

Title: Effects of whole-grain intake on glycemic control: a meta-analysis of randomized controlled trials

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Sources of Support:

None

Short running head:

Inverse association between whole-grain intake and fasting glucose concentration

Registry number and website:

This network meta-analysis was registered at www.crd.york.ac.uk/PROSPERO as CRD42019131128.

SUPPLEMENTAL METHODS

Search strategy

Pubmed

((((((((((((((((((((whole grain) OR grain) OR wholegrain) OR whole meal) OR whole wheat) OR wheat) OR rice) OR maize) OR oat) OR barley) OR corn) OR rye) OR millet) OR sorghum) OR triticale) OR canary seed) OR amaranth) OR buckwheat) OR quinoa)) AND (((((glucose) OR glycaemic control) OR glycemic control) OR insulin) OR insulin sensitivity). (Humans [ptyp] AND Clinical Trial [ptyp])

Embase

('whole grain' OR grain OR wholegrain OR 'whole meal' OR 'whole wheat' OR wheat OR rice OR maize OR oat OR barley OR corn OR rye OR millet OR sorghum OR triticale OR 'canary seed' OR amaranth OR buckwheat OR quinoa) AND (glucose OR 'glycemic control' OR 'glycaemic control' OR 'glucose control' OR insulin OR 'insulin sensitivity') AND [humans]/lim AND [clinical study]/lim AND [embase]/lim

Cochrane Library

(whole grain OR grain OR wholegrain OR whole meal OR whole wheat OR wheat OR rice OR maize OR oat OR barley OR corn OR rye OR millet OR sorghum OR triticale OR canary seed OR amaranth OR buckwheat OR quinoa) AND (glucose OR glycemic control OR glycaemic control OR glucose control OR insulin OR insulin sensitivity) in All Text

SUPPLEMENTAL TABLE 1Baseline and outcome data used in the meta-analysis¹

Author, publication year, Country	Group	Fasting glucose (mmol/L)	Fasting insulin (μ IU/mL)	HOMA-IR (units)	HbA1c (%)	2-h glucose (mmol/L)
Ampatzoglou, 2014, UK ^[1]	Mixed	Baseline (5.50 ± 0.57), outcome (5.40 ± 0.57)	Unavailable	Unavailable	Unavailable	Unavailable
	Control	Baseline (5.40 ± 0.57), outcome (5.40 ± 0.57)	Unavailable	Unavailable	Unavailable	Unavailable
Andersson, 2007, Sweden ^[2]	Mixed	Baseline (5.20 ± 0.80), outcome (5.30 ± 0.80)	Baseline (8.09 ± 3.30), outcome (8.29 ± 3.50)	Unavailable	Unavailable	Unavailable
	Control	Baseline (5.20 ± 0.90), outcome (5.20 ± 0.80)	Baseline (8.70 ± 4.41), outcome (8.29 ± 3.70)	Unavailable	Unavailable	Unavailable
Charlton, 2012, Australia ^[3]	Oat1	Baseline (4.85 ± 0.46), outcome (4.81 ± 0.51)	Baseline (8.92 ± 3.91), outcome (8.45 ± 7.43)	Unavailable	Unavailable	Unavailable
	Oat2	Baseline (4.96 ± 0.53), outcome (4.97 ± 0.61)	Baseline (10.16 ± 8.29), outcome (8.31 ± 8.93)	Unavailable	Unavailable	Unavailable
	Control	Baseline (4.86 ± 0.38), outcome (4.84 ± 0.32)	Baseline (9.10 ± 4.86), outcome (7.69 ± 4.46)	Unavailable	Unavailable	Unavailable
Connolly, 2016, UK ^[4]	Oat	Baseline (5.44 ± 0.55), outcome (5.33 ± 1.04)	Baseline (8.42 ± 5.04), outcome (8.66 ± 6.19)	Baseline (2.17 ± 1.48), outcome (2.21 ± 1.75)	Unavailable	Unavailable
	Control	Baseline (5.71 ± 0.71), outcome (5.82 ± 0.60)	Baseline (7.91 ± 5.53), outcome (10.23 ± 8.05)	Baseline (1.99 ± 1.48), outcome (2.63 ± 2.14)	Unavailable	Unavailable
Giacco, 2013, Finland/Italy ^[7]	Mixed	Baseline (5.89 ± 0.56), outcome (5.94 ± 0.56)	Baseline (13.51 ± 7.60), outcome (14.90 ± 8.01)	Unavailable	Unavailable	Unavailable
	Control	Baseline (6.06 ± 0.56), outcome (6.00 ± 0.61)	Baseline (13.41 ± 6.49), outcome (13.41 ± 6.80)	Unavailable	Unavailable	Unavailable

Supplementary Material

Author, publication year, Country	Group	Fasting glucose (mmol/L)	Fasting insulin (μ IU/mL)	HOMA-IR (units)	HbA1c (%)	2-h glucose (mmol/L)
Giacco, 2014, Finland/Italy ^[6]	Mixed	Baseline (5.60 \pm 0.60), outcome (5.70 \pm 0.70)	Baseline (15.00 \pm 9.01), outcome (16.00 \pm 8.01)	Baseline (4.02 \pm 2.61), outcome (3.99 \pm 2.22)	Unavailable	Unavailable
	Control	Baseline (5.80 \pm 0.50), outcome (5.80 \pm 0.70)	Baseline (14.00 \pm 6.00), outcome (14.00 \pm 8.01)	Baseline (3.50 \pm 1.61), outcome (3.24 \pm 1.62)	Unavailable	Unavailable
Giacco, 2009, Finland/Italy ^[5]	Wheat	Baseline (5.21 \pm 0.49), outcome (5.02 \pm 0.97)	Baseline (unavailable), outcome (9.44 \pm 3.66)	Unavailable	Unavailable	Unavailable
	Control	Baseline (5.21 \pm 0.49), outcome (5.42 \pm 0.52)	Baseline (unavailable), outcome (9.14 \pm 2.40)	Unavailable	Unavailable	Unavailable
Jackson, 2014, USA ^[8]	Mixed	Baseline (unavailable), outcome (-0.24 \pm 0.29)	Baseline (unavailable), outcome (-0.70 \pm 3.36)	Baseline (unavailable), outcome (-0.20 \pm 0.96)	Unavailable	Unavailable
	Control	Baseline (unavailable), outcome (-0.06 \pm 0.31)	Baseline (unavailable), outcome (-0.90 \pm 3.50)	Baseline (unavailable), outcome (-0.20 \pm 1.00)	Unavailable	Unavailable
Karl, 2017, USA ^[9]	Mixed	Baseline (5.06 \pm 0.56), outcome (-0.18 \pm 0.45)	Baseline (8.50 \pm 5.50), outcome (-0.80 \pm 0.84)	Baseline (2.40 \pm 1.40), outcome (-0.20 \pm 1.29)	Unavailable	Unavailable
	Control	Baseline (5.06 \pm 0.61), outcome (-0.06 \pm 0.63)	Baseline (9.50 \pm 6.40), outcome (-0.60 \pm 4.03)	Baseline (2.30 \pm 1.50), outcome (0.02 \pm 1.29)	Unavailable	Unavailable
Katcher, 2008, USA ^[10]	Mixed	Baseline (5.34 \pm 0.42), outcome (-0.07 \pm 0.26)	Baseline (15.00 \pm 7.60), outcome (-0.70 \pm 4.70)	Unavailable	Unavailable	Baseline (7.64 \pm 2.09), outcome (-0.22 \pm 1.81)
	Control	Baseline (5.32 \pm 0.31), outcome (-0.08 \pm 0.37)	Baseline (13.80 \pm 6.50), outcome (-2.00 \pm 5.90)	Unavailable	Unavailable	Baseline (7.62 \pm 2.12), outcome (-0.18 \pm 1.70)
Kazemzadeh, 2014-1, Iran ^[11]	Brown rice	Baseline (5.06 \pm 1.02), outcome (4.95 \pm 1.32)	Unavailable	Unavailable	Unavailable	Unavailable
	Control	Baseline (5.12 \pm 1.44), outcome (4.95 \pm 1.52)	Unavailable	Unavailable	Unavailable	Unavailable

Supplementary Material

Author, publication year, Country	Group	Fasting glucose (mmol/L)	Fasting insulin (μ IU/mL)	HOMA-IR (units)	HbA1c (%)	2-h glucose (mmol/L)
Kazemzadeh, 2014-2, Iran ^[11]	Brown rice	Baseline (5.00 \pm 1.54), outcome (5.00 \pm 1.10)	Unavailable	Unavailable	Unavailable	Unavailable
	Control	Baseline (5.06 \pm 1.50), outcome (4.84 \pm 1.41)	Unavailable	Unavailable	Unavailable	Unavailable
Kikuchi, 2019, Japan ^[12]	Wheat	Baseline (4.89 \pm 0.44), outcome (4.93 \pm 0.42)	Baseline (8.30 \pm 9.50), outcome (6.70 \pm 4.00)	Unavailable	Unavailable	Unavailable
	Control	Baseline (4.92 \pm 0.67), outcome (4.92 \pm 0.58)	Baseline (8.10 \pm 6.50), outcome (9.30 \pm 13.50)	Unavailable	Unavailable	Unavailable
Kirwan, 2016, USA ^[13]	Mixed	Baseline (4.93 \pm 1.02), outcome (-0.17 \pm 0.68)	Baseline (19.60 \pm 10.50), outcome (-2.90 \pm 7.03)	Baseline (4.50 \pm 3.00), outcome (-0.80 \pm 1.76)	Baseline (5.90 \pm 0.50), outcome (-0.13 \pm 0.37)	Unavailable
	Control	Baseline (4.96 \pm 0.86), outcome (0.07 \pm 0.56)	Baseline (22.60 \pm 14.90), outcome (-3.70 \pm 13.78)	Baseline (5.20 \pm 4.00), outcome (-0.60 \pm 3.08)	Baseline (5.80 \pm 0.50), outcome (-0.07 \pm 0.20)	Unavailable
Kondo, 2016, Japan ^[14]	Brown rice	Baseline (6.79 \pm 1.02), outcome (6.35 \pm 0.86)	Baseline (5.10 \pm 5.36), outcome (5.04 \pm 6.58)	Baseline (1.92 \pm 2.42), outcome (1.83 \pm 3.02)	Baseline (6.70 \pm 0.60), outcome (6.50 \pm 0.40)	Unavailable
	Control	Baseline (7.04 \pm 1.30), outcome (6.98 \pm 1.54)	Baseline (5.50 \pm 2.91), outcome (5.99 \pm 4.05)	Baseline (2.02 \pm 1.24), outcome (2.09 \pm 1.34)	Baseline (6.80 \pm 0.60), outcome (6.70 \pm 0.60)	Unavailable
Kristensen, 2012, Denmark ^[15]	Wheat	Baseline (5.73 \pm 0.55), outcome (5.70 \pm 0.55)	Baseline (7.62 \pm 1.48), outcome (7.37 \pm 1.85)	Baseline (1.91 \pm 0.92), outcome (1.80 \pm 1.05)	Baseline (5.63 \pm 0.25), outcome (5.72 \pm 0.18)	Unavailable
	Control	Baseline (5.63 \pm 0.41), outcome (5.55 \pm 0.41)	Baseline (7.45 \pm 1.52), outcome (7.20 \pm 1.69)	Baseline (2.01 \pm 1.22), outcome (1.80 \pm 0.99)	Baseline (5.62 \pm 0.17), outcome (5.71 \pm 0.17)	Unavailable
Liatis, 2009, Greece ^[16]	Wheat	Baseline (8.81 \pm 2.39), outcome (-0.72 \pm 0.93)	Baseline (18.56 \pm 21.03), outcome (-3.23 \pm 10.78)	Baseline (6.36 \pm 4.18), outcome (-2.08 \pm 5.93)	Baseline (7.29 \pm 1.61), outcome (-0.28 \pm 0.35)	Unavailable
	Control	Baseline (7.73 \pm 2.63), outcome (-0.07 \pm 1.41)	Baseline (10.75 \pm 5.10), outcome (-3.77 \pm 7.45)	Baseline (3.60 \pm 1.85), outcome (1.33 \pm 2.80)	Baseline (6.91 \pm 1.50), outcome (-0.13 \pm 0.45)	Unavailable

Supplementary Material

Author, publication year, Country	Group	Fasting glucose (mmol/L)	Fasting insulin (μ IU/mL)	HOMA-IR (units)	HbA1c (%)	2-h glucose (mmol/L)
Liu, 2018, China ^[17]	Wheat	Baseline (8.75 \pm 2.31), outcome (8.30 \pm 1.72)	Baseline (13.32 \pm 9.45), outcome (12.10 \pm 6.47)	Baseline (1.54 \pm 0.59), outcome (1.43 \pm 0.51)	Baseline (7.13 \pm 1.21), outcome (6.79 \pm 1.41)	Unavailable
	Control	Baseline (8.85 \pm 2.73), outcome (8.29 \pm 2.53)	Baseline (12.83 \pm 12.86), outcome (11.71 \pm 11.02)	Baseline (1.36 \pm 0.44), outcome (1.34 \pm 0.55)	Baseline (7.08 \pm 1.40), outcome (6.90 \pm 1.46)	Unavailable
Malik, 2019, USA ^[18]	Brown rice	Baseline (4.81 \pm 0.63), outcome (0.00 \pm 0.59)	Baseline (12.90 \pm 8.20), outcome (0.36 \pm 8.13)	Unavailable	Baseline (5.60 \pm 0.52), outcome (-0.04 \pm 0.27)	Unavailable
	Control	Baseline (4.81 \pm 0.63), outcome (0.04 \pm 0.69)	Baseline (12.90 \pm 8.20), outcome (0.90 \pm 9.37)	Unavailable	Baseline (5.60 \pm 0.52), outcome (-0.01 \pm 0.38)	Unavailable
Malin, 2019, USA ^[19]	Mixed	Baseline (5.22 \pm 0.56), outcome (5.07 \pm 0.42)	Baseline (23.00 \pm 9.73), outcome (15.90 \pm 6.49)	Unavailable	Unavailable	Baseline (8.71 \pm 2.33), outcome (8.27 \pm 2.27)
	Control	Baseline (5.25 \pm 0.52), outcome (5.14 \pm 0.46)	Baseline (21.60 \pm 12.98), outcome (17.10 \pm 9.73)	Unavailable	Unavailable	Baseline (8.35 \pm 2.12), outcome (8.48 \pm 1.96)
	Rye	Baseline (unavailable), outcome (5.60 \pm 0.90)	Baseline (unavailable), outcome (6.08 \pm 3.65)	Unavailable	Unavailable	Unavailable
McIntosh, 2003, Australia ^[21]	Wheat	Baseline (unavailable), outcome (5.59 \pm 0.69)	Baseline (unavailable), outcome (6.65 \pm 4.13)	Unavailable	Unavailable	Unavailable
	Control	Baseline (unavailable), outcome (5.64 \pm 0.85)	Baseline (unavailable), outcome (6.83 \pm 4.29)	Unavailable	Unavailable	Unavailable
Pereira, 2002, USA ^[22]	Mixed	Baseline (5.30 \pm 0.46), outcome (5.20 \pm 0.27)	Baseline (24.33 \pm 8.07), outcome (20.30 \pm 1.86)	Unavailable	Unavailable	Unavailable
	Control	Baseline (5.30 \pm 0.46), outcome (5.30 \pm 0.27)	Baseline (24.33 \pm 8.07), outcome (24.46 \pm 1.86)	Unavailable	Unavailable	Unavailable

Supplementary Material

Author, publication year, Country	Group	Fasting glucose (mmol/L)	Fasting insulin (μ IU/mL)	HOMA-IR (units)	HbA1c (%)	2-h glucose (mmol/L)
Pick, 1998, Canada ^[23]	Barley	Baseline (unavailable), outcome (8.06 \pm 0.83)	Baseline (unavailable), outcome (14.25 \pm 2.35)	Unavailable	Baseline (unavailable), outcome (7.32 \pm 0.30)	Unavailable
	Control	Baseline (unavailable), outcome (7.67 \pm 0.83)	Baseline (unavailable), outcome (15.83 \pm 2.35)	Unavailable	Baseline (unavailable), outcome (7.37 \pm 0.30)	Unavailable
Pins, 2002, USA ^[24]	Wheat	Baseline (6.58 \pm 1.53), outcome (5.90 \pm 1.57)	Unavailable	Unavailable	Unavailable	Unavailable
	Control	Baseline (6.51 \pm 1.90), outcome (6.66 \pm 2.01)	Unavailable	Unavailable	Unavailable	Unavailable
Roager, 2017, Denmark ^[25]	Mixed	Baseline (5.70 \pm 0.50), outcome (5.60 \pm 0.60)	Baseline (9.63 \pm 4.16), outcome (9.75 \pm 4.55)	Baseline (2.90 \pm 1.40), outcome (2.90 \pm 1.50)	Baseline (5.40 \pm 0.30), outcome (5.40 \pm 0.30)	Unavailable
	Control	Baseline (5.70 \pm 0.60), outcome (5.60 \pm 0.60)	Baseline (10.67 \pm 5.15), outcome (10.91 \pm 5.44)	Baseline (3.20 \pm 1.70), outcome (3.20 \pm 1.80)	Baseline (5.40 \pm 0.30), outcome (5.50 \pm 0.30)	Unavailable
Schutte, 2018, Netherlands ^[26]	Wheat	Baseline (5.5 \pm 0.7), outcome (0.1 \pm 0.5)	Baseline (13.4 \pm 27.5), outcome (-2.0 \pm 31.5)	Baseline (2.1 \pm 1.1), outcome (-0.5 \pm 7.9)	Unavailable	Unavailable
	Control	Baseline (5.4 \pm 0.5), outcome (0.0 \pm 0.2)	Baseline (8.9 \pm 7.8), outcome (-0.4 \pm 5.0)	Baseline (2.2 \pm 2.0), outcome (0.1 \pm 0.6)	Unavailable	Unavailable
Shimabukuro,2013-1, Japan ^[27]	Brown rice	Baseline (6.20 \pm 1.10), outcome (6.00 \pm 1.00)	Baseline (8.93 \pm 5.04), outcome (8.50 \pm 3.60)	Baseline (2.89 \pm 1.40), outcome (2.23 \pm 0.95)	Baseline (5.74 \pm 0.55), outcome (5.72 \pm 0.45)	Unavailable
	Control	Baseline (6.20 \pm 1.10), outcome (6.00 \pm 0.90)	Baseline (8.93 \pm 5.04), outcome (8.93 \pm 3.74)	Baseline (2.89 \pm 1.40), outcome (2.51 \pm 1.33)	Baseline (5.74 \pm 0.55), outcome (5.90 \pm 1.55)	Unavailable
Shimabukuro,2013-2, Japan ^[27]	Brown rice	Baseline (6.00 \pm 1.10), outcome (6.20 \pm 2.30)	Baseline (8.35 \pm 3.17), outcome (11.09 \pm 6.77)	Baseline (2.79 \pm 1.24), outcome (2.34 \pm 1.75)	Baseline (5.78 \pm 0.81), outcome (6.19 \pm 1.55)	Unavailable
	Control	Baseline (6.00 \pm 1.10), outcome (6.70 \pm 2.60)	Baseline (8.35 \pm 3.17), outcome (11.81 \pm 7.63)	Baseline (2.79 \pm 1.24), outcome (3.83 \pm 8.10)	Baseline (5.78 \pm 0.81), outcome (5.83 \pm 1.43)	Unavailable

Supplementary Material

Author, publication year, Country	Group	Fasting glucose (mmol/L)	Fasting insulin (μ IU/mL)	HOMA-IR (units)	HbA1c (%)	2-h glucose (mmol/L)
Steven, 2017, USA ^[20]	Mixed	Baseline (5.22 \pm 0.56), outcome (-0.09 \pm 0.46)	Baseline (19.2 \pm 9.35), outcome (-3.5 \pm 7.11)	Unavailable	Unavailable	Baseline (8.45 \pm 2.39), outcome (-0.12 \pm 1.44)
	Control	Baseline (5.25 \pm 0.45), outcome (-0.08 \pm 0.25)	Baseline (20.9 \pm 12.35), outcome (-3.5 \pm 6.36)	Unavailable	Unavailable	Baseline (8.45 \pm 2.02), outcome (0.16 \pm 0.73)
Tighe, 2010-1, UK ^[28]	Mixed	Baseline (5.53 \pm 0.50), outcome (5.49 \pm 0.42)	Unavailable	Baseline (1.81 \pm 1.59), outcome (1.73 \pm 1.51)	Unavailable	Unavailable
	Control	Baseline (5.63 \pm 0.71), outcome (5.70 \pm 0.63)	Unavailable	Baseline (2.30 \pm 2.30), outcome (2.29 \pm 1.83)	Unavailable	Unavailable
Tighe, 2010-2, UK ^[28]	Wheat	Baseline (5.47 \pm 0.68), outcome (5.38 \pm 0.68)	Unavailable	Baseline (2.18 \pm 3.16), outcome (1.97 \pm 2.39)	Unavailable	Unavailable
	Control	Baseline (5.63 \pm 0.71), outcome (5.70 \pm 0.63)	Unavailable	Baseline (2.30 \pm 2.30), outcome (2.29 \pm 1.83)	Unavailable	Unavailable
Vitaglione, 2015, Slovenia ^[29]	Wheat	Baseline (5.22 \pm 0.70), outcome (5.55 \pm 0.73)	Baseline (16.04 \pm 11.84), outcome (15.58 \pm 6.74)	Unavailable	Unavailable	Unavailable
	Control	Baseline (5.33 \pm 0.53), outcome (5.24 \pm 0.57)	Baseline (14.47 \pm 5.78), outcome (13.85 \pm 4.56)	Unavailable	Unavailable	Unavailable
Wang, 2013, USA ^[30]	Brown rice	Baseline (5.06 \pm 0.44), outcome (5.17 \pm 0.50)	Baseline (6.30 \pm 5.00), outcome (5.50 \pm 5.00)	Baseline (1.50 \pm 1.20), outcome (1.30 \pm 1.20)	Baseline (5.90 \pm 0.20), outcome (5.90 \pm 0.20)	Unavailable
	Control	Baseline (5.06 \pm 0.44), outcome (4.95 \pm 0.39)	Baseline (5.10 \pm 4.00), outcome (5.20 \pm 4.00)	Baseline (1.10 \pm 1.00), outcome (1.10 \pm 0.80)	Baseline (5.80 \pm 0.20), outcome (5.80 \pm 0.20)	Unavailable
Zhang, 2011, China ^[31]	Brown rice	Baseline (6.19 \pm 1.36), outcome (0.01 \pm 1.10)	Baseline (unavailable), outcome (0.13 \pm 2.85)	Baseline (1.85 \pm 1.19), outcome (0.03 \pm 0.97)	Baseline (5.85 \pm 0.65), outcome (-0.07 \pm 0.95)	Unavailable
	Control	Baseline (6.49 \pm 1.49), outcome (-0.16 \pm 1.49)	Baseline (unavailable), outcome (0.19 \pm 5.51)	Baseline (1.68 \pm 1.03), outcome (0.07 \pm 1.92)	Baseline (5.85 \pm 0.82), outcome (0.20 \pm 2.14)	Unavailable

Supplementary Material

Author, publication year, Country	Group	Fasting glucose (mmol/L)	Fasting insulin (μ IU/mL)	HOMA-IR (units)	HbA1c (%)	2-h glucose (mmol/L)
Zhang, 2012, China ^[32]	Oat	Baseline (5.63 ± 0.89), outcome (5.34 ± 0.81)	Unavailable	Unavailable	Unavailable	Unavailable
	Control	Baseline (5.47 ± 0.89), outcome (5.29 ± 0.81)	Unavailable	Unavailable	Unavailable	Unavailable

¹HOMA, Homeostasis Model Assessment; HbA1c, Hemoglobin A1c.

SUPPLEMENTAL TABLE 2

Author, publication year	Adequacy of random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias
Ampatzoglou, 2014, UK ^[1]	Unclear	Unclear	Unclear	Unclear	Low	Low	Low
Andersson, 2007, Sweden ^[2]	Unclear	Low	Unclear	High	Low	Low	Low
Charlton, 2012, Australia ^[3]	Unclear	Unclear	High	Low	Low	Low	Low
Connolly, 2016, UK ^[4]	Unclear	Low	Low	Unclear	Low	Low	Unclear
Giacco, 2009, Finland/Italy ^[5]	Unclear	Unclear	Unclear	Unclear	Low	Unclear	Low
Giacco, 2013, Finland/Italy ^[6]	Low	Low	Low	Low	Unclear	Low	Unclear
Giacco, 2014, Finland/Italy ^[7]	Low	Low	High	Low	Low	Low	Low
Jackson, 2014, USA ^[8]	Unclear	High	Low	Low	Low	Low	Unclear
Karl, 2017, USA ^[9]	Low	Unclear	Low	Low	Low	Low	Low
Katcher, 2008, USA ^[10]	Unclear	Unclear	Unclear	High	Low	Low	Low
Kazemzadeh, Iran ^[11]	Unclear	Unclear	Unclear	Unclear	Low	Low	Low
Kikuchi, 2019, Japan ^[12]	Low	Low	Low	Unclear	Low	Low	Low
Kirwan, 2016, USA ^[13]	Unclear	Unclear	Low	Unclear	Low	Low	Low
Kondo, 2016, Japan ^[14]	Unclear	Unclear	Unclear	Unclear	Low	Low	Low
Kristensen, 2012, Denmark ^[15]	Unclear	Unclear	Low	Unclear	Low	Low	Low
Liatis, 2009, Greece ^[16]	Unclear	Unclear	Low	Unclear	Low	Low	Low
Liu, 2018, China ^[17]	Low	High	Low	Low	Low	Low	Low
Malik, 2019, USA ^[18]	Unclear	Unclear	Unclear	Unclear	Low	Low	Low
Malin, 2019, USA ^[19]	Unclear	Unclear	Low	Unclear	Low	Low	Low
McIntosh, 2003, Australia ^[21]	Low	Unclear	Low	Low	Low	Unclear	Low
Pereira, 2002, USA ^[22]	Unclear	Unclear	Low	Low	Low	Low	Low
Pick, 1998, Canada ^[23]	Low	Low	Low	Low	Unclear	Low	Unclear

Supplementary Material

Author, publication year	Adequacy of random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias
Pins, 2002, USA ^[24]	Low	Low	Low	Unclear	Low	Low	Low
Roager, 2017, Denmark ^[25]	Low	Low	High	Low	Low	Low	Low
Schutte, 2018, Netherlands ^[26]	Unclear	Unclear	Unclear	Unclear	Low	Low	Low
Shimabukuro, 2013, Japan ^[27]	Unclear	Low	Low	Unclear	Low	Low	Low
Steven, 2017, USA ^[20]	Unclear	Low	Low	Low	Low	Low	Low
Tighe, 2010, UK ^[28]	Unclear	Unclear	Low	Low	Low	Low	Low
Vitaglione, 2015, Slovenia ^[29]	Low	Low	Low	Low	Unclear	Low	Unclear
Wang, 2013, China ^[30]	Unclear	Unclear	Low	Low	Unclear	Low	Low
Zhang, 2011, China ^[31]	Unclear	Low	Low	Low	Low	Low	Low
Zhang, 2012, China ^[32]	Low	Unclear	Low	Low	Low	Low	Low

¹Judgements of review authors (Low, Unclear and High) for each risk of bias item according to the Cochrane Risk of Bias assessment tool. In this tool, studies were deemed to be at high, low or unclear risk of bias based on adequacy of random sequence generation, allocation concealment, blinding of personnel, blinding, incomplete outcome data, selective reporting, and other bias.

REFERENCES

1. Ampatzoglou A, Atwal KK, Maidens CM, et al. Increased whole grain consumption does not affect blood biochemistry, body composition, or gut microbiology in healthy, low-habitual whole grain consumers. *J Nutr.* 2015;145(2):215-221.
2. Andersson A, Tengblad S, Karlstrom B, et al. Whole-grain foods do not affect insulin sensitivity or markers of lipid peroxidation and inflammation in healthy, moderately overweight subjects. *J Nutr.* 2007;137(6):1401-1407.
3. Charlton KE, Tapsell LC, Batterham MJ, et al. Effect of 6 weeks' consumption of beta-glucan-rich oat products on cholesterol levels in mildly hypercholesterolaemic overweight adults. *Br J Nutr.* 2012;107(7):1037-1047.
4. Connolly ML, Tzounis X, Tuohy KM, et al. Hypocholesterolemic and Prebiotic Effects of a Whole-Grain Oat-Based Granola Breakfast Cereal in a Cardio-Metabolic "At Risk" Population. *Front Microbiol.* 2016;7:1675.
5. Giacco R, Clemente G, Cipriano D, et al. Effects of the regular consumption of wholemeal wheat foods on cardiovascular risk factors in healthy people. *Nutr Metab Cardiovasc Dis.* 2010;20(3):186-194.
6. Giacco R, Costabile G, Della Pepa G, et al. A whole-grain cereal-based diet lowers postprandial plasma insulin and triglyceride levels in individuals with metabolic syndrome. *Nutr Metab Cardiovasc Dis.* 2014;24(8):837-844.
7. Giacco R, Lappi J, Costabile G, et al. Effects of rye and whole wheat versus refined cereal foods on metabolic risk factors: a randomised controlled two-centre intervention study. *Clin Nutr.* 2013;32(6):941-949.
8. Harris Jackson K, West SG, Vanden Heuvel JP, et al. Effects of whole and refined grains in a weight-loss diet on markers of metabolic syndrome in individuals with increased waist circumference: a randomized controlled-feeding trial. *Am J Clin Nutr.* 2014;100(2):577-586.
9. Karl JP, Meydani M, Barnett JB, et al. Substituting whole grains for refined grains in a 6-wk randomized trial favorably affects energy-balance metrics in healthy men and postmenopausal women. *Am J Clin Nutr.* 2017;105(3):589-599.
10. Katcher HI, Legro RS, Kunselman AR, et al. The effects of a whole grain-enriched hypocaloric diet on cardiovascular disease risk factors in men and women with metabolic syndrome. *Am J Clin Nutr.* 2008;87(1):79-90.
11. Kazemzadeh M, Safavi SM, Nematollahi S, et al. Effect of Brown Rice Consumption on Inflammatory Marker and Cardiovascular Risk Factors among Overweight and Obese Non-menopausal Female Adults. *Int J Prev Med.* 2014;5(4):478-488.
12. Kikuchi Y, Nozaki S, Makita M, et al. Effects of Whole Grain Wheat Bread on Visceral Fat Obesity in Japanese Subjects: A Randomized Double-Blind Study. *Plant Foods Hum Nutr.* 2018;73(3):161-165.
13. Kirwan JP, Malin SK, Scelsi AR, et al. A Whole-Grain Diet Reduces Cardiovascular Risk Factors in Overweight and Obese Adults: A Randomized Controlled Trial. *J Nutr.* 2016;146(11):2244-2251.
14. Kondo K, Morino K, Nishio Y, et al. Fiber-rich diet with brown rice improves

- endothelial function in type 2 diabetes mellitus: A randomized controlled trial. *PLoS One*. 2017;12(6):e0179869.
15. Kristensen M, Toubro S, Jensen MG, et al. Whole grain compared with refined wheat decreases the percentage of body fat following a 12-week, energy-restricted dietary intervention in postmenopausal women. *J Nutr*. 2012;142(4):710-716.
 16. Liatis S, Tsapogas P, Chala E, et al. The consumption of bread enriched with betaglucan reduces LDL-cholesterol and improves insulin resistance in patients with type 2 diabetes. *Diabetes Metab*. 2009;35(2):115-120.
 17. Liu Y, Qiu J, Yue Y, et al. Dietary black-grained wheat intake improves glycemic control and inflammatory profile in patients with type 2 diabetes: a randomized controlled trial. *Ther Clin Risk Manag*. 2018;14:247-256.
 18. Malik VS, Sudha V, Wedick NM, et al. Substituting brown rice for white rice on diabetes risk factors in India: a randomised controlled trial. *Br J Nutr*. 2019;121(12):1389-1397.
 19. Malin SK, Kullman EL, Scelsi AR, et al. A Whole-Grain Diet Increases Glucose-Stimulated Insulin Secretion Independent of Gut Hormones in Adults at Risk for Type 2 Diabetes. *Mol Nutr Food Res*. 2019;63(7):e1800967.
 20. Malin SK, Kullman EL, Scelsi AR, et al. A whole-grain diet reduces peripheral insulin resistance and improves glucose kinetics in obese adults: A randomized-controlled trial. *Metabolism*. 2018;82:111-117.
 21. McIntosh GH, Noakes M, Royle PJ, et al. Whole-grain rye and wheat foods and markers of bowel health in overweight middle-aged men. *Am J Clin Nutr*. 2003;77(4):967-974.
 22. Pereira MA, Jacobs DR, Jr., Pins JJ, et al. Effect of whole grains on insulin sensitivity in overweight hyperinsulinemic adults. *Am J Clin Nutr*. 2002;75(5):848-855.
 23. Pick ME, Hawrysh ZJ, Gee MI, et al. Barley Bread products improve glycemic control of Type 2 subjects. *International Journal of Food Sciences and Nutrition*. 2009;49(1):71-78.
 24. Pins JJ, Geleva D, Keenan JM, et al. Do whole-grain oat cereals reduce the need for antihypertensive medications and improve blood pressure control? *J Fam Pract*. 2002;51(4):353-359.
 25. Roager HM, Vogt JK, Kristensen M, et al. Whole grain-rich diet reduces body weight and systemic low-grade inflammation without inducing major changes of the gut microbiome: a randomised cross-over trial. *Gut*. 2019;68(1):83-93.
 26. Schutte S, Esser D, Hoevenaars FPM, et al. A 12-wk whole-grain wheat intervention protects against hepatic fat: the Graandioos study, a randomized trial in overweight subjects. *Am J Clin Nutr*. 2018;108(6):1264-1274.
 27. Shimabukuro M, Higa M, Kinjo R, et al. Effects of the brown rice diet on visceral obesity and endothelial function: the BRAVO study. *Br J Nutr*. 2014;111(2):310-320.
 28. Tighe P, Duthie G, Vaughan N, et al. Effect of increased consumption of whole-grain foods on blood pressure and other cardiovascular risk markers in healthy middle-aged persons: a randomized controlled trial. *Am J Clin Nutr*.

- 2010;92(4):733-740.
29. Vitaglione P, Mennella I, Ferracane R, et al. Whole-grain wheat consumption reduces inflammation in a randomized controlled trial on overweight and obese subjects with unhealthy dietary and lifestyle behaviors: role of polyphenols bound to cereal dietary fiber. *Am J Clin Nutr.* 2015;101(2):251-261.
 30. Wang B, Medapalli R, Xu J, et al. Effects of a whole rice diet on metabolic parameters and inflammatory markers in prediabetes. *e-SPEN Journal.* 2013;8(1):e15-e20.
 31. Zhang G, Pan A, Zong G, et al. Substituting white rice with brown rice for 16 weeks does not substantially affect metabolic risk factors in middle-aged Chinese men and women with diabetes or a high risk for diabetes. *J Nutr.* 2011;141(9):1685-1690.
 32. Zhang J, Li L, Song P, et al. Randomized controlled trial of oatmeal consumption versus noodle consumption on blood lipids of urban Chinese adults with hypercholesterolemia. *Nutr J.* 2012;11:54.

SUPPLEMENTAL TABLE 3

Pooled effects of whole grain consumption on glucose control and insulin sensitivity

Variables	No. of studies	Sample size (treatment/control) ¹	Net change (95% CI)	Test of heterogeneity ²		
				<i>P</i>	<i>I</i> ² (%)	<i>P</i> ³
Fasting glucose (mmol/L)	32	1346/1257	-0.05 (-0.10, -0.01)	0.129	21.3	0.027
Fasting insulin (mIU/mL)	27	1013/965	-0.12 (-0.52, 0.29)	0.907	0.0	0.578
HOMA-IR (units)	16	673/640	-0.04 (-0.15, 0.08)	0.536	0.0	0.469
HbA1c ⁴ (%)	10	539/523	-0.02 (-0.08, 0.04)	0.870	35.8	0.112
2-h glucose (mmol/L)	3	52/52	-0.18 (-0.78, 0.41)	0.550	0.0	0.935

¹ Numbers of subjects in the treatment and control groups.

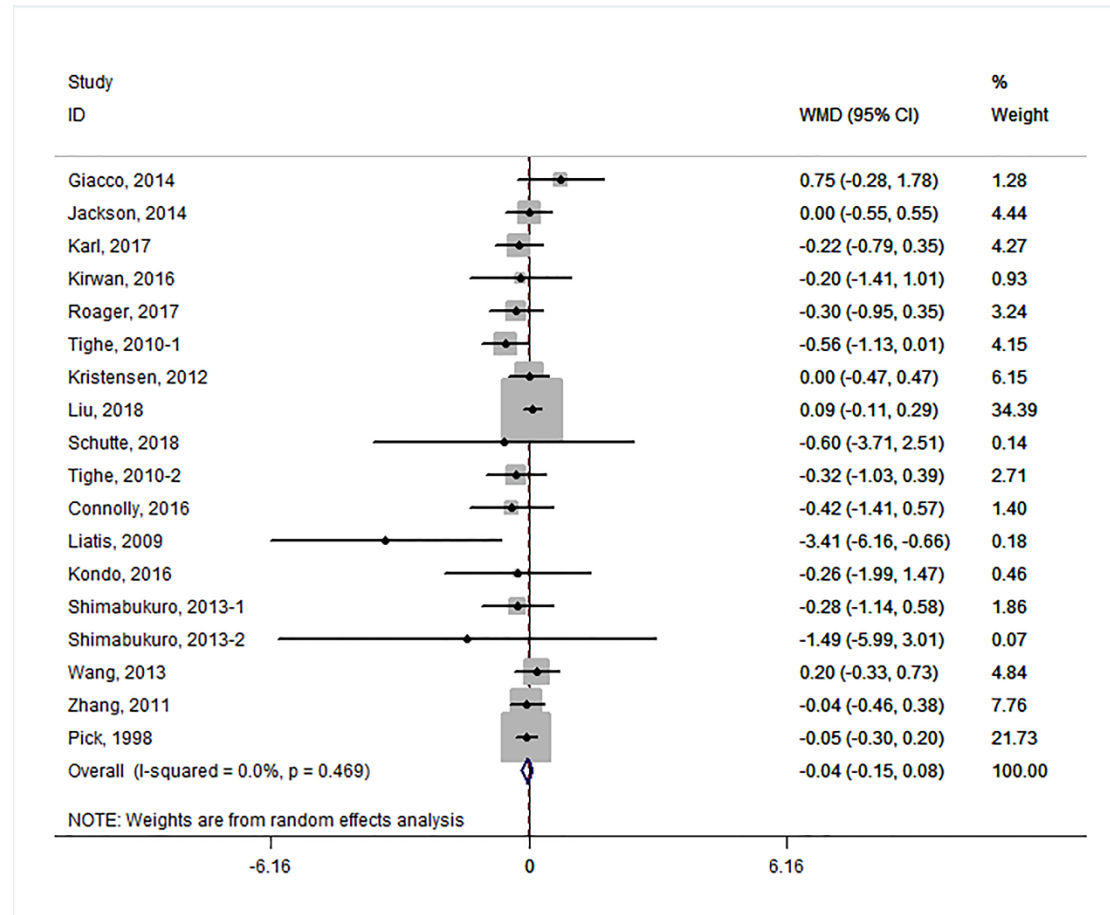
² *P* for heterogeneity was assessed by using Cochran's test, and *P* < 0.1 was considered to indicate significant heterogeneity across studies. The *I*² statistic was calculated by using Cochran's test, and an *I*² > 50% was considered to indicate significant heterogeneity across studies.

³ *P* for meta-analysis: *P* < 0.05 was considered to indicate significant effect of whole grain on fasting glucose and insulin concentrations by using a fixed-effects or random-effects model.

⁴ HbA1c, glycated hemoglobin.

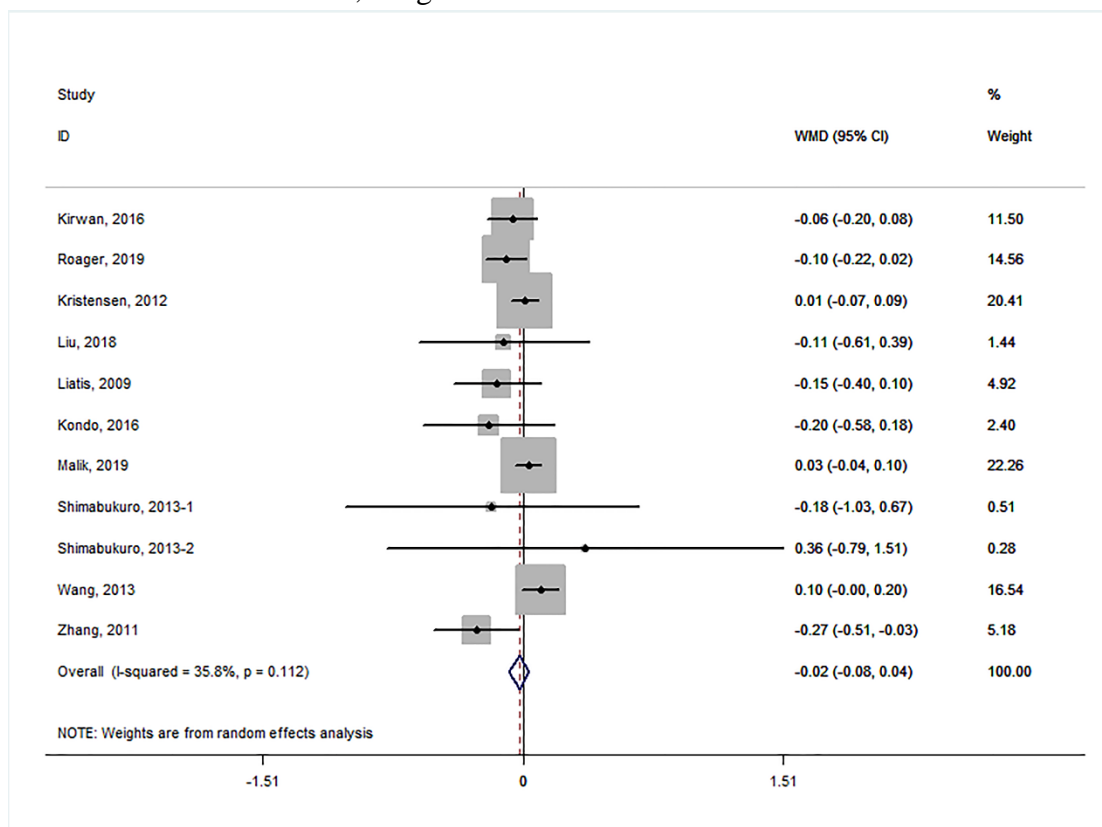
SUPPLEMENTAL FIGURE 1

Meta-analysis of the effects of whole grain on HOMA-IR. Weight was assigned with STATA (version 14.2; Stata Corp) by using the number of subjects and the SD. Sizes of the data markers indicate the weight of each study in this analysis. The diamond represents the overall estimated effect, and the result was obtained from a fixed-effects model. WMD, weighted mean difference.

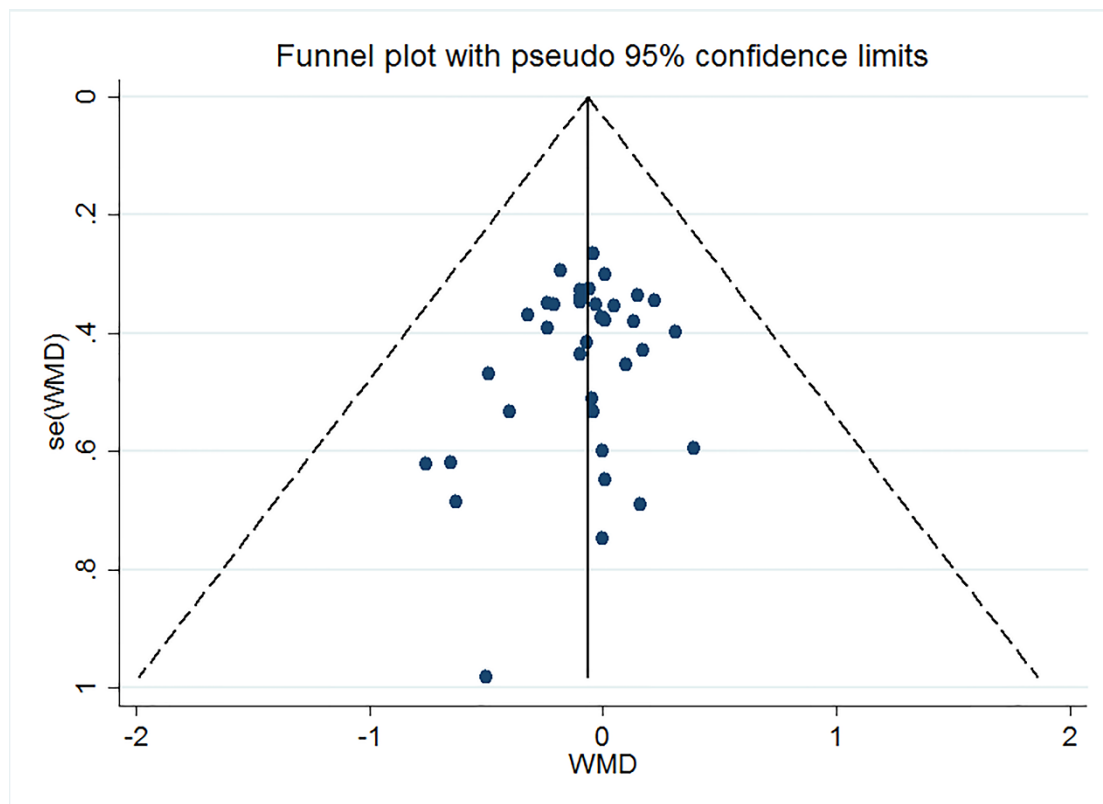


SUPPLEMENTAL FIGURE 2

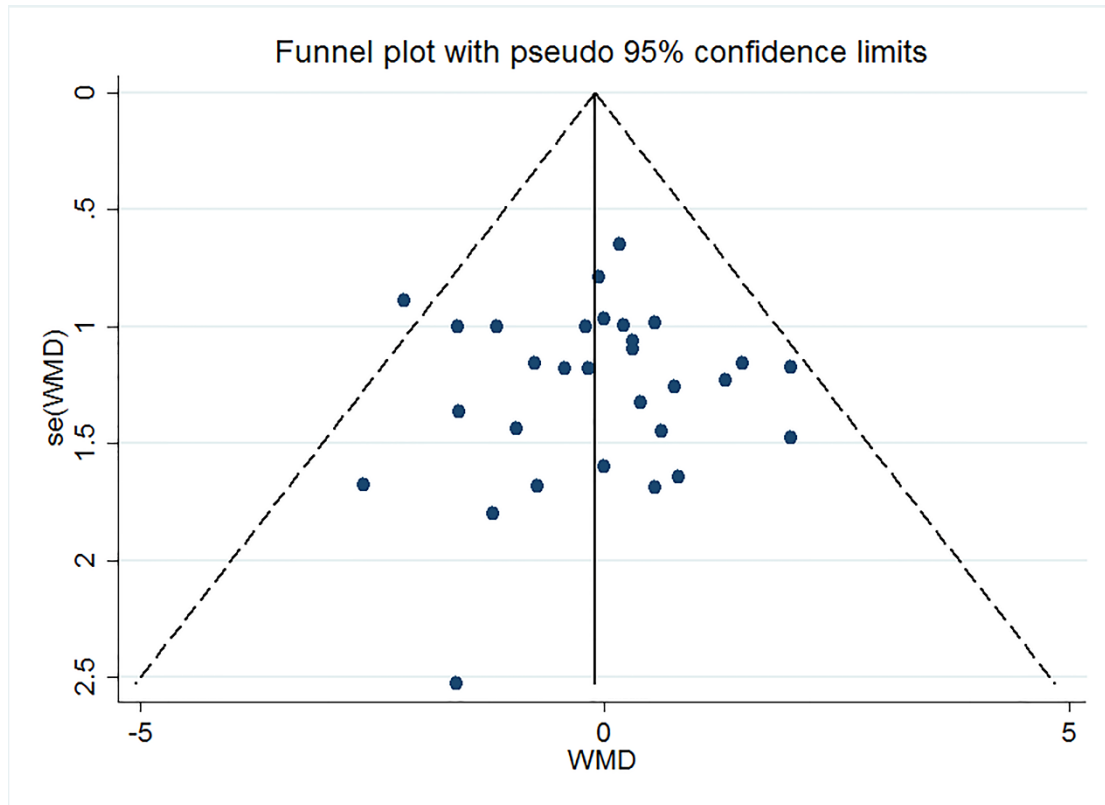
Meta-analysis of the effects of whole grain on HbA1c. Weight was assigned with STATA (version 14.2; Stata Corp) by using the number of subjects and the SD. Sizes of the data markers indicate the weight of each study in this analysis. The diamond represents the overall estimated effect, and the result was obtained from a fixed-effects model. WMD, weighted mean difference.



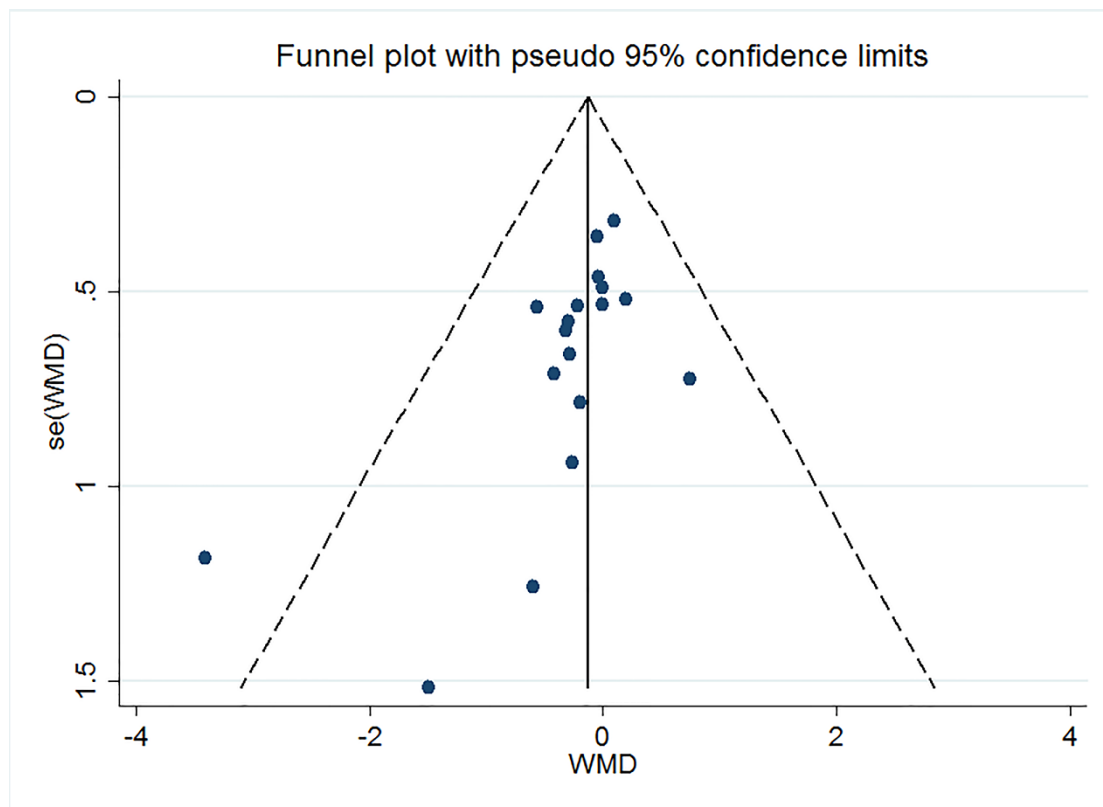
SUPPLEMENTAL FIGURE 3 Funnel plots for the studies of the association of whole grain and fasting glucose concentrations.



SUPPLEMENTAL FIGURE 4 Funnel plots for the studies of the association of whole grain and fasting insulin concentrations.



SUPPLEMENTAL FIGURE 5 Funnel plots for the studies of the association of whole grain and HOMA-IR.



SUPPLEMENTAL FIGURE 6 Funnel plots for the studies of the association of whole grain and HbA1c.

