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Diabetes Mellitus Type 2

Main article: [Diabetes mellitus](#)

Diabetes mellitus type 2 or **type 2 diabetes** (formerly called **non -insulin-dependent diabetes mellitus (NIDDM)**, or **adult-onset diabetes**) is a disorder that is characterized by high blood glucose in the context of [insulin resistance](#) and relative insulin deficiency.^[1] Diabetes is often initially managed by increasing [exercise](#) and [dietary modification](#). As

the condition progresses, medications are typically needed.

There are an estimated 23.6 million people in the U.S. (7.8% of the population) with diabetes with 17.9 million being diagnosed,^[2] 90% of whom are type 2.^[3] With prevalence rates doubling between 1990 and 2005, [CDC](#) has

characterized the increase as an [epidemic](#).^[4] Traditionally considered a disease of adults, type 2 diabetes is

increasingly diagnosed in children in parallel to rising obesity rates^[5] due to alterations in dietary patterns as well as in life styles during childhood.^[6]

Unlike [type 1 diabetes](#), there is very little tendency toward [ketoacidosis](#) in type 2 diabetes, though it is not unknown.^[7]

One effect that can occur is [nonketonic hyperglycemia](#) which also is quite dangerous, though it must be treated very differently. Complex and multifactorial metabolic changes very often lead to damage and function impairment of many [organs](#), most importantly the [cardiovascular](#) system in both types. This leads to substantially increased [morbidity](#) and [mortality](#) in people with both type 1 and type 2 diabetes, but the two have quite different origins and treatments despite the similarity in [complications](#).

Signs and symptoms

The symptoms of type 2 diabetes include:

Early symptoms may be nothing more than chronic fatigue, generalised weakness and malaise (feeling of unease)

[Excessive urine production](#)

[Excessive thirst and increased fluid intake](#)

Blurred vision (typically from lens shape alterations, due to [osmotic](#) effects, e.g., high blood glucose levels)

Unexplained [weight loss](#)

Lethargy

Itching of external genitalia

Excessive bowel movements

Cause

Medical conditions

There are many factors which can potentially give raise or exacerbate type 2 diabetes. These include obesity, [hypertension](#), elevated [cholesterol](#) ([combined hyperlipidemia](#)), and with the condition often termed [Metabolic syndrome](#) (it is also known as Syndrome X, Reavan's syndrome, or CHAOS). Other causes include [acromegaly](#), [Cushing's](#)

syndrome, thyrotoxicosis, pheochromocytoma, chronic pancreatitis, cancer and drugs. Additional factors found to increase the risk of type 2 diabetes include aging, [8] high-fat diets [9] and a less active lifestyle. [10]

Genetics

There is also a strong inheritable genetic connection in type 2 diabetes: having relatives (especially first degree) with type 2 increases risks of developing type 2 diabetes very substantially. In addition, there is also a mutation to the Islet Amyloid Polypeptide gene that results in an earlier onset, more severe, form of diabetes. [11][12]

About 55 percent of type 2 patients are obese at diagnosis [13] —chronic obesity leads to increased insulin resistance that can develop into Type 2, most likely because adipose tissue (especially that in the abdomen around internal organs) is a (recently identified) source of several chemical signals to other tissues (hormones and cytokines).

Other research shows that type 2 diabetes causes obesity as an effect of the changes in metabolism and other deranged cell behavior attendant on insulin resistance. [14]

However, environmental factors (almost certainly diet and weight) play a large part in the development of Type 2 in addition to any genetic component. This can be seen from the adoption of the Type 2 epidemiological pattern in those who have moved to a different environment as compared to the same genetic pool who have not. Immigrants to Western developed countries, for instance, as compared to lower incidence countries of origins. [15]

Medications

Some drugs, used for any of several conditions, can interfere with the insulin regulation system, possibly producing drug induced hyperglycemia. Some examples follow, giving the biochemical mechanism in each case:

Atypical Antipsychotics - Alter receptor binding characteristics, leading to increased insulin resistance.

Beta-blockers - Inhibit insulin secretion.

Calcium Channel Blockers - Inhibits secretion of insulin by interfering with cytosolic calcium release.

Corticosteroids - Cause peripheral insulin resistance and gluconeogenesis.

Fluoroquinolones - Inhibits insulin secretion by blocking ATP sensitive potassium channels.

Niacin - causes increased insulin resistance due to increased free fatty acid mobilization.

Phenothiazines - Inhibit insulin secretion.

Protease Inhibitors - Inhibit the conversion of proinsulin to insulin.

Somatropin - May decrease sensitivity to insulin, especially in those susceptible.

Thiazide Diuretics - Inhibit insulin secretion due to hypokalemia. They also cause increased insulin resistance due to increased free fatty acid mobilization.

Pathophysiology

Insulin resistance means that body cells do not respond appropriately when insulin is present. Unlike type 1 diabetes mellitus, insulin resistance is generally "post-receptor", meaning it is a problem with the cells that respond to insulin rather than a problem with the production of insulin.

Other important contributing factors:

increased hepatic glucose production (e.g., from glycogen → glucose conversion), especially at inappropriate times (typical cause is deranged insulin levels, as those levels control this function in liver cells)

decreased insulin-mediated [glucose](#) transport in (primarily) [muscle](#) and adipose tissues (receptor and post-receptor defects)

impaired beta-cell function—loss of early phase of insulin release in response to hyperglycemic stimuli

This is a more complex problem than type 1, but is sometimes easier to treat, especially in the early years when insulin is often still being produced internally. Type 2 may go unnoticed for years before diagnosis, since symptoms are typically milder (e.g., no ketoacidosis, coma, etc) and can be sporadic. However, severe complications can result from improperly managed type 2 diabetes, including [renal failure](#), [erectile dysfunction](#), blindness, slow healing wounds (including surgical incisions), and [arterial](#) disease, including [coronary artery disease](#). The onset of type 2 has been most common in [middle age](#) and [later life](#), although it is being more frequently seen in adolescents and young adults due to an increase in child obesity and inactivity. A type of diabetes called MODY is increasingly seen in adolescents, but this is classified as a diabetes due to a specific cause and not as type 2 diabetes.

Diabetes mellitus with a known etiology, such as secondary to other diseases, known [gene defects](#), trauma or surgery, or the effects of drugs, is more appropriately called secondary diabetes mellitus or diabetes due to a specific cause. Examples include diabetes mellitus such as MODY or those caused by hemochromatosis, pancreatic insufficiencies, or certain types of medications (e.g., long-term [steroid](#) use).

Diagnosis

The World Health Organization definition of diabetes is for a single raised glucose reading with symptoms, otherwise raised values on two occasions, of either: ^[17]

fasting plasma glucose ≥ 7.0 mmol/l (126 mg/dl)

or

With a [glucose tolerance test](#), two hours after the oral dose a plasma glucose ≥ 11.1 mmol/l (200 mg/dl)

Screening and prevention

Prevention

Onset of type 2 diabetes can often be delayed through proper nutrition and regular exercise. ^[18]

Interest has arisen in preventing diabetes due to research on the benefits of treating patients before overt diabetes. Although the U.S. Preventive Services Task Force concluded that "the evidence is insufficient to recommend for or against routinely screening asymptomatic adults for type 2 diabetes, impaired glucose tolerance, or impaired fasting glucose," ^{[19][20]} this was a grade I recommendation when published in 2003. However, the USPSTF does recommend screening for diabetics in adults with hypertension or hyperlipidemia (grade B recommendation).

In 2005, an evidence report by the [Agency for Healthcare Research and Quality](#) concluded that "there is evidence that combined diet and exercise, as well as drug therapy (metformin, acarbose), may be effective at preventing progression to DM in IGT subjects". ^[21]

Milk has also been associated with the prevention of diabetes. A questionnaire study was done by Choi et al. of 41,254 men which including a 12 year follow up showed this association. In this study, it was found that diets high in low-fat dairy might lower the risk of type 2 diabetes in men. Even though these benefits are being considered linked to milk consumption, the effect of diet is only one factor that is affecting the body's overall health. [22]

Accuracy of tests for early detection

If a 2-hour postload glucose level of at least 11.1 mmol/L (≥ 200 mg/dL) is used as the reference standard, the fasting plasma glucose > 7.0 mmol/L (126 mg/dL) diagnoses *current* diabetes with [20] :

sensitivity about 50%

specificity greater than 95%

A *random* capillary blood glucose > 6.7 mmol/L (120 mg/dL) diagnoses *current* diabetes with [23] :

sensitivity = 75%

specificity = 88%

Glycosylated hemoglobin values that are elevated (over 5%), but not in the diabetic range (not over 7.0%) are predictive of *subsequent* clinical diabetes in US female health professionals. [24] In this study, 177 of 1061

patients with glycosylated hemoglobin value less than 6% became diabetic within 5 years compared to 282 of 26281 patients with a glycosylated hemoglobin value of 6.0% or more. This equates to a glycosylated hemoglobin value of 6.0% or more having:

sensitivity = 16.7%

specificity = 98.9%

Benefit of early detection

Since publication of the USPSTF statement, a *randomized controlled trial* of prescribing acarbose to patients with "high-risk population of men and women between the ages of 40 and 70 years with a *body mass index* (BMI), calculated as weight in kilograms divided by the square of height in meters, between 25 and 40. They were eligible for the study if they had *IGT* according to the *World Health Organization* criteria, plus impaired fasting glucose (a fasting plasma glucose concentration of between 100 and 140 mg/dL or 5.5 and 7.8 mmol/L) found a *number needed to treat* of 44 (over 3.3 years) to prevent a major cardiovascular event. [25]

Other studies have shown that lifestyle changes, [26] *xenical* [27] and *metformin* [28] can delay the onset of diabetes.

Management

Main article: [Diabetes management](#)

Left untreated, diabetes mellitus type 2 is a chronic, progressive condition, but there are well-established treatments which can delay or prevent entirely the formerly inevitable consequences of the condition. Often, the condition is viewed as progressive since poor management of blood sugar leads to a myriad of steadily worsening complications. However, if blood sugar is properly maintained, then the condition is, in a limited sense, cured - that

is, patients are at no heightened risk for neuropathy, [blindness](#), or any other high blood sugar complication, though the underlying issue, a tendency to hyperglycemia has not been addressed directly. A study at UCLA in 2005 showed that the Pritikin Program of diet and exercise brought dramatic improvement to a group of diabetics and pre-diabetics in only three weeks, so that about half no longer met the criteria for the condition. [29] [30] [31]

There are two main goals of treatment:

1. reduction of mortality and concomitant morbidity (from assorted diabetic complications)
2. preservation of quality of life

The first goal can be achieved through close glycemic control (i.e., to near 'normal' blood glucose levels); the reduction in severity of diabetic side effects has been very well demonstrated in several large [clinical trials](#) and is established beyond controversy. The second goal is often addressed (in developed countries) by support and care from teams of diabetic health workers (usually physician, PA, nurse, dietitian or a certified diabetic educator). Endocrinologists, family practitioners, and general internists are the physician specialties most likely to treat people with diabetes. Knowledgeable patient participation is vital to clinical success, and so patient education is a crucial aspect of this effort.

Type 2 is initially treated by adjustments in diet and exercise, and by weight loss, most especially in obese patients. The amount of weight loss which improves the clinical picture is sometimes modest (2–5 kg or 4.4-11 lb); this is almost certainly due to currently poorly understood aspects of fat tissue activity, for instance chemical signaling (especially in visceral fat tissue in and around abdominal organs). In many cases, such initial efforts can substantially restore insulin sensitivity. In some cases strict diet can adequately control the glycemic levels.

Diabetes education is an integral component of medical care. Among adults with diagnosed diabetes, 12% take both insulin and oral medications, 19% take insulin only, 53% take oral medications only, and 15% do not take either insulin or oral medications.

Goals

Treatment goals for type 2 diabetic patients are related to effective control of blood glucose, [blood pressure](#) and [lipids](#) to minimize the risk of long-term consequences associated with diabetes. They are suggested in clinical practice guidelines released by various national and international diabetes agencies.

The targets are:

Hb_{A1c} of 6% [32] to 7.0% [33]

Preprandial blood glucose: 4.0 to 6.0 mmol/L (72 to 108 mg/dl) [34]

2-hour [postprandial](#) blood glucose: 5.0 to 8.0 mmol/L (90 to 144 mg/dl) [34]

In older patients, clinical practice guidelines by the [American Geriatrics Society](#) states "for frail older adults, persons with life expectancy of less than 5 years, and others in whom the risks of intensive glycemic control appear to outweigh the benefits, a less stringent target such as Hb_{A1c} of 8% is appropriate". [35]

Lifestyle modification

Exercise

In September 2007, a joint [randomized controlled trial](#) by the [University of Calgary](#) and the [University of Ottawa](#) found that "Either aerobic or resistance training alone improves glycemic control in type 2 diabetes, but the improvements are greatest with combined aerobic and resistance training than either alone." ^{[36][37]} The combined program reduced the HbA1c by 0.5 percentage point. Other studies have established that the amount of exercise needed is not large or extreme, but must be consistent and continuing. Examples might include a brisk 45 minute walk every other day.

Theoretically, exercise does have benefits in that exercise would stimulate the release of certain [ligands](#) that cause GLUT4 to be released from internal [endosomes](#) to the cell membrane. Insulin though, which no longer works effectively in those afflicted with type 2 diabetes, causes GLUT1 to be placed into the membrane. Though they have different structures, they both perform the same function of increasing intake of glucose into the cell from the blood serum. Exercise also allows for the uptake of glucose independently of insulin, i.e. by adrenaline.

Dietary management

Main article: [Diabetic diet](#)

Modifying the diet to limit and control glucose (or glucose equivalent, e.g., starch) intake, and in consequence, blood glucose levels, is known to assist type 2 patients, especially early in the course of the condition's progression. Additionally, weight loss is recommended and is often helpful in persons suffering from type 2 diabetes (see above).

Several dietary modifications using dietary supplements are sometimes recommended to those with type 2; there are studies suggesting that there is some beneficial effect for some of these. See the discussion below.

Monitoring of blood glucose

Main article: [Blood glucose monitoring](#)

Self-monitoring of blood glucose may not improve outcomes in some cases, that is among "reasonably well controlled non-insulin treated patients with type 2 diabetes". ^[38] Nevertheless, it is very strongly recommended for patients in whom it can assist in maintaining proper glycemic control, and is well worth the cost (sometimes considerable) if it does. It is the only source of current information on the glycemic state of the body, as changes are rapid and frequent, depending on food, exercise, and medication (dosage and timing with respect to both diet and exercise), and secondarily, on time of day, stress (mental and physical), infection, etc.

The [National Institute for Health and Clinical Excellence](#) (NICE), UK released updated diabetes recommendations on 30 May 2008. They indicate that self-monitoring of blood glucose levels for people with newly diagnosed type 2 diabetes should be part of a structured self-management education plan. ^[39] However, a recent study found that a treatment strategy of intensively lowering blood sugar levels (below 6%) in patients with additional [cardiovascular disease](#) risk factors poses more harm than benefit, and so there appear to be limits to benefit of intensive blood glucose control in some patients. ^{[40][41]}

Medications

Main article: [Anti-diabetic drug](#)

There are several drugs available for type 2 diabetics—most are unsuitable or even dangerous for use by type 1 diabetics. They fall into several classes and are not equivalent, nor can they be simply substituted one for another. All are prescription drugs.

One of the most widely used drugs now used for type 2 diabetes is the [biguanide metformin](#); it works primarily by reducing liver release of blood glucose from glycogen stores and secondarily by provoking some increase in cellular uptake of glucose in body tissues. Both historically, and currently, the most commonly used drugs are in the [Sulfonylurea](#) group, of which several members (including [glibenclamide](#) and [gliclazide](#)) are widely used; these increase glucose stimulated [insulin secretion](#) by the pancreas and so lower blood glucose even in the face of insulin resistance.

Newer drug classes include:

[Thiazolidinediones](#) (TZDs) ([rosiglitazone](#), [pioglitazone](#), and [troglitazone](#) -- the last, as Rezulin, was withdrawn from the US market because of an increased risk of systemic acidosis). These increase tissue insulin sensitivity by affecting gene expression

[α-glucosidase inhibitors](#) ([acarbose](#) and [miglitol](#)) which interfere with absorption of some glucose containing nutrients, reducing (or at least slowing) the amount of glucose absorbed

[Meglitinides](#) which stimulate insulin release ([nateglinide](#), [repaglinide](#), and their analogs) quickly; they can be taken with food, unlike the sulfonylureas which must be taken prior to food (sometimes some hours before, depending on the drug)

Peptide analogs which work in a variety of ways:

Incretin mimetics which increase insulin output from the beta cells among other effects. These includes the Glucagon-like peptide (GLP) analog [exenatide](#), sometimes referred to as *lizard spit* as it was first identified in [Gila monster](#) saliva

Dipeptidyl peptidase-4 (DPP-4) inhibitors increase [Incretin](#) levels ([sitagliptin](#)) by decreasing their deactivation rates

Amylin agonist analog, which slows gastric emptying and suppresses glucagon ([pramlintide](#))

Oral

A systematic review of randomized controlled trials found that [metformin](#) and second-generation sulfonylureas are the preferred choices for most with type 2 diabetes, especially those early in the course of the condition. ^[42]

Failure of response after a time is not unknown with most of these agents: the initial choice of anti-diabetic drug has been compared in a [randomized controlled trial](#) which found "cumulative incidence of monotherapy failure at 5 years to be 15% with rosiglitazone, 21% with metformin, and 34% with glyburide". ^[43] Of these, rosiglitazone users showed more weight gain and edema than did non-users. ^[43] Rosiglitazone may increase risk of death

from cardiovascular causes though the causal connection is unclear. [44] Pioglitazone and rosiglitazone may also increase the risk of fractures. [45][46]

For patients who also have heart failure, [metformin](#) may be the best tolerated drug. [47]

The variety of available agents can be confusing, and the clinical differences among type 2 diabetes patients compounds the problem. At present, choice of drugs for type 2 diabetics is rarely straightforward and in most instances has elements of repeated trial and adjustment.

Injectable peptide analogs

DPP-4 inhibitors lowered HbA1c by 0.74% (points), comparable to other antidiabetic drugs. [48] GLP-1 analogs resulted in weight loss and had more gastrointestinal side effects, while DPP-4 inhibitors were weight neutral and increased risk for infection and headache, but both classes appear to present an alternative to other antidiabetic drugs.

Insulin

In rare cases, if antidiabetic drugs fail (i.e., the clinical benefit stops), insulin therapy may be necessary – usually in addition to oral medication therapy – to maintain normal or near normal glucose levels. [49][50]

Typical total daily dosage of insulin is 0.6 U/kg. [51] But, of course, best timing and indeed total amounts depend on diet (composition, amount, and timing) as well the degree of insulin resistance. More complicated estimations to guide initial dosage of insulin are: [52]

For men, $[(\text{fasting plasma glucose [mmol/liter]} - 5) \times 2] \times (\text{weight [kg]} \div (14.3 \times \text{height [m]})) - \text{height [m]}$

For women, $[(\text{fasting plasma glucose [mmol/liter]} - 5) \times 2] \times (\text{weight [kg]} \div (13.2 \times \text{height [m]})) - \text{height [m]}$

The initial insulin regimen are often chosen based on the patient's blood glucose profile. [53] Initially, adding nightly insulin to patients failing oral medications may be best. [54] Nightly insulin combines better with [metformin](#)

than with [sulfonylureas](#). [51] The initial dose of nightly insulin (measured in IU/d) should be equal to the fasting blood glucose level (measured in mmol/L). If the fasting glucose is reported in mg/dl, multiply by 0.05551 to convert to mmol/L. [55]

When nightly insulin is insufficient, choices include:

Premixed insulin with a fixed ratio of short and intermediate acting insulin; this tends to be more effective than long acting insulin, but is associated with increased hypoglycemia. [56][57] . [58] Initial total daily dosage of

biphasic insulin can be 10 units if the fasting plasma glucose values are less than 180 mg/dl or 12 units when the fasting plasma glucose is above 180 mg/dl". [57] A guide to titrating fixed ratio insulin is available. [53]

Long acting insulins such as [insulin glargine](#) and [insulin detemir](#). A [meta-analysis](#) of randomized controlled trials by the [Cochrane Collaboration](#) found "only a minor clinical benefit of treatment with long-acting insulin

analogues for patients with diabetes mellitus type 2". [59] More recently, a randomized controlled trial found that although long acting insulins were less effective, they were associated with reduced hypoglycemic episodes. [56]

Insulin Pump therapy in Type 2 diabetes is gradually becoming popular. In an original published study, in addition to reduction of blood sugars, there is evidence of profound benefits in resistant neuropathic pain and also improvements in sexual performance. [60]

Gastric bypass surgery

Gastric Bypass procedures are currently considered an [elective procedure](#) with no universally accepted algorithm to decide who should have the surgery. In the diabetic patient, certain types result in 99-100% prevention of insulin resistance and 80-90% clinical resolution or remission of type 2 diabetes. In 1991, the NIH (National Institutes of Health) Consensus Development Conference on Gastrointestinal Surgery for Obesity proposed that the [body mass index](#) (BMI) threshold to consider surgery should drop from 40 to 35 in the appropriate patient. More recently, the [American Society for Bariatric Surgery](#) (ASBS) and the ASBS Foundation suggested that the BMI threshold be lowered to 30 in the presence of severe co-morbidities. [61] Debate has flourished about the role of gastric

bypass surgery in type 2 diabetics since the publication of The Swedish Obese Subjects Study. The largest prospective series showed a large decrease in the occurrence of type 2 diabetes in the post-gastric bypass patient at both 2 years ([odds ratio](#) was 0.14) and at 10 years (odds ratio was 0.25). [62]

A study of 20-years of Greenville (US) gastric bypass patients found that 80% of those with type 2 diabetes before surgery no longer required insulin or oral agents to maintain normal glucose levels. Weight loss occurred rapidly in many people in the study who had had the surgery. The 20% who did not respond to bypass surgery were, typically, those who were older and had had diabetes for over 20 years. [63]

In January 2008, The Journal of the [American Medical Association](#) (JAMA) published the first randomized controlled trial comparing the efficacy of laparoscopic adjustable gastric banding against conventional medical therapy in the obese patient with type 2 diabetes. Laparoscopic Adjustable Gastric Banding results in remission of type 2 diabetes among affected patients diagnosed within the previous two years according to a randomized controlled trial. [64] The [relative risk reduction](#) was 69.0%. For patients at similar risk to those in this study (87.0% had type 2), this leads to an [absolute risk reduction](#) of 60%. 1.7 patients must be treated for one to benefit ([number needed to treat](#) = 1.7). Click here to adjust these results for patients at higher or lower risk of type 2 diabetics.

These results have not yet produced a clinical standard for surgical treatment of Type 2 patients, as the mechanism, if any, is currently obscure. Surgical cure of Type 2 diabetes must be, as a result, considered currently experimental.

Epidemiology

About 90–95% of all North American cases of diabetes are type 2, ^[65] and about 20% of the population over the age of 65 has diabetes mellitus type 2. The fraction of type 2 diabetics in other parts of the world varies substantially, almost certainly for environmental and lifestyle reasons, though these are not known in detail. Diabetes affects over 150 million people worldwide and this number is expected to double by 2025. ^[65]

According to CDC, about 23.613 million people in the United States, or 8% of the population, have diabetes. The total prevalence of diabetes increased 13.5% from 2005-2007. It is thought that only 24% of diabetes is now undiagnosed, down from an estimated 30% in 2005 and from the previously estimated 50% in ca 1995.

References

1. ^ Robbins and Cotran, Pathologic Basis of Disease, 7th Ed. pp 1194-1195.
2. ^ American Diabetes Association title =Total Prevalence of Diabetes and Pre-diabetes url =<http://www.diabetes.org/diabetes-statistics/prevalence.jsp> | accessdate =2008-11-29
3. ^ Inzucchi SE, Sherwin RS, The Prevention of Type 2 Diabetes Mellitus. *Endocrinol Metab Clin N Am* 34 (2205) 199-219.
4. ^ Gerberding, Julie Louise (2007-05-24). *Diabetes*. Atlanta: Centres for Disease Control. <http://www.cdc.gov/nccdphp/publications/aag/ddt.htm>. Retrieved 2007-09-14.
5. ^ Diabetes rates are increasing among youth [NIH](#), November 13, 2007
6. ^ Steinberger J, Moran A, Hong CP, Jacobs DR Jr, Sinaiko AR: Adiposity in childhood predicts obesity and insulin resistance in young adulthood. *J Pediatr* 138:469–473, 2001
7. ^ Brian J. Welch, MD and Ivana Zib, MD: Case Study: Diabetic Ketoacidosis in Type 2 Diabetes: "Look Under the Sheets", *Clinical Diabetes*, October 2004, vol. 22 no. 4, 198-200
8. ^ Jack L, Boseman L, Vinicor F (April 2004). "Aging Americans and diabetes. A public health and clinical response". *Geriatrics* **59** (4): 14–7. PMID 15086069.
9. ^ Lovejoy JC (October 2002). "The influence of dietary fat on insulin resistance". *Curr. Diab. Rep.* **2** (5): 435–40. doi:10.1007/s11892-002-0098-y. PMID 12643169.
10. ^ Hu FB (February 2003). "Sedentary lifestyle and risk of obesity and type 2 diabetes". *Lipids* **38** (2): 103–8. doi:10.1007/s11745-003-1038-4. PMID 12733740.
11. ^ Sakagashira S, Sanke T, Hanabusa T, *et al.* (September 1996). "Missense mutation of amylin gene (S20G) in Japanese NIDDM patients". *Diabetes* **45** (9): 1279–81. doi:10.2337/diabetes.45.9.1279. PMID 8772735.
12. ^ Cho YM, Kim M, Park KS, Kim SY, Lee HK (May 2003). "S20G mutation of the amylin gene is associated with a lower body mass index in Korean type 2 diabetic patients". *Diabetes Res. Clin. Pract.* **60** (2): 125–9. doi:10.1016/S0168-8227(03)00019-6. PMID 12706321. <http://linkinghub.elsevier.com/retrieve/pii/S0168822703000196>. Retrieved 19 July 2008.
13. ^ Eberhart, M. S.; Ogden, C, Engelgau, M, Cadwell, B, Hedley, A. A., Saydah, S. H., (November 2004). "Prevalence of Overweight and Obesity Among Adults with Diagnosed Diabetes --- United States, 1988--1994 and 1999--2002". *Morbidity and Mortality Weekly Report* (Centers for Disease Control and Prevention) **53** (45): 1066–8. PMID 15549021. <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5345a2.htm>. Retrieved 19 July 2008.
14. ^ Camastra S, Bonora E, Del Prato S, Rett K, Weck M, Ferrannini E (December 1999). "Effect of obesity and insulin resistance on resting and glucose-induced thermogenesis in man. EGIR (European Group for the Study of Insulin Resistance)". *Int. J. Obes. Relat. Metab. Disord.* **23** (12): 1307–13. doi:10.1038/sj.ijo.0801072. PMID 10643689.
15. ^ Cotran, Kumar, Collins; **Robbins Pathologic Basis of Disease**, Saunders Sixth Edition, 1999; 913-926.
16. ^ "www.who.int" (pdf). *World Health Organization*. http://www.who.int/diabetes/publications/Definition%20and%20diagnosis%20of%20diabetes_new.pdf.

17. ^ World Health Organization. "Definition, diagnosis and classification of diabetes mellitus and its complications: Report of a WHO Consultation. Part 1. Diagnosis and classification of diabetes mellitus". <http://www.who.int/diabetes/publications/en/>. Retrieved 29 May 2007.
18. ^ Raina Elley C, Kenealy T (December 2008). "Lifestyle interventions reduced the long-term risk of diabetes in adults with impaired glucose tolerance". *Evid Based Med* **13** (6): 173. doi:10.1136/ebm.13.6.173. PMID 19043031.
19. ^ U.S. Preventive Services Task Force (February 2003). "Screening for type 2 diabetes mellitus in adults: recommendations and rationale". *Ann. Intern. Med.* **138** (3): 212–4. PMID 12558361. <http://www.annals.org/cgi/pmidlookup?view=long&pmid=12558361>. Retrieved 19 July 2008.
20. ^ ^{a b} Harris R, Donahue K, Rathore SS, Frame P, Woolf SH, Lohr KN (February 2003). "Screening adults for type 2 diabetes: a review of the evidence for the U.S. Preventive Services Task Force". *Ann. Intern. Med.* **138** (3): 215–29. PMID 12558362. <http://www.annals.org/cgi/pmidlookup?view=long&pmid=12558362>. Retrieved 19 July 2008.
21. ^ Santaguida PL, Balion C, Hunt D, et al. (August 2005). "Diagnosis, prognosis, and treatment of impaired glucose tolerance and impaired fasting glucose" (PDF). *Evid Rep Technol Assess (Summ)* (128): 1–11. PMID 16194123. <http://www.ahrq.gov/downloads/pub/evidence/pdf/imp glucose/imp glucose.pdf>. Retrieved 19 July 2008.
22. ^ Choi HK, Willett WC, Stampfer P, Vasson MP, Maubois JL, Beaufriere B (2005). "Dairy consumption and risk of type 2 diabetes mellitus in men". *Archives of Internal Medicine* **165**: 997–1003.
23. ^ Rolka DB, Narayan KM, Thompson TJ, et al. (2001). "Performance of recommended screening tests for undiagnosed diabetes and dysglycemia". *Diabetes Care* **24** (11): 1899–903. doi:10.2337/diacare.24.11.1899. PMID 11679454.
24. ^ Pradhan AD, Rifai N, Buring JE, Ridker PM (2007). "Hemoglobin A1c predicts diabetes but not cardiovascular disease in nondiabetic women". *Am. J. Med.* **120** (8): 720–7. doi:10.1016/j.amjmed.2007.03.022. PMID 17679132.
25. ^ Chiasson JL, Josse RG, Gomis R, Hanefeld M, Karasik A, Laakso M (July 2003). "Acarbose treatment and the risk of cardiovascular disease and hypertension in patients with impaired glucose tolerance: the STOP-NIDDM trial". *JAMA* **290** (4): 486–94. doi:10.1001/jama.290.4.486. PMID 12876091. <http://jama.ama-assn.org/cgi/pmidlookup?view=long&pmid=12876091>. Retrieved 19 July 2008.
26. ^ Lindström J, Ilanne-Parikka P, Peltonen M, et al. (November 2006). "Sustained reduction in the incidence of type 2 diabetes by lifestyle intervention: follow-up of the Finnish Diabetes Prevention Study". *Lancet* **368** (9548): 1673–9. doi:10.1016/S0140-6736(06)69701-8. PMID 17098085. [http://linkinghub.elsevier.com/retrieve/pii/S0140-6736\(06\)69701-8](http://linkinghub.elsevier.com/retrieve/pii/S0140-6736(06)69701-8). Retrieved 19 July 2008.
27. ^ Torgerson JS, Hauptman J, Boldrin MN, Sjöström L (January 2004). "XENical in the prevention of diabetes in obese subjects (XENDOS) study: a randomized study of orlistat as an adjunct to lifestyle changes for the prevention of type 2 diabetes in obese patients". *Diabetes Care* **27** (1): 155–61. doi:10.2337/diacare.27.1.155. PMID 14693982. <http://care.diabetesjournals.org/cgi/pmidlookup?view=long&pmid=14693982>. Retrieved 19 July 2008.

28. ^ Knowler WC, Barrett-Connor E, Fowler SE, *et al.* (February 2002). "Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin". *N. Engl. J. Med.* **346** (6): 393–403.
doi:10.1056/NEJMoa012512. PMID 11832527. [PMC](#) 1370926.
<http://content.nejm.org/cgi/pmidlookup?view=short&pmid=11832527&promo=ONFLNS19>. Retrieved 19 July 2008.
29. ^ "Physical activity and dietary intervention for chronic diseases: a quick fix after all?", Frank W. Booth & Manu V. Chakravarthy, *J Appl Physiol*, May 1, 2006; 100(5): 1439 - 1440.
30. ^ Roberts CK, Won D, Pruthi S, Kurtovic S, Sindhu RK, Vaziri ND, and Barnard RJ. "Effect of a short-term diet and exercise intervention on oxidative stress, inflammation, MMP-9, and monocyte chemotactic activity in men with metabolic syndrome factors", *J Appl Physiol* 100: 1657-1665, 2006. First published December 15, 2005
31. ^ "Three-week diet curbs diabetes", [New Scientist](#), 13 January 2006 by Shaoni Bhattacharya.
32. ^ American Diabetes (January 2006). "Standards of medical care in diabetes--2006". *Diabetes Care* **29 Suppl 1**: S4–42. PMID 16373931.
<http://care.diabetesjournals.org/cgi/pmidlookup?view=long&pmid=16373931>. Retrieved 19 July 2008.
33. ^ Qaseem A, Vijan S, Snow V, Cross JT, Weiss KB, Owens DK (September 2007). "Glycemic control and type 2 diabetes mellitus: the optimal hemoglobin A1c targets. A guidance statement from the American College of Physicians". *Ann. Intern. Med.* **147** (6): 417–22. PMID 17876024.
<http://www.annals.org/cgi/content/full/147/6/417>. Retrieved 19 July 2008.
34. ^ ^{a b} "Clinical Practice Guidelines". <http://www.diabetes.ca/cpg2003/chapters.aspx>. Retrieved 19 July 2008.
35. ^ Brown AF, Mangione CM, Saliba D, Sarkisian CA (May 2003). "Guidelines for improving the care of the older person with diabetes mellitus". *J Am Geriatr Soc* **51** (5 Suppl Guidelines): S265–80.
doi:10.1046/j.1532-5415.51.5s.1.x. PMID 12694461. <http://www.blackwell-synergy.com/openurl?genre=article&sid=nlm:pubmed&issn=00028614&date=2003&volume=51&issue=5%20Suppl%20Guidelines&spage=S265>. Retrieved 19 July 2008.
36. ^ Sigal RJ, Kenny GP, Boulé NG, *et al.* (2007). "Effects of aerobic training, resistance training, or both on glycemic control in type 2 diabetes: a randomized trial". *Ann. Intern. Med.* **147** (6): 357–69. PMID 17876019. <http://www.annals.org/cgi/content/full/147/6/357>. Non-technical summary
37. ^ Song S. "Study: The Best Exercise for Diabetes". *Time Inc.*
<http://www.time.com/time/health/article/0,8599,1662683,00.html?xid=newsletter-weekly>. Retrieved 28 September 2007.
38. ^ Farmer A, Wade A, Goyder E, *et al.* (2007). "Impact of self monitoring of blood glucose in the management of patients with non-insulin treated diabetes: open parallel group randomised trial". *BMJ* **335** (7611): 132. doi:10.1136/bmj.39247.447431.BE. PMID 17591623.
39. ^ "Clinical Guideline:The management of type 2 diabetes (update)".
<http://www.nice.org.uk/guidance/index.jsp?action=byID&o=11983>.
40. ^ Gerstein, H. C., M. E. Miller, *et al.* (2008). "Effects of intensive glucose lowering in type 2 diabetes.". *New England Journal of Medicine, the* **358** (358(24)): 2545–59. doi:10.1056/NEJMoa0802743. PMID 18539917.

41. ^ http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2007.pdf
42. ^ Bolen S et al. Systematic Review: Comparative Effectiveness and Safety of Oral Medications for Type 2 Diabetes Mellitus. *Ann Intern Med* 2007;147:6
43. ^ ^{a b} Kahn SE, Haffner SM, Heise MA, et al. (2006). "Glycemic durability of rosiglitazone, metformin, or glyburide monotherapy". *N. Engl. J. Med.* **355** (23): 2427–43. doi:10.1056/NEJMoa066224. PMID 17145742.
44. ^ "NEJM -- Effect of Rosiglitazone on the Risk of Myocardial Infarction and Death from Cardiovascular Causes". <http://content.nejm.org/cgi/content/full/NEJMoa072761>. Retrieved 21 May 2007.
45. ^ "MedWatch - 2007 Safety Information Alerts (Actos (pioglitazone))". <http://www.fda.gov/medwatch/safety/2007/safety07.htm#actos>. Retrieved 21 May 2007.
46. ^ "MedWatch - 2007 Safety Information Alerts (Rosiglitazone)". <http://www.fda.gov/medwatch/safety/2007/safety07.htm#rosiglitazone>. Retrieved 21 May 2007.
47. ^ Eurich DT, McAlister FA, Blackburn DF, et al. (2007). "Benefits and harms of antidiabetic agents in patients with diabetes and heart failure: systematic review". *BMJ* **335** (7618): 497. doi:10.1136/bmj.39314.620174.80. PMID 17761999.
48. ^ Amori RE, Lau J, Pittas AG (2007). "Efficacy and safety of incretin therapy in type 2 diabetes: systematic review and meta-analysis". *JAMA* **298** (2): 194–206. doi:10.1001/jama.298.2.194. PMID 17622601. <http://jama.ama-assn.org/cgi/pmidlookup?view=long&pmid=17622601>.
49. ^ Diabetes . MyOptumHealth. (Report). Retrieved on Jan 21, 2010.
50. ^ Diabetes and Medication . Diabetes New Zealand. (Report). Retrieved on Jan 21, 2010.
51. ^ ^{a b} Yki-Järvinen H, Ryysy L, Nikkilä K, Tulokas T, Vanamo R, Heikkilä M (March 1999). "Comparison of bedtime insulin regimens in patients with type 2 diabetes mellitus. A randomized, controlled trial". *Ann. Intern. Med.* **130** (5): 389–96. PMID 10068412. <http://www.annals.org/cgi/pmidlookup?view=long&pmid=10068412>. Retrieved 19 July 2008.
52. ^ Holman RR, Turner RC (January 1985). "A practical guide to basal and prandial insulin therapy". *Diabet. Med.* **2** (1): 45–53. doi:10.1111/j.1464-5491.1985.tb00592.x. PMID 2951066.
53. ^ ^{a b} Mooradian AD, Bernbaum M, Albert SG (July 2006). "Narrative review: a rational approach to starting insulin therapy". *Ann. Intern. Med.* **145** (2): 125–34. PMID 16847295.
54. ^ Yki-Järvinen H, Kauppila M, Kujansuu E, et al. (November 1992). "Comparison of insulin regimens in patients with non-insulin-dependent diabetes mellitus". *N. Engl. J. Med.* **327** (20): 1426–33. PMID 1406860.
55. ^ Kratz A, Lewandowski KB (October 1998). "Case records of the Massachusetts General Hospital. Weekly clinicopathological exercises. Normal reference laboratory values". *N. Engl. J. Med.* **339** (15): 1063–72. doi:10.1056/NEJM199810083391508. PMID 9761809. <http://content.nejm.org/cgi/pmidlookup?view=short&pmid=9761809&promo=ONFLNS19>. Retrieved 19 July 2008.
56. ^ ^{a b} Holman RR, Thorne KI, Farmer AJ, et al. (October 2007). "Addition of biphasic, prandial, or basal insulin to oral therapy in type 2 diabetes". *N. Engl. J. Med.* **357** (17): 1716–30. doi:10.1056/NEJMoa075392.

- PMID 17890232. <http://content.nejm.org/cgi/pmidlookup?view=short&pmid=17890232&promo=ONFLNS19>. Retrieved 19 July 2008.
57. ^{a b} Raskin P, Allen E, Hollander P, *et al.* (February 2005). "Initiating insulin therapy in type 2 Diabetes: a comparison of biphasic and basal insulin analogs". *Diabetes Care* **28** (2): 260–5. doi:10.2337/diacare.28.2.260. PMID 15677776. <http://care.diabetesjournals.org/cgi/pmidlookup?view=long&pmid=15677776>. Retrieved 19 July 2008.
 58. ^a Malone JK, Kerr LF, Campaigne BN, Sachson RA, Holcombe JH (December 2004). "Combined therapy with insulin lispro Mix 75/25 plus metformin or insulin glargine plus metformin: a 16-week, randomized, open-label, crossover study in patients with type 2 diabetes beginning insulin therapy". *Clin Ther* **26** (12): 2034–44. doi:10.1016/j.clinthera.2004.12.015. PMID 15823767. [http://linkinghub.elsevier.com/retrieve/pii/S0149-2918\(04\)00085-2](http://linkinghub.elsevier.com/retrieve/pii/S0149-2918(04)00085-2). Retrieved 19 July 2008.
 59. ^a Horvath K, Jeitler K, Berghold A, *et al.* (2007). "Long-acting insulin analogues versus NPH insulin (human isophane insulin) for type 2 diabetes mellitus". *Cochrane Database Syst Rev* (2): CD005613. doi:10.1002/14651858.CD005613.pub3. PMID 17443605.
 60. ^a Jothydev Kesavadev, Shyam Balakrishnan, Ahammed S, Sunitha Jothydev, *et al.* (2009). "Reduction of glycosylated hemoglobin following 6 months of continuous subcutaneous insulin infusion in an Indian population with type 2 diabetes". *Diabetes Technol Ther* **11** (8): 517–521. doi:10.1089/dia.2008.0128. PMID 19698065.
 61. ^a Cummings DE, Flum DR (2008). "Gastrointestinal surgery as a treatment for diabetes". *JAMA* **299** (3): 341–3. doi:10.1001/jama.299.3.341. PMID 18212321. <http://jama.ama-assn.org/cgi/pmidlookup?view=long&pmid=18212321>.
 62. ^a Folli F, Pontiroli AE, Schwesinger WH (2007). "Metabolic aspects of bariatric surgery". *Med. Clin. North Am.* **91** (3): 393–414, x. doi:10.1016/j.mcna.2007.01.005. PMID 17509385. [http://linkinghub.elsevier.com/retrieve/pii/S0025-7125\(07\)00006-5](http://linkinghub.elsevier.com/retrieve/pii/S0025-7125(07)00006-5).
 63. ^a Gastric Bypass Surgery - Diabetes Health
 64. ^a Dixon JB, O'Brien PE, Playfair J, *et al.* (2008). "Adjustable gastric banding and conventional therapy for type 2 diabetes: a randomized controlled trial". *JAMA* **299** (3): 316–23. doi:10.1001/jama.299.3.316. PMID 18212316. <http://jama.ama-assn.org/cgi/pmidlookup?view=long&pmid=18212316>.
 65. ^{a b} Zimmet P, Alberti KG, Shaw J (December 2001). "Global and societal implications of the diabetes epidemic". *Nature* **414** (6865): 782–7. doi:10.1038/414782a. PMID 11742409. <http://www.nature.com/nature/journal/v414/n6865/abs/414782a.html>. Retrieved 19 July 2008.

External links

Diabetes mellitus type 2 at the [Open Directory Project](#)

Diabetes mellitus type 2

Organizations

IDF Diabetes Atlas

International Diabetes Federation

World Diabetes Day (International Diabetes Federation)

Diabetes UK - Largest organisation in the UK working for people with diabetes

American Diabetes Association

Types and Pathogenesis of Diabetes

Authorities

National Diabetes Information Clearinghouse

Centers for Disease Control (Endocrine pathology)

Further reading

Diabetes Symptoms Revisited: Are They Too Vague and Too Late?

ABC Radio National transcript on hypothesised aetiology involving gut hormone

Does what we eat manage Type 2 Diabetes effectively?