Larsen PhD[1] | Margriet Westerterp-Plantenga PhD[2] | Ian Macdonald PhD[3] | J. Alfredo Martinez PhD[4,5,6] | Svetoslav Handjiev PhD[7] | Sally Poppitt PhD[8] | Sylvia Hansen MSc[9] | Christian Ritz PhD[1] | Arne Astrup DMSc[1] | Laura Pastor-Sanz PhD[1] | Finn Sandø-Pedersen MSc[1] | Kirsi H. Pietiläinen PhD[10,11] | Jouko Sundvall MSc[12] | Mathijs Drummen MSc[13] | Moira A. Taylor PhD[14] | Santiago Navas-Carretero PhD[4,5] | Teodora Handjieva-Darlenska PhD[7] | Shannon Brodie APD[15] | Marta P. Silvestre PhD[8] | Maija Huttunen-Lenz PhD[9] | Jennie Brand-Miller PhD[15] | Mikael Fogelholm ScD[16] | Anne Raben PhD[1]

Note: Christensen (2018)

Reduced carbohydrate higher protein weight loss diets showed 100% remission rate as measured by OGTT.

Remission of pre-diabetes to normal glucose tolerance in obese adults with high protein versus high carbohydrate diet: randomized control trial

Frankie B Stentz,[1] Amy Brewer,[1] Jim Wan,[2] Channing Garber,[1] Blake Daniels,[1] Chris Sands,[1] Abbas E Kitabchi[1]

Conclusions: This is the first dietary intervention feeding study, to the best of our knowledge, to report 100% remission of pre-diabetes with a HP diet and significant improvement in metabolic parameters and anti-inflammatory effects compared with a HC diet at 6 months.

Note: Stentz (2016)

Maintaining healthy body composition in the context of healthy diet and lifestyle seems to be the way forward. Easier said than done?

Review

Dietary Interventions for the Prevention of Type 2 Diabetes in High-Risk Groups: Current State of Evidence and Future Research Needs

Nicola D. Guess

Department of Nutritional Sciences, King's College London, 150 Stamford Street, Room 4.13, London SE1 9NH, UK; Nicola.Guess@kcl.ac.uk; Tel.: +44-(0)20-7848-4356

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Abstract: A series of large-scale randomised controlled trials have demonstrated the effectiveness of lifestyle change in preventing type 2 diabetes in people with impaired glucose tolerance. Participants in these trials consumed a low-fat diet, lost a moderate amount of weight and/or increased their physical activity. Weight loss appears to be the primary driver of type 2 diabetes risk reduction, with individual dietary components playing a minor role. The effect of weight loss via other dietary approaches, such as low-carbohydrate diets, a Mediterranean dietary pattern, intermittent fasting or very-low-energy diets, on the incidence of type 2 diabetes has not been tested.

Note: Guess (2018)

1. Making key bits of information accessible to healthcare professionals and patients.
2. Increasing the number of remissions – eg. Virta aims for 100M by 2025.
3. Reducing the number of patients (incl. with prediabetes) who develop Type 2 Diabetes
4. Greater role for technology to improve results and sustainability
5. A series of trials looking into whole-food based low energy diets as an alternative to total diet replacement.



Note: JV

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Email: jan.vyjidak@gmail.com

Twitter: @janvyjidak

Facebook: jan.vyjidak.5

Web: www.janvyjidak.com, www.neslazeno.cz