

# Clinical trials of metformin

TrialResults-center [www.trialresultscenter.org](http://www.trialresultscenter.org)

## 1 diabetes type 2

Trial	Treatments	Patients	Trials design and methods
<b>metformin vs Acarbose</b>			
Maji vs acarbose n=48/48 follow-up: 156	500 versus Acarbose	-	
<b>lifestyle modification + metformin vs control</b>			
IDDP (Ramachandran) , 2006 n=531 follow-up: 2.5 y	advice on lifestyle modification, metformin, or both versus given standard health care advice (control)	native Asian Indians with impaired glucose tolerance	Parallel groups open India
Jarret , 1979 n=204 follow-up: 4.3 y	carbohydrate restriction with phenformin 50 mg daily versus carbohydrate restriction alone	men with impaired glucose toleranc	Parallel groups open
<b>metformin vs control</b>			
James , 2005 n=10/10 follow-up: 8 weeks	metformin 1 g BID versus no treatment	Abdominal obesity with insulin resistance[	
<b>metformin vs Glibenclamide</b>			
Yki-Yarvinen vs glibenclamide , 1999 n=19/22 follow-up: 52	2.000 versus Glibenclamide	-	
Kahn (ADOPT) vs glibenclamide n=1454/1441 follow-up: 208	2.000 versus Glibenclamide	-	
<b>metformin vs Glimepiride</b>			
Yamanouchi vs glimepiride , 2005 n=39/37 follow-up: 52	750 versus Glimepiride	-	

continued...

Trial	Treatments	Patients	Trials design and methods
<b>metformin vs Glipizide/</b>			
Vahatalo vs glipizide/glimepiride n=26/15 follow-up: 52	2.500- versus Glipizide/	-	
<b>metformin vs Insulin</b>			
Yki-Yarvinen vsinsulin n=19/24 follow-up: 52	2.000 versus Insulin	-	
Klein , 1991 n=25/25 follow-up: 52	2.550 versus Insulin	-	
Barnett , 2008 n=211/235 follow-up: 128	NR versus Insulin	-	
<b>nateglinide + metformin vs metformin</b>			
Horton DOUBLON , 2000 n=172/178 follow-up: 24 weeks	nateglinide (120 mg, ac) and metformin (500 mg, tid) versus 500 mg metformin three times a day	-	
<b>repaglinide + metformin vs metformin</b>			
AGEE-1411 [NCT01465152] n=NA follow-up:	-	-	open Spain
<b>saxagliptin plus metformin XR 1500mg vs metformin up to 2000mg</b>			
CV181-085 [NCT00918138] n=NA follow-up:	Saxagliptin in Combination With Metformin XR 1500 mg versus Up-titrated Metformin XR to 2000 mg	Subjects With Type 2 Diabetes Who Have Inadequate Glycemic Control With Diet and Exercise and a Stable Dose of Metformin XR 1500 mg	
<b>metformin vs None</b>			
Vahatalo vs control , 2007 n=26/11 follow-up: 52	2.500 versus None	-	
Maji vs control , 2005 n=48/90 follow-up: 156	500 versus None	-	

continued...

Trial	Treatments	Patients	Trials design and methods
UKPDS 34 vs control n=342/411 follow-up: 556	2.550 versus None	-	
UKPDS 34 bis n=268/269 follow-up: 343	2.550 versus None	-	
Zhang n=49/45 follow-up: 76	750 versus None	-	
Ramachandran n=262/269 follow-up: 156	500 versus None	-	
<b>BIAsp 30)twice-daily + metformin vs once-daily glargine + metformin + secretagogues</b>			
Ligthelm , 2011 n=NA follow-up: 24 weeks	biphasic insulin aspart 70/30 (BIAsp 30)twice-daily + metformin versus once-daily glargine + metformin + secretagogues	type 2 diabetic patients who were not maintaining glycemic control on basal insulin and oral antidiabetic drugs	Parallel groups open-label
<b>metformin vs Pioglitazone</b>			
Yamanouchi vs pioglitazone n=39/38 follow-up: 52	750 versus Pioglitazone	-	
Shernthaner , 2004 n=597/597 follow-up: 52	2.000 versus Pioglitazone	-	
Derosa , 2009 n=67/69 follow-up: 64	3.000 versus Pioglitazone	-	
Charbonnel , 2005 n=320/319 follow-up: 104	2.550 versus Pioglitazone	-	
<b>metformin vs placebo</b>			
Baillargeon , 2004 n=32/32 follow-up: 26 weeks	metformin 850 mg BID versus placebo	Non obese women with PCOS	

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
Hermann , 2001 n=16/19 follow-up: 52 weeks	metformin 65279;1.700 versus Placebo	obese and overweight type 2 diabetes patients treated with insulin for at least 1 year, and with poor glycaemic control (HbA1c >upper reference level + 2% )	Parallel groups double-blind
Bridger , 2006 n=11/11 follow-up: 12 weeks	metformin 750 mg BID versus placebo	Adolescents with PCOS and insulin resistance	
Charles , 1998 n=227/230 follow-up: 52 weeks	metformin 850 mg BID versus placebo	Abdominal obesity	
Charles , 2000 n=83/85 follow-up: 13 weeks	metformin 850 mg BID versus placebo	Abdominal obesity, hypertension, and elevated triglycerides	
Choux , 2003 n=15/17 follow-up: 13 weeks	metformin 500 mg TID versus placebo	PCO	
Crave , 1995 n=12/12 follow-up: 17 weeks	metformin 850 mg BID versus placebo	Overweight with PCO	
EDIT (Holman) , 2003 n=631 follow-up:	metformin 500 mg three times/day, versus placebo	(WHO 1985 criteria)	UK
Douek , 2005 n=92/91 follow-up: 52	2.000 versus Placebo	-	
HOME , 2009 [NCT00375388] n=196/194 follow-up: 4.3 y	metformin 850 mg versus placebo	patients with DM2 treated with insulin	Parallel groups double-blind The Netherlands
Fleming , 2002 n=45/47 follow-up: 17 weeks	metformin 850 mg BID versus placebo	PCO	
Gregorio , 1999 n=89/85 follow-up: 76	1.700 versus Placebo	-	
Teupe , 1991 n=50/50 follow-up: 104	1.700 versus Placebo	Type 2 diabetic patients	Parallel groups open Canada

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
Freemark , 2001 n=16/16 follow-up: 26 weeks	metformin 500 mg BID versus placebo	Insulin resistance and family history of diabetes	
Gambineri , 2004 n=10/10 follow-up: 26 weeks	metformin 850 mg BID versus placebo	Obesity and PCOS	
Giugliano , 1993 n=12/12 follow-up: 12 weeks	metformin 850 mg BID versus placebo	Hypertension with normal glucose tolerance	
Hoeger , 2004 n=18/20 follow-up: 48 weeks	metformin 850 mg BID + lifestyle modification versus placebo + lifestyle modification	Overweight with PCOS[	
Kooy (HOME) , 2009 n=196/194 follow-up: 220	2.000 versus Placebo	Patients with type 2 diabetes	Parallel groups double blind
Kay , 2001 n=12/12 follow-up: 8 weeks	metformin 850 mg BID versus placebo	Adolescents with morbid obesity	
Kelly , 2002 n=16/16 follow-up: 26 weeks	metformin 500 mg TID versus placebo	PCO	
Kocak , 2002 n=28/28 follow-up: 8 weeks	metformin 850 mg BID versus placebo	PCO	
Lehtovirta , 2001 n=20/20 follow-up: 26 weeks	metformin 500 mg BID versus placebo	Overweight with impaired glucose tolerance and family history of diabetes	
palomba n=15/15 follow-up: 52	1.700 versus Placebo	-	
Ibanez n=12/12 follow-up: 52	850 versus Placebo	-	
Harborne n=26/26 follow-up: 52	1.500 versus Placebo	-	

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
Li , 1999 n=33/37 follow-up: 12 months	metformin 250 mg three times/day versus placebo	patients with impaired glucose tolerance (WHO 1985 criteria)	Parallel groups double blind China
Li n=33/37 follow-up: 52	2.000 versus Placebo	-	
Moggetti , 2000 n=12/11 follow-up: 26 weeks	metformin 500 mg TID versus placebo	PCOS with normal glucose tolerance	
Martinez n=35/73 follow-up: 52	1.700 versus Placebo	-	
Morel , 1999 n=19/19 follow-up: 8 weeks	metformin 850 mg BID versus placebo	Impaired glucose tolerance	
Gambineri n=40/40 follow-up: 52	1.700 versus Placebo	-	
Lund n=49/51 follow-up: 52	2.000 versus Placebo	-	
BIGPRO (Charles) n=164/160 follow-up: 52	1.700 versus Placebo	-	
Ng , 2001 n=10/10 follow-up: 12 weeks	metformin 500 mg TID versus placebo	PCO	
Orchard , 2005 n=1073/1082 follow-up: 156 weeks	metformin 850 mg BID versus placebo	Impaired glucose tolerance	
Stakos vs placebo n=59/97 follow-up: 104	500 versus Placebo	-	
Shuster n=45/81 follow-up: 104	500 versus Placebo	-	

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
Pasquali , 2000 n=20/20 follow-up: 26 weeks	metformin 850 mg BID versus placebo	Abdominal obesity with and without PCO	
DPP (Knowler) n=1073/1082 follow-up: 156	1.700 versus Placebo	-	
Ibanez 62 n=19/19 follow-up: 208	425 versus Placebo	-	
Rodriguez , 2004 n=10/11 follow-up: 20 weeks	metformin 1.7 g/d versus placebo	Obesity with insulin resistance	
Rodriguez-Moctezuma , 2004 n=12/11 follow-up: 8 weeks	metformin 850 mg BID versus placebo	Family history of diabetes	
Sirtori , 1984 n=15/15 follow-up: 26 weeks	metformin 850 mg BID versus placebo	Peripheral vascular disease	
Srinivasan , 2006 n=28/28 follow-up: 26 weeks	metformin 1 g BID versus placebo	Children and adolescents with obesity and insulin resistance	
Stakos , 2005 n=59/97 follow-up: 104 weeks	metformin 500 mg/d versus placebo	African-Americans with insulin resistance and family history of diabetes	
Sturrock , 2002 n=17/17 follow-up: 13 weeks	metformin 1500 mg/d versus placebo	PCO	
Tang , 2006 n=69/74 follow-up: 26 weeks	metformin 850 mg BID versus placebo	Obesity with PCO	
US-DPP (metformin) (Knowler) , 2002 n=3234 follow-up: 2.8 years	metformin 850mg twice daily versus placebo	nondiabetic patients with elevated glucose and high risk for diabetes	Parallel groups double blind USA
Vitale , 2005 n=32/33 follow-up: 13 weeks	metformin 500 mg BID versus placebo	Metabolic syndrome	
<b>rosiglitazone and metformin vs placebo</b>			

continued...

<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>CANOE , 2010</b> [NCT00116932] n=103/104 follow-up: 3.9y (median)	rosiglitazone (2 mg) and metformin (500 mg) twice-daily versus placebo	patients with impaired glucose tolerance	Parallel groups double-blind
<b>pioglitazone + metformin vs placebo (add on MET)</b>			
<b>PNFP-027</b> n=168/160 follow-up: 16 wk	Pioglitazone + metformin versus Placebo +metformin	patients with type 2 diabetes	Parallel groups
<b>metformin + repaglinide vs repaglinide</b>			
<b>AGEE-1411</b> [NCT01465152] n=NA follow-up: 24 weeks	metformin and repaglinide versus repaglinide	subjects with type 2 diabetes in which diet and exercise have failed	open Spain
<b>repaglinide + metformin vs repaglinide</b>			
<b>AGEE-3705</b> [NCT00819741] n=NA follow-up:	repaglinide plus metformin versus repaglinide alone	Chinese subjects with type 2 diabetes having an HbA1c (glycosylated haemoglobin A1c) over 8.5 % and who never have taken oral sugar-lowering drugs before	open China
<b>AGEE-3018</b> n=NA follow-up:	-	-	
<b>metformin vs Rosiglitazone</b>			
<b>maji vs rosiglitazone</b> n=48/48 follow-up: 156	500 versus Rosiglitazone	-	
<b>ADOPT vs rosiglitazone</b> n=1454/1456 follow-up: 208	2.000 versus Rosiglitazone	-	
<b>RECORD</b> n=1122/1103 follow-up: 260	2.550 versus Rosiglitazone	-	
<b>Tomazic</b> n=30/30 follow-up: 52	1.000 versus Rosiglitazone	-	
<b>repaglinide + metformin vs rosiglitazone + metformin</b>			

continued...



<b>Trial</b>	<b>Treatments</b>	<b>Patients</b>	<b>Trials design and methods</b>
<b>Raskin , 2009</b> [NCT00399711] n=NA follow-up: 26 weeks	repaglinide and metformin fixed dose combination tablet given as twice daily versus twice daily rosiglitazone and metformin fixed dose combination	subjects with type 2 diabetes currently on monotherapy	open USA
<b>repaglinide + metformin vs SU or MET</b>			
<b>AGEE-3017</b> [NCT00568984] n=NA follow-up:	combination therapy of repaglinide and metformin versus conventional treatment with a sulphonylurea or metformin in monotherapy	-	China
<b>pioglitazone + metformin vs sulfonylurea + metformin</b>			
<b>EC410</b> n=317/313 follow-up: 104 wk	Pioglitazone + metformin versus Sulfonylurea + metformin	patients with type 2 diabetes	Parallel groups
<b>metformin vs Vildagliptin</b>			
<b>Schweizer , 2007</b> n=254/526 follow-up: 52	2.000 versus Vildagliptin	-	
<b>metformin vs Glipizide</b>			
<b>Campbell , 1994</b> n=24/24 follow-up: 52	1.000 versus Glipizide	-	
<b>Stakos vs glipizide</b> n=59/25 follow-up: 104	500 versus Glipizide	-	
<b>metformin vs glyburide</b>			
<b>ADOPT , 2006</b> [NCT00279045] n=1454/1441 follow-up: 4 years (median)	metformin, versus glyburide	recently diagnosed type 2 diabetes	Parallel groups
<b>metformin vs SU/Insulin</b>			
<b>UKPDS (vs SU or INS)</b> n=342/951 follow-up: 556	2.550 versus SU/Insulin	Type 2 diabetic patients	Parallel groups open UK

More details and results :

- antidiabetic drugs for diabetes type 2 in all types of patients at <http://www.trialresultscenter.org/go-Q81>
- insulin sensitizers - glitazones for diabetes type 2 in all type of patients at <http://www.trialresultscenter.org/go-Q321>
- prevention for diabetes type 2 in all type of patients at <http://www.trialresultscenter.org/go-Q341>
- insulin sensitizer for diabetes type 2 in all type of patients at <http://www.trialresultscenter.org/go-Q377>
- insulin secretagogues for diabetes type 2 in all type of patients at <http://www.trialresultscenter.org/go-Q409>
- prevention for diabetes type 2 in people with impaired glucose tolerance at <http://www.trialresultscenter.org/go-Q416>
- insulin therapy for diabetes type 2 in all type of patients at <http://www.trialresultscenter.org/go-Q548>
- insulin secretagogues - Meglitinides (glinides) for diabetes type 2 in all types of patients at <http://www.trialresultscenter.org/go-Q549>
- insulin secretagogues - DPP-4 inhibitors for diabetes type 2 in all types of patients at <http://www.trialresultscenter.org/go-Q550>
- insulin sensitizer - biguanides for diabetes type 2 in all type of patients at <http://www.trialresultscenter.org/go-Q551>
- glucose lowering for cardiovascular prevention for diabetes type 2 in all type of patients at <http://www.trialresultscenter.org/go-Q576>
- glucose lowering for cardiovascular prevention for diabetes type 2 in meta-regression at <http://www.trialresultscenter.org/go-Q692>

## References

### **Maji vs acarbose, :**

#### **IDDP (Ramachandran), 2006:**

Ramachandran A, Snehalatha C, Mary S, Mukesh B, Bhaskar AD, Vijay V The Indian Diabetes Prevention Programme shows that lifestyle modification and metformin prevent type 2 diabetes in Asian Indian subjects with impaired glucose tolerance (IDPP-1). *Diabetologia* 2006;49:289-97 [16391903] [10.1007/s00125-005-0097-z](https://doi.org/10.1007/s00125-005-0097-z)

#### **Jarret, 1979:**

Jarrett RJ, Keen H, Fuller JH, McCartney M Worsening to diabetes in men with impaired glucose tolerance ("borderline diabetes"). *Diabetologia* 1979;16:25-30 [761734]

#### **James, 2005:**

James AP, Watts GF, Mamo JC The effect of metformin and rosiglitazone on postprandial lipid metabolism in obese insulin-resistant subjects. *Diabetes Obes Metab* 2005;7:381-9 [15955124] [10.1111/j.1463-1326.2004.00407.x](https://doi.org/10.1111/j.1463-1326.2004.00407.x)

#### **Yki-Yarvinen vs glibenclamide, 1999:**

Yki-Jrvinen H, Ryysy L, Nikkil K, Tulokas T, Vanamo R, Heikkil M Comparison of bedtime insulin regimens in patients with type 2 diabetes mellitus. A randomized, controlled trial. *Ann Intern Med* 1999;130:389-96 [10068412]

**Kahn (ADOPT) vs glibenclamide, :**

Kahn SE, Haffner SM, Heise MA, Herman WH, Holman RR, Jones NP, Kravitz BG, Lachin JM, O'Neill MC, Zinman B, Viberti G Glycemic durability of rosiglitazone, metformin, or glyburide monotherapy. *N Engl J Med* 2006;355:2427-43 [[17145742](#)] [10.1056/NEJMoa066224](#)

**Yamanouchi vs glimepiride, 2005:**

Yamanouchi T, Sakai T, Igarashi K, Ichiyonagi K, Watanabe H, Kawasaki T Comparison of metabolic effects of pioglitazone, metformin, and glimepiride over 1 year in Japanese patients with newly diagnosed Type 2 diabetes. *Diabet Med* 2005;22:980-5 [[16026361](#)] [10.1111/j.1464-5491.2005.01656.x](#)

**Vahatalo vs glipizide/glimepiride, :****Yki-Yarvinen vs insulin, :****Klein, 1991:**

Klein W Sulfonylurea-metformin-combination versus sulfonylurea-insulin-combination in secondary failures of sulfonylurea monotherapy. Results of a prospective randomized study in 50 patients. *Diabetes Metab* 1991;17:235-40 [[1936483](#)]

**Barnett, 2008:**

Barnett AH, Lange P, Dreyer M, Serdarevic-Pehar M Long-term tolerability of inhaled human insulin (Exubera) in patients with poorly controlled type 2 diabetes. *Int J Clin Pract* 2007;61:1614-25 [[17877648](#)] [10.1111/j.1742-1241.2007.01522.x](#)

**Horton DOUBLON, 2000:**

Horton ES, Foley JE, Shen SG, Baron MA Efficacy and tolerability of initial combination therapy with nateglinide and metformin in treatment-naïve patients with type 2 diabetes. *Curr Med Res Opin* 2004;20:883-9 [[15200747](#)] [10.1185/030079903125003881](#)

Horton ES, Clinkingbeard C, Gatlin M, Foley J, Mallows S, Shen S Nateglinide alone and in combination with metformin improves glycemic control by reducing mealtime glucose levels in type 2 diabetes. *Diabetes Care* 2000;23:1660-5 [[11092289](#)]

**AGEE-1411, :****CV181-085, :****Vahatalo vs control, 2007:**

Vahatalo M, Rinnemaa T, Viikari J Recognition of fasting or overall hyperglycaemia when starting insulin treatment in patients with type 2 diabetes in general practice. *Scand J Prim Health Care* 2007;25:147-53 [[17846932](#)] [10.1080/02813430701507719](#)

**Maji vs control, 2005:**

Maji D, Roy RU, Das S Prevention of type 2 diabetes in the prediabetic population. *J Indian Med Assoc* 2005;103:609-11 [[16570766](#)]

**UKPDS 34 vs control, :****UKPDS 34 bis, :****Zhang, :**

Zhang JL, Zheng X, Zou DJ, Qiu JL, Zhao XX, Qin YW Effect of metformin on weight gain during antihypertensive treatment with a beta-blocker in Chinese patients. *Am J Hypertens* 2009;22:884-90 [[19574961](#)] [10.1038/ajh.2009.93](#)

**Ramachandran, :**

Ramachandran A, Snehalatha C, Mary S, Mukesh B, Bhaskar AD, Vijay V The Indian Diabetes Prevention Programme shows that lifestyle modification and metformin prevent type 2 diabetes in Asian Indian subjects with impaired glucose tolerance (IDPP-1). *Diabetologia* 2006;49:289-97 [[16391903](#)] [10.1007/s00125-005-0097-z](#)

**Ligthelm, 2011:**

Ligthelm RJ, Gylvin T, DeLuzio T, Raskin P A comparison of twice-daily biphasic insulin aspart 70/30 and once-daily insulin glargine in persons with type 2 diabetes mellitus inadequately controlled on basal insulin and oral therapy: a randomized, open-label study. *Endocr Pract* 2011;17:41-50 [[20713345](#)] [10.4158/EP10079.OR](#)

**Yamanouchi vs pioglitazone, 0:**

**Shernthaner, 2004:**

Schernthaner G, Matthews DR, Charbonnel B, Hanefeld M, Brunetti P Efficacy and safety of pioglitazone versus metformin in patients with type 2 diabetes mellitus: a double-blind, randomized trial. *J Clin Endocrinol Metab* 2004;89:6068-76 [[15579760](#)] [10.1210/jc.2003-030861](#)

**Derosa, 2009:**

Derosa G, Maffioli P, Salvadeo SA, Ferrari I, Gravina A, Mereu R, Palumbo I, D'Angelo A, Cicero AF Direct comparison among oral hypoglycemic agents and their association with insulin resistance evaluated by euglycemic hyperinsulinemic clamp: the 60's study. *Metabolism* 2009;58:1059-66 [[19394976](#)] [10.1016/j.metabol.2009.03.007](#)

**Charbonnel, 2005:**

Charbonnel B, Schernthaner G, Brunetti P, Matthews DR, Urquhart R, Tan MH, Hanefeld M Long-term efficacy and tolerability of add-on pioglitazone therapy to failing monotherapy compared with addition of gliclazide or metformin in patients with type 2 diabetes. *Diabetologia* 2005;48:1093-104 [[15889234](#)] [10.1007/s00125-005-1751-1](#)

**Baillargeon, 2004:**

Baillargeon JP, Jakubowicz DJ, Iuorno MJ, Jakubowicz S, Nestler JE Effects of metformin and rosiglitazone, alone and in combination, in nonobese women with polycystic ovary syndrome and normal indices of insulin sensitivity. *Fertil Steril* 2004;82:893-902 [[15482765](#)] [10.1016/j.fertnstert.2004.02.127](#)

**Hermann, 2001:**

Hermann LS, Kaln J, Katzman P, Lager I, Nilsson A, Norrhamn O, Sartor G, Ugander L Long-term glycaemic improvement after addition of metformin to insulin in insulin-treated obese type 2 diabetes patients. *Diabetes Obes Metab* 2001;3:428-34 [[11903415](#)]

**Bridger, 2006:**

Bridger T, MacDonald S, Baltzer F, Rodd C Randomized placebo-controlled trial of metformin for adolescents with polycystic ovary syndrome. *Arch Pediatr Adolesc Med* 2006;160:241-6 [[16520442](#)] [10.1001/archpedi.160.3.241](#)

**Charles, 1998:**

Charles MA, Morange P, Eschwge E, Andr P, Vague P, Juhan-Vague I Effect of weight change and metformin on fibrinolysis and the von Willebrand factor in obese nondiabetic subjects: the BIGPRO1 Study. *Biguanides and the Prevention of the Risk of Obesity*. *Diabetes Care* 1998;21:1967-72 [[9802752](#)]

**Charles, 2000:**

Charles MA, Eschwge E, Grandmottet P, Isnard F, Cohen JM, Bensoussan JL, Berche H, Chapiro O, Andr P, Vague P, Juhan-Vague I, Bard JM, Safar M Treatment with metformin of non-diabetic men with hypertension, hypertriglyceridaemia and central fat distribution: the BIGPRO 1.2 trial. *Diabetes Metab Res Rev* 2000;16:2-7 [[10707032](#)]

**Choux, 2003:**

Chou KH, von Eye Corleta H, Capp E, Spritzer PM Clinical, metabolic and endocrine parameters in response to metformin in obese women with polycystic ovary syndrome: a randomized, double-blind and placebo-controlled trial. *Horm Metab Res* 2003;35:86-91 [[12734787](#)] [10.1055/s-2003-39056](#)

**Crave, 1995:**

Crave JC, Fimbel S, Lejeune H, Cugnardey N, Dchaud H, Pugeat M Effects of diet and metformin administration on sex hormone-binding globulin, androgens, and insulin in hirsute and obese women. *J Clin Endocrinol Metab* 1995;80:2057-62 [[7608255](#)]

**EDIT (Holman), 2003:**

Holman RR, Blackwell L, Stratton IM, Manley SE, Tucker L, Frighi V. *Diabet Med* 2003;20(suppl 2):15

**Douek, 2005:**

Douek IF, Allen SE, Ewings P, Gale EA, Bingley PJ Continuing metformin when starting insulin in patients with Type 2 diabetes: a double-blind randomized placebo-controlled trial. *Diabet Med* 2005;22:634-40 [[15842521](#)] [10.1111/j.1464-5491.2005.01475.x](#)

**HOME, 2009:**

Kooy A, de Jager J, Lehert P, Bets D, Wulfel MG, Donker AJ, Stehouwer CD Long-term effects of metformin on metabolism and microvascular and macrovascular disease in patients with type 2 diabetes mellitus. *Arch Intern Med* 2009;169:616-25 [[19307526](#)] [10.1001/archinternmed.2009.20](#)

**Fleming, 2002:**

Fleming R, Hopkinson ZE, Wallace AM, Greer IA, Sattar N Ovarian function and metabolic factors in women with oligomenorrhea treated with metformin in a randomized double blind placebo-controlled trial. *J Clin Endocrinol Metab* 2002;87:569-74 [[11836287](#)]

**Gregorio, 1999:**

Gregorio F, Ambrosi F, Manfrini S, Velussi M, Carle F, Testa R, Merante D, Filipponi P Poorly controlled elderly Type 2 diabetic patients: the effects of increasing sulphonylurea dosages or adding metformin. *Diabet Med* 1999;16:1016-24 [[10656230](#)]

**Teupe, 1991:**

Teupe B, Bergis K Prospective randomized two-years clinical study comparing additional metformin treatment with reducing diet in type 2 diabetes. *Diabete Metab* 1991;17:213-7 [[1936479](#)]

**Freemark, 2001:**

Freemark M, Bursey D The effects of metformin on body mass index and glucose tolerance in obese adolescents with fasting hyperinsulinemia and a family history of type 2 diabetes. *Pediatrics* 2001;107:E55 [[11335776](#)]

**Gambineri, 2004:**

Gambineri A, Pelusi C, Genghini S, et al Effect of flutamide and metformin administered alone or in combination in dieting obese women with polycystic ovary syndrome *H Clin Endocrinol (Oxf)*. 2004; 60:241-249

**Giugliano, 1993:**

Giugliano D, De Rosa N, Di Maro G, Marfella R, Acampora R, Buoninconti R, D'Onofrio F Metformin improves glucose, lipid metabolism, and reduces blood pressure in hypertensive, obese women. *Diabetes Care* 1993;16:1387-90 [[8269798](#)]

**Hoeger, 2004:**

Hoeger KM, Kochman L, Wixom N, Craig K, Miller RK, Guzick DS A randomized, 48-week, placebo-controlled trial of intensive lifestyle modification and/or metformin therapy in overweight women with polycystic ovary syndrome: a pilot study. *Fertil Steril* 2004;82:421-9 [[15302293](#)] [10.1016/j.fertnstert.2004.02.104](#)

**Kooy (HOME), 2009:**

Kooy A, de Jager J, Lehert P, Bets D, Wulfel MG, Donker AJ, Stehouwer CD Long-term effects of metformin on metabolism and microvascular and macrovascular disease in patients with type 2 diabetes mellitus. *Arch Intern Med* 2009;169:616-25 [[19307526](#)]

**Kay, 2001:**

Kay JP, Alemzadeh R, Langley G, D'Angelo L, Smith P, Holshouser S Beneficial effects of metformin in normoglycemic morbidly obese adolescents. *Metabolism* 2001;50:1457-61 [[11735093](#)] [10.1053/meta.2001.28078](#)

**Kelly, 2002:**

Kelly CJ, Gordon D The effect of metformin on hirsutism in polycystic ovary syndrome. *Eur J Endocrinol* 2002;147:217-21 [[12153743](#)]

**Kocak, 2002:**

Kocak M, Caliskan E, Sinsir C, Haberal A Metformin therapy improves ovulatory rates, cervical scores, and pregnancy rates in clomiphene citrate-resistant women with polycystic ovary syndrome. *Fertil Steril* 2002;77:101-6 [[11779598](#)]

**Lehtovirta, 2001:**

Lehtovirta M, Forsn B, Gullström M, Hggbloom M, Eriksson JG, Taskinen MR, Groop L Metabolic effects of metformin in patients with impaired glucose tolerance. *Diabet Med* 2001;18:578-83 [[11553189](#)]

**palomba, :**

Palomba S, Falbo A, Russo T, Manguso F, Tolino A, Zullo F, De Feo P, Orio F Jr Insulin sensitivity after metformin suspension in normal-weight women with polycystic ovary syndrome. *J Clin Endocrinol Metab* 2007;92:3128-35 [[17519312](#)] [10.1210/jc.2007-0441](#)

**Ibanez, :**

Ibez L, Ferrer A, Ong K, Amin R, Dunger D, de Zegher F Insulin sensitization early after menarche prevents progression from precocious pubarche to polycystic ovary syndrome. *J Pediatr* 2004;144:23-9 [[14722514](#)] [10.1016/j.jpeds.2003.08.015](#)

**Harborne, :**

Harborne L, Fleming R, Lyall H, Sattar N, Norman J Metformin or antiandrogen in the treatment of hirsutism in polycystic ovary syndrome. *J Clin Endocrinol Metab* 2003;88:4116-23 [[12970273](#)]

**Li, 1999:**

Li CL, Pan CY, Lu JM, Zhu Y, Wang JH, Deng XX, Xia FC, Wang HZ, Wang HY Effect of metformin on patients with impaired glucose tolerance. *Diabet Med* 1999;16:477-81 [[10391395](#)]

**Li, :**

Li CL, Pan CY, Lu JM, Zhu Y, Wang JH, Deng XX, Xia FC, Wang HZ, Wang HY Effect of metformin on patients with impaired glucose tolerance. *Diabet Med* 1999;16:477-81 [[10391395](#)]

**Moggetti, 2000:**

Moggetti P, Castello R, Negri C, Tosi F, Perrone F, Caputo M, Zanolin E, Muggeo M Metformin effects on clinical features, endocrine and metabolic profiles, and insulin sensitivity in polycystic ovary syndrome: a randomized, double-blind, placebo-controlled 6-month trial, followed by open, long-term clinical evaluation. *J Clin Endocrinol Metab* 2000;85:139-46 [[10634377](#)]

**Martinez, :**

Martnez E, Domingo P, Ribera E, Milinkovic A, Arroyo JA, Conget I, Prez-Cuevas JB, Casamitjana R, de Lazzari E, Bianchi L, Montserrat E, Roca M, Burgos R, Arnaiz JA, Gatell JM Effects of metformin or gemfibrozil on the lipodystrophy of HIV-infected patients receiving protease inhibitors. *Antivir Ther* 2003;8:403-10 [[14640387](#)]

**Morel, 1999:**

Morel Y, Golay A, Perneger T, Lehmann T, Vadas L, Pasik C, Reaven GM Metformin treatment leads to an increase in basal, but not insulin-stimulated, glucose disposal in obese patients with impaired glucose tolerance. *Diabet Med* 1999;16:650-5 [[10477209](#)]

**Gambineri, :**

Gambineri A, Patton L, Vaccina A, Cacciari M, Morselli-Labate AM, Cavazza C, Pagotto U, Pasquali R Treatment with flutamide, metformin, and their combination added to a hypocaloric diet in overweight-obese women with polycystic ovary syndrome: a randomized, 12-month, placebo-controlled study. *J Clin Endocrinol Metab* 2006;91:3970-80 [[16868063](#)] [10.1210/jc.2005-2250](#)

**Lund, :**

Lund SS, Tarnow L, Astrup AS, Hovind P, Jacobsen PK, Alibegovic AC, Parving I, Pietraszek L, Frandsen M, Rossing P, Parving HH, Vaag AA Effect of adjunct metformin treatment in patients with type-1 diabetes and persistent inadequate glycaemic control. A randomized study. PLoS One 2008;3:e3363 [[18852875](#)] [10.1371/journal.pone.0003363](#)

**BIGPRO (Charles), :**

Charles MA, Morange P, Eschwge E, Andr P, Vague P, Juhan-Vague I Effect of weight change and metformin on fibrinolysis and the von Willebrand factor in obese nondiabetic subjects: the BIGPRO1 Study. Biguanides and the Prevention of the Risk of Obesity. Diabetes Care 1998;21:1967-72 [[9802752](#)]

**Ng, 2001:**

Ng EH, Wat NM, Ho PC Effects of metformin on ovulation rate, hormonal and metabolic profiles in women with clomiphene-resistant polycystic ovaries: a randomized, double-blinded placebo-controlled trial. Hum Reprod 2001;16:1625-31 [[11473953](#)]

**Orchard, 2005:**

Orchard TJ, Temprosa M, Goldberg R, Haffner S, Ratner R, Marcovina S, Fowler S The effect of metformin and intensive lifestyle intervention on the metabolic syndrome: the Diabetes Prevention Program randomized trial. Ann Intern Med 2005;142:611-9 [[15838067](#)]

**Stakos vs placebo, :****Shuster, :**

Shuster D, Gaillard T, Rhinesmith S, Habash D, Osei K Impact of metformin on glucose metabolism in nondiabetic, obese African Americans: a placebo-controlled, 24-month randomized study. Diabetes Care 2004;27:2768-9 [[15505024](#)]

**Pasquali, 2000:**

Pasquali R, Gambineri A, Biscotti D, Vicennati V, Gagliardi L, Colitta D, Fiorini S, Cognigni GE, Filicori M, Morselli-Labate AM Effect of long-term treatment with metformin added to hypocaloric diet on body composition, fat distribution, and androgen and insulin levels in abdominally obese women with and without the polycystic ovary syndrome. J Clin Endocrinol Metab 2000;85:2767-74 [[10946879](#)]

**DPP (Knowler), :****Ibanez 62, 0:**

Ibez L, Lpez-Bermejo A, Daz M, Marcos MV, de Zegher F Metformin treatment for four years to reduce total and visceral fat in low birth weight girls with precocious pubarche. J Clin Endocrinol Metab 2008;93:1841-5 [[18319306](#)] [10.1210/jc.2008-0013](#)

**Rodriguez, 2004:**

Rodriguez Y, Giri M, Feyen E, Christophe AB Effect of metformin vs. placebo treatment on serum fatty acids in non-diabetic obese insulin resistant individuals. Prostaglandins Leukot Essent Fatty Acids 2004;71:391-7 [[15519498](#)] [10.1016/j.plefa.2004.08.004](#)

**Rodriguez-Moctezuma, 2004:**

Rodriguez-Moctezuma JR, Robles-Lpez G, Lpez-Carmona JM, Gutierrez-Rosas MJ Effects of metformin on the body composition in subjects with risk factors for type 2 diabetes. Diabetes Obes Metab 2005;7:189-92 [[15715892](#)] [10.1111/j.1463-1326.2004.00385.x](#)

**Sirtori, 1984:**

Sirtori CR, Franceschini G, Gianfranceschi G, Sirtori M, Montanari G, Bosisio E, Mantero E, Bondioli A Metformin improves peripheral vascular flow in nonhyperlipidemic patients with arterial disease. J Cardiovasc Pharmacol 1984;6:914-23 [[6209500](#)]

**Srinivasan, 2006:**

Srinivasan S, Ambler GR, Baur LA, Garnett SP, Tepsa M, Yap F, Ward GM, Cowell CT Randomized, controlled trial of metformin for obesity and insulin resistance in children and adolescents: improvement in body composition and fasting insulin. *J Clin Endocrinol Metab* 2006;91:2074-80 [[16595599](#)] [10.1210/jc.2006-0241](#)

**Stakos, 2005:**

Stakos DA, Schuster DP, Sparks EA, Wooley CF, Osei K, Boudoulas H Long term cardiovascular effects of oral antidiabetic agents in non-diabetic patients with insulin resistance: double blind, prospective, randomised study. *Heart* 2005;91:589-94 [[15831640](#)] [10.1136/hrt.2003.027722](#)

**Sturrock, 2002:**

Sturrock ND, Lannon B, Fay TN Metformin does not enhance ovulation induction in clomiphene resistant polycystic ovary syndrome in clinical practice. *Br J Clin Pharmacol* 2002;53:469-73 [[11994052](#)]

**Tang, 2006:**

Tang T, Glanville J, Hayden CJ, White D, Barth JH, Balen AH Combined lifestyle modification and metformin in obese patients with polycystic ovary syndrome. A randomized, placebo-controlled, double-blind multicentre study. *Hum Reprod* 2006;21:80-9 [[16199429](#)] [10.1093/humrep/dei311](#)

**US-DPP (metformin) (Knowler), 2002:**

Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, Nathan DM Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 2002;346:393-403 [[11832527](#)]

**Vitale, 2005:**

Vitale C, Mercurio G, Cornoldi A, Fini M, Volterrani M, Rosano GM Metformin improves endothelial function in patients with metabolic syndrome. *J Intern Med* 2005;258:250-6 [[16115299](#)] [10.1111/j.1365-2796.2005.01531.x](#)

**CANOE, 2010:**

Zinman B, Harris SB, Neuman J, Gerstein HC, Retnakaran RR, Raboud J, Qi Y, Hanley AJ Low-dose combination therapy with rosiglitazone and metformin to prevent type 2 diabetes mellitus (CANOE trial): a double-blind randomised controlled study. *Lancet* 2010 Jul 10;376:103-11 [[20605202](#)] [10.1016/S0140-6736\(10\)60746-5](#)

**PNFP-027, :**

**AGEE-1411, 0:**

**AGEE-3705, 0:**

**AGEE-3018, :**

**maji vs rosiglitazone, :**

**ADOPT vs rosiglitazone, :**

**RECORD, :**

**Tomazic, :**

Tomazic J, Karner P, Vidmar L, Maticic M, Sharma PM, Janez A Effect of metformin and rosiglitazone on lipid metabolism in HIV infected patients receiving protease inhibitor containing HAART. *Acta Dermatovenerol Alp Panonica Adriat* 2005;14:99-105 [[16200335](#)]

**Raskin , 2009:**

Raskin P, Lewin A, Reinhardt R, Lyness W Twice-daily dosing of a repaglinide/metformin fixed-dose combination tablet provides glycaemic control comparable to rosiglitazone/metformin tablet. *Diabetes Obes Metab* 2009 Sep;11:865-73 [[19476470](#)] [10.1111/j.1463-1326.2009.01062.x](#)

**AGEE-3017, 0:**

**EC410, :**

**Schweizer, 2007:**



Schweizer A, Couturier A, Foley JE, Dejager S Comparison between vildagliptin and metformin to sustain reductions in HbA(1c) over 1 year in drug-naive patients with Type 2 diabetes. Diabet Med 2007;24:955-61 [[17509069](#)] [10.1111/j.1464-5491.2007.02191.x](#)

**Campbell, 1994:**

Campbell IW, Menzies DG, Chalmers J, McBain AM, Brown IR One year comparative trial of metformin and glipizide in type 2 diabetes mellitus. Diabete Metab 1994;20:394-400 [[7843470](#)]

**Stakos vs glipizide, :**

Stakos DA, Schuster DP, Sparks EA, Wooley CF, Osei K, Boudoulas H Long term cardiovascular effects of oral antidiabetic agents in non-diabetic patients with insulin resistance: double blind, prospective, randomised study. Heart 2005;91:589-94 [[15831640](#)] [10.1136/hrt.2003.027722](#)

**ADOPT, 2006:**

Kahn SE, Haffner SM, Heise MA, Herman WH, Holman RR, Jones NP, Kravitz BG, Lachin JM, O'Neill MC, Zinman B, Viberti G Glycemic durability of rosiglitazone, metformin, or glyburide monotherapy. N Engl J Med 2006 Dec 7;355:2427-43 [[17145742](#)]

**UKPDS (vs SU or INS), 0:**

Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). UK Prospective Diabetes Study (UKPDS) Group. Lancet 1998;352:854-65 [[9742977](#)]

## 2 impaired fasting glucose

17

Trial	Treatments	Patients	Trials design and methods
<b>metformin vs placebo</b>			
<a href="#">US-DPP (metformin) (Knowler) , 2002</a> n=3234 follow-up: 2.8 years	metformin 850mg twice daily versus placebo	nondiabetic patients with elevated glucose and high risk for diabetes	Parallel groups double blind USA
<b>rosiglitazone and metformin vs placebo</b>			
<a href="#">CANOE , 2010</a> [NCT00116932] n=103/104 follow-up: 3.9y (median)	rosiglitazone (2 mg) and metformin (500 mg) twice-daily versus placebo	patients with impaired glucose tolerance	Parallel groups double-blind

More details and results :

- prevention for impaired fasting glucose in all type of patients at <http://www.trialresultscenter.org/go-Q342>

### References

**US-DPP (metformin) (Knowler), 2002:**

Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, Nathan DM Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 2002;346:393-403 [[11832527](#)]

**CANOE, 2010:**

Zinman B, Harris SB, Neuman J, Gerstein HC, Retnakaran RR, Raboud J, Qi Y, Hanley AJ Low-dose combination therapy with rosiglitazone and metformin to prevent type 2 diabetes mellitus (CANOE trial): a double-blind randomised controlled study. *Lancet* 2010 Jul 10;376:103-11 [[20605202](#)] [10.1016/S0140-6736\(10\)60746-5](#)

Entry terms: pioglitazone, Actos, Metformin, Dimethylguanylguanidine, Dimethylbiguanidine, Glucophage, , saxagliptin, saxagliptin, Onglyza, BMS 477118, BMS477118, BMS-477118, , dapagliflozin, dapagliflozin, forxiga, BMS 512148, BMS512148, BMS-512148,