Li Ka Shing Oborowski Degner Seminar Hall

University of Alberta, Edmonton

Collip Centenary Lecture

Celebrating 100 years of Insulin and Diabetes Research

The Discovery of Insulin to present day clinical care:

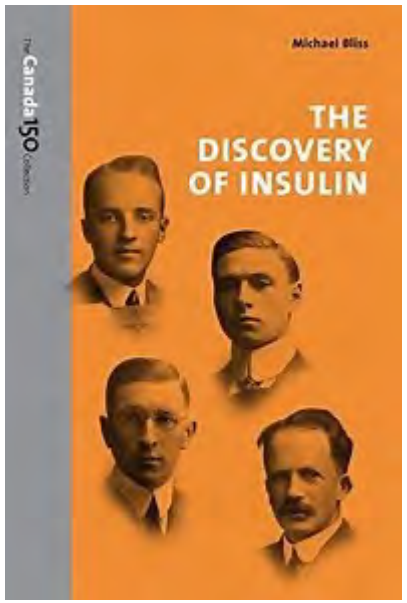
Collip and Colleagues, Complex Care, and Care in the Community

Professor Vinod Patel

FRCP MRCGP DRCOG MD

Warwick Medical School, The University of Warwick, UK

George Eliot Hospital NHS Trust, Nuneaton, UK



Grateful thanks to Professor Michael Overduin and Dr Rajiv Nair

The Discovery of Insulin to present day clinical care:

Collip and Colleagues, Complex Care, and Care in the Community

Structure

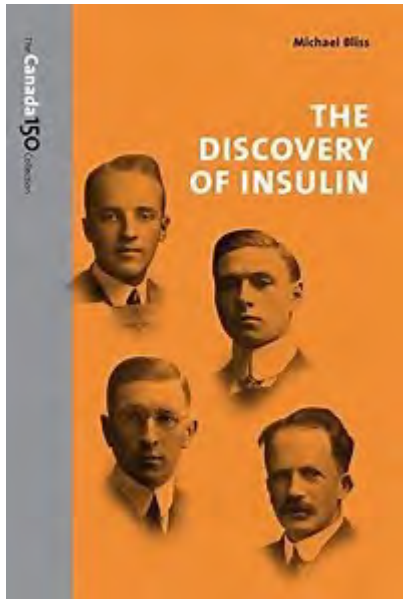
Burden of Diabetes

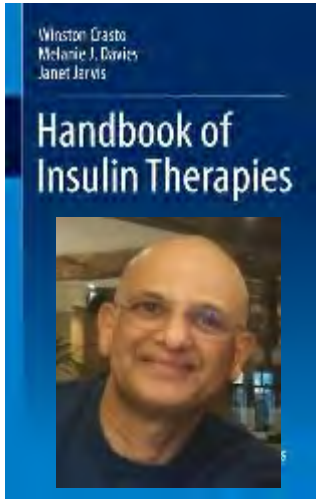
Brief History of Diabetes

Components of Diabetes Care

Caring for the Community

Conclusion





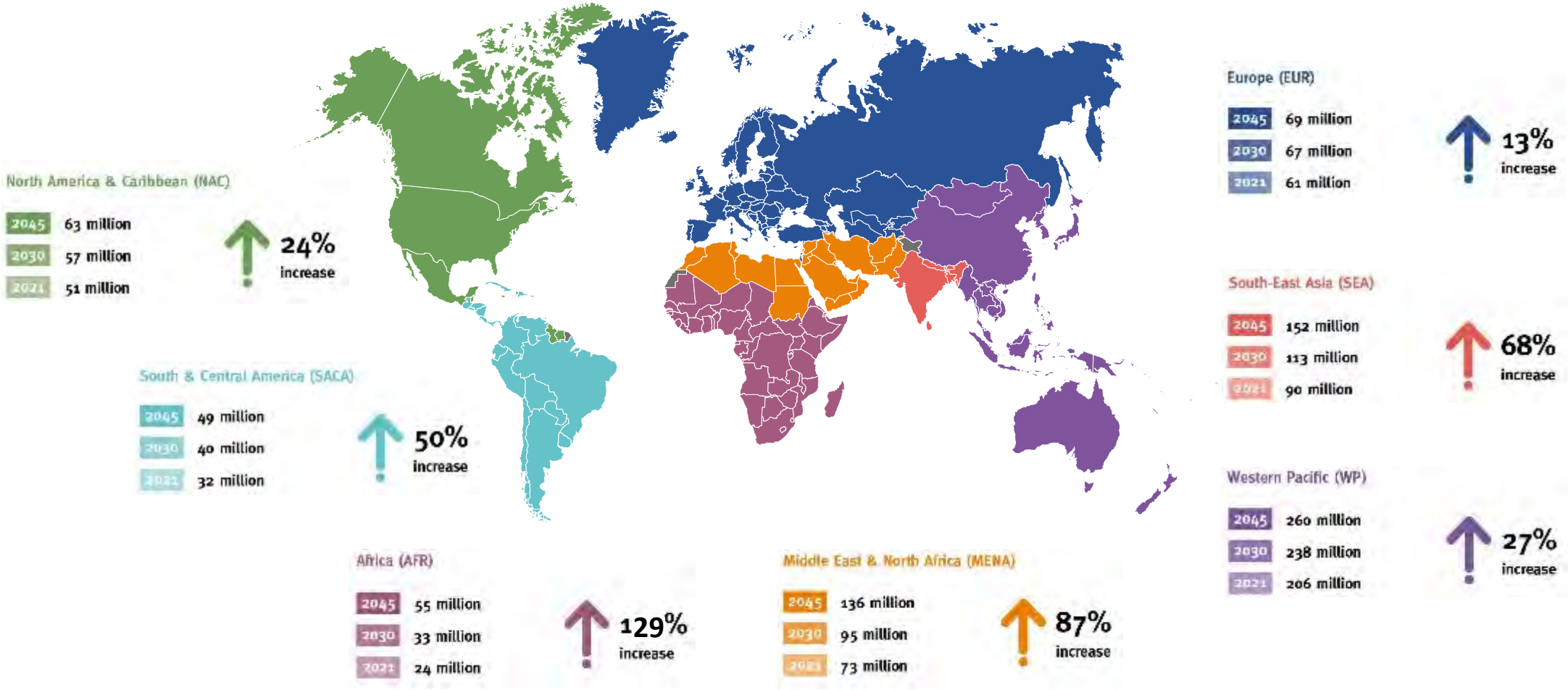
Acknowledgments: The public-domain images used, especially those from the UK Welcome History of Medicine Museum Collection and Lilly slides

Disclosures: There are no conflicts of Interest to declare

Dedicated to my Colleagues- Past and Present

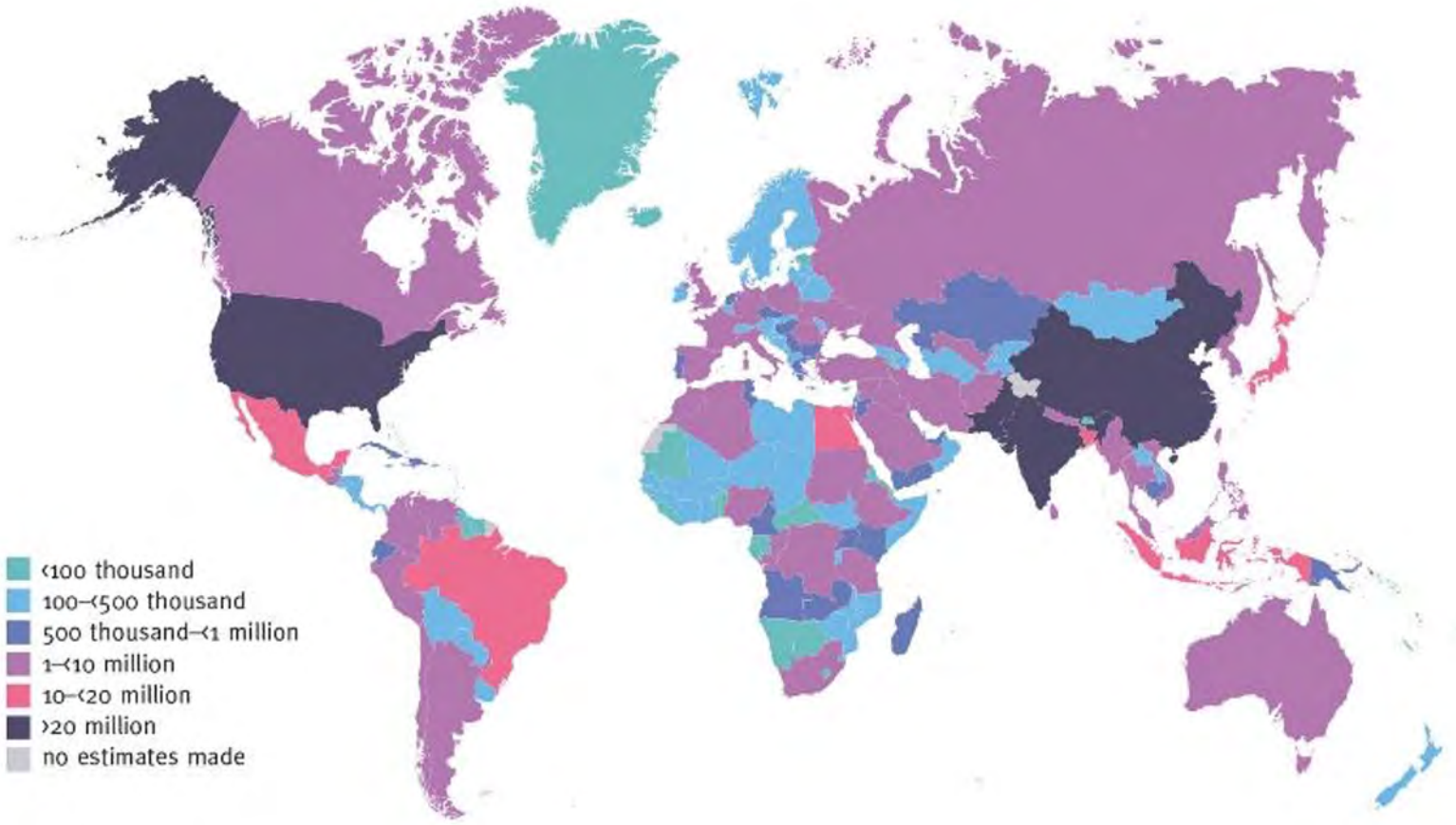
Number of people with diabetes

Aged 20–79 years globally and by IDF region



Number of adults with diabetes

Aged 20–79 years, 2021



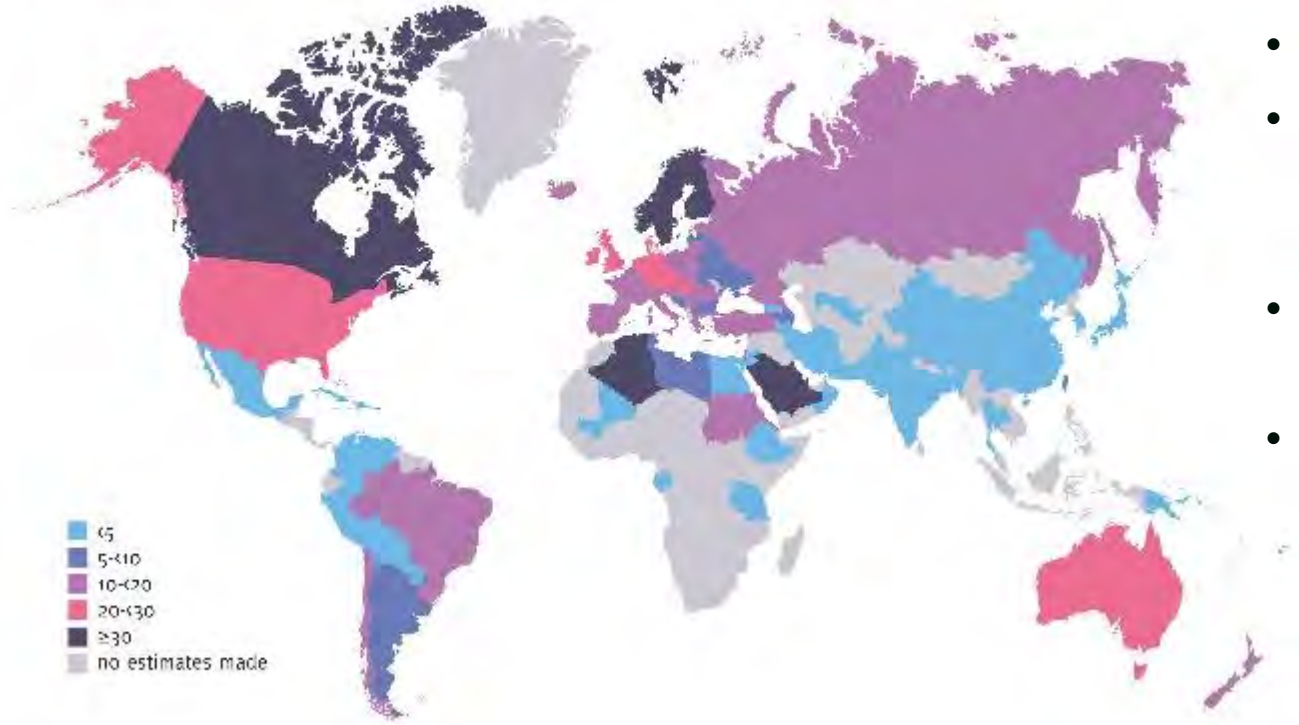
Key messages

- Diabetes is a serious, chronic condition that occurs when the body cannot produce enough insulin or cannot effectively use the insulin it does produce
- Type 1 diabetes is the major type of diabetes in childhood but can occur at any age. It cannot be prevented. People with type 1 diabetes require insulin to survive
- Type 2 diabetes accounts for the vast majority (over 90%) of diabetes worldwide. Evidence exists that type 2 diabetes can be prevented or delayed, and there is accumulating evidence that remission of type 2 diabetes may sometimes be possible
- 'Prediabetes' is a term used increasingly to describe people with impaired glucose tolerance and/or impaired fasting glucose. It indicates a higher risk of developing type 2 diabetes and diabetes-related complications.
- Pregnant women with gestational diabetes can have babies that are large for gestational age, increasing the risk of pregnancy and birth complications for the mother and baby

Age-sex standardised incidence rates of type 1 diabetes

Per 100,000 population per annum in children and adolescents aged 0–14 years and incidence of adult-onset type 1 diabetes in adults aged 20–40 years

Map 3.4 Age-sex standardised incidence rates (per 100,000 population per annum) of type 1 diabetes in children and adolescents aged 0–14 years



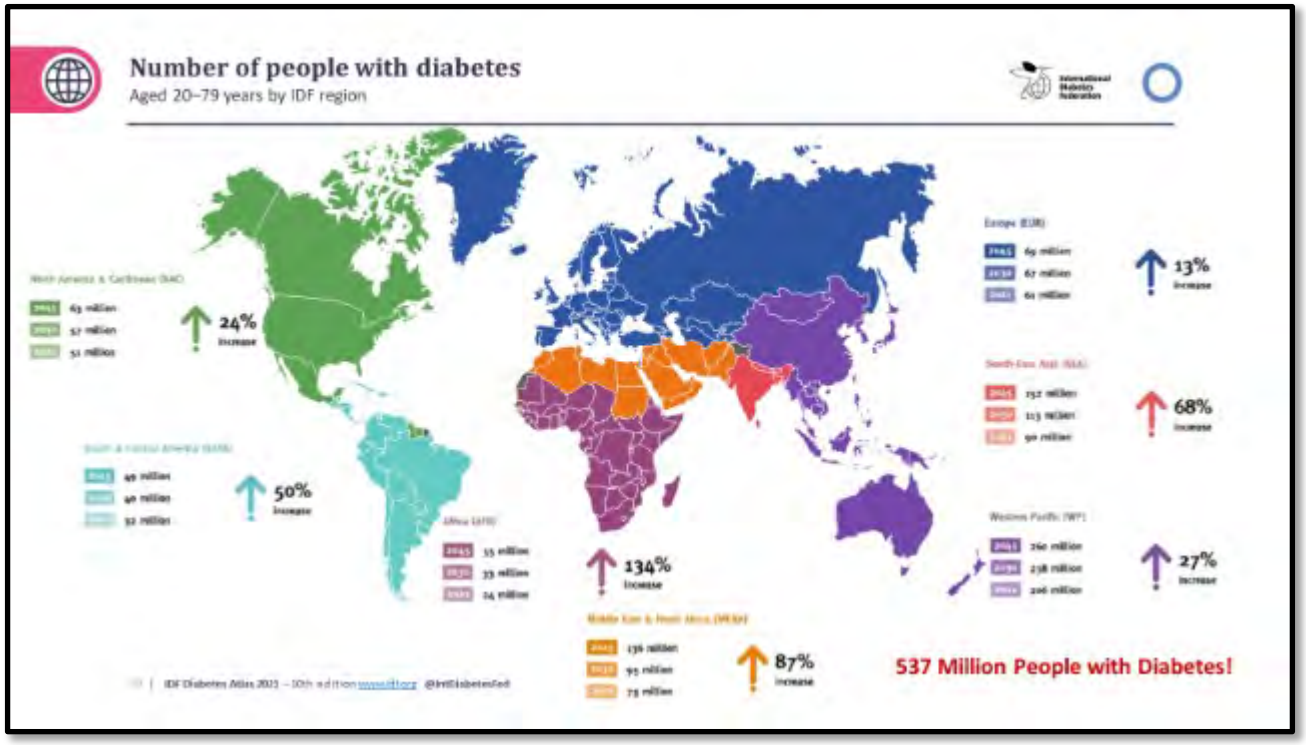
Facts about Type Diabetes

- 2021: 8·4 million people withT1D
- 1·5 million (18%) <20 years, 5·4 million (64%) were aged 20–59 years, and 1·6 million (19%) were aged 60 years or older.
- One fifth (1·8 million) were in were in low-income and lower-middle-income countries.
- Remaining life expectancy of a 10-year-old diagnosed with type 1 diabetes in 2021 ranged from a mean of 13 years in low-income countries to 65 years in high-income countries.

Global incidence, prevalence, and mortality of type 1 diabetes in 2021 with projection to 2040: a modelling study. Gregory, Gabriel AHarding, Jessica L et al. Lancet Diabetes & Endocrinology, Volume 10, Issue 10, 741 - 760

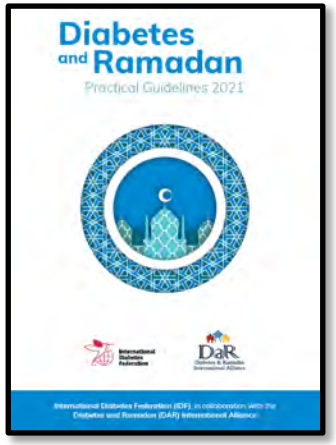
Number of people with diabetes

Aged 20–79 years by IDF region



WHO estimate that 10% of the World's Adult Population have Diabetes

Global Area	Estimated Muslim Population	Proportion of Global Muslims
North America	3,480,000	0.2%
South America	840,000	<0.1%
Europe	43,470,000	2.7%
Middle East North Africa	310,070,000	19.8%
Sub-Sahara Africa	248.420,000	15.5%
Asia Pacific	986,420,000	61.7%

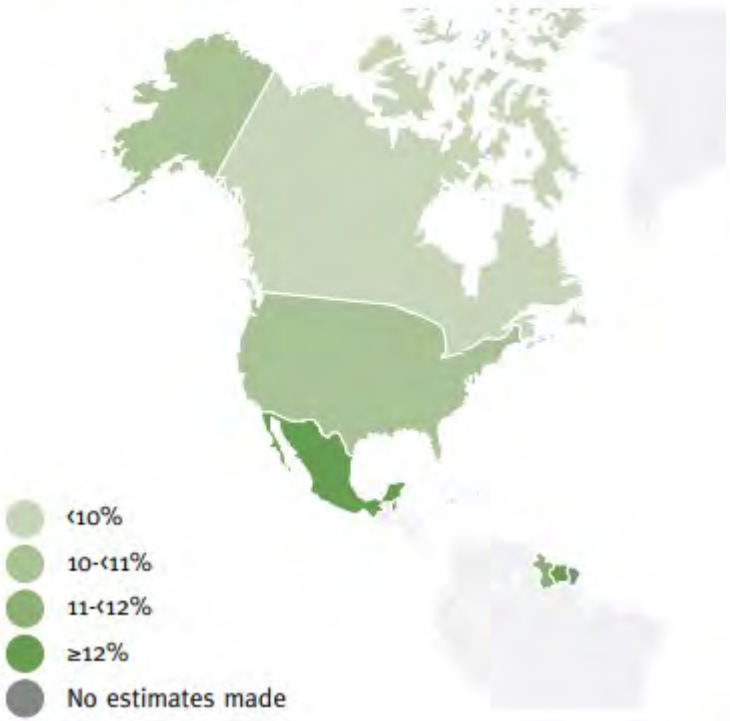


537 Million People with Diabetes!

IDF Data:

North American and Caribbean Region

Map 5.4 Age-adjusted comparative prevalence (%) of diabetes (20–79 years) in IDF North American and Caribbean Region in 2021



Type 1 diabetes (0–19 years)	
Number of children and adolescents with type 1 diabetes	192,500
Number of newly diagnosed children and adolescents each year	24,400

Top 5 countries for number of people with diabetes (20–79 years)	2011	2021
United States of America	23.7m	32.2m
Mexico	10.3m	14.1m
Canada	2.7m	3m
Haiti	295,500	548,700
Jamaica	258,500	231,100

Highlights

- 1 in 7 adults have diabetes – 51 million.
- The North America and Caribbean Region has the second highest diabetes prevalence (14%) of all IDF Regions.
- 1 in 4 people living with diabetes are undiagnosed.
- The North America and Caribbean Region has the highest diabetes-related expenditure (USD 415 billion) associated with diabetes, 43% of global expenditure.
- The North America and Caribbean Region has the second highest number of children and adolescents with type 1 diabetes – 193,000 in total.
- The North America and Caribbean Region has the highest average cost per person with diabetes (20-79y) – USD 8,208.
- 1 in 6 live births are affected by hyperglycaemia in pregnancy.

Diabetes in Canada: Basic Statistics from Diabetes Canada

- **Canadians:** 30% live with diabetes or prediabetes; 10% have a diagnosis of diabetes 14% with undiagnosed). Estimated lifespan reduction 5 to 15 years. Double vs standardised mortality
- **Age-adjusted prevalence** (5.0% in the general population):
  - **17.2% among First Nations individuals living on reserve**
  - 10.3% among First Nations individuals living off-reserve
  - 7.3% among Métis people
  - **14.4% South Asian descent**
  - 12.9% African descent
  - 9.4% Arab/West Asian descent
  - 8.2% East/Southeast Asian descent
  - South Asian and Black adults: x 8.1 times and x 6.6 times higher, vs White adults
  - (13). Further, the prevalence of diabetes

Risk factors: Non-completion of high school x 5.2 vs University Educated. Unemployed x 2.9, food security, the built environment, social support, and access to health care

Potentially Modifiable risk factors:

- 46.2% of adults and 57.1% of youth are physically inactive
- 35.6% of adults overweight, 28.2% of adults obesity, 23.2% of youth overweight or obesity;
- 74.6% not eating enough fruits and vegetables
- 12.9% are current tobacco smokers

DIABETES CANADA

Diabetes in Canada: Basic Statistics from Diabetes Canada

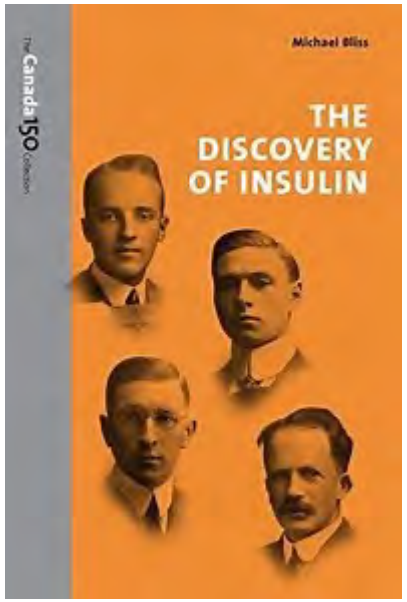
- **Indigenous women** are at an elevated risk of diabetes in pregnancy in North America
- **Cree communities** in Quebec are a distinct First Nation (North American Indian) group characterised by the highest reported prevalence of diabetes in pregnancy in Canada—affecting 15%–18% of Cree mothers
- **Both diabetes in pregnancy and infant hospitalisation rates** were much higher comparing:
  - Cree (23.7% and 29.0%)
  - Other First Nations (12.4% and 34.1%)
  - Non-Indigenous (5.9% and 15.5%) communities.

Huang R, Xiao L, Zhu J*, et al*
Population-based birth cohort study on diabetes in pregnancy and infant hospitalisations in Cree, other First Nations and non-Indigenous communities in Quebec
BMJ Open 2023;**13:**e074518. doi: 10.1136/bmjopen-2023-074518

DIABETES CANADA

A Brief History of Insulin

Professor Vinod Patel
FRCP, MRCGP, DRCOG MD, FHEA
Professor, Diabetes and Clinical Skills
Warwick Medical School, The University of Warwick
Hon Consultant in Endocrinology and Diabetes, Acute Medicine
George Eliot Hospital NHS Trust, Nuneaton



Based on John R. White. Diabetes Spectrum 2014 May; 27(2): 82-86
And other resources including Banting House Resources, London, Ontario, Canada

Diabetes Mellitus: A History

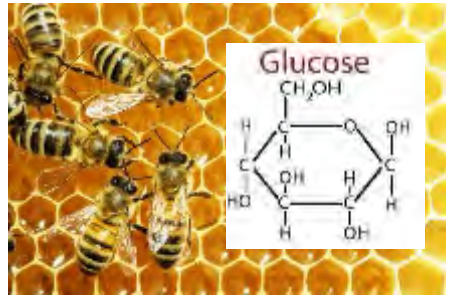
Ebers Papyrus and after
A disease characterised by the ‘too great emptying of urine’ finds its place in antiquity in Egyptian manuscripts dating back to 1500 B.C

Indian physicians called it *madhumeha* (‘honey urine’) because it attracted ants. Sushruta, and the surgeon Charaka (400–500 A.D.) were able to identify the two types, later to be named Type I (young) and Type 2 diabetes (wealthy, older, larger)

Aretaeus the Cappadocian history attributes the first complete descriptions in the first century A.D. to him. Coined the word *diabetes* (Greek, ‘siphon’) and dramatically stated *“… no essential part of the drink is absorbed by the body while great masses of the flesh are liquefied into urine”*

Avicenna (980–1037 A.D.), the great Persian physician, in *The Canon of Medicine* not only referred to abnormal appetite and observed diabetic gangrene but also concocted a mixture of seeds (lupin, fenugreek, zedoary) as a panacea

John Rollo: The term *mellitus* (Latin, ‘sweet like honey’) by this British Surgeon-General in 1798, to distinguish this diabetes from diabetes *insipidus* in which the urine was tasteless.



? Ironic!

Diabetes Mellitus: A History

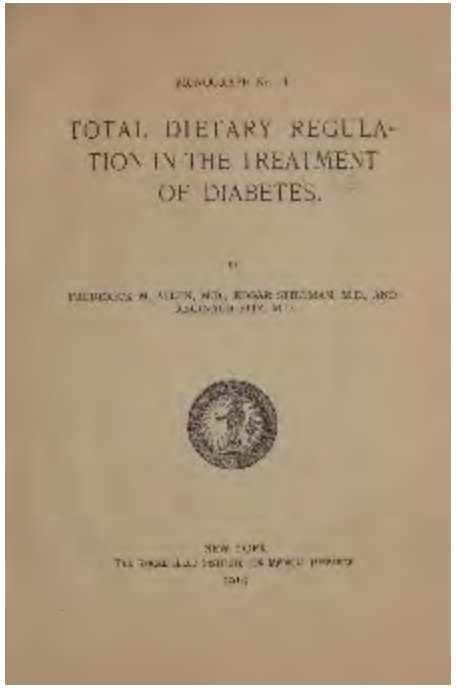
Discovery of the role of the pancreas

Joseph von Mering and Oskar Minkowski in 1889 discovered the role of pancreas in diabetes. They found that dogs whose pancreas was removed developed all the signs and symptoms of diabetes and died shortly afterwards.

In 1910, **Sir Edward Albert Sharpey-Schafer** found that diabetes resulted from lack of insulin. He termed the chemical regulating blood sugar as insulin from the Latin “insula”, meaning island, in reference to the insulin-producing islets of Langerhans in the pancreas.

Starvation treatment

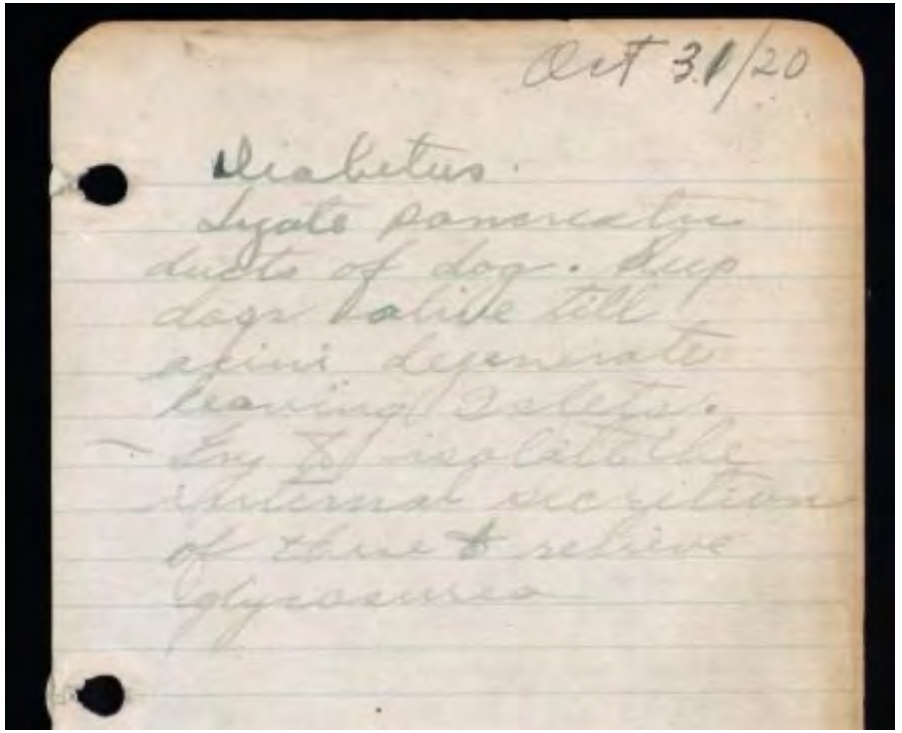
In 1919 **Dr Frederick Allen** of the Rockefeller Institute in New York published his “Total Dietary Regulations in the Treatment of Diabetes” that introduced a therapy of strict dieting or starvation treatment – as a way to manage diabetes.



Banting's Original Idea

31 October 1920

- In the early hours of October 31, 1920, in London, Ontario, 28-year-old Dr. Frederick G. Banting woke up suddenly.
- He had had a flash of insight for a novel experiment to isolate the elusive internal secretion of the pancreas as a means of treating diabetes.
- Banting, had been reading about carbohydrate metabolism and diabetes.
- After a few hours of disturbed sleep, he awoke with a compelling idea that he quickly jotted down in a notebook.



The note made by Banting in the middle of the night. It reads: ***"Diabetus – Ligate pancreatic ducts of dog – Keep dogs alive till acini degenerate leaving Islets – Try to insolate the internal secretion of these to relieve glycosurea"***
University of Toronto; The Discovery and Early Development of Insulin

? Just the two spelling mistakes?

A History of Insulin: Banting, Macleod, Best

- Before the 1920s, no effective pharmacological agents for T1DM or T2DM. T1DM was often a fatal malady
- Captain Dr. Frederick Banting, surgeon in World War I wounded by shrapnel (Military Cross)
- Toronto, Canada. Saw one patient in first month (seeking a prescription for ethanol), Banting embarked upon a career in academic medicine.
- Taught carbohydrate metabolism- led to interest in diabetes. He extracted matter from canine pancreas glands that had an impact on hyperglycaemia in other diabetic animals.
- While in Toronto for a friend's wedding, Banting is able to secure a meeting with the head of physiology at the University of Toronto, Dr. John J. R. Macleod, to speak about his pancreatic extract idea.
- His student, Charles Best, worked on various extraction processes. December 1921, process via equal parts of ground-up beef pancreas and slightly acidic alcohol. Filtered, washed twice with toluene, and filter sterilized. This test solution was given to dogs to determine potency.

Dog #408

4 August 1921 –

- Dog #408 receives an injection of the extract, successfully dropping its blood glucose

- The dog remained in good condition.
- Banting and Best referred to their pancreatic extract as “Isletin” for the first time

- Dog #408 would eventually die of an infection, after successfully receiving injections for a number of hours.

- Banting and Best had learned much about “Isletin” and its anti-diabetic properties and were eager to send a report to Macleod.

A History of Insulin

- Leonard Thompson was the first patient to receive insulin. 14-year-old, weight 65 lb (29.5kg). Pale, smelled of acetone, was losing hair, had a distended abdomen, described as looking like the victim of a concentration camp. Charity patient.
- 11 January 1922, House Officer, Ed Jeffery, injected 7.5 ml of Banting and Best's extract (thick brown muck) into **each** buttock of the patient. Sterile abscess at the site of one injections.
- **Bit Missing here!**
- Push to perfect the extraction process and commercialize insulin was on. Banting's team entered into an agreement with Eli Lilly and Company, and, by July 1922, the first bottles of Lilly's Iletin (insulin) arrived in Banting's office.
- Insulin was commercially available in the United States by 1923.

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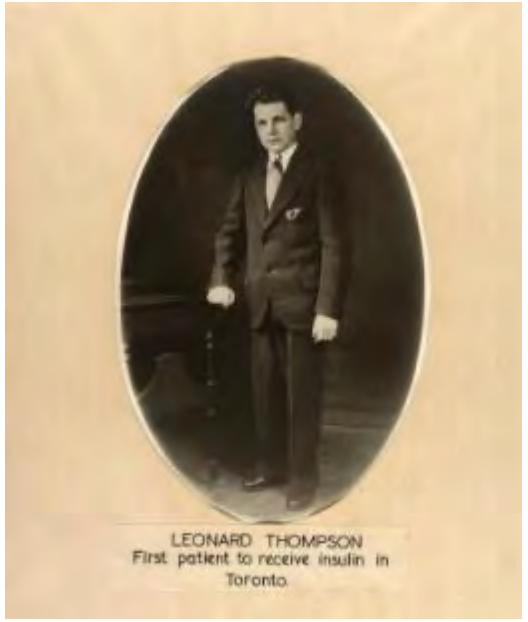
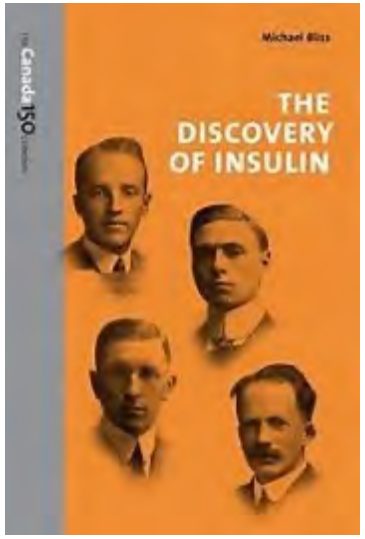


Collip and the Missing Bit from most Histories of Insulin 1

- 11 January 1922….injected 7.5 ml of Banting and Best's…… extract (thick brown muck) into **each** buttock of the patient…

- **Bit Missing here!**

- …blood glucose dropped from .440 to .320. – 24.4 mmol/l to 17.8 mmol/l, urine glucose from 91.5g to 84g (per 24 hrs), Rothera ketones test strongly positive.
- "No clinical benefit was evidenced"- referenced to Banting, Best, Collip, Campbell, and Fletcher 1922** "another crushing defeat for Banting"**
- And Collip had **not** been allowed to supply the extract.



Work on diabetes shows progress against disease
Toronto medical men hoping that cure is close at hand
A boy is treated
Effect of first treatment was so good that injections are continued

14 January 1922 – The press coverage begins.


WORK ON DIABETES SHOWS PROGRESS AGAINST DISEASE

Toronto Medical Men Hoping That Cure is Close at Hand.

A BOY IS TREATED

Effect of First Treatment Was So Good That Injections Are Continued

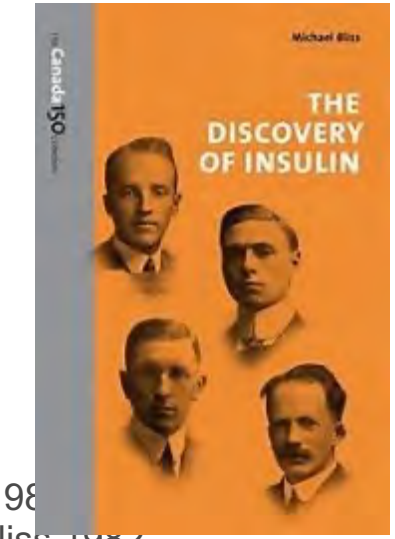
*Banting A Biography. Michael Bliss 1984. General Source.
**The Discovery of Insulin. Michael Bliss 1982.

Collip and the Missing Bit from most Histories of Insulin 2

- 11 January 1922….injected 7.5 ml of Banting and Best's…… extract ("thick brown muck") into **each** buttock of the patient…

- **Bit Missing here!**

- 20 December 2021: Banting and Best had tried oral extract on Dr Joe Gilchrist- failed. Then *'failed for the seventh straight time to reduce an animal's blood sugar'**
- 22 December 1921: Collip found that one of the extract-treated dogs had restoration of liver glycogen. And that his extract could relieve ketonuria.
- Collip: had shown restoration of two key metabolic defects in a dying diabetes dog versus just a glucose-lowering effect. Also that his extract induced severe hyppoglycaemia- corrected by glucose injection in rabbits ("insulin shock)
- 30 December 2021: Yale University presentation by Banting- criticism of experiments- including no temperature records- but verified that the extract had reduced glucose in at least 50% of the dogs tested
- Motivation for going for the clinical testing of the extract on a dying human.



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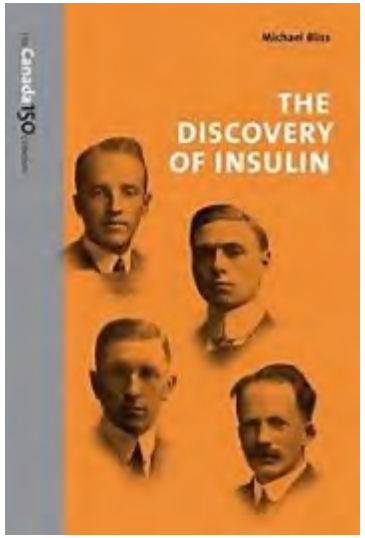
*Banting A Biography. Michael Bliss 198
**The Discovery of Insulin. Michael Bliss 1982.

Collip and the Missing Bit from most Histories of Insulin 3

- 11 January 1922 Banting and Best's extract. And Collip had **not** been allowed to supply the extract. Collip continued to refine his extraction process. 16th Jan 1922- discovered that he could create an "alcohol trap" to refine the purification of insulin via its precipitation.

- 23 January 1922….second injection- this time Collip's extraction. **"The results were spectacular."**

Extract →	Banting & Best	Collip
Date of Injection	11 January 1922	23 January 1922
Blood Glucose	17.8 mmol/l	Normal (<10mmol/l)
Rothera Ketones Test	Strongly Positive	Negative (Normal)
Urine Glucose	Strongly Positive	"almost disappeared"
Leonard Thompson	**"No clinical benefit"**	**"visibly brightened…more active"**



- Banting's own words: **"These results were not as encouraging as those obtained by Zuelzer in 1908"*****

*Banting A Biography. Michael Bliss 1984. General Source.
**The Discovery of Insulin. Michael Bliss 1982.
*** History of Insulin. Frederick Banting 19

The tragedy of Georg Ludwig Zülzer

- In 1908, in Germany **Zülzer** showed that pancreatic extracts could reduce the sugars and ketones in the urine of six diabetic patients
- At least one of those patients came out of a diabetic coma. Calling his preparation "**Acomatol**". But as supplies ran out, the patient died.
- Convinced of its effectiveness in treating diabetes, a patent was filed
- Extracts had caused fever, shivering and vomiting in patients
- In his patent application there was a technique to use alcohol to overcome this issue
- Soon his preparations were causing no signs of fever, shivering or vomiting. But test animals became convulsive and sometimes slipped into a coma. This insuli was too pure!
- But with the outbreak of WW1 in 1914, Zuelzer's research on insulin was brought to an abrupt halt from which it never recovered.
- Severe blow to hear about the Nobel Prize

XXIV.

Ueber Versuche einer specifischen Fermenttherapie des Diabetes.

Vorläufige Mittheilung.

Von

G. Zuelzer.

In einer früheren Mittheilung habe ich zu zeigen versucht, dass zwischen den Producten der inneren Pankreas- und der Nebennierensecretion gewisse nahe, antagonistische Beziehungen bestehen, u. a. dass es möglich ist, durch Injection eines bestimmten Pankreasextractes den Adrenalin-diabetes zu unterdrücken. Seither ist es mir gelungen, die Wirksamkeit dieses Pankreasextractes so zu erhöhen, dass $^1/_{20}$—$^1/_{10}$ der früher noth-wendigen Menge, nämlich 0,2—0,5 g intravenös injicirt, bereits genügen, jene Suppression der Adrenalin-Glykosurie zu erzielen. Zur Herstellung des Pankreaspräparates wird die Bauchspeicheldrüse vom lebenden Thiere, welches auf der Höhe der Verdauung befindlich ist, ent-nommen, nachdem die Drüse 1—$1^1/_2$ Stunden gestaut wurde. Die weitere Bereitung des Präparates geschieht durch Eiweissfällung, die ich bisher auf verschiedene Weise vorgenommen habe, ohne dass jedoch das Ziel, vollkommen verlustlos ein eiweissfreies Präparat zu gewinnen, erreicht wäre. Mit der Herstellung aber eines wirksamen Pankreaspräparates schien auch der Versuch gerechtfertigt, den Pankreasdiabetes, sowohl den experimentellen beim Hunde, wie auch den genuinen menschlichen Diabetes durch das gleiche Präparat zu beeinflussen. Theoretisch war dazu die Grundlage durch die Hormon-lehre Starlings[2]) — er versteht unter Hormonen die Producte der inneren Secretion der verschiedenen Organe — bereits geschaffen; auch hatte dieser Forscher auf Grund seiner übrigen Versuche, auf die hier nur hingewiesen werden soll, es bereits als wahrscheinlich bezeichnet, dass es gelingen werde, durch intravenöse Injection geeigneter Pankreas-extracte die Zuckerausscheidung beim menschlichen Diabetiker günstig zu beeinflussen.

Pflüger hat jüngst ausgesprochen, dass er nicht eher an die innere Secretion des Pankreas glauben werde, bis der Nachweis erbracht sei,

1) Congress für Innere Med. 1907.
2) Centralblatt für die Physiologie und Pathologie des Stoffwechsels. 1906.

Convincing the world

Nicolae Paulescu: It was actually revealed that during the summer of 1921, at the same time as Banting and Best started their work, that Romanian scientist had already published similar experiments in a European scientific journal, in French
But Paulescu's scientific work has since been overshadowed by the ugly revelation of his anti-Semitic politics and the role that he played in inciting the Holocaust in Romania.

Charles Best in a re-constructed lab

Charles Best: When asked whether researchers such as Paulescu, Zuelzer, Kleiner, deserved any credit for the discovery of insulin, his reply spoke volumes:

"None of them convinced the world of what they had … This is the most important thing in any discovery. You've got to convince the scientific world. And we did."

The discovery of insulin: a story of monstrous egos and toxic rivalries
Insulin – the Crooked Timber: A History from Thick Brown Muck to Wall Street Gold' OUP. 2022
Kersten Hall 2022. Leeds UK

Gift to the World

Patented Oct. 9, 1923. 1,469,994

UNITED STATES PATENT OFFICE.

FREDERICK G. BANTING AND CHARLES HERBERT BEST, OF TORONTO, ONTARIO, AND JAMES BERTRAM COLLIP, OF EDMONTON, ALBERTA, CANADA, ASSIGNORS TO THE GOVERNORS OF THE UNIVERSITY OF TORONTO, OF TORONTO, ONTARIO, CANADA.

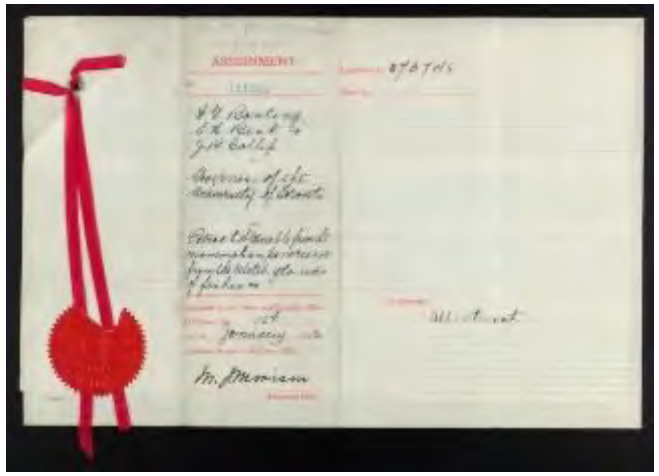
EXTRACT OBTAINABLE FROM THE MAMMALIAN PANCREAS OR FROM THE RELATED GLANDS IN FISHES, USEFUL IN THE TREATMENT OF DIABETES MELLITUS, AND A METHOD OF PREPARING IT.

No Drawing. Application filed January 11, 1923. Serial No. 612,138.

To all whom it may concern:

Be it known that we, FREDERICK G. BANTING and CHARLES HERBERT BEST, of the city of Toronto, in the county of York and Province of Ontario, Dominion of Canada, and JAMES BERTRAM COLLIP, formerly of the said city of Toronto, and now of the University of Alberta, in the city of Edmonton, in the Province of Alberta, Dominion of Canada, British subjects, have invented an extract obtainable from the mammalian pancreas or from the related glands of fishes, useful in the treatment of diabetes mellitus, and a prepare the extract containing the secretion or hormone in practically pure form and to devise suitable means for obtaining the maximum yield of it.

This was done by extracting the internal secretion or hormone from the fresh pancreas of mammalia, or, from the fresh pancreas of cartilaginous fishes, or, from fresh related glands, (principal Islets), of bony fishes, with a solvent capable of preserving the activity of the internal secretion or hormone and then separating it practically free from injurious substances including inert asso-



Canada and US Patents for Insulin

Nobel Prize for Medicine Awarded To Doctors Banting and MacLeod

(Special Cable to The Globe and The Chicago Tribune. Copyright, 1923.)

DR. F. G. BANTING

STOCKHOLM, Oct. 25.—The Council of Teachers of the Karolinska Institute this evening decided to give the Nobel Prize to the Canadian professors of the University of Toronto, Doctors F. G. Banting and J. J. R. MacLeod, for the discovery of insulin.

The Nobel Prize in 1922 was awarded to a professor of University College, London, Archibald Hill, because of his discoveries in the physiology of the muscles, and the second half to a professor of the University of Kiel, Otto Meyerhof, for his researches concerning oxygen, lactic acid and consumption of muscles.

This is only the second time that a Nobel Prize, for outstanding service in the field of medicine, has been awarded in America. It is the first time that any Nobel Prize has ever fallen to the lot of a Canadian.

The previous award of the prize in medicine on this continent was made to Dr. Alexis Carrel in 1912, for his work in connection with surgery of the blood vessels and transplantation of tissues and organs.

DR. J. J. R. MACLEOD.

The other Nobel awards made to Americans are: One in physics to A. A. Michelson, one in chemistry to T. W. Richards, and prizes for efforts in furthering peace to the late Theodore Roosevelt, Honorable Elihu Root, and ex-President Woodrow Wilson.

The total value of the award to be divided between Dr. Banting and Dr. MacLeod amounts to about $40,000. It is understood that the prize was awarded jointly, in view of the fact that Professor MacLeod, as head of the Department of Physiology at the University of Toronto, directed the work in the laboratories where Dr. Banting conducted the investigations which led up to the discovery of insulin.

Professor MacLeod has not yet returned to Toronto from England, where he has been for the past month or two, and Dr. Banting could not be reached at his home here.

CANADIAN PACIFIC RAILWAY COMPANY'S TELEGRAPH

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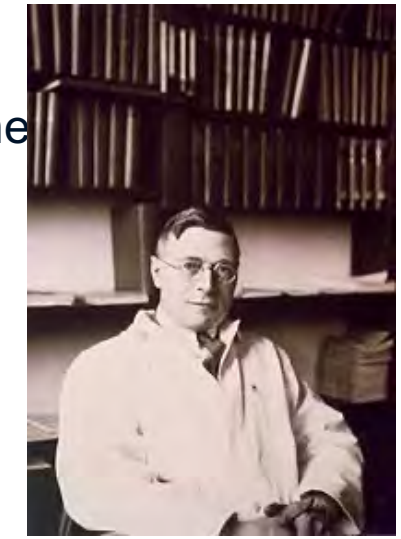
"It is not within the power of the properly constructed human mind to he satisfied. Progress would cease if this were the case."

– Sir Frederick Grant Banting

SPRINGER NATURE
On This Day

James Bertram Collip (1892-1965)

- Born in Belleville Ontario 20 November 1892, education began in a one-room schoolhouse, then Trinity College in Toronto (15). Medical school not possible- too young. Enrolled in Biochemistry and Physiology (Hons), top of class in 1912. PhD under Prof AB Macallum in Toronto. His first scientific paper published when 21 yrs old.
- Research at University of Alberta for almost five years. In 1921, he was Associate Professor of Biochemistry at the University of Alberta with 24 publications. Research in Chicago, Sheffield, and Glasgow.
- In 1921, Collip arrived in Toronto, on a sabbatical, to work with Prof JJR Macleod.
- Rockefeller Fellowship: early December 1921 Collip joined in the effort to purify the pancreatic extract so that it could be administered to humans.



- Early January 1922, Collip wrote enthusiastically to President of U of A detailing success of the insulin experiments – stayed as Assistant Professor in Pathological Chemistry at University of Toronto.
- Collip contributions in human insulin therapy, his extract:
  - Clearance of ketones from diabetic urine
  - Processed glucose to glycogen in the liver.
  - Observed and cured "insulin shock", with glucose injection
  - First to produce a form of animal pancreatic extract pure enough, and not toxic to be injected into a human patient with clinical improvement

https://insulin.library.utoronto.ca/about/collip

James Bertram Collip (1892-1965)

- May 1922: returned to the University of Alberta now as the Chair of the Department of Biochemistry. In Edmonton, researched alternative sources of insulin continuing his research with the help of JJR Macleod and a Carnegie grant. Collip first looked to clams, yeast, vegetables, including potato peelings as a source of insulin- March 1923 presented "glucokinin“
- October 1923, Nobel Prize was announced, JJR Macleod made it known that he would share his prize with Collip. At U of A , 1922 and 1927, Collip published over forty articles, and awarded D.Sc. and M.D
- In 1938: Associate Committee on Medical Research of the National Research Council, chaired by FG Banting. In 1939 Collip VC, then 1941, after Banting's sudden death, Chair

- McGill University in Montreal, then as Dean of the U of A Medical School (from 1948). Research into parathyroid and ACTH isolation.
- Collip and Banting had met the day before Banting’s death. Terrible shock to Collip, for in the years since the discovery of insulin, the two men had formed a friendship.
- Acting Lieutenant-Colonel, Royal Canadian Army Medical Corps from 1942 to 1944 and was promoted to Acting Colonel in 1944. Collip also received many honorary degrees including those from Harvard and Oxford Universities.
- Collip died on 19 June 1965 after suffering a stroke. He and his wife had three children.

https://insulin.library.utoronto.ca/about/collip

Frederick Grant Banting
1891-1941

Banting developed the research idea and in collaboration with Banting made most of the experiments and surgeries.

Charles Herbert Best
1899-1978

Best collaborated with Banting on most of the experiments and surgeries that led to the discovery of insulin.

John James Rickard MacLeod
1876-1935

MacLeod provided the laboratry and scientific guidance through all research steps. He had an active role in the final steps of isolating and purifying of insulin.

James Bertram Collip
1892-1965

Collip played a central role isolating and purifying insulin.

DR. COLLIP'S PART IN INSULIN DISCOVERY

University of Alberta Professor to Get Fourth Part of the Nobel Prize

EDMONTON, Nov. 8.—The report that Dr. Collip, of the University of Alberta, would share in the Nobel prize for his part in the discovery of insulin, has been received with much satisfaction, and has apparently cleared up some misunderstanding. Insulin was discovered by four men, Drs. Banting, Best, MacLeod and Collip, each doing some part in the work. When the announcement was first made, the names of the four men were included. But later when the Dominion parliament recognized the discoverers, the name of Dr. Collip was omitted. When the Nobel prize was first announced it was to be shared between Dr. Banting and Dr. MacLeod. The former announced that he had shared his part of the prize with Dr. Best, and now Dr. MacLeod has announced that he has shared his part with Dr. Collip. Each of the four will get $10,000. Here is the statement made by Dr. MacLeod:

"Dr. Collip made a very important contribution to the work, and his share was equal to that of the others," said Dr. MacLeod.

"Dr. Banting and Dr. Best showed by their experiments that insulin was present in extracts of the pancreas. It was then that Dr. Collip came in and, with his assistance, it was shown that it was possible to induce insulin suitable to continued use. His skill in bio-chemistry made his services very valuable in the preparation and purefaction of insulin. He worked on the insulin experiments for about six months," said Dr. MacLeod, "and it was his insulin that was used in the first clinics. His name is on the first clinical papers."

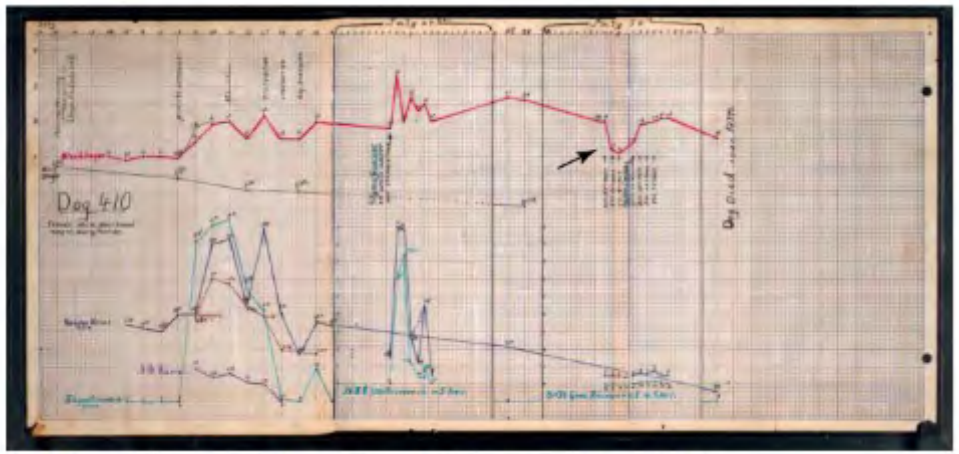


Figure 4. Variation of glycaemia (arrow) of the first dog (nº 410) treated with intravenous insulin extracts, on 30 July 1921.

Cardoso, Luís et al. "Banting and Best: The Extraordinary Discovery of Insulin." *Revista Portuguesa de Endocrinologia, Diabetes e Metabolismo* 12 (2017): 106-115.

Vision of Ezekiel

When insulin was first used to treat patients in the early 1920s, diabetes specialist Elliott Joslin likened its power to the **'Vision of Ezekiel'** , the Old Testament prophet who is said to have seen a valley of dry bones rise up and be restored to life.

(One patient was) just about the weight of her bones and a human soul
Elliott Joslin, MD

Hall, Kersten T., *Insulin - The Crooked Timber: A History from Thick Brown Muck to Wall Street Gold* (Oxford, 2022)

Teddy Ryder

- Born in New Jersey in 1916. Age 4, diagnosed with Type 1 diabetes. Allen diet- starvation diet of about 500-600 cals
- Most such patients only live 6 to 12 months. Teddy later recalled that at five-years-old he was “twenty-six or seven pounds” and could only walk up three or four steps before he needed help. His uncle, Dr Morton Ryder, personally contacted Banting to ask to include Teddy in the trials.
- Banting initially stated that he did not have enough insulin to treat Teddy along with his seven other patients but to bring him in September .
- Dr Ryder wrote to Banting saying that Teddy would survive until then as he was so weak- **“did not have the energy to play by himself”**.
- Banting agreed to treat Teddy and on July 10th, 1922 he was one of the first people to receive insulin. Within two weeks of starting the treatment, Ryder began to gain weight.
- September 1922: **Teddy his sixth birthday party and Banting attended. Teddy returned home in October 1922** and continued his treatment.

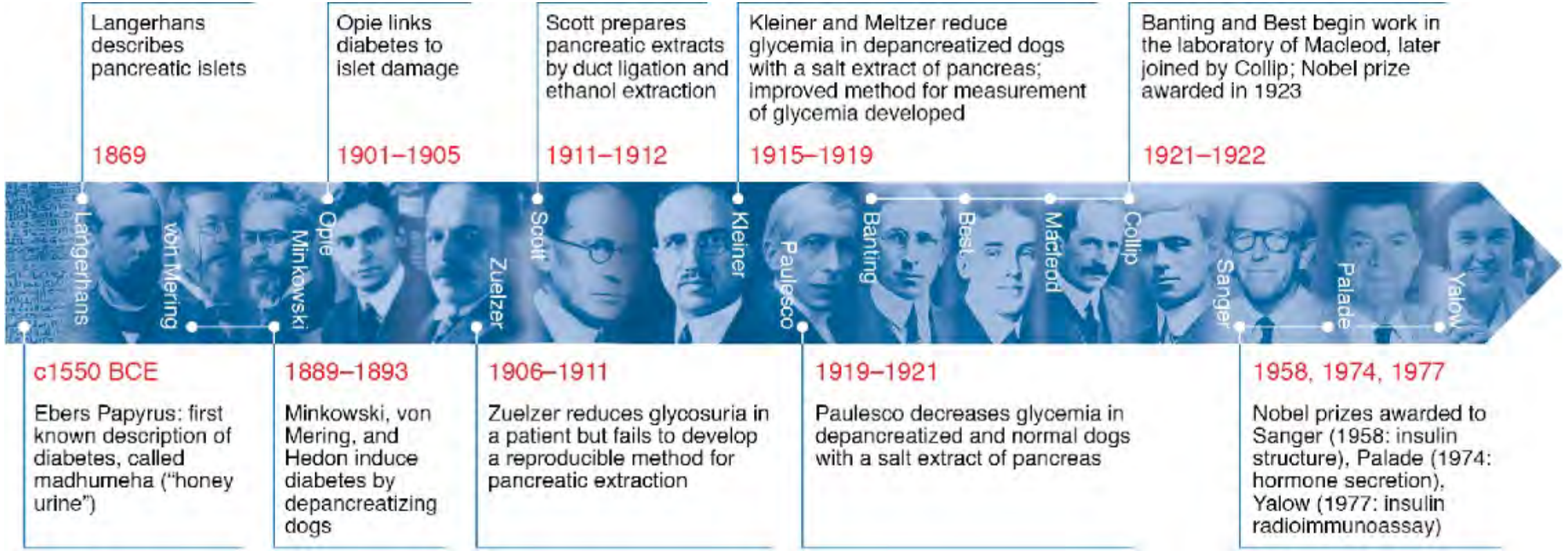
Dear Dr. Banting …..

Teddy Ryder

DEAR DR. BANTING.
I WISH
YOU COULD COME TO
SEE ME. I AM A FAT
BOY NOW AND I FEEL
FINE. I CAN CLIMB A TREE.
MARGARET WOULD
LIKE TO SEE YOU.
LOTS OF LOVE FROM
TEDDY RYDER

- Ryder went on to become a librarian in Hartford, Connecticut.
- He had no serious complications from diabetes the rest of his life.
- In 1990, he attended an unveiling of an exhibit at the University of Toronto honouring the discovery of insulin.
- He revealed his own before and after insulin treatment pictures in the exhibit as he stood in front of the crowd as a healthy man.
- Ryder died of heart failure at the age of 76 in 1993. At the time, he was the longrest-treated person using insulin in the world.

Based on a post by Rachel Delle Palme, Banting House NHSC. London, Ontario, Canada



Lewis, Gary Franklin and Patricia Lee Brubaker. "The discovery of insulin revisited: lessons for the modern era." *The Journal of clinical investigation* 131 1 (2021)

International Trial of the Edmonton Protocol for Islet Transplantation

Background

Islet transplantation offers the potential to improve glycemic control in a subgroup of patients with type 1 diabetes mellitus- the **Edmonton protocol**.

Methods

36 subjects with type 1 DM underwent islet transplantation at nine international sites. Islets were prepared from pancreases of deceased donors and were transplanted within 2 hours after purification. The **primary end point was defined as insulin independence** with adequate glycemic control 1 year after the final transplantation.

Results

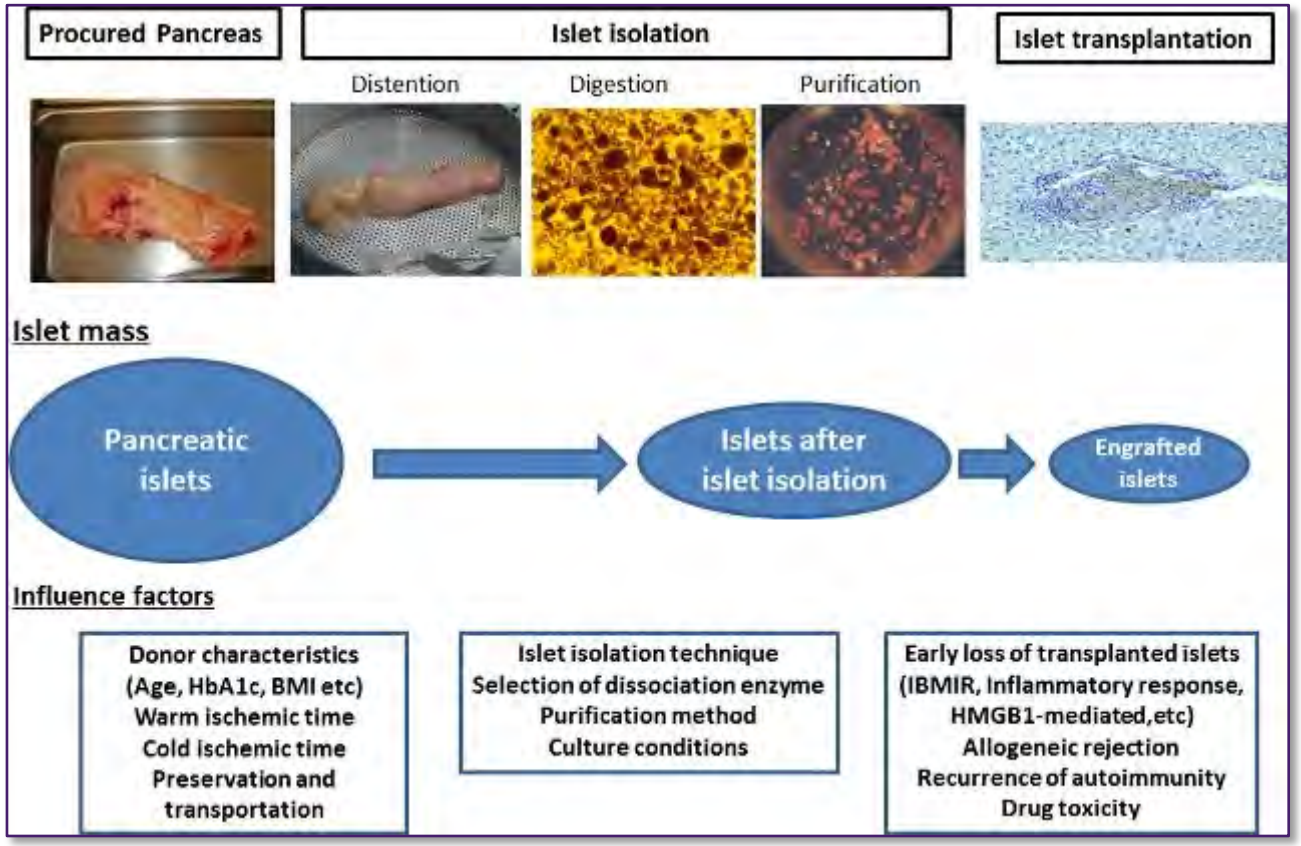
Of the 36 subjects, **16 (44%) met the primary end point**, 10 (28%) had partial function, and 10 (28%) had complete graft loss 1 year after the final transplantation. **A total of 21 subjects (58%) attained insulin independence with good glycemic control at any point throughout the trial**. Of these subjects, 16 (76%) required insulin again at 2 years; 5 of the 16 subjects who reached the primary end point (31%) remained insulin-independent at 2 years.

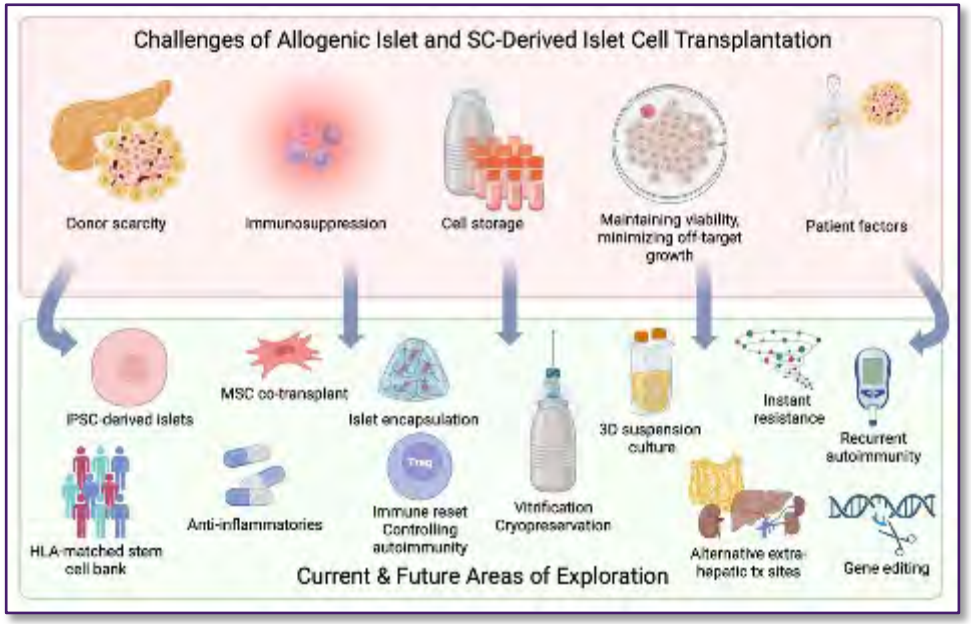
Conclusions

Islet transplantation with the use of the Edmonton protocol can successfully restore long-term endogenous insulin production and glycemic stability in subjects with type 1 diabetes mellitus and unstable control, but insulin independence is usually not sustainable. (ClinicalTrials.gov number, NCT00014911.)

Shapiro AJ, Ricordi C, Hering BJ, Auchincloss H, Lindblad R, Robertson RP, Secchi A, Brendel MD, Berney T, Brennan DC, Cagliero E. International trial of the Edmonton protocol for islet transplantation. New England Journal of Medicine. 2006 Sep 28;355(13):1318-30.

Edmonton Protocol

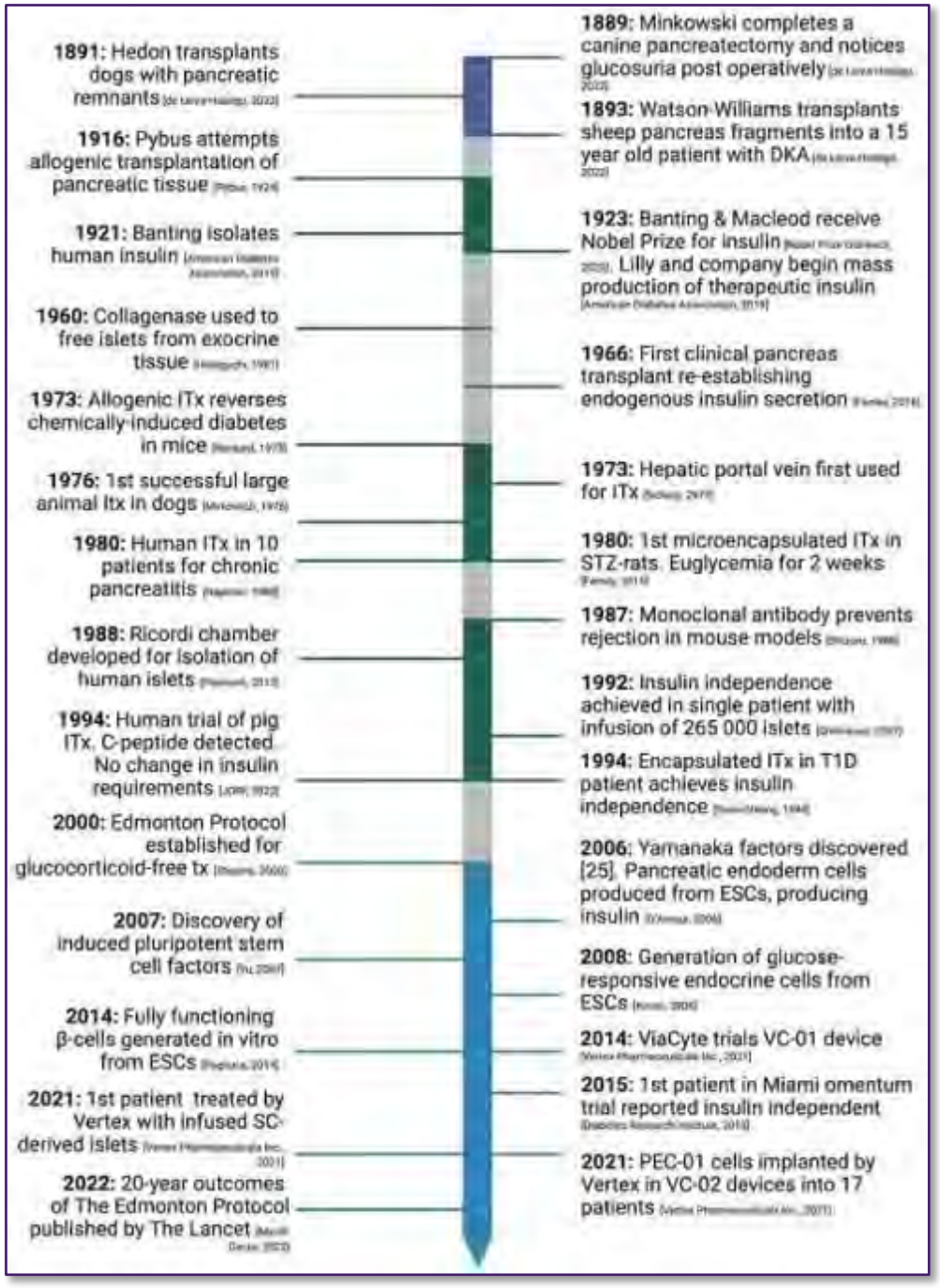


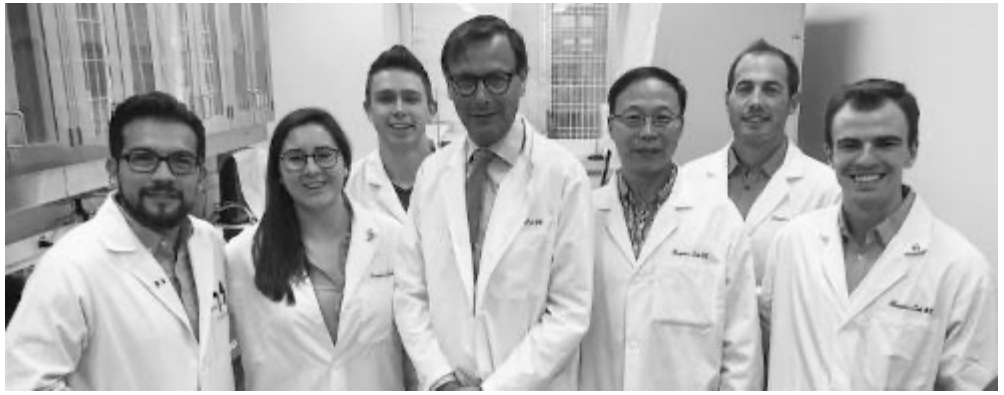


Prof Michael Overduin

He would surely understand this slide!

Recruitment of Ahsa1 to Hsp90 is regulated by a conserved peptide that inhibits ATPase stimulation
Hussein SK, Bhat R, **Overduin M**, LaPointe P. EMBO Reports ? Pending





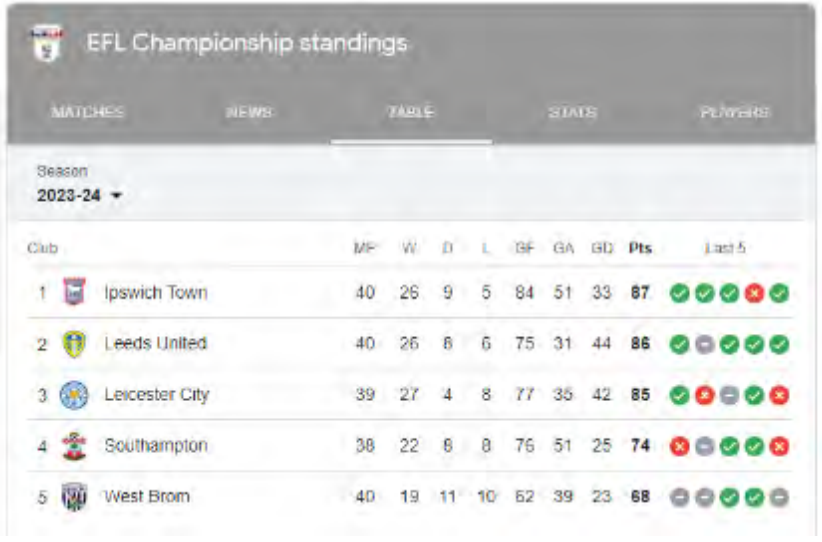
Prof James Shapiro and Colleagues

Scientist, researcher and transplant surgeon

Good to meet him someday?

The history of islet cell transplantation (ITx) and landmark discoveries from 1889 to 2021

DKA = diabetic ketoacidosis; ITx = islet cell transplantation; Tx = transplantation; ESC = embryonic stem cell. Czarnecka, Z.; Dadheech, N.; Razavy, H.; Pawlick, R.; Shapiro, A.M.J. The Current Status of Allogenic Islet Cell Transplantation. *Cells* **2023**, *12*, 2423. https://doi.org/10.3390/cells12202423



Islet transplant patient #252: ‘A second chance at a better life’

Procedure developed at U of A guides islet cell transplants for people with Type 1 diabetes around the worl

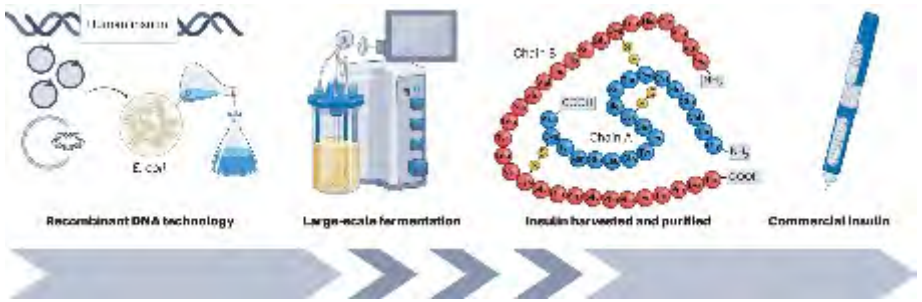
Nina Greene with her husband, Brent. Since receiving an transplant of insulin-producing islet cells in January 2017.

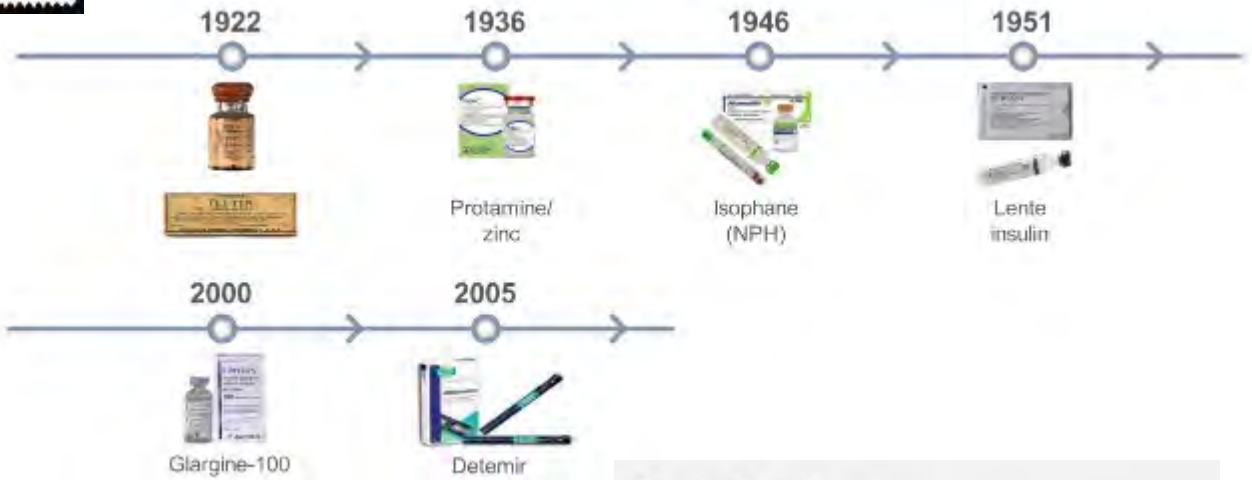
Technically, Greene still has diabetes, but **she hasn’t had to take insulin since September 2019, after she received a transplant of islet cells**, which produce insulin.

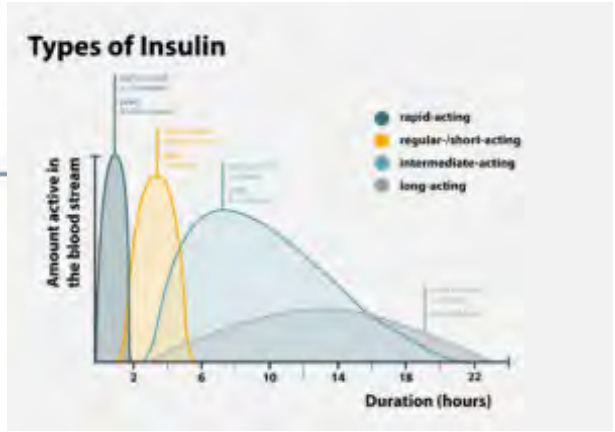
Today, she is **living a life she could only dream of before the transplant**. Every morning when she wakes up, she feels optimistic.

UofA Website accessed March 2024

Insulin therapy: An historical overview







Fiasp and Lyumjev

Hybrid Closed-Loop Systems

Roll out 2024-2029

Professor Partha Kar

NHS England National Specialty Advisor, Diabetes

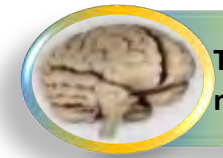
Kirby. Br J Diabetes Vasc. Dis. 2012, 12:315-320

Objectives for Our Diabetes Care

Reduce Complications of Type 1 & 2 diabetes

A chronic, lifelong condition with considerable morbidity and mortality

Macrovascular complications



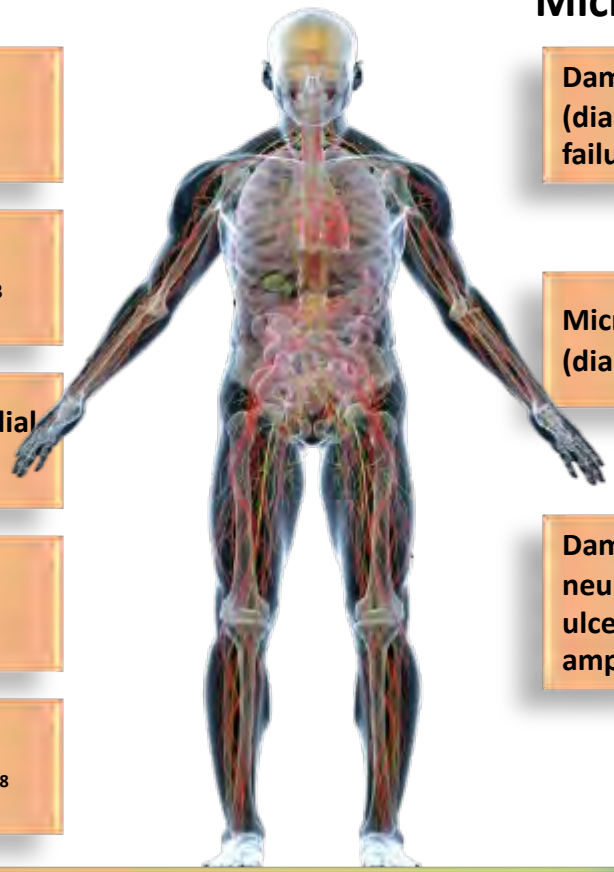
The risk of stroke in newly treated type 2 diabetes is more than double that of the general population[2]

People with diabetes are twice more likely to have cardiovascular disease than someone without diabetes[3]

There is almost a 10% increase in the risk of myocardial infarction[6]

Hypertension is a significant risk factor for the complications of type 2 diabetes [7]

Peripheral vascular disease affects 1 in 3 people with diabetes and increases the risk of heart attack and stroke[8]

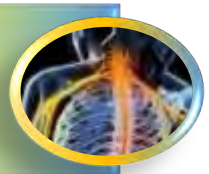


Microvascular complications

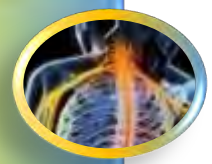
Damage to the kidney filtering systems from diabetes (diabetic nephropathy) is a leading cause of kidney failure[4]

Microvascular damage to the retina from diabetes (diabetic retinopathy) is a leading cause of blindness[5]

Damage to the nerves from diabetes (diabetic neuropathy) is a leading cause of foot wounds and ulcers which frequently lead to foot and leg amputation[9] · Erectile Dysfunction.



Others: Obesity, Depression, Anxiety, Dementia, Heart Failure, Increased cancer risks, Increased risk of death from Covid-19, Increased Cancer risk



Live longer, better lives without complications

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2. Jeerakathil T *et al. Stroke* 2007;**38(6):**1739–1743.
3. World Heart Federation. Cardiovascular Risk Factors – Diabetes. Available at: www.worldheart.org/cardiovascular-health/cardiovascular-disease-risk-factors/diabetes/ (Accessed May 2010)
4. Hovind P *et al. Kidney Int* 2001;**59(2):**702–709; 5. Fong DS *et al., Diabetes Care*. **2004;27(10):**2540–2553; 6. Deshpande AD *et al. Phys Ther* 2008;**88**:1254–1264.
7. Adler AI *et al.* on behalf of the UK Prospective Diabetes Study Group. *BMJ* 2000;**321**:412-9.
8. Peripheral artery disease. Available at: www.diabetes.co.uk/diabetes-complications/peripheral-artery-disease.html (Accessed June 2014)
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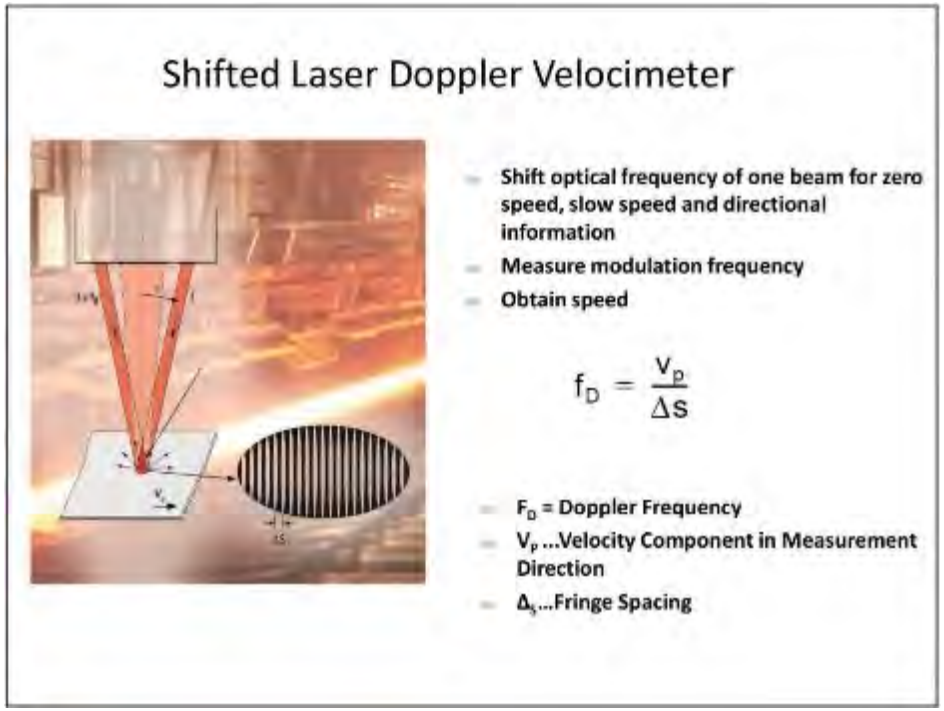
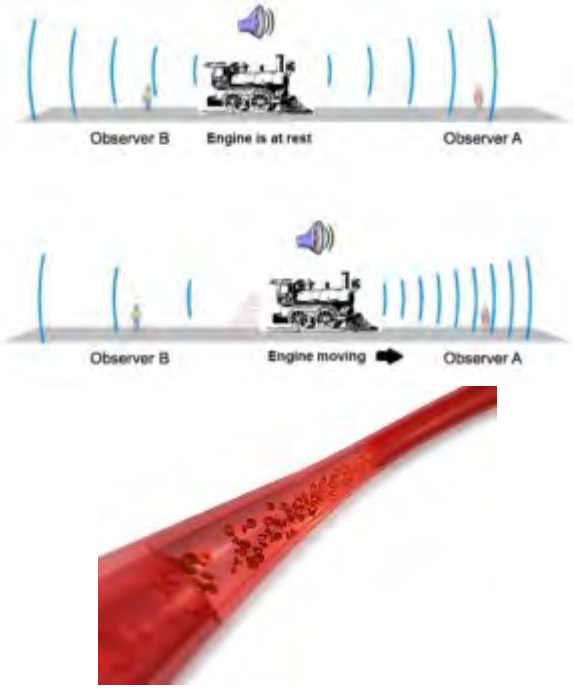
Diabetic Retinopathy: Evaluating Autoregulation by Determining Flow Under Limits

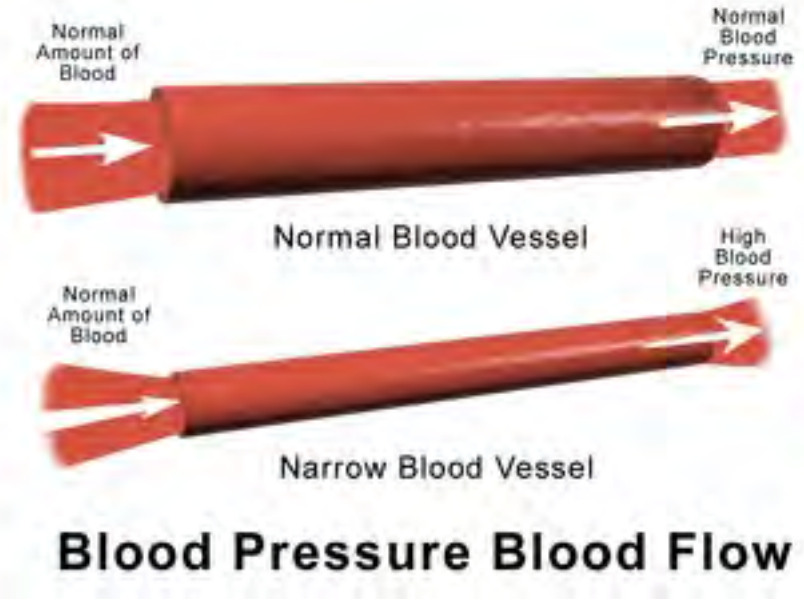
Laser Doppler Velocimeter

Prof Eva Kohner
Died 2021 age 92

- Retinal Blood Flow Under Different Circumstances







Accurate vessel width measurement from fundus photographs: a new concept

Salwan M B Rassam, Vinod Patel, Olaf Brinchmann-Hansen, Oddbjørn Engvold, Eva M Kohner

Abstract

Accurate determination of retinal vessel width measurement is important in the study of the haemodynamic changes that accompany various physiological and pathological states. Currently the width at the half height of the transmittance and densitometry profiles are used as a measure of retinal vessel width. A consistent phenomenon of two 'kick points' on the slopes of the transmittance and densitometry profiles near the base, has been observed. In this study, mathematical models have been formulated to describe the characteristic curves of the transmittance and the densitometry profiles. They demonstrate the kick points being coincident with the edges of the blood column. The horizontal distance across the kick points would therefore indicate the actual blood column width. To evaluate this hypothesis, blood was infused through two lengths of plastic tubing of known diameters, and photographed. In comparison with the known diameters, the half height underestimated the blood column width by 7·33% and 6·46%, while the kick point method slightly overestimated it by 1·40% and 0·34%. These techniques were applied to monochromatic fundus photographs. In comparison with the kick point method, the half height underestimated the blood column width in veins by 16·67% and in arteries by 15·86%. The characteristics of the kick points and their practicality have been discussed. The kick point method may provide the most accurate measurement of vessel width possible from these profiles.

(Br J Ophthalmol 1994; 78: 24–29)

Diabetic Retinopathy Unit, Department of Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, London
S M B Rassam
V Patel
E M Kohner

Department of Ophthalmology, University Hospital of Trondheim, N-7006 Trondheim, Norway
O Brinchmann-Hansen

Institute of Theoretical Astrophysics, University of Oslo, PO Box 1029, Blindern N-0315, Oslo 3, Norway
O Engvold

Correspondence to Professor Eva M Kohner, Diabetic Retinopathy Unit, Department of Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, Du Cane Road, London W12 0NN.

Accepted for publication 17 August 1993

The retinal vessels are the only part of the central circulation that can be viewed directly and studied in detail. Retinal vessel width changes have been utilised in the study of various physiological and pathological conditions.[1–3] With the developments of new techniques that accurately measure the velocity of red cells such as bidirectional laser Doppler velocimetry[4] and scanning laser ophthalmoscopy,[5] precise measurements of retinal vessel width become important for the determination of retinal volume blood flow. At present, the most commonly used techniques in determining vessel width from retinal photographs are microdensitometry which measures the density profile, film scanners that record photographic image transmittance, and film densities to provide film exposure profiles.[1–3] The only available method to derive an estimate of the vessel width from these profiles, uses the arbitrary assumption of the width at the half height of the profiles as a measure of the blood column width (Fig 1).[6] The width at the half height using these techniques is dependent on the characteristic photosensitivity calibration curves of the photographic film used. This is potentially another source of error.

At the Hammersmith hospital, a computer assisted digital image analyser is used to measure the light transmittance through film negatives of monochromatic fundus photographs,[7 8] and displays them on a screen as transmittance profiles. Two distinct skew points termed 'kick points' have been observed on the slopes in the transmittance profiles near the base of the curves (Fig 1). These kick points are also seen in densitometry profiles.[7 9] We set out to determine the source of these kick points, and to study the relation between the blood column and the vessel wall using mathematical models of hypothetical artery and vein. These models were tested using plastic tubing and human retinal photographs.

Materials and method

MATHEMATICAL MODEL

The mathematical models of the hypothetical

Figure 1 Monochromatic fundus photograph, displaying the transmittance profile of a vessel from the photographic negative. The half height, the kick points, and the slope reflectances thereon.

And how to measure the blood vessels….

Rejected multiple times… until **Olaf and Oddbjorn** stepped in from the **Oslo Institute of Theoretical Astro-physics!**

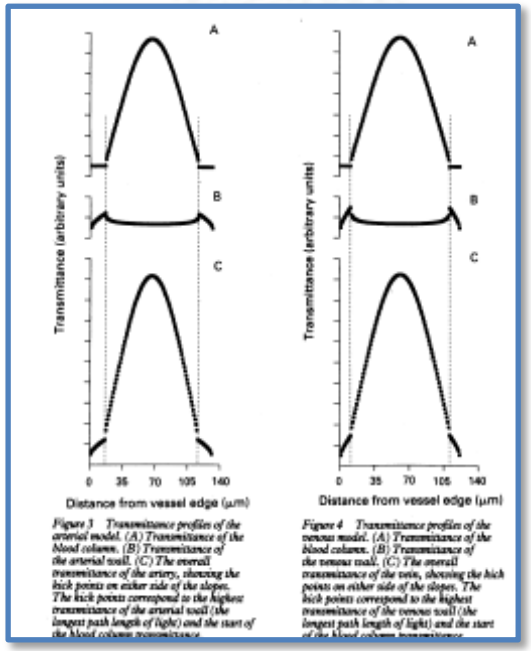


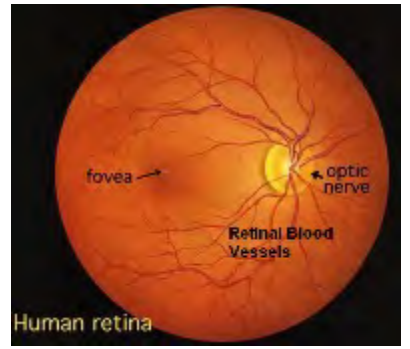
Figure 3 Transmittance profiles of the arterial model. (A) Transmittance of the blood column. (B) Transmittance of the arterial wall. (C) The overall transmittance of the artery, showing the kick points on either side of the slopes. The kick points correspond to the highest transmittance of the arterial wall (the longest path length of light) and the start of the blood column transmittance.

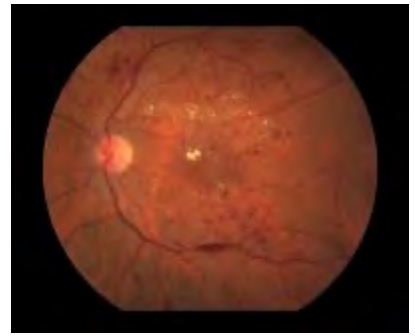
Figure 4 Transmittance profiles of the venous model. (A) Transmittance of the blood column. (B) Transmittance of the venous wall. (C) The overall transmittance of the vein, showing the kick points on either side of the slopes. The kick points correspond to the highest transmittance of the venous wall (the longest path length of light) and the start of the blood column transmittance.

Main research findings ever!

In Diabetes retinal blood flow is increased:

- **OBJECTIVES**--(a) To report on retinal blood flow, (b) to formulate a haemodynamic model for the pathogenesis of diabetic retinopathy
- **DESIGN**--Laser-Doppler velocimetry and computerised image analysis
- **SETTING**--Diabetic retinopathy outpatient clinic
- **SUBJECTS**--24 non-diabetic controls and 76 diabetic subjects were studied , 12 had no DR, 27 background DR, 13 pre-proliferative DR, 12 proliferative DR, 12 post laser.
- **MAIN OUTCOME MEASURES-**-Retinal blood flow and conductance
- **RESULTS**- Controls 9.52 microliters/min and diabetic patients with no diabetic retinopathy (9.12 ul/min), RBF increased in all grades of DR (background 12.13 ul/min, pre-proliferative 15.27 ul/min, proliferative 13.88 ul/min). Significant decrease in flow after laser (4.48 ul/min). Results independent of age, sex, type of diabetes, duration of diabetes, glycated haemoglobin concentration, blood glucose concentration, blood pressure, and intraocular pressure.
- **CONCLUSIONS**--Retinal blood flow is significantly increased in diabetic retinopathy. This has implications for controlling hypertension and hyperglycaemia as a strategy in reducing morbidity from diabetic retinopathy.





Patel V et al, BMJ 1994

WARWICK
MEDICAL SCHOOL

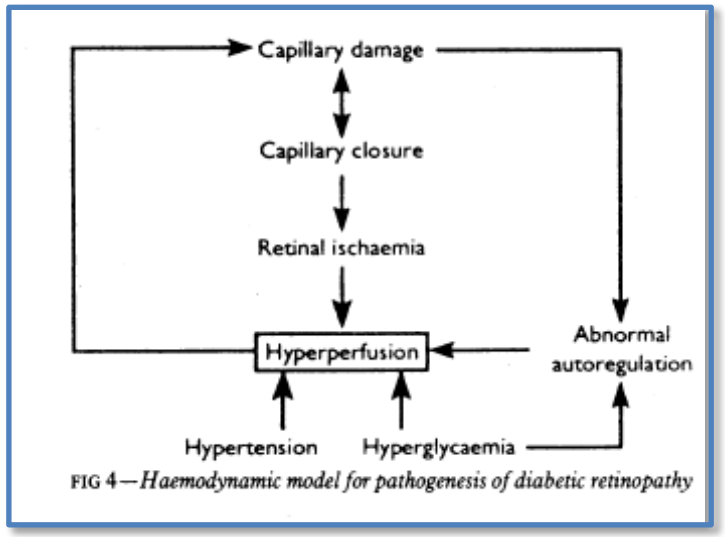


FIG 4—*Haemodynamic model for pathogenesis of diabetic retinopathy*

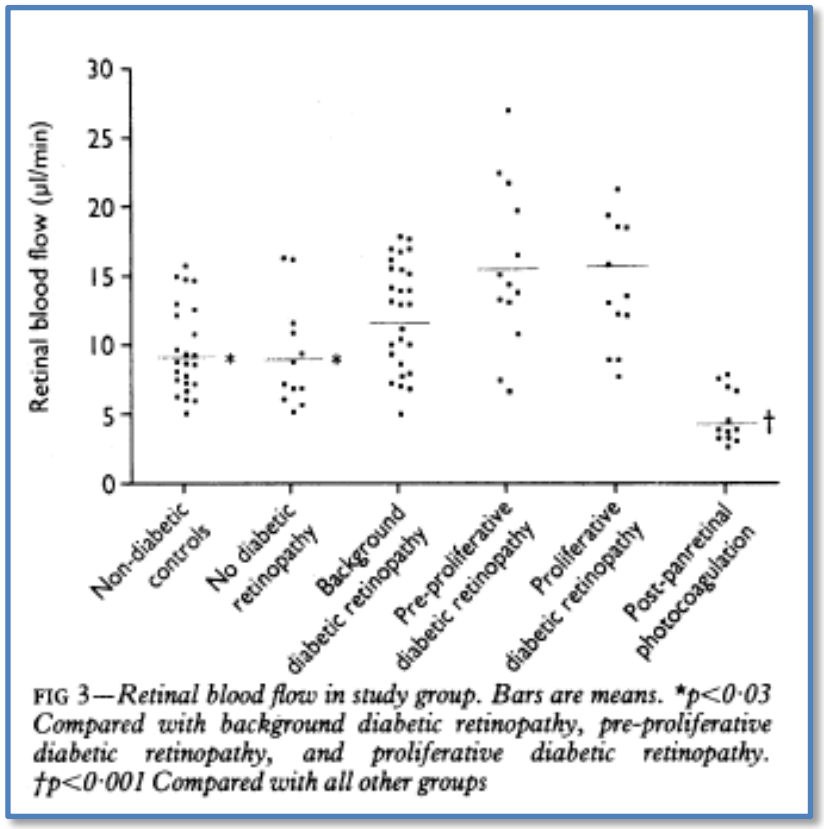
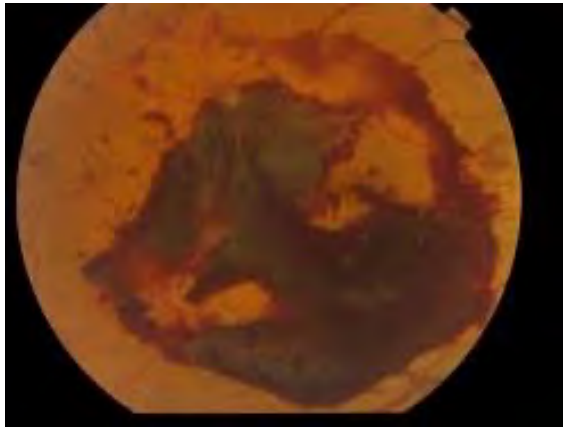
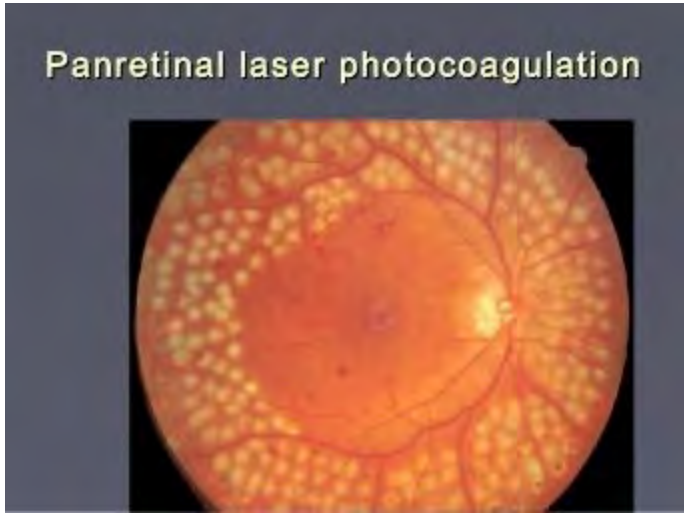


FIG 3—*Retinal blood flow in study group. Bars are means. *p<0·03 Compared with background diabetic retinopathy, pre-proliferative diabetic retinopathy, and proliferative diabetic retinopathy. †p<0·001 Compared with all other groups*





Oxygen reactivity in diabetes: *hypertension and hyperglycaemia*

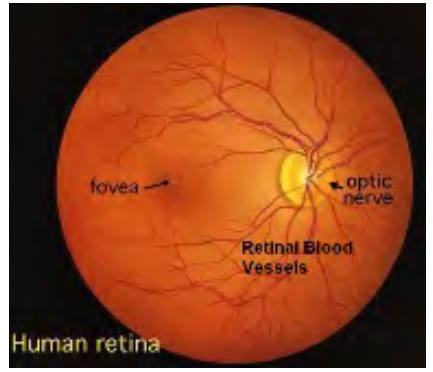
WARWICK MEDICAL SCHOOL

Abstract

Aim: LDV to define retinal vascular autoregulation to 60% oxygen breathing (vasoconstriction). Normotensive & hypertensive diabetic subjects under conditions of relative normoglycaemia (< 10 mmol) and hyperglycaemia (> 15 mmol) controls

Results: RBF significantly higher in diabetic subjects when hypertensive and hyperglycaemic than in the same diabetic subjects when normotensive and normal glucose

- **Normotensive controls** oxygen reactivity was **41.16** ± 14.09%
- **Normotensive 'hyperglycaemic**' diabetic subjects reduced to **21.75** ± 15.56%
- **Hypertensive diabetes, controlled BP, 'normoglycaemia' 30.49** ± 14.20%
- **Hypertensive diabetes, uncontrolled BP, 'normoglycaemia' 26.91** ± 13.43%
- **Hypertensive diabetes, controlled BP , 'hyperglycaemia' 18.36** ± 11.42%
- **Hypertensive diabetes uncontrolled BP, 'hyperglycaemia' 17.17** ± 13.24%, all $p < 0.05$



Conclusion: Retinal vascular reactivity is impaired in diabetes, both when they are normotensive and when they are hypertensive. Hyperglycaemia, to a degree commonly encountered in clinical practice, impairs retinal vascular auto-regulation even further.

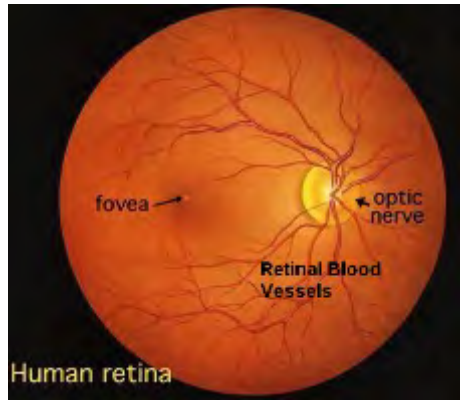
Patel V et al 1994 Clin Sci

Effect of ACE-I Perindopril and ß-blockade Atenolol on retinal blood flow in hypertensive diabetic subjects

WARWICK MEDICAL SCHOOL

Aim: ACE-I on the diabetic retinal circulation not been studied previously.

Subjects: 45 hypertensive diabetes subjects, RCT, over a period of 12 months. LDV. BP changes similar: perindopril [PE]: 152.1± 3.3/97.2 ± 1.7 to 136.8 ±3.4/85.8 ±2.1; atenolol: 158.9 ±5.1/97.5 ±1.6 to 137.9 ±3.4/85.1 ±1.6; P = .607



- **RBF decreased 17.19** ± 2.21 ul/min, to **14.18** ± 1.50 ul/min in the PE group P = .208
- **Increased with atenolol 15.80** ± 1.24 ul/min, to **16.99** ± 1.18 ul/min P = .399
- **Comparison**: **PE -7.16%** ± 11.49%; **atenolol, +15.31%** ± 9.51% P < .05
- Increase in RBF in 33.3% PE, 70.6% atenolol
- No significant changes in retinal vascular permeability
- Albuminuria decreased to a greater degree with PE, but did not reach significance (PE, 112.1 ± 39.5 mg/24 h to 88.6 ± 30.5 mg/24 h; atenolol, 87.3 ±51.7 mg/24 h to 82.1 ± 47.7 mg/24 h).
- **Conclusion:** ACE inhibition may promote a hemodynamic milieu in the hypertensive diabetic retinal circulation that serves to protect against the progression of diabetic retinopathy, whereas beta-blockade has the opposite effect.

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Key to the Knowledge

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J Endocrinol Thyroid Res

The THOR Effect: Thyroid Hormone Offsets Retinopathy

Sankarnarayanan Sailesh*, Harpal S Randeva, Chris JO Callaghan, Paul OHare, Paul O Hare, Sam Philip, Ponnusamy Saravanan and Vinod Patel

Warwick Medical School, UK

Submission: July 21, 2017; **Published:** February 20, 2018

***Corresponding author:** Sankaranarayanan Sailesh, MBBS, MD, FRCP, University Hospital Coventry & Warwickshire NHS Trust, Clifford Bridge Road, Coventry CV22DX, UK, Tel: +44-2476-965972; Fax: +44-2476-965964; Email: sailesh.sankar@uhcw.nhs.uk

Abstract

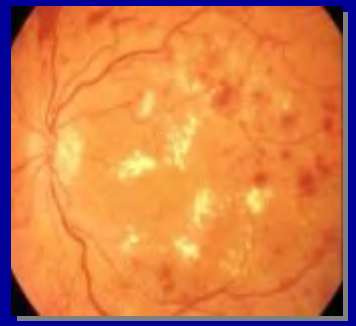
Objective: Thyroid status has been implicated in macrovascular disease both in patients with and without diabetes, however its effect on microvascular complications has not been explored. We assessed the prevalence and time to development of diabetic retinopathy in patients with type 2 diabetes with and without thyroxine treatment.

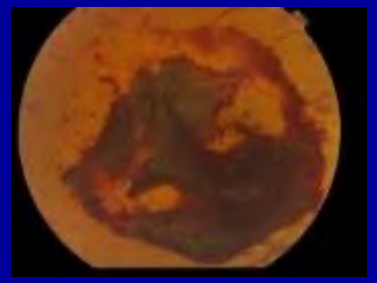
Research design and methods: The prevalence of retinopathy was determined, in a retrospective cohort study from a secondary care referral diabetes clinic patients with type 2 diabetes and coexisting treated hypothyroidism (THD; n=147) and duration matched controls without hypothyroidism (DM2; n=383), Using Kaplan-Meier survival analysis and Cox Proportional Hazards regression model we estimated the time to development of retinopathy in the two groups.

Results: Prevalence of retinopathy was 27.9% in THD group, as compared to 55.1% in the DM2 group ($p<0.001$). THD were less than one-third as likely to have concurrent retinopathy than, DM2 patients (OR=0.32; 95% CI=0.21 to 0.48; $p<0.001$). There was a significant difference in the median time to retinopathy between THD and DM2 patients (21.0yrs vs. 13.0yrs: Log-Rank $p<0.001$). Risk of developing retinopathy in THD patients was two-fifths of that of DM2 patients (hazard ratio=0.418; $p<0.001$) in a time-dependent variable analysis. The risk of developing retinopathy was concomitantly lower for patients with longer duration of hypothyroidism and thyroxine treatment prior to diagnosis of diabetes (Hazard ratio=0.957:p= 0.004).

Conclusion: A significant sparing effect on development of retinopathy was noted in type 2 diabetic patients with concomitant hypothyroidism (on thyroxine). The exact mechanism(s) for these observations remain to be elucidated.

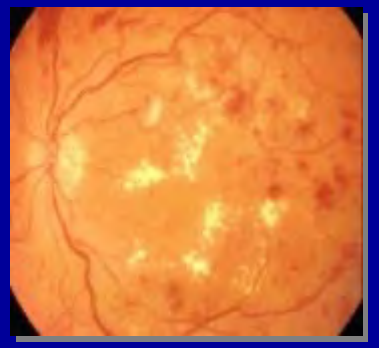
Keywords: Type 2 diabetes; Hypothyroidism; Diabetic retinopathy; Thyroxine





Model For the Pathogenesis of Diabetic Retinopathy

Maculopathy



Capillary Damage +
Hypercholesterolaemia

Endothelial Damage

Capillary Non perfusion

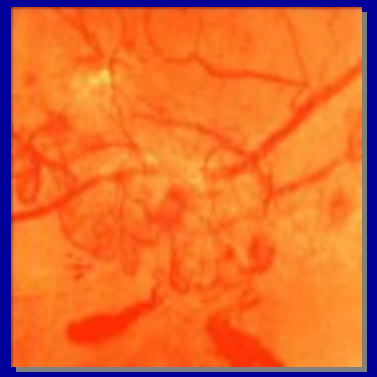
Retinal Ischaemia

Vasoactive Factors

Growth Factors

Pericyte loss in Capillaries and Vein

New Vessels



HYPERPERFUSION

Abnormal Autoregulation

HYPERTENSION

HYPERGLYCAEMIA

ACE-I

May protect

Patel V et al 1994 Clin Sci

Trials and Tribulations of Ideas for Improving Diabetes Care:
My Life in Acronyms

CARDS: Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative ***Atorvastatin*** Diabetes Study

ASCOT: Long-term mortality after ***blood pressure-lowering and lipid-lowering*** treatment in patients with hypertension in the Anglo-Scandinavian Cardiac Outcomes Trial

ADVANCE: Action in Diabetes and Vascular Disease: ***Preterax and Diamicron*** Modified Release Controlled Evaluation

RENAAL: Effects of ***losartan*** on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy

DIRECT: The DIabetic Retinopathy ***Candesartan*** Trials

REACH : A twenty-six week, randomized, open-label, 2-arm parallel group real world pragmatic trial to assess the clinical and health outcomes benefit of ***Toujeo®*** compared to standard of care insulin for initiating basal insulin in insulin naïve patients with uncontrolled type 2 diabetes mellitus, with 6-month extension

REGAIN: A twenty-six week, randomized, open-label, 2-arm parallel group real world pragmatic trial to assess the clinical and health outcomes benefit of transition to Toujeo® compared to standard of care insulin, in basal insulin treated patients with uncontrolled type 2 diabetes mellitus, with six-month extension

ReFLeCT : A multi-centre, prospective, non-interventional study of insulin ***degludec*** investigating the safety and effectiveness in a real world population with type 1 and 2 diabetes mellitus

SUSTAIN 10 . Efficacy and safety of ***semaglutide*** 1.0 mg once-weekly versus liraglutide 1.2 mg once-daily as add-on to 1-3 oral anti-diabetic drugs (OADs) in subjects with type 2 diabetes

Trials and Tribulations of Ideas for Improving Diabetes Care:
My Life in Acronyms

VESALIUS : A Double-blind, Randomized, Placebo-controlled, Multicenter Study to evaluate the Impact of ***Evolocumab*** on Major Cardiovascular Events In Patients at High Cardiovascular Risk Without Prior Myocardial Infarction or Stroke

FREMS PDPN: The Utility of Frequency-Modulated Electromagnetic Neural Stimulation (FREMS) as a Third Line Treatment in Patients with Painful Diabetes-Related Peripheral Neuropathy: A Randomised Controlled Trial

Begin: EASY AM - A trial comparing efficacy and safety of NN1250 (SIBA) and insulin ***glargine*** in subjects with type 2 diabetes A 26-week randomised, confirmatory, controlled, open label, multicentre, multinational treat to target trial comparing efficacy and safety of SIBA 200 U/mL three times weekly injected in the morning and insulin glargine once daily in a population of insulin naïve subjects with type 2 diabetes mellitus currently treated with oral anti-diabetic drugs (OADs) qualifying for intensified treatment

LEADER: ***Liraglutid***e Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results

LANSCAPE: Comparison of a basal plus one insulin regimen (insulin glargine/insulin glulisine) with a biphasic insulin regimen (insulin ***aspart/insulin aspart protamine*** 30/70) in type 2 diabetes patients following basal insulin optimisation.

PRiDE: ***Micronutrients*** in Pregnancy as a Risk Factor for gestational Diabetes and Effects on mother and baby

Trials and Tribulations of Ideas for Improving Diabetes Care:
My Life in Acronyms

COMBO: Use ***of Duloxetine or Pregabalin*** in Monotherapy versus Combination Therapy of Both Drugs in Patients with Painful Diabetic Neuropathy "The COMBO - DN (COmbination vs Monotherapy of pregaBalin and dulOxetine in Diabetic Neuropathy) Study"

MARS : A Multicenter, Randomized, Double-Blind, Placebo-Controlled, ParallelGroup Trial to Evaluate the Efficacy and Safety of E2007 in Patients with Painful Diabetic Neuropathy

ELIXA: A randomized, double-blind, placebo-controlled, parallel-group, multicenter study to evaluate cardiovascular outcomes during treatment with lixisenatide in type 2 diabetic patients after an Acute Coronary Syndrome event

EXAMINE: A Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate Cardiovascular Outcomes Following Treatment with ***Alogliptin*** in Addition to Standard of Care in Subjects with Type 2 Diabetes and Acute Coronary Syndrome

PIONEER REAL : A multi-centre, prospective, non-interventional single-arm study investigating clinical parameters associated with the use of once-daily oral ***semaglutide*** in a real-world adult population with type 2 diabetes in the United Kingdom

SURE: A multi-centre, prospective, non-interventional study investigating the effectiveness of once-weekly subcutaneous ***semaglutide*** in a real world adult population with type 2 diabetes

FOCUS: A research study to look at how ***semaglutide*** compared to placebo affects diabetic eye disease in people with type 2 diabetes

Trials and Tribulations of Ideas for Improving Diabetes Care:

My Life in Acronyms

ICCD : TRIAL OF ***INTERMEDIATE CARE CLINICS*** FOR DIABETES

ADDRESS-2: An incident and High Risk Type 1 Diabetes Research Cohort –After Diabetes Diagnosis REsearch Support System-2

DARE : Diabetes Alliance for research in England

FOURIER: A Double-blind, Randomized, Placebo-controlled, Multicenter Study Assessing the Impact of Additional LDL-Cholesterol Reduction on Major Cardiovascular Events When ***AMG 145*** is Used in Combination With Statin Therapy In Patients with Clinically Evident Cardiovascular Disease

Omneon-18 : A Randomised, Double-Blind, Placebo-Controlled, Multicentre Study to Assess Cardiovascular Outcomes Following Treatment with MK-3102 in Subjects with Type 2 Diabetes Mellitus

DEVOTE: (***Degludec*** CV Outcomes Trial) A trial comparing cardiovascular safety of insulin degludec versus insulin glargine in subjects with type 2 diabetes at high risk of cardiovascular events

CDRC: The Chronic Disease Research into Diabetes study

EASE 2 : A Phase III, randomised, double-blind, placebo-controlled, parallel group, efficacy, safety and tolerability trial of once daily, oral doses of ***Empagliflozin*** as Adjunctive to insulin thErapy over 52 weeks in patients with Type 1 Diabetes Mellitus (EASE-2)

EASE 3 : A Phase III, randomised, double blind, placebo-controlled, parallel group, efficacy, safety and tolerability trial of once daily, oral doses of ***Empagliflozin*** as Adjunctive to inSulin thErapy over 26 weeks in patients with Type 1 Diabetes Mellitus (EASE-3)

Alphabet Strategy for Diabetes Care: "Checklist"

A Safety "Checklist", Patient-Centred, Multi-Professional, Evidence-based Approach

National Diabetes Audit Eight Process Checks

- HbA1c, BP, cholesterol
- Urine albumin, Creatinine
- Foot examination
- BMI and smoking

(Eye screening)

National Diabetes Audit Targets:

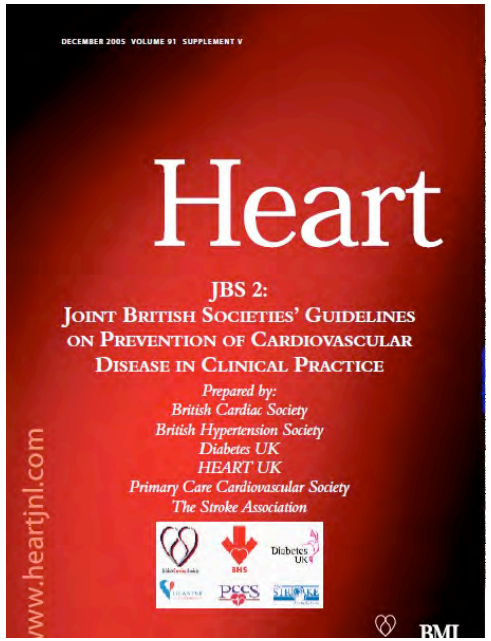
BP: ≤140/80 mmHg
HbA1c: ≤58 mmol/mol
Cholesterol: <5 mmol/L

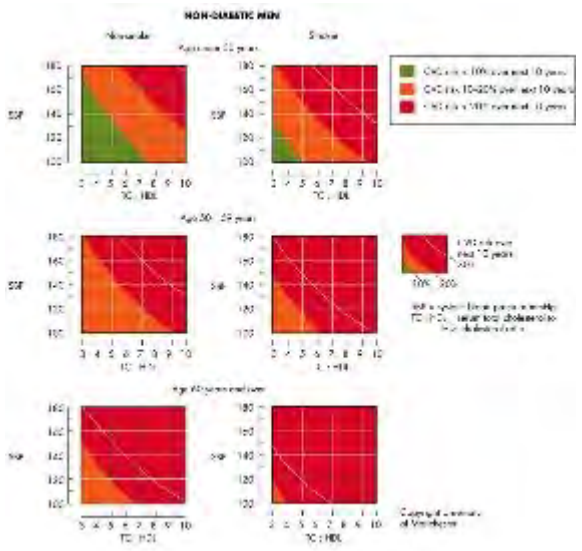
New Target Statins:
Primary & Secondary Prevention of CHD

Upreti R, Lee JD, Kotecha S, Patel V.
Alphabet strategy for diabetes care: A checklist approach in the time of COVID-19 and beyond.
World J Diabetes. 2021 Apr 15;12(4):407-419. doi: 10.4239/wjd.v12.i4.407.

Lee J, Saravanan P, Patel V. **Alphabet Strategy for diabetes care: A multi-professional, evidence-based, outcome-directed approach to management**. World journal of diabetes 2015. 6. 874-9. 10.4239/wjd.v6.i6.874.

- **Advice:**
  - Diet and weight control, Physical activity, not smoking, Good Infection Control Measures, Appropriate PPE, COVID-19 Symptoms, appropriate vaccinations
- **Blood Pressure:**
  - aim ≤ 140/80,
  - CVD or CKD ≤ 130/80
- **Cholesterol & CKD Prevention**
  - Most Atorvastatin 20mg or 80mg, TC ≈ 4 mmol/l
  - UACR yearly and treat
- **Diabetes Control:**
  - HbA1c < 59 (7.5%) usual target, ideal < 48 (6.5%)
  - Outcome based Rx: usually SGLT2-i, ? GLP-RA
  - Safer insulins where needed
- **Eyes:**
  - check yearly at least
- **Feet:**
  - daily self-care, HCP check yearly at least
- **Guardian Drugs:**
  - ?Aspirin 75mg (CVD atheroma), ?ACE-i, ARBs (esp CKD, HF, CVD), appropriate SGLT2-i (NICE NG-28), GLP-RA
- **Healthcare Professional Advice:** (with kindness and compassion)
  - Contraception & Pre-conception Advice
  - Driving and Occupation Advice
  - Hospital Admission Care
  - Other individualised advice eg Ramadan, Travel





Alphabet Strategy in the JBS-2 Guidelines 2006

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The main components of diabetes care can usefully be remembered, both by healthcare professionals and those with diabetes, by using the "Alphabet Strategy"[68]:

•**A**dvice—Education, self management, concordance with treatment. Special focus on smoking cessation, diet, physical activity, and weight reduction.

•**B**lood pressure targets—Blood pressure < 130/80 mm Hg, which may require combinations of a diuretic, ACE inhibitor/ARB, and a CCB (audit standard < 140/90 mm Hg).

•**C**holesterol and LDL cholesterol targets—Total cholesterol < 4.0 mmol/l *and* LDL cholesterol < 2.0 mmol/l *or* a 25% reduction in total cholesterol *and* a 30% reduction in LDL cholesterol, which ever gets the person to the lowest absolute level. A non-HDL cholesterol < 3.0 mmol/l and triglycerides < 1.7 mmol/l are preferred values but are not targets. Nor is there a target for HDL cholesterol, but values below 1.0 mmol/l in men (1.2 mmol/l in women) are associated with an increased risk of CVD.

•**D**iabetes control—A normal HbA1c% is ideal but the practical target is ⩽ 6.5%. Metformin is the first choice for most people with type 2 diabetes, especially if overweight. Early recourse to multiple therapies and insulin will be needed if targets are not reached. While the evidence is limited, attention to glycaemic control in the context of acute coronary syndromes is advised, and the DIGAMI protocol may be an appropriate strategy.

•**E**ye care—Yearly digital photography is recommended with appropriate ophthalmological referral if retinopathy is present, and management of all other CVD risk factors.

•**F**eet care—Yearly examination with appropriate referral as required, and management of all other CVD risk factors.

•"**G**uardian" drugs for cardiovascular prevention—Aspirin 75 mg daily is indicated for people with diabetes who meet any of the following criteria:

- established atherosclerotic disease
- ≥ 50 years, or who are younger but have had the disease for more than 10 years, or who are already receiving treatment for hypertension.

A statin is appropriate in most people with diabetes in order to achieve the total and LDL cholesterol targets.
ACE inhibitor/ARB therapy is indicated when there is microalbuminuria or proteinuria or diabetic nephropathy.

Risk Factor Control. Mortality and CVD Outcomes in Patients with Type 2 Diabetes

% increased risk			
399	288	210	39

Diabetes Patients are at higher risk of CVD and Death, investigation into risk factor control and effect on these outcomes

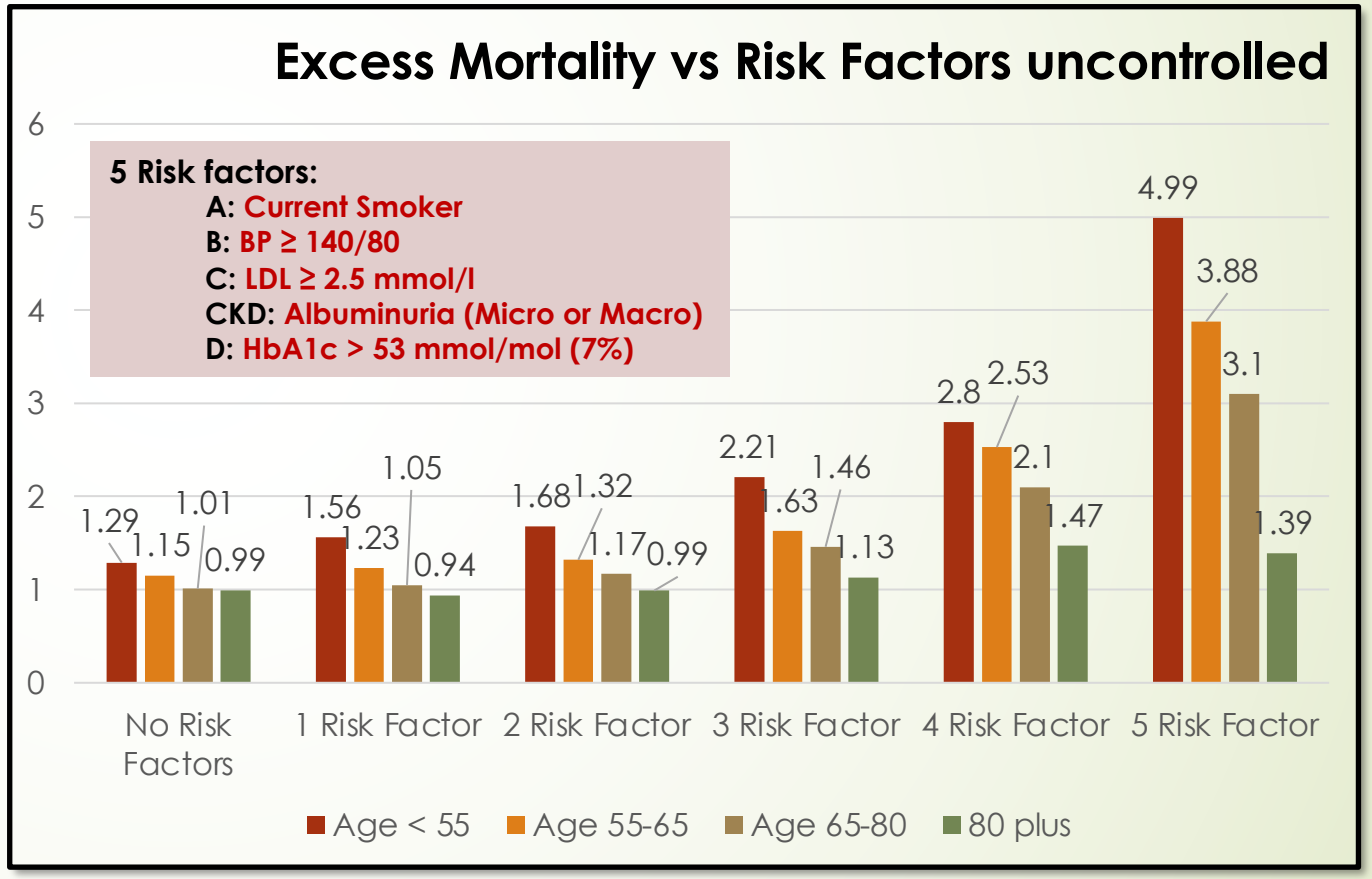
Cohort Study: 271,174 T2DM Pts followed for 5.7 years median. Swedish database. 1,355,870 controls matched for age, sex, country

5 Risk factors:

- **HbA1c > 53 mmol/mol (7%)**
- **BP ≥ 140/80**
- **Albuminuria (Micro or Macro)**
- **Current Smoker**
- **LDL ≥ 2.5 mmol/l**

Age groups: < 55, ≥55-65, , ≥65-80, ≥80

Models adjusted for Socio-economic status (income, marital status, immigrant status, educational level). Deaths adjusted for CHD, HF. MI adjusted for AF and HF. Heart failure adjusted for AF and CHD. Stroke adjusted for AF, HF and CHD.



Similar Trends for:

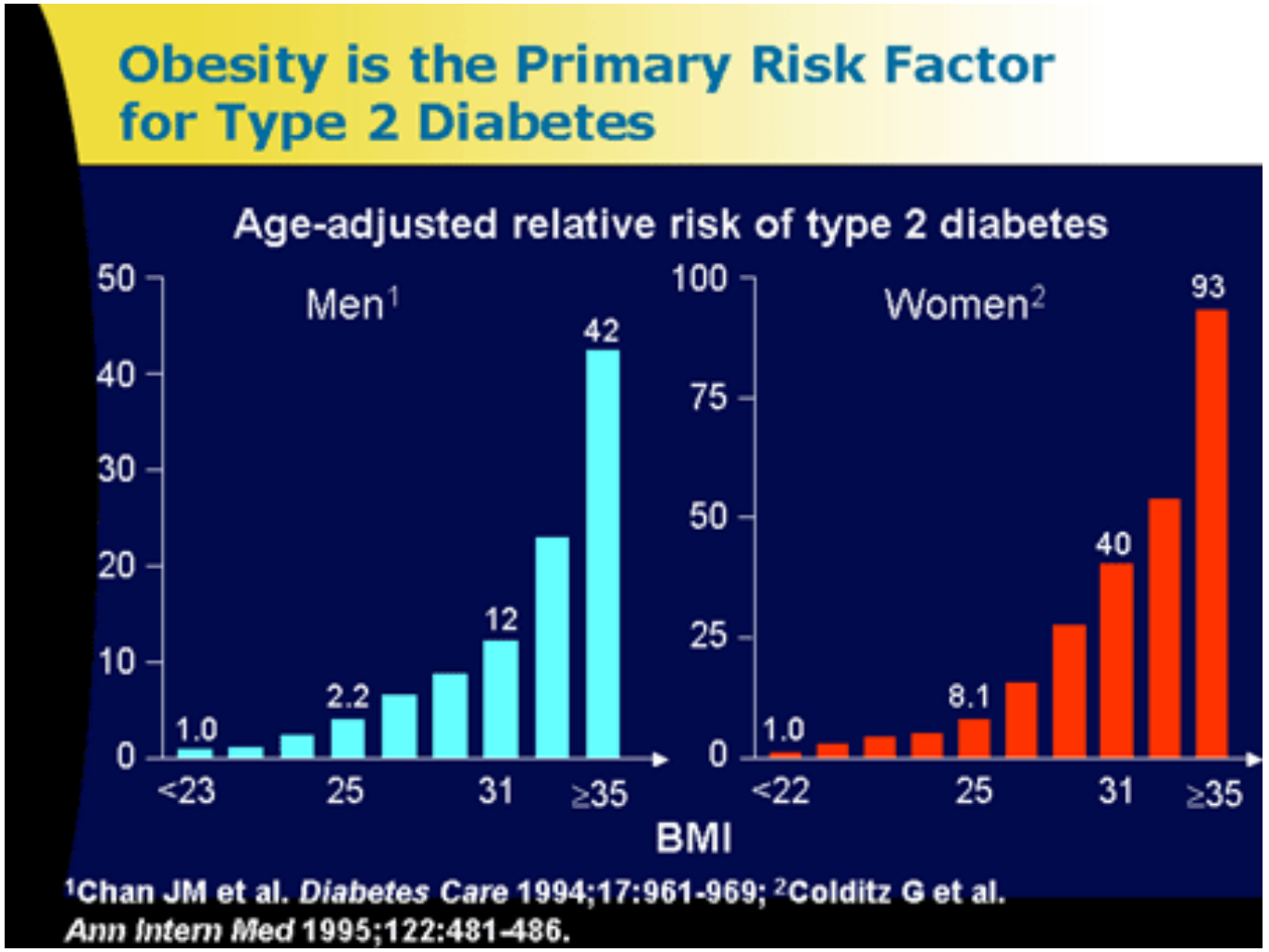
- **Excess MI**
- **Excess Stroke**
- **Excess Heart Failure**

Rawshani A et a. NEJM 2018;379:633-644.

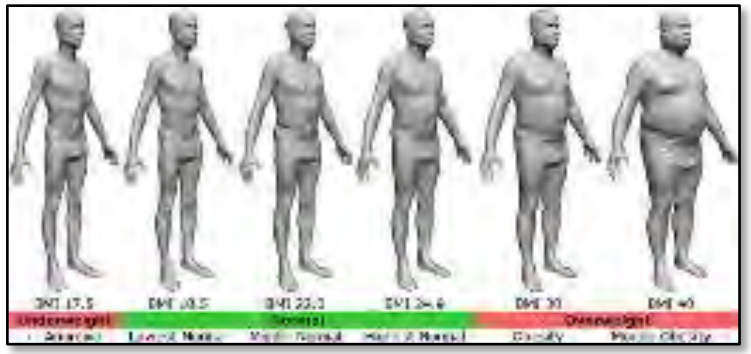
Prevention of Diabetes

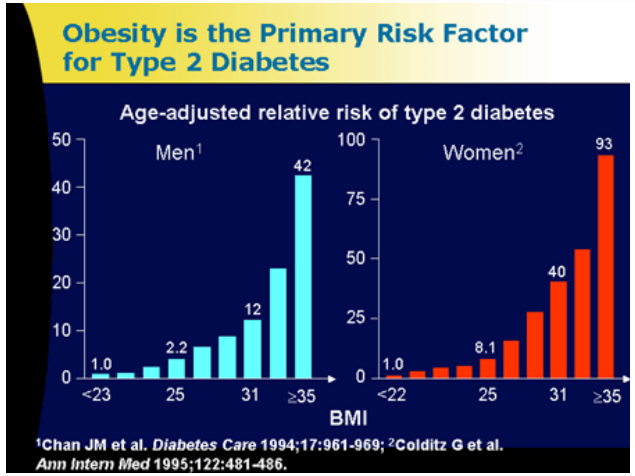
- Overweight and Obesity prevention, Optimising Physical Activity
- Balanced diet (less carbohydrate-rich diet)

What is the % increase in risk of Diabetes with a BMI of <23 versus ≥ 35



Men: …%
Women: …%





What is the % increase in risk of Diabetes BMI of <23 versus ≥ 35 ?

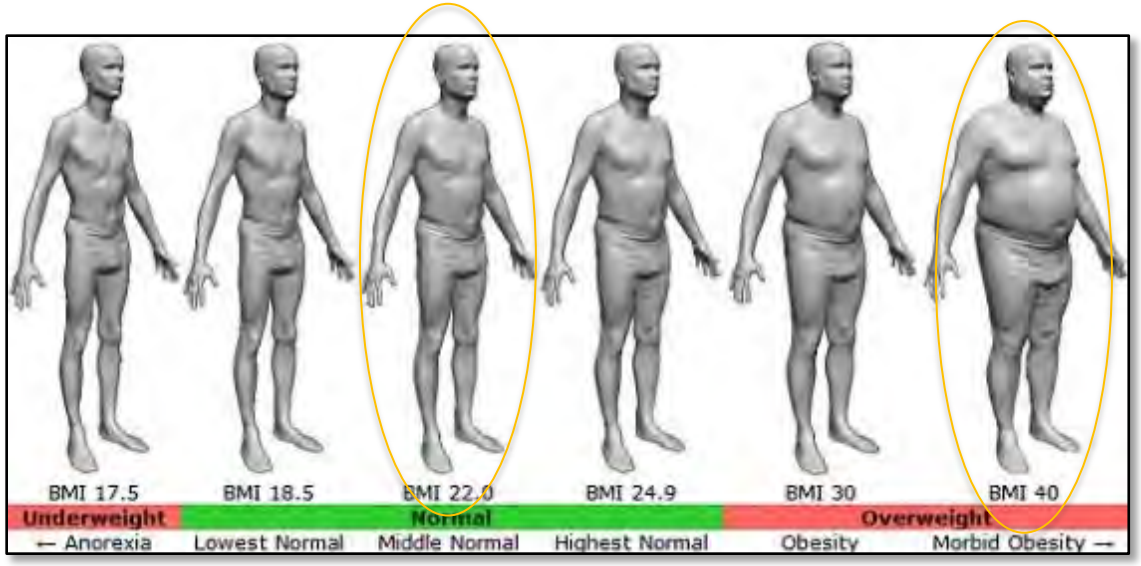
A: Men **42%**, Women **93%**

B: Men **100%**, Women **120%**

C: Men **420%**, Women **600%**

D: Men **4100%**, Women **9200%**

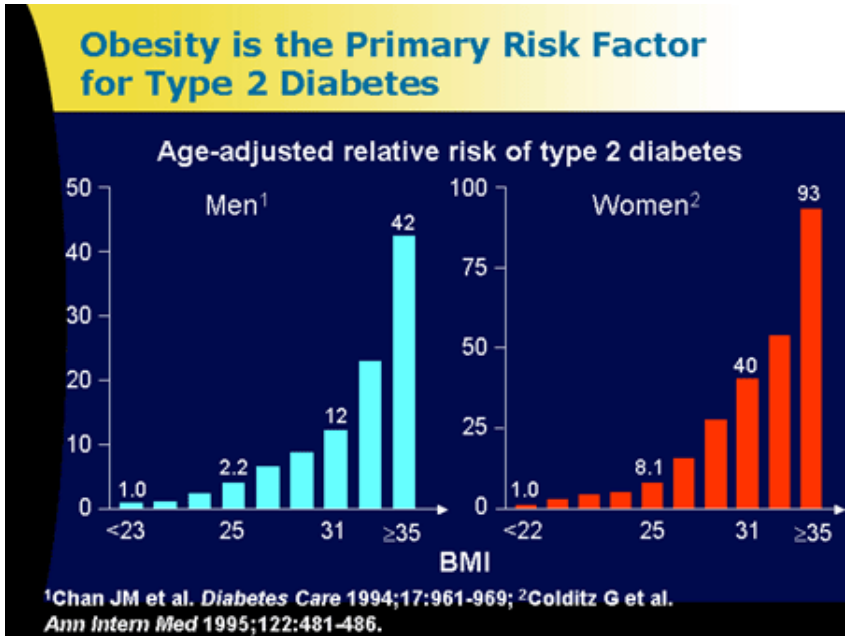
E: Men **200%**, Women **300%**

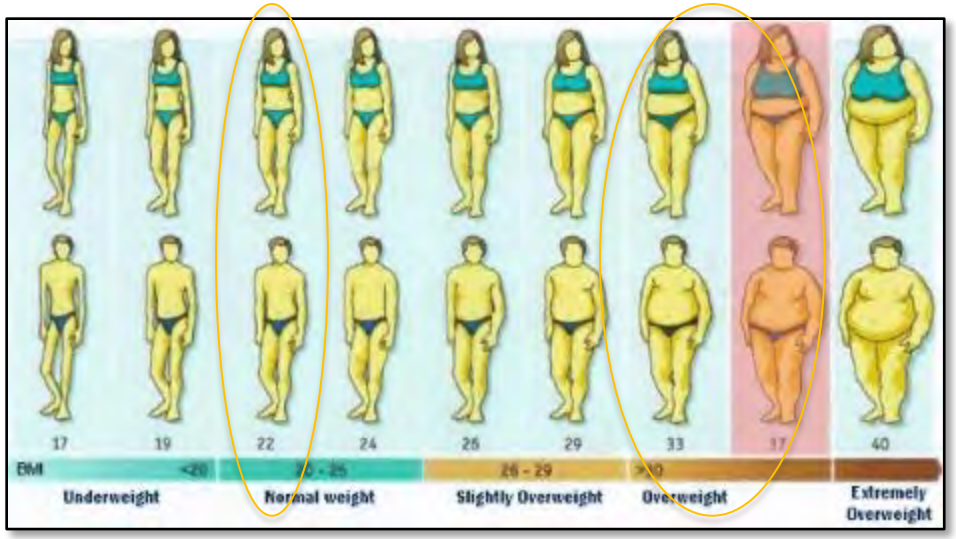


Actually!

Men: 4100 %
Women: 9200%

What is the % increase in risk of Diabetes: BMI of <23 versus ≥ 35



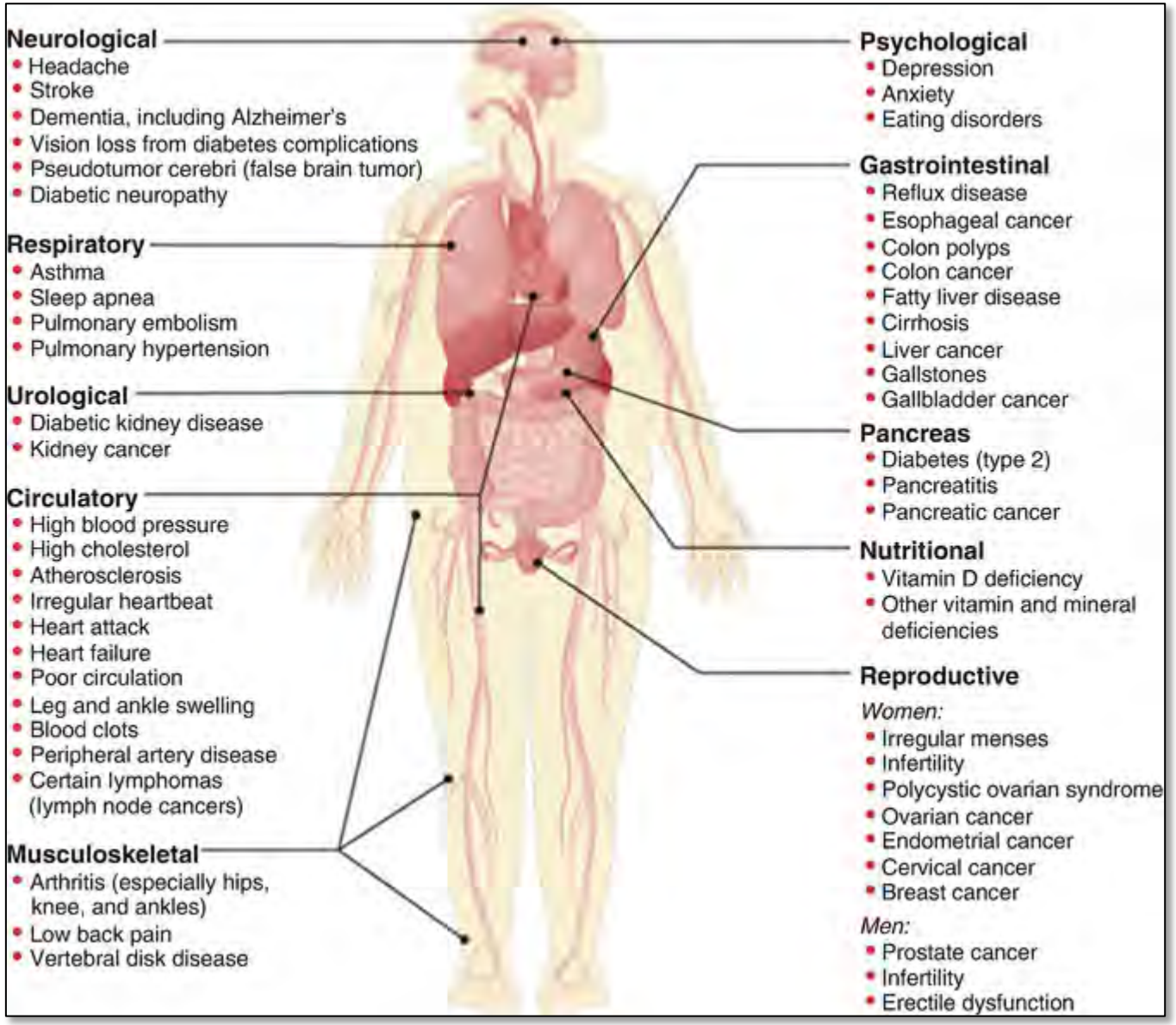


Medical Complications Resulting from Severe Obesity

Kastanias, P., Mackenzie, K., Robinson, S., Wang, W. (2017).

Medical Complications Resulting from Severe Obesity.

In: Sockalingam, S., Hawa, R. (eds) Psychiatric Care in Severe Obesity. Springer, Cham. https://doi.org/10.1007/978-3-319-42536-8_5



Calories per gram of macronutrients:

Nutrient	kcal/g	Satiety
Carb	4	+
Protein	4	+++
Fat	9	++
Alcohol	7	-ve

Mifflin-St Jeor Equation

- 40yr male
- 170cm tall
- 80kg weight
- sedentary lifestyle requires 2000kcal/day to maintain their bodyweight

The PLATE Idea
Protein Limits Action Towards Eating

Deepa Lad and Sheena Bageerutty

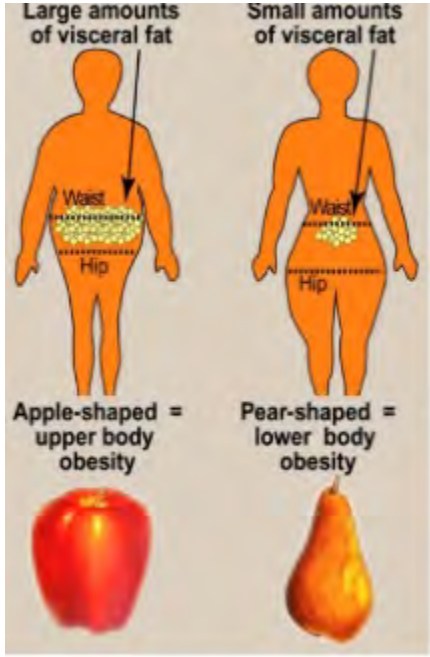
- **Protein requirement** = 80g
- This is 80 x 4 = **"Protein Calories" = 320 calories**
- Person X should be on a $\frac{320 \text{ kcal}}{2000 \text{ kcal}}$ = **16%** of calories from protein in the diet

- Patient eats **2000 kcals of Curry and rice or Pizza and chips:** only **12%** of calories come from protein.
- This is 12% of 2000 = 240 calories from Protein = **60g of Protein**

- **Protein Deficit is 20g** (80g – 60g)

- To have **Satiety, extra 20g of protein are needed**

- Person X eats 2000 cals of Curry and less rice or Pizza with Salad:
  - **16%** of calories come from protein.
  - This is 16% of 2000 = 320 calories from Protein = 80g of Protein
  - Protein needs satisfied
  - **No Protein Deficit**



Mackintosh JE, Mistry JP, Ali SN, Patel V. **Potential prevention of diabetes and obesity by achieving macronutrient balance: a guide for diet and fast food.** British journal of diabetes. 2020 Jun 5;20(1):61-9.

COMMENTARY

Potential prevention of diabetes and obesity by achieving macronutrient balance: a guide for diet and fast food

JAMES EL MACKINTOSH,[1] JEMINIE PATEL MISTRY,[2] SARAH N ALI,[3] VINOD PATEL[1]

Abstract

Protein is the most satiating macronutrient. Animal studies have indicated that there may be a discrete amount of protein that an individual seeks to consume each day. Given this to be true, a person will continue to eat until this amount of protein has been consumed. Once the target is met, hunger signals are switched off. By altering the proportion of protein in a diet, you can affect how many calories are required to meet this target. A diet with a protein content >15% drives weight loss through the reduction of calories consumed to meet protein needs. We hypothesise that changing the proportion of calories from protein in a person's diet from 12% to 20% could alter their total intake by 1000 kcal each day. This equates to a weight change of 0.9 kg each week. Maintaining a healthy weight is not as simple as changing a single variable. Eating habits in the UK are governed by a range of complex interdependent factors including hunger, emotions, cost, accessibility, education and culture. However, we suggest that by addressing satiety, and thereby hunger, we may remove a significant barrier for those trying to alter their diet for weight loss.

Key words: macronutrients, protein, weight loss, fast food, satiety

Introduction

The UK is undergoing an obesity epidemic. In England, 64% of adults are classified as overweight or obese.[1] In 2017/18 there were 10,660 hospital admissions directly attributable to obesity and 711,000 admissions where obesity was a factor.[2] It is estimated that the NHS spent £6.1 billion on overweight and obesity-related ill health in 2014–2015.[3] This problem is widely acknowledged by healthcare professionals, government policy makers and the general public. However, obesity is still on the rise. If trends persist, one in three people in the UK will be obese and one in 10 will have type 2 diabetes (T2DM).[4]

Being overweight or obese is the main modifiable risk factor for developing diabetes.[5] Furthermore, men with body mass index (BMI) ≥35 kg/m² have a relative risk of developing T2DM 42.1 times greater than men with BMI ≤23 kg/m².[5] Diabetes directly costs the UK £6.8 billion a year.[6] The annual spend on the treatment of obesity and diabetes is greater than the amount spent on the police, the fire service and the judicial system combined.[7] Unfortunately, the factors affecting eating habits in the UK are numerous and complex. This makes it difficult to give advice that will work for the whole population. In a survey of over 3,000 people, respondents stated that two of the main difficulties in trying to eat more healthily was increased cost and time constraints.[8]

The impact of cost was further demonstrated in a systematic review showing a significant difference in fruit and vegetable consumption between socioeconomic groups, with those in the lowest group consuming the least.[9]

One study showed that distributing the same amount of energy over more meals throughout the day improved satiety.[10] Another study, looking at meal duration, found that group having the longer meal felt fuller and less hungry.[11] These results show how time constraints could impact food consumption.

Stress affects eating habits and is out of the control of the individual, as are cost and time constraints. One review found that stress increases the drive to eat higher calorie or more 'palatable' food via its interaction with central reward pathways.[12]

Current weight loss advice is to restrict calories consumed, for which there is strong research evidence.[13–15] This is the foundation on which almost all 'weight loss diets' are based. Unfortunately, research has shown that people struggle to maintain successful weight loss over a long period of time. For example, in one study only 12% of the 192 participants maintained at least 75% of their weight loss three years later, and 80% gained more weight than they had originally lost.[16]

The biggest factor determining success of weight loss diets is sustainability (or can be thought of as compliance).[17,18] Adherence to a dietary weight loss intervention is strongly associated with weight loss success over the short and long term.[19,20]

There has been a shift in culture accompanying the obesity crisis, which has seen fast food making up a larger proportion of the nation's diet. More than one-quarter (27.1%) of adults and

Too Much Carb and not enough Protein

A Barrier to Preventing Diabetes and Good Diabetes Control in South Asian and some other communities?

Mackintosh JE, Mistry JP, Ali SN, Patel V. Potential prevention of diabetes and obesity by achieving macronutrient balance: a guide for diet and fast food. British journal of diabetes. 2020 Jun 5;20(1):61-9.

Primary care-led weight management for remission of type 2 diabetes (DiRECT)

M Lean et al Lancet 2018;391:541–551,

- **Population:** 20–65 years, Type 2 DM diagnosed ≤ 6 yrs, BMI 27–45 kg/m^2, and not on insulin
- **Results:** Diabetes remission in 68 (46%) intervention group, 6 (4%) controls
- **Remission rate:**
  - 0% in 76 participants who gained weight
  - 7% (6) of 89 participants who maintained 0–5 kg weight loss
  - 34%(19) of 56 participants with 5–10 kg loss
  - 57% (16) of 28 participants with 10–15 kg loss
  - 86% (31) of 36 participants who lost 15 kg or more
- **Conclusion:** At 12 months, almost half of participants achieved remission and off antidiabetic drugs. Remission of type 2 diabetes is a practical target for primary care

Diabetes Care ABCDEFG Plan

Advice	No smoking, cholesterol, healthy food, weight, exercise.
Blood Pressure	Know your blood pressure target.
Cholesterol	Know your cholesterol target to stop blood clots.
Diabetes Control	Monitor your blood glucose regularly.
Eyes	Eyes checked every year.
Feet	Examine feet daily, see a professional every year.
Guardian Drugs	Talk to your care team for treatment options.

The content of these materials was developed by Dr Vinod Patel and the Diabetes Care Team at George Eliot Hospital NHS Trust.

Alphabet Strategy: Advice, Blood Pressure, Cholesterol, Diabetes Control, Eye Examination, Foot Care, Guardian Drugs

Advice on Diabetes

Eat healthy food	Aim for 5 portions of fruit or veg a day.
Exercise regularly	Aim for 30 mins brisk walking a day.
Don't smoke	Smoking increases heart and lung problems.
Control your weight	Being overweight increases heart problems.
Plan your journeys	Keep glucose and monitor in your car.
Don't drink too much	Alcohol lowers blood sugar.

The content of these materials was developed by Dr Vinod Patel and the Diabetes Care Team at George Eliot Hospital NHS Trust.

Alphabet Strategy: Advice, Blood Pressure, Cholesterol, Diabetes Control, Eye Examination, Foot Care, Guardian Drugs

Advice on Diabetes

A hypo is when your blood sugar is less than 4 mmol/L.

A hypo is caused by

- not enough food
- vomiting
- increased activity
- too much insulin
- alcohol
- being hot or cold

Watch out for

- lack of concentration
- shaking
- hunger
- drowsiness
- headache
- sweating

Driving Advice

Blood sugar to be 5mmol/L. After a hypo wait 45 mins to drive.

If you feel a hypo, stop and eat some sugar.

The content of these materials was developed by Dr Vinod Patel and the Diabetes Care Team at George Eliot Hospital NHS Trust.

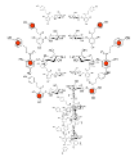
Alphabet Strategy: Advice, Blood Pressure, Cholesterol, Diabetes Control, Eye Examination, Foot Care, Guardian Drugs

Diabetes Care Plan

A Safety "Checklist", Patient-Centred, Multi-Professional, Evidence-based Approach

Our patient spend **3 hours** a year with HCP in Diabetes Care- the other **8763 hours** looking after themselves!

- **Patient Information:** Background and Personal Targets based on National Diabetes Audit
- **Diabetes UK 15 Healthcare Essentials:** Brief summary of main points
- **Reducing Complication:** Statement for information and endorsing collaborative care
- **Key Contacts:** Table of key contacts and roles, patient to fill in details



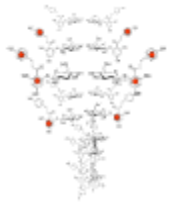
- Your diabetes should not prevent you living a normal, healthy life. This Care Plan using the Alphabet Approach can help you.
- You should work towards achieving your personalised targets for BP, cholesterol and diabetes control. National targets have been advised by Diabetes UK.
- Diabetes UK has stated 15 Healthcare Essential Standards that everyone with diabetes should receive. This includes:
  - **Specialist team to provide long term care**
  - **Safe driving and work-related advice**
  - **High-quality care if admitted to hospital**
  - **Specialist care if planning to have a baby**
  - **Opportunity to discuss any sexual problems**
  - **Access to psychological support if needed**
- These targets and Healthcare Essential Standards will help you reduce the risk of all the **complications of diabetes including: heart disease, strokes, amputation, blindness, kidney disease and hospital admissions for complications.** A good outcome to a pregnancy would also be far more likely for mother and baby.

Key Contact	How can they help	Contact Details
GP Practice Nurse	Management and Co-ordination of Care	
Pharmacist	Help with medicines	
Podiatrist	Foot care	
Dentist	Oral care	
Dietitian	Diet	
Diabetes UK	Support / Info	
Eye Screening	Annual screening	
Hospital Team	Specialist Care	

Diabetes Care Plan

A Safety "Checklist", Patient-Centred, Multi-Professional, Evidence-based Approach

- **Alphabet Strategy Information:** Notes of each aspect of care
- **Personal Targets:** as agreed by patient with HCP advice
- **Result 1:** Result at current review, or previous result to compare to Result 2
- **Result 2:** Result at current review, to compare to Result 1
- **National Targets:** Usual National Targets to guide collaborative agreed personalised targets for the patient



Date:	Your target	Result 1	Result 2	National Targets
Advice on Lifestyle: •Weight and Body Mass Index:				≤25
•Stop smoking: if you smoke				Non smoker
•Diet and Physical activity				Within 12 mths diagnosis
Blood Pressure: • **Yearly check:** High BP can cause heart disease, stroke, eye and kidney disease				140/80 or less
Cholesterol and CKD Prevention • **High cholesterol** can cause heart disease, stroke and poor circulation the legs with risk of amputation				Less than 5 mmol/l
• **CKD: Chronic Kidney Disease** Prevention -Yearly kidney tests (Creatinine and UACR)				Kidney tests yearly
Diabetes Control: • **HbA1c test:** measures the amount of glucose sticking to your blood in the last 2 months • **Hypo avoidance:** essential to avoid low glucose levels of less than 4 • **Driving:** Remember to check before driving: glucose 5 or more to drive				HbA1c 58 mmol/mol or less (7.5%)
Eyes: • It is important that your eyes are examined yearly. Treatment may be needed to stop blindness				Annual check
Footcare: • Examine your feet daily: check for heat (infection), ulcers, numbness, circulation. Yearly HCP examination.				Daily and annual check
Guardian Drugs / Flu jab • Take your medications as advised. Many are essential to avoid heart and kidney disease.				? taken regularly

MY DIABETES SELF MANAGEMENT PLAN: Title Calling Name Surname

Keep this safe & accessible in an emergency with any other care plans, and bring to your diabetes check-ups

Birmingham and Solihull NHS

www.diabetes.org.uk

Alphabet Strategy — Advice, Blood Pressure, Cholesterol, Diabetes Control, Eye Examination, Foot Care, Guardian Drugs

- Your diabetes should not prevent you living a normal, healthy life.
- This will be helped by you working towards and achieving the appropriate targets for blood pressure, cholesterol and diabetes control. Targets have been advised by Diabetes UK.
- Diabetes UK has suggested the 15 Healthcare Essential Standards that everyone with diabetes should receive

These targets and Healthcare Essential Standards will help you reduce the risk of all the **complications of diabetes including: heart disease, strokes, amputation, blindness and kidney disease.**

Care Plan	Diabetes checks	National Targets	My Latest Result	My Goal
Advice on Lifestyle	**Body Mass Index:** indicates weight/body shape	18.5 - 25	Single Code Entry: Body mass index Single Code Entry: Waist circumference Single Code Entry: O/E - weight	
	Stop smoking: if you smoke	Stop	Single Code Entry: Current smoker...	Single Code Entry: Smoking cessation advice
	Dietary Advice:	Healthy	Single Code Entry: Health ed. - diet	
	Physical activity:	Healthy	Single Code Entry: Health ed. - exercise	
	Group education course:	Learn	Single Code Entry: Referral to diabetes structured education programme...	
	Flu vaccination: available free	Annual	Single Code Entry: 1st intramuscular seasonal influenza vacc given by other HCP... Single Code Entry: Pneumococcal vaccination given...	
Blood pressure	**BP**: if high can harm heart, brain, eyes, kidneys	<140/80	Single Code Entry: O/E - blood pressure reading	Single Code Entry: Target systolic blood pressure Single Code Entry: Target diastolic blood pressure Single Code Entry: Provision of written information about diabetes and high BP
Cholesterol & CKD prevention	**Cholesterol:** if high can harm heart, brain, circulation	<4.0	Single Code Entry: Serum cholesterol	Single Code Entry: Target cholesterol level Single Code Entry: Provsn written information about diabetes & high cholesterol
	Kidney tests: to prevent Chronic Kidney Disease (CKD) blood test eGFR, urine test for UACR	eGFR>60	Single Code Entry: GFR calculated abbreviated MDRD	
		Urine ACR<3	Single Code Entry: Urine albumin:creatinine ratio	
Diabetes Control	**HbA1c**: measures the amount of glucose sticking to your blood in the last 2 months	<58	Single Code Entry: Haemoglobin A1c level - IFCC standardised	Single Code Entry: HbA1c target level - IFCC standardised Single Code Entry: Provision written information abt diabetes & high HbA1c levl
	Home glucose test:	5-8	Single Code Entry: Self monitoring of blood glucose	
	Have you been having hypos?		Single Code Entry: Recurrent severe hypos	Single Code Entry: Hypoglycaemia education
Eyes	**Retinopathy screening**: annually to prevent blindness	Annual	Single Code Entry: Digital retinal screening	
Footcare	**Foot checks**: check your feet daily, annual diabetic clinic check for numbness, circulation and damage	Daily Self Care	Single Code Entry: O/E - Right diabetic foot at low risk...	
		Annual Clinic	Single Code Entry: O/E - Left diabetic foot at low risk...	
Healthcare Professional	☐ Advised to inform DVLA and advised to inform/liaise with Occupational Health ☐ Specialist care if diabetes related hospital admission ☐ Contraception advice for fertile women			

Advice	☐ Referral to pre-conception clinic if planning a baby ☐ Erectile Dysfunction discussed ☐ Mental Health and Wellbeing discussed	
Follow up plan	☐ 3 months ☐ 6 months ☐ 12 months ☐ Other:	Today's date: **Short date letter merged**

Medications: Title Calling Name Surname	**Additional Info**
Medication	

Diabetes self-management plan agreed - **Short date letter merged**

Name of professional - Current User Patient Signature - .....

Birmingham and Solihull CCG

My Diabetes Self Management Plan

Works through GP Systems- eg EMIS, and printable to give or post to patients

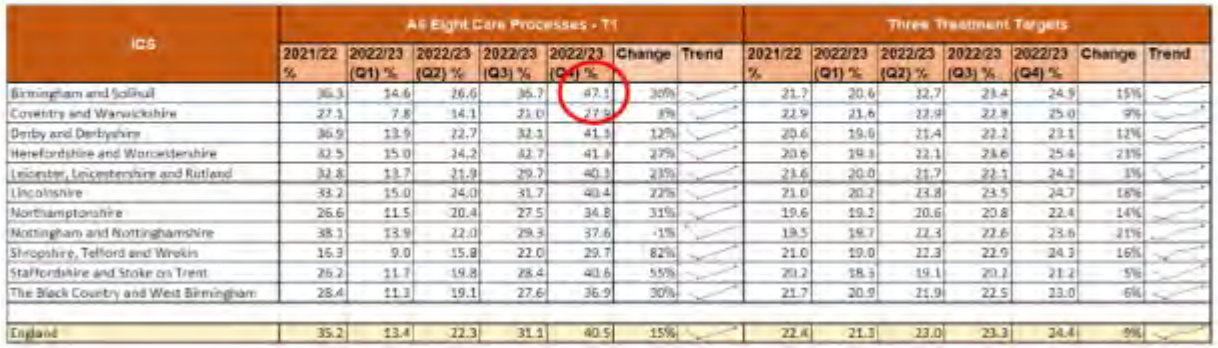
NDA Data 2021- 2023: NHS England- Midland ICB Areas

Type 2 Diabetes Mellitus

ICS	All Eight Care Processes - T2							Three Treatment Targets						
	2021/22 %	2022/23 (Q1) %	2022/23 (Q2) %	2022/23 (Q3) %	2022/23 (Q4) %	Change	Trend	2021/22 %	2022/23 (Q1) %	2022/23 (Q2) %	2022/23 (Q3) %	2022/23 (Q4) %	Change	Trend
Birmingham and Solihull	51.6	21.9	39.2	52.1	64.3	25%		37.4	33.2	35.2	36.0	38.2	2%	
Coventry and Warwickshire	32.5	11.5	30.7	31.8	40.1	24%		38.3	33.9	37.4	38.3	40.0	5%	
Derby and Derbyshire	48.7	20.9	35.1	47.8	58.6	20%		33.9	31.0	34.5	35.0	35.3	4%	
Herefordshire and Worcestershire	47.9	21.7	35.5	48.6	59.0	23%		36.2	33.7	37.1	38.0	39.2	8%	
Leicester, Leicestershire and Rutland	46.7	18.5	31.8	43.3	54.6	17%		36.3	32.4	35.6	36.7	38.2	5%	
Lincolnshire	47.5	20.2	33.3	45.0	55.8	18%		36.6	34.2	36.7	37.7	38.2	4%	
Northamptonshire	38.8	16.7	21.3	39.4	49.1									
Nottingham and Nottinghamshire	47.0	19.5	31.9	43.8	55.0									
Shropshire, Telford and Wrekin	26.1	12.3	22.5	32.7	42.5									
Staffordshire and Stoke on Trent	38.5	16.6	29.5	41.6	55.5									
The Black Country and West Birmingham	44.2	17.8	31.9	43.3	55.3									
England	47.9	19.5	33.5	46.2	57.8									

NDA Data 2021- 2023: NHS England- Midland ICB Areas

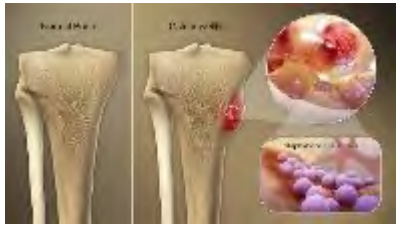
Type 1 Diabetes Mellitus



ICS	All Eight Care Processes - T1							Three Treatment Targets						
	2021/22 %	2022/23 (Q1) %	2022/23 (Q2) %	2022/23 (Q3) %	2022/23 (Q4) %	Change	Trend	2021/22 %	2022/23 (Q1) %	2022/23 (Q2) %	2022/23 (Q3) %	2022/23 (Q4) %	Change	Trend
Birmingham and Solihull	36.3	14.6	26.6	36.7	47.1	30%		21.7	20.6	22.7	23.4	24.9	15%	
Coventry and Warwickshire	27.1	7.8	14.1	21.0	27.9	3%		22.9	21.6	22.9	22.9	25.0	9%	
Derby and Derbyshire	36.9	13.9	22.7	32.3	41.3	12%		20.6	19.6	21.4	22.2	23.1	12%	
Herefordshire and Worcestershire	32.5	15.0	24.2	32.7	41.3	27%		20.6	19.3	22.1	23.6	25.4	23%	
Leicester, Leicestershire and Rutland	32.8	13.7	21.9	29.7	40.3	23%		23.6	20.0	21.7	22.1	24.3	3%	
Lincolnshire	33.2	15.0	24.0	31.7	40.4	22%		21.0	20.2	23.8	23.5	24.7	18%	
Northamptonshire	26.6	11.5	20.4	27.5	34.8	31%		19.6	19.2	20.6	20.8	22.4	14%	
Nottingham and Nottinghamshire	38.1	13.9	22.0	29.3	37.6	-1%		19.5	19.7	22.3	22.6	23.6	21%	
Shropshire, Telford and Wrekin	16.3	9.0	15.8	22.0	29.7	82%		21.0	19.0	22.3	22.9	24.3	16%	
Staffordshire and Stoke on Trent	26.2	11.7	19.8	28.4	40.6	55%		20.2	18.3	19.1	20.2	21.2	5%	
The Black Country and West Birmingham	28.4	11.3	19.1	27.6	36.9	30%		21.7	20.9	21.9	22.5	23.0	6%	
England	35.2	13.4	22.3	31.1	40.5	15%		22.4	21.3	23.0	23.3	24.4	9%	

Clinical Cases Published

1	**Osteomyelitis, discitis, epidural and psoas abscess** secondary to Salmonella enterica BMJ Cases 2015	
2	**Systemic corticosteroids for the outpatient treatment of necrobiosis lipoidica in a diabetic patient** Journal of Dermatological Treatment 2007	
3	**Fatal emphysematous pyelonephritis with gas in the spinal extradural space in a patient with diabetes** Diabetic Medicine 2001	
4	**Herbal Remedy for Diabetes: Two Case Reports** Experimental and Clinical Endocrinology & Diabetes 2009	
5	**Isolated Thyroxine Malabsorption Treated With Intramuscular Thyroxine Injections** American Journal of the Medical Sciences 2009	
6	**Granuloma annulare and perinephric abscess in undiagnosed diabetes mellitus** Br J Diabetes Vasc Dis 2003	
7	**An unusual cause of a foot ulcer in a patient with type 1 diabetes** Br J Diabetes Vasc Dis 2004	
8	**Allergic reaction to blue cheese: serendipity or actual causation?** The New Zealand Medical Journal 2008	
9	**Eruptive Xanthomata in uncontrolled diabetes** Br J Diabetes Vasc Dis 2002;2:60-1	
10	**A successful spontaneous pregnancy in abetalipoproteinemia: Amsterdam or the art of vitamin replacement?** BMJ Case Reports 2014	
11 & 12	**A Lump in the Chest?** BMJ 1995	**Cultural barriers to diabetes care in South Asians: arranged marriage – arranged complications?**. Pract Diab Int, 2004
13	**Pneumococcal septic arthritis** Rheumatol Pract 1986	
14	**Tree Frog Fingers: ? A New Sign in Cushing's Syndrome** Postgrad Medical Journal 1998	
15	**Diagonal earlobe creases and atheromatous disease: a postmortem study** J R Coll Physicians Lond 1992;26:274-77.	
? 16	**Young Doctor: "Type 1 " diabetes for 10 years- 10 000 insulin injections, 5000 fingerpick tests to a tablet a day and better control- HNF1α Diabetes-**	



Tree Frog Fingers Sign

(PS Same School as David Attenborough)

Some Case Reports with Dr Rajiv Nair

Farrar H, Abbey A, Patel V, Nair R.
Osteomyelitis, discitis, epidural and psoas abscess secondary to Salmonella enterica in a man with diabetes mellitus and newly diagnosed α-thalassaemia trait. *BMJ Case Rep. 2015 Jan 21;2015:bcr2014207008*.

Othonos N, Patel V, Nair R, Ayre S, Saravanan P.
Diabetes: The forgotten complications of parathyroidectomy
Endocrine Abstracts (2014) **34** P148 | DOI:

Sukumar N, Nair R, Patel V.
Non-type 1 non-type 2 diabetes mellitus. *British Journal of Diabetes & Vascular Disease*. 2011;11(5):262-265.

Abstract 1

We report the case of a 65-year-old man with type 2 diabetes mellitus and α-thalassaemia trait. Investigations for relapsing and remitting fever found vertebral osteomyelitis, discitis and epidural and psoas abscess secondary to Salmonella enterica.

Abstract 2

Monogenic forms of b-cell diabetes have been broadly divided according to age of presentation, into neonatal and adolescent/adult forms (the latter previously termed maturity onset diabetes of the young – MODY). Herein we describe the identification of monogenic diabetes in a lady with a long-term history of treatment for type 1 diabetes diagnosed in early adulthood.

Dr Rajiv Nair

Skydiving doctor helps raise money for Nuneaton's George Eliot Hospital

Cultural Competence

"The ability of systems to provide care to patients with diverse values, beliefs, and behaviours including tailoring delivery to meet patients' social, cultural and linguistic needs"

Betancourt & Carrillo (2002)

Betancourt & Carrillo. Cultural Competence In Healthcare: Emerging Frameworks and Practical Approaches. (2002)

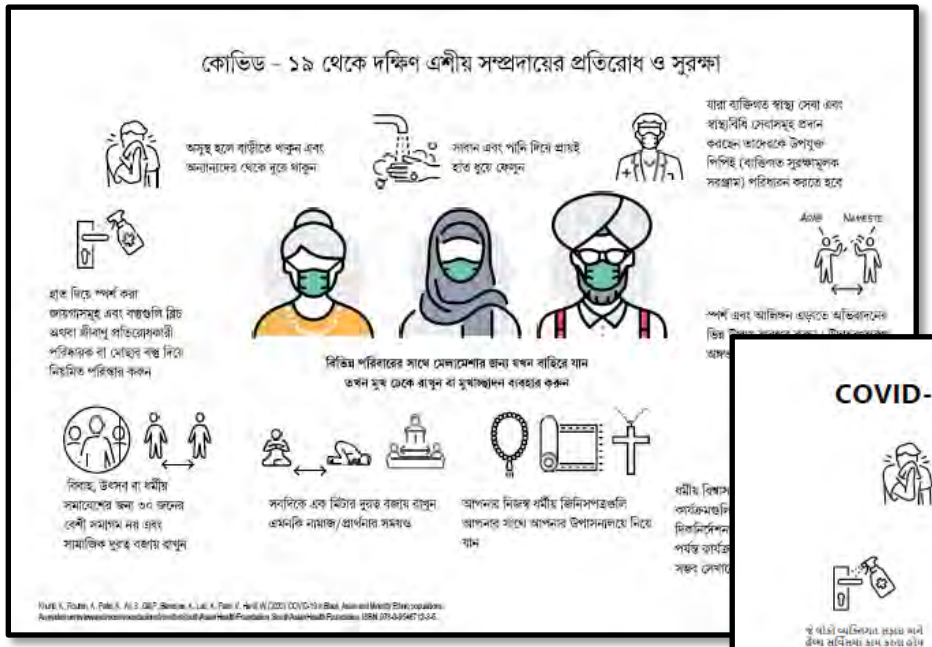
Health Inequalities:

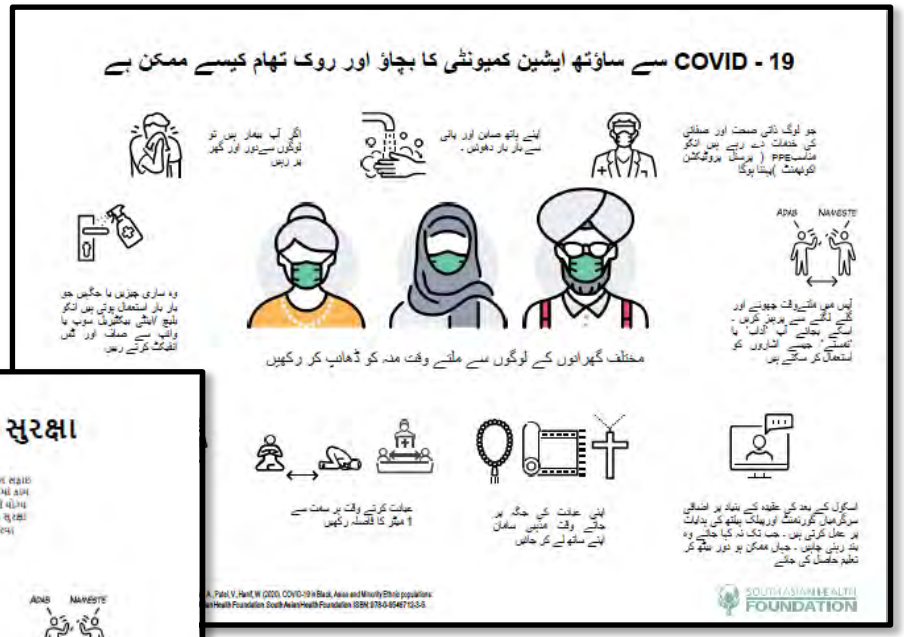
Avoidable inequalities that are unfair or unjust

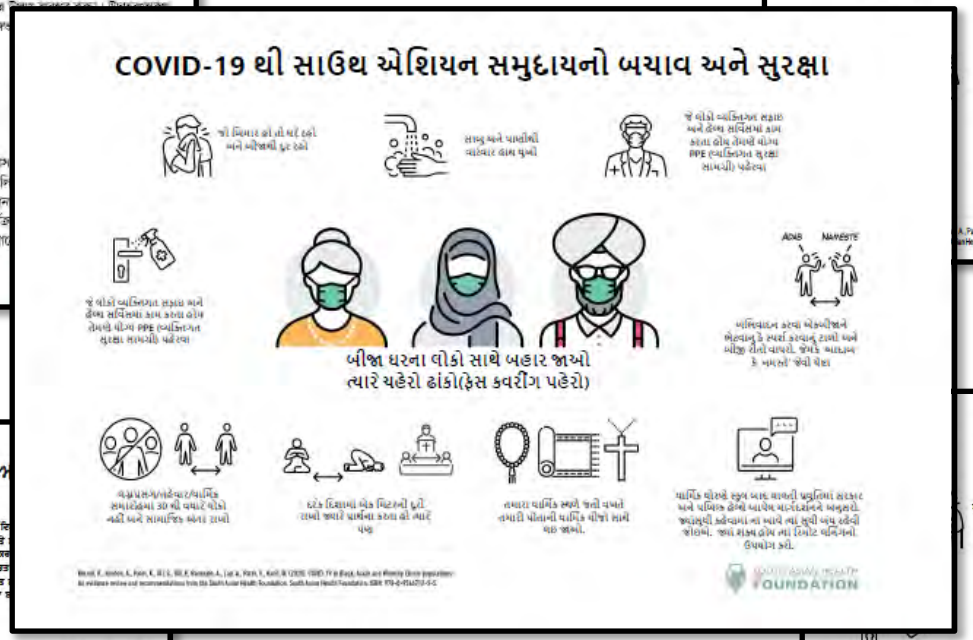
Braveman & Gruskin (2003) Defining Equity in Health

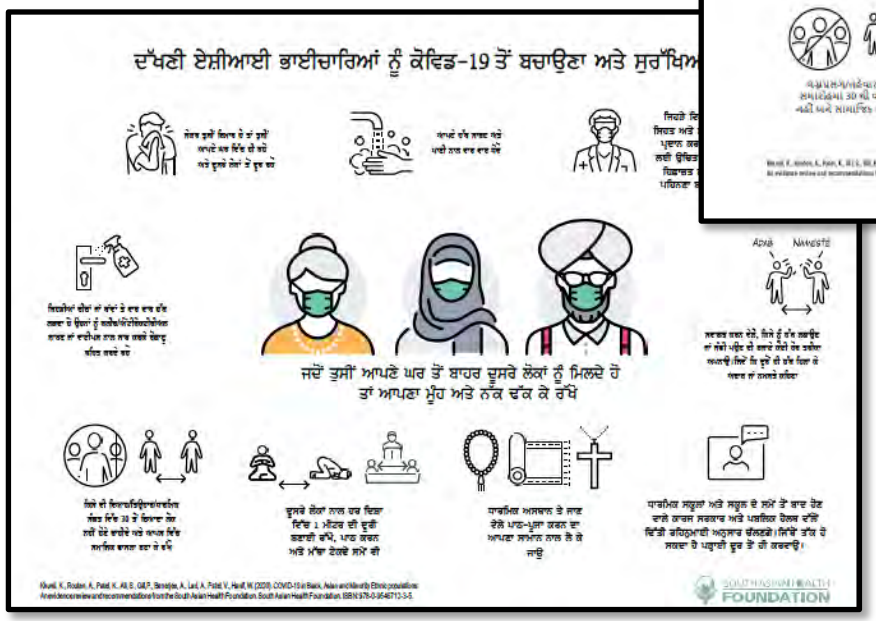
COVID-19 Guidelines

SOUTH ASIAN HEALTH FOUNDATION

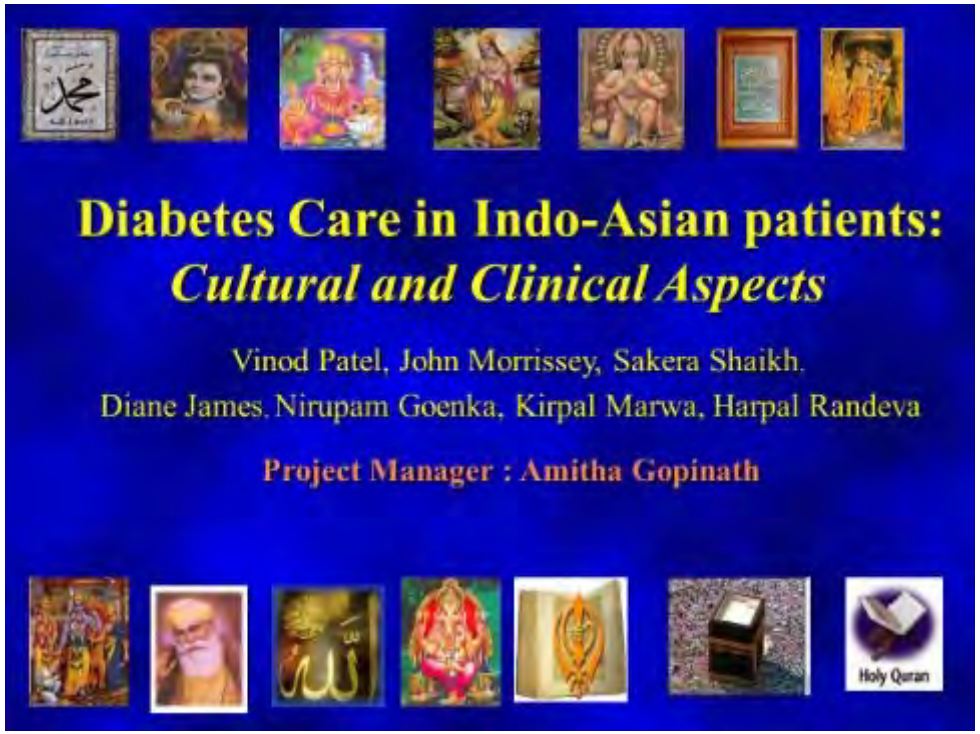








Bengali, Urdu, Gujarati, Hindi, Punjabi



Diabetes care in the Sikh patient: cultural and clinical aspects

NIRUPAM GOENKA,[1] KIRPAL MARWA,[1] HARPAL S RANDEVA,[2] JOHN MORRISSEY,[3] VINOD PATEL[3]

"*Realisation of Truth is higher than all else. Higher still is Truthful Living*"
(Guru Nanak, Sri Rag)

The Sikh religion

The word 'Sikh' in the Punjabi language means 'disciple' and the Sikh religion today has a following of over 20 million people worldwide. Sikhs are the disciples of God who follow the writings and teaching of the Ten Sikh Gurus. The Sikh religion originated in the Punjab region of India. The founder of the Sikh religion was Guru Nanak who was born in 1469. He preached a message of love and understanding and criticised some specific practices and rituals of certain Hindu and Muslim sects. Guru Nanak passed on the leadership of this new religion to nine successive Gurus. The final living Guru, Guru Gobind Singh, died in 1708.

Sikhism has been revolutionary in many ways, especially in its view of women. At the time of the Gurus, women were not considered the equals of men in society. Men were allowed polygamy but widows were not allowed to remarry and were encouraged to burn themselves on their husband's funeral pyre (sati). Child marriage and female infanticide were prevalent and often given religious sanction.

In this climate the Gurus preached that women were equal to men, worthy of praise and deserving of education, and the cruel customs of sati and female infanticide were condemned. Sikhs were also taught that women wearing veil was unnecessary and widows were encouraged to remarry. The Sikh religion was also innovative in its condemnation of a 'priestly' class and in holding the belief that people of different religions were equally capable of reaching salvation whilst following their own religion.

[1]Department of Diabetes and Endocrinology, University Hospital Aintree, Liverpool.
[2]Department of Diabetes and Endocrinology, University Hospitals of Coventry and Warwickshire.
[3]Diabetes and Endocrinology Centre, George Eliot Hospital NHS Trust, Nuneaton, Warwickshire.
Correspondence to: Dr Vinod Patel
Diabetes and Endocrinology Centre, George Eliot Hospital NHS Trust, College Street, Nuneaton, Warwickshire, CV10 7DJ, UK
Tel: +44 (0)2476 351351 | Fax: +44 (0)2476 865210
E-mail: vinod.patel@cwh-tr.nhs.uk
Br J Diabetes Vasc Dis (2002) 2 207-09

The Golden Temple - The Harimandir Sahib (meaning Temple of God) is also commonly known as the Golden Temple or Darbar Sahib (Divine Court). It is situated in the city of Amritsar in Punjab. The Golden Temple is a living symbol of the spiritual and historical traditions of the Sikhs.

During his life, the last living Sikh Guru, Guru Gobind Singh (1666–1708), established the Khalsa order (meaning 'the pure'), soldier-saints. The Khalsa uphold the highest Sikh virtues of commitment and dedication to their faith. The Khalsa are men and women who strictly follow the Sikh code of conduct and wear the prescribed physical articles of the faith (the five Ks, see table 1).

The spiritual head is not a living person as such, but a religious scripture called the Sri Guru Granth Sahib, the Eternal Guru of the Sikhs. It contains the poetry of the Gurus as well as the writings of saints of other faiths whose thoughts were consistent with those of the Sikh Gurus. In this regard, Sikhism can be regarded as a multi-faith eclectic religion to a greater extent than the other main faiths.

Diabetes care and Ramadan: to fast or not to fast?

SAKERA SHAIKH, DIANE JAMES, JOHN MORRISSEY, VINOD PATEL

"In the month of Ramadan the Quran was revealed.... Therefore whoever of you is present in that month let him fast. But he who is ill or on a journey shall fast a similar number of days later on. God desires your well-being not your discomfort."

The Quran

Introduction

The devout Muslim will wish to follow the instruction of Allah, revealed to Muhammed, to fast from dawn to sunset for the whole month of Ramadan. This practice may place Muslim patients with diabetes at risk. Diabetes affects over 20% of the Muslim population in Britain, five times its prevalence in the white Caucasian population.[1]

With advice, support and careful attention to glycaemic control most patients can fast safely. However, in the absence of such precautions patients may be at hazard of hypoglycaemia or ketoacidosis. For some patients fasting is dangerous and they should be advised to seek exemption. This short article offers a guide to the care of the Muslim patient with diabetes during Ramadan.

Islam

Islam is not only a religion but an entire way of life. The core beliefs of Islam are that there is only one God, Allah, that Muhammed was a prophet sent by Allah to mankind, and that the Quran, the revelations by Allah to Muhammed, is the word of God.

The Arabic word Islam means submission and obedience. Submission is acceptance of Allah's commands. Obedience means putting Allah's commands into practice.[2] One who accepts the Islamic way of life and acts accordingly is a Muslim. There are approximately one billion Muslims in the world, about 1.6 million in the United Kingdom.[3]

The Islamic perception of healthcare has religious, cultural and scientific dimensions. The relative importance given to each varies between cultures and according to the strength of an individual's religious belief. It is believed that cure comes solely from Allah and that doctors, teachers of religion and other such individuals are merely God's instruments.[4] The Muslim may seek treatment by modern medicine but simultaneously approach the learned teacher, *alim*, for help and advice based on the Quran.

Fasting

Fasting is abstention from food and drink from dawn to sunset. This also involves abstaining from intravenous fluid and intravenous, oral, anal and nasal medication. Fasting cultivates the spirit of sacrifice and teaches self-discipline and sympathy for the hungry and poor.[5] A pre-dawn meal (*suhr*) is taken before the start of the fasting day[6] and a larger meal after sunset.

Fasting during Ramadan (*sawm*) is one of the five pillars of Islam, the duties which form the basis of the Muslim way of life.[7,8] The others are *shahadah*, a declaration of faith, *salah*, five compulsory daily prayers, *zakat*, alms for the poor and needy, and *hajj*, pilgrimage to Mecca.

Ramadan is the ninth month of the Islamic year. Islam follows the lunar calendar in which one year equals twelve lunar months, 354 days. Each day in the Islamic year falls eleven days earlier each solar year. Ramadan therefore circulates through the seasons. When Ramadan falls during the winter months in Britain a fast can last ten hours, in summer up to nineteen. In the year 2001 of the Christian calendar Ramadan commences in November.

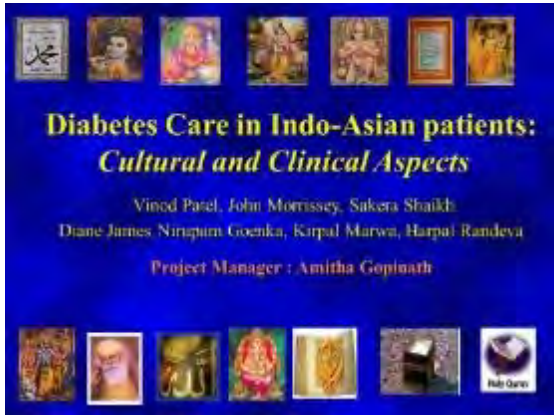
Exemptions from fasting

Fasting is obligatory upon every responsible and healthy Muslim. To miss a fast intentionally without valid reason is a sin, subject to a penalty of fasting for two months or providing a meal for sixty people.[9,10] However, some individuals are exempt:

- Children under the age of puberty.
- Those with learning difficulties and unable to understand the nature and purpose of the fast.
- The old and frail.
- The acutely unwell.
- Those with chronic illnesses for whom fasting may be detrimental to health.

Correspondence to: Mrs Sakera Shaikh
Diabetes and Endocrinology Centre, George Eliot Hospital NHS Trust, College Street, Nuneaton, Warwickshire, CV10 7DJ, UK.
Tel: +44 (0)2476 351351; Fax: +44 (0)2476 865310
Email: sakera.shaikh@virgin.net

Br J Diabetes Vasc Dis 2001;1:65–67



Diabetes care in the Hindu patient: cultural and clinical aspects

VINOD PATEL,[1] JOHN MORRISSEY,[1] NIRUPAM GOENKA,[2] DIANE JAMES,[1] SAKERA SHAIKH[1]

"Sattvic (good) people like food which is pure, which gives health, mental power, strength and long life, which has taste, is soothing and nourishing, and which makes glad the heart."

Bhagavad Gita (The Song of God) 17:8[1]

Introduction

In the UK about one third of Indo-Asians are Hindus. The prevalence of diabetes in these people is 15.2%, compared with 3.8% in the white Caucasian population, and a further 16.2% have impaired glucose tolerance (IGT).[2] Management should embrace an aggressive approach to coronary risk factors, especially diet and exercise. Recent evidence shows it is possible to reduce progression to diabetes in individuals with IGT.

Food, and the sharing of it, is particularly important in Hindu culture and the Western approach to dietary management of diabetes is not always appropriate. Specific advice is needed at the times of the many Hindu festivals, which may involve fasting, feasting or both.

Hinduism

Hinduism has no common roots with the Abrahamic religions (Judaism, Christianity and Islam) and embraces concepts which are not readily comprehensible to the Western mind. At the heart of Hinduism is the relentless pursuit of Absolute Truth and higher consciousness with the ultimate aim of uniting the individual soul (Atman) with God (Brahman).

Hinduism is often mistakenly regarded as a polytheistic idol-worshipping religion. In fact the various images are manifestations of the multiple facets of God and are used as aids to prayer and meditation (figures 1 and 2).

Hinduism has no formal book of catechism for all its aspects. Hindus revere the Vedas (akin to the Old Testament) as the foundation scriptures and the Bhagavad Gita and the Upanishads (akin to the New Testament) as their ultimate distillation. Hindus in UK courts swear an oath on the Bhagavad Gita. Hinduism emphasises the spirit of balance in all aspects of life and this can be used positively to influence diabetes care.

> Hinduism emphasises the spirit of balance in all aspects of life

Diabetes mellitus is well known in Hindu culture: it was described in the Ayurvedic texts several centuries BC. It was divided into a fatal condition of childhood (type 1 diabetes) and a condition of affluence and obesity in middle age (type 2 diabetes). Hindu physicians recognised the sweetness of diabetic urine by observing its attraction for ants. diabetes was therefore known as 'madhumeh', honeyed urine.[3]

Treatment of the condition included diet and various herbal remedies, especially *Momordica charantia* (karela, bitter gourd). This has proven hypoglycaemic properties: it reduces both hepatic gluconeogenesis and intestinal glucose absorption.[4] Indo-Asian diabetic patients may use karela and other bitters, often based on fenugreek, along with prescribed drugs without realising the need to communicate this to the diabetes care team.[5,6]

The festivals of Hinduism

Hinduism is characterised by its many festivals, with periods of feasting or fasting from one to nine days. Their timing is based on the lunar calendar, consequently they occur on different dates in the solar calendar from year to year. Devout Hindus often fast on specific days in the Hindu lunar calendar: the main such observance is **Poonam** which is the day of the full moon.

- **Diwali and New Year's day**. In 2001 AD these occur on 14th and 16th November respectively. The 'festival of lights' (Diwali) is the most important in the Hindu year, has a significance similar to Christmas and is usually celebrated with

Diabetes and Endocrinology Centre, George Eliot Hospital NHS Trust, Nuneaton
Department of Diabetes and Endocrinology, University Hospital Aintree, Liverpool
Correspondence to: Dr Vinod Patel
Diabetes and Endocrinology Centre, George Eliot Hospital NHS Trust, College Street, Nuneaton, Warwickshire, CV10 7DJ, UK.
Tel: +44 (0)2476 351351; Fax: +44 (0)2476 865310
Email: vinod.patel@geh-tr.wmids.nhs.uk

Br J Diabetes Vasc Dis 2001;1:152–5

Treatment Changes during Ramadan

- As you know some treatments will need adjusting, for example, some drugs need changing as you cannot drink fluids as normal
- We would advise you to change your treatment as below
- **Please go back to your normal times and doses after Ramadan**

Current Treatment	Ramadan
	Sehri (morning)
	Iftari (evening)

For further details contact

Diabetes Nurses: 024-76865210
Multi Lingual Co Worker: 024 76865595

Ramadan and Diabetes

Fasting safely during the Holy month of Ramadan

General Advice

- The Diabetes Care Team would like to help you Fast safely during Ramadan. We provide Ramadan diabetes advice in the local community and also at the hospital
- Over-eating during Ramadan and Eid can increase your blood sugars and make you put on weight
- Fasting allows you to abstain from smoking, Ramadan is a good time to stop smoking!
- Eat 5 portions of fruit and vegetables a day
- Ramadan is a good time to make small lifestyle changes. These changes will help you to have good control of your diabetes and reduce chance of a heart attack or stroke

Ramadan
Patient Education

Diet

- When you open your Fast limit the amount of sweet foods such as dates, milkshakes, jelabi and burfi.
- At **Sehri** and **Iftari** time eat more starchy foods, such as basmati rice, chapatti, brown bread and cereals.
- Eat more fruit, vegetables, dhal and low fat yoghurts.
- All drinks should be sugar-free, avoid adding sugar to tea and coffee. Limit the amount of salt you add to food.
- To avoid dehydration make sure you drink plenty of water before starting the Fast
- When you break your Fast, try not to have too many fried foods such as samosas, paratha and pakoras!

Medication

- During Ramadan it is very important to keep taking your regular tablets. Some tablets will need adjusting
- Your tablets will keep your blood glucose in control and keep you feeling well.
- If you decide to Fast and you are on insulin, you will need to be very careful, your insulin dose will need to change. Do not stop your insulin
- **For further advice contact the diabetes team at the hospital or your own GP.**

Diabetes Control

- Check your blood glucose regularly, it should be between 4 – 7
- When your blood glucose drops below 4, you may be at risk of having a hypo. You may feel weakness, sweating, trembling, tingling in the lips and fingers and slurred speech. If this happens then you must take 2 3 glucose tablets followed by a snack.

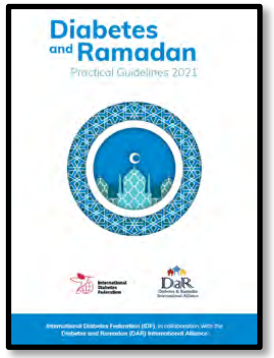
Clinical Care during Ramadan
Focus on Diabetes

People with **diabetes** observing **Ramadan fasts** are at a **higher risk** of complications (hypoglycaemia, hyperglycaemia, ketoacidosis) due to changes in eating patterns and circadian rhythms

Current guidelines highlight the role of **pre-Ramadan risk stratification** and **counselling** by HCPs with emphasis on the need for advice on adequate dietary and fluid intake, BG monitoring and awareness of when to break the fast

Based on robust evidence, guidelines exist to provide **clinically-relevant recommendations** on **lifestyle modifications** and **glucose-lowering therapies**

An **individualised patient-centric treatment plan** is essential to not only achieve optimal glycaemic outcomes but also enable people with diabetes to observe a **risk-free** month of fasting during Ramadan



You Tube: Managing Type 2 Diabetes During Ramadan London Mosque Imam Doctor Patel
https://youtu.be/dGyUzIkU_ZI

ACRONYM:
Archive of Clinical Research Outputs to Navigate Your Clinical Management

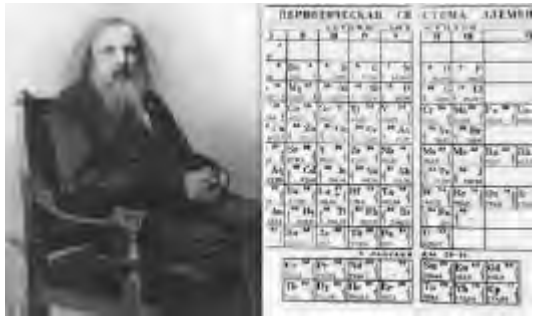
A Resource for Teaching Evidence-based Diabetes Clinical Care

Clinical Faculty
Friends of Vinod Patel
Warwick Medical School, George Eliot Hospital NHS Trust, Nuneaton

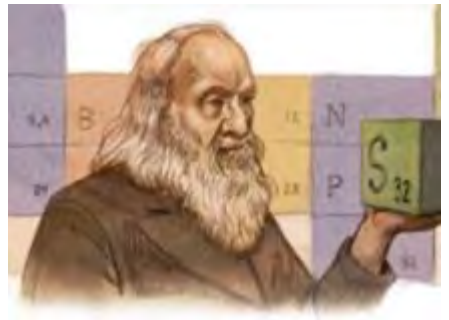


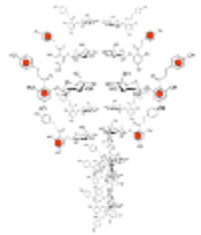


Student Faculty		
Hannah **Abebe**	Mara **Bortnowschi**	Rebecca **Campbell**



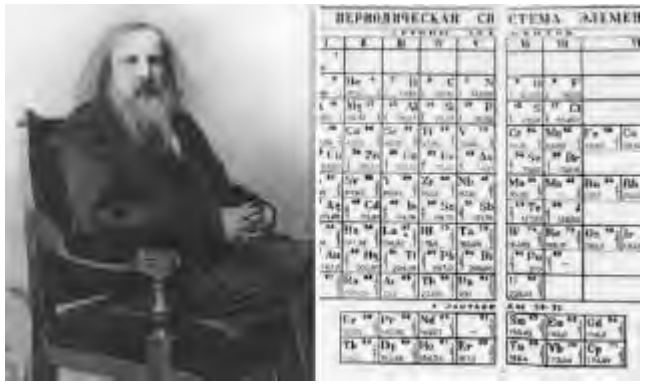






Our Community of People with Diabetes

	***1: Infant***	**Adam Eaton:** 5 year old. No significant past medical history apart from prematurity and neonatal jaundice. His mother had gestational diabetes. Adam is in the 90 percentile for weight at his infant school. Loves playing computer games.
	***2: Child***	**Bedi Bishan:** 15 years old now having developed Type 1 diabetes at the age of 11. He has taken well to using the Flash Monitoring device for glucose measurements. He craves carbohydrates and really does not like PE.
	***3: Pregnant***	**Camilla Begum:** is 29 years old and pregnant with her second child. She had difficulty conceiving and had a diagnosis of PCOS. She has Gestational diabetes. She is happy to stick to her diet and take metformin but is very reluctant to take insulin. Her husband has type 2 diabetes and wants advice on observing Ramadan.
	***4: Self-employed***	**Daniella Deronton:** is 48 years old and work as a part-time taxi driver and as an odd-jobs business. This can include fitting windows and guttering on houses. She is overweight and desperate to lose weight with a pending wedding and daughter's graduation. She had been told that she has pre-diabetes
	***5: Teaching Assistant***	**Eliot Evans:** is a 58 year old assistant Science Teacher and in charge of the Chemistry and Physics Labs at the local academy. He recently had a heart attack and has a foot ulcer that has proven very slow to improve. Does not want Covid-19 vaccine. He had type 2 diabetes and is very reluctant to have statins and indeed any further drug therapy.
	***6: Retired Nurse***	**Felix Kanhai** is 67 years old and recently retired and looking forward to spending time with his allotment and want to continue to singing activities. He is looking to visiting family in the Caribbean . He hope to travel with his family on a cruise.
	***7: Residential Care***	**Georgina Sklodowska:** an 83 year old woman, now living alone. She was recently admitted overnight to hospital having had a fall. She is an amateur artist and now has difficulty holding paintbrushes.

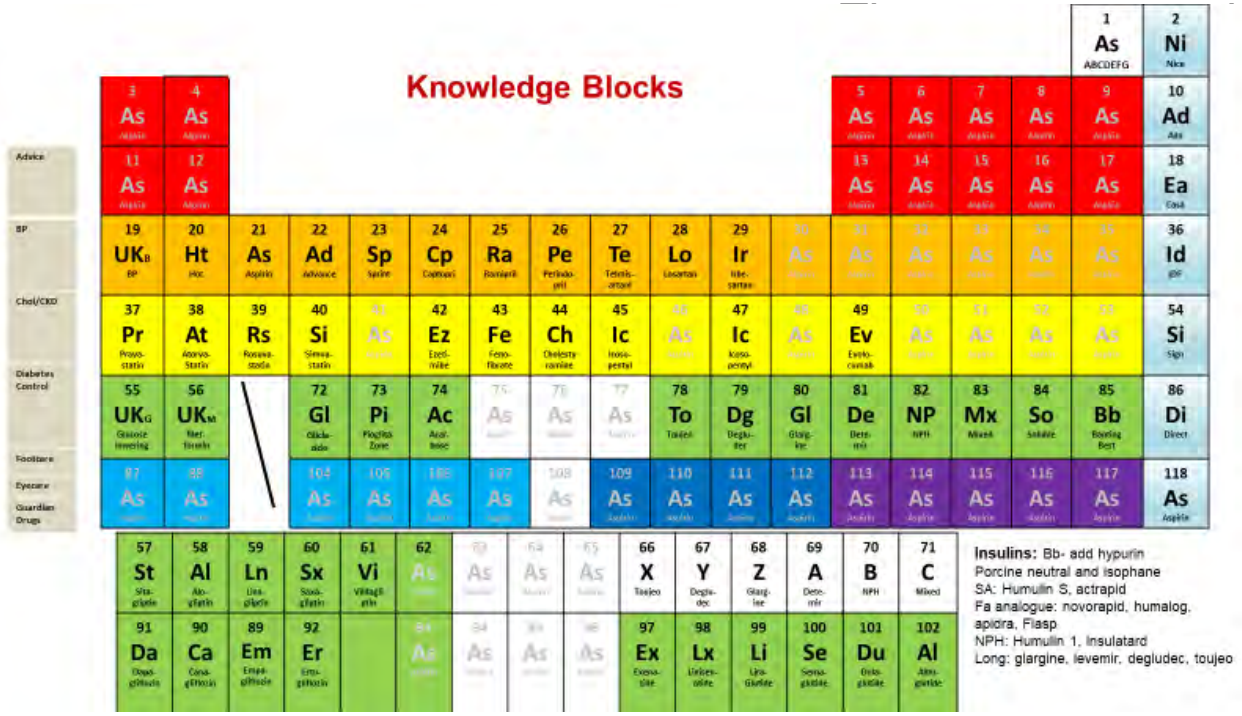


DMITRI Project

Diabetes Management Informed by Trials Research Integration

The Central Idea

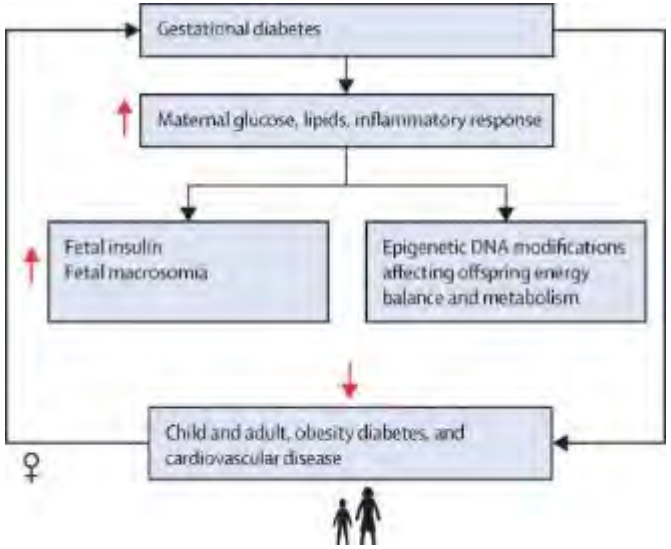
- To create an educational resource that will be useful for Clinicians and Patients across a broad spectrum of clinical scenarios in Diabetes Care
- This will encompass advice on general health, therapies specific to diabetes and special circumstances in relation to their life-journey or culture

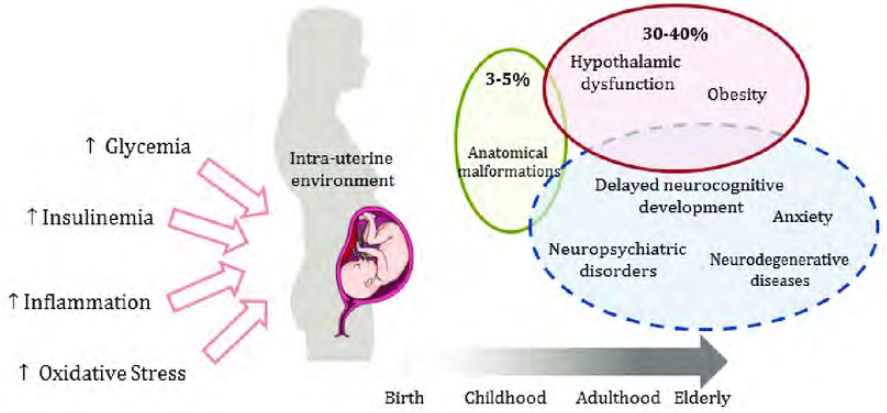


e used to provide patients with evidence-based
empower them to plan a shared and agreed
nt plan

Gestational Diabetes (GDM)

- GDM is defined as hyperglycaemia that begins or is first diagnosed in pregnancy. It is associated with increased pregnancy complications and long-term metabolic risks for the woman and the offspring.
- However, the current diagnostic and management strategies recommended by national and international guidelines are mainly focused on short-term risks during pregnancy and delivery.
- Good evidence for long-term risk in women with gestational diabetes and their offspring.
- A shift is needed in the thinking about GDM; moving from the perception of a short-term condition that confers increased risks of large babies to a potentially modifiable long-term condition that contributes to the growing burden of childhood obesity and cardiometabolic disorders in women and the future generation.





Saravanan P; Diabetes in Pregnancy Working Group; Maternal Medicine Clinical Study Group; RCOG UK. Gestational diabetes: opportunities for improving maternal and child health. Lancet Diabetes Endocrinol. 2020 Sep;8(9):793-800. doi: 10.1016/S2213-8587(20)30161-3.

Prof P Saravanan

Preventing Death, CVD and Micro-vascular Complications in Type 1 Patients:

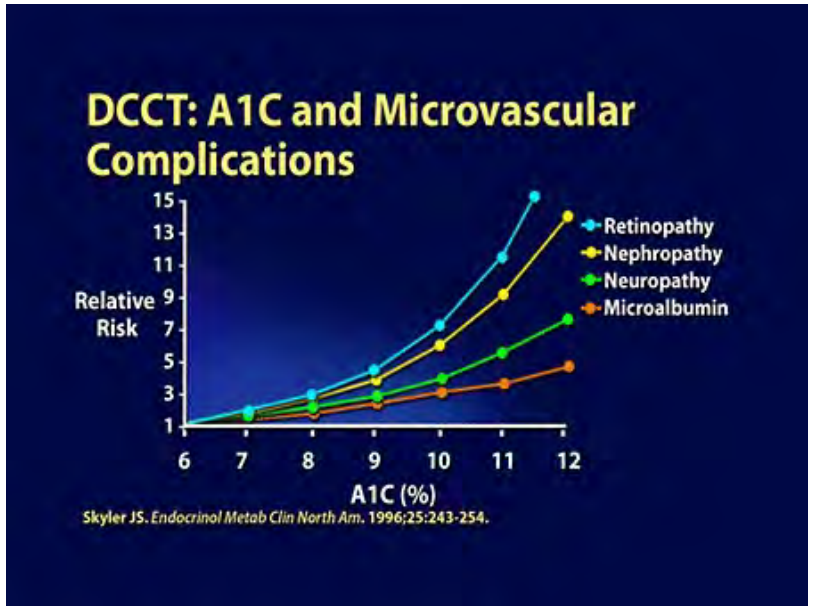
The Triple Shield of BP control, lipid-lowering and Glycaemic control

- *Huo et al 2016:* Type 1 diabetes 12.2 years of life lost on average
- *Hero et al 2016:* 24230 Type 1 patients, Cohort Study, 5387 (22%) on lipid-lowering (97% statins), rest 18843 not, 6 year follow up, Sweden
- Statin Treatment associated with:
  - **40% CVD reduction**
  - **44% Stroke reduction**
  - **22% MI reduction**
  - **44% Death reduction**
- Number needed to save one death was 297 treatment years or 50 patients treated for 6 years.

One key message- always- is to consider Statins for all Type 1 patients according to NICE Guidelines

All over 40 years of age or if > 10 years diabetes duration

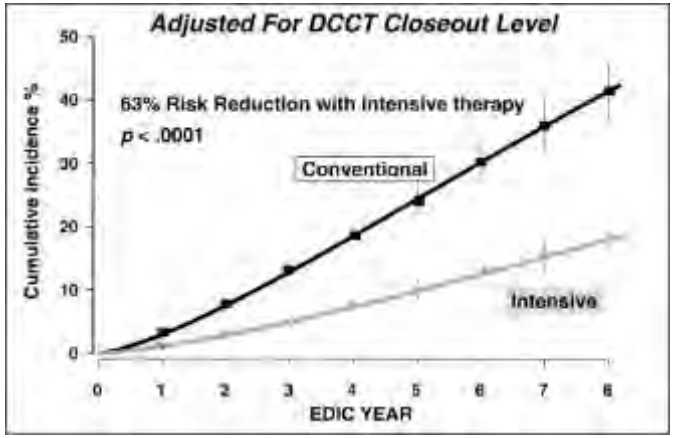
Effective Contraception Essential in females



Hypertension and Cholesterol Goals

Driven mainly by strong relationships (RR range 1.8-12.1) with mortality, CAD, and overt nephropathy, suggested goal levels are as follows:

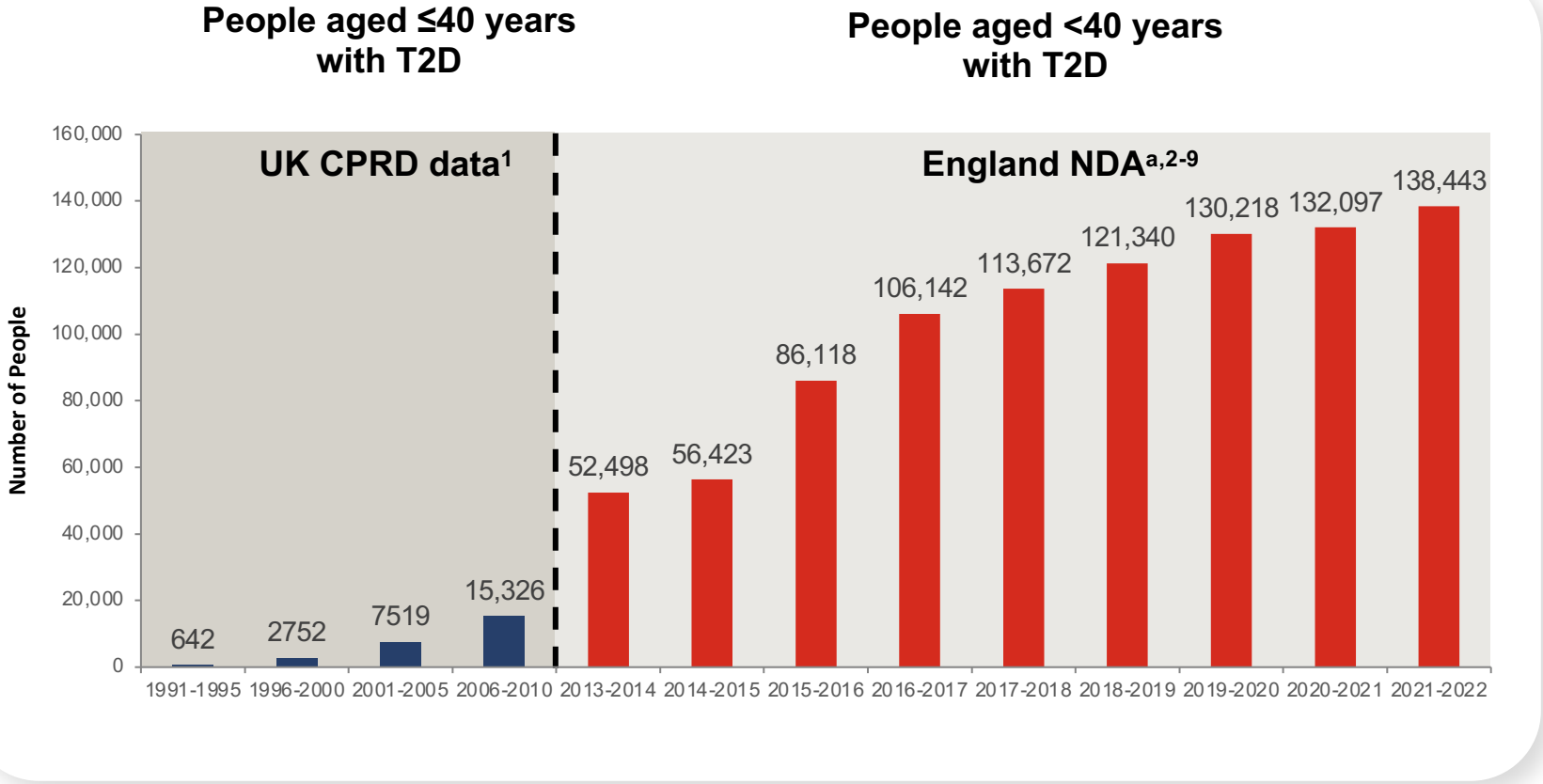
- **LDL chol. <2.6 mmol/l, HDL chol. >1.1 mmol/l, trigs. <1.7mmol/l**
- **Systolic BP <120 mmHg, Diastolic BP <80 mmHg**
- Age, sex, glycaemic control had little influence on these independent goals.

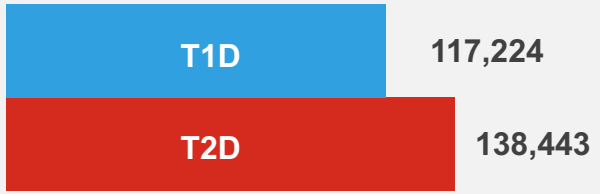


HbA1c:
9% vs 7%
75 vs 53 mmol/mol

Orchard TJ et al. Lipid and BP goals for type 1 diabetes: 10-year incidence data from the Pittsburgh Epidemiology of Diabetes Complications Study. Diabetes Care. 2001 Jun;24(6):1053-9. doi: 10.2337/diacare.24.6.1053. PMID: 11375370.

T2D Onset in Younger People is a Growing Problem





younger people (<40 years) in England in 2021-2022[9]

T2D is now more prevalent than T1D in younger people in England[7-9]

[a]Listed as Type 2 and other registrations.

Notes: There is no standard definition for younger adults, however the National Diabetes Audit (NDA) typically includes people aged <40 years. Two different datasets covering different geographical regions are shown in the graph and cannot be compared directly but show a trend in onset of diabetes in younger people.

CPRD=Clinical Practice Research Datalink; NDA=National Diabetes Audit; T2D=Type 2 Diabetes.

1. Holden SE, et al. *Diabetes Obes Metab*. 2013;15(9):844-852. 2. National Diabetes Audit 2013-15. 3. National Diabetes Audit 2014-16.
4. National Diabetes Audit, 2016-2017. 5. National Diabetes Audit 2017-2018. 6. National Diabetes Audit, 2018-2019. 7. National Diabetes Audit 2019-2020.
8. National Diabetes Audit 2020-2021. 9. National Diabetes Audit 2021-2022.

Preventing Death, CVD and Micro-vascular Complications in Type 2 Patients:

The Triple Shield of BP control, lipid-lowering and Glycaemic control

Primary Prevention: Atorvastatin 10mg

Treatment Effect on the Primary Endpoint

Event	Placebo*	Atorva*	Hazard Ratio	Risk Reduction (CI)
Primary endpoint**	127 (9.0%)	83 (5.8%)		37% (17- 52) p=0.001
Acute coronary events	77 (5.5%)	51 (3.6%)		36% (9- 55)
Coronary revascularisation	34 (2.4%)	24 (1.7%)		31% (-16- 59)
Stroke	39 (2.8%)	21 (1.5%)		48% (11- 69)

.2 .4 .6 .8 1.2

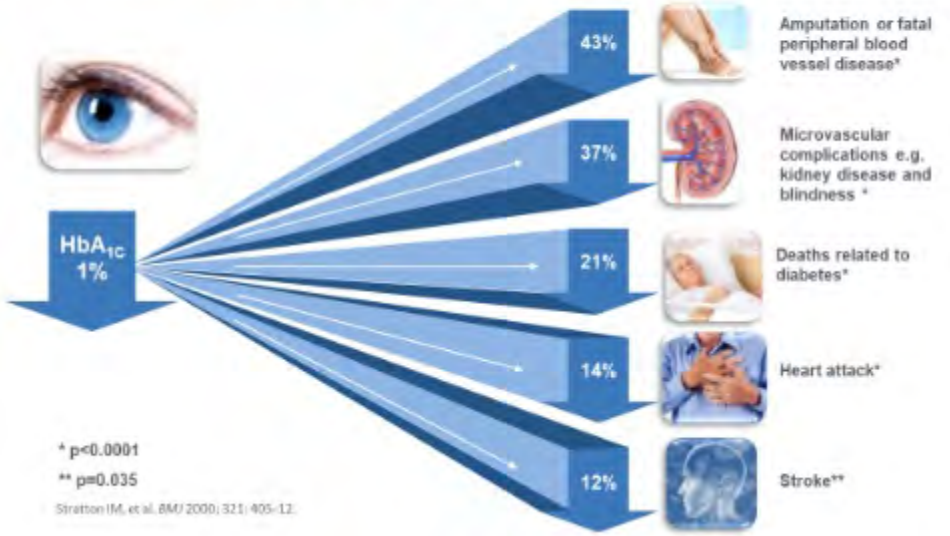
Favours Atorvastatin Favours Placebo

**Fatal MI ,Other acute CHD death, non fatal MI, unstable angina, CABG, Fatal stroke, non fatal stroke

* N (% randomised)

Diabetes Control: UKPDS

1% (10 mmol/l) decrease in HbA_{1c} associated with reduction in complications



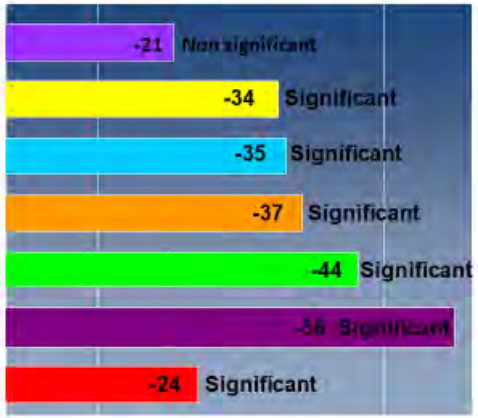
* p<0.0001

** p=0.035

Stratton IM, et al. BMJ 2000; 321: 405-12.

Blood Pressure

UKPDS 38: 154/87 versus 144/82

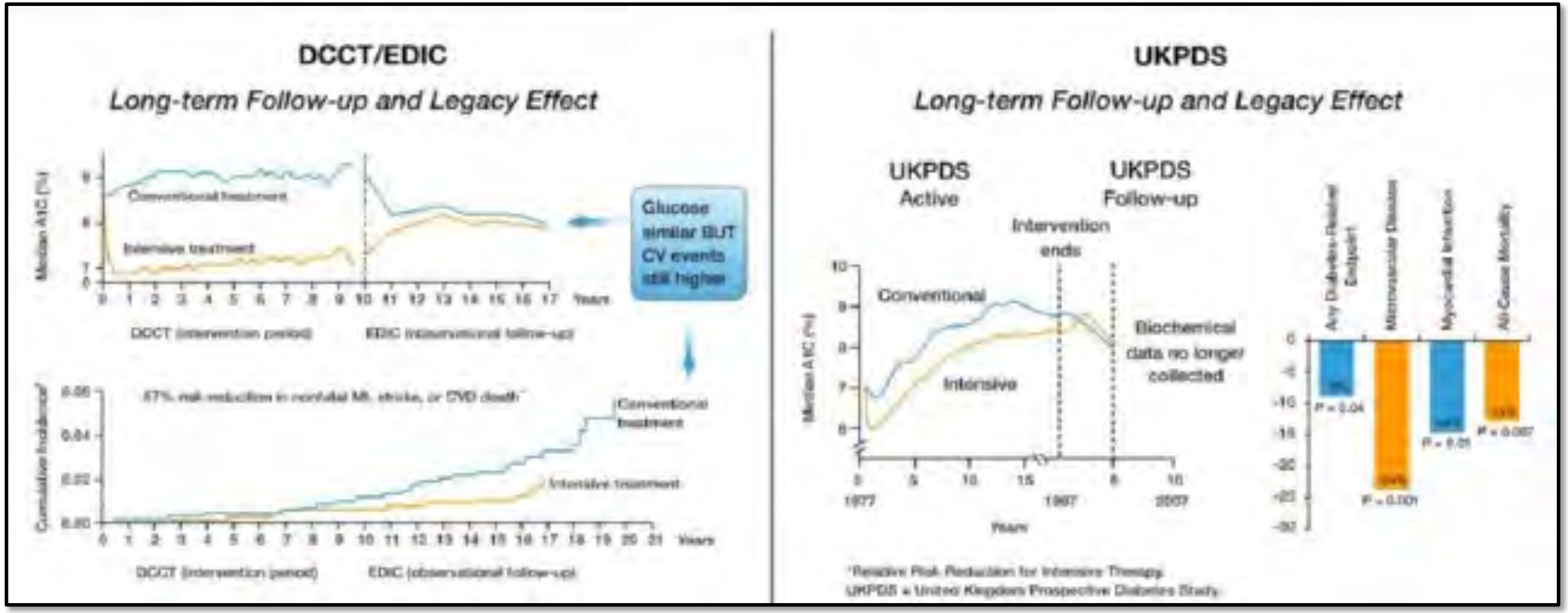


- MI
- Microvascular endpoint –34%
- Heart failure –35%
- Stroke –37%
- All macrovascular endpoints –44%
- Retinal photocoagulation –56%
- Any diabetes-related endpoint –24%

Deaths reduced by 32%

UK Prospective Diabetes Study (UKPDS) Group (38). BMJ 1998;317:703-713

Beneficial legacy effect of good glycaemic control in Type 1 and Type 2 Diabetes



DCCT/EDIC Long term follow up and metabolic memory in Type 1 diabetes and Type 2 UKPDS: long term follow up and legacy effect.

Program uses novel approach to improve diabetes care in First Nations communities

It never occurred to Peter Young that he might get diabetes ….he had lost a childhood friend to an uncontrolled diabetic foot infection. **“I didn’t know how diabetes works,”** said the 44-year old member of the Bigstone Cree Nation in Wabasca, 322 kilometres north of Edmonton.

So when the telltale signs of Type 2 diabetes began to plague him last summer—lightheadedness, an unquenchable thirst, urinating every hour**—“I didn’t have a clue.” “When the doctor gave me the news, I got in my truck and I just cried,”** Young said. **“It was such a shock. I thought, ‘My life is over, I can’t have any fun stuff anymore.’”**

An innovative new program co-developed with the First Nations and ….and researchers at the University of Alberta, is revolutionizing care and improving outcomes for First Nations members across the province. Young, … has now wrestled his blood sugars back into the normal range with a daily regimen of medication, exercise, meal planning and finger-prick blood tests when needed…

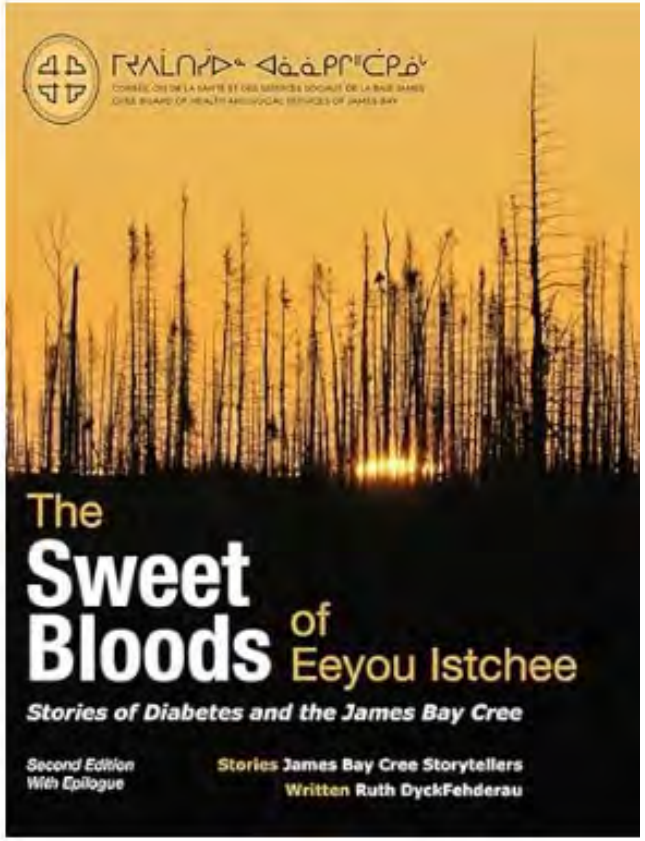
“I’m not eating as many fatty foods, I'm eating lots more fruit and drinking lots more water. If I have something sweet, I'll walk it off.”

U of A epidemiologist Dean Eurich says the RADAR program has helped more than 700 people with Type 2 diabetes improve their health with culturally appropriate support that is adaptable to each community's specific needs… improved by an average of 10% in key metrics such as blood sugar, BP and cholesterol levels.

U of A Website accessed March 21 2024. Adapted

The Sweet Bloods of Eeyou Istchee: Stories of Diabetes and the James Bay Cree

Ruth DyckFehderau and the James Bay Cree Storytellers



From the Review

This is an important book. In this time, when our Cree communities and other Indigenous groups are facing down a **brutal and pervasive diabetes epidemic**, *Sweet Bloods* offers a Talking Circle in print: frank, funny, and emotional stories of James Bay Cree people living with the disease. Once you start this book, you'll want to read to the end. -- **Bella M. Petawabano**

The stories contained in *The Sweet Bloods of Eeyou Istchee* are incredible. They are life lessons, they are tales of warning, they are songs of resilience, they are prayers for a healthier life-- **Joseph Boyden**

Ruth

While I was working on Sweet Bloods, many storytellers informed me that their diabetes began in the Indian Residential Schools (when they were receiving fewer than 600 cals/day) ...

Helping Everyone Achieve Longer Term Health

? An evidence-based U of A Faculty Approach

Our Area of Care and Influence?

- **Autonomy:** the patient has the right to refuse or choose their treatment (*Voluntas aegroti suprema lex.*)
- **Beneficience:** a practitioner should act in the best interest of the patient (*Salus aegroti suprema lex.*)
- **Non-maleficence:** do no harm (*Primum non nocere*)
- **Justice:** distribution of scarce health resources, based on fairness and equality. Addressing Health Inequalities. Addressing Socio-economic Deprivation (*iustitia*)

Dr Rashmi Shukla

Philosophy Politics, Economics	10 Fold Path Idea
Overall Philosophy	1.**Good Mental Health:** Connect with people and foster good relationships, Be active, Learn new skills, Give to others, Pay attention to the present moment (mindfulness), time in Nature
Personal Lifestyle Advice	2.**Never Smoking:** Not smoking or cessation. Advise vaping if last resort for nicotine replacement. 3. **Higher Diet Quality Score:** Alternative Healthy Eating Index Diet of 60 points or more 4. **Physical Activity: Moderate to Vigorous:** Moderate or more physical activity, 3 Mets or more, 30 mins 5 hours. 5. **Moderate or No Alcohol intake:** 14 units per weeks, if you chose to drink
Personal Clinical Factors	6. **Body Mass Index or Body Shape:** Optimising body shape for the frame that you have- Ecto, Meso, Endo. 7. **Blood Pressure Control:** Optimising BP for the age group 8. **Cholesterol Care- Statins:** Statins for most over the age of 50 or so.
Clinical Care	9. **Clinical Care and Interventions:** Vaccinations, screening, treatments, surgeries
The Planet	10. **Planetary Health:** Addressing Inequalities, Climate change, Biodiversity, Pollution, Peace vs War, Crime, Sustainability

Bechman N, Thornby J, Brandstatter E, Hewitt D, Patel V. Helping Everyone Achieve Long Term Health Passport: exploring potential use of the HEALTH Passport in primary and secondary schools. J Public Health (Oxf). 2023 Jun 14;45(2):e234-e240. doi: 10.1093/pubmed/fdac039. PMID: 35403188.

Alphabet Strategy for Diabetes Care: "Checklist"

A Safety "Checklist", Patient-Centred, Multi-Professional, Evidence-based Approach

National Diabetes Audit Eight Process Checks

- HbA1c, BP, cholesterol
- Urine albumin, Creatinine
- Foot examination
- BMI and smoking

(Eye screening)

National Diabetes Audit Targets:

BP: ≤140/80 mmHg
HbA1c: ≤58 mmol/mol
Cholesterol: <5 mmol/L

New Target Statins:
Primary & Secondary Prevention of CHD

Upreti R, Lee JD, Kotecha S, Patel V.
Alphabet strategy for diabetes care: A checklist approach in the time of COVID-19 and beyond.
World J Diabetes. 2021 Apr 15;12(4):407-419. doi: 10.4239/wjd.v12.i4.407.

Lee J, Saravanan P, Patel V. **Alphabet Strategy for diabetes care: A multi-professional, evidence-based, outcome-directed approach to management**. World journal of diabetes 2015. 6. 874-9. 10.4239/wjd.v6.i6.874.

- **Advice:**
  - Diet and weight control, Physical activity, not smoking, Good Infection Control Measures, Appropriate PPE, COVID-19 Symptoms, appropriate vaccinations
- **Blood Pressure:**
  - aim ≤ 140/80,
  - CVD or CKD ≤ 130/80
- **Cholesterol & CKD Prevention**
  - Most Atorvastatin 20mg or 80mg, TC ≈ 4 mmol/l
  - UACR yearly and treat
- **Diabetes Control:**
  - HbA1c < 59 (7.5%) usual target, ideal < 48 (6.5%)
  - Outcome based Rx: usually SGLT2-i, ? GLP-RA
  - Safer insulins where needed
- **Eyes:**
  - check yearly at least
- **Feet:**
  - daily self-care, HCP check yearly at least
- **Guardian Drugs:**
  - ?Aspirin 75mg (CVD atheroma), ?ACE-i, ARBs (esp CKD, HF, CVD), appropriate SGLT2-i (NICE NG-28), GLP-RA
- **Healthcare Professional Advice:** (with kindness and compassion)
  - Contraception & Pre-conception Advice
  - Driving and Occupation Advice
  - Hospital Admission Care
  - Other individualised advice eg Ramadan, Travel

George Eliot Hospital NHS Trust

THE UNIVERSITY OF WARWICK

Collaborative Care and Research
Partnership of patients and Colleagues
Common Endeavours

NHS
George Eliot Hospital
NHS Trust

Our vision is to EXCEL at patient care

The Discovery of Insulin to present day clinical care:

Collip and Colleagues, Complex Care, and Care in the Community

Conclusions

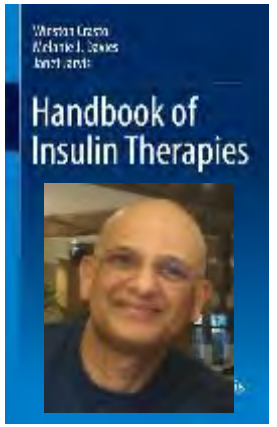
Collip and Colleagues: ***Important of collaborative research and Clinical Care- there was "Glory Enough for All" and is …***

Burden of Diabetes: ***Urgent need to address, especially prevention of diabetes, diabetes complications, pancreatic transplant research***

Complex Care: ***Need for Healthcare Professional and Patients to implement effective evidence-based care***

Caring for the Community: ***Cultural competence, Individualised, Ethical Clinical Care***

Canadian Film: 1988,
Dir. Eric Till, Nine Gemini Awards



Dedicated to my Colleagues- Past and Present

Thank You all for Attending

Dr Winston Crasto