

Insulin Resistance and Pre-diabetes

What is insulin resistance?

Insulin resistance is a condition in which the body produces insulin but does not use it properly. Insulin, a hormone made by the pancreas, helps the body use glucose for energy. Glucose is a form of sugar that is the body's main source of energy.

The body's digestive system breaks food down into glucose, which then travels in the bloodstream to cells throughout the body. Glucose in the blood is called blood glucose, also known as blood sugar. As the blood glucose level rises after a meal, the pancreas releases insulin to help cells take in and use the glucose.

When people are insulin resistant, their muscle, fat, and liver cells do not respond properly to insulin. As a result, their bodies need more insulin to help glucose enter cells. The pancreas tries to keep up with this increased demand for insulin by producing more. Eventually, the pancreas fails to keep up with the body's need for insulin. Excess glucose builds up in the bloodstream, setting the stage for diabetes. Many people with insulin resistance have high levels of both glucose and insulin circulating in their blood at the same time.

Insulin resistance increases the chance of developing type 2 diabetes and heart disease. Learning about insulin resistance is the first step toward making lifestyle changes that can help prevent diabetes and other health problems.

What causes insulin resistance?

Scientists have identified specific genes that make people more likely to develop insulin resistance and diabetes. Excess weight and lack of physical activity also contribute to insulin resistance.

Many people with insulin resistance and high blood glucose have other conditions that increase the risk of developing type 2 diabetes and damage to the heart and blood vessels, also called cardiovascular disease. These conditions include having excess weight around the waist, high blood pressure, and abnormal levels of cholesterol and triglycerides in the blood. Having several of these problems is called metabolic syndrome or insulin resistance syndrome, formerly called syndrome X.

Metabolic Syndrome

Metabolic syndrome is defined as the presence of any three of the following conditions:

- waist measurement of 40 inches or more for men and 35 inches or more for women

- triglyceride levels of 150 milligrams per deciliter (mg/dL) or above, or taking medication for elevated triglyceride levels
- HDL, or “good,” cholesterol level below 40 mg/dL for men and below 50 mg/dL for women, or taking medication for low HDL levels
- blood pressure levels of 130/85 or above, or taking medication for elevated blood pressure levels
- fasting blood glucose levels of 100 mg/dL or above, or taking medication for elevated blood glucose levels

Source: Grundy SM, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute scientific statement. *Circulation*. 2005;112:2735–2752.

Similar definitions have been developed by the World Health Organization and the American Association of Clinical Endocrinologists.

What is pre-diabetes?

Pre-diabetes is a condition in which blood glucose levels are higher than normal but not high enough for a diagnosis of diabetes. This condition is sometimes called impaired fasting glucose (IFG) or impaired glucose tolerance (IGT), depending on the test used to diagnose it. The U.S. Department of Health and Human Services estimates that about one in four U.S. adults aged 20 years or older—or 57 million people—had pre-diabetes in 2007.

People with pre-diabetes are at increased risk of developing type 2 diabetes, formerly called adult-onset diabetes or noninsulin-dependent diabetes. Type 2 diabetes is sometimes defined as the form of diabetes that develops when the body does not respond properly to insulin, as opposed to type 1 diabetes, in which the pancreas makes little or no insulin.

Studies have shown that most people with pre-diabetes develop type 2 diabetes within 10 years, unless they lose 5 to 7 percent of their body weight—about 10 to 15 pounds for someone who weighs 200 pounds—by making changes in their diet and level of physical activity. People with pre-diabetes also are at increased risk of developing cardiovascular disease.

What are the symptoms of insulin resistance and pre-diabetes?

Insulin resistance and pre-diabetes usually have no symptoms. People may have one or both conditions for several years without noticing anything. People with a severe form of insulin resistance may have dark patches of skin, usually on the back of the neck. Sometimes people have a dark ring around their neck. Other possible sites for dark patches include elbows, knees, knuckles, and armpits. This condition is called acanthosis nigricans.

How are insulin resistance and pre-diabetes diagnosed?

Health care providers use blood tests to determine whether a person has pre-diabetes but do not usually test for insulin resistance. Insulin resistance can be assessed by measuring the level of insulin in the blood. However, the test that most accurately measures insulin resistance, called the euglycemic clamp, is too costly and complicated to be used in most doctors' offices. The clamp is a research tool used by scientists to learn more about glucose metabolism. If tests indicate pre-diabetes or metabolic syndrome, insulin resistance most likely is present.

Diabetes and pre-diabetes can be detected with one of the following tests:

- **Fasting glucose test.** This test measures blood glucose in people who have not eaten anything for at least 8 hours. This test is most reliable when done in the morning. Fasting glucose levels of 100 to 125 mg/dL are above normal but not high enough to be called diabetes. This condition is called pre-diabetes or IFG. People with IFG often have had insulin resistance for some time. They are much more likely to develop diabetes than people with normal blood glucose levels.
- **Glucose tolerance test.** This test measures blood glucose after people fast for at least 8 hours and 2 hours after they drink a sweet liquid provided by a doctor or laboratory. A blood glucose level between 140 and 199 mg/dL means glucose tolerance is not normal but is not high enough for a diagnosis of diabetes. This form of pre-diabetes is called IGT and, like IFG, it points toward a history of insulin resistance and a risk for developing diabetes.

People whose test results indicate they have pre-diabetes should have their blood glucose levels checked again in 1 to 2 years.

Risk Factors for Pre-diabetes and Type 2 Diabetes

The American Diabetes Association recommends that testing to detect pre-diabetes and type 2 diabetes be considered in adults without symptoms who are overweight or obese and have one or more additional risk factors for diabetes. In those without these risk factors, testing should begin at age 45.

Risk factors for pre-diabetes and diabetes—in addition to being overweight or obese or being age 45 or older—include the following:

- being physically inactive
- having a parent or sibling with diabetes
- having a family background that is African American, Alaska Native, American Indian, Asian American, Hispanic/Latino, or Pacific Islander
- giving birth to a baby weighing more than 9 pounds or being diagnosed with gestational diabetes—diabetes first found during pregnancy
- having high blood pressure—140/90 or above—or being treated for high blood pressure
- having an HDL, or “good,” cholesterol level below 35 mg/dL or a triglyceride level above 250 mg/dL

- having polycystic ovary syndrome, also called PCOS
- having impaired fasting glucose (IFG) or impaired glucose tolerance (IGT) on previous testing
- having other conditions associated with insulin resistance, such as severe obesity or acanthosis nigricans
- having a history of cardiovascular disease

If test results are normal, testing should be repeated at least every 3 years. Health care providers may recommend more frequent testing depending on initial results and risk status.

Can insulin resistance and pre-diabetes be reversed?

Yes. Physical activity and weight loss help the body respond better to insulin. By losing weight and being more physically active, people with insulin resistance or pre-diabetes may avoid developing type 2 diabetes.

The Diabetes Prevention Program (DPP) and other large studies have shown that people with pre-diabetes can often prevent or delay diabetes if they lose a modest amount of weight by cutting fat and calorie intake and increasing physical activity—for example, walking 30 minutes a day 5 days a week. Losing just 5 to 7 percent of body weight prevents or delays diabetes by nearly 60 percent. In the DPP, people aged 60 or older who made lifestyle changes lowered their chances of developing diabetes by 70 percent. Many participants in the lifestyle intervention group returned to normal blood glucose levels and lowered their risk for developing heart disease and other problems associated with diabetes. The DPP also showed that the diabetes drug metformin reduced the risk of developing diabetes by 31 percent.

People with insulin resistance or pre-diabetes can help their body use insulin normally by being physically active, making wise food choices, and reaching and maintaining a healthy weight. Physical activity helps muscle cells use blood glucose for energy by making the cells more sensitive to insulin.

Body Mass Index (BMI)

BMI is a measurement of body weight relative to height. Adults aged 20 or older can use the BMI table below to find out whether they are normal weight, overweight, obese, or extremely obese. To use the table, follow these steps:

- Find the person's height in the left-hand column.
- Move across the row to the number closest to that person's weight.
- Check the number at the top of that column.

The number at the top of the column is the person's BMI. The words above the BMI number indicate whether the person is normal weight, overweight, obese, or extremely

obese. People who are overweight, obese, or extremely obese should consider talking with a doctor about ways to lose weight to reduce the risk of diabetes.

The BMI table has certain limitations. It may overestimate body fat in athletes and others who have a muscular build and underestimate body fat in older adults and others who have lost muscle. BMI for children and teens must be determined based on age and sex in addition to height and weight. Information about BMI in children and teens, including a BMI calculator, is available from the Centers for Disease Control and Prevention (CDC) at www.cdc.gov/nccdphp/dnpa/bmi. The CDC website also has a BMI calculator for adults.

Body Mass Index Table

	Normal						Overweight					Obese					
BMI	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35
Height (inches)	Body Weight (pounds)																
58	91	96	100	105	110	115	119	124	129	134	138	143	148	153	158	162	167
59	94	99	104	109	114	119	124	128	133	138	143	148	153	158	163	168	173
60	97	102	107	112	118	123	128	133	138	143	148	153	158	163	168	174	179
61	100	106	111	116	122	127	132	137	143	148	153	158	164	169	174	180	185
62	104	109	115	120	126	131	136	142	147	153	158	164	169	175	180	186	191
63	107	113	118	124	130	135	141	146	152	158	163	169	175	180	186	191	197
64	110	116	122	128	134	140	145	151	157	163	169	174	180	186	192	197	204
65	114	120	126	132	138	144	150	156	162	168	174	180	186	192	198	204	210
66	118	124	130	136	142	148	155	161	167	173	179	186	192	198	204	210	216
67	121	127	134	140	146	153	159	166	172	178	185	191	198	204	211	217	223
68	125	131	138	144	151	158	164	171	177	184	190	197	203	210	216	223	230
69	128	135	142	149	155	162	169	176	182	189	196	203	209	216	223	230	236
70	132	139	146	153	160	167	174	181	188	195	202	209	216	222	229	236	243
71	136	143	150	157	165	172	179	186	193	200	208	215	222	229	236	243	250
72	140	147	154	162	169	177	184	191	199	206	213	221	228	235	242	250	258
73	144	151	159	166	174	182	189	197	204	212	219	227	235	242	250	257	265
74	148	155	163	171	179	186	194	202	210	218	225	233	241	249	256	264	272
75	152	160	168	176	184	192	200	208	216	224	232	240	248	256	264	272	279
76	156	164	172	180	189	197	205	213	221	230	238	246	254	263	271	279	287

Body Mass Index Table 2 of 2

	Obese				Extreme Obesity														
BMI	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54
Height (inches)	Body Weight (pounds)																		
58	172	177	181	186	191	196	201	205	210	215	220	224	229	234	239	244	248	253	258
59	178	183	188	193	198	203	208	212	217	222	227	232	237	242	247	252	257	262	267
60	184	189	194	199	204	209	214	219	224	229	234	239	244	249	254	259	264	269	274
61	190	195	200	205	210	215	220	225	230	235	240	245	250	255	260	265	270	275	280
62	196	201	206	211	216	221	226	231	236	241	246	251	256	261	266	271	276	281	286
63	202	207	212	217	222	227	232	237	242	247	252	257	262	267	272	277	282	287	292
64	208	213	218	223	228	233	238	243	248	253	258	263	268	273	278	283	288	293	298
65	214	219	224	229	234	239	244	249	254	259	264	269	274	279	284	289	294	299	304
66	220	225	230	235	240	245	250	255	260	265	270	275	280	285	290	295	300	305	310
67	226	231	236	241	246	251	256	261	266	271	276	281	286	291	296	301	306	311	316
68	232	237	242	247	252	257	262	267	272	277	282	287	292	297	302	307	312	317	322
69	238	243	248	253	258	263	268	273	278	283	288	293	298	303	308	313	318	323	328
70	244	249	254	259	264	269	274	279	284	289	294	299	304	309	314	319	324	329	334
71	250	255	260	265	270	275	280	285	290	295	300	305	310	315	320	325	330	335	340
72	256	261	266	271	276	281	286	291	296	301	306	311	316	321	326	331	336	341	346
73	262	267	272	277	282	287	292	297	302	307	312	317	322	327	332	337	342	347	352
74	268	273	278	283	288	293	298	303	308	313	318	323	328	333	338	343	348	353	358

Body Mass Index Table 2 of 2

	Obese				Extreme Obesity															
BMI	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	
Height (inches)	Body Weight (pounds)																			
75	28 7	29 5	30 3	31 1	31 9	32 7	33 5	34 3	35 1	35 9	36 7	37 5	38 3	39 1	39 9	40 7	41 5	42 3	43 1	
76	29 5	30 4	31 2	32 0	32 8	33 6	34 4	35 3	36 1	36 9	37 7	38 5	39 4	40 2	41 0	41 8	42 6	43 5	44 3	

Source: Adapted from *Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults: The Evidence Report*, National Institutes of Health, 1998.

Can medicines help reverse insulin resistance or pre-diabetes?

Clinical trials have shown that people at high risk for developing diabetes can be given treatments that delay or prevent onset of diabetes. The first therapy should always be an intensive lifestyle modification program because weight loss and physical activity are much more effective than any medication at reducing diabetes risk.

Several drugs have been shown to reduce diabetes risk to varying degrees. No drug is approved by the U.S. Food and Drug Administration to treat insulin resistance or pre-diabetes or to prevent type 2 diabetes. The American Diabetes Association recommends that metformin is the only drug that should be considered for use in diabetes prevention. Other drugs that have delayed diabetes have side effects or haven't shown long-lasting benefit. Metformin use was recommended only for very high-risk individuals who have both forms of pre-diabetes (IGT and IFG), have a BMI of at least 35, and are younger than age 60. In the DPP, metformin was shown to be most effective in younger, heavier patients.

Points to Remember

- Insulin resistance is a condition in which the body's cells do not use insulin properly. Insulin helps cells use blood glucose for energy.
- Insulin resistance increases the risk of developing pre-diabetes, type 2 diabetes, and cardiovascular disease.
- Pre-diabetes is a condition in which blood glucose levels are higher than normal but not high enough for a diagnosis of diabetes.
- Causes of insulin resistance and pre-diabetes include genetic factors, excess weight, and lack of physical activity.
- Being physically active, making wise food choices, and reaching and maintaining a healthy weight can help prevent or reverse insulin resistance and pre-diabetes.
- The Diabetes Prevention Program (DPP) study confirmed that people at risk for developing type 2 diabetes can prevent or delay the onset of diabetes by losing 5

to 7 percent of their body weight through regular physical activity and a diet low in fat and calories.

Hope through Research

Researchers continue to follow DPP participants to learn about the long-term effects of the study. Other research sponsored by the National Institutes of Health builds on the findings from the DPP, including research focusing on lowering diabetes risk in children. Once considered an adult disease, type 2 diabetes is becoming more common in children, and researchers are seeking ways to reverse this trend.

The National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) sponsors the HEALTHY study, which is part of a broad research initiative called STOPP T2D (Studies to Treat or Prevent Pediatric Type 2 Diabetes). The study seeks to improve the treatment and prevention of type 2 diabetes in youth, exploring the roles of nutrition, physical activity, and behavior change in lowering risk for type 2 diabetes in children. The participating 42 middle schools are randomly assigned to a program group implementing changes or a comparison group. Students in the program group have healthier choices from the cafeteria and vending machines; longer, more intense periods of physical activity; and activities and awareness campaigns that promote long-term healthy behaviors. Results from the HEALTHY study are expected in 2009.

The NIDDK also sponsors the TODAY (Treatment Options for Type 2 Diabetes in Adolescents and Youth) study, which focuses on treatment of type 2 diabetes in children and teens at 13 sites. The TODAY study will evaluate the effects of three treatment approaches on control of blood glucose levels, insulin production, insulin resistance, and other outcomes. Each approach involves medication, but one of the three treatment groups will also receive an intensive lifestyle intervention to help the participants lose weight and increase physical fitness. More information about the TODAY study is available at www.todaystudy.org.

Participants in clinical trials can play a more active role in their own health care, gain access to new research treatments before they are widely available, and help others by contributing to medical research. For information about current studies, visit www.ClinicalTrials.gov.

For More Information

For more information about the DPP and the risk of developing diabetes, see these publications:

- [Diabetes Prevention Program](#)
- [Am I at Risk for Type 2 Diabetes?](#)

These publications are available at www.diabetes.niddk.nih.gov or by calling 1-800-860-8747.

American Diabetes Association

1701 North Beauregard Street
Alexandria, VA 22311
Phone: 1-800-DIABETES (342-2383)
Email: AskADA@diabetes.org
Internet: www.diabetes.org

National Diabetes Education Program

1 Diabetes Way
Bethesda, MD 20814-9692
Phone: 1-888-693-NDEP (6337)
TTY: 1-866-569-1162
Fax: 703-738-4929
Email: ndep@mail.nih.gov
Internet: www.ndep.nih.gov

National Heart, Lung, and Blood Institute Information Center

P.O. Box 30105
Bethesda, MD 20824-0105
Phone: 301-592-8573
Fax: 301-592-8563
Email: nhlbiinfo@nhlbi.nih.gov
Internet: www.nhlbi.nih.gov

The National Diabetes Information Clearinghouse collects resource information about diabetes for the NIDDK Reference Collection. This database provides titles, abstracts, and availability information for health information and health education resources.

This publication may contain information about medications. When prepared, this publication included the most current information available. For updates or for questions about any medications, contact the U.S. Food and Drug Administration toll-free at 1-888-INFO-FDA (463-6332) or visit www.fda.gov. Consult your doctor for more information.

National Diabetes Information Clearinghouse

1 Information Way
Bethesda, MD 20892-3560
Phone: 1-800-860-8747
TTY: 1-866-569-1162
Fax: 703-738-4929
Email: ndic@info.niddk.nih.gov
Internet: www.diabetes.niddk.nih.gov

The National Diabetes Information Clearinghouse (NDIC) is a service of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). The NIDDK is part of the National Institutes of Health of the U.S. Department of Health and Human Services. Established in 1978, the Clearinghouse provides information about diabetes to people with diabetes and to their families, health care professionals, and the public. The NDIC answers inquiries, develops and distributes publications, and works closely with professional and patient organizations and Government agencies to coordinate resources about diabetes.

Publications produced by the Clearinghouse are carefully reviewed by both NIDDK scientists and outside experts. This publication was originally reviewed by George A. Bray, M.D., Pennington Biomedical Research Center, Louisiana State University, and Richard F. Hamman, M.D., Dr.P.H., Department of Preventive Medicine and Biometrics, University of Colorado Health Sciences Center.

This publication is not copyrighted. The Clearinghouse encourages users of this publication to duplicate and distribute as many copies as desired.

NIH Publication No. 09-4893
October 2008