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Insulin resistance and high carbohydrate diets cause the majority of “chronic diseases of lifestyle”: Implications for the health industry

Timothy David Noakes

OMS, MBChB, MD, DSc, PhD (hc), FACSM, (hon) FFSEM (UK), (hon) FFSEM (Ire)

@ProfTimNoakes

The Noakes Foundation

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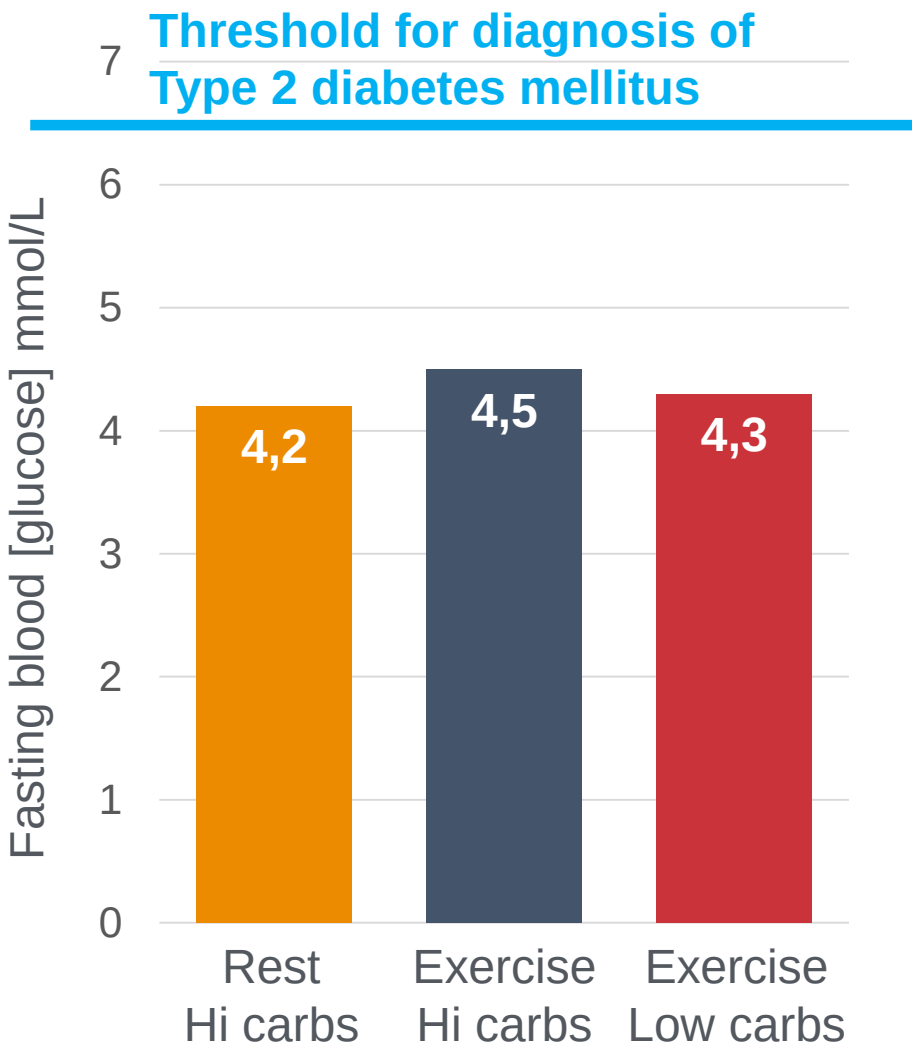
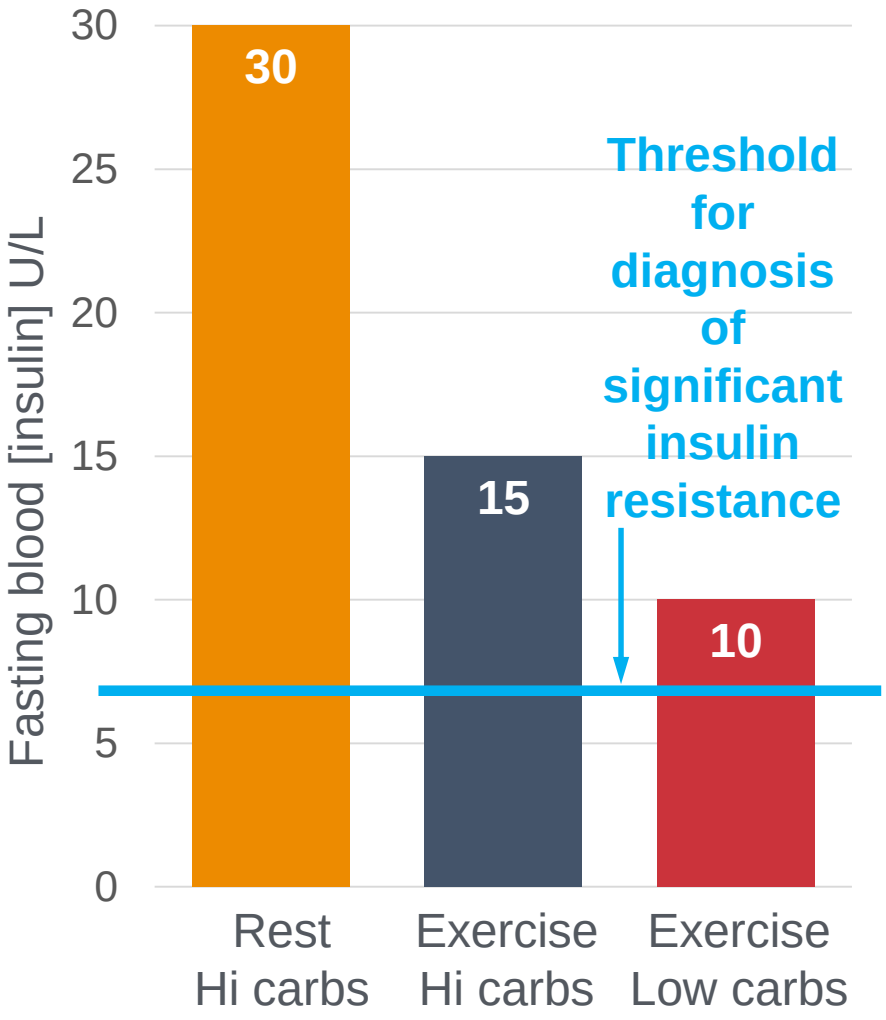
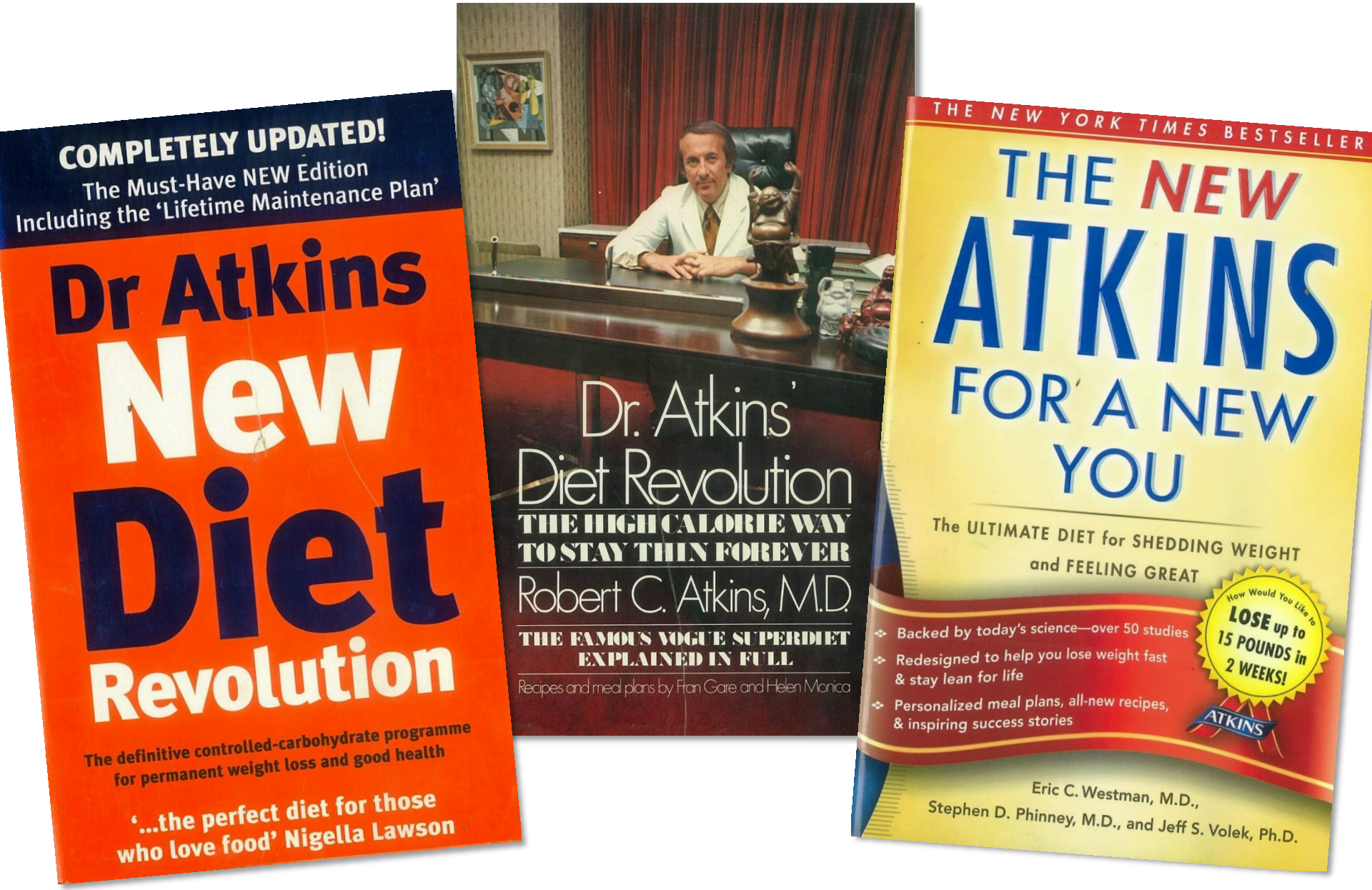
SECTION COLLOQUIUM 2019

THE NOAKES FOUNDATION

THE 28 YEAR OLD TIM NOAKES IS A WALKING T2DM TIME BOMB WITH PROFOUND INSULIN RESISTANCE







JONNO PROUDFOOT - DAVID GRIER - PROF TIM NOAKES -

The Real Meal Revolution is one of the sources of dietary information used by the Virta Health company whose goal is to ”reverse” type 2 diabetes mellitus in 100 million persons by the year 2015.

GREEN is an all-you-can-eat list – you can choose anything you like without worrying about the carbohydrate content as all the foods will be between 0 to 5g/100g. It will be almost impossible to overdo your carbohydrate intake by sticking to this group of foods. Over-eating protein is not recommended, so eat a moderate amount of animal protein at each meal. Include as much fat as you are comfortable with – bearing in mind that Banting is high in fat. Caution: even though these are all-you-can-eat foods, only eat when hungry, stop when full and do not overeat. The size and thickness of your palm without fingers is a good measure for a serving of animal protein.

ANIMAL PROTEIN (unless these have a rating, they are all 0g/100g)

All meat, poultry and game
All eggs
All offal
All natural and cured meats (pancetta, parma ham, coppa etc)
All natural and cured sausages (salami, chorizo etc)
All seafood (except swordfish and tilefish – high mercury content)
Broths

FATS

Avocado oil
Butter
Cheese – firm, natural, full-fat, aged cheeses (not processed)
Coconut oil
Duck fat
Ghee
Lard
Macadamia oil
Full-fat mayonnaise (not from seed oils – see recipe for coconut mayo in "Basics")
Olive oil
Any rendered animal fat

NUTS AND SEEDS

Almonds
Flaxseeds (watch out for pre-ground flaxseeds, they go rancid quickly and become toxic)
Macadamia nuts
Pecan nuts
Pine nuts
Pumpkin seeds
Sunflower seeds
Walnuts

VEGETABLES

Cauliflower
Broccoli
Pumpkin
Courgettes
Aubergines
Tomatoes
Asparagus
Avocado
Artichoke hearts
Brussels sprouts
Celery
Cabbage
Peppers
Spring onions
Leeks
Onions
Olives
Radishes
Mushrooms
Sauerkraut
All green leafy vegetables (spinach, cabbage, lettuces etc)
Any other vegetables grown above the ground

SWEETENERS

Stevia powder
Xylitol granules
Erythritol granules

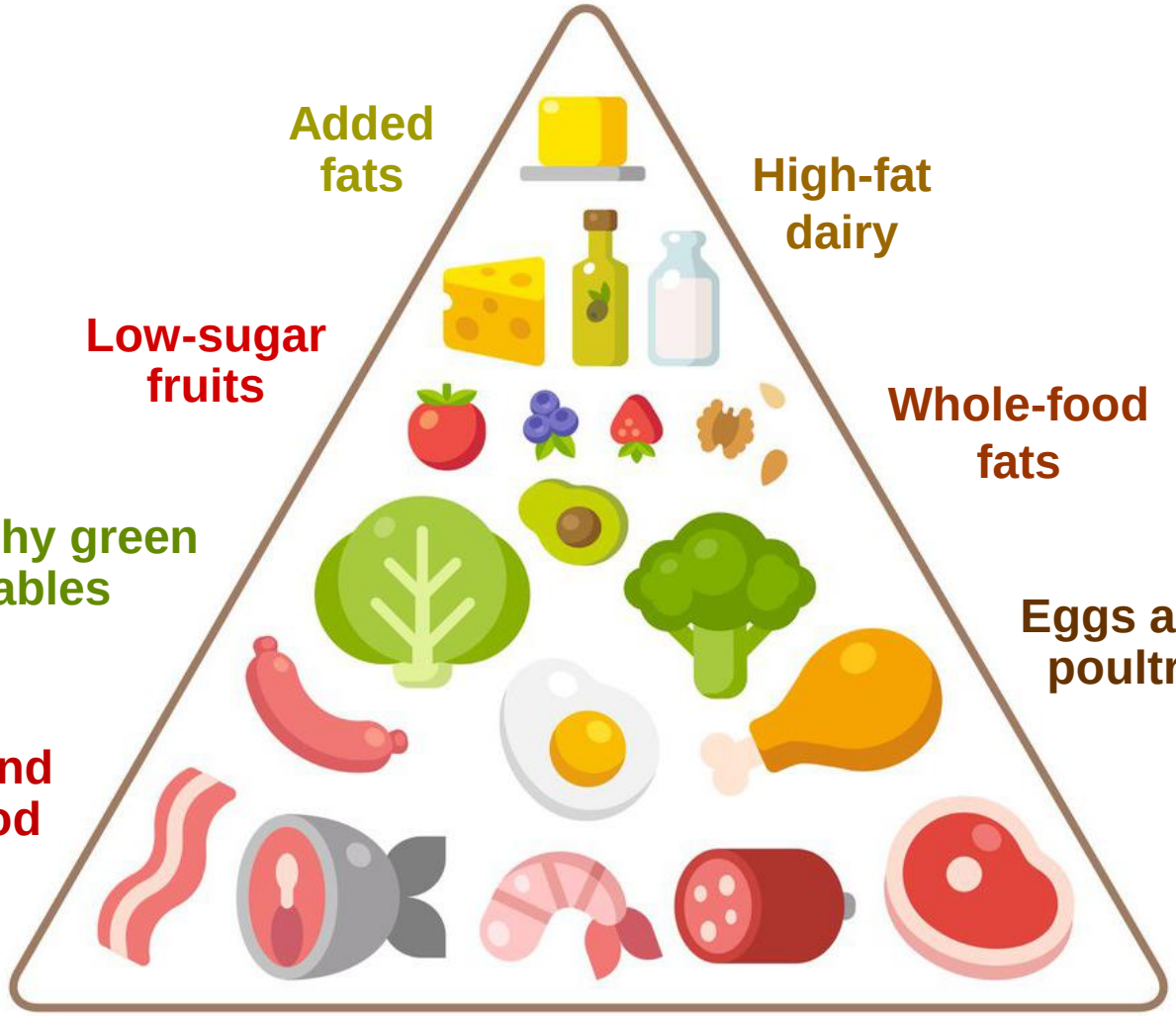
BEVERAGES

Spirits
Dry wines
Coffees and teas
Water

FLAVOURINGS AND CONDIMENTS

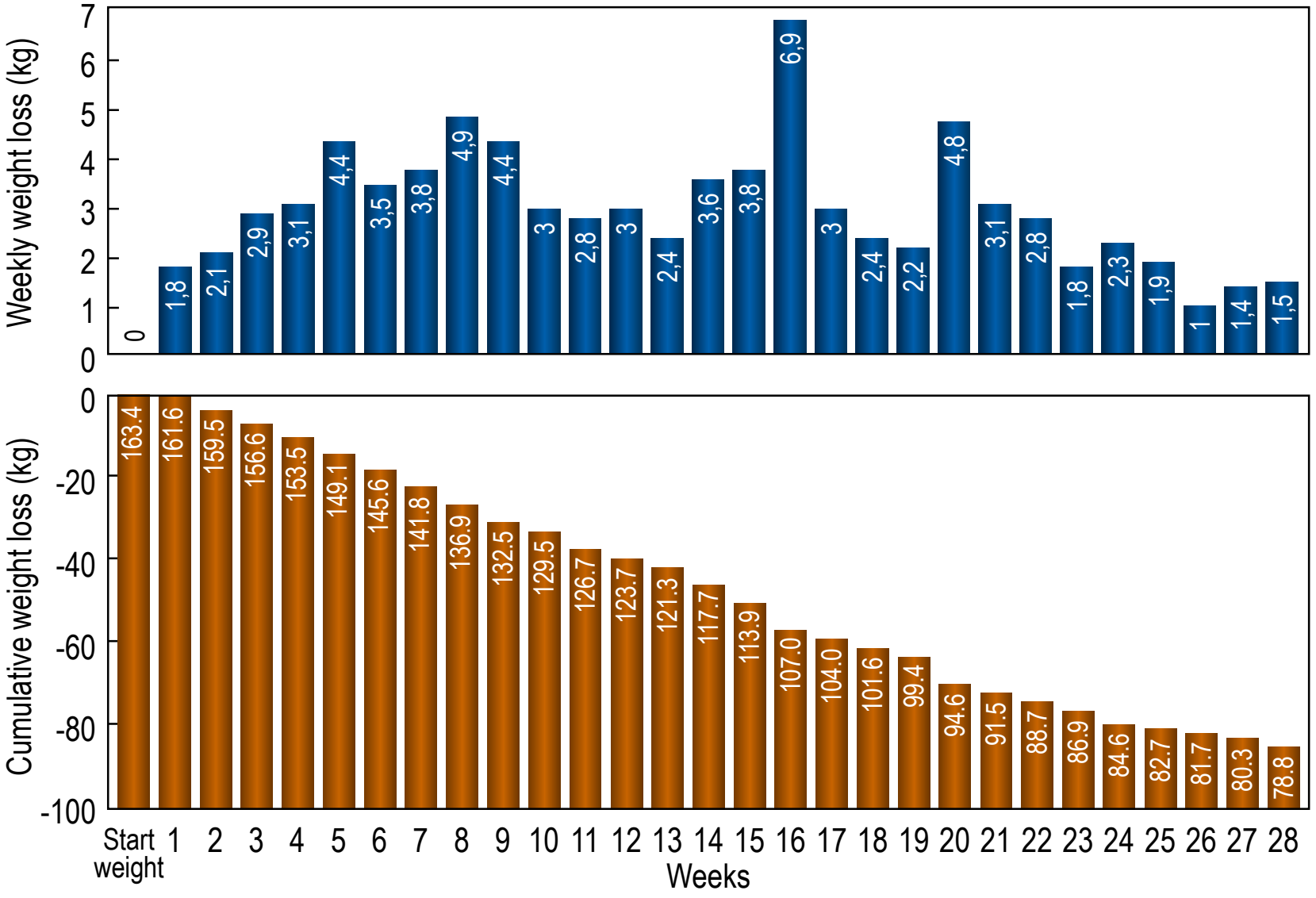
All flavourings and condiments are okay, including lemon and lime juice, provided they do not contain sugars and preservatives or vegetable oils.

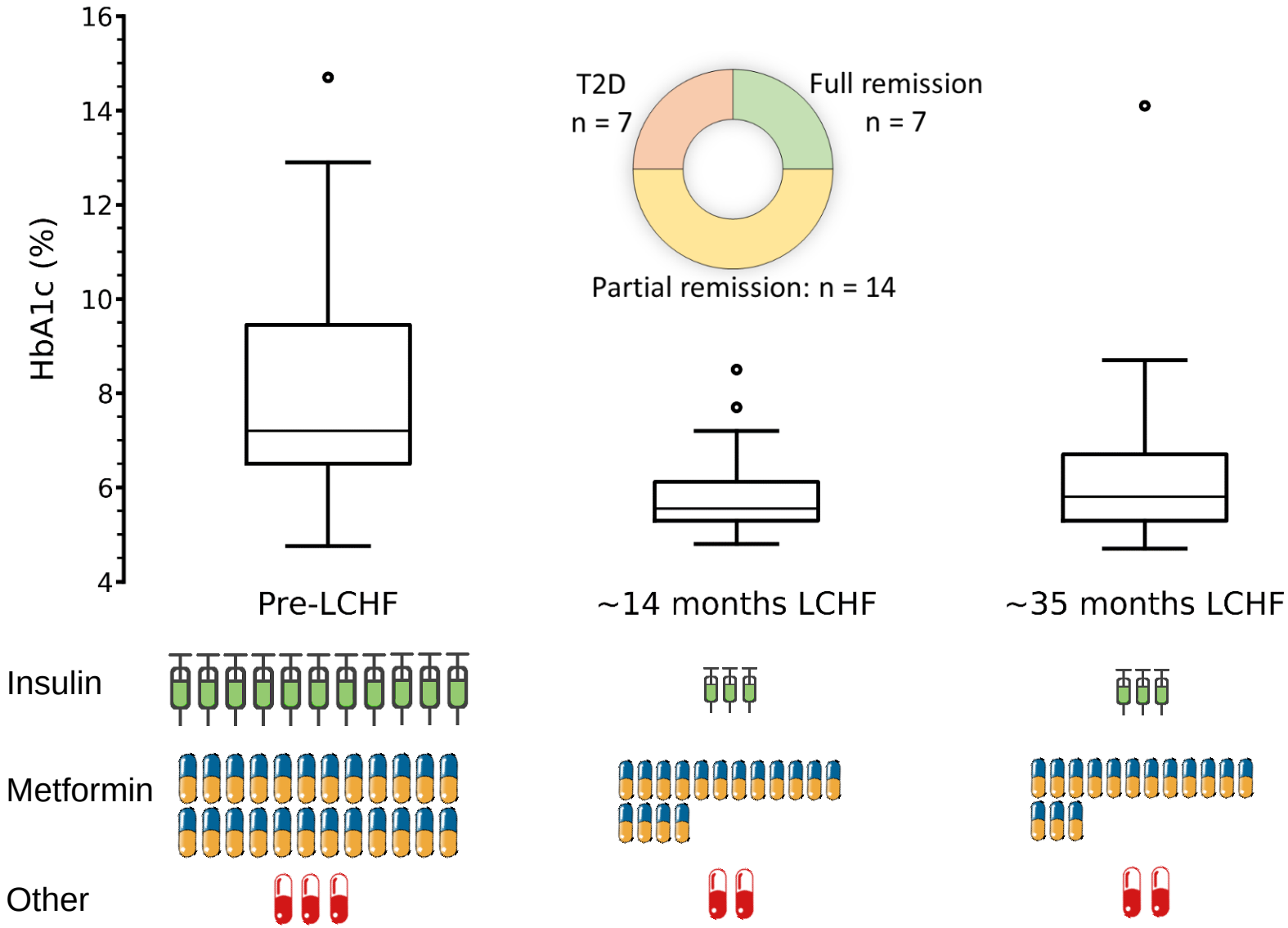
THE NOAKES FOUNDATION



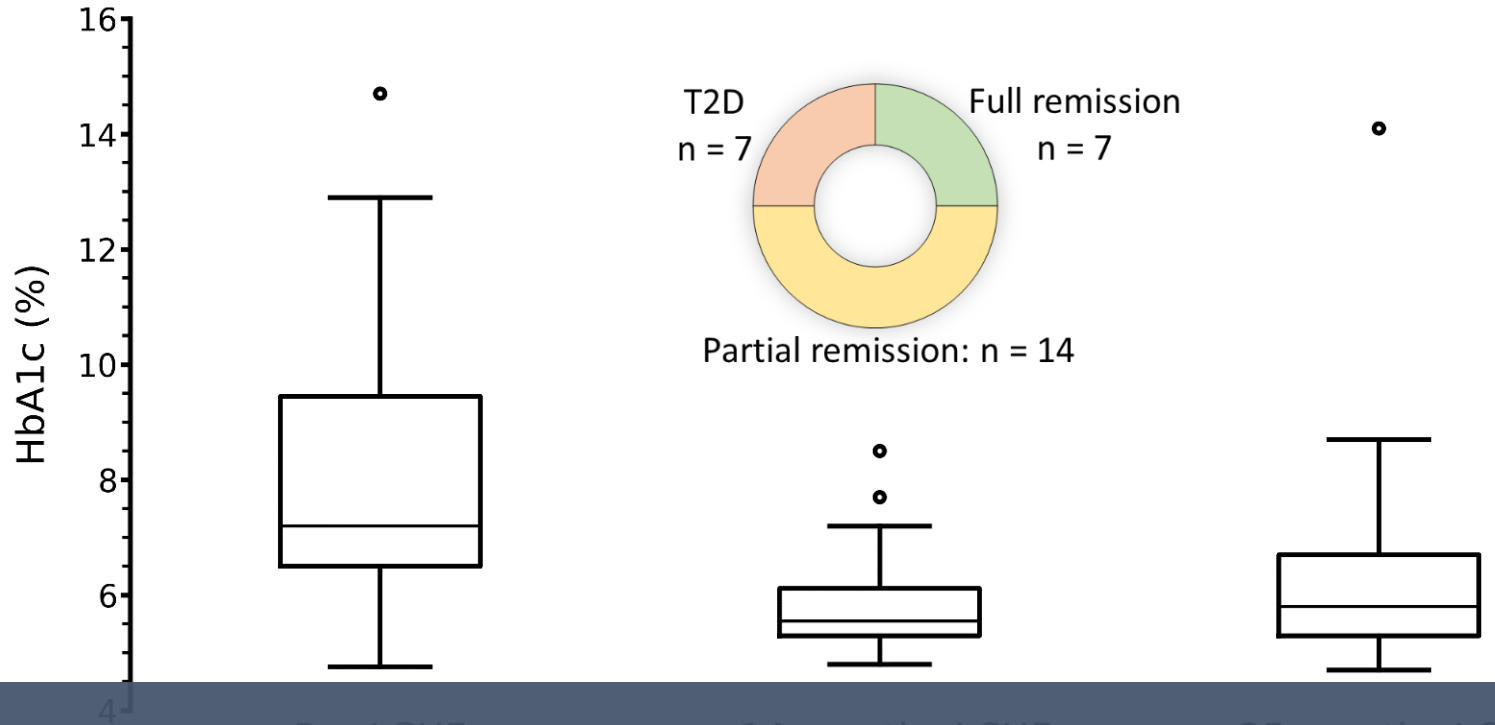
EXCLUDE:

WEIGHT LOSS IN 44 YEAR OLD MALE





HbA1c and number of participants taking insulin, metformin or other T2D medications (symbols). Relative size of medication symbols indicates average dose. Pie chart: Proportion of participants achieving complete or partial T2D remission at first assessment.

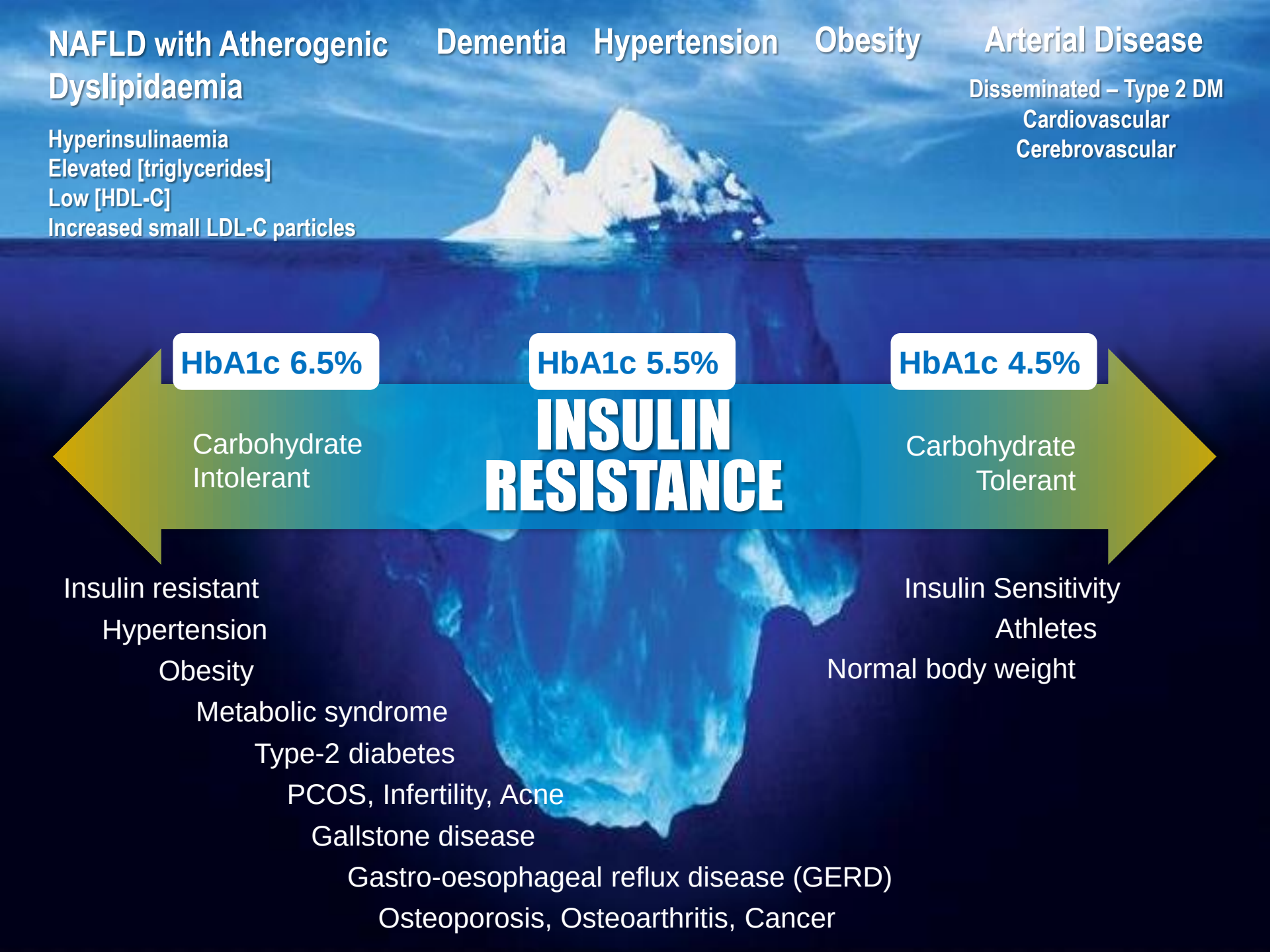


75% of this highly selected group of persons with T2DM were able to put their diabetes "into remission" as a result of information they received from books, the internet, social media and other persons with T2DM.

Sami Inkinen and Virta Health represent the future of medical care of chronic disease

Goals

- **To reverse diabetes in 100 million persons with T2DM by 2025**
- **For Virta Health to become the Amazon of medical care**


NAFLD with Atherogenic Dyslipidaemia
Hyperinsulinaemia
Elevated [triglycerides]
Low [HDL-C]
Increased small LDL-C particles
Dementia
Hypertension
Obesity
Arterial Disease
Disseminated – Type 2 DM
Cardiovascular
Cerebrovascular
HbA1c 6.5%
HbA1c 5.5%
HbA1c 4.5%
INSULIN RESISTANCE
Carbohydrate Intolerant
Carbohydrate Tolerant
Insulin resistant
Hypertension
Obesity
Metabolic syndrome
Type-2 diabetes
PCOS, Infertility, Acne
Gallstone disease
Gastro-oesophageal reflux disease (GERD)
Osteoporosis, Osteoarthritis, Cancer
Insulin Sensitivity
Athletes
Normal body weight

Gerald M. Reaven, MD: Demonstration of the Central Role of Insulin Resistance in Type 2 Diabetes and Cardiovascular Disease

Fredric B. Kraemer[1] *and Henry N. Ginsberg*[2]

Diabetes Care 2014;37:1178–1181 | DOI: 10.2337/dc13-2668

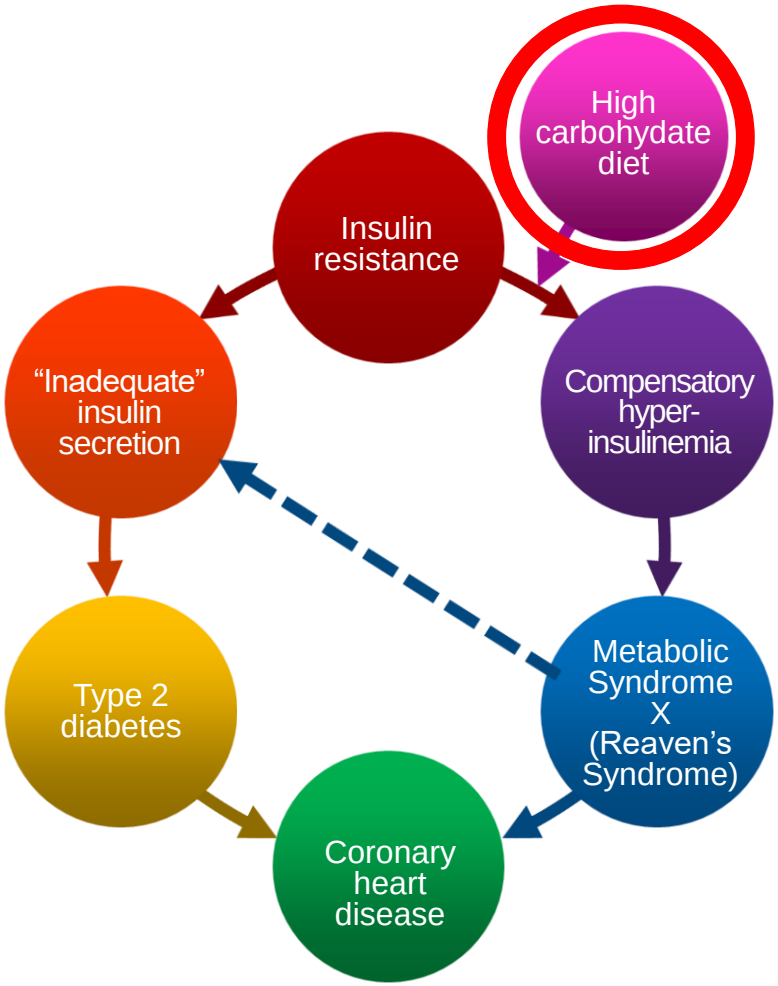
Gerald M. Reaven, MD, could easily be epitomized as the "Father of Insulin Resistance." (For those who do not know Dr. Reaven, he would humbly raise objection to being called Dr. Reaven rather than Jerry.) That said, Jerry is credited with developing the insulin suppression test, the first quantitative method to measure insulin-mediated glucose uptake in humans (1). Using this technique, he established the importance of insulin resistance in human disease, and importantly, in type 2 diabetes (2,3). In nondiabetic individuals, he demonstrated the role of insulin resistance/compensatory group of clinical abnormalities, initially designated Syndrome X, is an important factor leading to cardiovascular disease. Syndrome X was introduced to the medical community in his now famous Banting Lecture in 1988 (13) and only later became known as metabolic syndrome.

Jerry was born in Gary, IN, on 28 July 1928, but spent most of his precollege years living in Cleveland, OH, thus accounting for his lifelong allegiance to the Cleveland Indians baseball team and a great deal of frustration on his part during their many less-than-stellar seasons. Jerry matriculated at the Uni-

Gerald M. Reaven, MD

Eve were stationed in several locations in Europe, providing time for explora-

LINK BETWEEN INSULIN RESISTANCE & CORONARY HEART DISEASE



Weight gain
Atherogenic dyslipidaemia
Visceral adiposity
Endothelial dysfunction
Hypertension
Hyperuricemia
Systemic inflammation
Mitochondrial dysfunction
Impaired exercise performance

Increasing insulin resistance

Reaven G. Insulin resistance and CHD in non-diabetic subjects. Atheroscler Throm Vasc Biol 2012;32:1754-59

Deleterious Metabolic Effects of High-Carbohydrate, Sucrose-Containing Diets in Patients with Non-Insulin-Dependent Diabetes Mellitus

ANN M. COULSTON, M.S.
CLARIE B. HOLLENBECK, Ph.D.
ARTHUR L.M. SWISLOCKI, M.D.
Y-D. IDA CHEN, Ph.D.
GERALD M. REAVEN, M.D.
Stanford, California
and
Palo Alto, California

The effects of variations in dietary carbohydrate and fat intake on various aspects of carbohydrate and lipid metabolism were studied in patients with non-insulin-dependent diabetes mellitus (NIDDM). Two test diets were utilized, and they were consumed in random order over two 15-day periods. One diet was low in fat and high in carbohydrate, and corresponded closely to recent recommendations made by the American Diabetes Association (ADA), containing (as percent of total calories) 20 percent protein, 20 percent fat, and 60 percent carbohydrate, with 10 percent of total calories as sucrose. The other diet contained 20 percent protein, 40 percent fat, and 40 percent carbohydrate, with sucrose accounting for 3 percent of total calories. Although plasma fasting glucose and insulin concentrations were similar with both diets, incremental glucose and insulin responses from 8 a.m. to 4 p.m. were higher ($p < 0.01$), and mean (± SEM) 24-hour urine glucose excretion was significantly greater (55 ± 16 versus 26 ± 4 g/24 hours $p < 0.02$) in response to the low-fat, high-carbohydrate diet. In addition, fasting and postprandial triglyceride levels were increased ($p < 0.001$ and $p < 0.05$, respectively) and high-density lipoprotein (HDL) cholesterol concentrations were reduced ($p < 0.02$) when patients with NIDDM ate the low-fat, high-carbohydrate diet. Finally, since low-density lipoprotein (LDL) concentrations did not change with diet, the HDL/LDL cholesterol ratio fell in response to the low-fat, high-carbohydrate diet. These results document that low-fat, high-carbohydrate diets, containing moderate amounts of sucrose, similar in composition to the recommendations of the ADA, have deleterious metabolic effects when consumed by patients with NIDDM for 15 days. Until it can be shown that these untoward effects are evanescent, and that long-term ingestion of similar diets will result in beneficial metabolic changes, it seems prudent to avoid the use of low-fat, high-carbohydrate diets containing moderate amounts of sucrose in patients with NIDDM.

From the Department of Medicine, Stanford University School of Medicine Stanford, California, and Geriatric Research, Education and Clinical Center, Veterans Administration Medical Center, Palo Alto, California. This was supported by grants from the Research Service of the Veterans Administration, National Institutes of Health (RR-70-22, HL-08506, AM-07217), and the Nora Eccles Treadwell Foundation. Requests for reprints should be addressed to Dr. Gerald M. Reaven, Veterans Administration Medical Center, (GRECC 640/182B), 3801 Miranda Avenue, Palo Alto, California 94304. Manuscript submitted December 12, 1985, and accepted May 20, 1986.

Along with the recent emphasis on improved glycemic control and the use of home blood glucose monitoring in patients with diabetes has been renewed interest in the composition of the diabetic diet. In particular, attention has been focused on dietary manipulations aimed at reducing the risk of coronary artery disease in patients with diabetes. Although there can be no disagreement with this goal, we are concerned about the means currently being advocated to accomplish this task. The American Diabetes Association (ADA) has followed the lead of the American Heart Association [1] in recommending that dietary carbohydrate content be

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doi: 10.2337/diacare.12.2.94
Diabetes Care **February 1989** vol. 12 no. 2 **94-101**

Persistence of Hypertriglyceridemic Effect of Low-Fat High-Carbohydrate Diets in NIDDM Patients

Ann M Coulston, MS, RD, Clarie B Hollenbeck, PhD, Arthur L M Swislocki, MD and Gerald M Reaven, MD

+ Author Affiliations

Address correspondence and reprint requests to Gerald M. Reaven, MD, Veterans Administration Medical Center, GRECC/182B, 3801 Miranda Avenue, Palo Alto, CA 94304.

Abstract

Although low-fat high-carbohydrate diets are recommended for patients with non-insulin-dependent diabetes mellitus (NIDDM) in an effort to reduce the risk of coronary artery disease (CAD), the results of short-term studies have shown that these diets can lead to changes in carbohydrate and lipid metabolism associated with an increased risk of CAD. This study has extended these earlier observations by determining the metabolic effects of such diets over a longer period in these patients. The comparison diets contained either 40 or 60% of the total calories as carbohydrates, with reciprocal changes in fat content from 40 to 20% consumed in random order for 6 wk in a crossover experimental design. The ratio of polyunsaturated to saturated fat and the total cholesterol intake were held constant in the two diets. Plasma glucose and insulin concentrations were significantly ($P < .001$) elevated throughout the day when patients consumed the 60% carbohydrate diet, and 24-h urinary glucose excretion more than doubled (0.8 vs. 1.8 mol/24 h). Fasting plasma total and very-low-density lipoprotein (VLDL) triglyceride (TG) concentrations increased by 30% ($P < .001$) after 1 wk on the 60% carbohydrate diet, and the magnitude of carbohydrate-induced hypertriglyceridemia persisted unchanged throughout the 6-wk study period. Total plasma cholesterol concentrations were similar after both diets. However, VLDL cholesterol (VLDL-chol) was significantly increased, whereas both low-density lipoprotein (LDL-) and high-density lipoprotein (HDL-) chol concentrations were significantly decreasedafter consumption of the 60% carbohydrate diet. Consequently, neither total-chol-to-HDL-chol nor LDL-chol-to-HDL-chol ratios changed. The results of this study indicate that high-carbohydrate diets lead to several changes in carbohydrate and lipid metabolism in patients with NIDDM that could lead to an increased risk of CAD, and these effects persist for >6 wk. Given these results, it seems reasonable to suggest that the routine recommendation of low-fat high-carbohydrate diets for patients with NIDDM be reconsidered.

JAMA The Journal of the American Medical Association

ARTICLE | May 11, 1994

Effects of Varying Carbohydrate Content of Diet in Patients With Non—Insulin-Dependent Diabetes Mellitus

Abhimanyu Garg, MBBS, MD; John P. Bantle, MD; Robert R. Henry, MD; Ann M. Coulston, RD; Kay A. Griver, RD; Susan K. Raatz, MS, RD; Linda Brinkley, RD; Y-D. Ida Chen, PhD; Scott M. Grundy, MD, PhD; Beverley A. Huet, MS; Gerald M. Reaven, MD

JAMA. 1994;271(18):1421-1428. doi:10.1001/jama.1994.03510420053034.

ABSTRACT

Objective. —To study effects of variation in carbohydrate content of diet on glycemia and plasma lipoproteins in patients with non—insulin-dependent diabetes mellitus (NIDDM).

Design. —A four-center randomized crossover trial.

Setting. —Outpatient and inpatient evaluation in metabolic units.

Patients. —Forty-two NIDDM patients receiving glipizide therapy.

Interventions. —A high-carbohydrate diet containing 55% of the total energy as carbohydrates and 30% as fats was compared with a high—monounsaturated-fat diet containing 40% carbohydrates and 45% fats. The amounts of saturated fats, polyunsaturated fats, cholesterol, sucrose, and protein were similar. The study diets, prepared in metabolic kitchens, were provided as the sole nutrients to subjects for 6 weeks each. To assess longer-term effects, a subgroup of 21 patients continued the diet they received second for an additional 8 weeks.

Main Outcome Measures. —Fasting plasma glucose, insulin, lipoproteins, and glycosylated hemoglobin concentrations. Twenty-four-hour profiles of glucose, insulin, and triglyceride levels.

Results. —The site of study as well as the diet order did not affect the results. Compared with the high—monounsaturated-fat diet, the high-carbohydrate diet increased fasting plasma triglyceride levels and very low-density lipoprotein cholesterol levels by 24% ($P<.0001$) and 23% ($P=.0001$), respectively, and increased daylong plasma triglyceride, glucose, and insulin values by 10% ($P=.03$), 12% ($P<.0001$), and 9% ($P=.02$), respectively. Plasma total cholesterol, low-density lipoprotein cholesterol, and high-density lipoprotein cholesterol levels remained unchanged. The effects of both diets on plasma glucose, insulin, and triglyceride levels persisted for 14 weeks.

Conclusions. —In NIDDM patients, high-carbohydrate diets compared with high—monounsaturated-fat diets caused persistent deterioration of glycemic control and accentuation of hyperinsulinemia, as well as increased plasma triglyceride and very-low-density lipoprotein cholesterol levels, which may not be desirable.(*JAMA*. 1994;271:1421-1428)

THREE CRITICAL STUDIES BY DR REAVEN IN THE 1980's.

These results document that low-fat, high-carbohydrate diets, containing moderate amounts of sucrose, similar in composition to the recommendations of the ADA, have deleterious metabolic effects when consumed by patients with NIDDM for 15 days. Until it can be shown that these untoward effects are evanescent, and that long-term ingestion of similar diets will result in beneficial metabolic changes, it seems prudent to avoid the use of low-fat, high-carbohydrate diets containing moderate amounts of sucrose in patients with NIDDM.

The results of this study indicate that high-carbohydrate diets lead to several changes in carbohydrate and lipid metabolism in patients with NIDDM that could lead to an increased risk of CAD, and these effects persist for >6 wk. Given these results, it seems reasonable to suggest that the routine recommendation of low-fat high-carbohydrate diets for patients with NIDDM be reconsidered.

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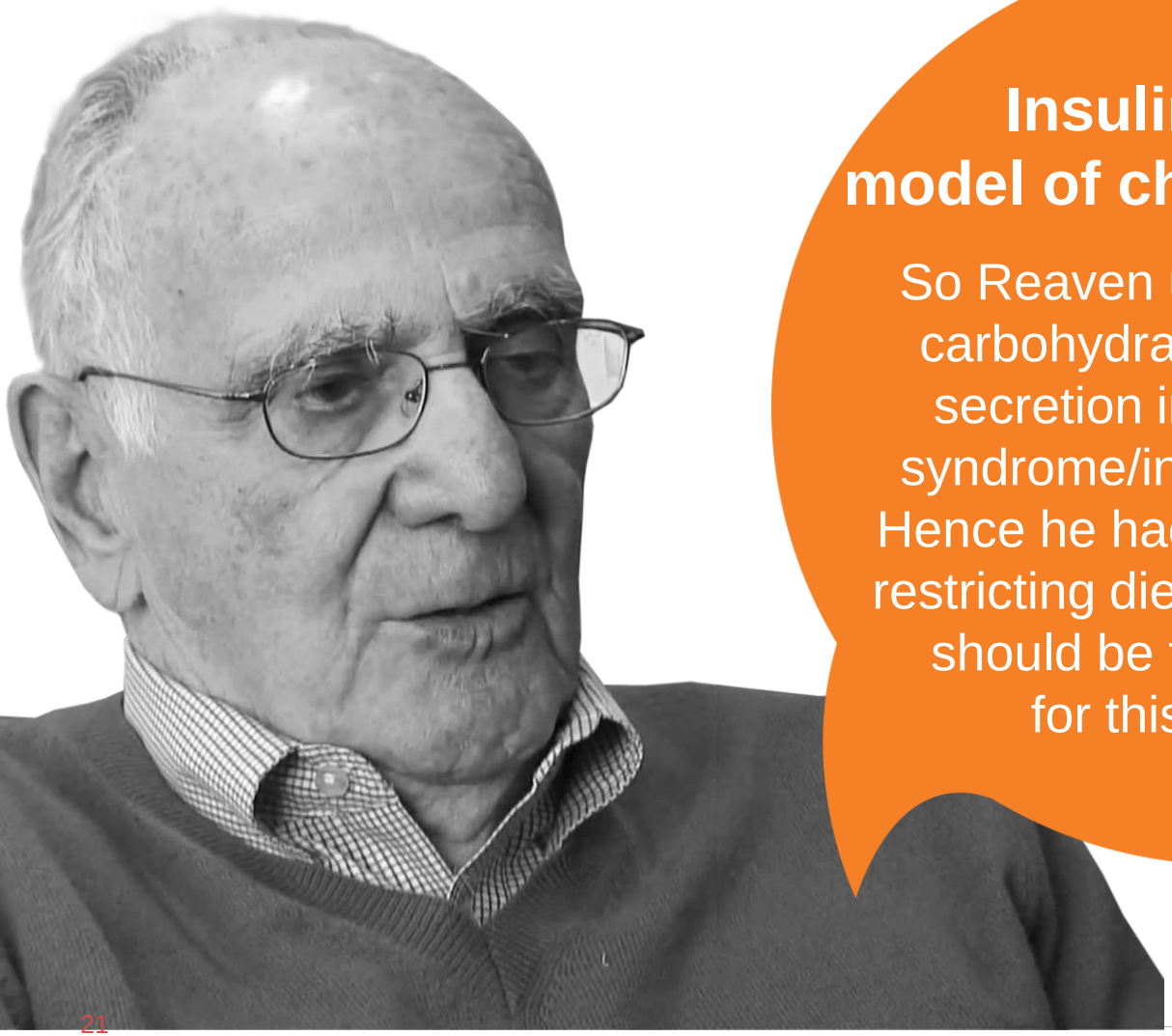
CARBOHYDRATE CONSUMPTION IN METABOLIC SYNDROME



Insulinocentric model of chronic ill health

So Reaven understands that carbohydrates drive insulin secretion in the metabolic syndrome/insulin resistance. Hence he had to conclude that restricting dietary carbohydrate should be the key therapy for this condition.

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ATVB in Focus
Metabolic Syndrome and Insulin Resistance:
Mechanisms and Consequences

Series Editor: Ann Marie Schmidt

Insulin Resistance and Coronary Heart Disease in Nondiabetic Individuals

Gerald Reaven

Abstract—The goal of this review was to summarize evidence supporting the view that insulin resistance/compensatory hyperinsulinemia play an important role in the pathogenesis of coronary heart disease (CHD) in nondiabetic individuals. Results of case–control and epidemiological studies in nondiabetic individuals will be reviewed to examine the link between insulin resistance/compensatory hyperinsulinemia, associated abnormalities, and CHD. The primary focus of the review will be on the central role that dyslipidemia plays in the link between insulin resistance/compensatory hyperinsulinemia and CHD. Additional issues to be addressed include the following: (1) the relationship among obesity, insulin resistance, and CHD; (2) a listing of other abnormalities that contribute to risk of CHD in insulin-resistant individuals; and (3) discussion of the importance of differential tissue insulin sensitivity in the development of abnormalities that increase CHD risk in insulin-resistant, nondiabetic individuals. The information will reflect the author's decision as to what issues are believed to be central to the relationship between insulin resistance and CHD. Resistance to insulin-mediated glucose disposal and hyperinsulinemia is a common finding in apparently healthy individuals and is associated with a number of abnormalities that greatly increase risk of CHD. (*Arterioscler Thromb*

Key Words: insulin ■ insulin resistance ■ coronary heart disease ■ hyperinsulinemia ■ atherogenic lipoproteins

A "healthy balanced diet" **must minimize insulin secretion at all times** in those with insulin resistance.

Original Article

Ten-Year Mortality in the WISE Study (Women's Ischemia Syndrome Evaluation)

Tanya S. Kenkre, PhD, MPH; Pankaj Malhotra, MD; B. Delia Johnson, PhD; Eileen M. Handberg, PhD; Diane V. Thompson, MS; Oscar C. Marroquin, MD; William J. Rogers, MD; Carl J. Pepine, MD; C. Noel Bairey Merz, MD; Sheryl F. Kelsey, PhD

Background—The WISE study (Women's Ischemia Syndrome Evaluation) was a prospective cohort study of 936 clinically stable symptomatic women who underwent coronary angiography to evaluate symptoms and signs of ischemia. Long-term mortality data for such women are limited.

Methods and Results—Obstructive coronary artery disease (CAD) was defined as ≥50% stenosis on angiography by core laboratory. We conducted a National Death Index search to assess the mortality of women who were alive at their final WISE contact date. Death certificates were obtained. All deaths were adjudicated as cardiovascular or noncardiovascular by a panel of WISE cardiologists masked to angiographic data. Multivariate Cox proportional hazards regression was used to identify significant independent predictors of mortality. At baseline, mean age was 58±12 years; 176 (19%) were non-white, primarily black; 25% had a history of diabetes mellitus, 59% hypertension, 55% dyslipidemia, and 59% had a body mass index ≥30. During a median follow-up of 9.5 years (range, 0.2–11.5 years), a total of 184 (20%) died. Of these, 115 (62%) were cardiovascular deaths; 31% of all cardiovascular deaths occurred in women without obstructive CAD (<50% stenosis). Independent predictors of mortality were obstructive CAD, age, baseline systolic blood pressure, history of diabetes mellitus, history of smoking, elevated triglycerides, and estimated glomerular filtration rate.

Conclusions—Among women referred for coronary angiography for signs and symptoms of ischemia, 1 in 5 died from predominantly cardiac pathogeneses within 9 years of angiographic evaluation. A majority of the factors contributing to the risk of death seem to be modifiable by existing therapies. Of note, 1 in 3 of the deaths in this cohort occurred in women without obstructive CAD, a condition often considered benign and without guideline-recommended treatments. Clinical trials are needed to provide treatment guidance for the group without obstructive CAD. (***Circ Cardiovasc Qual Outcomes*****. 2017;10:e003863. DOI: 10.1161/CIRCOUTCOMES.116.003863.)**

Key Words: acute coronary syndrome ■ coronary artery disease ■ ischemia ■ mortality ■ women

About 190 000 American women die each year from cardiovascular disease, predominately ischemic heart disease (IHD) and related conditions, and current projections indicate that this statistic will dramatically increase with our aging population.[1] In fact, since 1984, more women have died annually from IHD than men.[2] Notably, IHD is the leading killer of women at all ages, with annual mortality rates greater than all forms of cancers combined.[3]

Clear sex differences in presentation, pathophysiology, and management underscore the need for an increased understanding of IHD in women. For instance, pathology reports demonstrate a higher frequency of coronary plaque erosion and distal embolization as pathogenic in younger women as compared with plaque rupture in men.[4–6] A review of data from randomized acute coronary syndrome clinical trials suggest a higher 30-day mortality rate after acute coronary syndrome in women versus men, 9.6% versus 5.3% (odds ratio, 1.91; 95% confidence interval [CI], 1.83–2.00).[7] Furthermore, women who are symptomatic more often have persistent and refractory chest pain requiring more hospitalizations compared with men, accompanied by lower ratings of general well-being, and limitations in activities of daily living.[8,9] Interestingly, these adverse outcomes are experienced by women despite possessing lower syntax scores than males. A variety of reports document that across all ages and diagnoses, more than half of women with clinically stable symptoms presenting to coronary angiography do not have obstructive coronary artery disease (CAD),[10] for which evidence-based guidelines do not exist. Moreover, sex-related variability in medical care may contribute to a higher case fatality rate for IHD in women.[11] In women, IHD is relatively more expensive to treat than it is in men; resource consumption in females is characterized by

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From the Department of Epidemiology, Graduate School of Public Health, University of Pittsburgh, PA (T.S.K., B.D.J., O.C.M., S.F.K.); Barbra Streisand Women's Heart Center, Cedars-Sinai Heart Institute, Los Angeles, CA (P.M., C.N.B.M.); Division of Cardiovascular Medicine, College of Medicine, University of Florida, Gainesville (E.M.H., C.J.P.); Division of Cardiology, Department of Medicine, Allegheny General Hospital, Pittsburgh, PA (D.V.T.); Heart and Vascular Institute, University of Pittsburgh Medical Center, PA (O.C.M.); and Division of Cardiovascular Disease, School of Medicine, University of Alabama at Birmingham (W.J.R.).

Correspondence to Tanya S. Kenkre, PhD, MPH, Epidemiology Data Center, University of Pittsburgh, 4420 Bayard St, Suite 600, Pittsburgh, PA 15260. E-mail KenkreT@edc.pitt.edu

Circ Cardiovasc Qual Outcomes **is available at http://circoutcomes.ahajournals.org** **DOI: 10.1161/CIRCOUTCOMES.116.003863**

SIGNIFICANT INDEPENDENT PREDICTORS OF CARDIAC MORTALITY IN WISE

	n=748, 85 Events	
	HR (95% CI)	P Value
Hx diabetes mellitus	2.60 (1.64–4.12)	<0.0001
Smoking history	2.10 (1.34–3.30)	0.001
Hypertension*	1.96 (1.04–3.70)	0.038
Obstructive CAD	1.71 (1.05–2.80)	0.032
Triglycerides (log)	1.49 (1.04–2.14)	0.030
Age	1.03 (1.01–1.05)	0.007
Ever HRT use	0.60 (0.39–0.94)	0.025
GFR (log)	0.43 (0.28–0.67)	0.0002

*Hypertension defined as SBP >140, DBP >90, or self-reported history of HTN.

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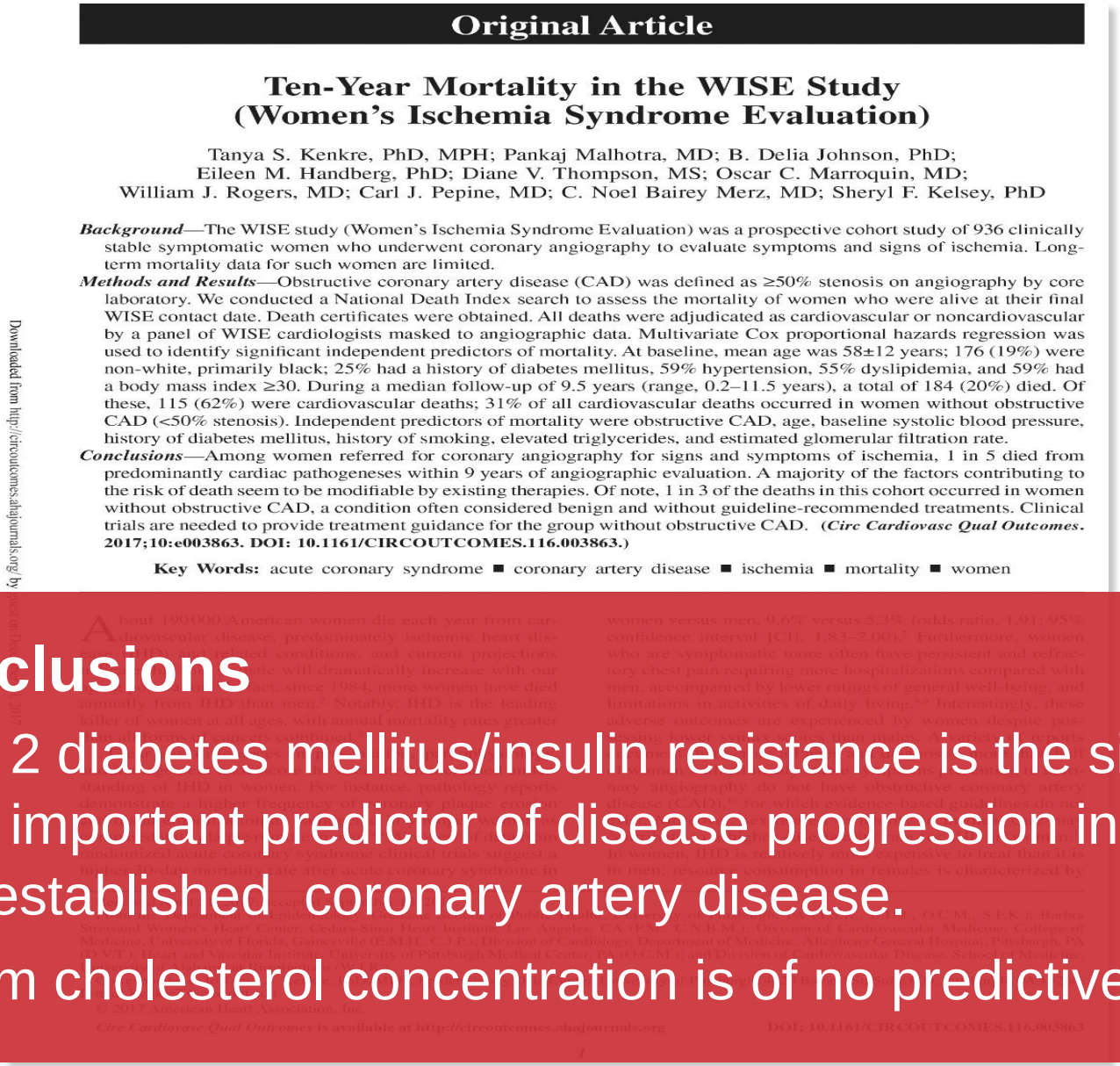

Original Article

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Conclusions—Among women referred for coronary angiography for signs and symptoms of ischemia, 1 in 5 died from predominantly cardiac pathogeneses within 9 years of angiographic evaluation. A majority of the factors contributing to the risk of death seem to be modifiable by existing therapies. Of note, 1 in 3 of the deaths in this cohort occurred in women without obstructive CAD, a condition often considered benign and without guideline-recommended treatments. Clinical trials are needed to provide treatment guidance for the group without obstructive CAD. (***Circ Cardiovasc Qual Outcomes*****. 2017;10:e003863. DOI: 10.1161/CIRCOUTCOMES.116.003863.)**

Key Words: acute coronary syndrome ■ coronary artery disease ■ ischemia ■ mortality ■ women

Conclusions

Type 2 diabetes mellitus/insulin resistance is the single most important predictor of disease progression in women with established coronary artery disease.

Serum cholesterol concentration is of no predictive value.

THE NOAKES FOUNDATION

THE PREVALENCE OF ABNORMAL GLUCOSE REGULATION IN CHD

European Heart Journal (2004) 25, 1880–1890

ELSEVIER

EUROPEAN SOCIETY OF CARDIOLOGY

Clinical research

The prevalence of abnormal glucose regulation in patients with coronary artery disease across Europe

The Euro Heart Survey on diabetes and the heart

Małgorzata Bartnik[a,b,*], Lars Rydén[a], Roberto Ferrari[c], Klas Malmberg[a], Kalevi Pyörälä[d], Maarten Simoons[e], Eberhard Standl[f], Jordi Soler-Soler[g], John Öhrvik[h], on behalf of the Euro Heart Survey Investigators

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[b] 3rd Department of Cardiology, Silesian School of Medicine, Górnośląskie Centrum Medyczne, Katowice, Poland
[c] Chair of Cardiology, University of Ferrara and Fondazione S. Maugeri, Ferrara, Italy
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[e] Thoraxcenter, Department of Cardiology, Erasmus University Medical Center, Rotterdam, The Netherlands
[f] Department of Medicine (Endocrinology), Teaching Hospital, Munich-Schwabing, Germany
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Received 6 April 2004; revised 8 July 2004; accepted 20 July 2004

See page 1865 for the editorial comment on this article (doi:10.1016/j.ehj.2004.07.027)

KEYWORDS
Coronary artery disease;
Diabetes mellitus;
Impaired glucose tolerance;
Oral glucose tolerance test

Aim The objective behind the Euro Heart Survey on diabetes and the heart was to study the prevalence of abnormal glucose regulation in adult patients with coronary artery disease (CAD).
Methods and results The survey engaged 110 centres in 25 countries recruiting 4196 patients referred to a cardiologist due to CAD out of whom 2107 were admitted on an acute basis and 2854 had an elective consultation. Patient data were collected via a web-based case record form. An oral glucose tolerance test (OGTT) was used for the characterisation of the glucose metabolism.
Thirty-one per cent of the patients had diabetes. An OGTT was performed on the 1920 patients without known diabetes, of whom 923 had acute and 997 had a stable manifestation of CAD, respectively. In patients with acute CAD, 36%had impaired glucose regulation and 22%newly detected diabetes. In the stable group these proportions were 37%and 14%
Conclusion This survey demonstrates that normal glucose regulation is less common than abnormal glucose regulation in patients with CAD. OGTT easily discloses the glucometabolic state and should be a routine procedure. The knowledge of glucometabolic state among these patients should influence their future management because it has great potential to improve the outcome.

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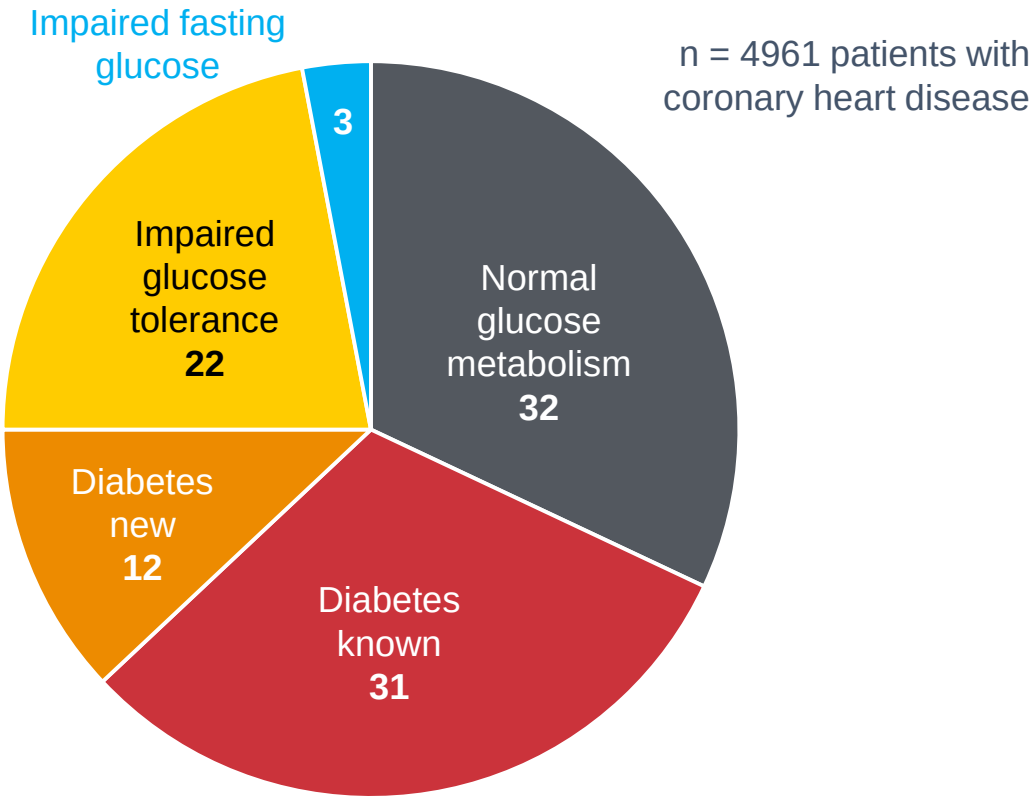
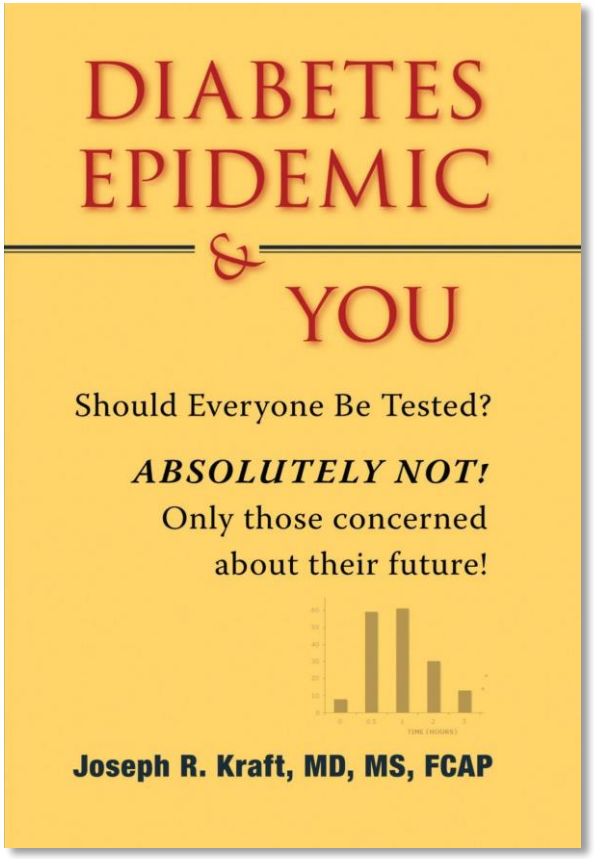
0195-668X/ $ - see front matter
doi:10.1016/j.ehj.2004.07.027

THE PREVALENCE OF ABNORMAL GLUCOSE REGULATION IN CHD IS >66%



Bartnik M et al. European Heart Journal 2004; 25: 1880-1890

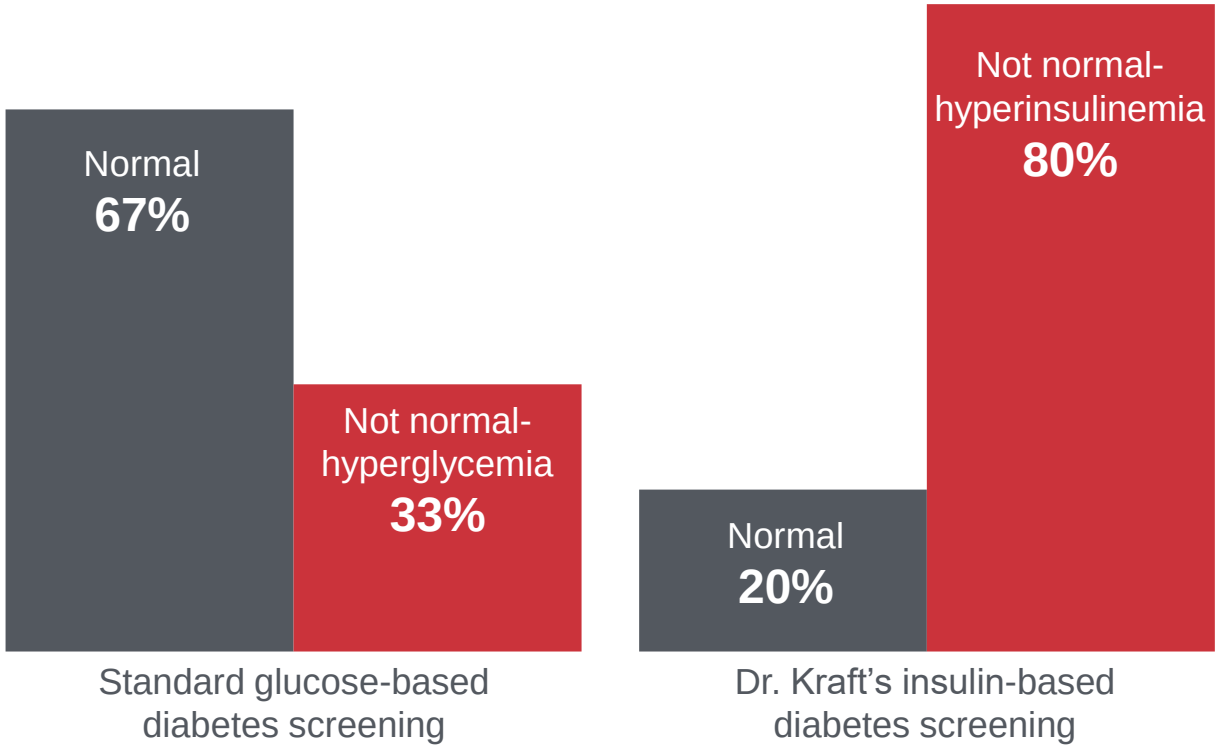
DR. KRAFT IDENTIFIES NEED TO MEASURE INSULIN RESPONSE TO GLUCOSE TOLERANCE TESTS



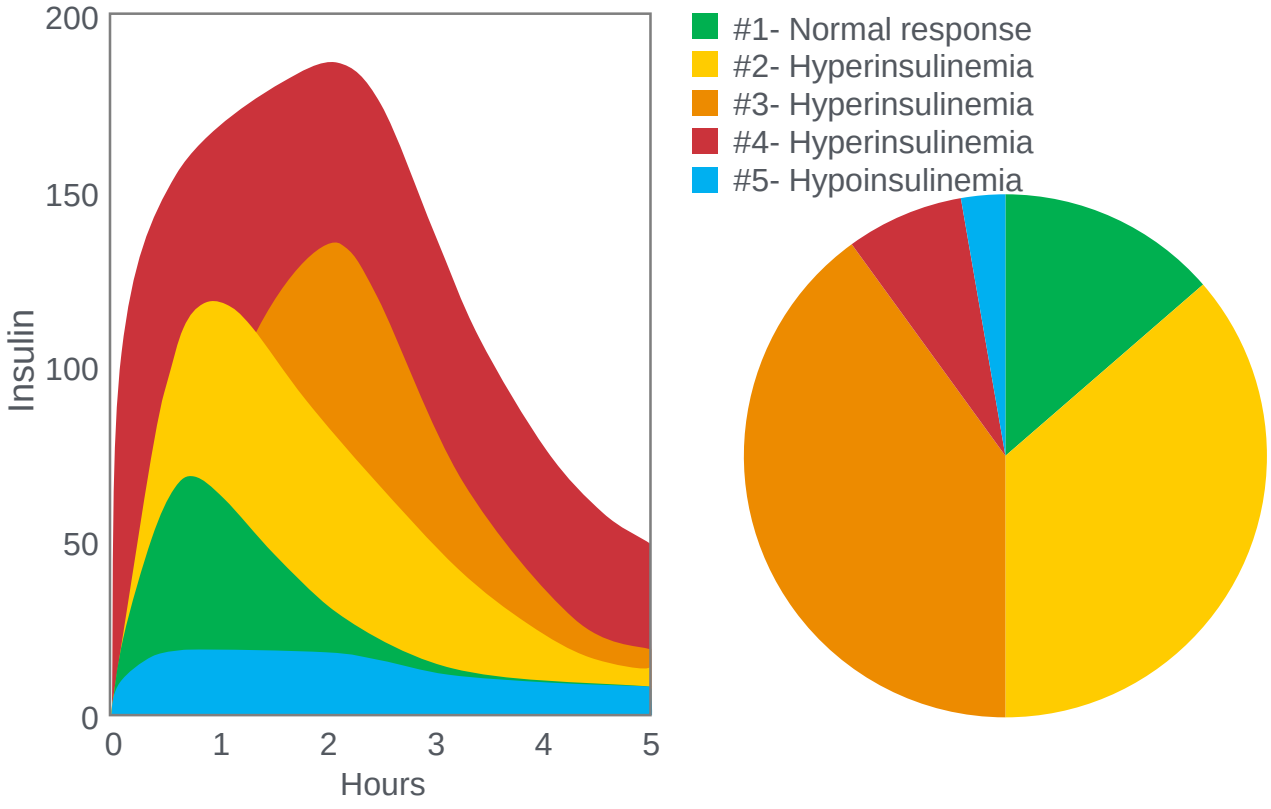
Standard glucose tolerance testing misses **78%** of those who actually have an abnormal hyperinsulinemic response which represents early diabetes. Dr. Kraft's glucose tolerance test **with insulin levels** reveals this underlying insulin resistance!

THE NOAKES FOUNDATION

STANDARD GLUCOSE-BASED DIABETES SCREENING VS DR. KRAFT'S INSULIN-BASED DIABETES SCREENING



THE FIVE DYNAMIC PATTERNS OF INSULIN SECRETION IN RESPONSE TO GLUCOSE INGESTION



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ABNORMAL GLUCOSE TOLERANCE PREDICTS OUTCOME FOLLOWING MYOCARDIAL INFARCTION

European Heart Journal (2004) 25, 1990–1997

Clinical research

Newly detected abnormal glucose tolerance: an important predictor of long-term outcome after myocardial infarction[q]

M. Bartnik[a,*], K. Malmberg[a], A. Norhammar[a], Å. Tenerz[b], J. Öhrvik[c], L. Rydén[a]

[a] Department of Cardiology, Karolinska University Hospital Solna, Stockholm, Sweden
[b] Department of Medicine, Västerås Hospital, Sweden
[c] Department of Epidemiology and Biostatistics, Karolinska Institute, 171 76 Stockholm, Sweden

Received 3 September 2004; revised 19 September 2004; accepted 28 September 2004
Available online 5 November 2004

See page 1969 for the editorial comment on this article (doi:10.1016/j.ehj.2004.10.003)

KEYWORDS
Prognosis;
Myocardial infarction;
Survival;
Abnormal glucose tolerance

Aims Recent data revealed that patients with myocardial infarction (MI) have a high prevalence of previously unknown diabetes mellitus (DM) and impaired glucose tolerance (IGT). The added prognostic importance of this finding has not been prospectively explored. To investigate whether a newly detected abnormal glucose tolerance (IGT or DM) assessed early after an MI, is related to long-term prognosis.
Methods and results Patients (n = 168; age 63.5 ± 9.3 years) with MI, no previous DM and admission blood glucose <11.0 mmol/l were followed for major cardiovascular events defined as the composite of cardiovascular death, non-fatal MI, non-fatal stroke or severe heart failure (HF). According to an oral glucose tolerance test (OGTT) before hospital discharge, 55 patients had normal and 113 abnormal glucose tolerance (GT). During the follow-up of median 34 months there were eight cardiovascular deaths, 15 patients had a recurrent MI, six had a stroke and ten severe HF. All patients who died from cardiovascular causes had abnormal GT. The composite cardiovascular event occurred in 31 (18%) patients. The probability of remaining free from cardiovascular events was significantly higher in patients with normal than abnormal GT (p = 0.002). Together with previous MI, abnormal GT was the strongest predictor of future cardiovascular events (hazard ratio 4.18; CI 1.26–13.84; p = 0.019).
Conclusions Abnormal glucose tolerance is a strong risk factor for future cardiovascular events after myocardial infarction. Since it is common and possible to detect even during the hospital phase it may be a target for novel secondary preventive efforts.

Introduction

People with impaired glucose tolerance have a cardiovascular mortality rate twice that of their counterparts with normal glucose tolerance.[1,2] It is only in the recent decade that blood glucose has been recognized as an independent risk factor for cardiovascular morbidity and

[q] The study was supported by the Swedish Heart and Lung Foundation, AFA Insurance, King Gustaf V's and Queen Victoria's Foundation and Aventis Pharma. These grants, obtained in competition, were totally unrestricted and unconditional.
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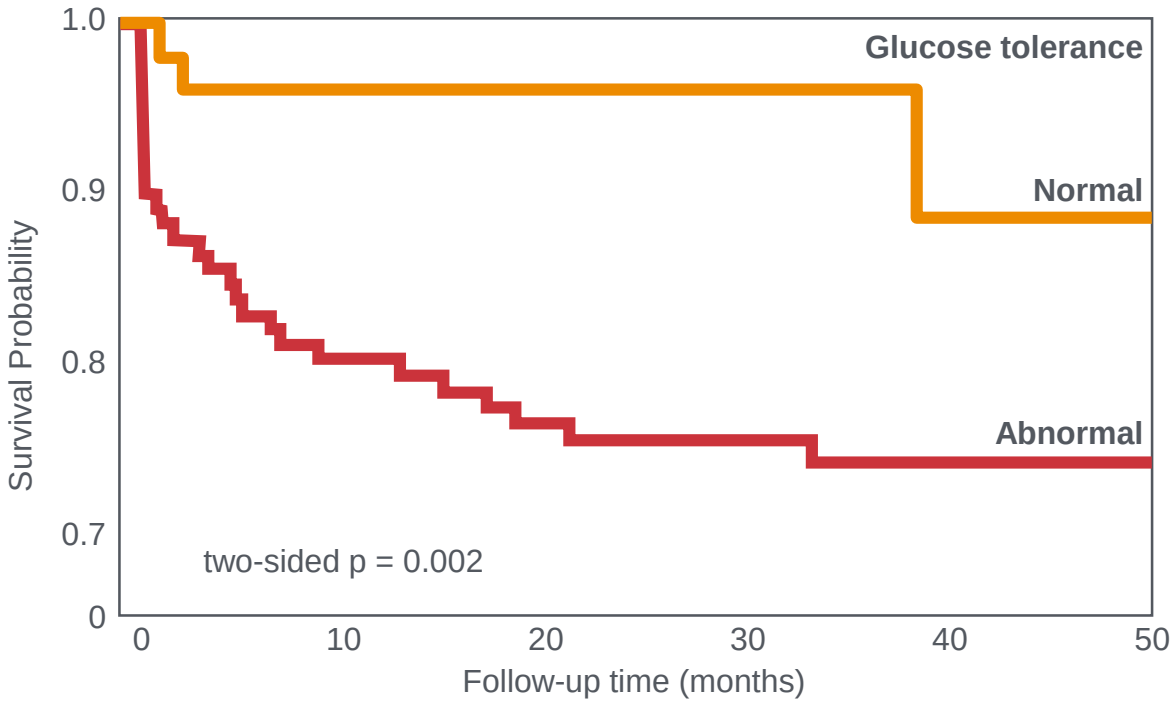
doi:10.1016/j.ehj.2004.09.021

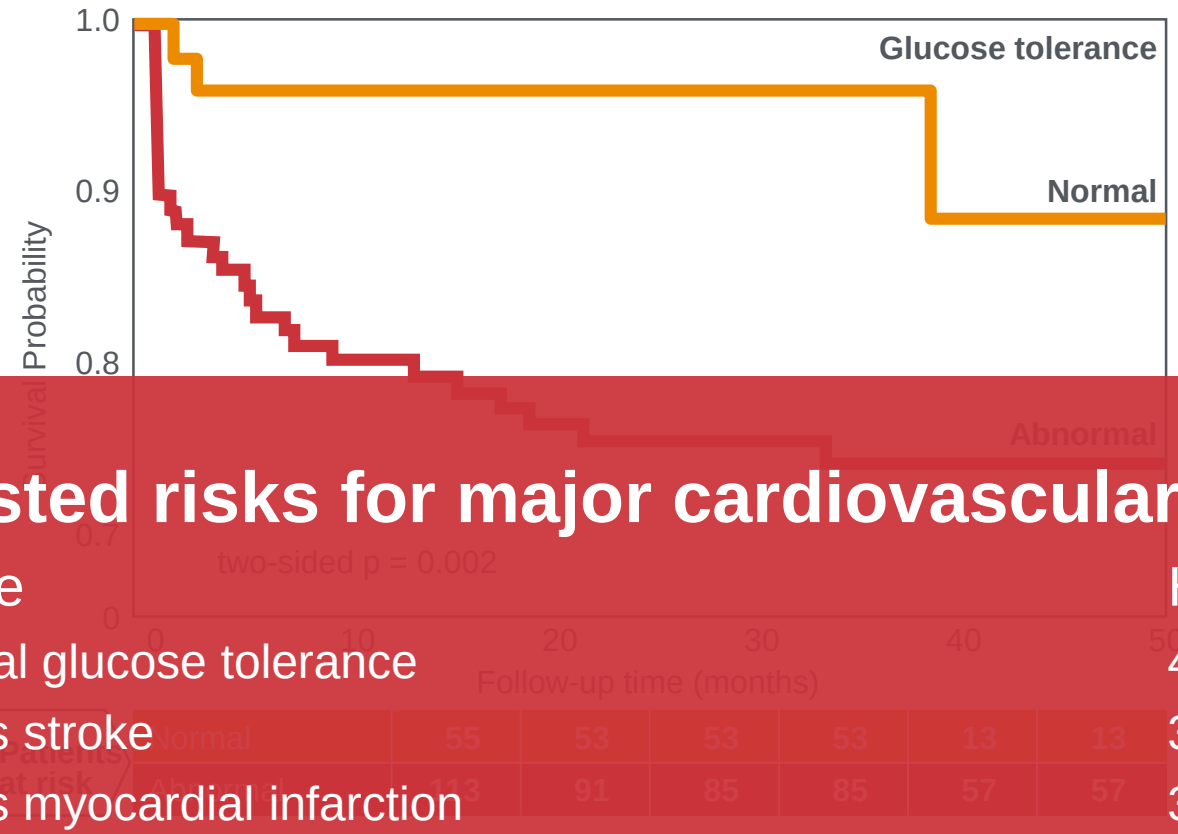
ABNORMAL GLUCOSE TOLERANCE PREDICTS OUTCOME FOLLOWING MYOCARDIAL INFARCTION



Patients at risk							
Normal	55	53	53	53	13	13
Abnormal	113	91	85	85	57	57

Bartnik M et al. European Heart Journal 2004; 25; 1990-1997

ABNORMAL GLUCOSE TOLERANCE PREDICTS OUTCOME FOLLOWING MYOCARDIAL INFARCTION



Adjusted risks for major cardiovascular events

Variable	Hazard Ratio
Abnormal glucose tolerance	4.18
Previous stroke	3.68
Previous myocardial infarction	3.38

Bartnik M et al. European Heart Journal 2004; 25; 1990-1997

Diabesity 2015; 1 (4): 34-43 doi: 10.15562/diabesity.2015.19
www.diabesity.ejournals.ca

REVIEW

Hyperinsulinemia: A unifying theory of chronic disease?

Catherine A.P Crofts*[1], Caryn Zinn[1], Mark C Wheldon[2], Grant M Schofield[1]

ABSTRACT

Globally, there is an increasing prevalence of non-communicable diseases. The morbidity and mortality from these conditions confer a greater economic societal burden. Epidemiological research associates insulin resistance in the etiology of these diseases, but there is limited evidence for the mechanism of damage. Emerging research suggests that hyperinsulinemia, a symptom of insulin resistance, may cause these pathological changes, and therefore be an independent contributor to these diseases. This review shows that hyperinsulinemia, or excessive insulin secretion, should be considered independently to insulin resistance, defined as glucose uptake rate, even though the two conditions are intertwined and will co-exist under normal conditions. Hyperinsulinemia directly and indirectly contributes to a vast array of metabolic diseases including all inflammatory conditions, all vascular diseases, gestational and type 2 diabetes, non-alcoholic fatty liver disease, obesity and certain cancers and dementias. The mechanisms include increased production of: insulin growth factor-1; reactive oxidative species and advanced glycation end-products; and triglyceride and fatty acids. Hyperinsulinemia also directly and indirectly affects many other hormones and cytokine mechanisms including leptin, adiponectin and estrogen. There is limited research standardizing the hyperinsulinemia diagnostic process. Methodological concerns and lack of standardized reference ranges preclude the use of fasting insulin. Most research has also focused on insulin resistance and it is unknown whether these methods translate to hyperinsulinemia.

Keywords: *Hyperinsulinemia, hyperglycemia, type 2 diabetes, insulin resistance, secretagogue, syndrome x*

Introduction

Impaired insulin homeostasis encompasses both hyperinsulinemia and hypoinsulinemia. Although the latter is well recognised as type 1 diabetes, there is little literature on the former, despite being first

It is well recognised that earliest detection of any disease state allows for the best possible outcomes. It is agreed that hyperinsulinemia precedes hyperglycemia, by up to 24 years.[3, 4, 6] There is a strong

THE MEDICAL CONSEQUENCES OF HYPERINSULINAEMIA AND HIGH CARBOHYDRATE DIETS

NEUROPSYCHIATRIC

Alzheimers / other dementias
Peripheral neuropathy
Retinopathy
Neuro-psychiatric disorders
Parkinson's disease
Autism

GASTROINTESTINAL

Diabetes: Type 2 / Gestational
Hypertriglyceridaemia
Non-alcoholic fatty liver disease
Ulcerative colitis

ENDOCRINE

Chronic inflammation
Fatty liver
Obesity
PCOS

CANCER

Breast, ovarian colon bladder, pancreas, liver, prostate

Tinnitus
Vertigo
Meniere's disease
Periodontal disease

CIRCULATORY

Atherosclerosis
Cardiomyopathy
Endothelial dysfunction (microvascular disease and peripheral vascular disease)
Stroke
Thrombosis (DVT)
Hypertension

SKELETAL

Osteoporosis

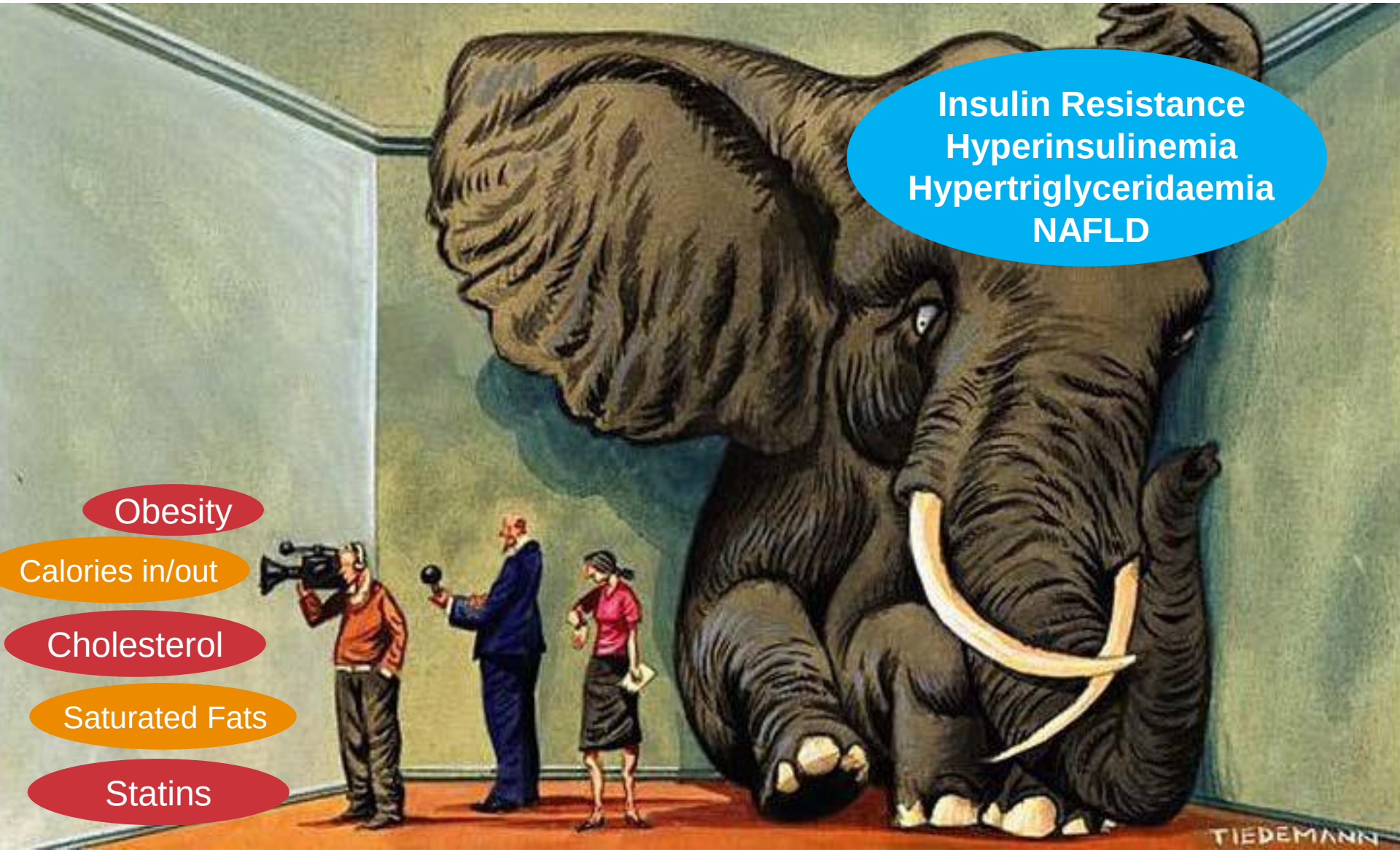
INFLAMMATION

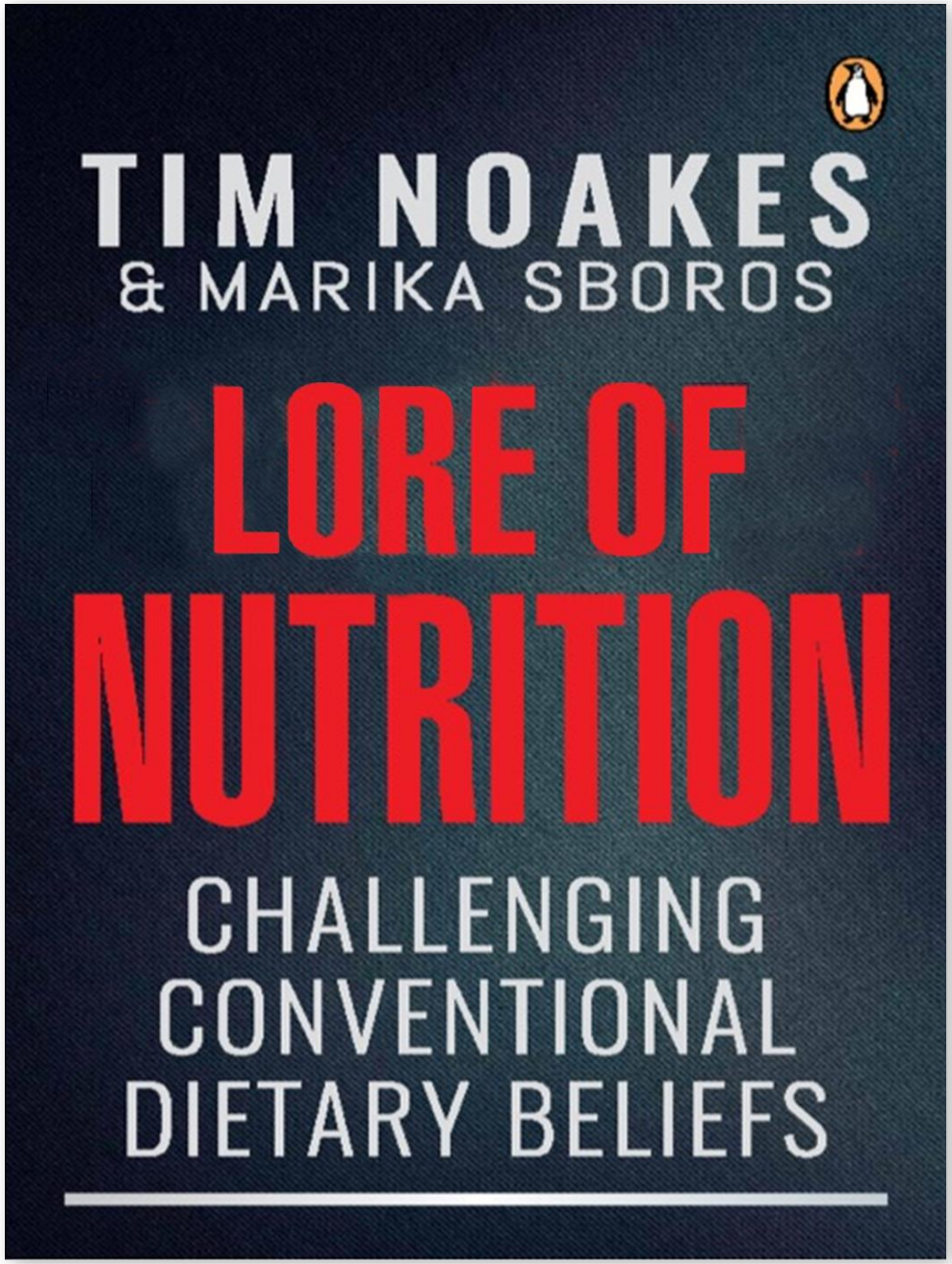
Osteoarthritis
Rheumatoid arthritis

UROLOGY

Nephropathy, erectile dysfunction

Crofts, Zinn, Wheldon & Schofield. Diabesity: (2015).





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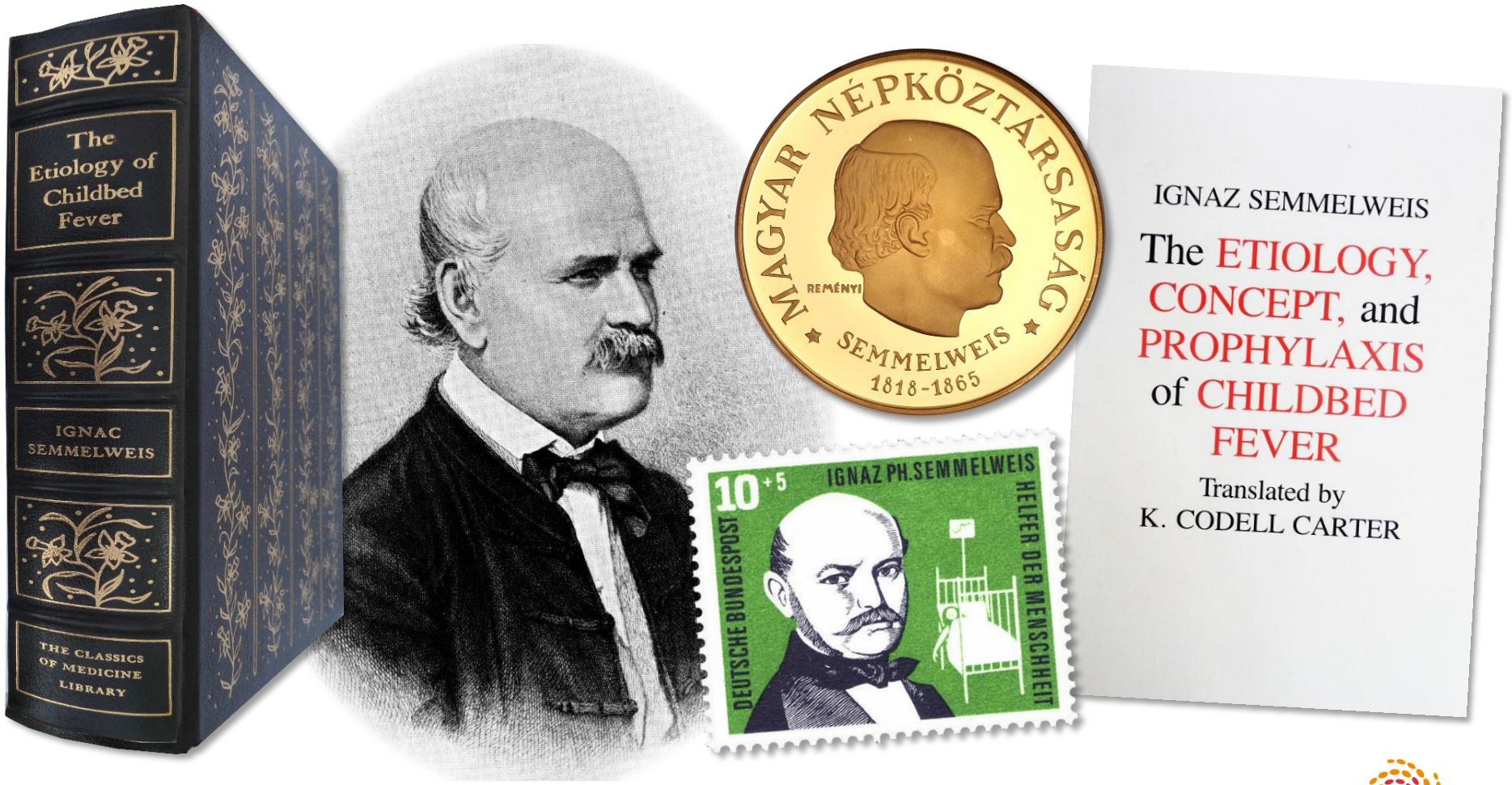
THE MESSAGE OF IGNAZ SEMMELWEIS



THE NOAKES FOUNDATION

The Semmelweis reflex or "Semmelweis effect" is a metaphor for the reflex-like tendency to reject new evidence or new knowledge because it contradicts established norms, beliefs or paradigms.

THE MESSAGE OF IGNAZ SEMMELWEIS

COGNITIVE DISSONANCE

82% of all deaths from childbed fever (puerperal sepsis) would have been prevented if obstetricians had adopted Semmelweis' findings and simply washed their hands.

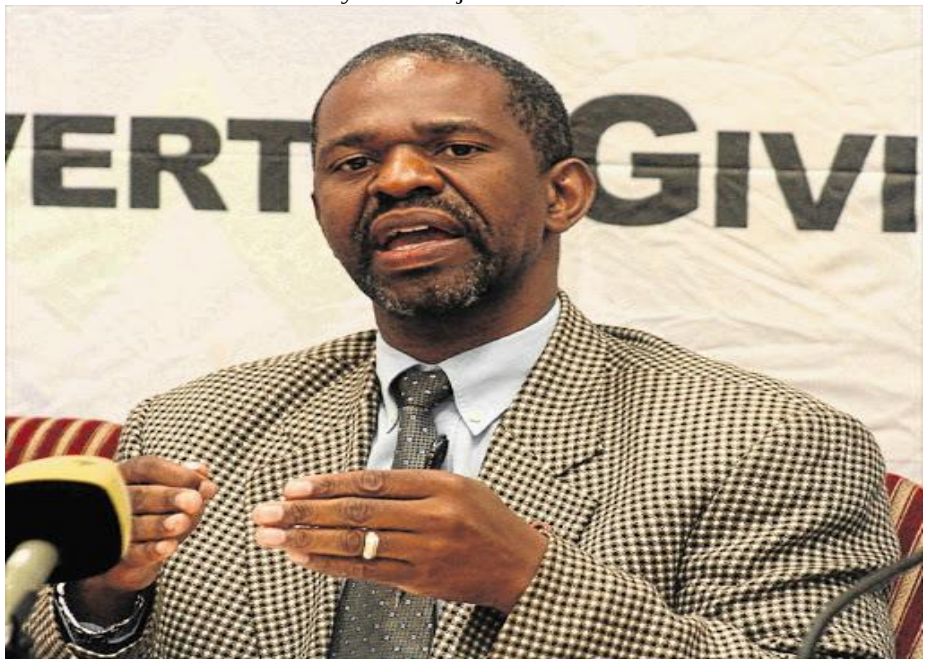
They did not because they could not conceive that doctors were killing their patients.

Does the same apply to those promoting the current nutritional guidelines especially for those with insulin resistance/T2DM?

South Africa

Diabetes claims around 2,500 leg amputations a year in KZN

11 November 2018 - 15:31 By Iavan Pijoos



KZN health MEC Sibongiseni Dhlomo. (File photo)
Image: Sunday Times

Diabetes claims around 2,500 leg amputations a year in KwaZulu-Natal, the department of health in the province said on Sunday.

The province's health MEC Sibongiseni Dhlomo sounded the alarm and urged citizens to fight back against diabetes and other non-communicable diseases.

"Diabetes, alongside other non-communicable diseases such as hypertension, heart disease, stroke and others, has exploded and become a major problem," he said.

Dhlomo was speaking at the 5km Durban Wellness Festival on the beachfront on Sunday morning.

According to the department, roughly six leg amputations are done per day at government hospitals around KwaZulu-Natal.

"We all must therefore try and increase awareness about these diseases. That is why we are also urging our fellow compatriots to make lifestyle adjustments.

"Getting engaged in regular exercise, getting rid of bad habits like smoking, and alcohol and substance abuse; and following a healthy and balanced diet, can delay the onset of diabetes and these other diseases," he said.

He urged everyone to get screened and tested for diabetes at least once a year, especially those with a family history of the sickness.

"Each and every person must know about diabetes. They must know about it more than healthcare professionals.

"Even if you're diagnosed with diabetes, it should not automatically follow that next year we are amputating your leg. There's a lot you can do to delay the

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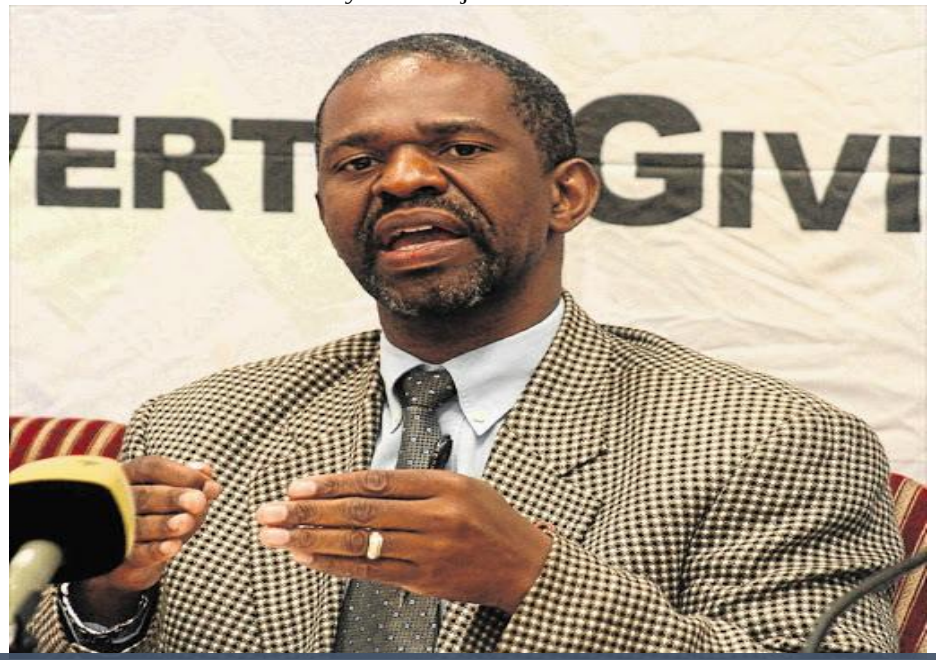

KZN health MEC Sibongiseni Dhlomo. (File photo)
Image: Sunday Times

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44

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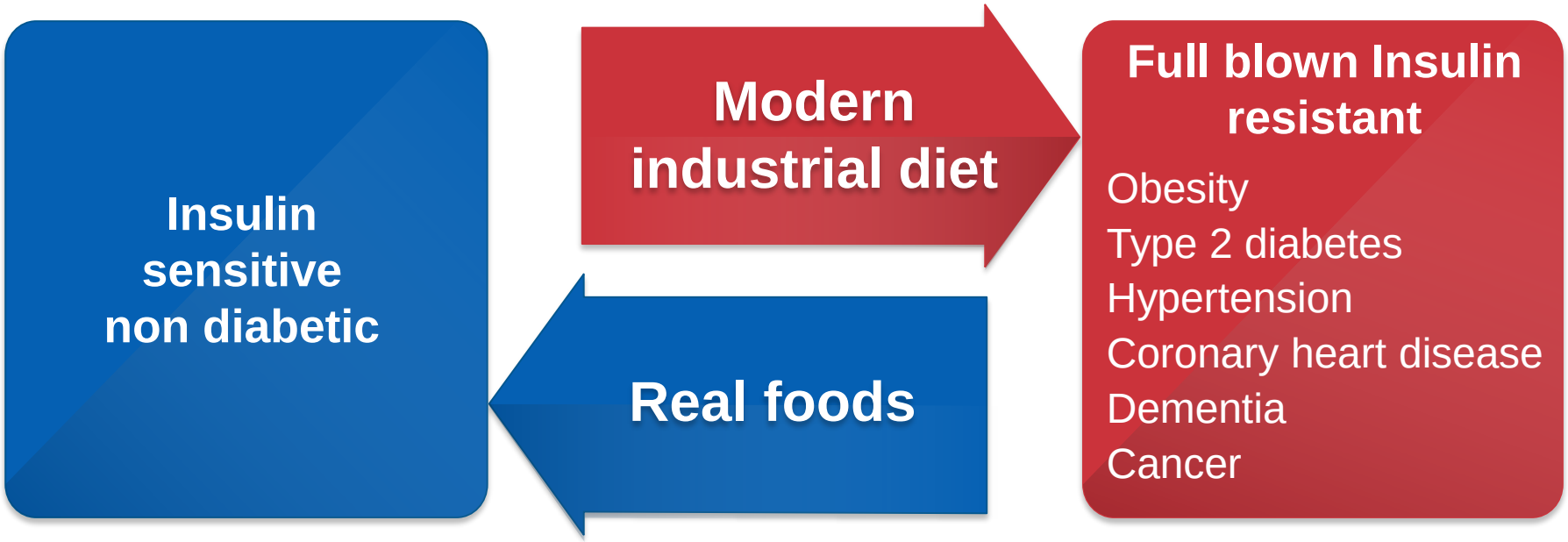
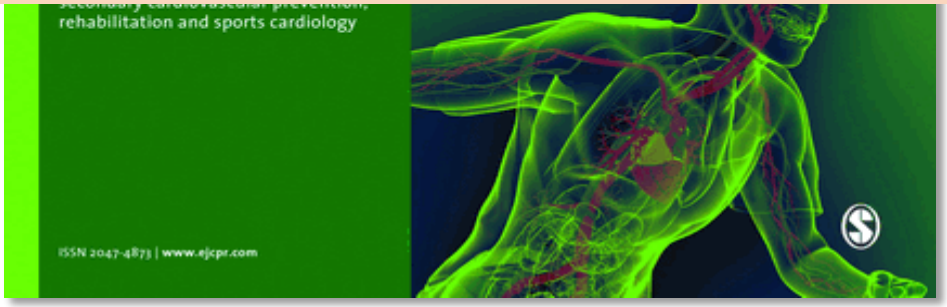
THE HUMAN CHRONIC DISEASE **SPECTRUM**



BASELINE CHARACTERISTICS OF PARTICIPANTS GROUPED ACCORDING TO SEX-SPECIFIC QUARTERS OF GAMMA-GLUTAMYLTRANSFERASE (GGT)

Presence of Non-Alcoholic Fatty Liver Disease	Least		More	Most
Variables	Q1	Q2	Q3	Q4
Mean body mass index, kg/m2 (SD)	28.6 (6.6)	29.5 (6.8)	31.1 (7.5)	30.3 (7.3)
Mean fasting blood glucose, mmol/l (SD)	5.9 (2.7)	6.2 (2.8)	6.6 (3.3)	6.6 (2.8)
Mean HbAlc, % (SD)	6.1 (1.3)	6.2 (1.3)	6.4 (1.6)	6.4 (1.5)
Mean triglycerides, mmol/l (SD)	1.2 (0.6)	1.4 (0.8)	1.5 (0.8)	1.8 (1.2)
Mean HDL cholesterol, mmol/l (SD)	1.3 (0.3)	1.3 (0.3)	1.2 (0.4)	1.3 (0.4)
Mean total cholesterol, mmol/l (SD)	5.4 (1.1)	5.5 (1.2)	5.6 (1.1)	5.7 (1.3)
Metabolic syndrome (JIS) Three components or more, *n* (%)	137 (46.9)	163 (59.9)	212 (66.7)	205 (64.9)



THE NOAKES FOUNDATION

This group of Capetonians is suffering from NAFLD, hyperinsulinaemia and carbohydrate intoxication.

What dietary advice should they receive?

What advice are they likely to receive?

THE NOAKES FOUNDATION

HEALTHCARE DELIVERY

A successful lifestyle intervention model replicated in diverse clinical settings

S Mark,[1] MSc, PhD; **S du Toit**,[2] MD; **T D Noakes**,[3] MD, DSc; **K Nordli**;[2] **D Coetzee**,[4] MD; **M Makin**,[4] MD; **S van der Spuy**,[4] MD; **J Frey**,[4] MD; **J Wortman**,[5] MD

[1] *Approach Analytics, Nanaimo, British Columbia, Canada*
[2] *Valemount Health Center, British Columbia, Canada*
[3] *Department of Human Biology, Faculty of Health Sciences, University of Cape Town; Sports Science Institute of South Africa, Cape Town, South Africa*
[4] *Omineca Medical Clinic, Vanderhoof, British Columbia, Canada*
[5] *Department of Family Practice, Faculty of Medicine, University of British Columbia, Vancouver, Canada*

Corresponding author: *S Mark (sean@approachanalytics.com)*

Lifestyle interventions (LIs) can treat metabolic syndrome and prevent type 2 diabetes mellitus, but they remain underutilised in routine practice. In 2010, an LI model was created in a rural primary care practice and spread with few resources to four other rural practices. A retrospective chart review evaluated changes in health indicators in two practice environments by following 372 participants, mainly women (mean age 52 years). Participants had a mean body mass index of 37 kg/m^2 at baseline and lost an average of 12% of their initial body weight as a result of the intervention. Among participants at the first intervention site for whom cardiometabolic data were available, the prevalence of metabolic syndrome decreased from 58% at baseline to 19% at follow-up. Taken as a whole, our experience suggests that LIs are feasible and deliver meaningful results in routine primary care practice.

S Afr Med J 2016;106(8):763-766. DOI:10.7196/SAMJ.2016.v106i8.10136

Lifestyle interventions (LIs) can treat metabolic syndrome and reduce the incidence of type 2 diabetes mellitus (T2DM) in high-risk individuals.[1] However, realising the health benefits of LIs in routine clinical practice remains elusive.[2] In January 2010, an LI model was created in a rural primary care practice and spread to four other rural communities. We present changes in health indicators among participants in two physician-led interventions.

instructed to avoid foods containing sugar and other refined carbohydrates, in addition to restricting the consumption of dietary fat. To assist in appetite control, participants were instructed not to undertake moderate or vigorous physical activity until they had reached their weight-loss goal. After reaching their target weight, a high-fat diet was used for weight maintenance. The use of a high-fat diet was predicated on the high prevalence of insulin resistance in

“As a physician you give prescriptions every month for chronic conditions and you don't see any improvements in health; actually, things tend to get worse over time. So we started to question: as physicians practicing recommended guidelines, why aren't we seeing the desired improvements in health? Why is evidence based medicine not working?

“So we started these group-based lifestyle interventions with obese, pre-diabetic and diabetic patient and tracked patient outcomes with the electronic medical record data - practice based evidence. And what we found was participants' health improved; they reduced their need for medication and their control improved. And then things took off from there...”

DR STEFAN DU TOIT

Table 1. Characteristics at baseline and follow-up of participants at S1 in a service contract primary care practice in rural BC, Canada (*N*=139)

Characteristic	Baseline	Follow-up	Change	*p*-value
Age (years), mean (SD)	52.4 (13.1)	-	-	-
Sex, % female	80.4	-	-	-
Height (m), mean (SD)	1.7 (0.1)	-	-	-
Weight (kg), mean (SD)	97.2 (22.6)	84.2 (20.6)	−12.8 (8.9)	<0.0001
BMI (kg/m^2), mean (SD)	35.4 (7.0)	30.7 (6.4)	−4.7 (3.2)	<0.0001
% with elevated waist circumference	90.7	66.2	−24.5	<0.0001
% with metabolic syndrome	57.6	19.4	−38.2	<0.0001
% with PHQ-9 score ≥10	23.7	7.9	−15.8	<0.0001
PHQ-9 score (*n*=111), mean (SD)	7.0 (5.2)	3.4 (4.6)	−3.6 (4.6)	<0.0001
Blood pressure (mmHg, *n*=119), mean (SD)	136.6/85.4	122.5/77.0	−14.1/8.4	<0.0001
HDL-C (mmol/L, *n*=119), mean (SD)	1.34 (0.35)	1.42 (0.35)	0.08 (0.27)	0.0019
LDL-C (mmol/L), mean (SD)	3.31 (1.04)	2.90 (0.88)	−0.41 (0.97)	<0.0001
Triglyceride concentration (mmol/L), mean (SD)	1.63 (0.80)	1.08 (0.59)	−0.56 (0.64)	<0.0001
Triglyceride/HDL-C ratio, mean (SD)	1.36 (0.91)	0.84 (0.73)	−0.52 (0.77)	<0.0001
Fasting blood glucose concentration (mmol/L, *n*=111), mean (SD)	5.91 (1.74)	5.32 (1.17)	−0.59 (1.47)	<0.0001
HbA1c concentration (%, *n*=18), mean (SD)	7.47 (1.64)	6.95 (1.09)	−0.52 (1.91)	0.089

HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol.

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Characteristic	Baseline	Follow-up	Change	*p*-value
Age (years), mean (SD)	52.4 (13.1)	-	-	-
Sex, % female	80.4	-	-	-
Height (m), mean (SD)	1.7 (0.1)	-	-	-
Weight (kg), mean (SD)	97.2 (22.6)	84.2 (20.6)	−12.8 (8.9)	<0.0001
BMI (kg/m^2), mean (SD)	35.4 (7.0)	30.7 (6.4)	−4.7 (3.2)	<0.0001
% with elevated waist circumference	90.7	66.2	−24.5	<0.0001
% with metabolic syndrome	57.6	19.4	−38.2	<0.0001
% with PHQ-9 score ≥10	23.7	7.9	−15.8	<0.0001

These data show that the metabolic syndrome can be reversed by a high fat diet as part of a lifestyle intervention program, in those with insulin resistance.

This outcome is not produced by conventional medical management using standard pharmacotherapy.

VIRTAHEALTH – TELEMEDICINE FOR TYPE 2 DIABETES

What does the Virta Treatment include?

Physician 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 you 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.

Diabetes Ther
https://doi.org/10.1007/s13300-018-0373-9

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ORIGINAL RESEARCH

Effectiveness and Safety of a Novel Care Model for the Management of Type 2 Diabetes at 1 Year: An Open-Label, Non-Randomized, Controlled Study

Sarah J. Hallberg · Amy L. McKenzie · Paul T. Williams · Nasir H. Bhanpuri · Anne L. Peters · Wayne W. Campbell · Tamara L. Hazbun · Brittanie M. Volk · James P. McCarter · Stephen D. Phinney · Jeff S. Volek

Received: December 28, 2017

ABSTRACT

Introduction: Carbohydrate restriction markedly improves glycemic control in patients with type 2 diabetes (T2D) but necessitates prompt medication changes. Therefore, we assessed the effectiveness and safety of a novel care model providing continuous remote care with medication management based on biometric feedback combined with the metabolic approach of nutritional ketosis for T2D management.

Methods: We conducted an open-label, non-randomized, controlled, before-and-after 1-year study of this continuous care intervention (CCI) and usual care (UC). Primary outcomes were glycosylated hemoglobin (HbA_{1c}), weight, and medication use. Secondary outcomes included fasting serum glucose and insulin, HOMA-IR, blood lipids and lipoproteins, liver and kidney function markers, and high-sensitivity C-reactive protein (hsCRP).

Results: 349 adults with T2D enrolled: CCI: $n = 262$ [mean (SD); 54 (8) years, 116.5 (25.9) kg, 40.4 (8.8) kg m^2, 92% obese, 88% prescribed T2D medication]; UC: $n = 87$ (52 (10) years, 105.6 (22.15) kg, 36.72 (7.26) kg m^2, 82% obese, 87% prescribed T2D medication]. 218 participants (83%) remained enrolled in the CCI at 1 year. Intention-to-treat analysis of the CCI (mean ± SE) revealed HbA_{1c} declined from

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Electronic supplementary material The online version of this article (https://doi.org/10.1007/s13300-018-0373-9) contains supplementary material, which is available to authorized users.

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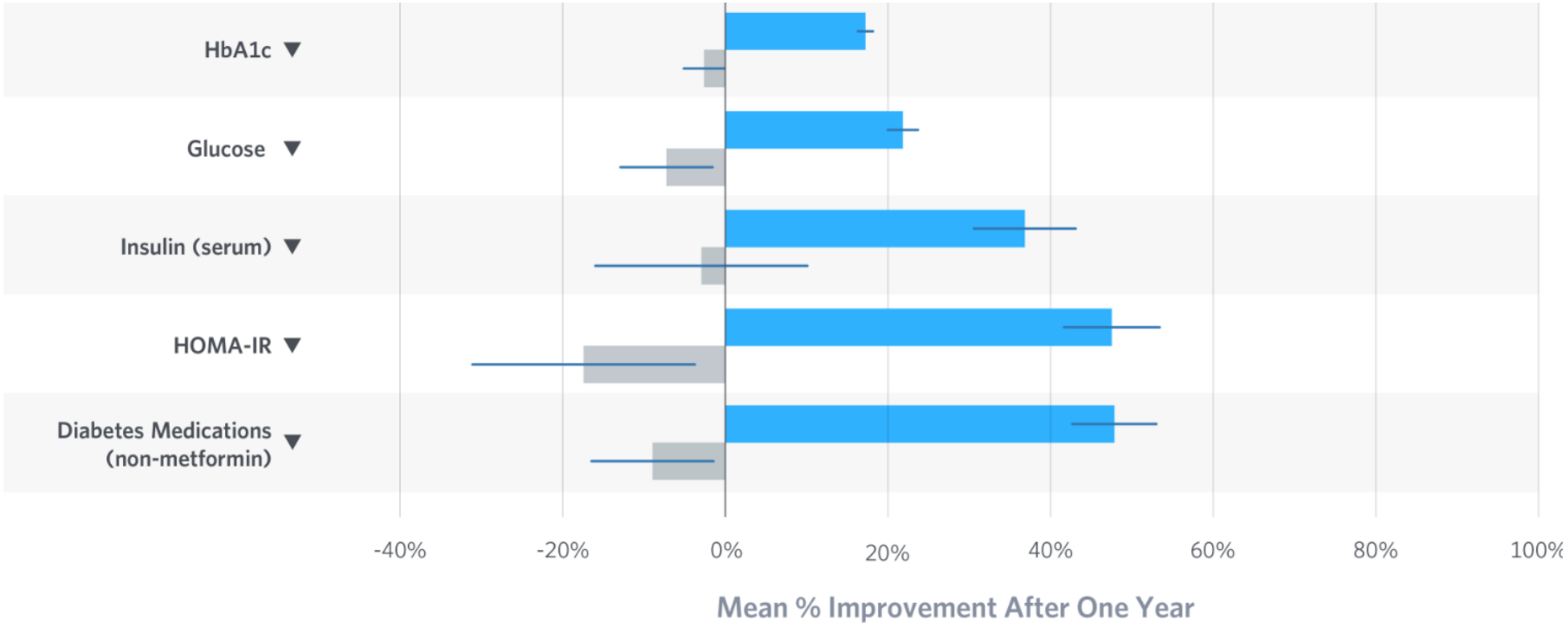
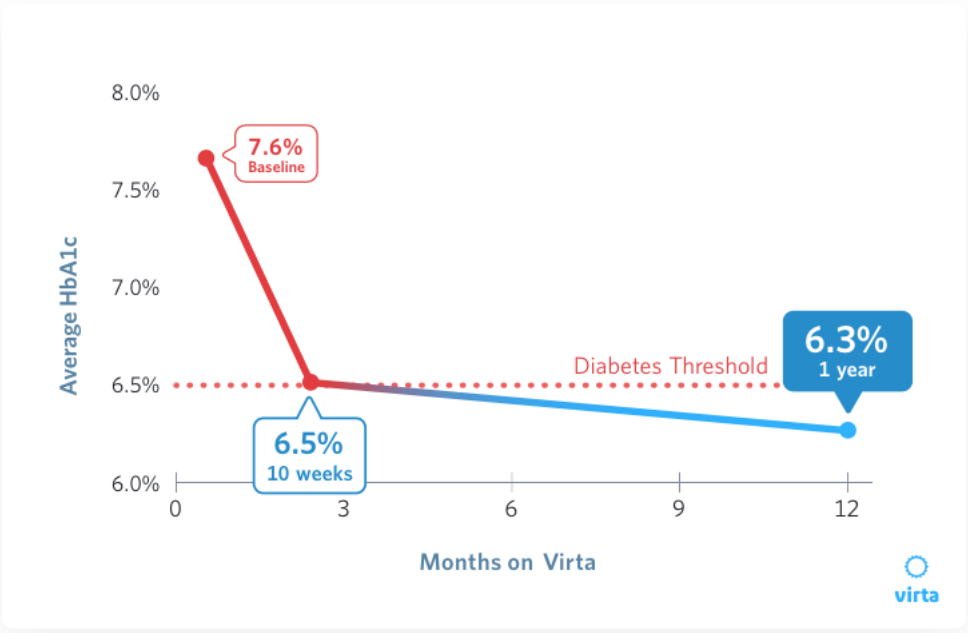
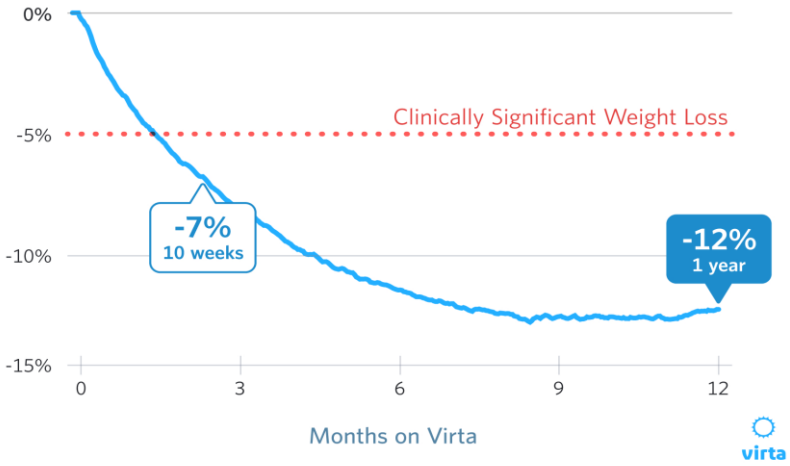
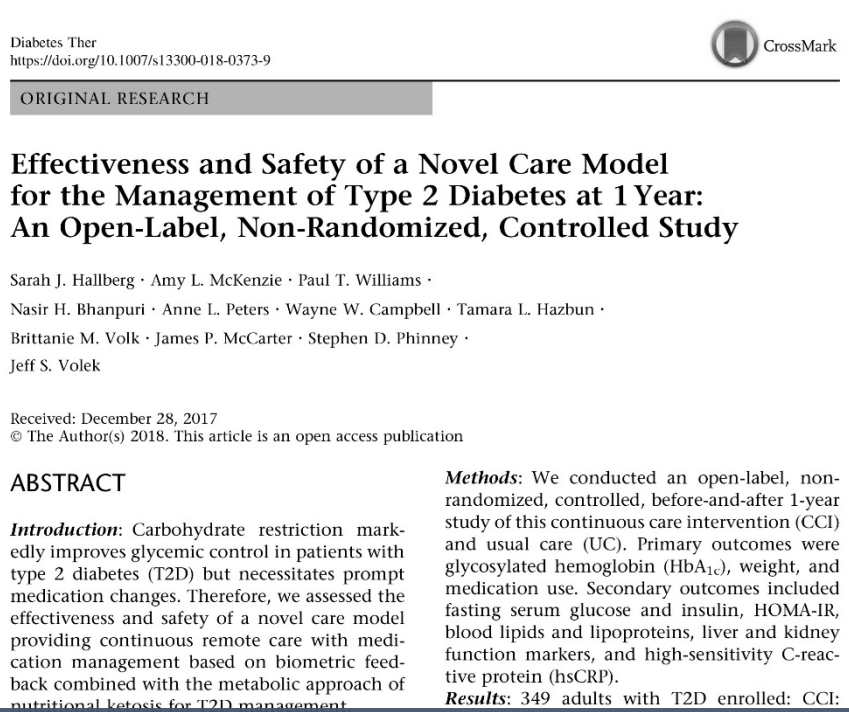




The Virta Treatment: Weight Loss (% of Starting Body Weight)





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ORIGINAL RESEARCH

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- **60% of patients reversed their Type 2 diabetes**
- **94% of patients reduced or eliminated insulin**
- **1.3% average HbA1c reduction at 1 year**
- **30 lbs (12%) average weight loss at 1 year**

Bhanpuri et al. Cardiovasc Diabetol (2018) 17:56
https://doi.org/10.1186/s12933-018-0698-8

Cardiovascular Diabetology

ORIGINAL INVESTIGATION Open Access

Cardiovascular disease risk factor responses to a type 2 diabetes care model including nutritional ketosis induced by sustained carbohydrate restriction at 1 year: an open label, non-randomized, controlled study

Nasir H. Bhanpuri[1*], Sarah J. Hallberg[1,2], Paul T. Williams[3], Amy L. McKenzie[1], Kevin D. Ballard[4], Wayne W. Campbell[5], James P. McCarter[1,6], Stephen D. Phinney[1] and Jeff S. Volek[1,7]

Abstract

Background: Cardiovascular disease (CVD) is a leading cause of death among adults with type 2 diabetes mellitus (T2D). We recently reported that glycemic control in patients with T2D can be significantly improved through a continuous care intervention (CCI) including nutritional ketosis. The purpose of this study was to examine CVD risk factors in this cohort.

Methods: We investigated CVD risk factors in patients with T2D who participated in a 1 year open label, non-randomized, controlled study. The CCI group (n = 262) received treatment from a health coach and medical provider. A usual care (UC) group (n = 87) was independently recruited to track customary T2D progression. Circulating biomarkers of cholesterol metabolism and inflammation, blood pressure (BP), carotid intima media thickness (cIMT), multi-factorial risk scores and medication use were examined. A significance level of $P < 0.0019$ ensured two-tailed significance at the 5% level when Bonferroni adjusted for multiple comparisons.

Results: The CCI group consisted of 262 participants (baseline mean (SD): age 54 (8) year, BMI 40.4 (8.8) kg m^{-2}). Intention-to-treat analysis (% change) revealed the following at 1-year: total LDL-particles (LDL-P) (− 4.9%, $P = 0.02$), small LDL-P (− 20.8%, $P = 1.2 \times 10^{-12}$), LDL-P size (+ 1.1%, $P = 6.0 \times 10^{-10}$), ApoB (− 1.6%, $P = 0.37$), ApoA1 (+ 9.8%, $P < 10^{-16}$), ApoB/ApoA1 ratio (− 9.5%, $P = 1.9 \times 10^{-7}$), triglyceride/HDL-C ratio (− 29.1%, $P < 10^{-16}$), large VLDL-P (− 38.9%, $P = 4.2 \times 10^{-15}$), and LDL-C (+ 9.9%, $P = 4.9 \times 10^{-5}$). Additional effects were reductions in blood pressure, high sensitivity C-reactive protein, and white blood cell count (all $P < 1 \times 10^{-7}$) while cIMT was unchanged. The 10-year atherosclerotic cardiovascular disease (ASCVD) risk score decreased − 11.9% ($P = 4.9 \times 10^{-5}$). Antihypertensive medication use was discontinued in 11.4% of CCI participants ($P = 5.3 \times 10^{-5}$). The UC group of 87 participants [baseline mean (SD): age 52 (10) year, BMI 36.7 (7.2) kg m^{-2}] showed no significant changes. After adjusting for baseline differences when comparing CCI and UC groups, significant improvements for the CCI group included small LDL-P, ApoA1, triglyceride/HDL-C ratio, HDL-C, hsCRP, and LP-IR score in addition to other biomarkers that were previously reported. The CCI group showed a greater rise in LDL-C.

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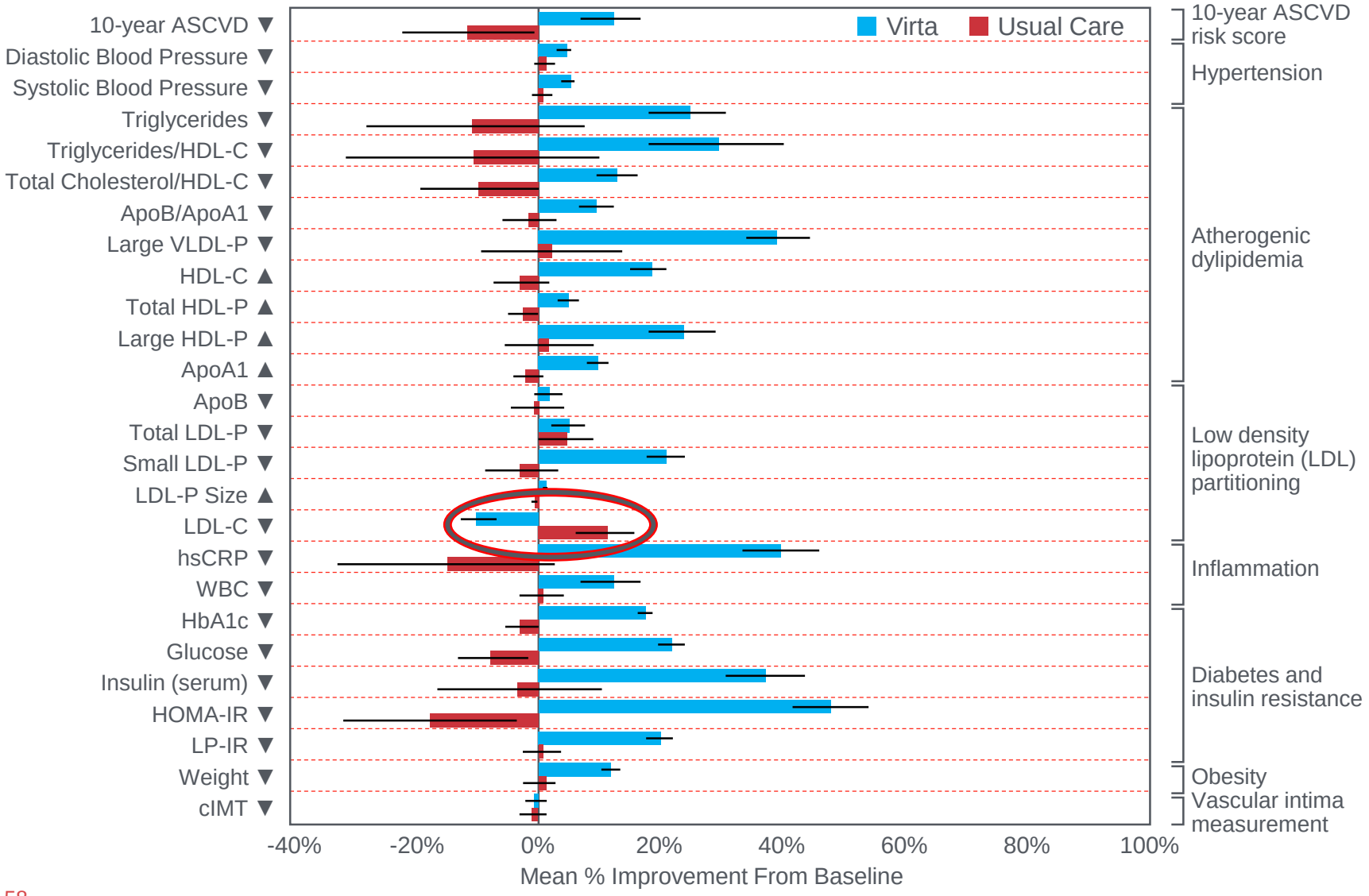
VIRTA HEALTH STUDY: CHANGES IN CVS RISK FACTORS



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Conclusions

A T2D intervention combining technology-enabled continuous remote care with individualized plans encouraging nutritional ketosis has demonstrated diabetes status improvement while improving many CVD risk factors including atherogenic dyslipidemia, inflammation and blood pressure while decreasing use of antihypertensive mediations.

BMJ Open

Post hoc analyses of surrogate markers of non-alcoholic fatty liver disease (NAFLD) and liver fibrosis in patients with type 2 diabetes in a digitally supported continuous care intervention: an open-label, non-randomised controlled study

Eduardo Vilar-Gomez,[1] Shaminie J Athinarayanan,[2] Rebecca N Adams,[2] Sarah J Hallberg,[2,3] Nasir H Bhanpuri,[2] Amy L McKenzie,[2] Wayne W Campbell,[4] James P McCarter,[2,5] Stephen D Phinney,[2] Jeff S Volek,[2,6] Naga Chalasani[1]

To cite: Vilar-Gomez E, Athinarayanan SJ, Adams RN, *et al*. Post hoc analyses of surrogate markers of non-alcoholic fatty liver disease (NAFLD) and liver fibrosis in patients with type 2 diabetes in a digitally supported continuous care intervention: an open-label, non-randomised controlled study. *BMJ Open* 2019;**9**:e023597. doi:10.1136/bmjopen-2018-023597

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ABSTRACT

Objective One year of comprehensive continuous care intervention (CCI) through nutritional ketosis improves glycosylated haemoglobin(HbA1c), body weight and liver enzymes among patients with type 2 diabetes (T2D). Here, we report the effect of the CCI on surrogate scores of non-alcoholic fatty liver disease (NAFLD) and liver fibrosis.

Methods This was a non-randomised longitudinal study, including adults with T2D who were self-enrolled to the CCI (n=262) or to receive usual care (UC, n=87) during 1 year. An NAFLD liver fat score (N-LFS) >−0.640 defined the presence of fatty liver. An NAFLD fibrosis score (NFS) of >0.675 identified subjects with advanced fibrosis. Changes in N-LFS and NFS at 1 year were the main endpoints.

Results At baseline, NAFLD was present in 95% of patients in the CCI and 90% of patients in the UC. At 1 year, weight loss of ≥5% was achieved in 79% of patients in the CCI versus 19% of patients in UC (p<0.001). N-LFS mean score was reduced in the CCI group (−1.95±0.22, p<0.001), whereas it was not changed in the UC (0.47±0.41, p=0.26) (CCI vs UC, p<0.001). NFS was reduced in the CCI group (−0.65±0.06, p<0.001) compared with UC (0.26±0.11, p=0.02) (p<0.001 between two groups). In the CCI group, the percentage of individuals with a low probability of advanced fibrosis increased from 18% at baseline to 33% at 1 year (p<0.001).

Conclusions One year of a digitally supported CCI significantly improved surrogates of NAFLD and advanced fibrosis in patients with T2D.

Trial registration number NCT02519309; Results.

Strengths and limitations of this study

- This is a longitudinal study including 262 continuous care intervention and 87 usual care patients with type 2 diabetes who have higher risk in developing non-alcoholic fatty liver disease (NAFLD).
- This study performed exploratory association analyses to demonstrate the relationship between glycaemic improvements and improvements in alanine aminotransferase levels.
- The assessment of resolution of steatosis and fibrosis is limited by the sensitivity and specificity of the non-invasive markers used in the study.
- The patients were restricted in their carbohydrate intake and monitored for their nutritional ketosis state, but dietary energy, macronutrient and micronutrient intakes were not assessed.

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is an important cause of chronic liver disease, hepatocellular carcinoma and liver transplant worldwide and is associated with increased risk of heart disease, diabetes, chronic kidney disease and malignancies.[1–4] NAFLD is highly prevalent (~70%) among patients with obesity and type 2 diabetes (T2D).[5] T2D is usually associated with the more aggressive form of NAFLD, including non-alcoholic steatohepatitis (NASH; indicating significant hepatocellular injury) and advanced fibrosis[6] and is linked with high risk for all-cause and liver-related mortality.[7–10] Currently, there are no approved pharmacological interventions for NASH. Weight loss (WL) via lifestyle changes including dietary modification and exercise is the first-line intervention used in treating and improving NAFLD/NASH.[11 12] However, the majority of patients do not achieve or

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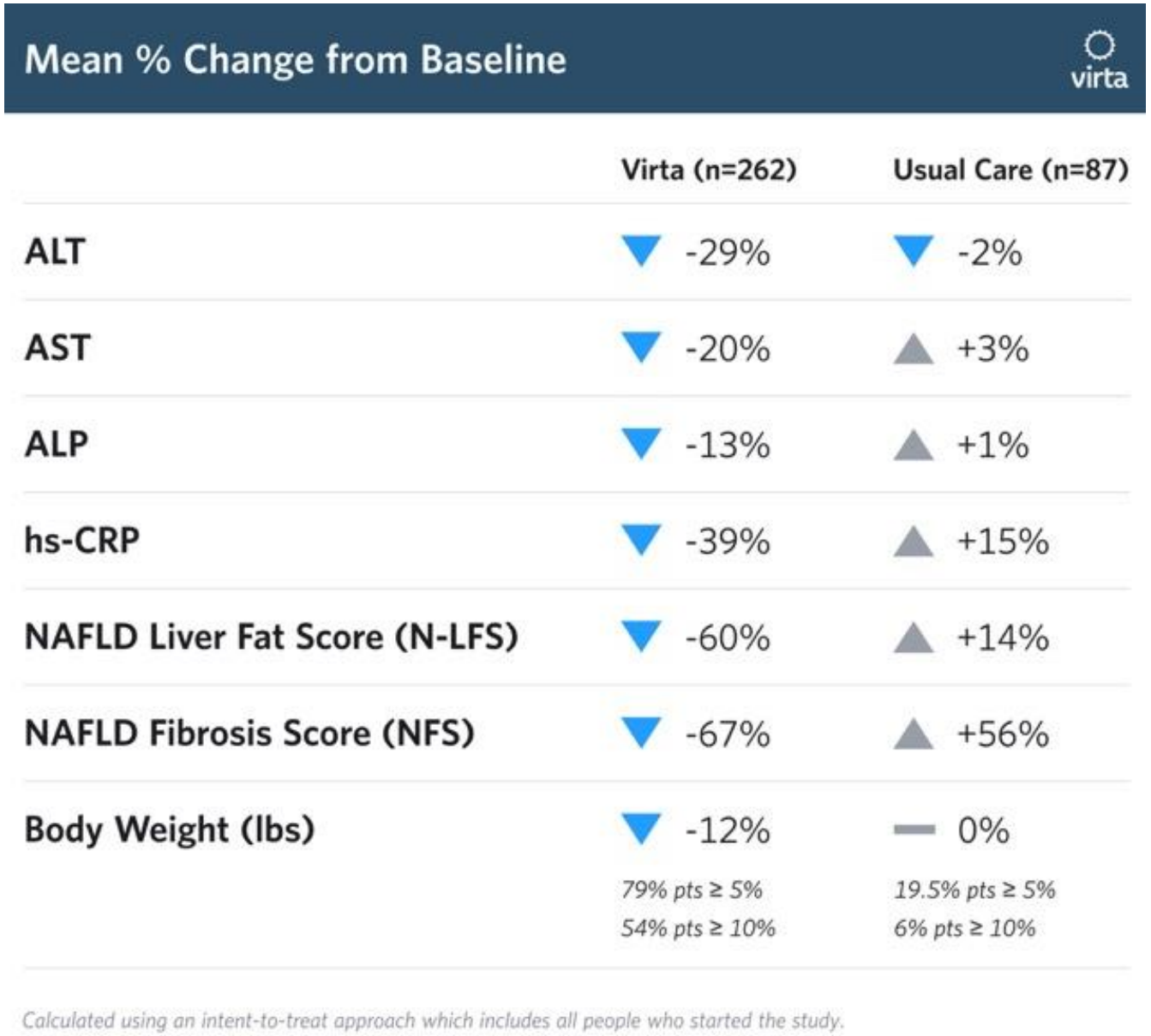

Open access Research

BMJ Open

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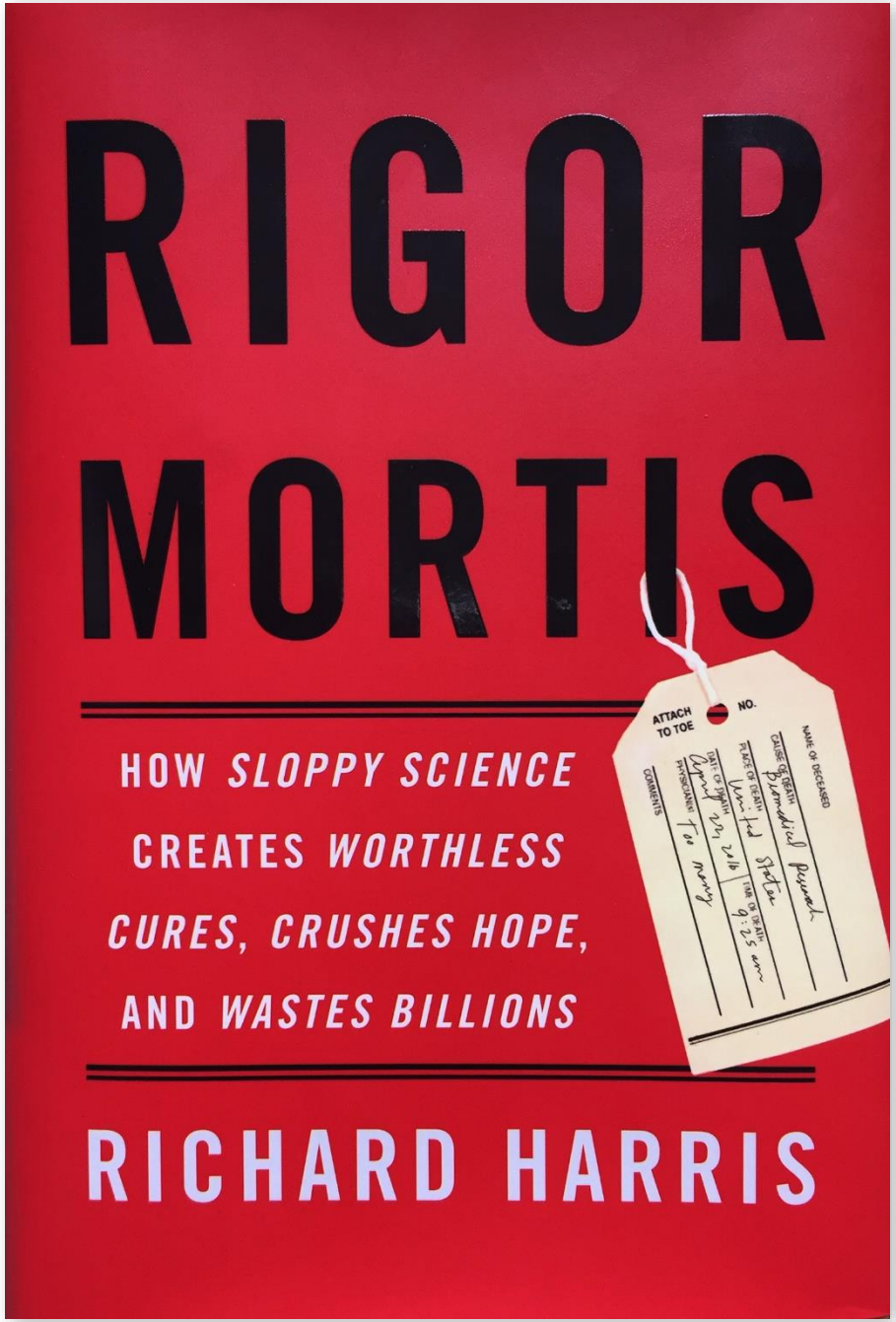

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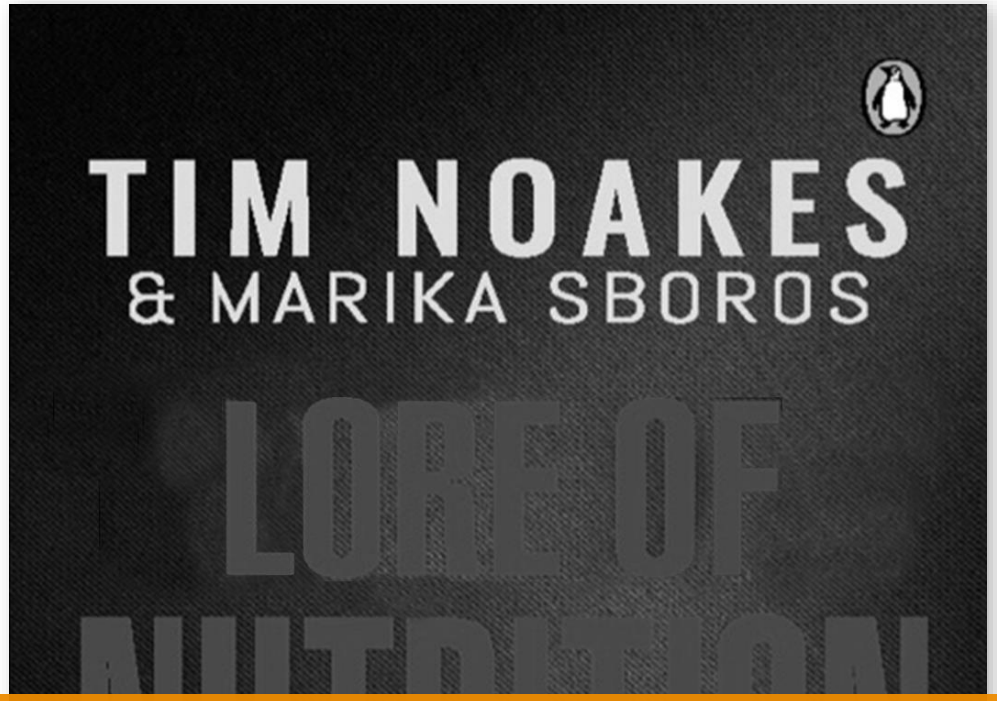
"Biomedical science – the research that underlies our treatments and cures is in deep crisis. Every year, American taxpayers spend more than $30 billion funding it. And half of that work, by some estimates is wrong".

Richard Harris. Rigor Mortis. How sloppy science creates worthless cures, crushes hope, and wastes billions. 2017

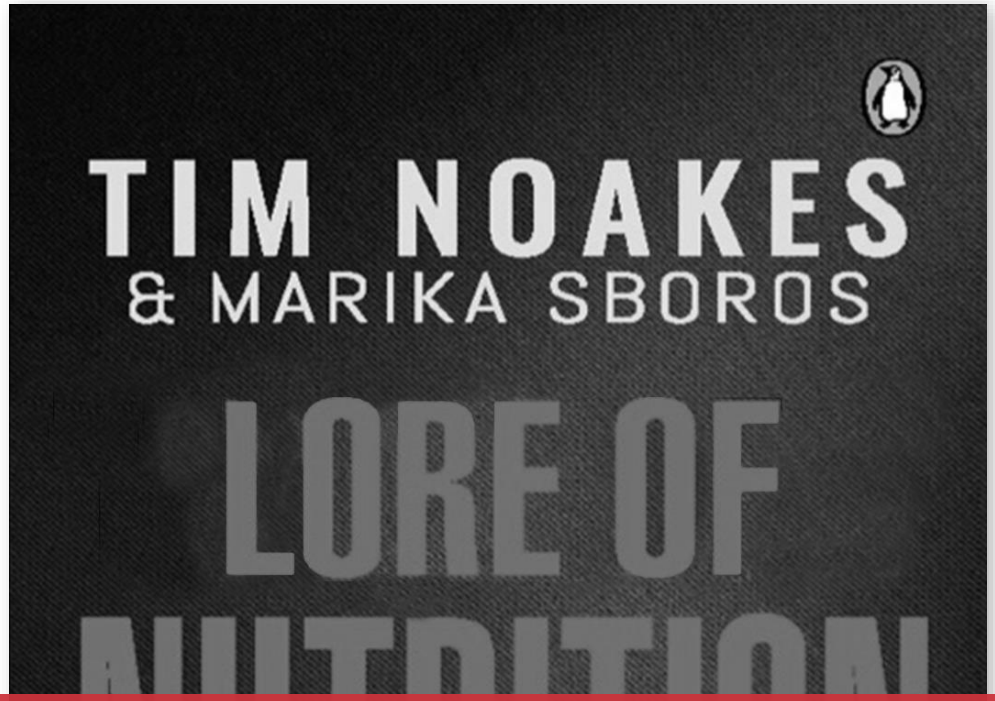


The pending revolution in (wellness) medicine

The growth of social media and the democratization of access to medical information heralds the end of (paternalistic) medicine as we currently practice and understand it.

The future of (wellness) medicine is that patients will control all aspects of their interactions with the medical profession.

The patient will decide when she consults the profession; she will decide whom she consults; she will decide what information she accepts and what she rejects; and she will decide what is best for her health.



The pending revolution in (wellness) medicine

The biggest change is that patients will choose non-pharmacological interventions to maintain their wellness.

This is because pharmacological agents do not produce health/wellness and thus they become irrelevant in this new health/wellness model.