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Meta-analysis

Surrogate measures of insulin sensitivity vs the hyperinsulinaemic–euglycaemic clamp: a meta-analysis

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Abstract

Aims/hypothesis We aimed to identify which surrogate index of insulin sensitivity has the strongest correlation with the reference measurement, the hyperinsulinaemic–euglycaemic clamp (HEC), to determine which surrogate measure should be recommended for use in large-scale studies.

Methods A literature search (1979–2012) was conducted to retrieve all articles reporting bivariate correlations between the HEC and surrogate measures of insulin sensitivity (in fasting samples or during the OGTT). We performed a random effects meta-analysis for each surrogate measure to integrate the correlation coefficients of the different studies.

Results The OGTT-based surrogate measures with the strongest pooled correlations (*r*) to the HEC were the Stumvoll metabolic clearance rate (MCR; *r*=0.70 [95% CI 0.61, 0.77], *n*=5), oral glucose insulin sensitivity (OGIS; *r*=0.70 [0.57, 0.80], *n*=6), the Matsuda index (*r*=0.67 [0.61, 0.73], *n*=19), the Stumvoll insulin sensitivity index (ISI; *r*=0.67 [0.60, 0.72], *n*=8) and the Gutt index (*r*=0.65 [0.60, 0.69], *n*=6). The fasting surrogate indices that correlated most strongly with the HEC and had narrow 95% CIs were the revised QUICKI (*r*=0.68 [0.58, 0.77], *n*=7), the QUICKI (*r*=0.61 [0.55, 0.65], *n*=35), the log HOMA-IR (*r*=−0.60 [−0.66, −0.53], *n*=22) and the HOMA of insulin sensitivity (computer generated, HOMA-%S) (*r*=0.57 [0.46, 0.67], *n*=5).

Conclusions/interpretation The revised QUICKI fasting surrogate measure appears to be as good as the OGTT-based Stumvoll MCR, OGIS, Matsuda, Stumvoll ISI and Gutt indices for estimating insulin sensitivity. It can therefore be recommended as the most appropriate index for use in large-scale clinical studies.

Keywords Glucose, Hyperinsulinaemic–euglycaemic clamp, Insulin, Insulin sensitivity, Meta-analysis, Surrogate markers

Abbreviations

FIRI	Fasting insulin resistance index
G_0	Fasting glucose
HEC	Hyperinsulinaemic–euglycaemic clamp
HOMA-%S	HOMA of insulin sensitivity (computer generated)
I_0	Fasting insulin
IGT	Impaired glucose tolerance
ISI	Insulin sensitivity index

M_{BSA}	Glucose infusion rate (mg/min) per m^2 body surface area
M_{BW}	Glucose infusion rate (mg/min) per kg body weight
M_{BW}/I	M_{BW} /steady state insulin
M_{BW}/G	M_{BW} /steady state glucose
M_{BW}/(G×ΔI)	M_{BW}/(steady state glucose concentration × increment in insulin concentration)
MCR	Metabolic clearance rate
M_{LBM}	Glucose infusion rate (mg/min) per kg lean body mass
M_{LBM}/I	M_{LBM} /steady state insulin
M_{LBM}/(G×ΔI)	M_{LBM}/(steady state glucose concentration × increment in insulin concentration)
NGT	Normal glucose tolerance
OGIS	Oral glucose insulin sensitivity

Introduction

An estimated 371 million people worldwide have diabetes mellitus, and the number is rising every year [1]. Impaired insulin sensitivity is a key abnormality underlying the development of type 2 diabetes, and mean insulin sensitivity is lower in these individuals compared with healthy controls. Even if there is no cut-off value to distinguish healthy from insulin-resistant individuals, measuring insulin sensitivity is of major importance to identify individuals at risk of developing diabetes and to evaluate diabetes-focused interventions [2, 3]. 'Insulin sensitivity' is an umbrella term for many different physiological processes. The most important elements of insulin sensitivity are glucose clearance in peripheral tissues (i.e. peripheral insulin sensitivity) and insulin-mediated suppression of hepatic glucose production (i.e. hepatic insulin sensitivity).

The purpose of this meta-analysis was to compare different measurements of peripheral insulin sensitivity and determine which technique is the most appropriate for large-scale clinical studies. The hyperinsulinaemic–euglycaemic clamp (HEC) is considered the 'gold standard' measure of peripheral insulin sensitivity, although it does not simulate the

physiological state of continuously changing glucose and insulin levels or hepatic insulin extraction, nor the feedback mechanism between glucose and insulin [4].

During the HEC, insulin is infused at a constant rate and the amount of glucose needed to maintain euglycaemia provides a measure of insulin sensitivity. Since muscle takes up over 70% of infused glucose, the HEC is the standard test for peripheral insulin sensitivity [5]. However, HEC is costly, time consuming and invasive, and requires trained staff; surrogate measures of insulin sensitivity are therefore necessary in epidemiological or large-scale intervention studies. These surrogate measures are based on insulin and/or glucose samples taken either in the fasting state or during the OGTT.

Surrogate indices based on fasting glucose and fasting insulin primarily reflect hepatic insulin sensitivity [6, 7]. In most individuals, hepatic insulin sensitivity is closely related to peripheral insulin sensitivity. Therefore, fasting surrogate measures show at least moderate correlations (r>0.5) with the HEC [7, 8].

Surrogate indices based on changes in insulin and glucose during the OGTT incorporate both peripheral and hepatic insulin sensitivity: hepatic glucose production changes most during the first hour of the OGTT, and peripheral glucose uptake is best measured during the second hour [7]. Gastric emptying, glucose absorption, insulin secretion and incretin hormones also influence OGTT results.

We undertook a meta-analysis to determine which surrogate measure(s) of insulin sensitivity should be used in clinical studies. We also aimed to establish whether fasting surrogate measures can be used instead of the more time-consuming OGTT-based measures.

Methods

Data sources and searches We searched Medline from 1979 until 2 March 2012 via PubMed. We chose 1979 as the start date because the HEC was first described by DeFronzo in that year [4]. We used the following Medical Subject Headings in our search: glucose

clamp technique; insulin resistance; and humans. We identified other potentially eligible studies by browsing the reference lists of suitable articles.

Study selection We read the abstracts of all articles and then read the entire article if the study seemed eligible. We included studies that reported bivariate correlation coefficients between the HEC reference method and surrogate measures for insulin sensitivity based on blood samples. The article was included in our analysis if the HEC glucose infusion rate *M* value was reported as M_{BW}, M_{BW}/I, M_{LBM}, M_{LBM}/I, M_{BW}/(G×ΔI), M_{LBM}/(G×ΔI), M_{BW}/I, M_{BW}/G or M_{BSA} (see main abbreviations list for definitions). We included studies that reported surrogate measures based on the OGTT or on fasting samples (fasting glucose, fasting insulin or both). We excluded articles not published in English, animal studies and studies conducted in children. Some of the relevant articles were intervention studies. If the articles contained correlation coefficients before and after the intervention, we used the mean of both for our meta-analysis. If a study reported correlation coefficients for two different insulin doses, we used the stronger of the coefficients. In several articles, the authors reported correlation coefficients with an opposite sign to the one expected (e.g. r=0.5 instead of r=−0.5). If the opposite correlation coefficients were significant or stronger than 0.2, we contacted the authors (n=12) via email. Four authors replied that they wanted only to describe the strength of the correlation (i.e. without the sign) or that the reported sign was incorrect. In those cases, we changed the sign in the relevant meta-analyses. The remaining eight authors did not respond. We therefore also performed a separate subgroup analysis excluding the correlation coefficients with signs opposite to those expected.

Data extraction and quality assessment We extracted the following information from each retrieved article: (1) name of the first author; (2) year of publication; (3) country in which the study was performed; (4) subject category (type 2 diabetes, impaired glucose tolerance,

normal glucose tolerance, other disease, healthy); (5) number of study participants; (6) proportion of men and women; (7) age (mean and SD); (8) BMI (mean and SD); (9) insulin dose of the HEC; (10) target blood glucose of the HEC; (11) duration of the HEC; (12) how insulin sensitivity measured by the HEC was expressed (e.g. M_{LBM}/I); (13) the method of determining correlation (Pearson's *r* or Spearman's ρ); and (14) the correlation coefficients between the HEC and the different surrogate measures (see electronic supplementary material [ESM] Table 1). We used the following questions to assess the quality and identify possible confounders of the different studies: (1) Is the study population evenly distributed between both sexes? (2) Are study participants with different levels of insulin sensitivity included? (3) Do study participants have medical conditions that might interfere with the measurement of insulin sensitivity? (4) Is diabetes diagnosed using OGTT, fasting glucose or medical history? (5) Is the insulin dose of the HEC appropriate for the study population? (6) How long was the HEC? (7) Was glucose during OGTT/fasting samples analysed as blood glucose or plasma/serum glucose (ESM Table 1)?

Data synthesis and analysis Combining Pearson's *r* with the more conservative Spearman's ρ could have introduced bias into the meta-analysis. We therefore converted Spearman's ρ into Pearson's *r* according to Rupinski and Dunlap using the following formula: $r=2\sin(\rho\times\pi/6)$ [9]. If a study reported R^2 (together with a graph indicating the direction) or a standardised (beta) coefficient instead of a correlation coefficient, we calculated the correlation coefficient. We combined the following ways of measuring correlation into a single meta-analysis: (1) x; (2) $\log x$; and (3) $1/x$ (the sign of the correlation coefficient was converted for the latter). Stumvoll and Mari used regression analysis to derive the Stumvoll insulin sensitivity index (ISI), the Stumvoll metabolic clearance rate (MCR) and oral glucose insulin sensitivity (OGIS) indices [10, 11]. We did not include these correlation coefficients in our meta-analysis because using the same population for both the development and

validation of the index would introduce bias. Both of these papers report additional correlation coefficients based on a validation analysis, and we used these for our meta-analysis.

To assess the differences between types of clamp measurement (M_{BW}, M_{LBM}, M_{BW}/I and M_{LBM}/I), we performed a separate subgroup analysis for each. To compare these different measures, we identified all surrogate measures (fasting and OGTT based) that were reported in 15 or more articles and in which the pooled correlation with the HEC was at least moderate (r>0.5 or <−0.5). For each surrogate measure (Matsuda, AUC insulin, QUICKI, fasting insulin and HOMA-IR), we conducted separate meta-analyses for all clamp measurements reported in at least two articles.

In another subgroup analysis, we compared surrogate measures in individuals with normal glucose tolerance (NGT), impaired glucose tolerance (IGT) and type 2 diabetes. For this comparison, we report surrogate measures only when correlation coefficients were available in at least one article for each of the subgroups.

We used the random effects model of DerSimonian and Laird for our random effects meta-analyses [12]. Before conducting the meta-analyses, we transformed all correlation coefficients to Fisher's z scale (zr) to stabilise the variances [13]. After the meta-analyses, we transformed the z-values back to correlation coefficients before plotting them in the graphs. We considered the random effects model to be most appropriate because characteristics (e.g. age and weight) differed among the study participants. Therefore, we were unable to assume that the effect size would be the same across studies, which is a required assumption for the fixed effect meta-analysis.

We used the Q-statistic, which follows a χ^2 distribution, to test for heterogeneity [14]. If there is significant heterogeneity, then a fixed effect meta-analysis is not recommended. We next used the I^2 statistic to quantify heterogeneity. A high I^2 (>75%) indicates that a large

proportion of the observed variance is caused by a genuine difference between the correlation coefficients of the included studies, and a low I^2 (<25%) means that most of the observed variance is the result of random error.

We used Begg and Mazumdar's rank correlation test [15] and funnel plots [16] to estimate publication bias. In the funnel plots, we plotted *z*-transformed correlation coefficients (*zr*) on the *x*-axis and SE on the *y*-axis. Asymmetry in a funnel plot reveals publication bias if small studies (i.e. with large SEs) exhibit strong correlation coefficients and there is a lack of small studies with weak correlation coefficients.

We conducted the meta-analysis, the heterogeneity test and Begg and Mazumdar's rank correlation test in IBM SPSS Statistics for Mac, Version 20.0 (Armonk, NY, IBM Corp.) using a syntax written by Field and Gillett [17, 18]. The funnel plots were produced in R (version 2.15.1, R Foundation for Statistical Computing, Vienna, Austria) using a code written by Vevea and Woods [19] and applying a script from Field and Gillett to feed SPSS data into R [18]. We visualised meta-analysis results using PRISM 5.0b (GraphPad Software, San Diego, CA).

Results

We retrieved 1,753 articles from our database search and included 120 of these in our meta-analysis. ESM Fig. 1 shows details of the selection process. Characteristics of the studies included in the meta-analysis are summarised in ESM Table 1.

OGTT-based and fasting surrogate measures compared with the HEC We pooled a total of 120 studies that included correlations between surrogate measures and the HEC. We report in detail only meta-analyses based on five or more articles. ESM Fig. 2 shows the random effects meta-analyses for correlations between the HEC and surrogate measures based on the OGTT. ESM Fig. 3 depicts correlations between fasting surrogate measures and the HEC.

Details of study participants and their characteristics can be found in ESM Table 1. Results of meta-analyses of fewer than five articles are included in ESM Tables 2 and 3. Table 1 contains the mathematical formulas of the relevant surrogate indices.

Each meta-analysis resulted in a pooled correlation coefficient. Of the OGTT-based surrogate measures, the Stumvoll MCR, OGIS, Matsuda, Stumvoll ISI and Gutt indices exhibited the strongest correlations with the HEC (ESM Fig. 2). Other OGTT-based indices exhibited weaker correlations with the HEC [e.g. insulin (120 min)]. Fig. 1 summarises the results of all meta-analyses (based on more than five studies) in a single graph to compare the pooled correlation coefficients and their respective 95% CIs.

Of the fasting surrogate measures, the pooled correlation coefficients of the QUICKI, revised QUICKI, HOMA-IR, HOMA of insulin sensitivity (HOMA-%S; computer generated) and fasting insulin exhibited the strongest correlations with the HEC and narrow 95% CIs (Fig. 1 and ESM Fig. 3). The QUICKI exhibited a stronger correlation than the HOMA-IR with the HEC. A separate meta-analysis revealed that the QUICKI and the log-transformed HOMA-IR had equally strong pooled correlations with the HEC (log HOMA-IR r=−0.60 [95% CI 0.66, −0.53], n=22; QUICKI r=0.61 [0.56, 0.66], n=36). Similarly, the correlation between fasting insulin and the HEC was stronger if log-transformed insulin was used (log fasting insulin r=−0.56 [−0.60, −0.51], n=17; fasting insulin r=−0.53 [−0.49, −0.56], n=71).

When we compared fasting surrogate measures to OGTT-based measures, we observed that only the correlation between the revised QUICKI and the HEC was as strong as those of HEC with the OGTT-based surrogate indices Stumvoll MCR, OGIS, Matsuda, Stumvoll ISI and Gutt (Fig. 1).

Heterogeneity analysis There was significant heterogeneity (p<0.05) in all meta-analyses based on five or more articles, except for correlation coefficients between the Gutt index and

the HEC (p=0.85). We therefore did not continue with fixed effect meta-analyses, but relied on the random effects meta-analyses. The reasons for such high levels of heterogeneity may be the different insulin doses used for the HECs, heterogeneous study populations with different levels of insulin sensitivity and, in some meta-analyses, outliers with correlation coefficients with signs opposite to those expected.

Publication bias The Begg and Mazumdar rank correlation test did not reveal a statistically significant publication bias, except for meta-analyses between the HEC and the I_0/G_0 and Gutt (p=0.02 and p=0.04, respectively). Although the funnel plot of the Gutt meta-analysis was slightly asymmetrical, this was caused by the inclusion of several small studies with weaker correlation coefficients, which argues against publication bias. Even the funnel plot for the meta-analysis between the HEC and I_0/G_0 exhibited clear asymmetry, which in this case was caused by three studies that reported positive correlation coefficients. Outliers of this type also caused clear asymmetry in other funnel plots [HOMA-IR, fasting insulin resistance index (FIRI), G_0/I_0, insulin (120 min)], but we did not interpret this as publication bias. There was some evidence of publication bias in the funnel plots of the revised QUICKI, HOMA-%S and glucose (120 min) meta-analyses. However, the Begg test did not reveal publication bias in these three meta-analyses. All funnel plots are shown in ESM Fig. 4.

Quality assessment Because of interference with the measurement of insulin sensitivity, we removed study participants with type 1 diabetes, insulinoma and renal failure (ESM Fig. 1). Furthermore we found the insulin dose used during the HEC to substantially influence the study quality. In our opinion, eight studies report an insulin dose that is too low for the population studied (ESM Table 1). However, we decided to keep these studies in our meta-analysis because all other studies that examined individuals with different levels of insulin sensitivity had used an inappropriate insulin dose for part of their study population.

We assessed whether the quality of the eight studies included in the meta-analysis of the revised QUICKI differed from the quality of all 120 studies combined (ESM Table 1). The only difference was that more studies in the revised QUICKI meta-analysis had an even sex distribution in the study population (i.e. as many men as women in four of seven studies). Only 33% of all 120 studies had evenly distributed study populations. The studies included in the revised QUICKI meta-analysis were comparable with the combined group of 120 studies in all other aspects of quality assessment.

Subgroup analyses After our attempts to contact the relevant authors, several meta-analyses still included outliers (the sign of the correlation coefficient was opposite to that expected, e.g. r=0.5 instead of r=−0.5). We therefore conducted additional meta-analyses without these outliers (data not shown). The pooled correlation coefficients did not change for QUICKI or fasting insulin when the outliers were removed. However, the removal of outliers resulted in slightly larger pooled correlation coefficients for HOMA-IR, insulin (120 min), FIRI, fasting glucose, I_0/G_0 and G_0/I_0. The remaining meta-analyses did not contain outliers.

Another subgroup analysis showed that the Matsuda, AUC insulin, QUICKI and fasting insulin exhibited stronger correlations with M values normalised to insulin (M_{BW}/I and M_{LBM}/I) than with those not normalised to insulin (M_{BW} and M_{LBM}; ESM Figs 5–8). Only for HOMA-IR was the M_{LBM} value correlation stronger than that of the M_{LBM}/I estimate (ESM Fig. 9). However, when we conducted a meta-analysis without the outliers (i.e. positive signs for all correlation coefficients), both M values for HOMA-IR normalised to insulin exhibited stronger correlations with the HEC compared with M values not normalised to insulin (data not shown).

We also conducted meta-analyses to test our hypothesis that the HEC correlates more strongly with surrogate measures for insulin sensitivity in individuals with IGT than in those with NGT or type 2 diabetic patients (ESM Table 4). According to our analyses, this is the

case for several surrogate measures (e.g. Matsuda, Stumvoll MCR, Stumvoll ISI, revised QUICKI), but not for others (e.g. OGIS, QUICKI, HOMA).

Discussion

Several surrogate markers for insulin sensitivity have been developed for use in clinical studies when the accepted reference method, HEC, is not practicable. We have correlated these surrogate measures of insulin sensitivity with the HEC in a meta-analysis. Based on this analysis, we recommend that the primary choice of surrogate index for estimating insulin sensitivity should be the revised QUICKI. This index is easy to perform because only fasting blood samples are needed and the correlation with the HEC is approximately as strong as that of OGTT-based indices. However, NEFA analyses are needed to construct this index. If NEFA analyses are not available, then any of the following OGTT-based indices could be employed as a second-choice measurement: Stumvoll MCR, OGIS, Matsuda, Stumvoll ISI and Gutt. If estimations must rely on fasting levels without NEFA analysis, then the best choice would be the QUICKI, the log-transformed HOMA-IR or the HOMA-%S.

However, the strength of correlation of the different surrogate measures with the HEC is moderate at best. This leads us directly to cost–benefit considerations. When conducting a small study, the HEC reference method should be used. However, in epidemiological or large-scale intervention studies, practical considerations will determine which of the aforementioned indices should be used. The overlapping CIs of the different meta-analyses suggest that there is no difference in correlation strength between these indices.

Some surrogate measures show a poor correlation with the HEC [e.g. I_0/G_0, G_0/I_0, insulin (120 min) and fasting glucose]. When using the I_0/G_0 or G_0/I_0 ratio, high insulin and high glucose levels will cancel each other out, so indices containing $G_0 \times I_0$ or G_0+I_0 are always preferred. Although insulin during the OGTT [e.g. insulin (120 min)] exhibits a fairly good correlation with the HEC in a healthy population, it is of less value in a diabetic population

because it is strongly influenced by islet dysfunction (ESM Table 4). Fasting glucose shows only a very limited variation in a healthy population and is regulated by several factors besides insulin sensitivity, such as islet function and hepatic glucose release. It is therefore a poor index to distinguish between various degrees of insulin sensitivity among healthy subjects.

After excluding study participants with medical conditions that might interfere with the measurement of insulin sensitivity, the quality of the remaining studies was still variable. This was probably caused by a disproportionately low insulin dose being administered during the HEC. During the HEC, the aim is to completely suppress hepatic glucose production to enable an accurate estimation of peripheral insulin sensitivity. Incomplete suppression will lead to the underestimation of insulin sensitivity. If the same dose of insulin is used for healthy/normal weight and type 2 diabetic individuals, then some participants will be examined with an inappropriate dose (because overweight and diabetic individuals need higher insulin doses to suppress hepatic glucose production) [4, 20], which indirectly affects correlations with surrogate indices. Furthermore, despite the assumption of a steady state condition, the amount of infused glucose continues to rise even at the end of the examination [21–23]. This means that the same participant may exhibit better insulin sensitivity during a longer HEC than during a shorter one, which makes comparisons difficult among clamp examinations of different durations. In addition, the glucose infusion rate is higher at the second examination than at the first within the same individual [22]. One possible explanation is that reduced stress causes the increase in insulin sensitivity.

Surrogate measures of insulin sensitivity (both fasting and OGTT based) have previously been validated mostly by determining their correlation coefficients to the HEC, in line with our analysis [24, 25]. However, it should be emphasised that fasting indices mainly measure hepatic insulin sensitivity and the HEC mainly measures muscle insulin sensitivity, while

OGTT-based indices measure both types of insulin sensitivity [7, 26]. There are other differences among these three methods of measuring insulin sensitivity. For example, although the HEC is the accepted reference measurement for insulin sensitivity, it does not reflect physiological conditions. Furthermore, arterialised blood is used during the HEC to measure glucose, while venous blood samples are taken for the surrogate measures. The same amount of glucose is always administered during the OGTT, in contrast to the fixed insulin dose but variable glucose infusion administered during the HEC. Although some consider the OGTT to be a more physiological examination in which the glucose load mimics that of a meal, this is disputed [27]. All of these factors help to explain why the correlation strength between surrogate measures and HEC is moderate at best.

Furthermore, there are several sources of error in insulin concentrations, which form part of most surrogate indices. For example, insulin assays show varying degrees of cross-reactivity with proinsulin and its partially processed products. While this is an important source of error in a radioimmunoassay, cross-reactivity to proinsulin is as low as 5.3% in the newer, specific insulin assays [28]. Insulin assays seem to exhibit most variability at low insulin levels, which could cause lower correlation coefficients in healthy individuals vs type 2 diabetic patients [29].

Matthews and collaborators originally recommended that three blood samples should be obtained for insulin analyses (one every 5 min, to account for the periodicity in insulin secretion) [30]. However, few of the studies included in our meta-analysis collected more than one sample for insulin analysis. This methodology may therefore introduce an error, especially for normal weight subjects, because pulsatile insulin decreases with IGT and diabetes [31, 32]. Finally, insulin levels are also regulated by beta cell and liver function (via effects on insulin clearance), in addition to insulin sensitivity.

It has been suggested that surrogate measures of insulin sensitivity show weaker

correlations with the HEC in healthy normal weight individuals than in insulin-resistant individuals [27]. In our meta-analysis, that was true for some of the surrogate indices but not for all. Generally, the strength of the correlation between a surrogate measure and the HEC in individuals with different levels of insulin sensitivity (NGT, IGT and type 2 diabetes) depends on the insulin dose administered during the clamp [29]. Lower insulin doses favour strong correlations for individuals with NGT, and higher insulin doses increase the correlation coefficient for insulin-resistant individuals. In many of the studies included in our meta-analysis, the same insulin dose was used for all study participants. This favours stronger correlations for insulin-sensitive groups. Furthermore, lower insulin doses will measure hepatic insulin sensitivity instead of peripheral glucose uptake, which strengthens correlations with the fasting surrogate measures relative to OGTT-based indices [33]. We therefore cannot draw conclusions from our meta-analyses about the NGT, IGT and type 2 diabetes subgroups.

Our analysis did not reveal a difference between the *M* value normalised to body weight and the *M* value normalised to lean body mass. However, *M* values normalised to insulin (M_{BW}/I and M_{LBM}/I) exhibited stronger correlations with all tested surrogate measures compared with *M* values not normalised to insulin (M_{BW} and M_{LBM}). Related to this, Bokemark et al showed that clamp examinations 2 weeks apart in the same individual exhibit a stronger correlation if insulin sensitivity is calculated using *M* values normalised to insulin and not *M* values without normalisation [22]. In addition, the distribution of insulin sensitivity in the population studied increases if the *M* value is normalised to insulin because it then becomes possible to detect small differences in insulin sensitivity [2].

In summary, we recommend that either the revised QUICKI fasting surrogate measurement or the OGTT-based indices (Stumvoll, OGIS, Matsuda and Gutt) should be used in future clinical studies. However, these indices need further validation against the

HEC and should be compared in a single study.

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Duality of interest

The authors declare that there is no duality of interest associated with this manuscript.

Contribution statement

JO designed the study; collected, analysed and interpreted the data; drafted and reviewed the manuscript; and approved the final version for publication. BA and TO designed the study; analysed and interpreted the data; drafted and reviewed the manuscript; and approved the final version for publication. JO is responsible for the overall integrity of the work.

References

1. International Diabetes Federation (2012) Diabetes: facts and figures. Available from www.idf.org/worlddiabetesday/toolkit/gp/facts-figures, accessed 3 October 2013

2. Ferrannini E, Mari A (1998) How to measure insulin sensitivity. J Hypertens 16: 895–906

3. Taylor R (2012) Insulin resistance and type 2 diabetes. Diabetes 61: 778–779

4. DeFronzo RA, Tobin JD, Andres R (1979) Glucose clamp technique: a method for quantifying insulin secretion and resistance. Am J Physiol 237: E214–223

5. Shulman GI, Rothman DL, Jue T, Stein P, DeFronzo RA, Shulman RG (1990) Quantitation of muscle glycogen synthesis in normal subjects and subjects with non-insulin-dependent diabetes by 13C nuclear magnetic resonance spectroscopy. N Engl J Med 322: 223–228

6. DeFronzo RA, Ferrannini E, Simonson DC (1989) Fasting hyperglycemia in non-insulin-dependent diabetes mellitus: contributions of excessive hepatic glucose production and impaired tissue glucose uptake. Metabolism 38: 387–395

7. Abdul-Ghani MA, Matsuda M, Balas B, DeFronzo RA (2007) Muscle and liver insulin resistance indexes derived from the oral glucose tolerance test. Diabetes Care 30: 89–94

8. Bonora E, Targher G, Alberiche M, et al. (2000) Homeostasis model assessment closely mirrors the glucose clamp technique in the assessment of insulin sensitivity: studies in subjects with various degrees of glucose tolerance and insulin sensitivity. Diabetes Care 23: 57–63

9. Rupinski MT, Dunlap WP (1996) Approximating pearson product-moment correlations from Kennall's tau and Spearman's rho. Educ Psychol Meas 56: 419–429

10. Stumvoll M, Mitrakou A, Pimenta W, et al. (2000) Use of the oral glucose tolerance test to assess insulin release and insulin sensitivity. Diabetes Care 23: 295–301

11. Mari A, Pacini G, Murphy E, Ludvik B, Nolan JJ (2001) A model-based method for assessing insulin sensitivity from the oral glucose tolerance test. Diabetes Care 24: 539–548

12. DerSimonian R, Laird N (1986) Meta-analysis in clinical trials. Control Clin Trials 7: 177–188

13. Hedges LV, Vevea JL (1998) Fixed- and random-effects models in meta-analysis. Psychol Methods 3: 486–504

14. Hedges LV, Olkin I (1985) Statistical methods for meta-analysis. Academic Press, Orlando, FL, USA

15. Begg CB, Mazumdar M (1994) Operating characteristics of a rank correlation test for publication bias. Biometrics 50: 1088–1101

16. Macaskill P, Walter SD, Irwig L (2001) A comparison of methods to detect publication bias in meta-analysis. Stat Med 20: 641–654

17. Field AP, Gillett R (2010) How to do a meta-analysis. The British journal of mathematical and statistical psychology 63: 665–694

18. Field A, Gillett R (2010) Meta-analysis program & datasets. Available from www.statisticshell.com/meta_analysis/how_to_do_a_meta_analysis.html, accessed 2 November 2012

19. Vevea JL, Woods CM (2005) Publication bias in research synthesis: sensitivity analysis using a priori weight functions. Psychol Methods 10: 428–443

20. DeFronzo RA, Soman V, Sherwin RS, Hendler R, Felig P (1978) Insulin binding to monocytes and insulin action in human obesity, starvation, and refeeding. J Clin Invest 62: 204–213

21. Bergman RN, Finegood DT, Ader M (1985) Assessment of insulin sensitivity in vivo. Endocr Rev 6: 45–86

22. Bokemark L, Froden A, Attvall S, Wikstrand J, Fagerberg B (2000) The euglycemic hyperinsulinemic clamp examination: variability and reproducibility. Scand J Clin Lab Invest 60: 27–36

23. Karelis AD, Henry JF, Malita F, et al. (2004) Comparison of insulin sensitivity values using the hyperinsulinemic euglycemic clamp: 2 vs 3 hours. Diabetes Metab 30: 413–414

24. Bastard JP, Vandernotte JM, Faraj M, et al. (2007) Relationship between the hyperinsulinemic-euglycaemic clamp and a new simple index assessing insulin sensitivity in overweight and obese postmenopausal women. Diabetes Metab 33: 261–268

25. Piche ME, Lemieux S, Corneau L, Nadeau A, Bergeron J, Weisnagel SJ (2007) Measuring insulin sensitivity in postmenopausal women covering a range of glucose tolerance: comparison of indices derived from the oral glucose tolerance test with the euglycemic-hyperinsulinemic clamp. Metabolism 56: 1159–1166

26. Matsuda M, DeFronzo RA (1999) Insulin sensitivity indices obtained from oral glucose tolerance testing: comparison with the euglycemic insulin clamp. Diabetes Care 22: 1462–1470

27. Antuna-Puente B, Disse E, Rabasa-Lhoret R, Laville M, Capeau J, Bastard JP (2011) How can we measure insulin sensitivity/resistance? Diabetes Metab 37: 179–188

28. Petrie JR, Morris AD, Dorrian CA, Small M, Connell JM (1997) Specific insulin assays, insulin sensitivity and blood pressure. QJM 90: 465–475

29. Mather KJ, Hunt AE, Steinberg HO, et al. (2001) Repeatability characteristics of simple indices of insulin resistance: implications for research applications. J Clin Endocrinol Metab 86: 5457–5464

30. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC (1985) Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 28: 412–419

31. Gumbiner B, van Cauter E, Beltz WF, et al. (1996) Abnormalities of insulin pulsatility and glucose oscillations during meals in obese noninsulin-dependent diabetic patients: effects of weight reduction. J Clin Endocrinol Metab 81: 2061–2068

32. Polonsky KS, Given BD, Hirsch LJ, et al. (1988) Abnormal patterns of insulin secretion in non-insulin-dependent diabetes mellitus. N Engl J Med 318: 1231–1239

33. Monzillo LU, Hamdy O (2003) Evaluation of insulin sensitivity in clinical practice and in research settings. Nutr Rev 61: 397–412

34. Gutt M, Davis CL, Spitzer SB, et al. (2000) Validation of the insulin sensitivity index (ISI(0,120)): comparison with other measures. Diabetes Res Clin Pract 47: 177–184

35. Belfiore F, Iannello S, Volpicelli G (1998) Insulin sensitivity indices calculated from basal and OGTT-induced insulin, glucose, and FFA levels. Mol Genet Metab 63: 134–141

36. Cederholm J, Wibell L (1990) Insulin release and peripheral sensitivity at the oral glucose tolerance test. Diabetes Res Clin Pract 10: 167–175

37. Reaven GM, Moore J, Greenfield M (1983) Quantification of insulin secretion and in vivo insulin action in nonobese and moderately obese individuals with normal glucose tolerance. Diabetes 32: 600–604

38. Kolterman OG, Gray RS, Griffin J, et al. (1981) Receptor and postreceptor defects contribute to the insulin resistance in noninsulin-dependent diabetes mellitus. J Clin Invest 68: 957–969

39. Hollenbeck CB, Chen N, Chen YD, Reaven GM (1984) Relationship between the plasma insulin response to oral glucose and insulin-stimulated glucose utilization in normal subjects. Diabetes 33: 460–463

40. Perseghin G, Caumo A, Caloni M, Testolin G, Luzi L (2001) Incorporation of the fasting plasma FFA concentration into QUICKI improves its association with insulin sensitivity in nonobese individuals. J Clin Endocrinol Metab 86: 4776–4781

41. Katz A, Nambi SS, Mather K, et al. (2000) Quantitative insulin sensitivity check index: a simple, accurate method for assessing insulin sensitivity in humans. J Clin Endocrinol Metab 85: 2402–2410

42. Cleland SJ, Petrie JR, Morris AD, Ueda S, Dorrian CA, Connell JM (1996) FIRI: a fair insulin resistance index? Lancet 347: 770

43. McAuley KA, Williams SM, Mann JI, et al. (2001) Diagnosing insulin resistance in the general population. Diabetes Care 24: 460–464

44. Li G, Pan X (1995) A new insulin-sensitivity index for epidemiological study. Chin Med J (Engl) 108: 55–56

45. DeFronzo R, Deibert D, Hendler R, Felig P, Soman V (1979) Insulin sensitivity and insulin binding to monocytes in maturity-onset diabetes. J Clin Invest 63: 939–946

46. Hanson RL, Pratley RE, Bogardus C, et al. (2000) Evaluation of simple indices of insulin sensitivity and insulin secretion for use in epidemiologic studies. Am J Epidemiol 151: 190–198

Fig. 1 Summary of all meta-analyses. The figure shows the strength of the pooled correlations; negative pooled correlations are shown on the positive side to facilitate comparison. Figures in parentheses indicate the papers that first described the surrogate measure (e.g. Matsuda) or that first measured the correlation with the HEC (e.g. fasting insulin)

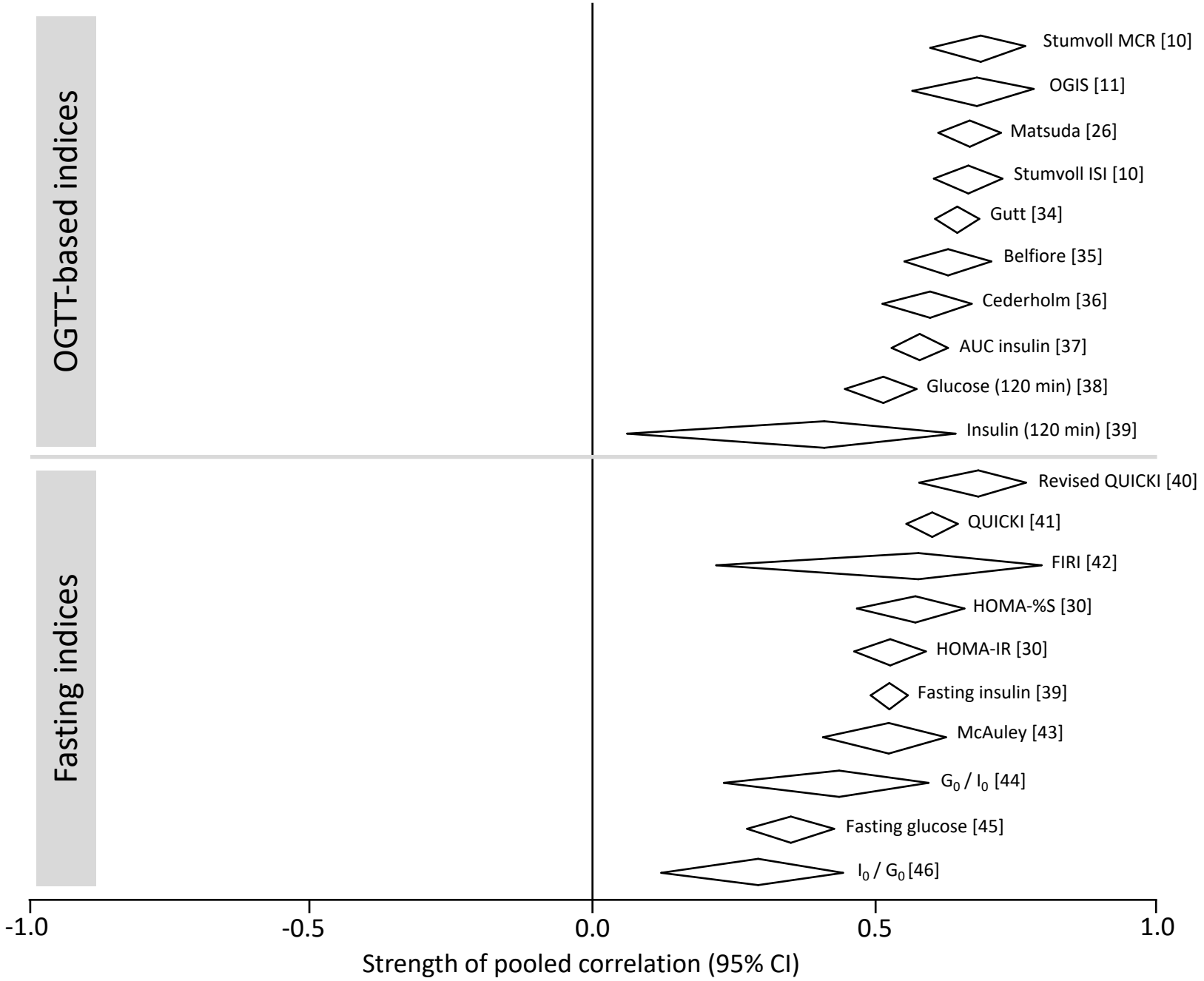
Table 1 Mathematical formulas of surrogate measures of insulin sensitivity based on the oral glucose tolerance test and fasting blood samples

Surrogate measure	Formula
OGTT-based indices	
Stumvoll MCR [10]	$18.8 - 0.271 \times BMI - 0.0052 \times I_{120} - 0.27 \times G_{90}$
Gutt [34]	$[75{,}000 + (G_0 - G_{120}) \times 0.19 \times BW] / (120 \times \log [(I_0 + I_{120}) / 2] \times [(G_0 + G_{120}) / 2])$
Stumvoll ISI [10]	$0.226 - 0.0032 \times BMI - 0.0000645 \times I_{120} - 0.00375 \times G_{90}$
OGIS [11]	http://webmet.pd.cnr.it/ogis/
Belfiore [35]	2 / [(AUC insulin + AUC glucose) + 1] (AUC glucose = $0.25 \times G_0 + 0.5 \times G_{30} + 0.5 \times G_{60} + 0.5 \times G_{90} + 0.25 \times G_{120}$)
Cederholm [36]	$[75{,}000 + (G_0 - G_{120}) \times 1.15 \times 180 \times 0.19 \times BW] / (120 \times I_{mean} \times G_{mean})$
Insulin (120 min)	I_{120}
Glucose (120 min)	G_{120}
AUC insulin[a]	$0.25 \times I_0 + 0.5 \times I_{30} + 0.5 \times I_{60} + 0.5 \times I_{90} + 0.25 \times I_{120}$
Matsuda [26]	$10{,}000 / \sqrt{G_0 \times I_0 \times G_{mean} \times I_{mean}}$
Fasting indices	
HOMA-IR [30]	$(G_0 \times I_0) / 22.5$
QUICKI [41]	$1 / (\log G_0 + \log I_0)$
Revised QUICKI [40]	$1 / (\log G_0 + \log I_0 + \log NEFA)$
HOMA-%S [30]	www.dtu.ox.ac.uk/homacalculator/index.php
FIRI [42]	$(G_0 \times I_0) / 25$
McAuley [43]	$e^{(2.63 - 0.28 \times \ln I_0 - 0.31 \times \ln TG)}$
I_0/G_0 [46]	Fasting insulin/fasting glucose
G_0/I_0 [44]	Fasting glucose/fasting insulin

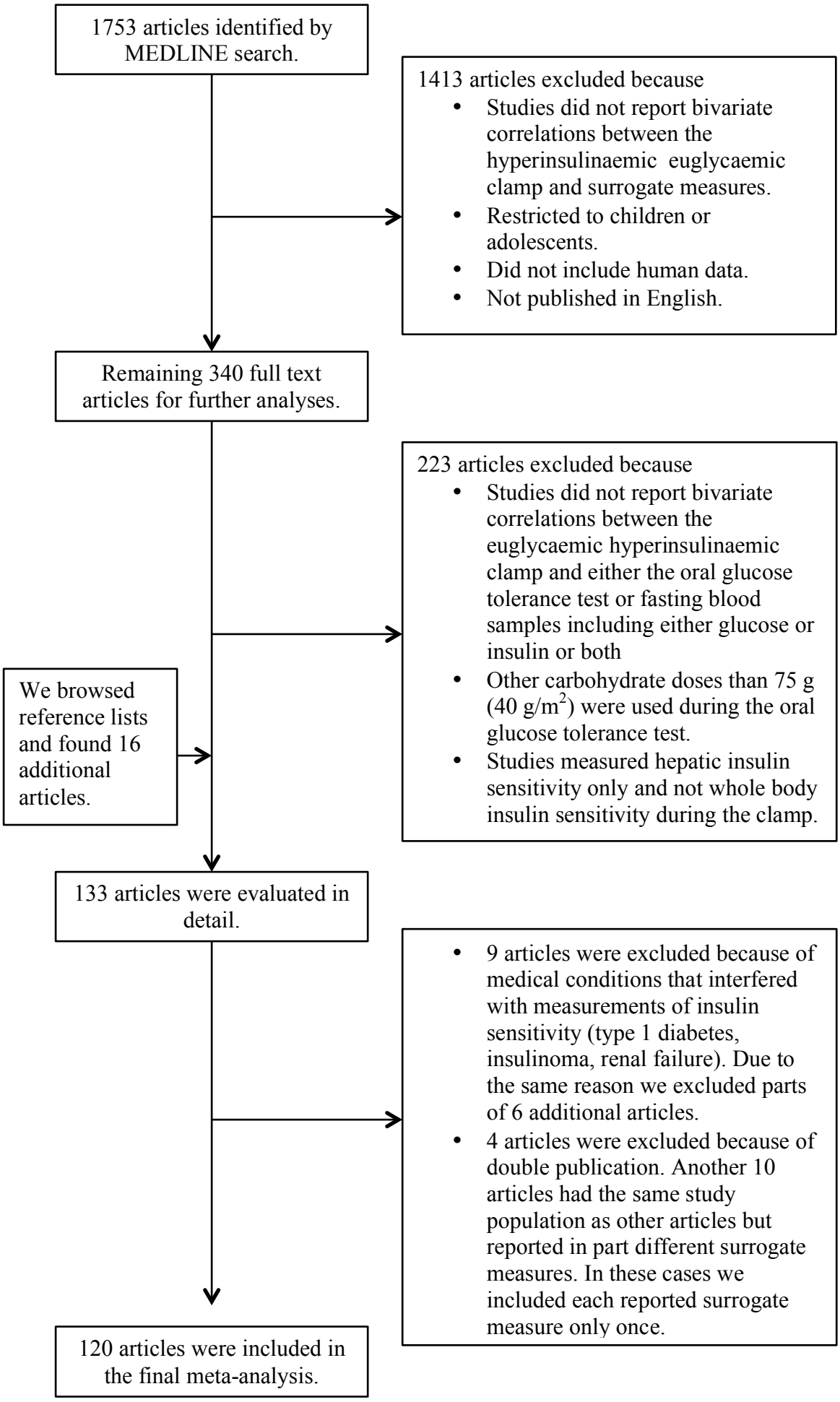
[a]AUC insulin is calculated according to the trapezoidal rule; however, the formula can differ if other measurement times are available

$I_{30}/I_{60}/I_{90}/I_{120}$, insulin 30, 60, 90 and 120 min after the administration of 75 g glucose; $G_{30}/G_{60}/G_{90}/G_{120}$, glucose 30, 60, 90 and 120 min after the administration of 75 g glucose; BW, body weight; I_{mean}, mean insulin during OGTT; G_{mean}, mean glucose during OGTT

Figure 1

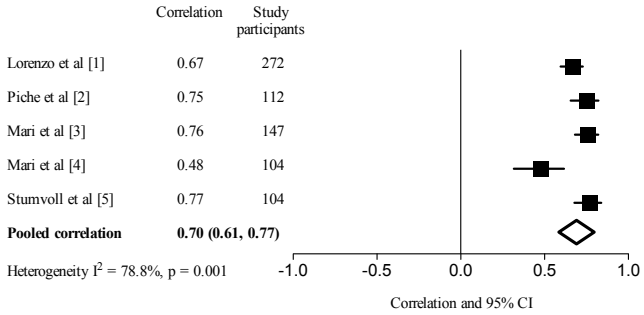

OGTT-based indices
Stumvoll MCR [10]
OGIS [11]
Matsuda [26]
Stumvoll ISI [10]
Gutt [34]
Belfiore [35]
Cederholm [36]
AUC insulin [37]
Glucose (120 min) [38]
Insulin (120 min) [39]
Fasting indices
Revised QUICKI [40]
QUICKI [41]
FIRI [42]
HOMA-%S [30]
HOMA-IR [30]
Fasting insulin [39]
McAuley [43]
G_0 / I_0 [44]
Fasting glucose [45]
I_0 / G_0 [46]
-1.0
-0.5
0.0
0.5
1.0
Strength of pooled correlation (95% CI)

ESM Fig. 1 Flow diagram of the search and selection process

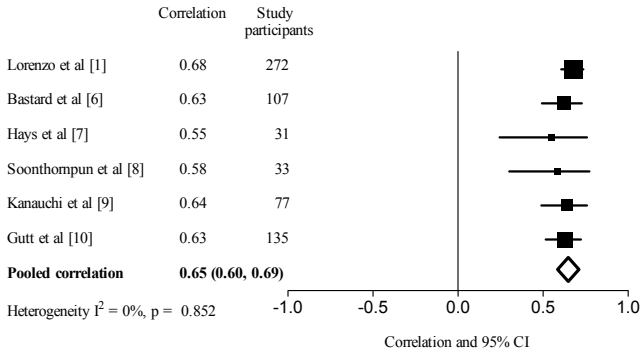


ESM Fig. 2 Meta-analyses of correlation coefficients between OGTT-based surrogate measures of insulin sensitivity and the hyperinsulinaemic euglycaemic clamp

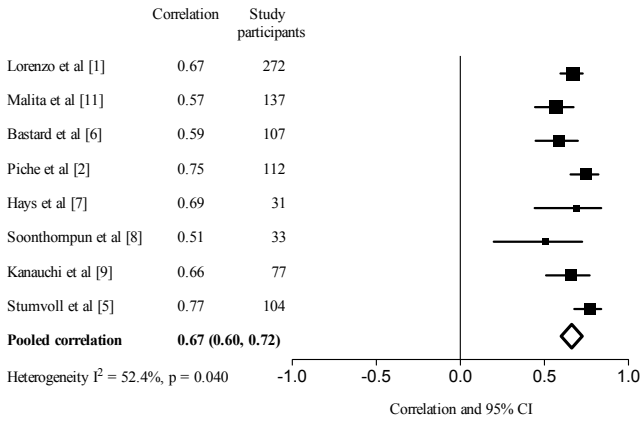
a) Stumvoll MCR



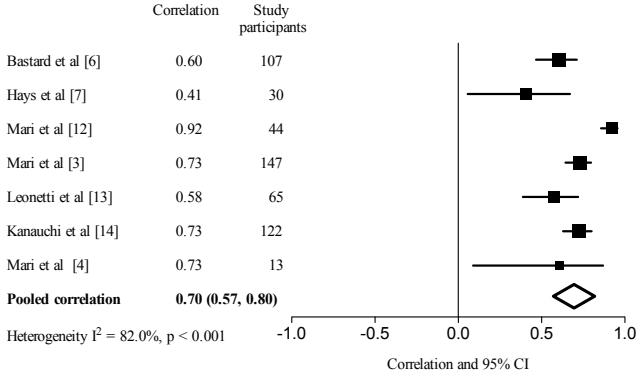
b) Gutt



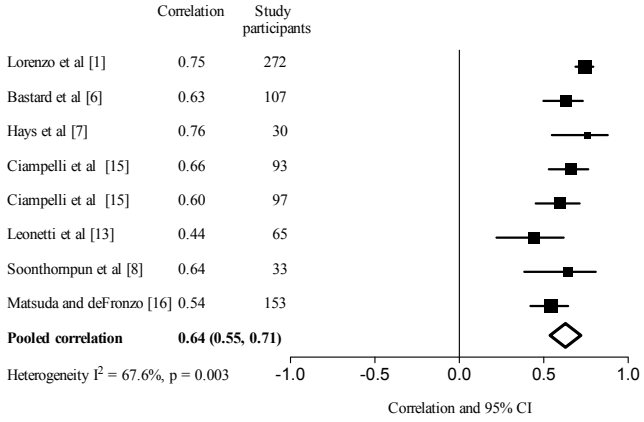
c) Stumvoll ISI



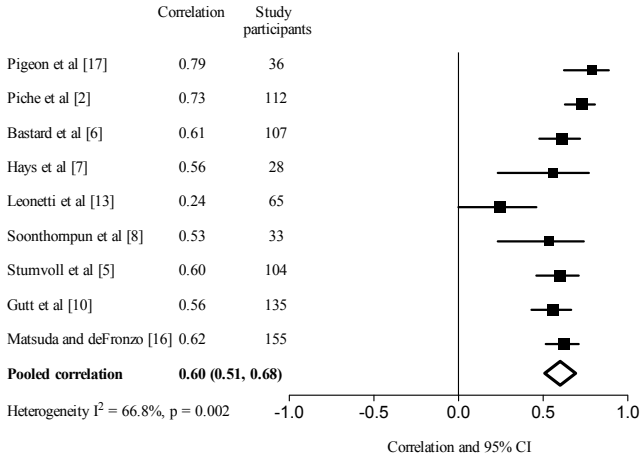
d) OGIS



e) Belfiore

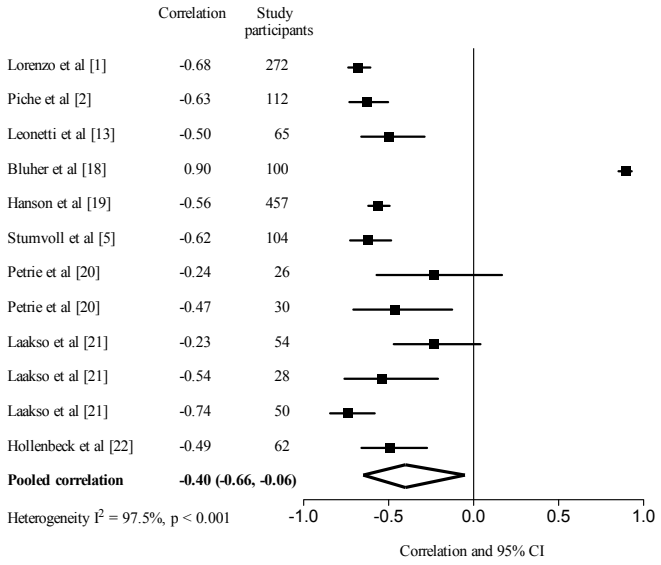


f) Cederholm

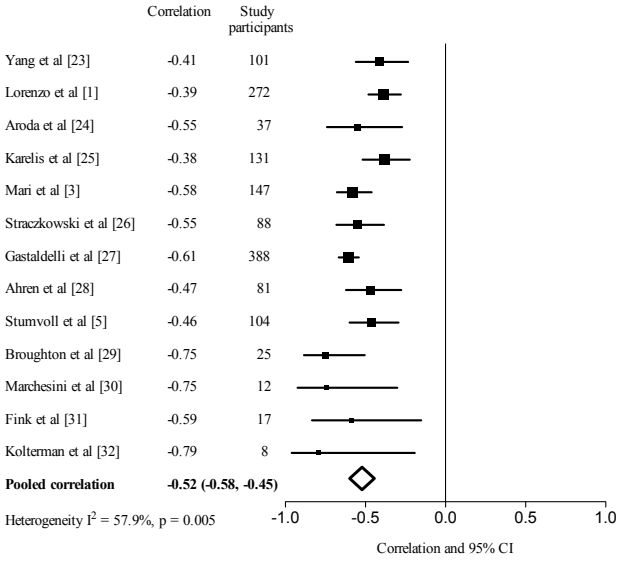


ESM Fig. 2 (continued)

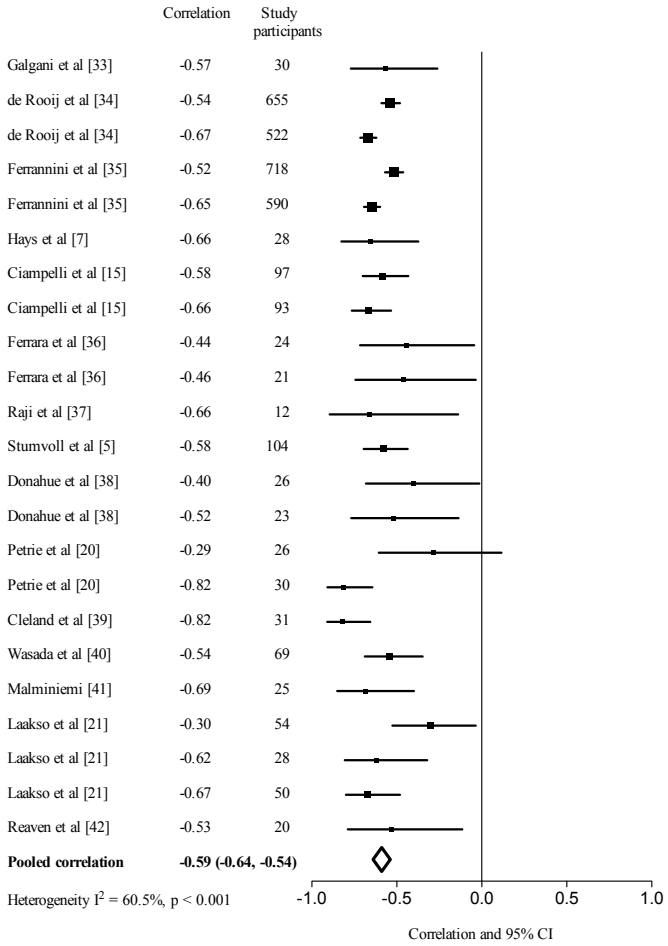
g) Insulin (120 min)



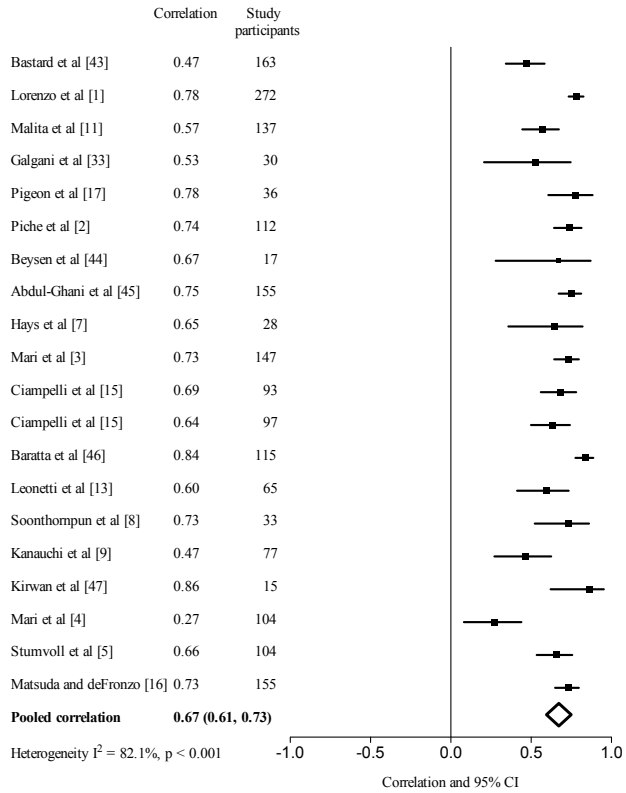
h) Glucose (120 min)



i) AUC insulin



j) Matsuda



References

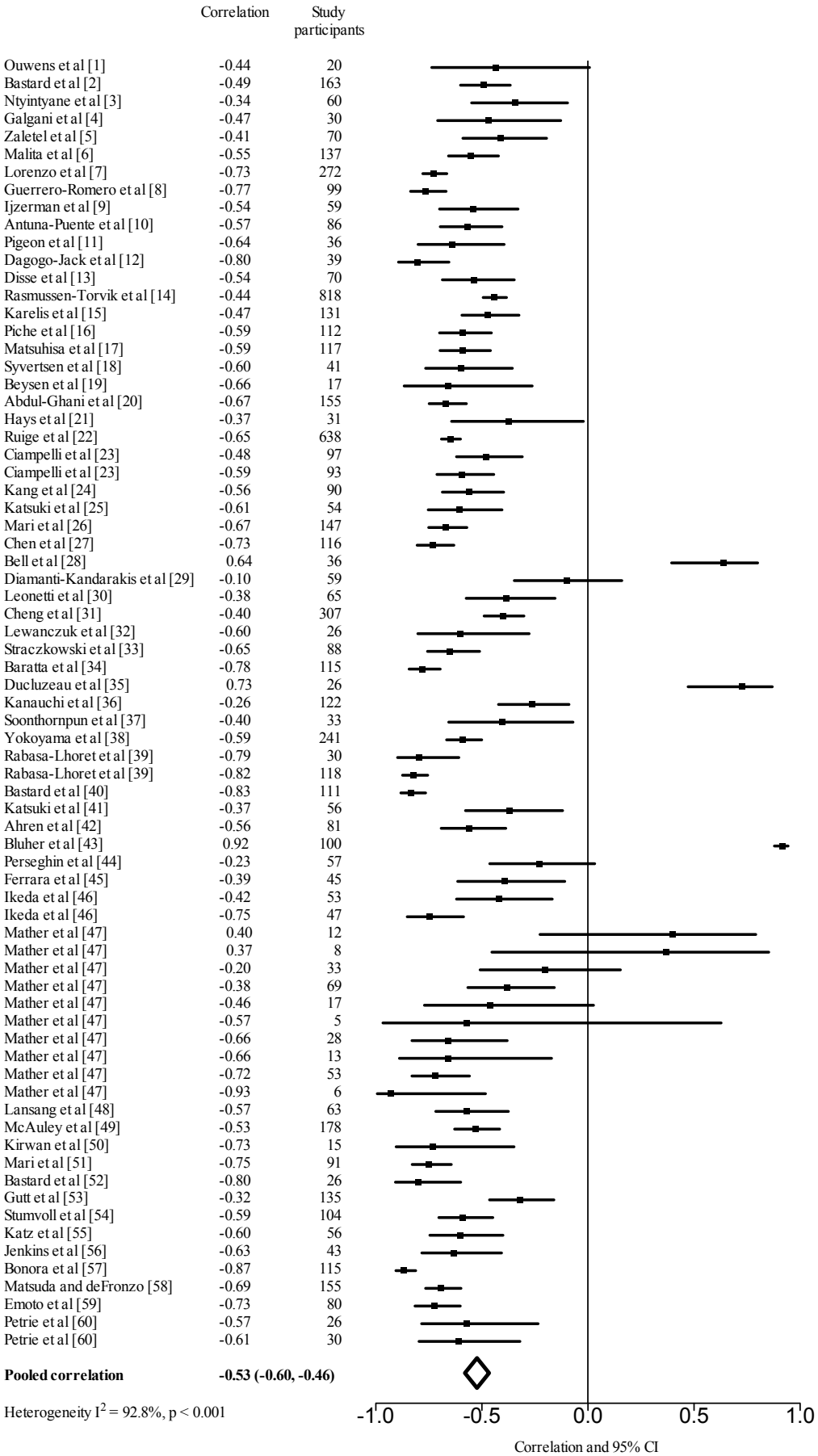
1. Lorenzo C, Haffner SM, Stancakova A, Laakso M (2010) Relation of direct and surrogate measures of insulin resistance to cardiovascular risk factors in nondiabetic finnish offspring of type 2 diabetic individuals. J Clin Endocrinol Metab 95: 5082-5090
2. Piche ME, Lemieux S, Corneau L, Nadeau A, Bergeron J, Weisnagel SJ (2007) Measuring insulin sensitivity in postmenopausal women covering a range of glucose tolerance: comparison of indices derived from the oral glucose tolerance test with the euglycemic-hyperinsulinemic clamp. Metabolism 56: 1159-1166
3. Mari A, Pacini G, Brazzale AR, Ahren B (2005) Comparative evaluation of simple insulin sensitivity methods based on the oral glucose tolerance test. Diabetologia 48: 748-751
4. Mari A, Pacini G, Murphy E, Ludvik B, Nolan JJ (2001) A model-based method for assessing insulin sensitivity from the oral glucose tolerance test. Diabetes Care 24: 539-548
5. Stumvoll M, Mitrakou A, Pimenta W, et al. (2000) Use of the oral glucose tolerance test to assess insulin release and insulin sensitivity. Diabetes Care 23: 295-301
6. Bastard JP, Vandernotte JM, Faraj M, et al. (2007) Relationship between the hyperinsulinemic-euglycaemic clamp and a new simple index assessing insulin sensitivity in overweight and obese postmenopausal women. Diabetes Metab 33: 261-268
7. Hays NP, Starling RD, Sullivan DH, Fluckey JD, Coker RH, Evans WJ (2006) Comparison of insulin sensitivity assessment indices with euglycemic-hyperinsulinemic clamp data after a dietary and exercise intervention in older adults. Metabolism 55: 525-532
8. Soonthornpun S, Setasuban W, Thamprasit A, Chayanunnukul W, Rattarasarn C, Geater A (2003) Novel insulin sensitivity index derived from oral glucose tolerance test. J Clin Endocrinol Metab 88: 1019-1023
9. Kanauchi M, Tsujimoto N, Hashimoto T (2002) Validation of simple indices to assess insulin sensitivity based on the oral glucose tolerance test in the Japanese population. Diabetes Res Clin Pract 55: 229-235
10. Gutt M, Davis CL, Spitzer SB, et al. (2000) Validation of the insulin sensitivity index (ISI(0,120)): comparison with other measures. Diabetes Res Clin Pract 47: 177-184
11. Malita FM, Messier V, Lavoie JM, Bastard JP, Rabasa-Lhoret R, Karelis AD (2010) Comparison between several insulin sensitivity indices and metabolic risk factors in overweight and obese postmenopausal women: a MONET study. Nutr Metab Cardiovasc Dis 20: 173-179
12. Mari A, Manco M, Guidone C, et al. (2006) Restoration of normal glucose tolerance in severely obese patients after bilio-pancreatic diversion: role of insulin sensitivity and beta cell function. Diabetologia 49: 2136-2143
13. Leonetti F, Iacobellis G, Zappaterreno A, et al. (2004) Insulin sensitivity assessment in uncomplicated obese women: comparison of indices from fasting and oral glucose load with euglycemic hyperinsulinemic clamp. Nutr Metab Cardiovasc Dis 14: 366-372
14. Kanauchi M (2003) Validation of the oral glucose insulin sensitivity index to assess insulin sensitivity in Japanese subjects for use in clinical practice. Eur J Clin Invest 33: 1022-1023
15. Ciampelli M, Leoni F, Cucinelli F, et al. (2005) Assessment of insulin sensitivity from measurements in the fasting state and during an oral glucose tolerance test in polycystic ovary syndrome and menopausal patients. J Clin Endocrinol Metab 90: 1398-1406
16. Matsuda M, DeFronzo RA (1999) Insulin sensitivity indices obtained from oral glucose tolerance testing: comparison with the euglycemic insulin clamp. Diabetes Care 22: 1462-1470
17. Pigeon E, Riou ME, St-Onge J, et al. (2009) Validation of a simple index (SIisOGTT) of insulin sensitivity in a population of sedentary men. Diabetes Metab 35: 398-403

18. Bluher M, Kratzsch J, Paschke R (2001) Plasma levels of tumor necrosis factor-alpha, angiotensin II, growth hormone, and IGF-I are not elevated in insulin-resistant obese individuals with impaired glucose tolerance. Diabetes Care 24: 328-334
19. Hanson RL, Pratley RE, Bogardus C, et al. (2000) Evaluation of simple indices of insulin sensitivity and insulin secretion for use in epidemiologic studies. Am J Epidemiol 151: 190-198
20. Petrie JR, Morris AD, Dorrian CA, Small M, Connell JM (1997) Specific insulin assays, insulin sensitivity and blood pressure. QJM 90: 465-475
21. Laakso M (1993) How good a marker is insulin level for insulin resistance? Am J Epidemiol 137: 959-965
22. Hollenbeck CB, Chen N, Chen YD, Reaven GM (1984) Relationship between the plasma insulin response to oral glucose and insulin-stimulated glucose utilization in normal subjects. Diabetes 33: 460-463
23. Yang S, Li Q, Song Y, et al. (2011) Serum complement C3 has a stronger association with insulin resistance than high-sensitivity C-reactive protein in women with polycystic ovary syndrome. Fertil Steril 95: 1749-1753
24. Aroda V, Ciaraldi TP, Chang SA, Dahan MH, Chang RJ, Henry RR (2008) Circulating and cellular adiponectin in polycystic ovary syndrome: relationship to glucose tolerance and insulin action. Fertil Steril 89: 1200-1208
25. Karelis AD, Pasternyk SM, Messier L, et al. (2007) Relationship between insulin sensitivity and the triglyceride-HDL-C ratio in overweight and obese postmenopausal women: a MONET study. Appl Physiol Nutr Metab 32: 1089-1096
26. Straczkowski M, Stepien A, Kowalska I, Kinalska I (2004) Comparison of simple indices of insulin sensitivity using the euglycemic hyperinsulinemic clamp technique. Med Sci Monit 10: CR480-484
27. Gastaldelli A, Ferrannini E, Miyazaki Y, Matsuda M, DeFronzo RA (2004) Beta-cell dysfunction and glucose intolerance: results from the San Antonio metabolism (SAM) study. Diabetologia 47: 31-39
28. Ahren B, Larsson H (2002) Quantification of insulin secretion in relation to insulin sensitivity in nondiabetic postmenopausal women. Diabetes 51 Suppl 1: S202-211
29. Broughton DL, Webster J, Taylor R (1992) Insulin sensitivity and secretion in healthy elderly human subjects with 'abnormal' glucose tolerance. Eur J Clin Invest 22: 582-590
30. Marchesini G, Bianchi GP, Forlani G, et al. (1987) Insulin resistance is the main determinant of impaired glucose tolerance in patients with liver cirrhosis. Dig Dis Sci 32: 1118-1124
31. Fink RI, Kolterman OG, Griffin J, Olefsky JM (1983) Mechanisms of insulin resistance in aging. J Clin Invest 71: 1523-1535
32. Kolterman OG, Gray RS, Griffin J, et al. (1981) Receptor and postreceptor defects contribute to the insulin resistance in noninsulin-dependent diabetes mellitus. J Clin Invest 68: 957-969
33. Galgani JE, de Jonge L, Rood JC, Smith SR, Young AA, Ravussin E (2010) Urinary C-peptide excretion: a novel alternate measure of insulin sensitivity in physiological conditions. Obesity (Silver Spring) 18: 1852-1857
34. de Rooij SR, Dekker JM, Kozakova M, et al. (2009) Fasting insulin has a stronger association with an adverse cardiometabolic risk profile than insulin resistance: the RISC study. Eur J Endocrinol 161: 223-230
35. Ferrannini E, Balkau B, Coppack SW, et al. (2007) Insulin resistance, insulin response, and obesity as indicators of metabolic risk. J Clin Endocrinol Metab 92: 2885-2892

36. Ferrara CM, Goldberg AP (2001) Limited value of the homeostasis model assessment to predict insulin resistance in older men with impaired glucose tolerance. Diabetes Care 24: 245-249
37. Raji A, Seely EW, Arky RA, Simonson DC (2001) Body fat distribution and insulin resistance in healthy Asian Indians and Caucasians. J Clin Endocrinol Metab 86: 5366-5371
38. Donahue RP, Prineas RJ, Donahue RD, et al. (1999) Is fasting leptin associated with insulin resistance among nondiabetic individuals? The Miami Community Health Study. Diabetes Care 22: 1092-1096
39. Cleland SJ, Petrie JR, Morris AD, Ueda S, Dorrian CA, Connell JM (1996) FIRI: a fair insulin resistance index? Lancet 347: 770
40. Wasada T, Arii H, Kuroki H, et al. (1995) The relationship between insulin resistance and insulin secretion in Japanese subjects with borderline glucose intolerance. Diabetes Res Clin Pract 30: 53-57
41. Malminiemi K (1995) Association between serum lipids, glucose tolerance, and insulin sensitivity during 12 months of celiprolol treatment. Cardiovasc Drugs Ther 9: 295-304
42. Reaven GM, Moore J, Greenfield M (1983) Quantification of insulin secretion and in vivo insulin action in nonobese and moderately obese individuals with normal glucose tolerance. Diabetes 32: 600-604
43. Bastard JP, Lavoie ME, Messier V, Prud'homme D, Rabasa-Lhoret R (2012) Evaluation of two new surrogate indices including parameters not using insulin to assess insulin sensitivity/resistance in non-diabetic postmenopausal women: a MONET group study. Diabetes Metab 38: 258-263
44. Beysen C, Murphy EJ, McLaughlin T, et al. (2007) Whole-body glycolysis measured by the deuterated-glucose disposal test correlates highly with insulin resistance in vivo. Diabetes Care 30: 1143-1149
45. Abdul-Ghani MA, Matsuda M, Balas B, DeFronzo RA (2007) Muscle and liver insulin resistance indexes derived from the oral glucose tolerance test. Diabetes Care 30: 89-94
46. Baratta R, Amato S, Degano C, et al. (2004) Adiponectin relationship with lipid metabolism is independent of body fat mass: evidence from both cross-sectional and intervention studies. J Clin Endocrinol Metab 89: 2665-2671
47. Kirwan JP, Huston-Presley L, Kalhan SC, Catalano PM (2001) Clinically useful estimates of insulin sensitivity during pregnancy: validation studies in women with normal glucose tolerance and gestational diabetes mellitus. Diabetes Care 24: 1602-1607

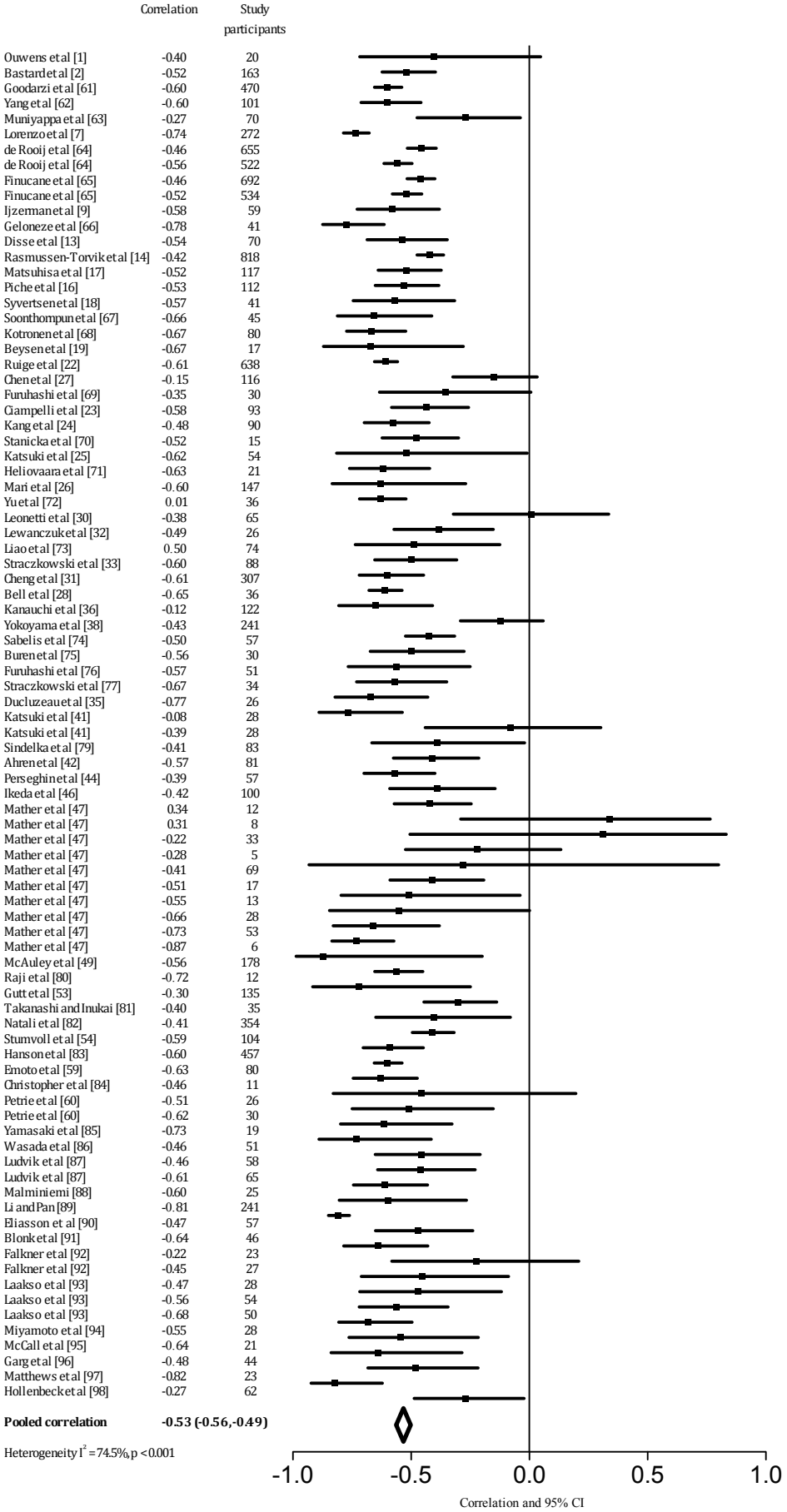
ESM Fig. 3 Meta-analyses of correlation coefficients between fasting surrogate measures of insulin sensitivity and the hyperinsulinaemic euglycaemic clamp

a) HOMA-IR



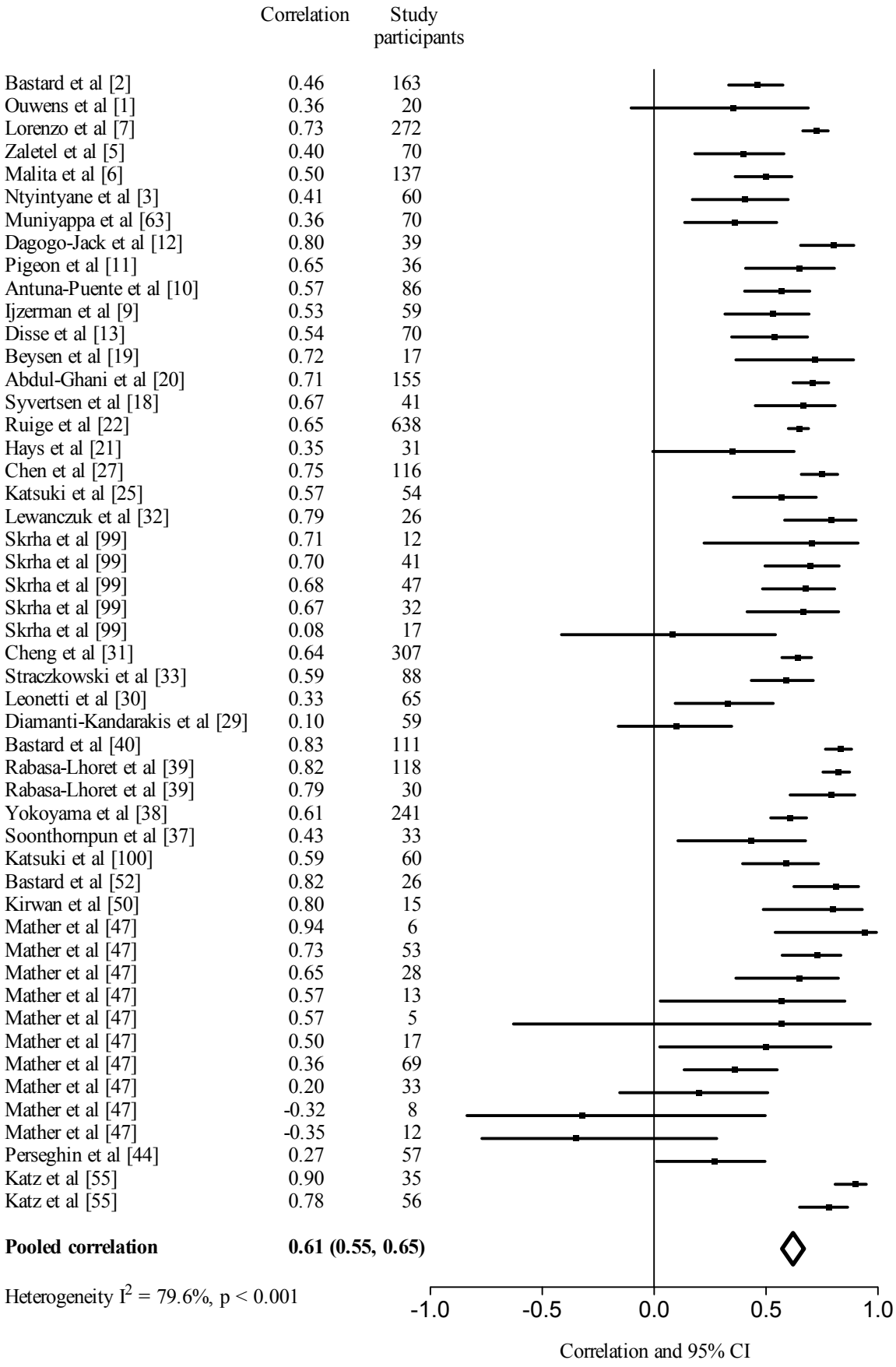
ESM Fig. 3 (continued)

b) Fasting insulin



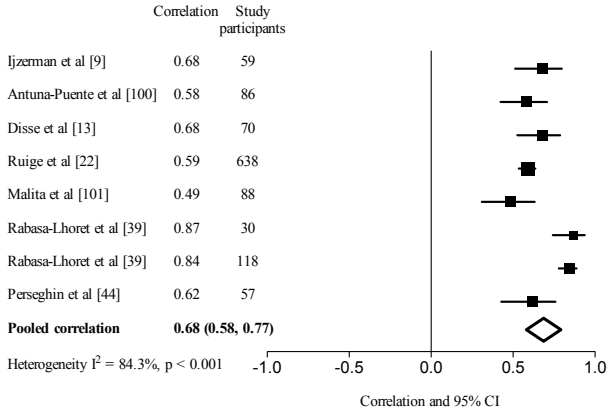
ESM Fig. 3 (continued)

c) QUICKI

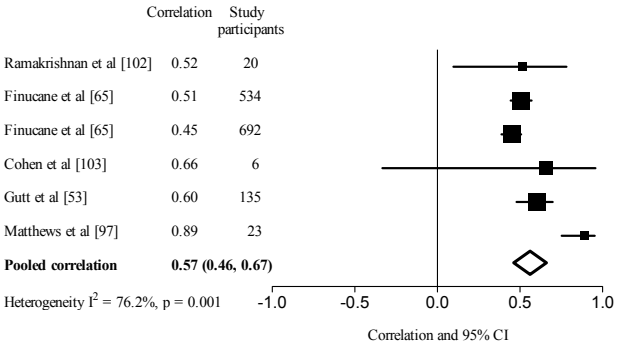


ESM Fig. 3 (continued)

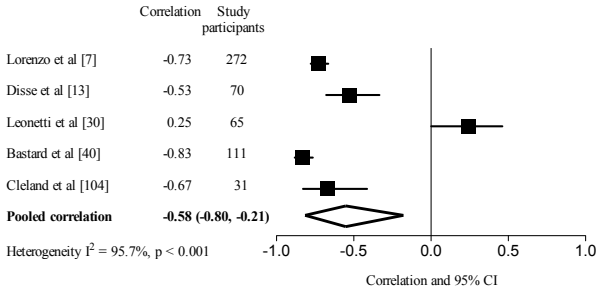
d) Revised QUICKI



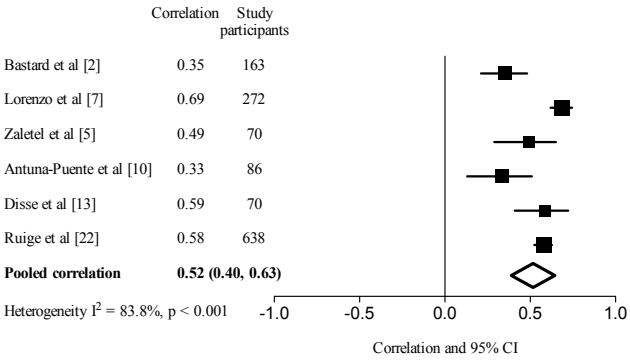
e) HOMA-%S



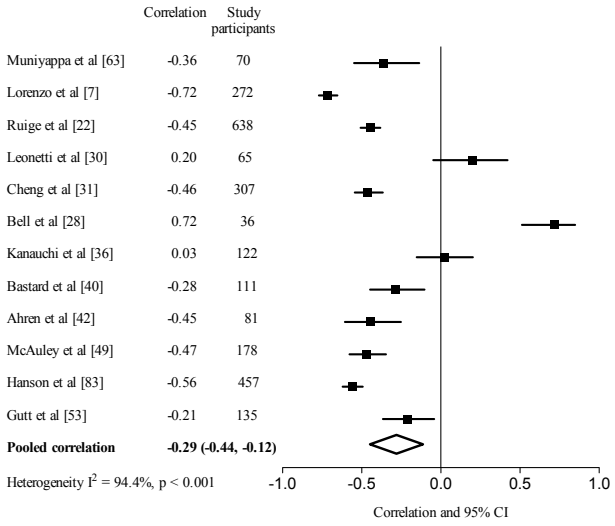
f) FIRI



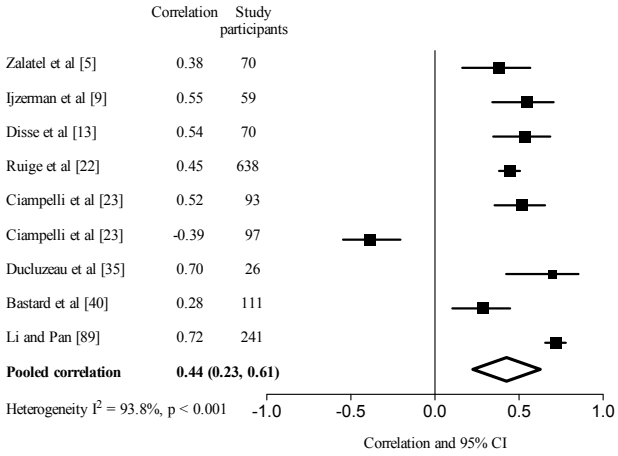
g) McAuley



h) I_0/G_0

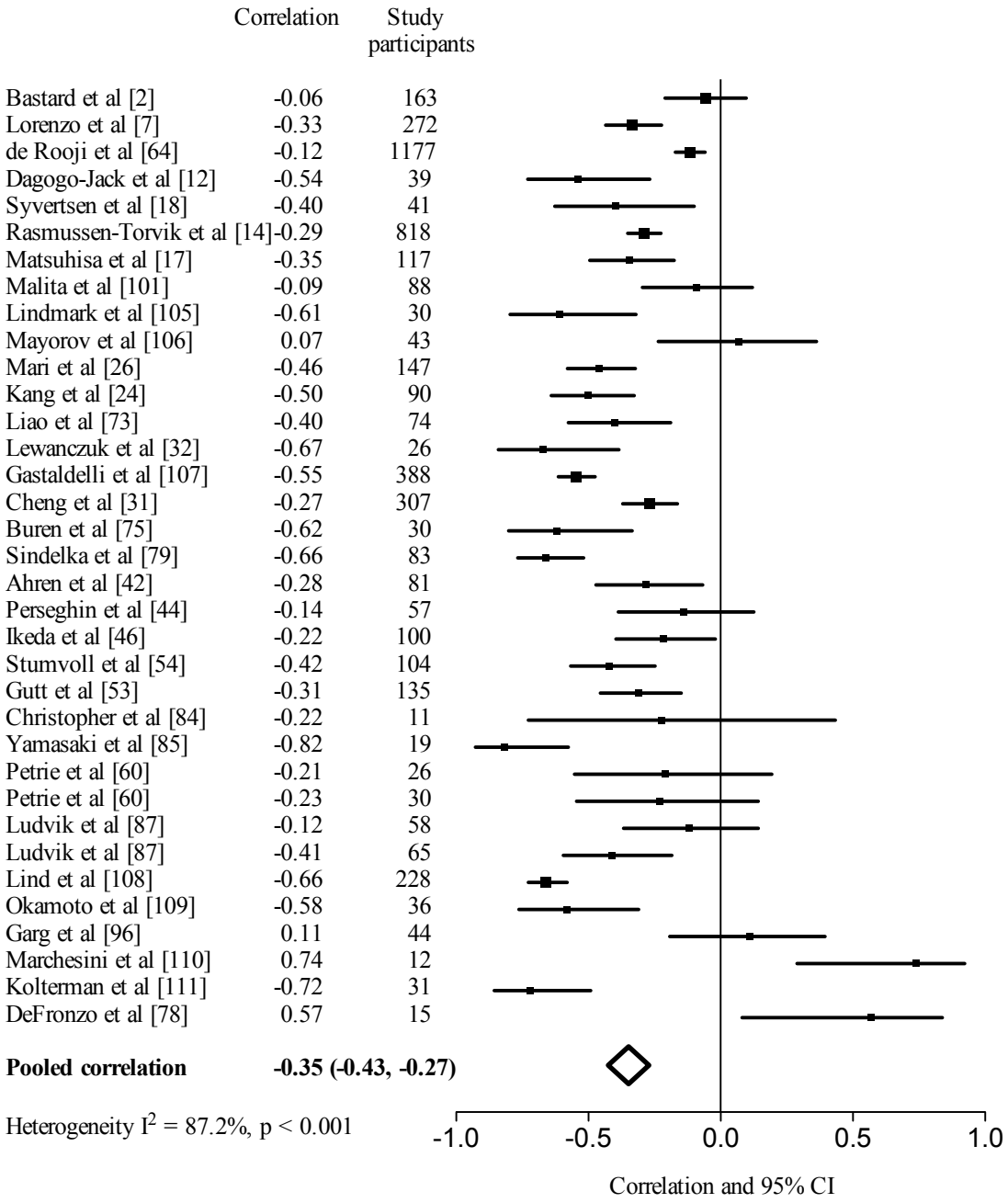


i) G_0/I_0



ESM Fig. 3 (continued)

j) Fasting glucose



References

1. Ouwens DM, Bekaert M, Lapauw B, et al. (2012) Chemerin as biomarker for insulin sensitivity in males without typical characteristics of metabolic syndrome. Arch Physiol Biochem 118: 135-138
2. Bastard JP, Lavoie ME, Messier V, Prud'homme D, Rabasa-Lhoret R (2012) Evaluation of two new surrogate indices including parameters not using insulin to assess insulin sensitivity/resistance in non-diabetic postmenopausal women: a MONET group study. Diabetes Metab 38: 258-263
3. Ntyintyane L, Panz V, Raal F, Gill G (2010) Comparison between surrogate indices of insulin sensitivity and resistance, and the hyperinsulinaemic euglycaemic glucose clamp in urban South African blacks with and without coronary artery disease. Diab Vasc Dis Res 7: 151-157
4. Galgani JE, de Jonge L, Rood JC, Smith SR, Young AA, Ravussin E (2010) Urinary C-peptide excretion: a novel alternate measure of insulin sensitivity in physiological conditions. Obesity (Silver Spring) 18: 1852-1857
5. Zaletel J, Barlovic DP, Prezelj J (2010) Adiponectin-leptin ratio: a useful estimate of insulin resistance in patients with Type 2 diabetes. J Endocrinol Invest 33: 514-518
6. Malita FM, Messier V, Lavoie JM, Bastard JP, Rabasa-Lhoret R, Karelis AD (2010) Comparison between several insulin sensitivity indices and metabolic risk factors in overweight and obese postmenopausal women: a MONET study. Nutr Metab Cardiovasc Dis 20: 173-179
7. Lorenzo C, Haffner SM, Stancakova A, Laakso M (2010) Relation of direct and surrogate measures of insulin resistance to cardiovascular risk factors in nondiabetic finnish offspring of type 2 diabetic individuals. J Clin Endocrinol Metab 95: 5082-5090
8. Guerrero-Romero F, Simental-Mendia LE, Gonzalez-Ortiz M, et al. (2010) The product of triglycerides and glucose, a simple measure of insulin sensitivity. Comparison with the euglycemic-hyperinsulinemic clamp. J Clin Endocrinol Metab 95: 3347-3351
9. Ijzerman RG, Stehouwer CD, Serne EH, et al. (2009) Incorporation of the fasting free fatty acid concentration into quantitative insulin sensitivity check index improves its association with insulin sensitivity in adults, but not in children. Eur J Endocrinol 160: 59-64
10. Antuna-Puente B, Disse E, Faraj M, et al. (2009) Evaluation of insulin sensitivity with a new lipid-based index in non-diabetic postmenopausal overweight and obese women before and after a weight loss intervention. Eur J Endocrinol 161: 51-56
11. Pigeon E, Riou ME, St-Onge J, et al. (2009) Validation of a simple index (SIisOGTT) of insulin sensitivity in a population of sedentary men. Diabetes Metab 35: 398-403
12. Dagogo-Jack S, Askari H, Tykodi G (2009) Glucoregulatory physiology in subjects with low-normal, high-normal, or impaired fasting glucose. J Clin Endocrinol Metab 94: 2031-2036
13. Disse E, Bastard JP, Bonnet F, et al. (2008) A lipid-parameter-based index for estimating insulin sensitivity and identifying insulin resistance in a healthy population. Diabetes Metab 34: 457-463
14. Rasmussen-Torvik LJ, Pankow JS, Jacobs DR, et al. (2007) Heritability and genetic correlations of insulin sensitivity measured by the euglycaemic clamp. Diabet Med 24: 1286-1289
15. Karelis AD, Pasternyk SM, Messier L, et al. (2007) Relationship between insulin sensitivity and the triglyceride-HDL-C ratio in overweight and obese postmenopausal women: a MONET study. Appl Physiol Nutr Metab 32: 1089-1096
16. Piche ME, Lemieux S, Corneau L, Nadeau A, Bergeron J, Weisnagel SJ (2007) Measuring insulin sensitivity in postmenopausal women covering a range of glucose tolerance: comparison of indices derived from the oral glucose tolerance test with the euglycemic-hyperinsulinemic clamp. Metabolism 56: 1159-1166
17. Matsuhisa M, Yamasaki Y, Emoto M, et al. (2007) A novel index of insulin resistance determined from the homeostasis model assessment index and adiponectin levels in Japanese subjects. Diabetes Res Clin Pract 77: 151-154

18. Syvertsen C, Halse J, Hoivik HO, et al. (2007) The effect of 6 months supplementation with conjugated linoleic acid on insulin resistance in overweight and obese. Int J Obes (Lond) 31: 1148-1154
19. Beysen C, Murphy EJ, McLaughlin T, et al. (2007) Whole-body glycolysis measured by the deuterated-glucose disposal test correlates highly with insulin resistance in vivo. Diabetes Care 30: 1143-1149
20. Abdul-Ghani MA, Matsuda M, Balas B, DeFronzo RA (2007) Muscle and liver insulin resistance indexes derived from the oral glucose tolerance test. Diabetes Care 30: 89-94
21. Hays NP, Starling RD, Sullivan DH, Fluckey JD, Coker RH, Evans WJ (2006) Comparison of insulin sensitivity assessment indices with euglycemic-hyperinsulinemic clamp data after a dietary and exercise intervention in older adults. Metabolism 55: 525-532
22. Ruige JB, Mertens IL, Bartholomeeusen E, Dirinck E, Ferrannini E, Van Gaal LF (2006) Fasting-based estimates of insulin sensitivity in overweight and obesity: a critical appraisal. Obesity (Silver Spring) 14: 1250-1256
23. Ciampelli M, Leoni F, Cucinelli F, et al. (2005) Assessment of insulin sensitivity from measurements in the fasting state and during an oral glucose tolerance test in polycystic ovary syndrome and menopausal patients. J Clin Endocrinol Metab 90: 1398-1406
24. Kang ES, Yun YS, Park SW, et al. (2005) Limitation of the validity of the homeostasis model assessment as an index of insulin resistance in Korea. Metabolism 54: 206-211
25. Katsuki A, Urakawa H, Gabazza EC, et al. (2005) Quantitative insulin sensitivity check index is a useful indicator of insulin resistance in Japanese metabolically obese, normal-weight subjects with normal glucose tolerance. Endocr J 52: 253-257
26. Mari A, Pacini G, Brazzale AR, Ahren B (2005) Comparative evaluation of simple insulin sensitivity methods based on the oral glucose tolerance test. Diabetologia 48: 748-751
27. Chen H, Sullivan G, Quon MJ (2005) Assessing the predictive accuracy of QUICKI as a surrogate index for insulin sensitivity using a calibration model. Diabetes 54: 1914-1925
28. Bell D, McAuley KA, Mann J, Murphy E, Williams S (2004) The hypertriglyceridaemic waist in New Zealand Maori. Asia Pac J Clin Nutr 13: 74-77
29. Diamanti-Kandarakis E, Kouli C, Alexandraki K, Spina G (2004) Failure of mathematical indices to accurately assess insulin resistance in lean, overweight, or obese women with polycystic ovary syndrome. J Clin Endocrinol Metab 89: 1273-1276
30. Leonetti F, Iacobellis G, Zappaterreno A, et al. (2004) Insulin sensitivity assessment in uncomplicated obese women: comparison of indices from fasting and oral glucose load with euglycemic hyperinsulinemic clamp. Nutr Metab Cardiovasc Dis 14: 366-372
31. Cheng C, Campbell KL, Kushner H, Falkner BE (2004) Correlation of oral glucose tolerance test-derived estimates of insulin sensitivity with insulin clamp measurements in an African-American cohort. Metabolism 53: 1107-1112
32. Lewanczuk RZ, Paty BW, Toth EL (2004) Comparison of the [13C]glucose breath test to the hyperinsulinemic-euglycemic clamp when determining insulin resistance. Diabetes Care 27: 441-447
33. Straczkowski M, Stepien A, Kowalska I, Kinalska I (2004) Comparison of simple indices of insulin sensitivity using the euglycemic hyperinsulinemic clamp technique. Med Sci Monit 10: CR480-484
34. Baratta R, Amato S, Degano C, et al. (2004) Adiponectin relationship with lipid metabolism is independent of body fat mass: evidence from both cross-sectional and intervention studies. J Clin Endocrinol Metab 89: 2665-2671
35. Ducluzeau PH, Cousin P, Malvoisin E, et al. (2003) Glucose-to-insulin ratio rather than sex hormone-binding globulin and adiponectin levels is the best predictor of insulin resistance in nonobese women with polycystic ovary syndrome. J Clin Endocrinol Metab 88: 3626-3631
36. Kanauchi M (2003) Validation of the oral glucose insulin sensitivity index to assess insulin sensitivity in Japanese subjects for use in clinical practice. Eur J Clin Invest 33: 1022-1023

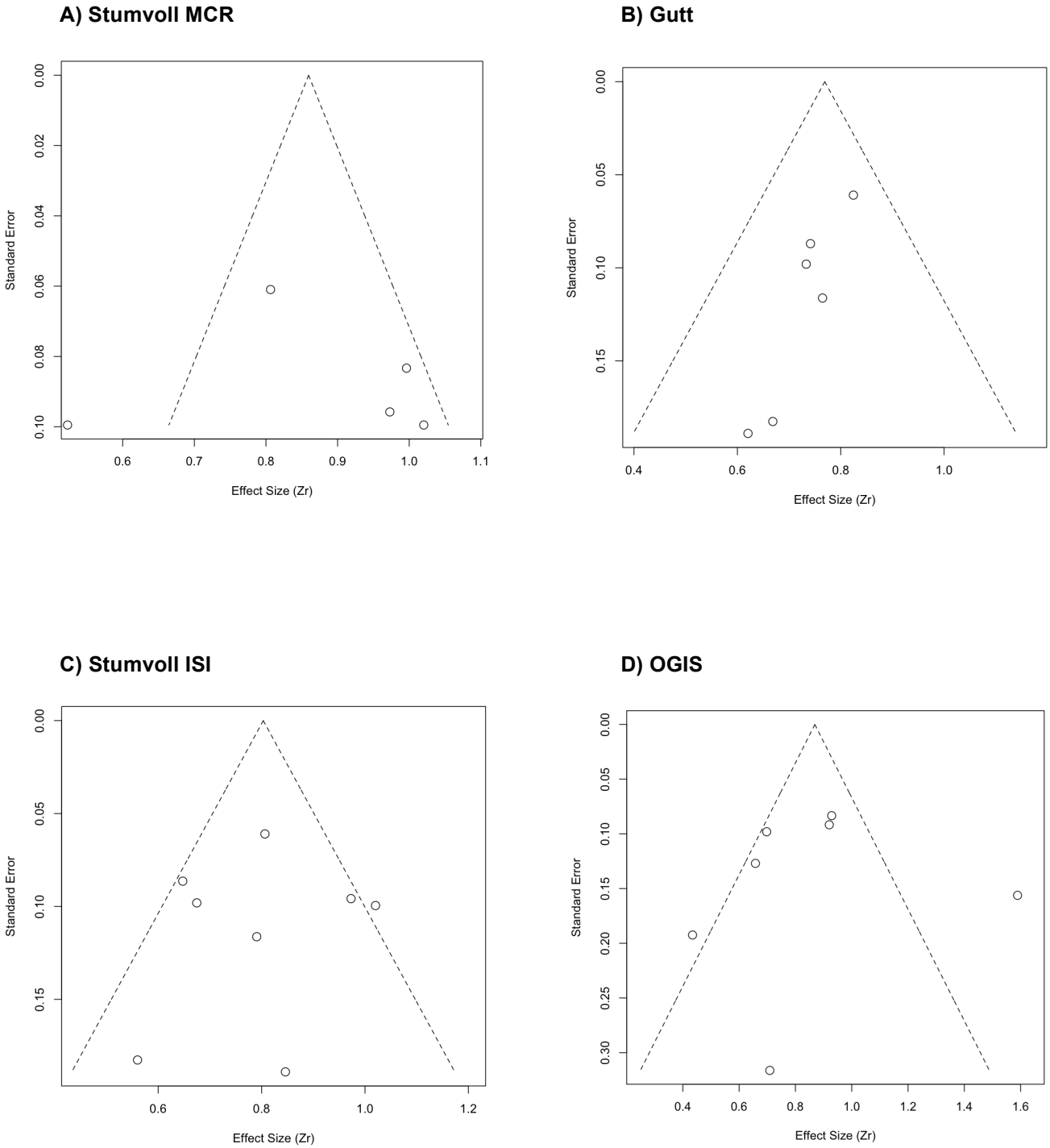
37. Soonthornpun S, Setasuban W, Thamprasit A, Chayanunnukul W, Rattarasarn C, Geater A (2003) Novel insulin sensitivity index derived from oral glucose tolerance test. J Clin Endocrinol Metab 88: 1019-1023
38. Yokoyama H, Emoto M, Fujiwara S, et al. (2003) Quantitative insulin sensitivity check index and the reciprocal index of homeostasis model assessment in normal range weight and moderately obese type 2 diabetic patients. Diabetes Care 26: 2426-2432
39. Rabasa-Lhoret R, Bastard JP, Jan V, et al. (2003) Modified quantitative insulin sensitivity check index is better correlated to hyperinsulinemic glucose clamp than other fasting-based index of insulin sensitivity in different insulin-resistant states. J Clin Endocrinol Metab 88: 4917-4923
40. Bastard JP, Rabasa-Lhoret R, Maachi M, et al. (2003) What kind of simple fasting index should be used to estimate insulin sensitivity in humans? Diabetes Metab 29: 285-288
41. Katsuki A, Sumida Y, Urakawa H, et al. (2002) Neither homeostasis model assessment nor quantitative insulin sensitivity check index can predict insulin resistance in elderly patients with poorly controlled type 2 diabetes mellitus. J Clin Endocrinol Metab 87: 5332-5335
42. Ahren B, Larsson H (2002) Quantification of insulin secretion in relation to insulin sensitivity in nondiabetic postmenopausal women. Diabetes 51 Suppl 1: S202-211
43. Bluher M, Kratzsch J, Paschke R (2001) Plasma levels of tumor necrosis factor-alpha, angiotensin II, growth hormone, and IGF-I are not elevated in insulin-resistant obese individuals with impaired glucose tolerance. Diabetes Care 24: 328-334
44. Perseghin G, Caumo A, Caloni M, Testolin G, Luzi L (2001) Incorporation of the fasting plasma FFA concentration into QUICKI improves its association with insulin sensitivity in nonobese individuals. J Clin Endocrinol Metab 86: 4776-4781
45. Ferrara CM, Goldberg AP (2001) Limited value of the homeostasis model assessment to predict insulin resistance in older men with impaired glucose tolerance. Diabetes Care 24: 245-249
46. Ikeda Y, Suehiro T, Nakamura T, Kumon Y, Hashimoto K (2001) Clinical significance of the insulin resistance index as assessed by homeostasis model assessment. Endocr J 48: 81-86
47. Mather KJ, Hunt AE, Steinberg HO, et al. (2001) Repeatability characteristics of simple indices of insulin resistance: implications for research applications. J Clin Endocrinol Metab 86: 5457-5464
48. Lansang MC, Williams GH, Carroll JS (2001) Correlation between the glucose clamp technique and the homeostasis model assessment in hypertension. Am J Hypertens 14: 51-53
49. McAuley KA, Williams SM, Mann JI, et al. (2001) Diagnosing insulin resistance in the general population. Diabetes Care 24: 460-464
50. Kirwan JP, Huston-Presley L, Kalhan SC, Catalano PM (2001) Clinically useful estimates of insulin sensitivity during pregnancy: validation studies in women with normal glucose tolerance and gestational diabetes mellitus. Diabetes Care 24: 1602-1607
51. Mari A, Pacini G, Murphy E, Ludvik B, Nolan JJ (2001) A model-based method for assessing insulin sensitivity from the oral glucose tolerance test. Diabetes Care 24: 539-548
52. Bastard JP, Robert JJ, Jardel C, Bruckert E, Grimaldi A, Hainque B (2001) Is quantitative insulin sensitivity check index, a fair insulin sensitivity index in humans? Diabetes Metab 27: 69-70
53. Gutt M, Davis CL, Spitzer SB, et al. (2000) Validation of the insulin sensitivity index (ISI(0,120)): comparison with other measures. Diabetes Res Clin Pract 47: 177-184
54. Stumvoll M, Mitrakou A, Pimenta W, et al. (2000) Use of the oral glucose tolerance test to assess insulin release and insulin sensitivity. Diabetes Care 23: 295-301
55. Katz A, Nambi SS, Mather K, et al. (2000) Quantitative insulin sensitivity check index: a simple, accurate method for assessing insulin sensitivity in humans. J Clin Endocrinol Metab 85: 2402-2410
56. Jenkins AB, Samaras K, Carey DG, Kelly P, Campbell LV (2000) Improved indices of insulin resistance and insulin secretion for use in genetic and population studies of type 2 diabetes mellitus. Twin Res 3: 148-151

57. Bonora E, Targher G, Alberiche M, et al. (2000) Homeostasis model assessment closely mirrors the glucose clamp technique in the assessment of insulin sensitivity: studies in subjects with various degrees of glucose tolerance and insulin sensitivity. Diabetes Care 23: 57-63
58. Matsuda M, DeFronzo RA (1999) Insulin sensitivity indices obtained from oral glucose tolerance testing: comparison with the euglycemic insulin clamp. Diabetes Care 22: 1462-1470
59. Emoto M, Nishizawa Y, Maekawa K, et al. (1999) Homeostasis model assessment as a clinical index of insulin resistance in type 2 diabetic patients treated with sulfonylureas. Diabetes Care 22: 818-822
60. Petrie JR, Morris AD, Dorrian CA, Small M, Connell JM (1997) Specific insulin assays, insulin sensitivity and blood pressure. QJM 90: 465-475
61. Goodarzi MO, Cui J, Chen YD, Hsueh WA, Guo X, Rotter JI (2011) Fasting insulin reflects heterogeneous physiological processes: role of insulin clearance. Am J Physiol Endocrinol Metab 301: E402-408
62. Yang S, Li Q, Song Y, et al. (2011) Serum complement C3 has a stronger association with insulin resistance than high-sensitivity C-reactive protein in women with polycystic ovary syndrome. Fertil Steril 95: 1749-1753
63. Muniyappa R, Irving BA, Unni US, et al. (2010) Limited predictive ability of surrogate indices of insulin sensitivity/resistance in Asian-Indian men. Am J Physiol Endocrinol Metab 299: E1106-1112
64. de Rooij SR, Dekker JM, Kozakova M, et al. (2009) Fasting insulin has a stronger association with an adverse cardiometabolic risk profile than insulin resistance: the RISC study. Eur J Endocrinol 161: 223-230
65. Finucane FM, Luan J, Wareham NJ, et al. (2009) Correlation of the leptin:adiponectin ratio with measures of insulin resistance in non-diabetic individuals. Diabetologia 52: 2345-2349
66. Geloneze B, Pereira JA, Pareja JC, et al. (2009) Overcoming metabolic syndrome in severe obesity: adiponectin as a marker of insulin sensitivity and HDL-cholesterol improvements after gastric bypass. Arq Bras Endocrinol Metabol 53: 293-300
67. Soonthornpun S, Setasuban W, Thamprasit A (2007) Correlation between change in serum homocysteine levels during hyperinsulinemia and insulin sensitivity. J Med Assoc Thai 90: 1506-1511
68. Kotronen A, Vehkavaara S, Seppala-Lindroos A, Bergholm R, Yki-Jarvinen H (2007) Effect of liver fat on insulin clearance. Am J Physiol Endocrinol Metab 293: E1709-1715
69. Furuhashi M, Ura N, Higashiura K, et al. (2005) Low adiponectin level in young normotensive men with a family history of essential hypertension. Hypertens Res 28: 141-146
70. Stanicka S, Vondra K, Pelikanova T, Vlcek P, Hill M, Zamrazil V (2005) Insulin sensitivity and counter-regulatory hormones in hypothyroidism and during thyroid hormone replacement therapy. Clin Chem Lab Med 43: 715-720
71. Heliovaara MK, Teppo AM, Karonen SL, Tuominen JA, Ebeling P (2005) Plasma IL-6 concentration is inversely related to insulin sensitivity, and acute-phase proteins associate with glucose and lipid metabolism in healthy subjects. Diabetes Obes Metab 7: 729-736
72. Yu Y, Suo L, Yu H, Wang C, Tang H (2004) Insulin resistance and endothelial dysfunction in type 2 diabetes patients with or without microalbuminuria. Diabetes Res Clin Pract 65: 95-104
73. Liao Y, Kwon S, Shaughnessy S, et al. (2004) Critical evaluation of adult treatment panel III criteria in identifying insulin resistance with dyslipidemia. Diabetes Care 27: 978-983
74. Sabelis LW, Senden PJ, Zonderland ML, et al. (2003) Determinants of insulin sensitivity in chronic heart failure. Eur J Heart Fail 5: 759-765
75. Buren J, Lindmark S, Renstrom F, Eriksson JW (2003) In vitro reversal of hyperglycemia normalizes insulin action in fat cells from type 2 diabetes patients: is cellular insulin resistance caused by glucotoxicity in vivo? Metabolism 52: 239-245

76. Furuhashi M, Ura N, Higashiura K, Murakami H, Shimamoto K (2003) Circulating resistin levels in essential hypertension. Clin Endocrinol (Oxf) 59: 507-510
77. Straczkowski M, Kowalska I, Stepien A, et al. (2003) Insulin resistance in the first-degree relatives of persons with type 2 diabetes. Med Sci Monit 9: CR186-190
78. DeFronzo R, Deibert D, Hendler R, Felig P, Soman V (1979) Insulin sensitivity and insulin binding to monocytes in maturity-onset diabetes. J Clin Invest 63: 939-946
79. Sindelka G, Skrha J, Prazny M, Haas T (2002) Association of obesity, diabetes, serum lipids and blood pressure regulates insulin action. Physiol Res 51: 85-91
80. Raji A, Seely EW, Arky RA, Simonson DC (2001) Body fat distribution and insulin resistance in healthy Asian Indians and Caucasians. J Clin Endocrinol Metab 86: 5366-5371
81. Takanashi K, Inukai T (2000) Insulin resistance and changes in the blood coagulation-fibrinolysis system after a glucose clamp technique in patients with type 2 diabetes mellitus. J Med 31: 45-62
82. Natali A, Toschi E, Camastra S, Gastaldelli A, Groop L, Ferrannini E (2000) Determinants of postabsorptive endogenous glucose output in non-diabetic subjects. European Group for the Study of Insulin Resistance (EGIR). Diabetologia 43: 1266-1272
83. Hanson RL, Pratley RE, Bogardus C, et al. (2000) Evaluation of simple indices of insulin sensitivity and insulin secretion for use in epidemiologic studies. Am J Epidemiol 151: 190-198
84. Christopher M, Hew FL, Oakley M, Rantzau C, Alford F (1998) Defects of insulin action and skeletal muscle glucose metabolism in growth hormone-deficient adults persist after 24 months of recombinant human growth hormone therapy. J Clin Endocrinol Metab 83: 1668-1681
85. Yamasaki Y, Kawamori R, Wasada T, et al. (1997) Pioglitazone (AD-4833) ameliorates insulin resistance in patients with NIDDM. AD-4833 Glucose Clamp Study Group, Japan. Tohoku J Exp Med 183: 173-183
86. Wasada T, Arii H, Kuroki H, et al. (1995) The relationship between insulin resistance and insulin secretion in Japanese subjects with borderline glucose intolerance. Diabetes Res Clin Pract 30: 53-57
87. Ludvik B, Nolan JJ, Baloga J, Sacks D, Olefsky J (1995) Effect of obesity on insulin resistance in normal subjects and patients with NIDDM. Diabetes 44: 1121-1125
88. Malminiemi K (1995) Association between serum lipids, glucose tolerance, and insulin sensitivity during 12 months of celiprolol treatment. Cardiovasc Drugs Ther 9: 295-304
89. Li G, Pan X (1995) A new insulin-sensitivity index for epidemiological study. Chin Med J (Engl) 108: 55-56
90. Eliasson B, Attvall S, Taskinen MR, Smith U (1994) The insulin resistance syndrome in smokers is related to smoking habits. Arterioscler Thromb 14: 1946-1950
91. Blonk MC, Jacobs MA, Friedberg CE, et al. (1994) Determinants of insulin sensitivity and consequences for lipoproteins and blood pressure in subjects with non-insulin-dependent diabetes mellitus. Metabolism 43: 501-508
92. Falkner B, Hulman S, Kushner H (1993) Insulin-stimulated glucose utilization and borderline hypertension in young adult blacks. Hypertension 22: 18-25
93. Laakso M (1993) How good a marker is insulin level for insulin resistance? Am J Epidemiol 137: 959-965
94. Miyamoto I, Miyakoshi H, Nagai Y, et al. (1992) Characterization of the insulin resistance in liver cirrhosis: a comparison with non-insulin dependent diabetes mellitus. Endocrinol Jpn 39: 421-429
95. McCall JL, Tuckey JA, Parry BR (1992) Serum tumour necrosis factor alpha and insulin resistance in gastrointestinal cancer. Br J Surg 79: 1361-1363
96. Garg A, Helderman JH, Koffler M, Ayuso R, Rosenstock J, Raskin P (1988) Relationship between lipoprotein levels and in vivo insulin action in normal young white men. Metabolism 37: 982-987

97. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC (1985) Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 28: 412-419
98. Hollenbeck CB, Chen N, Chen YD, Reaven GM (1984) Relationship between the plasma insulin response to oral glucose and insulin-stimulated glucose utilization in normal subjects. Diabetes 33: 460-463
99. Skrha J, Haas T, Sindelka G, et al. (2004) Comparison of the insulin action parameters from hyperinsulinemic clamps with homeostasis model assessment and QUICKI indexes in subjects with different endocrine disorders. J Clin Endocrinol Metab 89: 135-141
100. Katsuki A, Sumida Y, Gabazza EC, et al. (2002) QUICKI is useful for following improvements in insulin sensitivity after therapy in patients with type 2 diabetes mellitus. J Clin Endocrinol Metab 87: 2906-2908
101. Malita FM, Karelis AD, St-Pierre DH, et al. (2006) Surrogate indexes vs. euglycaemic-hyperinsulinemic clamp as an indicator of insulin resistance and cardiovascular risk factors in overweight and obese postmenopausal women. Diabetes Metab 32: 251-255
102. Ramakrishnan G, Unni US, Raj T, Thomas T, Vaz M, Kurpad AV (2009) A pilot study on hyperinsulinaemic euglycaemic clamp based insulin sensitivity in young adult Indian males with low body mass index. Indian J Med Res 129: 409-417
103. Cohen O, Epstein GS, Weisz B, Homko CJ, Sivan E (2006) Longitudinal assessment of insulin sensitivity in pregnancy. Validation of the homeostasis model assessment. Clin Endocrinol (Oxf) 64: 640-644
104. Cleland SJ, Petrie JR, Morris AD, Ueda S, Dorrian CA, Connell JM (1996) FIRI: a fair insulin resistance index? Lancet 347: 770
105. Lindmark S, Buren J, Eriksson JW (2006) Insulin resistance, endocrine function and adipokines in type 2 diabetes patients at different glycaemic levels: potential impact for glucotoxicity in vivo. Clin Endocrinol (Oxf) 65: 301-309
106. Mayorov AY, Naumenkova IV, Antsiferov MB, Dedov, II (2005) Influence of insulin treatment on insulin sensitivity in insulin requiring type 2 diabetes patients. Diabetes Res Clin Pract 68 Suppl1: S54-59
107. Gastaldelli A, Ferrannini E, Miyazaki Y, Matsuda M, DeFronzo RA (2004) Beta-cell dysfunction and glucose intolerance: results from the San Antonio metabolism (SAM) study. Diabetologia 47: 31-39
108. Lind L, Lithell H, Pollare T, Ljunghall S (1994) On the interplay between insulin secretion and sensitivity as determinants of glucose tolerance. Acta Diabetol 31: 26-30
109. Okamoto M, Okamoto M, Nishimura H, et al. (1991) Insulin-stimulated glucose uptake and fasting blood glucose. Endocrinol Jpn 38: 421-427
110. Marchesini G, Bianchi GP, Forlani G, et al. (1987) Insulin resistance is the main determinant of impaired glucose tolerance in patients with liver cirrhosis. Dig Dis Sci 32: 1118-1124
111. Kolterman OG, Gray RS, Griffin J, et al. (1981) Receptor and postreceptor defects contribute to the insulin resistance in noninsulin-dependent diabetes mellitus. J Clin Invest 68: 957-969

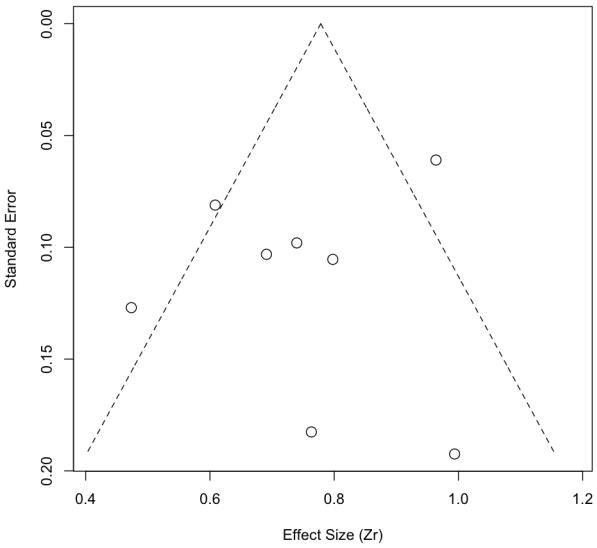
ESM Fig. 4 Funnel plots of meta-analyses between the hyperinsulinaemic euglycaemic clamp and surrogate measures based on the OGTT (A-J) and fasting samples (K-T)



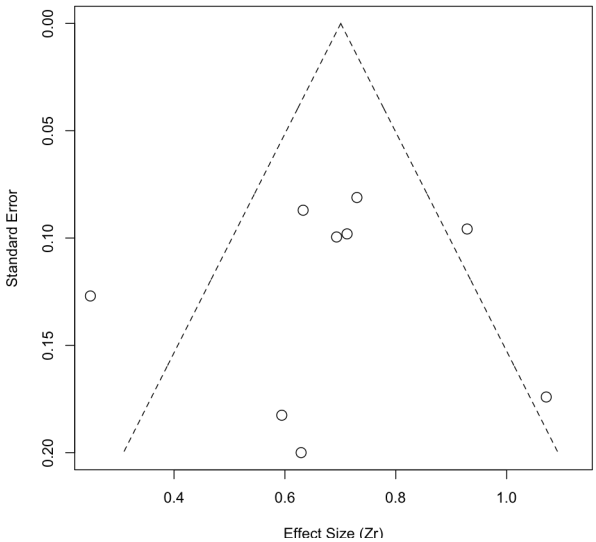
The correlation coefficients are transformed to Fisher's z scale (effect size (Zr)). Abbreviations: MCR, metabolic clearance rate. ISI, insulin sensitivity index. OGIS, oral glucose insulin sensitivity. HOMA-%S, HOMA-computer formula of insulin sensitivity. FIRI, fasting insulin resistance index. I_0, fasting insulin. G_0, fasting glucose.

ESM Fig. 4 (continued)

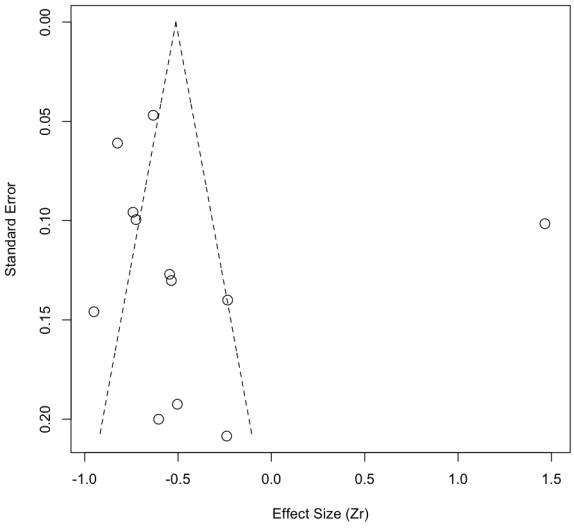
E) Belfiore



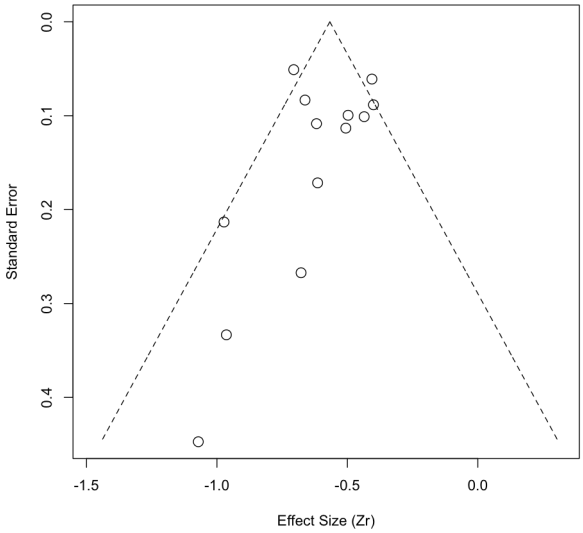
F) Cederholm



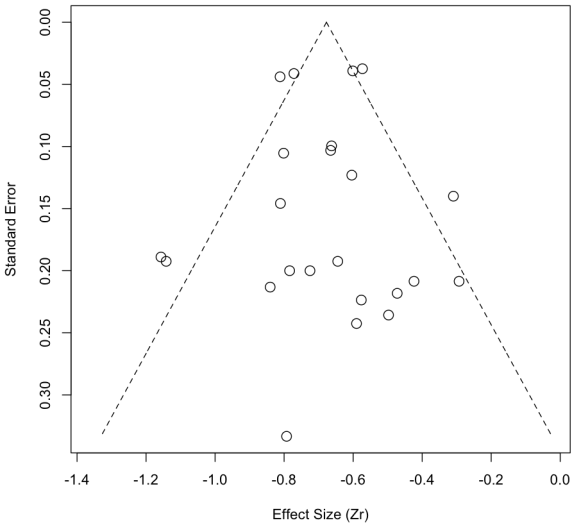
G) Insulin (120 min)



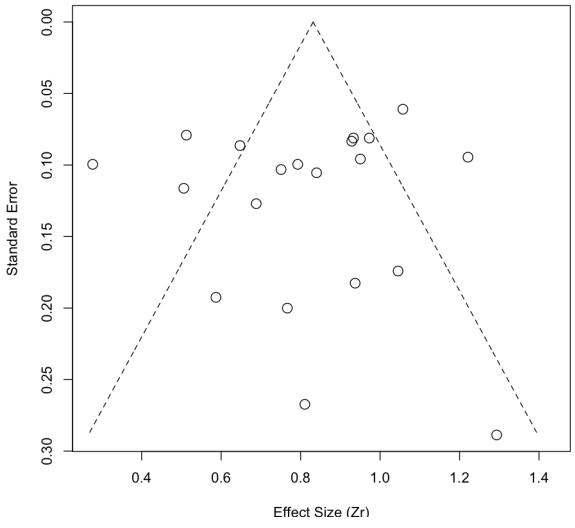
H) Glucose (120 min)



I) AUC insulin

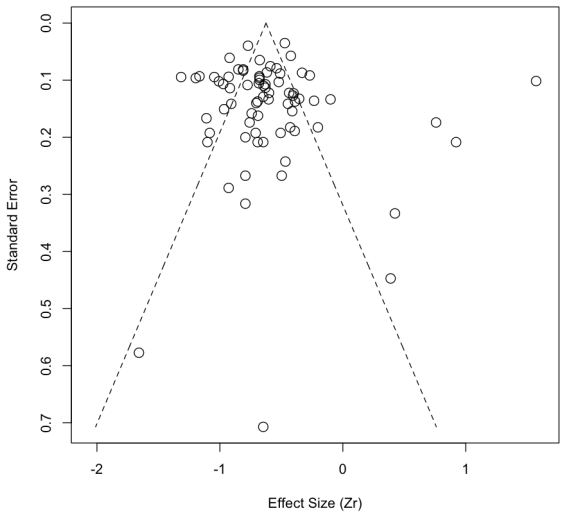


J) Matsuda

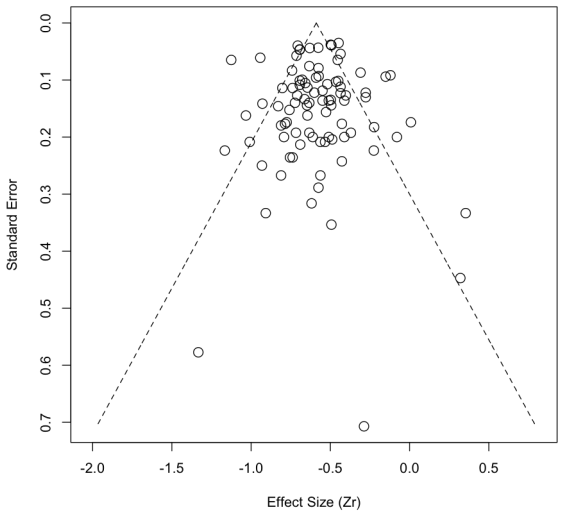


ESM Fig. 4 (continued)

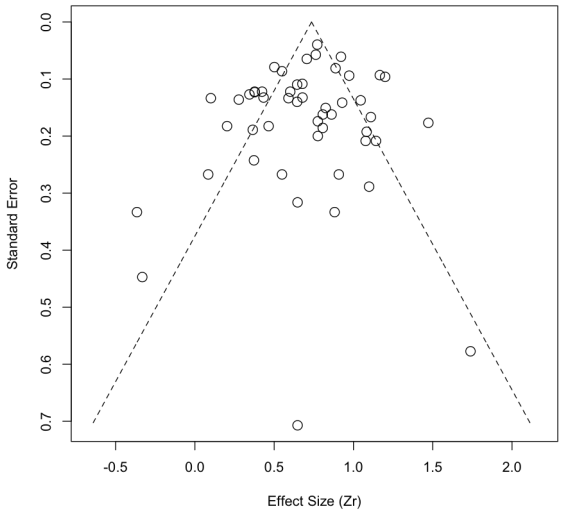
K) HOMA-IR



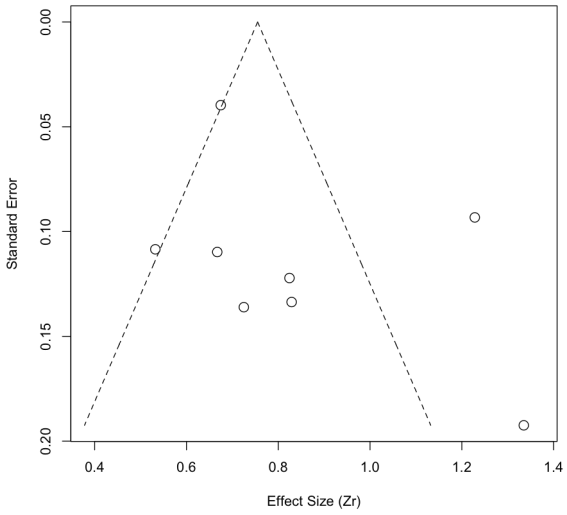
L) Fasting insulin



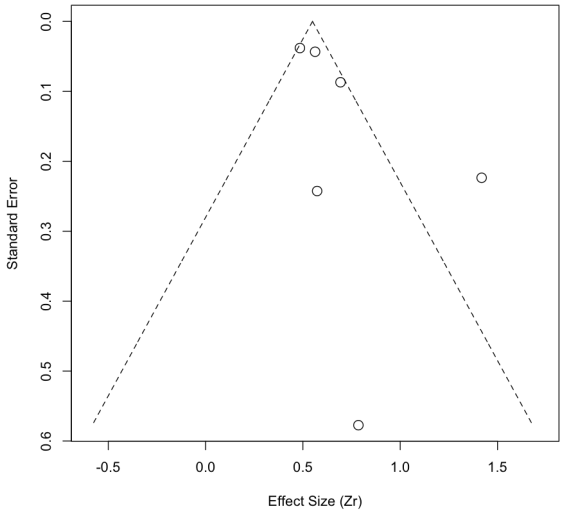
M) QUICKI



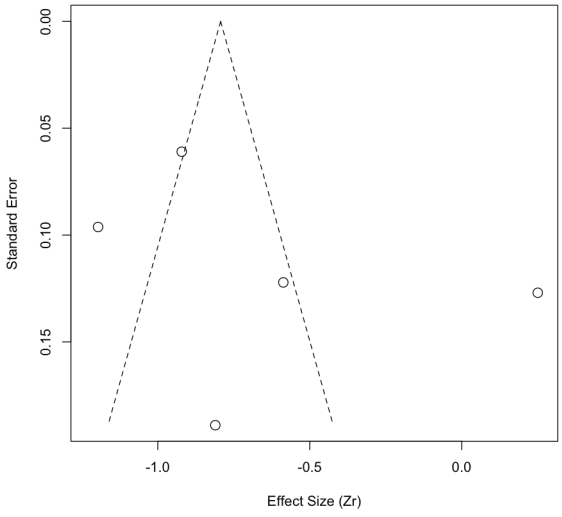
N) Revised QUICKI



O) HOMA-%S

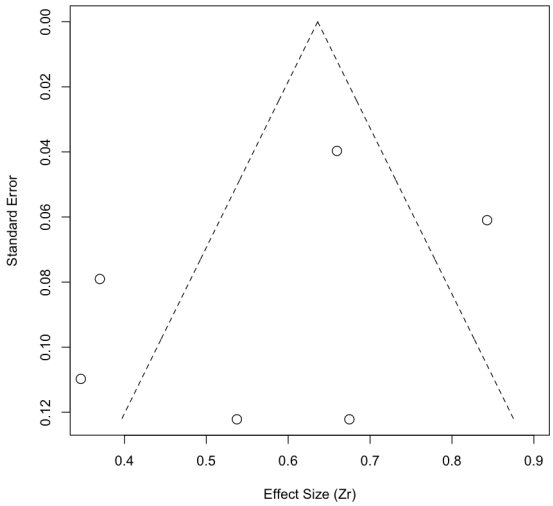


P) FIRI

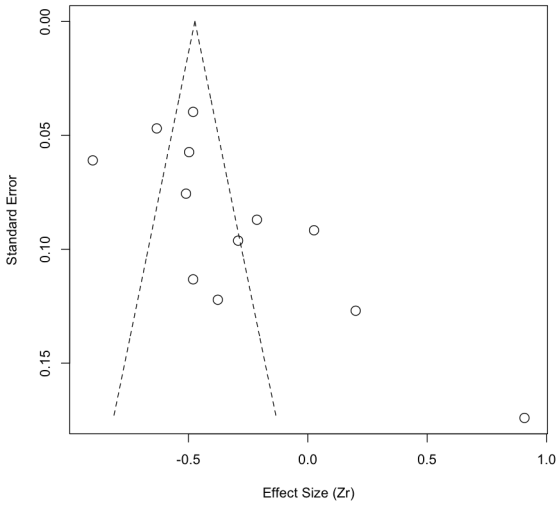


ESM Fig. 4 (continued)

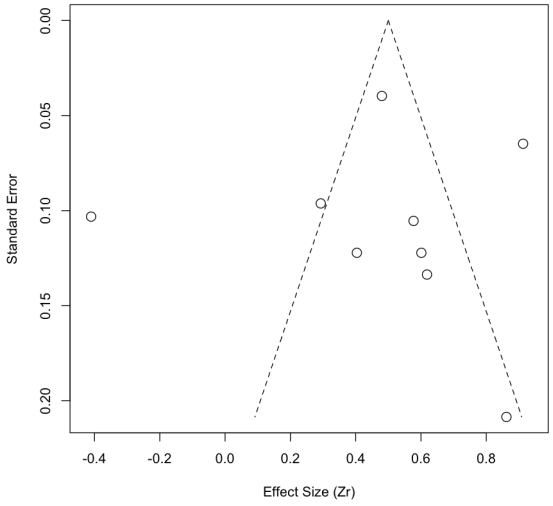
Q) McAuley



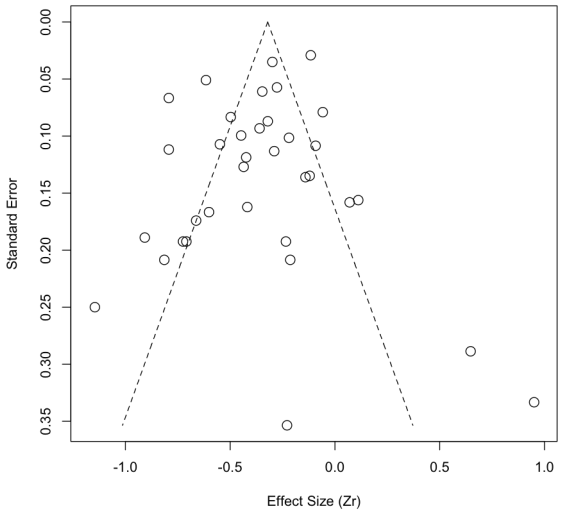
R) I_0 / G_0



S) G_0 / I_0

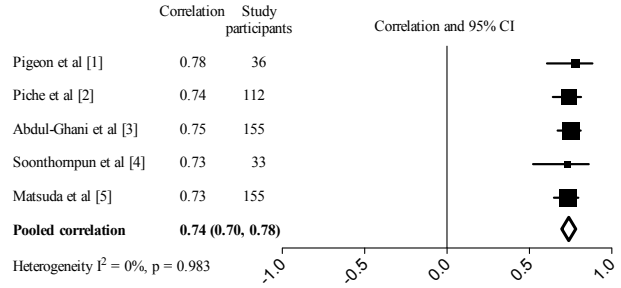


T) Fasting glucose

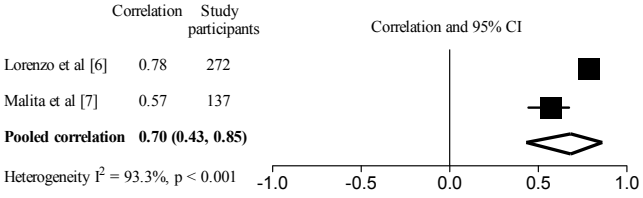


ESM Fig. 5 Meta-analyses of correlation coefficients between the Matsuda index and different clamp measurements

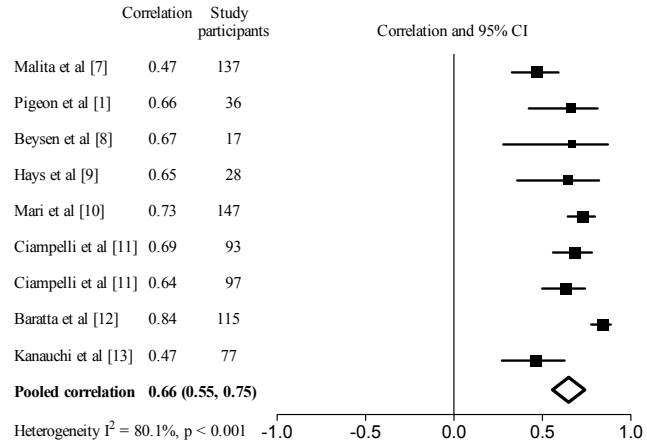
A) Matsuda index correlated with M_{BW}/I



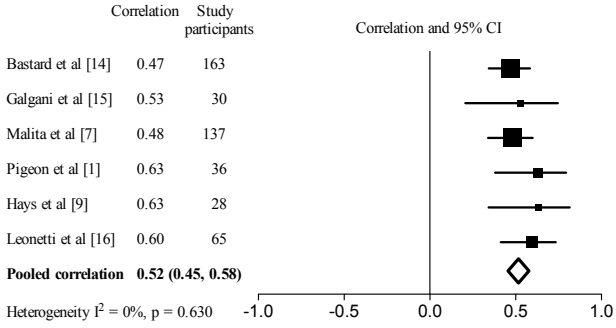
B) Matsuda index correlated with M_{LBM}/I



C) Matsuda index correlated with M_{BW}



D) Matsuda index correlated with M_{LBM}



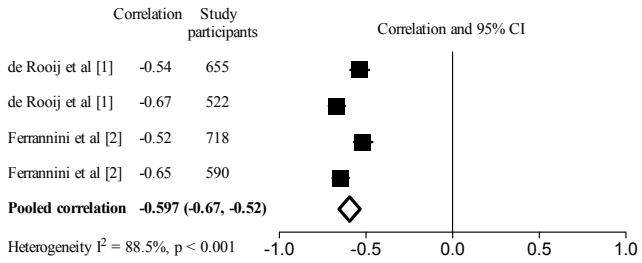
Abbreviations: M_{BW}, glucose infusion rate per kg body weight. M_{LBM}, glucose infusion rate per kg lean body mass. I, steady state insulin.

References

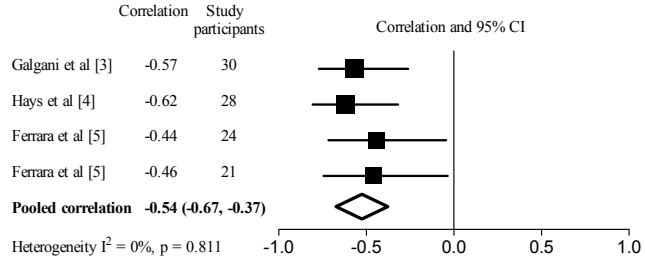
1. Pigeon E, Riou ME, St-Onge J, et al. (2009) Validation of a simple index (SIisOGTT) of insulin sensitivity in a population of sedentary men. Diabetes Metab 35: 398-403
2. Piche ME, Lemieux S, Corneau L, Nadeau A, Bergeron J, Weisnagel SJ (2007) Measuring insulin sensitivity in postmenopausal women covering a range of glucose tolerance: comparison of indices derived from the oral glucose tolerance test with the euglycemic-hyperinsulinemic clamp. Metabolism 56: 1159-1166
3. Abdul-Ghani MA, Matsuda M, Balas B, DeFronzo RA (2007) Muscle and liver insulin resistance indexes derived from the oral glucose tolerance test. Diabetes Care 30: 89-94
4. Soonthornpun S, Setasuban W, Thamprasit A, Chayanunnukul W, Rattarasarn C, Geater A (2003) Novel insulin sensitivity index derived from oral glucose tolerance test. J Clin Endocrinol Metab 88: 1019-1023
5. Matsuda M, DeFronzo RA (1999) Insulin sensitivity indices obtained from oral glucose tolerance testing: comparison with the euglycemic insulin clamp. Diabetes Care 22: 1462-1470
6. Lorenzo C, Haffner SM, Stancakova A, Laakso M (2010) Relation of direct and surrogate measures of insulin resistance to cardiovascular risk factors in nondiabetic finnish offspring of type 2 diabetic individuals. J Clin Endocrinol Metab 95: 5082-5090
7. Malita FM, Messier V, Lavoie JM, Bastard JP, Rabasa-Lhoret R, Karelis AD (2010) Comparison between several insulin sensitivity indices and metabolic risk factors in overweight and obese postmenopausal women: a MONET study. Nutr Metab Cardiovasc Dis 20: 173-179
8. Beysen C, Murphy EJ, McLaughlin T, et al. (2007) Whole-body glycolysis measured by the deuterated-glucose disposal test correlates highly with insulin resistance in vivo. Diabetes Care 30: 1143-1149
9. Hays NP, Starling RD, Sullivan DH, Fluckey JD, Coker RH, Evans WJ (2006) Comparison of insulin sensitivity assessment indices with euglycemic-hyperinsulinemic clamp data after a dietary and exercise intervention in older adults. Metabolism 55: 525-532
10. Mari A, Pacini G, Brazzale AR, Ahren B (2005) Comparative evaluation of simple insulin sensitivity methods based on the oral glucose tolerance test. Diabetologia 48: 748-751
11. Ciampelli M, Leoni F, Cucinelli F, et al. (2005) Assessment of insulin sensitivity from measurements in the fasting state and during an oral glucose tolerance test in polycystic ovary syndrome and menopausal patients. J Clin Endocrinol Metab 90: 1398-1406
12. Baratta R, Amato S, Degano C, et al. (2004) Adiponectin relationship with lipid metabolism is independent of body fat mass: evidence from both cross-sectional and intervention studies. J Clin Endocrinol Metab 89: 2665-2671
13. Kanauchi M, Tsujimoto N, Hashimoto T (2002) Validation of simple indices to assess insulin sensitivity based on the oral glucose tolerance test in the Japanese population. Diabetes Res Clin Pract 55: 229-235
14. Bastard JP, Lavoie ME, Messier V, Prud'homme D, Rabasa-Lhoret R (2012) Evaluation of two new surrogate indices including parameters not using insulin to assess insulin sensitivity/resistance in non-diabetic postmenopausal women: a MONET group study. Diabetes Metab 38: 258-263
15. Galgani JE, de Jonge L, Rood JC, Smith SR, Young AA, Ravussin E (2010) Urinary C-peptide excretion: a novel alternate measure of insulin sensitivity in physiological conditions. Obesity (Silver Spring) 18: 1852-1857
16. Leonetti F, Iacobellis G, Zappaterreno A, et al. (2004) Insulin sensitivity assessment in uncomplicated obese women: comparison of indices from fasting and oral glucose load with euglycemic hyperinsulinemic clamp. Nutr Metab Cardiovasc Dis 14: 366-372

ESM Fig. 6 Meta-analyses of correlation coefficients between AUC insulin and different clamp measurements

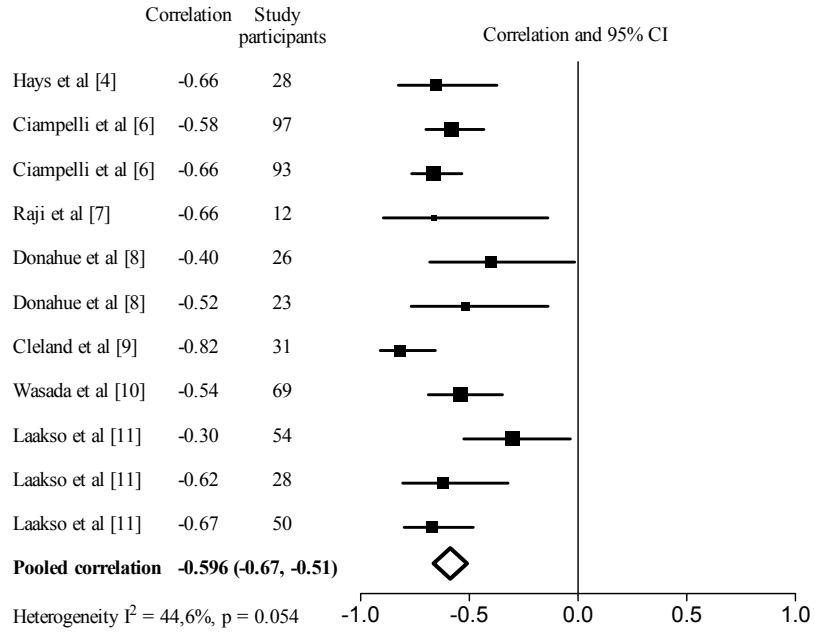
A) AUC insulin correlated with M_{LBM}/I



B) AUC insulin correlated with M_{LBM}



C) AUC insulin correlated with M_{BW}



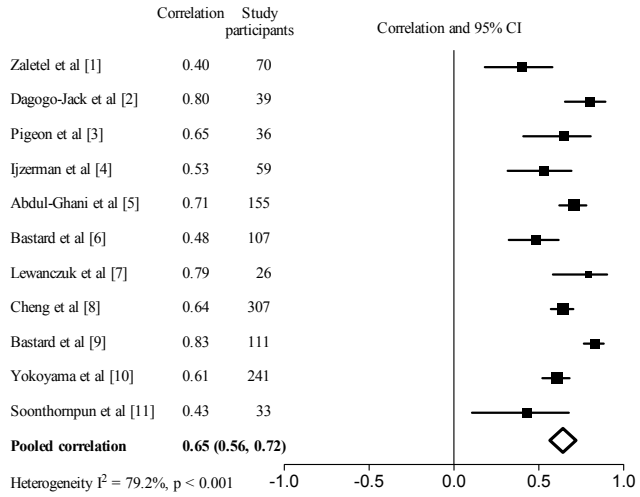
Abbreviations: M_{LBM}, glucose infusion rate per kg lean body mass. I, steady state insulin. M_{BW}, glucose infusion rate per kg body weight.

References

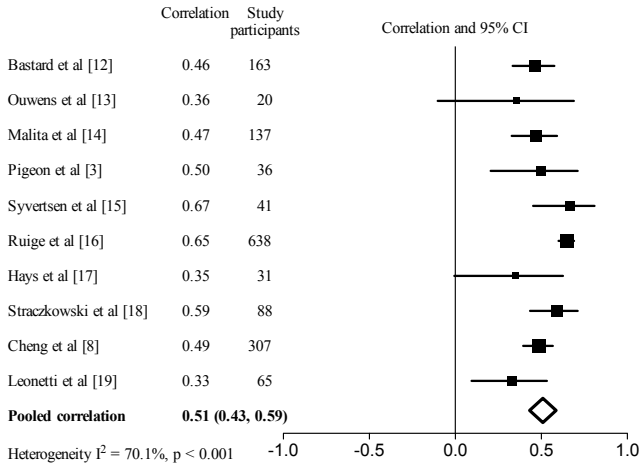
1. de Rooij SR, Dekker JM, Kozakova M, et al. (2009) Fasting insulin has a stronger association with an adverse cardiometabolic risk profile than insulin resistance: the RISC study. Eur J Endocrinol 161: 223-230
2. Ferrannini E, Balkau B, Coppack SW, et al. (2007) Insulin resistance, insulin response, and obesity as indicators of metabolic risk. J Clin Endocrinol Metab 92: 2885-2892
3. Galgani JE, de Jonge L, Rood JC, Smith SR, Young AA, Ravussin E (2010) Urinary C-peptide excretion: a novel alternate measure of insulin sensitivity in physiological conditions. Obesity (Silver Spring) 18: 1852-1857
4. Hays NP, Starling RD, Sullivan DH, Fluckey JD, Coker RH, Evans WJ (2006) Comparison of insulin sensitivity assessment indices with euglycemic-hyperinsulinemic clamp data after a dietary and exercise intervention in older adults. Metabolism 55: 525-532
5. Ferrara CM, Goldberg AP (2001) Limited value of the homeostasis model assessment to predict insulin resistance in older men with impaired glucose tolerance. Diabetes Care 24: 245-249
6. Ciampelli M, Leoni F, Cucinelli F, et al. (2005) Assessment of insulin sensitivity from measurements in the fasting state and during an oral glucose tolerance test in polycystic ovary syndrome and menopausal patients. J Clin Endocrinol Metab 90: 1398-1406
7. Raji A, Seely EW, Arky RA, Simonson DC (2001) Body fat distribution and insulin resistance in healthy Asian Indians and Caucasians. J Clin Endocrinol Metab 86: 5366-5371
8. Donahue RP, Prineas RJ, Donahue RD, et al. (1999) Is fasting leptin associated with insulin resistance among nondiabetic individuals? The Miami Community Health Study. Diabetes Care 22: 1092-1096
9. Cleland SJ, Petrie JR, Morris AD, Ueda S, Dorrian CA, Connell JM (1996) FIRI: a fair insulin resistance index? Lancet 347: 770
10. Wasada T, Arii H, Kuroki H, et al. (1995) The relationship between insulin resistance and insulin secretion in Japanese subjects with borderline glucose intolerance. Diabetes Res Clin Pract 30: 53-57
11. Laakso M (1993) How good a marker is insulin level for insulin resistance? Am J Epidemiol 137: 959-965

ESM Fig. 7 Meta-analyses of correlation coefficients between QUICKI and different clamp measurements

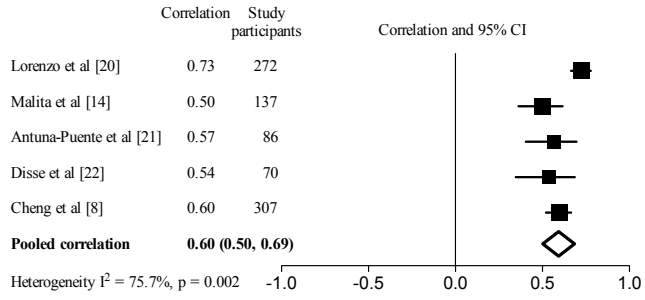
A) QUICKI correlated with M_{BW}/I



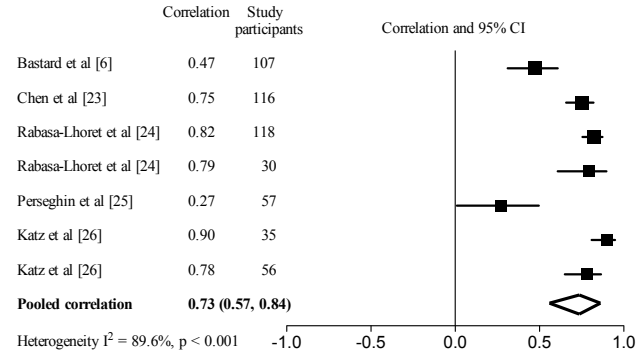
B) QUICKI correlated with M_{LBM}



C) QUICKI correlated with M_{LBM}/I



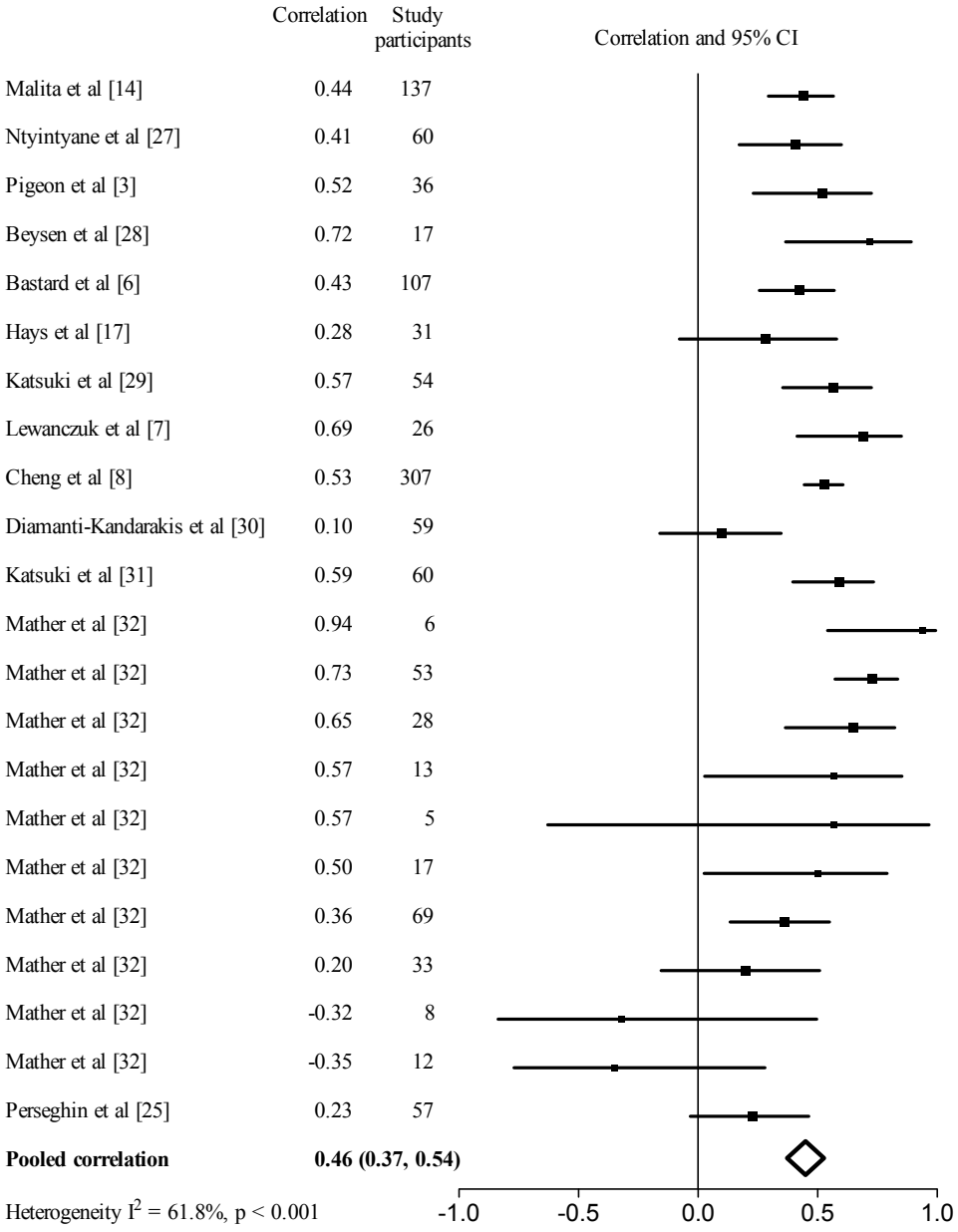
D) QUICKI correlated with $M_{BW}/(G*\Delta I)$



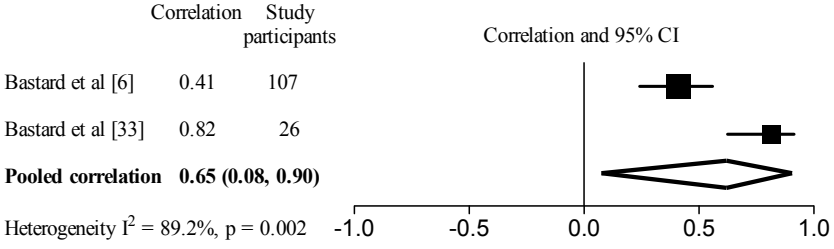
Abbreviations: M_{BW}, glucose infusion rate per kg body weight. I, steady state insulin. M_{LBM}, glucose infusion rate per kg lean body mass. G, steady state glucose. ΔI, increment of insulin concentration. M_{BSA}, glucose infusion rate per m^2 body surface area.

ESM Fig. 7 (continued)

E) QUICKI correlated with M_{BW}



F) QUICKI correlated with M_{BSA}



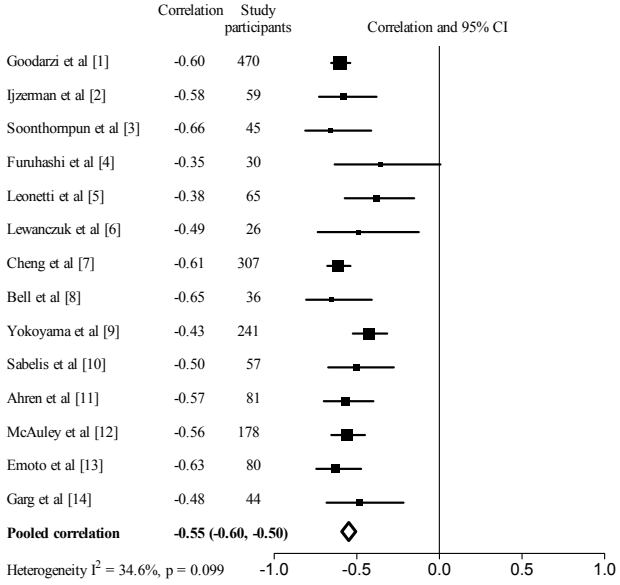
References

1. Zaletel J, Barlovic DP, Prezelj J (2010) Adiponectin-leptin ratio: a useful estimate of insulin resistance in patients with Type 2 diabetes. J Endocrinol Invest 33: 514-518
2. Dagogo-Jack S, Askari H, Tykodi G (2009) Glucoregulatory physiology in subjects with low-normal, high-normal, or impaired fasting glucose. J Clin Endocrinol Metab 94: 2031-2036
3. Pigeon E, Riou ME, St-Onge J, et al. (2009) Validation of a simple index (SIisOGTT) of insulin sensitivity in a population of sedentary men. Diabetes Metab 35: 398-403
4. Ijzerman RG, Stehouwer CD, Serne EH, et al. (2009) Incorporation of the fasting free fatty acid concentration into quantitative insulin sensitivity check index improves its association with insulin sensitivity in adults, but not in children. Eur J Endocrinol 160: 59-64
5. Abdul-Ghani MA, Matsuda M, Balas B, DeFronzo RA (2007) Muscle and liver insulin resistance indexes derived from the oral glucose tolerance test. Diabetes Care 30: 89-94
6. Bastard JP, Vandernotte JM, Faraj M, et al. (2007) Relationship between the hyperinsulinemic-euglycaemic clamp and a new simple index assessing insulin sensitivity in overweight and obese postmenopausal women. Diabetes Metab 33: 261-268
7. Lewanczuk RZ, Paty BW, Toth EL (2004) Comparison of the [13C]glucose breath test to the hyperinsulinemic-euglycemic clamp when determining insulin resistance. Diabetes Care 27: 441-447
8. Cheng C, Campbell KL, Kushner H, Falkner BE (2004) Correlation of oral glucose tolerance test-derived estimates of insulin sensitivity with insulin clamp measurements in an African-American cohort. Metabolism 53: 1107-1112
9. Bastard JP, Rabasa-Lhoret R, Maachi M, et al. (2003) What kind of simple fasting index should be used to estimate insulin sensitivity in humans? Diabetes Metab 29: 285-288
10. Yokoyama H, Emoto M, Fujiwara S, et al. (2003) Quantitative insulin sensitivity check index and the reciprocal index of homeostasis model assessment in normal range weight and moderately obese type 2 diabetic patients. Diabetes Care 26: 2426-2432
11. Soonthornpun S, Setasuban W, Thamprasit A, Chayanunnukul W, Rattarasarn C, Geater A (2003) Novel insulin sensitivity index derived from oral glucose tolerance test. J Clin Endocrinol Metab 88: 1019-1023
12. Bastard JP, Lavoie ME, Messier V, Prud'homme D, Rabasa-Lhoret R (2012) Evaluation of two new surrogate indices including parameters not using insulin to assess insulin sensitivity/resistance in non-diabetic postmenopausal women: a MONET group study. Diabetes Metab 38: 258-263
13. Ouwens DM, Bekaert M, Lapauw B, et al. (2012) Chemerin as biomarker for insulin sensitivity in males without typical characteristics of metabolic syndrome. Arch Physiol Biochem 118: 135-138
14. Malita FM, Messier V, Lavoie JM, Bastard JP, Rabasa-Lhoret R, Karelis AD (2010) Comparison between several insulin sensitivity indices and metabolic risk factors in overweight and obese postmenopausal women: a MONET study. Nutr Metab Cardiovasc Dis 20: 173-179
15. Syvertsen C, Halse J, Hoivik HO, et al. (2007) The effect of 6 months supplementation with conjugated linoleic acid on insulin resistance in overweight and obese. Int J Obes (Lond) 31: 1148-1154
16. Ruige JB, Mertens IL, Bartholomeeusen E, Dirinck E, Ferrannini E, Van Gaal LF (2006) Fasting-based estimates of insulin sensitivity in overweight and obesity: a critical appraisal. Obesity (Silver Spring) 14: 1250-1256
17. Hays NP, Starling RD, Sullivan DH, Fluckey JD, Coker RH, Evans WJ (2006) Comparison of insulin sensitivity assessment indices with euglycemic-hyperinsulinemic clamp data after a dietary and exercise intervention in older adults. Metabolism 55: 525-532
18. Straczkowski M, Stepien A, Kowalska I, Kinalska I (2004) Comparison of simple indices of insulin sensitivity using the euglycemic hyperinsulinemic clamp technique. Med Sci Monit 10: CR480-484
19. Leonetti F, Iacobellis G, Zappaterreno A, et al. (2004) Insulin sensitivity assessment in uncomplicated obese women: comparison of indices from fasting and oral glucose load with euglycemic hyperinsulinemic clamp. Nutr Metab Cardiovasc Dis 14: 366-372

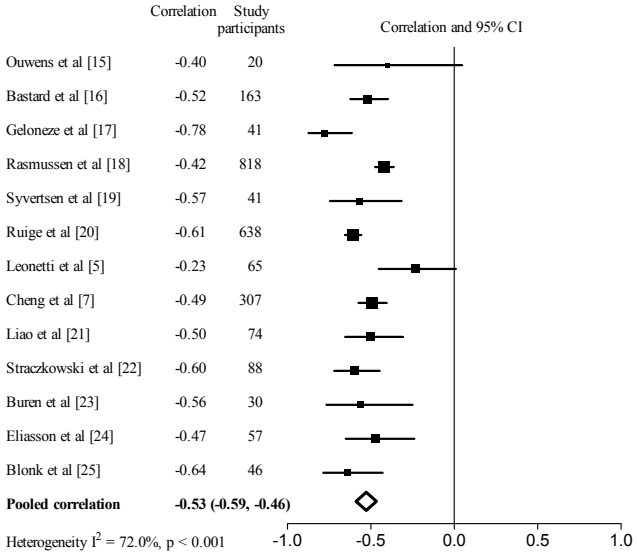
20. Lorenzo C, Haffner SM, Stancakova A, Laakso M (2010) Relation of direct and surrogate measures of insulin resistance to cardiovascular risk factors in nondiabetic finnish offspring of type 2 diabetic individuals. J Clin Endocrinol Metab 95: 5082-5090
21. Antuna-Puente B, Disse E, Faraj M, et al. (2009) Evaluation of insulin sensitivity with a new lipid-based index in non-diabetic postmenopausal overweight and obese women before and after a weight loss intervention. Eur J Endocrinol 161: 51-56
22. Disse E, Bastard JP, Bonnet F, et al. (2008) A lipid-parameter-based index for estimating insulin sensitivity and identifying insulin resistance in a healthy population. Diabetes Metab 34: 457-463
23. Chen H, Sullivan G, Quon MJ (2005) Assessing the predictive accuracy of QUICKI as a surrogate index for insulin sensitivity using a calibration model. Diabetes 54: 1914-1925
24. Rabasa-Lhoret R, Bastard JP, Jan V, et al. (2003) Modified quantitative insulin sensitivity check index is better correlated to hyperinsulinemic glucose clamp than other fasting-based index of insulin sensitivity in different insulin-resistant states. J Clin Endocrinol Metab 88: 4917-4923
25. Perseghin G, Caumo A, Caloni M, Testolin G, Luzi L (2001) Incorporation of the fasting plasma FFA concentration into QUICKI improves its association with insulin sensitivity in nonobese individuals. J Clin Endocrinol Metab 86: 4776-4781
26. Katz A, Nambi SS, Mather K, et al. (2000) Quantitative insulin sensitivity check index: a simple, accurate method for assessing insulin sensitivity in humans. J Clin Endocrinol Metab 85: 2402-2410
27. Ntyintyane L, Panz V, Raal F, Gill G (2010) Comparison between surrogate indices of insulin sensitivity and resistance, and the hyperinsulinaemic euglycaemic glucose clamp in urban South African blacks with and without coronary artery disease. Diab Vasc Dis Res 7: 151-157
28. Beysen C, Murphy EJ, McLaughlin T, et al. (2007) Whole-body glycolysis measured by the deuterated-glucose disposal test correlates highly with insulin resistance in vivo. Diabetes Care 30: 1143-1149
29. Katsuki A, Urakawa H, Gabazza EC, et al. (2005) Quantitative insulin sensitivity check index is a useful indicator of insulin resistance in Japanese metabolically obese, normal-weight subjects with normal glucose tolerance. Endocr J 52: 253-257
30. Diamanti-Kandarakis E, Kouli C, Alexandraki K, Spina G (2004) Failure of mathematical indices to accurately assess insulin resistance in lean, overweight, or obese women with polycystic ovary syndrome. J Clin Endocrinol Metab 89: 1273-1276
31. Katsuki A, Sumida Y, Gabazza EC, et al. (2002) QUICKI is useful for following improvements in insulin sensitivity after therapy in patients with type 2 diabetes mellitus. J Clin Endocrinol Metab 87: 2906-2908
32. Mather KJ, Hunt AE, Steinberg HO, et al. (2001) Repeatability characteristics of simple indices of insulin resistance: implications for research applications. J Clin Endocrinol Metab 86: 5457-5464
33. Bastard JP, Robert JJ, Jardel C, Bruckert E, Grimaldi A, Hainque B (2001) Is quantitative insulin sensitivity check index, a fair insulin sensitivity index in humans? Diabetes Metab 27: 69-70

ESM Fig. 8 Meta-analyses of correlation coefficients between fasting insulin and different clamp measurements

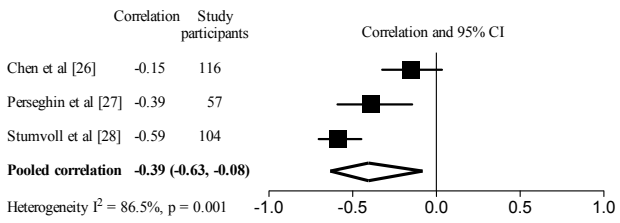
A) Fasting insulin correlated with M_{BW}/I



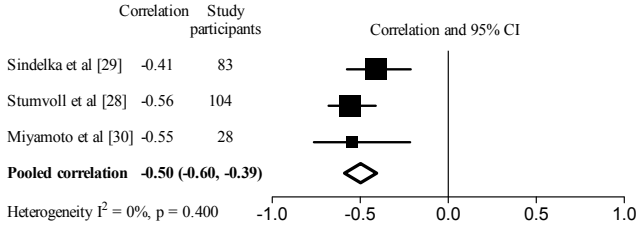
B) Fasting insulin correlated with M_{LBM}



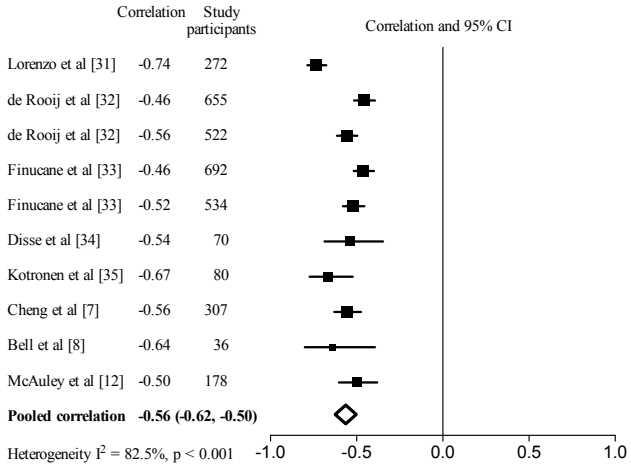
C) Fasting insulin correlated with $M_{BW}/(G*\Delta I)$



D) Fasting insulin correlated with M/G



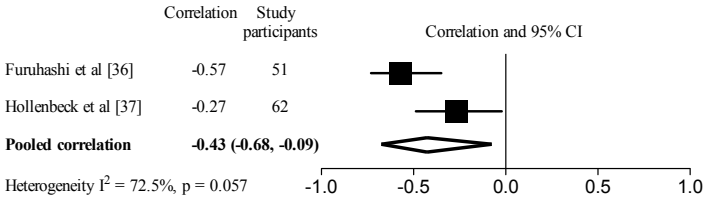
E) Fasting insulin correlated with M_{LBM}/I



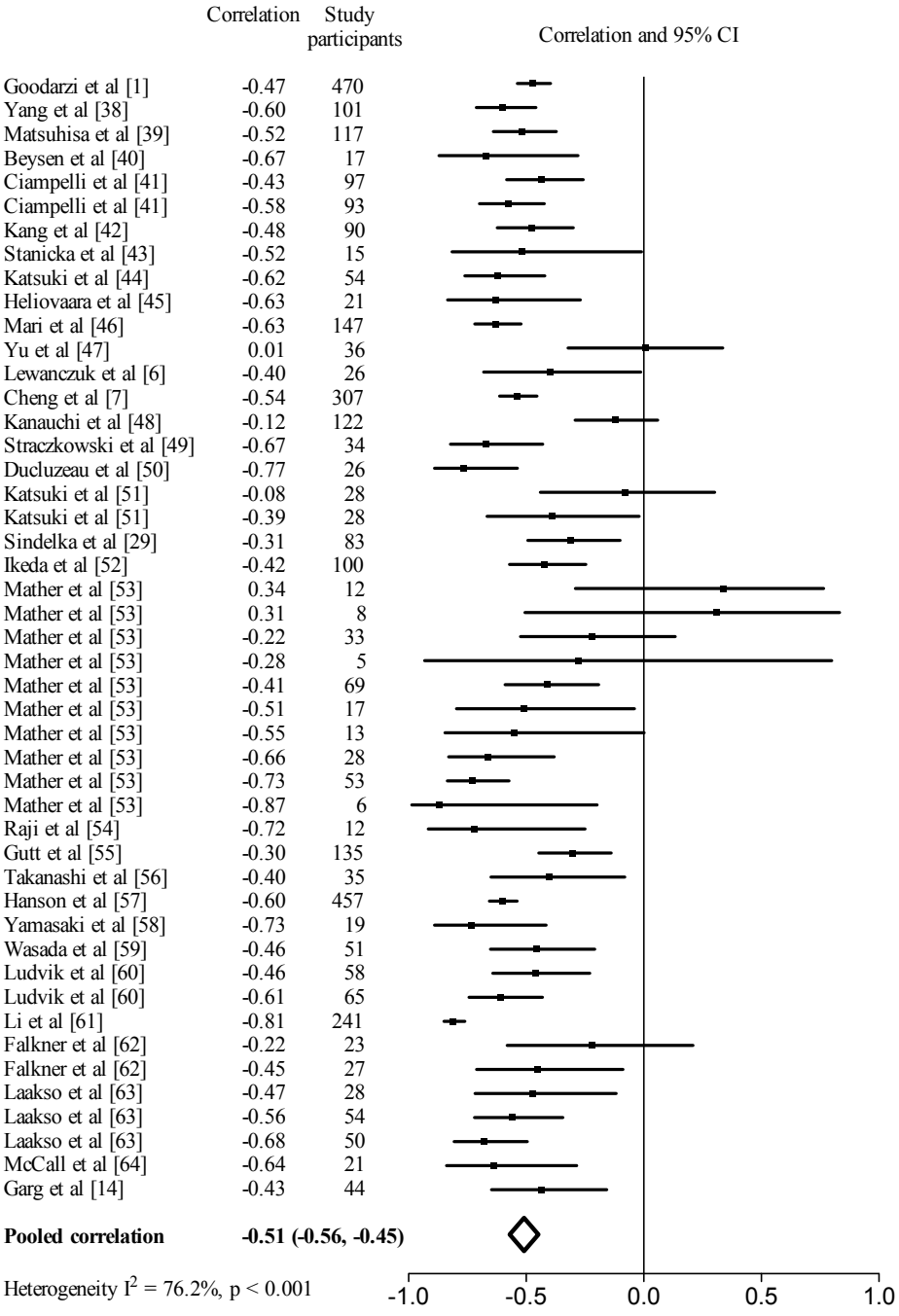
Abbreviations: M_{BW}, glucose infusion rate per kg body weight. I, steady state insulin. M_{LBM}, glucose infusion rate per kg lean body mass. G, steady state glucose. ΔI, increment of insulin concentration.

ESM Fig. 8 (continued)

F) Fasting insulin correlated with M_{BSA}



G) Fasting insulin correlated with M_{BW}



References

1. Goodarzi MO, Cui J, Chen YD, Hsueh WA, Guo X, Rotter JI (2011) Fasting insulin reflects heterogeneous physiological processes: role of insulin clearance. Am J Physiol Endocrinol Metab 301: E402-408
2. Ijzerman RG, Stehouwer CD, Serne EH, et al. (2009) Incorporation of the fasting free fatty acid concentration into quantitative insulin sensitivity check index improves its association with insulin sensitivity in adults, but not in children. Eur J Endocrinol 160: 59-64
3. Soonthornpun S, Setasuban W, Thamprasit A (2007) Correlation between change in serum homocysteine levels during hyperinsulinemia and insulin sensitivity. J Med Assoc Thai 90: 1506-1511
4. Furuhashi M, Ura N, Higashiura K, et al. (2005) Low adiponectin level in young normotensive men with a family history of essential hypertension. Hypertens Res 28: 141-146
5. Leonetti F, Iacobellis G, Zappaterreno A, et al. (2004) Insulin sensitivity assessment in uncomplicated obese women: comparison of indices from fasting and oral glucose load with euglycemic hyperinsulinemic clamp. Nutr Metab Cardiovasc Dis 14: 366-372
6. Lewanczuk RZ, Paty BW, Toth EL (2004) Comparison of the [13C]glucose breath test to the hyperinsulinemic-euglycemic clamp when determining insulin resistance. Diabetes Care 27: 441-447
7. Cheng C, Campbell KL, Kushner H, Falkner BE (2004) Correlation of oral glucose tolerance test-derived estimates of insulin sensitivity with insulin clamp measurements in an African-American cohort. Metabolism 53: 1107-1112
8. Bell D, McAuley KA, Mann J, Murphy E, Williams S (2004) The hypertriglyceridaemic waist in New Zealand Maori. Asia Pac J Clin Nutr 13: 74-77
9. Yokoyama H, Emoto M, Fujiwara S, et al. (2003) Quantitative insulin sensitivity check index and the reciprocal index of homeostasis model assessment in normal range weight and moderately obese type 2 diabetic patients. Diabetes Care 26: 2426-2432
10. Sabelis LW, Senden PJ, Zonderland ML, et al. (2003) Determinants of insulin sensitivity in chronic heart failure. Eur J Heart Fail 5: 759-765
11. Ahren B, Larsson H (2002) Quantification of insulin secretion in relation to insulin sensitivity in nondiabetic postmenopausal women. Diabetes 51 Suppl 1: S202-211
12. McAuley KA, Williams SM, Mann JI, et al. (2001) Diagnosing insulin resistance in the general population. Diabetes Care 24: 460-464
13. Emoto M, Nishizawa Y, Maekawa K, et al. (1999) Homeostasis model assessment as a clinical index of insulin resistance in type 2 diabetic patients treated with sulfonylureas. Diabetes Care 22: 818-822
14. Garg A, Helderman JH, Koffler M, Ayuso R, Rosenstock J, Raskin P (1988) Relationship between lipoprotein levels and in vivo insulin action in normal young white men. Metabolism 37: 982-987
15. Ouwens DM, Bekaert M, Lapauw B, et al. (2012) Chemerin as biomarker for insulin sensitivity in males without typical characteristics of metabolic syndrome. Arch Physiol Biochem 118: 135-138
16. Bastard JP, Lavoie ME, Messier V, Prud'homme D, Rabasa-Lhoret R (2012) Evaluation of two new surrogate indices including parameters not using insulin to assess insulin sensitivity/resistance in non-diabetic postmenopausal women: a MONET group study. Diabetes Metab 38: 258-263
17. Geloneze B, Pereira JA, Pareja JC, et al. (2009) Overcoming metabolic syndrome in severe obesity: adiponectin as a marker of insulin sensitivity and HDL-cholesterol improvements after gastric bypass. Arq Bras Endocrinol Metabol 53: 293-300
18. Rasmussen-Torvik LJ, Pankow JS, Jacobs DR, et al. (2007) Heritability and genetic correlations of insulin sensitivity measured by the euglycaemic clamp. Diabet Med 24: 1286-1289
19. Syvertsen C, Halse J, Hoivik HO, et al. (2007) The effect of 6 months supplementation with conjugated linoleic acid on insulin resistance in overweight and obese. Int J Obes (Lond) 31: 1148-1154

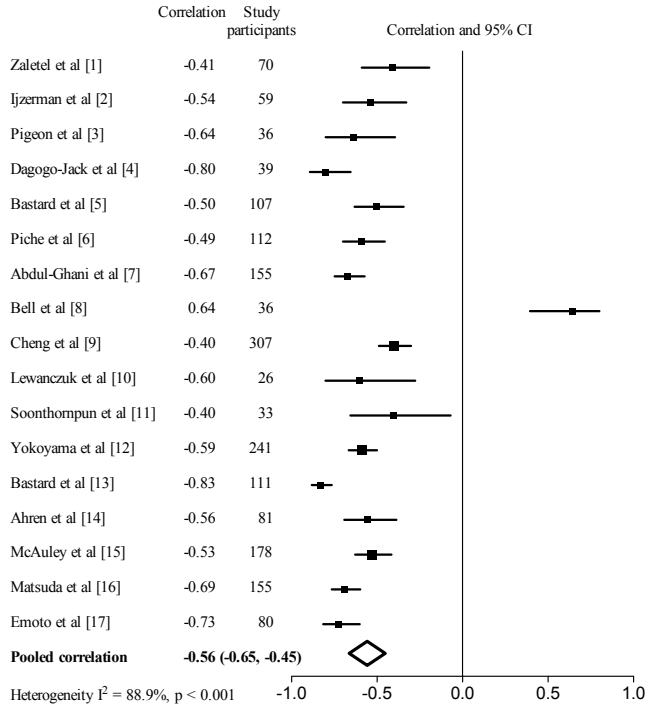
20. Ruige JB, Mertens IL, Bartholomeeusen E, Dirinck E, Ferrannini E, Van Gaal LF (2006) Fasting-based estimates of insulin sensitivity in overweight and obesity: a critical appraisal. Obesity (Silver Spring) 14: 1250-1256
21. Liao Y, Kwon S, Shaughnessy S, et al. (2004) Critical evaluation of adult treatment panel III criteria in identifying insulin resistance with dyslipidemia. Diabetes Care 27: 978-983
22. Straczkowski M, Stepien A, Kowalska I, Kinalska I (2004) Comparison of simple indices of insulin sensitivity using the euglycemic hyperinsulinemic clamp technique. Med Sci Monit 10: CR480-484
23. Buren J, Lindmark S, Renstrom F, Eriksson JW (2003) In vitro reversal of hyperglycemia normalizes insulin action in fat cells from type 2 diabetes patients: is cellular insulin resistance caused by glucotoxicity in vivo? Metabolism 52: 239-245
24. Eliasson B, Attvall S, Taskinen MR, Smith U (1994) The insulin resistance syndrome in smokers is related to smoking habits. Arterioscler Thromb 14: 1946-1950
25. Blonk MC, Jacobs MA, Friedberg CE, et al. (1994) Determinants of insulin sensitivity and consequences for lipoproteins and blood pressure in subjects with non-insulin-dependent diabetes mellitus. Metabolism 43: 501-508
26. Chen H, Sullivan G, Quon MJ (2005) Assessing the predictive accuracy of QUICKI as a surrogate index for insulin sensitivity using a calibration model. Diabetes 54: 1914-1925
27. Perseghin G, Caumo A, Caloni M, Testolin G, Luzi L (2001) Incorporation of the fasting plasma FFA concentration into QUICKI improves its association with insulin sensitivity in nonobese individuals. J Clin Endocrinol Metab 86: 4776-4781
28. Stumvoll M, Mitrakou A, Pimenta W, et al. (2000) Use of the oral glucose tolerance test to assess insulin release and insulin sensitivity. Diabetes Care 23: 295-301
29. Sindelka G, Skrha J, Prazny M, Haas T (2002) Association of obesity, diabetes, serum lipids and blood pressure regulates insulin action. Physiol Res 51: 85-91
30. Miyamoto I, Miyakoshi H, Nagai Y, et al. (1992) Characterization of the insulin resistance in liver cirrhosis: a comparison with non-insulin dependent diabetes mellitus. Endocrinol Jpn 39: 421-429
31. Lorenzo C, Haffner SM, Stancakova A, Laakso M (2010) Relation of direct and surrogate measures of insulin resistance to cardiovascular risk factors in nondiabetic finnish offspring of type 2 diabetic individuals. J Clin Endocrinol Metab 95: 5082-5090
32. de Rooij SR, Dekker JM, Kozakova M, et al. (2009) Fasting insulin has a stronger association with an adverse cardiometabolic risk profile than insulin resistance: the RISC study. Eur J Endocrinol 161: 223-230
33. Finucane FM, Luan J, Wareham NJ, et al. (2009) Correlation of the leptin:adiponectin ratio with measures of insulin resistance in non-diabetic individuals. Diabetologia 52: 2345-2349
34. Disse E, Bastard JP, Bonnet F, et al. (2008) A lipid-parameter-based index for estimating insulin sensitivity and identifying insulin resistance in a healthy population. Diabetes Metab 34: 457-463
35. Kotronen A, Vehkavaara S, Seppala-Lindroos A, Bergholm R, Yki-Jarvinen H (2007) Effect of liver fat on insulin clearance. Am J Physiol Endocrinol Metab 293: E1709-1715
36. Furuhashi M, Ura N, Higashiura K, Murakami H, Shimamoto K (2003) Circulating resistin levels in essential hypertension. Clin Endocrinol (Oxf) 59: 507-510
37. Hollenbeck CB, Chen N, Chen YD, Reaven GM (1984) Relationship between the plasma insulin response to oral glucose and insulin-stimulated glucose utilization in normal subjects. Diabetes 33: 460-463
38. Yang S, Li Q, Song Y, et al. (2011) Serum complement C3 has a stronger association with insulin resistance than high-sensitivity C-reactive protein in women with polycystic ovary syndrome. Fertil Steril 95: 1749-1753
39. Matsuhisa M, Yamasaki Y, Emoto M, et al. (2007) A novel index of insulin resistance determined from the homeostasis model assessment index and adiponectin levels in Japanese subjects. Diabetes Res Clin Pract 77: 151-154

40. Beysen C, Murphy EJ, McLaughlin T, et al. (2007) Whole-body glycolysis measured by the deuterated-glucose disposal test correlates highly with insulin resistance in vivo. Diabetes Care 30: 1143-1149
41. Ciampelli M, Leoni F, Cucinelli F, et al. (2005) Assessment of insulin sensitivity from measurements in the fasting state and during an oral glucose tolerance test in polycystic ovary syndrome and menopausal patients. J Clin Endocrinol Metab 90: 1398-1406
42. Kang ES, Yun YS, Park SW, et al. (2005) Limitation of the validity of the homeostasis model assessment as an index of insulin resistance in Korea. Metabolism 54: 206-211
43. Stanicka S, Vondra K, Pelikanova T, Vlcek P, Hill M, Zamrazil V (2005) Insulin sensitivity and counter-regulatory hormones in hypothyroidism and during thyroid hormone replacement therapy. Clin Chem Lab Med 43: 715-720
44. Katsuki A, Urakawa H, Gabazza EC, et al. (2005) Quantitative insulin sensitivity check index is a useful indicator of insulin resistance in Japanese metabolically obese, normal-weight subjects with normal glucose tolerance. Endocr J 52: 253-257
45. Heliovaara MK, Teppo AM, Karonen SL, Tuominen JA, Ebeling P (2005) Plasma IL-6 concentration is inversely related to insulin sensitivity, and acute-phase proteins associate with glucose and lipid metabolism in healthy subjects. Diabetes Obes Metab 7: 729-736
46. Mari A, Pacini G, Brazzale AR, Ahren B (2005) Comparative evaluation of simple insulin sensitivity methods based on the oral glucose tolerance test. Diabetologia 48: 748-751
47. Yu Y, Suo L, Yu H, Wang C, Tang H (2004) Insulin resistance and endothelial dysfunction in type 2 diabetes patients with or without microalbuminuria. Diabetes Res Clin Pract 65: 95-104
48. Kanauchi M (2003) Validation of the oral glucose insulin sensitivity index to assess insulin sensitivity in Japanese subjects for use in clinical practice. Eur J Clin Invest 33: 1022-1023
49. Straczkowski M, Kowalska I, Stepien A, et al. (2003) Insulin resistance in the first-degree relatives of persons with type 2 diabetes. Med Sci Monit 9: CR186-190
50. Ducluzeau PH, Cousin P, Malvoisin E, et al. (2003) Glucose-to-insulin ratio rather than sex hormone-binding globulin and adiponectin levels is the best predictor of insulin resistance in nonobese women with polycystic ovary syndrome. J Clin Endocrinol Metab 88: 3626-3631
51. Katsuki A, Sumida Y, Urakawa H, et al. (2002) Neither homeostasis model assessment nor quantitative insulin sensitivity check index can predict insulin resistance in elderly patients with poorly controlled type 2 diabetes mellitus. J Clin Endocrinol Metab 87: 5332-5335
52. Ikeda Y, Suehiro T, Nakamura T, Kumon Y, Hashimoto K (2001) Clinical significance of the insulin resistance index as assessed by homeostasis model assessment. Endocr J 48: 81-86
53. Mather KJ, Hunt AE, Steinberg HO, et al. (2001) Repeatability characteristics of simple indices of insulin resistance: implications for research applications. J Clin Endocrinol Metab 86: 5457-5464
54. Raji A, Seely EW, Arky RA, Simonson DC (2001) Body fat distribution and insulin resistance in healthy Asian Indians and Caucasians. J Clin Endocrinol Metab 86: 5366-5371
55. Gutt M, Davis CL, Spitzer SB, et al. (2000) Validation of the insulin sensitivity index (ISI(0,120)): comparison with other measures. Diabetes Res Clin Pract 47: 177-184
56. Takanashi K, Inukai T (2000) Insulin resistance and changes in the blood coagulation-fibrinolysis system after a glucose clamp technique in patients with type 2 diabetes mellitus. J Med 31: 45-62
57. Hanson RL, Pratley RE, Bogardus C, et al. (2000) Evaluation of simple indices of insulin sensitivity and insulin secretion for use in epidemiologic studies. Am J Epidemiol 151: 190-198
58. Yamasaki Y, Kawamori R, Wasada T, et al. (1997) Pioglitazone (AD-4833) ameliorates insulin resistance in patients with NIDDM. AD-4833 Glucose Clamp Study Group, Japan. Tohoku J Exp Med 183: 173-183
59. Wasada T, Arii H, Kuroki H, et al. (1995) The relationship between insulin resistance and insulin secretion in Japanese subjects with borderline glucose intolerance. Diabetes Res Clin Pract 30: 53-57

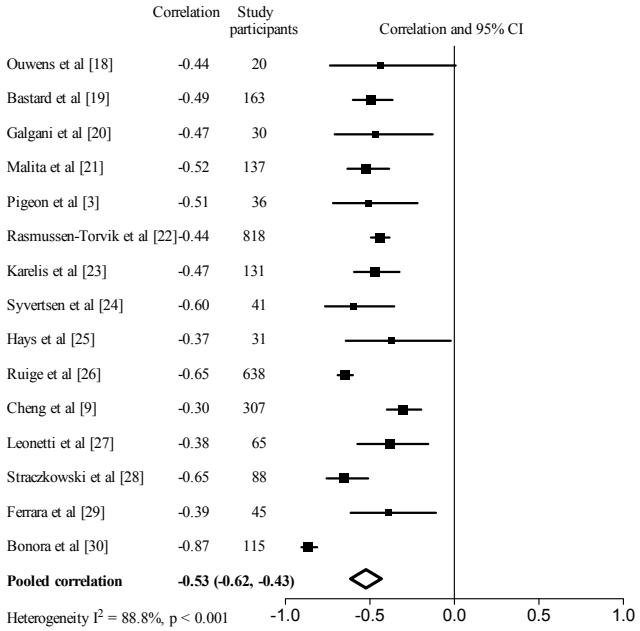
60. Ludvik B, Nolan JJ, Baloga J, Sacks D, Olefsky J (1995) Effect of obesity on insulin resistance in normal subjects and patients with NIDDM. Diabetes 44: 1121-1125
61. Li G, Pan X (1995) A new insulin-sensitivity index for epidemiological study. Chin Med J (Engl) 108: 55-56
62. Falkner B, Hulman S, Kushner H (1993) Insulin-stimulated glucose utilization and borderline hypertension in young adult blacks. Hypertension 22: 18-25
63. Laakso M (1993) How good a marker is insulin level for insulin resistance? Am J Epidemiol 137: 959-965
64. McCall JL, Tuckey JA, Parry BR (1992) Serum tumour necrosis factor alpha and insulin resistance in gastrointestinal cancer. Br J Surg 79: 1361-1363

ESM Fig. 9 Meta-analyses of correlation coefficients between HOMA-IR and different clamp measurements

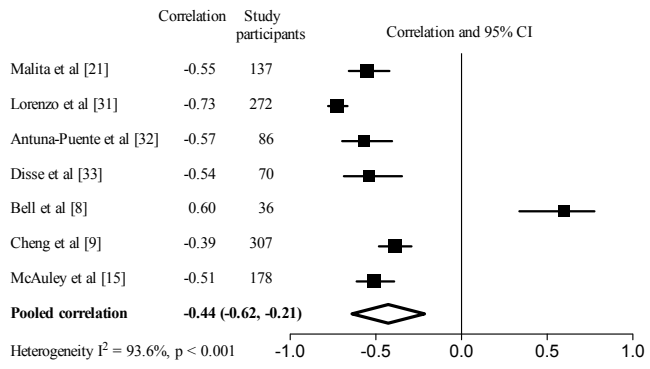
A) HOMA-IR correlated with M_{BW}/I



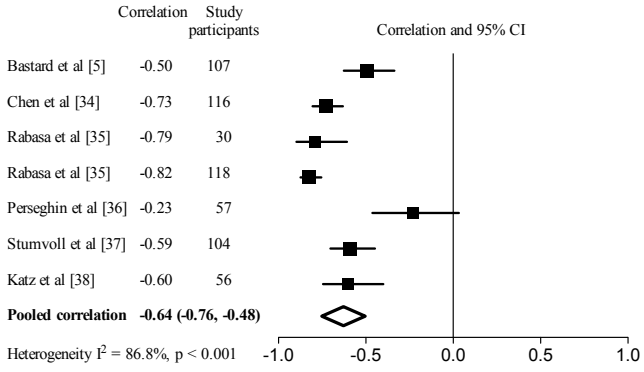
B) HOMA-IR correlated with M_{LBM}



C) HOMA-IR correlated with M_{LBM}/I



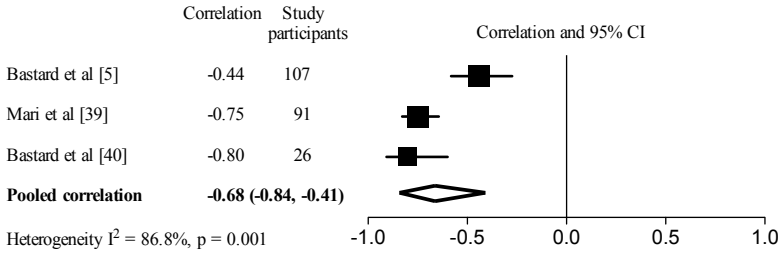
D) HOMA-IR correlated with $M_{BW}/(G*\Delta I)$



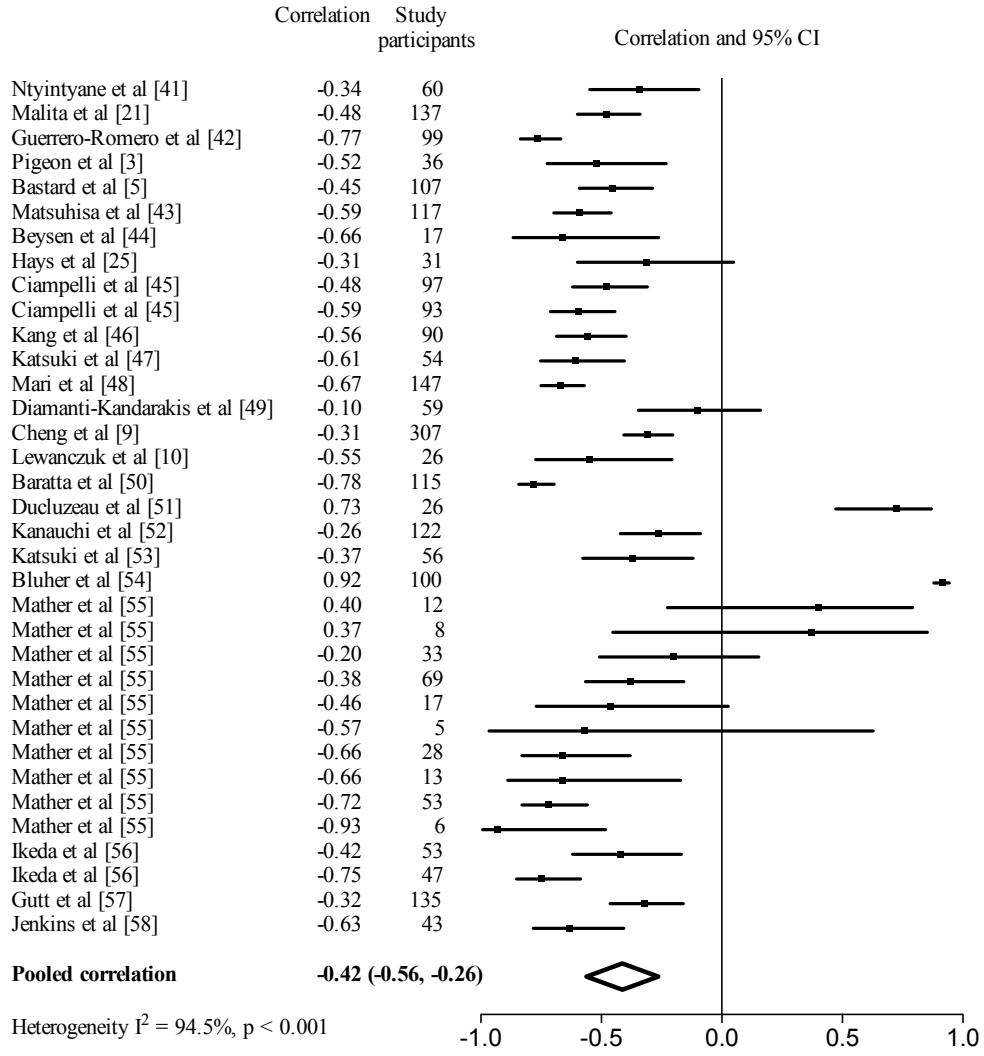
Abbreviations: M_{BW}, glucose infusion rate per kg body weight. I, steady state insulin. M_{LBM}, glucose infusion rate per kg lean body mass. G, steady state glucose. ΔI, increment of insulin concentration. M_{BSA}, glucose infusion rate per m^2 body surface area.

ESM Fig. 9 (continued)

E) HOMA-IR correlated with M_{BSA}



F) HOMA-IR correlated with M_{BW}



References

1. Zaletel J, Barlovic DP, Prezelj J (2010) Adiponectin-leptin ratio: a useful estimate of insulin resistance in patients with Type 2 diabetes. J Endocrinol Invest 33: 514-518
2. Ijzerman RG, Stehouwer CD, Serne EH, et al. (2009) Incorporation of the fasting free fatty acid concentration into quantitative insulin sensitivity check index improves its association with insulin sensitivity in adults, but not in children. Eur J Endocrinol 160: 59-64
3. Pigeon E, Riou ME, St-Onge J, et al. (2009) Validation of a simple index (SIisOGTT) of insulin sensitivity in a population of sedentary men. Diabetes Metab 35: 398-403
4. Dagogo-Jack S, Askari H, Tykodi G (2009) Glucoregulatory physiology in subjects with low-normal, high-normal, or impaired fasting glucose. J Clin Endocrinol Metab 94: 2031-2036
5. Bastard JP, Vandernotte JM, Faraj M, et al. (2007) Relationship between the hyperinsulinemic-euglycaemic clamp and a new simple index assessing insulin sensitivity in overweight and obese postmenopausal women. Diabetes Metab 33: 261-268
6. Piche ME, Lemieux S, Corneau L, Nadeau A, Bergeron J, Weisnagel SJ (2007) Measuring insulin sensitivity in postmenopausal women covering a range of glucose tolerance: comparison of indices derived from the oral glucose tolerance test with the euglycemic-hyperinsulinemic clamp. Metabolism 56: 1159-1166
7. Abdul-Ghani MA, Matsuda M, Balas B, DeFronzo RA (2007) Muscle and liver insulin resistance indexes derived from the oral glucose tolerance test. Diabetes Care 30: 89-94
8. Bell D, McAuley KA, Mann J, Murphy E, Williams S (2004) The hypertriglyceridaemic waist in New Zealand Maori. Asia Pac J Clin Nutr 13: 74-77
9. Cheng C, Campbell KL, Kushner H, Falkner BE (2004) Correlation of oral glucose tolerance test-derived estimates of insulin sensitivity with insulin clamp measurements in an African-American cohort. Metabolism 53: 1107-1112
10. Lewanczuk RZ, Paty BW, Toth EL (2004) Comparison of the [13C]glucose breath test to the hyperinsulinemic-euglycemic clamp when determining insulin resistance. Diabetes Care 27: 441-447
11. Soonthornpun S, Setasuban W, Thamprasit A, Chayanunnukul W, Rattarasarn C, Geater A (2003) Novel insulin sensitivity index derived from oral glucose tolerance test. J Clin Endocrinol Metab 88: 1019-1023
12. Yokoyama H, Emoto M, Fujiwara S, et al. (2003) Quantitative insulin sensitivity check index and the reciprocal index of homeostasis model assessment in normal range weight and moderately obese type 2 diabetic patients. Diabetes Care 26: 2426-2432
13. Bastard JP, Rabasa-Lhoret R, Maachi M, et al. (2003) What kind of simple fasting index should be used to estimate insulin sensitivity in humans? Diabetes Metab 29: 285-288
14. Ahren B, Larsson H (2002) Quantification of insulin secretion in relation to insulin sensitivity in nondiabetic postmenopausal women. Diabetes 51 Suppl 1: S202-211
15. McAuley KA, Williams SM, Mann JI, et al. (2001) Diagnosing insulin resistance in the general population. Diabetes Care 24: 460-464
16. Matsuda M, DeFronzo RA (1999) Insulin sensitivity indices obtained from oral glucose tolerance testing: comparison with the euglycemic insulin clamp. Diabetes Care 22: 1462-1470
17. Emoto M, Nishizawa Y, Maekawa K, et al. (1999) Homeostasis model assessment as a clinical index of insulin resistance in type 2 diabetic patients treated with sulfonylureas. Diabetes Care 22: 818-822
18. Ouwens DM, Bekaert M, Lapauw B, et al. (2012) Chemerin as biomarker for insulin sensitivity in males without typical characteristics of metabolic syndrome. Arch Physiol Biochem 118: 135-138
19. Bastard JP, Lavoie ME, Messier V, Prud'homme D, Rabasa-Lhoret R (2012) Evaluation of two new surrogate indices including parameters not using insulin to assess insulin sensitivity/resistance in non-diabetic postmenopausal women: a MONET group study. Diabetes Metab 38: 258-263

20. Galgani JE, de Jonge L, Rood JC, Smith SR, Young AA, Ravussin E (2010) Urinary C-peptide excretion: a novel alternate measure of insulin sensitivity in physiological conditions. Obesity (Silver Spring) 18: 1852-1857
21. Malita FM, Messier V, Lavoie JM, Bastard JP, Rabasa-Lhoret R, Karelis AD (2010) Comparison between several insulin sensitivity indices and metabolic risk factors in overweight and obese postmenopausal women: a MONET study. Nutr Metab Cardiovasc Dis 20: 173-179
22. Rasmussen-Torvik LJ, Pankow JS, Jacobs DR, et al. (2007) Heritability and genetic correlations of insulin sensitivity measured by the euglycaemic clamp. Diabet Med 24: 1286-1289
23. Karelis AD, Pasternyk SM, Messier L, et al. (2007) Relationship between insulin sensitivity and the triglyceride-HDL-C ratio in overweight and obese postmenopausal women: a MONET study. Appl Physiol Nutr Metab 32: 1089-1096
24. Syvertsen C, Halse J, Hoivik HO, et al. (2007) The effect of 6 months supplementation with conjugated linoleic acid on insulin resistance in overweight and obese. Int J Obes (Lond) 31: 1148-1154
25. Hays NP, Starling RD, Sullivan DH, Fluckey JD, Coker RH, Evans WJ (2006) Comparison of insulin sensitivity assessment indices with euglycemic-hyperinsulinemic clamp data after a dietary and exercise intervention in older adults. Metabolism 55: 525-532
26. Ruige JB, Mertens IL, Bartholomeeusen E, Dirinck E, Ferrannini E, Van Gaal LF (2006) Fasting-based estimates of insulin sensitivity in overweight and obesity: a critical appraisal. Obesity (Silver Spring) 14: 1250-1256
27. Leonetti F, Iacobellis G, Zappaterreno A, et al. (2004) Insulin sensitivity assessment in uncomplicated obese women: comparison of indices from fasting and oral glucose load with euglycemic hyperinsulinemic clamp. Nutr Metab Cardiovasc Dis 14: 366-372
28. Straczkowski M, Stepien A, Kowalska I, Kinalska I (2004) Comparison of simple indices of insulin sensitivity using the euglycemic hyperinsulinemic clamp technique. Med Sci Monit 10: CR480-484
29. Ferrara CM, Goldberg AP (2001) Limited value of the homeostasis model assessment to predict insulin resistance in older men with impaired glucose tolerance. Diabetes Care 24: 245-249
30. Bonora E, Targher G, Alberiche M, et al. (2000) Homeostasis model assessment closely mirrors the glucose clamp technique in the assessment of insulin sensitivity: studies in subjects with various degrees of glucose tolerance and insulin sensitivity. Diabetes Care 23: 57-63
31. Lorenzo C, Haffner SM, Stancakova A, Laakso M (2010) Relation of direct and surrogate measures of insulin resistance to cardiovascular risk factors in nondiabetic finnish offspring of type 2 diabetic individuals. J Clin Endocrinol Metab 95: 5082-5090
32. Antuna-Puente B, Disse E, Faraj M, et al. (2009) Evaluation of insulin sensitivity with a new lipid-based index in non-diabetic postmenopausal overweight and obese women before and after a weight loss intervention. Eur J Endocrinol 161: 51-56
33. Disse E, Bastard JP, Bonnet F, et al. (2008) A lipid-parameter-based index for estimating insulin sensitivity and identifying insulin resistance in a healthy population. Diabetes Metab 34: 457-463
34. Chen H, Sullivan G, Quon MJ (2005) Assessing the predictive accuracy of QUICKI as a surrogate index for insulin sensitivity using a calibration model. Diabetes 54: 1914-1925
35. Rabasa-Lhoret R, Bastard JP, Jan V, et al. (2003) Modified quantitative insulin sensitivity check index is better correlated to hyperinsulinemic glucose clamp than other fasting-based index of insulin sensitivity in different insulin-resistant states. J Clin Endocrinol Metab 88: 4917-4923
36. Perseghin G, Caumo A, Caloni M, Testolin G, Luzi L (2001) Incorporation of the fasting plasma FFA concentration into QUICKI improves its association with insulin sensitivity in nonobese individuals. J Clin Endocrinol Metab 86: 4776-4781
37. Stumvoll M, Mitrakou A, Pimenta W, et al. (2000) Use of the oral glucose tolerance test to assess insulin release and insulin sensitivity. Diabetes Care 23: 295-301
38. Katz A, Nambi SS, Mather K, et al. (2000) Quantitative insulin sensitivity check index: a simple, accurate method for assessing insulin sensitivity in humans. J Clin Endocrinol Metab 85: 2402-2410

39. Mari A, Pacini G, Murphy E, Ludvik B, Nolan JJ (2001) A model-based method for assessing insulin sensitivity from the oral glucose tolerance test. Diabetes Care 24: 539-548
40. Bastard JP, Robert JJ, Jardel C, Bruckert E, Grimaldi A, Hainque B (2001) Is quantitative insulin sensitivity check index, a fair insulin sensitivity index in humans? Diabetes Metab 27: 69-70
41. Ntyintyane L, Panz V, Raal F, Gill G (2010) Comparison between surrogate indices of insulin sensitivity and resistance, and the hyperinsulinaemic euglycaemic glucose clamp in urban South African blacks with and without coronary artery disease. Diab Vasc Dis Res 7: 151-157
42. Guerrero-Romero F, Simental-Mendia LE, Gonzalez-Ortiz M, et al. (2010) The product of triglycerides and glucose, a simple measure of insulin sensitivity. Comparison with the euglycemic-hyperinsulinemic clamp. J Clin Endocrinol Metab 95: 3347-3351
43. Matsuhisa M, Yamasaki Y, Emoto M, et al. (2007) A novel index of insulin resistance determined from the homeostasis model assessment index and adiponectin levels in Japanese subjects. Diabetes Res Clin Pract 77: 151-154
44. Beysen C, Murphy EJ, McLaughlin T, et al. (2007) Whole-body glycolysis measured by the deuterated-glucose disposal test correlates highly with insulin resistance in vivo. Diabetes Care 30: 1143-1149
45. Ciampelli M, Leoni F, Cucinelli F, et al. (2005) Assessment of insulin sensitivity from measurements in the fasting state and during an oral glucose tolerance test in polycystic ovary syndrome and menopausal patients. J Clin Endocrinol Metab 90: 1398-1406
46. Kang ES, Yun YS, Park SW, et al. (2005) Limitation of the validity of the homeostasis model assessment as an index of insulin resistance in Korea. Metabolism 54: 206-211
47. Katsuki A, Urakawa H, Gabazza EC, et al. (2005) Quantitative insulin sensitivity check index is a useful indicator of insulin resistance in Japanese metabolically obese, normal-weight subjects with normal glucose tolerance. Endocr J 52: 253-257
48. Mari A, Pacini G, Brazzale AR, Ahren B (2005) Comparative evaluation of simple insulin sensitivity methods based on the oral glucose tolerance test. Diabetologia 48: 748-751
49. Diamanti-Kandarakis E, Kouli C, Alexandraki K, Spina G (2004) Failure of mathematical indices to accurately assess insulin resistance in lean, overweight, or obese women with polycystic ovary syndrome. J Clin Endocrinol Metab 89: 1273-1276
50. Baratta R, Amato S, Degano C, et al. (2004) Adiponectin relationship with lipid metabolism is independent of body fat mass: evidence from both cross-sectional and intervention studies. J Clin Endocrinol Metab 89: 2665-2671
51. Ducluzeau PH, Cousin P, Malvoisin E, et al. (2003) Glucose-to-insulin ratio rather than sex hormone-binding globulin and adiponectin levels is the best predictor of insulin resistance in nonobese women with polycystic ovary syndrome. J Clin Endocrinol Metab 88: 3626-3631
52. Kanauchi M (2003) Validation of the oral glucose insulin sensitivity index to assess insulin sensitivity in Japanese subjects for use in clinical practice. Eur J Clin Invest 33: 1022-1023
53. Katsuki A, Sumida Y, Urakawa H, et al. (2002) Neither homeostasis model assessment nor quantitative insulin sensitivity check index can predict insulin resistance in elderly patients with poorly controlled type 2 diabetes mellitus. J Clin Endocrinol Metab 87: 5332-5335
54. Bluher M, Kratzsch J, Paschke R (2001) Plasma levels of tumor necrosis factor-alpha, angiotensin II, growth hormone, and IGF-I are not elevated in insulin-resistant obese individuals with impaired glucose tolerance. Diabetes Care 24: 328-334
55. Mather KJ, Hunt AE, Steinberg HO, et al. (2001) Repeatability characteristics of simple indices of insulin resistance: implications for research applications. J Clin Endocrinol Metab 86: 5457-5464
56. Ikeda Y, Suehiro T, Nakamura T, Kumon Y, Hashimoto K (2001) Clinical significance of the insulin resistance index as assessed by homeostasis model assessment. Endocr J 48: 81-86
57. Gutt M, Davis CL, Spitzer SB, et al. (2000) Validation of the insulin sensitivity index (ISI(0,120)): comparison with other measures. Diabetes Res Clin Pract 47: 177-184

58. Jenkins AB, Samaras K, Carey DG, Kelly P, Campbell LV (2000) Improved indices of insulin resistance and insulin secretion for use in genetic and population studies of type 2 diabetes mellitus. Twin Res 3: 148-151

ESM Table 1 Study characteristics

Study	Number of study participants (proportion of women)	Country	Subject category	Age (SD)	BMI (SD)	Insulin dose HEC (target blood glucose, duration)	Clamp measure	Method of correlation	Quality assessment[a]
Abdul-Ghani 2007 [1]	155 (63%)	USA	NGT, IGT	40 (12)	30.4 (6.1)	40 mU/m^2/min (fasting level, 120 min)	M_{BW}/I	Pearson	(1)0, (2)1, (3)2, (4)2, (5)1, (6)2, (7)2
Ahren 2002 [2]	81 (100%)	Sweden	Non-diabetic postmenopausal women	62 (1)	25.7 (3.4)	0.28 nmol/m^2/min (5 mmol/l, 120 min)	M_{BW}/I	Spearman	(1)0, (2)1, (3)2, (4)2, (5)1, (6)2, (7)2
Antuna-Puente 2009 [3]	86 (100%)	France	Postmenopausal women			75 mU/m^2/min (fasting level, 180 min)	M_{LBM}/I	Spearman	(1)0, (2)1, (3)2, (4)2, (5)1, (6)3, (7)2
Aroda 2008 [4]	37 (100%)	USA	PCOS and controls	29 (6)	35.5 (7.2)	300 mU/m^2/min (5 mmol/l, 180 min)	M_{BW}	Pearson	(1)0, (2)1, (3)2, (4)2, (5)1, (6)3, (7)2
Baratta 2004 [5]	115 (59%)	Italy	Non-diabetic	39 (14)	31.7 (9.7)	40 mU/m^2/min (fasting level, 120 min)	M_{BW}	Pearson	(1)1, (2)1, (3)2, (4)2, (5)1, (6)2, (7)2
Bastard 2001 [6]	26	France	T2DM and non-diabetic	43 (10)	29.8 (7.5)	40/400 mU/m^2/min (100 min)	M_{BSA}	Pearson	(1)0, (2)1, (3)2, (4)0, (5)1, (6)1, (7)2
Bastard 2003 [7]	111	France	NGT, IGT, T2DM		28.3 (5.7)	75 mU/m^2/min (180 min)	M_{BW}/I	Spearman	(1)0, (2)1, (3)2, (4)2, (5)1, (6)3, (7)2
Bastard 2007 [8]	107 (100%)	Canada	Non-diabetic postmenopausal women	58 (5)	32.4 (4.5)	75 mU/m^2/min (fasting level, 180 min)	M_{BW}, M_{LBM}, M_{BSA}, M_{BW}/I, M_{BW}/(G* ΔI)	Pearson	(1)0, (2)1, (3)2, (4)2, (5)1, (6)3, (7)2
Bastard 2012 [9]	163 (100%)	Canada	Postmenopausal women with NGT, IGT, IFG	57 (5)	33.1 (3.8)	75 mU/m^2/min (fasting level, 180 min)	M_{LBM}	Pearson	(1)0, (2)1, (3)2, (4)2, (5)1, (6)3, (7)0

Bell 2004 [10]	36 (78%)	New Zealand	NFG, IFG, T2DM	41 (9)	34.3 (5.9)	40 mU/m^2/min (4.5 mmol/l, 120 min)	M_{BW}/I, M_{LBM}/I	Pearson	(1)0, (2)1, (3)2, (4)1, (5)1, (6)2, (7)0
Beysen 2007 [11]	17 (71%)	USA	Non-diabetic patients with metabolic syndrome and controls	36 (13)	28.9 (7.4)	40 mU/m^2/min (5 mmol/l, 110 min)	M_{BW}	Pearson	(1)0, (2)1, (3)2, (4)1, (5)1, (6)1, (7)2
Blonk 1994 [12]	46 (57%)	The Netherlands	T2DM	59 (7)	29.9 (4.9)	65 mU/kg_{LBM}/h (5 mmol/l)	M_{LBM}	Pearson	(1)1, (2)0, (3)2, (4)0, (5)1, (6)0, (7)2
Bluher 2001 [13]	100 (55%)	Germany	NGT, IGT	38 (13)	26.8 (6.9)	0.28 nmol/m^2/min (5 mmol/l, 120 min)	M_{BW}	Spearman	(1)1, (2)1, (3)2, (4)2, (5)1, (6)2, (7)2
Bonora 2000 [14]	115 (57%)	Italy	T2DM and non-diabetic	48 (12)	27.8 (5.0)	20 mU/m^2/min (5 mmol/l, 240 min)	M_{LBM}	Pearson/Spearman	(1)1, (2)1, (3)2, (4)0, (5)0, (6)3, (7)2
Broughton 1992 [15]	25 (0%)	United Kingdom	NGT, IGT, T2DM	61 (13)	26.4 (3.4)	15/50 mU/kg/min (fasting level, 120/150 min)	M_{BW}/G	Pearson	(1)0, (2)1, (3)2, (4)2, (5)0, (6)3, (7)1
Buren 2003 [16]	30 (40%)	Sweden	T2DM and controls	58 (7)	27.4 (3.1)	56 mU/m^2/min (6 mmol/l, 120 min)	M_{LBM}	Pearson	(1)1, (2)1, (3)2, (4)0, (5)1, (6)2, (7)1
Chen 2005 [17]	116 (55%)	USA	NGT, IGT, T2DM	43 (11)	31.2 (7.7)	120 mU/m^2/min (fasting level, 240 min)	M_{BW}/(G*ΔI)	Pearson	(1)1, (2)1, (3)2, (4)2, (5)1, (6)3, (7)0
Cheng 2004 [18]	307 (65%)	USA	NGT, IGT, T2DM	332 (4)	30.4 (8.1	1 mU/kg/min (fasting level, 120 min)	M_{BW}, M_{LBM}, M_{BW}/I, M_{LBM}/I	Pearson	(1)0, (2)1, (3)2, (4)2, (5)1, (6)2, (7)2
Christopher 1998 [19]	11 (36%)	Australia	GH-deficit adults	42 (14)	25.5 (4.0)	40 mU/kg/h (fasting level, 150 min)	ΔRd_{LBM}/ΔI	Spearman	(1)0, (2)1, (3)1, (4)0, (5)1, (6)3, (7)2
Ciampelli 2005 [20]	93 (100%)	Italy	PCOS with NGT	25	29.8	40 mU/m^2/min (4.22 mmol/l)	M_{BW}	Spearman	(1)0, (2)1, (3)2, (4)2, (5)1, (6)0, (7)0
Ciampelli 2005 [20]	97 (100%)	Italy	Postmenopausal women with NGT	56	27.2	40 mu/m^2/min (4.22 mmol/l)	M_{BW}	Spearman	(1)0, (2)1, (3)2, (4)2, (5)1, (6)0, (7)0
Cleland 1996 [21]	31 (?)	Great Britain	Non-diabetic	44	27.7	(5.2 mmol/l, 180 min)	M_{BW}	Pearson	(1)0, (2)1, (3)2, (4)0, (5)0, (6)3, (7)0

Cohen 2006 [22]	6 (100%)	Israel	Pregnancy	27 (3)	31.0 (3.1)	7 pmol/kg/min (4.7 mmol/l, 240 min)	M_{BW}	Pearson	(1)0, (2)1, (3)1, (4)0, (5)1, (6)3, (7)0
Dagogo-Jack 2009 [23]	39 (59%)	USA	Non-diabetic	36 (11)	32.1 (9.9)	2 mU/kg/min (100 mg/dl, 180 min)	M_{BW}/I	Spearman	(1)1, (2)1, (3)2, (4)2, (5)1, (6)3, (7)2
DeFronzo 1979 [24]	15 (60%)	USA	T2DM	59 (12)		42.6 mU/m^2/min (fasting level, 120 min)	M_{BW}	Pearson	(1)1, (2)0, (3)2, (4)0, (5)1, (6)2, (7)2
de Rooij 2009 [25]	1177 (56%)	Europe	Healthy	44 (8)	24.9 (5.0)	240 pmol/m^2/min (5 mmol/l, 120 min)	M_{LBM}/I	Spearman	(1)1, (2)1, (3)2, (4)2, (5)1, (6)2, (7)2
de Rooij 2009 [25]	522 (0%)	Europe	Healthy men	43 (8)	26.2 (3.9)	240 pmol/m^2/min (5 mmol/l, 120 min)	M_{LBM}/I	Spearman	(1)0, (2)1, (3)2, (4)2, (5)1, (6)2, (7)2
de Rooij 2009 [25]	655 (100%)	Europe	Healthy women	44 (8)	24.4 (5.2)	240 pmol/m^2/min (5 mmol/l, 120 min)	M_{LBM}/I	Spearman	(1)0, (2)1, (3)2, (4)2, (5)1, (6)2, (7)2
Diamanti-Kandarakis 2004 [26]	59 (100%)	Greece	PCOS with NGT	23 (4)	28.9 (7.1)	40 mU/m^2/min (fasting level, 120 min)	M_{BW}	Pearson	(1)0, (2)0, (3)2, (4)2, (5)1, (6)2, (7)2
Disse 2008 [27]	70 (56%)	France	Healthy	43 (7)	23.6 (3.4)	40 mU/m^2/min (4.5 mmol/l, 120 min)	M_{LBM}/I	Spearman	(1)1, (2)1, (3)2, (4)2, (5)1, (6)2, (7)2
Donahue 1999 [28]	23 (0%)	USA	Non-diabetic men	35 (6)	27.3 (7.1)	40 μU/m^2/min (fasting level, 120 min)	M_{BW}	Pearson	(1)0, (2)1, (3)2, (4)2, (5)1, (6)2, (7)2
Donahue 1999 [28]	26 (100%)	USA	Non-diabetic women	36 (7)	27.5 (7.7)	40 μU/m^2/min (fasting level, 120 min)	M_{BW}	Pearson	(1)0, (2)1, (3)2, (4)2, (5)1, (6)2, (7)2
Ducluzeau 2003 [29]	26 (100%)	France	PCOS and controls	23 (5)	23.3 (3.9)	450 pmol/m^2/min (180 min)	M_{BW}	Spearman	(1)0, (2)1, (3)2, (4)2, (5)1, (6)3, (7)2
Eliasson 1994 [30]	57 (0%)	Sweden	Non-diabetic	49 (6)	23.7 (2.0)	1.0 mU/kg/min (5 mmol/l, 120 min)	M_{LBM}	Pearson	(1)0, (2)1, (3)2, (4)1, (5)1, (6)2, (7)1
Emoto 1999 [31]	80 (24%)	Japan	T2DM	53 (13)	23.3 (3.4)	1.25 mU/kg/min (5 mmol/l, 120 min)	M_{BW}/I	Pearson	(1)0, (2)0, (3)1, (4)0, (5)0, (6)2, (7)2
Falkner 1993 [32]	23 (30%)	USA	Non-diabetic	26 (2)	25.7 (4.2)	30 mU/m^2/min (120 min)	M_{BW}	Pearson	(1)0, (2)1, (3)2, (4)2, (5)1, (6)2, (7)2
Falkner 1993 [32]	27 (22%)	USA	Non-diabetic	26 (2)	28.9 (6.3)	30 mU/m^2/min (120 min)	M_{BW}	Pearson	(1)0, (2)1, (3)2, (4)2, (5)1, (6)2, (7)2

Ferrannini 2007 [33]	590 (0%)	Europe	Healthy men	43 (9)	26.0 (4.4)	240 pmol/m^2/min (5 mmol/l, 120 min)	M_{LBM}/I	Spearman	(1)0, (2)1, (3)2, (4)2, (5)1, (6)2, (7)2
Ferrannini 2007 [33]	718 (100%)	Europe	Healthy women	44 (8)	24.0 (5.3)	240 pmol/m^2/min (5 mmol/l, 120 min)	M_{LBM}/I	Spearman	(1)0, (2)1, (3)2, (4)2, (5)1, (6)2, (7)2
Ferrara 2001 [34]	45 (0%)	USA	NGT, IGT	61 (8)	29.5 (3.1)	600 pmol/m^2/min (fasting level)	M_{LBM}	Pearson	(1)0, (2)1, (3)2, (4)2, (5)1, (6)0, (7)2
Ferrara 2001 [34]	21 (0%)	USA	NGT	62 (9)	27.8 (2.6)	600 pmol/m^2/min (fasting level)	M_{LBM}	Pearson	(1)0, (2)0, (3)2, (4)2, (5)1, (6)0, (7)2
Ferrara 2001 [34]	24 (0%)	USA	IGT	61 (8)	30.9 (2.8)	600 pmol/m^2/min (fasting level)	M_{LBM}	Pearson	(1)0, (2)0, (3)2, (4)2, (5)1, (6)0, (7)2
Fink 1983 [35]	17 (35%)	USA	NGT	69 (4)	24.0 (2.1)	15/40 mU/m^2/min (85 mg/dl, 180min)	M_{BSA}	Pearson	(1)0, (2)0, (3)2, (4)2, (5)1, (6)3, (7)2
Finucane 2009 [36]	534 (0%)	United kingdom	Healthy	43 (8)	26.4 (2.4)	240 pmol/m^2/min (5 mmol/l)	M_{LBM}/I	Pearson	(1)0, (2)1, (3)2, (4)0, (5)1, (6)0, (7)0
Finucane 2009 [36]	692 (100%)	United kingdom	Healthy	44 (9)	24.8 (4.0)	240 pmol/m^2/min (5 mmol/l)	M_{LBM}/I	Pearson	(1)0, (2)1, (3)2, (4)0, (5)1, (6)0, (7)0
Furuhashi 2003 [37]	51 (55%)	Japan	Non-diabetic	46 (13)	24.5 (2.8)	40 mU/m^2/min (120 min)	M_{BSA}	Pearson	(1)1, (2)1, (3)2, (4)0, (5)1, (6)2, (7)2
Furuhashi 2005 [38]	30 (100%)	Japan	Healthy	24 (4)	24.5 (3.2)	40 mU/m^2/min (120 min)	M_{BW}/I	Spearman	(1)0, (2)1, (3)2, (4)0, (5)1, (6)2, (7)2
Galgani 2010 [39]	30 (50%)	USA	Non-diabetic	35 (12)	27.2 (4.0)	120 mU/m^2/min (5 mmol/l, 120 min)	M_{LBM}	Spearman	(1)0, (2)1, (3)2, (4)0, (5)0, (6)2, (7)2
Garg 1988 [40]	44 (0%)	USA	Healthy men	25 (3)	24.3 (2.7)	40 mU/m^2/min (fasting level, 240 min)	M_{BW}, M_{BW}/I	Pearson	(1)0, (2)1, (3)2, (4)1, (5)1, (6)3, (7)2
Gastaldelli 2004 [41]	388 (54%)	Italy	NGT, IGT, T2DM	46 (12)	29.9 (5.6)	240 pmol/m^2/min (5.3 mmol/l, 120/180 min)	M_{LBM}/I	Spearman	(1)1, (2)1, (3)2, (4)2, (5)1, (6)3, (7)2
Geloneze 2009 [42]	41 (100%)	Brasil	Non-diabetic	38 (14)	31.0 (14.0)	40 mU/m^2/min (120 min)	M_{LBM}	Spearman	(1)0, (2)1, (3)2, (4)2, (5)1, (6)2, (7)2
Goodarzi 2011 [43]	470 (58%)	USA	Non-diabetic			60 mU/m^2/min (97.5 mg/dl, 120 min)	M_{BW}/I	Pearson	(1)1, (2)1, (3)2, (4)2, (5)1, (6)2, (7)0

Guerrero-Romero 2010 [44]	99 (53%)	Mexico	T2DM and controls	40 (9)	30.8 (3.3)	40 μU/m^2/min (120 min)	M_{BW}	Pearson	(1)1, (2)1, (3)2, (4)2, (5)1, (6)2, (7)2
Gutt 2000 [45]	135 (63%)	USA	NGT, IGT, T2DM			(fasting level)	M_{BW}	Pearson	(1)0, (2)1, (3)2, (4)2, (5)0, (6)0, (7)1/2
Hanson 2000 [46]	457	USA	NGT, IGT				M_{BW}	Pearson	(1)0, (2)1, (3)2, (4)2, (5)0, (6)0, (7)2
Hays 2006 [47]	31 (58%)	USA	IGT	68 (20)	30.7 (3.9)	40 mU/m^2/min (fasting level, 120 min)	M_{BW}, M_{LBM}	Pearson	(1)1, (2)0, (3)2, (4)2, (5)0, (6)2, (7)2
Heliovaara 2005 [48]	21 (24%)	Finland	Healthy	28 (8)	24.1 (3.7)	40 mU/m^2/min (240 min)	M_{BW}	Spearman	(1)0, (2)1, (3)2, (4)0, (5)1, (6)3, (7)2
Hollenbeck 1984 [49]	62 (56%)	USA	NGT	42 (16)	23.2 (3.1)	40 mU/m^2/min (fasting level, 120 min)	M_{BSA}	Pearson	(1)1, (2)0, (3)2, (4)2, (5)1, (6)2, (7)2
Ijzerman 2009 [50]	59 (49%)	The Netherlands	Non-diabetic	44 (5)	24.9 (3.8)	60 mU/kg/h (5 mmol/l, 120 min)	M_{BW}/I	Pearson	(1)1, (2)1, (3)2, (4)0, (5)1, (6)2, (7)2
Ikeda 2001 [51]	100 (40%)	Japan	NGT, IGT, T2DM	44 (14)	24.8 (4.9)	1.12 mU/kg/min (5 mmol/l, 120 min)	M_{BW}	Pearson	(1)1, (2)1, (3)2, (4)2, (5)1, (6)2, (7)2
Ikeda 2001 [51]	47 (43%)	Japan	T2DM	52 (11)	25.5 (4.3)	1.12 mU/kg/min (5 mmol/l, 120 min)	M_{BW}	Pearson	(1)1, (2)0, (3)2, (4)2, (5)1, (6)2, (7)2
Ikeda 2001 [51]	53 (38%)	Japan	NGT, IGT	37 (12)	24.2 (5.3)	1.12 mU/kg/min (5 mmol/l, 120 min)	M_{BW}	Pearson	(1)0, (2)1, (3)2, (4)2, (5)1, (6)2, (7)2
Jenkins 2000 [52]	43 (81%)	Australia	Non-diabetic	39 (11)	25.6 (4.2)	(180 min)	M_{BW}	Pearson	(1)0, (2)1, (3)2, (4)0, (5)0, (6)3, (7)2
Kanauchi 2002 [53]	77 (27%)	Japan	NGT, IGT, type 2-diabetes	60 (10)	24.0 (10.0)	1.12 mU/kg/min (95 mg/dl, 120 min)	M_{BW}	Spearman	(1)0, (2)1, (3)2, (4)2, (5)1, (6)2, (7)2
Kanauchi 2003 [54]	122 (22%)	Japan	NGT, IFG, IGT, T2DM	60	24.4	1.12 mU/kg/min (95 mg/dl, 120 min)	M_{BW}	Pearson	(1)0, (2)1, (3)2, (4)2, (5)1, (6)2, (7)2
Kang 2005 [55]	90 (16%)	Korea	NGT, IGT, T2DM	46 (7)	24.1 (5.4)	120 pmol/m^2/min (5 mmol/l, 180 min)	M_{BW}	Pearson	(1)0, (2)1, (3)2, (4)2, (5)0, (6)3, (7)2
Karelis 2007 [56]	131 (100%)	Canada	Postmenopausal women	58 (5)	32.2 (4.3)	75 mU/m^2/min (fasting level, 180 min)	M_{LBM}	Pearson	(1)0, (2)1, (3)2, (4)2, (5)1, (6)3, (7)2

Katsuki 2002 [57]	60 (25%)	Japan	T2DM	55 (11)	23.1 (3.1)	13.44 pmol/kg/min (5.24 mmol/l, 120 min)	M_{BW}	Pearson	(1)0, (2)0, (3)2, (4)0, (5)1, (6)2, (7)2
Katsuki 2002 [58]	56 (43%)	Japan	T2DM	64 (11)	21.6 (1.9)	13.44 pmol/kg/min (5.24 mmol/l, 120 min)	M_{BW}	Pearson	(1)1, (2)0, (3)2, (4)0, (5)1, (6)2, (7)2
Katsuki 2002 [58]	28 (46%)	Japan	T2DM > 70 years old	73 (3)	21.2 (2.2)	13.44 pmol/kg/min (5.24 mmol/l, 120 min)	M_{BW}	Pearson	(1)1, (2)0, (3)2, (4)0, (5)1, (6)2, (7)2
Katsuki 2002 [58]	28 (39%)	Japan	T2DM < 70 years old	55 (9)	22.0 (1.4)	13.44 pmol/kg/min (5.24 mmol/l, 120 min)	M_{BW}	Pearson	(1)0, (2)0, (3)2, (4)0, (5)1, (6)2, (7)2
Katsuki 2005 [59]	54 (4%)	Japan	Non-diabetic	35 (8)	22.2 (1.9)	13.44 pmol/kg/min (5.24 mmol/l, 120 min)	M_{BW}	Pearson	(1)0, (2)0, (3)2, (4)2, (5)1, (6)2, (7)2
Katz 2000 [60]	56 (52%)	USA	T2DM and non-diabetic	37 (12)	30.5 (9.2)	120 mU/m^2/min (fasting level, 240 min)	$M_{BW}/(G^* \Delta I)$	Pearson	(1)1, (2)1, (3)2, (4)0, (5)1, (6)3, (7)0
Katz 2000 [60]	35	USA	Non-diabetic	35 (8)	32.3 (7.7)	120 mU/m^2/min (fasting level, 240 min)	$M_{BW}/(G^* \Delta I)$	Pearson	(1)?, (2)1, (3)2, (4)0, (5)1, (6)3, (7)0
Kirwan 2001 [61]	15 (100%)	USA	Pregnant women (NGT and gestational diabetes)	31 (4)	25.9 (6.7)	40 mU/m^2/min (5 mmol/l, 120 min)	$(M_{LBM} + EGO_{LMB})/I$	Pearson	(1)0, (2)1, (3)1, (4)2, (5)1, (6)2, (7)2
Kolterman 1981 [62]	8 (25%)	USA	IGT	44 (14)		120 (40, 240, 1200, 1800) mU/m^2/min (85 mg/dl, 140 min)	M_{BW}	Pearson	(1)0, (2)0, (3)0, (4)2, (5)1, (6)3, (7)2
Kolterman 1981 [62]	31 (51%)	USA	IGT and T2DM	51 (11)		120 (40, 240, 1200, 1800) mU/m^2/min (85 mg/dl, 140 min)	M_{BW}	Pearson	(1)1, (2)1, (3)0, (4)2, (5)1, (6)3, (7)2
Kotronen 2007 [63]	80 (29%)	Finland	Non-diabetic	43 (10)	26.7 (3.9)	0.3 mU/kg/min (5 mmol/l, 240 min)	M_{LBM}/I	Spearman	(1)0, (2)1, (3)2, (4)1, (5)0, (6)3, (7)2
Laakso 1993 [64]	50 (54%)	Finland	NGT	65 (7)	28 (7)	40 mU/m^2/min (5.5 mmol/l, 120 min)	M_{BW}	Pearson	(1)1, (2)0, (3)2, (4)2, (5)1, (6)2, (7)1
Laakso 1993 [64]	28 (46%)	Finland	IGT	64 (11)	28 (5)	40 mU/m^2/min (5.5 mmol/l, 120 min)	M_{BW}	Pearson	(1)1, (2)0, (3)2, (4)2, (5)1, (6)2, (7)1
Laakso 1993	54 (48%)	Finland	T2DM	61	29 (7)	40 mU/m^2/min (5.5	M_{BW}	Pearson	(1)1, (2)0, (3)2, (4)2,

[64]				(15)		mmol/l, 120 min)			(5)1, (6)2, (7)1
Lansang 2001 [65]	63 (22%)	USA	Non-diabetic	39 (11)		40 mU/m^2/min (120 min)	M_{BSA}/I	Pearson	(1)0, (2)1, (3)2, (4)0, (5)1, (6)2, (7)2
Leonetti 2004 [66]	65 (100%)	Italy	Obese women with NGT	35 (9)	35 (10)	1 mU/kg/min (fasting level, 120 min)	M_{LBM}	Pearson	(1)0, (2)0, (3)2, (4)2, (5)1, (6)2, (7)2
Lewanczuk 2004 [67]	26 (50%)	Canada	T2DM, healthy	42 (20)	30.4 (7.3)	20 mU/m^2/min (5mmol/l, 240 min)	M_{BW}, M_{BW}/I	Pearson	(1)1, (2)1, (3)2, (4)2, (5)0, (6)3, (7)2
Li 1995 [68]	241	China	NGT, IGT, T2DM				M_{BW}	Pearson	(1)0, (2)1, (3)2, (4)2, (5)0, (6)0, (7)2
Liao 2004 [69]	74 (54%)	USA	Non-diabetic	36 (11)	26.9 (4.7)	200 mU/m^2/min (5 mmol/l, 180 min)	M_{LBM}	Pearson	(1)1, (2)1, (3)2, (4)2, (5)0, (6)3, (7)2
Lind 1994 [70]	228 (43%)	Sweden	Healthy and T2DM	58 (12)	27.2 (4.8)	56 mU/m^2/min (5.1 mmol/l)	M_{BW}	Pearson	(1)1, (2)1, (3)2, (4)0, (5)1, (6)0, (7)0
Lindmark 2006 [71]	30 (40%)	Sweden	T2DM and controls	59 (7)	27.4 (3.1)	56 mU/m^2/min (6 mmol/l, 120 min)	M_{BW}	Pearson	(1)1, (2)0, (3)2, (4)0, (5)1, (6)2, (7)2
Lorenzo 2010 [72]	272 (53%)	Finland	Offspring of type 2-diabetics	35 (10)	26.2 (8.2)	(120 min)	M_{LBM}/I	Spearman	(1)1, (2)1, (3)2, (4)2, (5)0, (6)2, (7)2
Ludvik 1995 [73]	65 (9%)	USA	NGT	44 (8)	30.0 (6.0)	120 mU/m^2/min (300 min)	M_{BW}	Pearson	(1)0, (2)0, (3)2, (4)2, (5)1, (6)3, (7)2
Ludvik 1995 [73]	58 (16%)	USA	T2DM	53 (9)	32.1 (7.3)	120 mU/m^2/min (300 min)	M_{BW}	Pearson	(1)0, (2)0, (3)2, (4)2, (5)1, (6)3, (7)2
Malita 2006 [74]	88 (100%)	Canada	Non-diabetic postmenopausal women	58 (5)	32.5 (4.4)	74 mU/m^2/min (fasting level, 180 min)	M_{LBM}	Pearson	(1)0, (2)1, (3)2, (4)2, (5)1, (6)3, (7)2
Malita 2010 [75]	137 (100%)	Canada	Non-diabetic postmenopausal women	58 (5)	32.4 (4.6)	75 mU/m^2/min (fasting level, 180 min)	M_{BW}, M_{LBM}, M_{LBM}/I, $M_{LBM}/(G*\Delta I)$	Pearson	(1)0, (2)1, (3)2, (4)2, (5)1, (6)3, (7)2
Malminiemi 1995 [76]	25 (36%)	Finland	Hypertensive patients	50 (7)	27.9 (2.8)	40 mU/m^2/min (5 mmol/l, 120 min)	$M_{BW}/(G*I)$	Pearson	(1)0, (2)1, (3)2, (4)0, (5)1, (6)2, (7)2

Marchesini 1987 [77]	12 (50%)	Italy	Liver cirrhosis patients	56 (16)		40 mU/m^2/min (fasting level, 120 min)	M_{BW}/I	Pearson	(1)1, (2)1, (3)1, (4)0, (5)1, (6)2, (7)1
Mari 2001 [78]	104 (11%)	USA	NGT, IGT, type 2 diabetes	47 (10)	32.3 (7.0)	120 (300) mU/m^2/min (90 mg/dl, 240 min)	M_{BSA}	Pearson	(1)0, (2)1, (3)2, (4)2, (5)1, (6)3, (7)2
Mari 2001 [78]	13 (23%)	USA	IGT	52	34	300 mU/m^2/min (90 mg/dl, 240 min)	M_{BSA}	Pearson	(1)0, (2)0, (3)2, (4)2, (5)1, (6)3, (7)2
Mari 2005 [79]	147 (100%)	Sweden	Postmenopausal women			0.28 nmol/m^2/min (5 mmol/l, 120 min)	M_{BW}	Pearson	(1)0, (2)1, (3)2, (4)2, (5)1, (6)2, (7)1
Mari 2006 [80]	44	Italy	NGT, IGT, T2DM			240 pmol/m^2/min	M_{BW}	Pearson	(1)0, (2)1, (3)2, (4)2, (5)1, (6)0, (7)0
Mather 2001 [81]	69 (10%)	USA	Lean and healthy	39 (6)	22.8	40 mU/m^2/min (fasting level, 240 min)	M_{BW}	Pearson	(1)0, (2)1, (3)2, (4)0, (5)1, (6)3, (7)0
Mather 2001 [81]	28	USA	Obese and non-diabetic			40 mU/m^2/min (fasting level, 240 min)	M_{BW}	Pearson	(1)0, (2)1, (3)2, (4)0, (5)1, (6)3, (7)0
Mather 2001 [81]	12	USA	Lean and healthy			120 mU/m^2/min (fasting level, 240 min)	M_{BW}	Pearson	(1)0, (2)1, (3)2, (4)0, (5)1, (6)3, (7)0
Mather 2001 [81]	53	USA	Obese and non-diabetic			120 mU/m^2/min (fasting level, 240 min)	M_{BW}	Pearson	(1)0, (2)1, (3)2, (4)0, (5)1, (6)3, (7)0
Mather 2001 [81]	8	USA	Lean and healthy			300 mU/m^2/min (fasting level, 240 min)	M_{BW}	Pearson	(1)0, (2)1, (3)2, (4)0, (5)1, (6)3, (7)0
Mather 2001 [81]	13	USA	Obese and non-diabetic			300 mU/m^2/min (fasting level, 240 min)	M_{BW}	Pearson	(1)0, (2)1, (3)2, (4)0, (5)1, (6)3, (7)0
Mather 2001 [81]	5	USA	T2DM			300 mU/m^2/min (fasting level, 240 min)	M_{BW}	Pearson	(1)0, (2)0, (3)2, (4)0, (5)1, (6)3, (7)0
Mather 2001 [81]	33	USA	Lean and healthy			600 mU/m^2/min (fasting level, 240 min)	M_{BW}	Pearson	(1)0, (2)1, (3)2, (4)0, (5)1, (6)3, (7)0
Mather 2001 [81]	17	USA	Obese and non-diabetic			600 mU/m^2/min (fasting level, 240 min)	M_{BW}	Pearson	(1)0, (2)1, (3)2, (4)0, (5)1, (6)3, (7)0
Mather 2001 [81]	6	USA	T2DM			600 mU/m^2/min (fasting level, 240 min)	M_{BW}	Pearson	(1)0, (2)0, (3)2, (4)0, (5)1, (6)3, (7)0

Matsuda 1999 [82]	153 (57%)	USA	NGT, IGT, T2DM	43 (12)	31 (12)	40 mU/m^2/min (90 mg/dl, 120 min)	M_{BW}/I	Pearson	(1)1, (2)1, (3)2, (4)2, (5)1, (6)2, (7)2
Matsuhisa 2007 [83]	117	Japan	NGT, IGT, T2DM	53 (11)	26.0 (16.2)	(5.5 mmol/l)	M_{BW}	Pearson	(1)0, (2)1, (3)2, (4)2, (5)0, (6)0, (7)2
Matthews 1985 [84]	23	United kingdom	T2DM and non-diabetic			50 mU/min/70 kg ideal body weight (4.5 mmol/l)	(M_{BW}/I)* 0.18	Spearman	(1)0, (2)1, (3)2, (4)0, (5)1, (6)0, (7)2
Mayorov 2005 [85]	43 (65%)	Russia	T2DM	56 (9)	29.5 (5.3)	1 mU/kg/min (5.3 mmol/l, 240 min)	M_{BW}	Pearson	(1)0, (2)0, (3)1, (4)0, (5)0, (6)3, (7)2
McAuley 2001 [86]	178	New Zealand	Non-diabetic	47 (8)	27.5 (5.3)	40 mU/m^2/min (4.5 mmol/l, 120 min)	M_{BW}/I, M_{LBM}/I	Pearson	(1)0, (2)?, (3)2, (4)0, (5)1, (6)2, (7)0
McCall 1992 [87]	21 (43%)	Australia	Non-diabetic	64 (11)		20 mU/m^2/min (120 min)	MBW	Spearman	(1)1, (2)1, (3)2, (4)0, (5)0, (6)2, (7)0
Miyamoto 1992 [88]	28 (21%)	Japan	Livercirrosis	55 (11)	22.0 (3.7)	0.5/3/10 mU/kg/min (fasting level, 270 min)	M_{BW}/G	Pearson	(1)0, (2)?, (3)1, (4)0, (5)1, (6)3, (7)1
Muniyappa 2010 [89]	70 (0%)	USA	T2DM, IFG, NGT	30 (14)	21.0 (4.0)	40-60 mU/m^2/min (87.5 mg/dl, ca 120 min)	M_{BW}/ΔI	Pearson	(1)0, (2)1, (3)2, (4)0, (5)1, (6)2, (7)2
Natali 2000 [90]	354 (37%)	Europe	NGT	43 (15)	26.6 (6.0)	1 mU/kg/min (fasting level)	ΔRd_{BW}/ΔI	Pearson	(1)0, (2)0, (3)2, (4)2, (5)1, (6)0, (7)2
Ntyintyane 2010 [91]	60 (23%)	South Africa	NGT, IGT, T2DM	53 (9)	28.5 (5.6)	40 mU/m^2/min (5.1 mmol/l, 120 min)	M_{BW}	Pearson	(1)0, (2)1, (3)2, (4)2, (5)1, (6)2, (7)2
Okamoto 1991 [92]	36	Japan	NGT, IGT, T2DM	54 (23)	21.1 (3.2)	40 mU/m^2/min (fasting level, 120 min)	M_{BW}/G	Pearson	(1)0, (2)1, (3)2, (4)?, (5)1, (6)2, (7)1
Ouwens 2012 [93]	20 (0%)	Belgium	Healthy men	32 (6)	23.0 (2.3)	40 mU/m2/min (5 mmol/l, 120 min)	M_{LBM}	Pearson	(1)0, (2)1, (3)2, (4)0, (5)1, (6)2, (7)2
Perseghin 2001 [94]	57 (67%)	Italy	Healthy	26 (4)	21.4 (2.8)	40 mU/m^2/min (5 mmol/l, 150 min)	M_{BW}/(G*ΔI)	Pearson	(1)0, (2)1, (3)2, (4)0, (5)1, (6)3, (7)2
Petrie 1997 [95]	30 (10%)	Great Britain	Non-diabetic	43 (10)	27.8 (4.3)	1.5 mU/kg/min (5.2 mmol/l, 180 min)	ΔR_d/(G*ΔI)	Pearson	(1)0, (2)0, (3)2, (4)2, (5)1, (6)3, (7)0
Petrie 1997	26 (15%)	Great Britain	T2DM	58	28.3	1.5 mU/kg/min (5.2	ΔR_d/(G*	Pearson	(1)0, (2)0, (3)2, (4)2,

[95]				(10)	(5.2)	mmol/l, 180 min)	ΔI)		(5)1, (6)3, (7)0
Piche 2007 [96]	112 (100%)	Canada	Postmenopausal women	59	28.7	40 mU/m^2 /min (fasting level, 120 min after steady state)	M_{BW}/I	Pearson	(1)0, (2)1, (3)2, (4)2, (5)1, 6(3), (7)2
Pigeon 2009 [97]	36 (0%)	Canada	Sedentary men with NGT and IGT	43 (5)	31.4 (5.8)	40 mU/m^2/min (5.5 mmol/l, 120 min)	M_{BW}, M_{LBM}, M_{BW}/I	Pearson	(1)0, (2)1, (3)2, (4)2, (5)1, (6)2, (7)2
Rabasa-Lhoret 2003 [98]	30 (50%)	France	NGT	31 (10)	27.2 (6.8)	40 mU/m^2/min (5 mmol/l, 180 min)	M_{BW}/(G* ΔI)	Spearman	(1)1, (2)0, (3)2, (4)2, (5)1, (6)3, (7)2
Rabasa-Lhoret 2003 [98]	118 (69%)	France	NGT, IGT, T2DM	42 (15)	27.6 (5.6)	75 mU/m^2/min (5 mmol/l, 180 min)	M_{BW}/(G* ΔI)	Spearman	(1)0, (2)1, (3)2, (4)2, (5)1, (6)3, (7)2
Raji 2001 [99]	12 (58%)	USA	Healthy	34 (10)	23 (2)	40 mU/m^2/min (fasting level, 120 min)	M_{BW}	Pearson	(1)1, (2)1, (3)2, (4)0, (5)1, (6)2, (7)2
Ramakrishnan 2009 [100]	20 (0%)	India	Non-diabetic			40 mU/m^2/min (90 mg/dl, 120 min)	M_{BW}/I	Spearman	(1)0, (2)1, (3)2, (4)1, (5)1, (6)2, (7)2
Rasmussen-Torvik 2007 [101]	818 (51%)	USA	Parents and their 18-year old children	30 (15)	26.6 (6.4)	1 mU/kg/min (5.6 mmol/l, 180 min)	M_{LBM}	Pearson	(1)1, (2)1, (3)2, (4)1, (5)1, (6)3, (7)0
Reaven 1983 [102]	20 (60%)	USA	NGT	41 (14)	27.0 (5.1)	40 mU/m^2/min (fasting level, 120 min)	M_{BSA}	Pearson	(1)1, (2)0, (3)2, (4)2, (5)1, (6)2, (7)2
Ruige 2006 [103]	638 (40%)	Europe	Non-diabetic			240 pmol/m^2/min (fasting level, 120 min)	M_{LBM}	Spearman	(1)1, (2)1, (3)2, (4)2, (5)1, (6)2, (7)2
Sabelis 2003 [104]	57 (0%)	The Netherlands	Non-diabetic	62 (9)	26.9 (3.3)	3 mU/kg/min (180 min)	M_{BW}/I	Pearson	(1)0, (2)1, (3)2, (4)1, (5)0, (6)3, (7)2
Sindelka 2002 [105]	83	Czech Republic	T2DM and controls	46	31.4 (8.7)	1 mU/kg/min (fasting level, 120 min)	M_{BW}, M_{BW}/G	Pearson	(1)0, (2)1, (3)2, (4)2, (5)1, (6)2, (7)2
Skrha 2004 [106]	41	Czech Republic	T2DM	51	32.6 (7.1)	1 mU/kg/min (fasting level, 120 min)	M_{BW}(G*I)	Spearman	(1)0, (2)0, (3)2, (4)2, (5)1, (6)2, (7)2
Skrha 2004	17	Czech	Primary	49	28.2	1 mU/kg/min (fasting	M_{BW}(G*I	Spearman	(1)0, (2)0, (3)2, (4)2,

[106]		Republic	hyperaldosteronism		(4.4)	level, 120 min)	)		(5)1, (6)2, (7)2
Skrha 2004 [106]	12	Czech Republic	High renin hypertension	52	27.1 (2.7)	1 mU/kg/min (fasting level, 120 min)	M_{BW}(G*I)	Spearman	(1)0, (2)0, (3)2, (4)2, (5)1, (6)2, (7)2
Skrha 2004 [106]	32 (100%)	Czech Republic	PCOS	24	24.2 (4.8)	1 mU/kg/min (fasting level, 120 min)	M_{BW}(G*I)	Spearman	(1)0, (2)0, (3)2, (4)2, (5)1, (6)2, (7)2
Skrha 2004 [106]	47	Czech Republic	Healthy	33	26.6 (9.4)	1 mU/kg/min (fasting level, 120 min)	M_{BW}(G*I)	Spearman	(1)0, (2)0, (3)2, (4)2, (5)1, (6)2, (7)2
Soonthornpun 2003 [107]	33 (52%)	Thailand	NGT	31 (8)	22.0 (3.9)	50 mU/m^2/min (5 mmol/l, 120 min)	M_{BW}/I	Pearson	(1)1, (2)0, (3)2, (4)2, (5)1, (6)2, (7)2
Soonthornpun 2007 [108]	45 (58%)	Thailand	NGT, IGT, T2DM	40 (12)	25.0 (5.3)	50 mU/m^2/min (5 mmol/l, 120 min)	M_{BW}/I	Pearson	(1)1, (2)1, (3)2, (4)2, (5)1, (6)2, (7)2
Stanicka 2005 [109]	15 (100%)	Czech Republic	Post thyroid cancer	33 (8)	24.6 (3.0)	1 mU/kg/min (5 mmol/l, 120 min)	M_{BW}	Pearson	(1)0, (2)1, (3)1, (4)0, (5)1, (6)2, (7)2
Straczkowski 2003 [110]	34 (59%)	Poland	NGT	25 (4)	21.5 (1.9)	50 mU/kg/h (5 mmol/, 120 min)	M_{BW}	Pearson	(1)1, (2)0, (3)2, (4)2, (5)1, (6)2, (7)2
Straczkowski 2004 [111]	88 (59%)	Poland	NGT, IGT	36 (8)	28.5 (6.5)	50 mU/kg/h (5 mmol/l, 120 min)	M_{LBM}	Pearson	(1)1, (2)1, (3)2, (4)2, (5)1, (6)2, (7)2
Stumvoll 2000 [112]	104 (63%)		Non-diabetic	45 (10)	27.6 (0.5)	1 mU/kg/min (5 mmol/l, 180 min)	M/G	Pearson	(1)0, (2)0, (3)2, (4)2, (5)1, (6)3, (7)2
Syvertsen 2007 [113]	41 (68%)	Norway	Overweight			1 mU/kg/min (5 mmol/l, 177 min)	M_{LBM}	Spearman	(1)0, (2)1, (3)2, (4)0, (5)1, (6)3, (7)0
Takanashi 2000 [114]	35 (46%)	Japan	T2DM	58 (12)	24.8 (1.6)	(100 mg/dl)	M_{BW}	Pearson	(1)1, (2)0, (3)2, (4)0, (5)0, (6)0, (7)2
Wasada 1995 [115]	51 (33%)	Japan	IGT	50	23.7	1.12 mU/kg/min (80 mg/dl, 90 min)	M_{BW}	Spearman	(1)0, (2)0, (3)2, (4)2, (5)1, (6)1, (7)2
Wasada 1995 [115]	69 (35%)	Japan	NGT, IGT	47	23.5	1.12 mU/kg/min (80 mg/dl, 90 min)	M_{BW}	Spearman	(1)0, (2)1, (3)2, (4)2, (5)1, (6)1, (7)2
Yamasaki 1997 [116]	19 (35%)	Japan	T2DM	58 (9)	23.9 (3.4)	9 µmol/kg/min (5.3 mmol/l, 120 min)	M_{BW}	Spearman	(1)0, (2)0, (3)1, (4)1, (5)0, (6)2, (7)2
Yang 2011	101 (100%)	China	PCOS			120 mU/m^2/min (5.2	M_{BW}	Pearson	(1)0, (2)1, (3)2, (4)0,

[117]						mmol/l, 180 min)			(5)1, (6)3, (7)2
Yokoyama 2003 [118]	241 (33%)	Japan	T2DM and controls	52 (14)	23.2 (3.2)	1.25 mU/kg/min (5 mmol/l, 120 min)	M_{BW}/I	Pearson	(1)0, (2)1, (3)2, (4)0, (5)1, (6)2, (7)2
Yu 2004 [119]	36 (53%)	China	T2DM and controls	55 (7)	22.8 (2.0)	120 mU/m^2/min (90 mg/dl, 240 min)	M_{BW}	Pearson	(1)1, (2)1, (3)2, (4)0, (5)1, (6)3, (7)2
Zaletel 2010 [120]	70 (50%)	Slovenia	T2DM	61 (9)	30.5 (5.2)	2 mU/kg/min (90 mg/dl, 120 min)	M_{BW}/I	Pearson	(1)1, (2)0, (3)2, (4)0, (5)1, (6)2, (7)0

[a] Quality assessment:

(1) Study participants of both sexes: *0: Gender is not reported or unevenly distributed study population (more uneven than 60% : 40%). 1: Evenly distributed study population.*

(2) Study participants with different levels of insulin sensitivity: *0: Study participants are a subgroup of insulin sensitivity (NGT or IGT or T2DM). 1: Study participants with different levels of insulin sensitivity.*

(3) Medical conditions that might interfere with measurement of insulin sensitivity: *0: Medical conditions that clearly interfere with measurement of insulin sensitivity. 1: Medical conditions that may interfere with measurement of insulin sensitivity. 2: No other medical conditions reported that obviously interfere with measurement of insulin sensitivity.*

(4) Diagnostic criteria for diabetes: *0: Not reported or by medical history. 1: fasting glucose. 2: OGTT.*

(5) Insulin dose of hyperinsulinaemic euglycaemic clamp: *0: not reported or clearly inappropriate for all subgroups of the study population. 1: appropriate for the study population.*

(6) Duration of hyperinsulinaemic euglycaemic clamp: *0: not reported. 1: shorter than 120 min. 2: 120 min. 3: longer than 120 min.*

(7) Blood glucose or plasma/serum glucose during OGTT/fasting samples: *0: not reported. 1: blood glucose. 2: plasma glucose / serum glucose.*

Abbreviations: HEC, hyperinsulinaemic euglycaemic clamp. NGT, normal glucose tolerance. IGT, impaired glucose tolerance. T2DM, type 2 diabetes mellitus. M_{BW} , glucose infusion rate per kg body weight. M_{LBM} , glucose infusion rate per kg lean body mass. I, steady state insulin. G, steady state glucose concentration. ΔI, increment in insulin concentration (basal to steady state). ΔRd_{BW} , increment in glucose uptake (basal to steady state, per kg body weight). ΔRd_{LBM} , increment in glucose uptake (basal to steady state, per kg lean body mass).

References

1. Abdul-Ghani MA, Matsuda M, Balas B, DeFronzo RA (2007) Muscle and liver insulin resistance indexes derived from the oral glucose tolerance test. Diabetes Care 30: 89-94
2. Ahren B, Larsson H (2002) Quantification of insulin secretion in relation to insulin sensitivity in nondiabetic postmenopausal women. Diabetes 51 Suppl 1: S202-211
3. Antuna-Puente B, Disse E, Faraj M, et al. (2009) Evaluation of insulin sensitivity with a new lipid-based index in non-diabetic postmenopausal overweight and obese women before and after a weight loss intervention. Eur J Endocrinol 161: 51-56
4. Aroda V, Ciaraldi TP, Chang SA, Dahan MH, Chang RJ, Henry RR (2008) Circulating and cellular adiponectin in polycystic ovary syndrome: relationship to glucose tolerance and insulin action. Fertil Steril 89: 1200-1208
5. Baratta R, Amato S, Degano C, et al. (2004) Adiponectin relationship with lipid metabolism is independent of body fat mass: evidence from both cross-sectional and intervention studies. J Clin Endocrinol Metab 89: 2665-2671
6. Bastard JP, Robert JJ, Jardel C, Bruckert E, Grimaldi A, Hainque B (2001) Is quantitative insulin sensitivity check index, a fair insulin sensitivity index in humans? Diabetes Metab 27: 69-70
7. Bastard JP, Rabasa-Lhoret R, Maachi M, et al. (2003) What kind of simple fasting index should be used to estimate insulin sensitivity in humans? Diabetes Metab 29: 285-288
8. Bastard JP, Vandernotte JM, Faraj M, et al. (2007) Relationship between the hyperinsulinemic-euglycaemic clamp and a new simple index assessing insulin sensitivity in overweight and obese postmenopausal women. Diabetes Metab 33: 261-268
9. Bastard JP, Lavoie ME, Messier V, Prud'homme D, Rabasa-Lhoret R (2012) Evaluation of two new surrogate indices including parameters not using insulin to assess insulin sensitivity/resistance in non-diabetic postmenopausal women: a MONET group study. Diabetes Metab 38: 258-263
10. Bell D, McAuley KA, Mann J, Murphy E, Williams S (2004) The hypertriglyceridaemic waist in New Zealand Maori. Asia Pac J Clin Nutr 13: 74-77
11. Beysen C, Murphy EJ, McLaughlin T, et al. (2007) Whole-body glycolysis measured by the deuterated-glucose disposal test correlates highly with insulin resistance in vivo. Diabetes Care 30: 1143-1149
12. Blonk MC, Jacobs MA, Friedberg CE, et al. (1994) Determinants of insulin sensitivity and consequences for lipoproteins and blood pressure in subjects with non-insulin-dependent diabetes mellitus. Metabolism 43: 501-508
13. Bluher M, Kratzsch J, Paschke R (2001) Plasma levels of tumor necrosis factor-alpha, angiotensin II, growth hormone, and IGF-I are not elevated in insulin-resistant obese individuals with impaired glucose tolerance. Diabetes Care 24: 328-334
14. Bonora E, Targher G, Alberiche M, et al. (2000) Homeostasis model assessment closely mirrors the glucose clamp technique in the assessment of insulin sensitivity: studies in subjects with various degrees of glucose tolerance and insulin sensitivity. Diabetes Care 23: 57-63

15. Broughton DL, Webster J, Taylor R (1992) Insulin sensitivity and secretion in healthy elderly human subjects with 'abnormal' glucose tolerance. Eur J Clin Invest 22: 582-590
16. Buren J, Lindmark S, Renstrom F, Eriksson JW (2003) In vitro reversal of hyperglycemia normalizes insulin action in fat cells from type 2 diabetes patients: is cellular insulin resistance caused by glucotoxicity in vivo? Metabolism 52: 239-245
17. Chen H, Sullivan G, Quon MJ (2005) Assessing the predictive accuracy of QUICKI as a surrogate index for insulin sensitivity using a calibration model. Diabetes 54: 1914-1925
18. Cheng C, Campbell KL, Kushner H, Falkner BE (2004) Correlation of oral glucose tolerance test-derived estimates of insulin sensitivity with insulin clamp measurements in an African-American cohort. Metabolism 53: 1107-1112
19. Christopher M, Hew FL, Oakley M, Rantzau C, Alford F (1998) Defects of insulin action and skeletal muscle glucose metabolism in growth hormone-deficient adults persist after 24 months of recombinant human growth hormone therapy. J Clin Endocrinol Metab 83: 1668-1681
20. Ciampelli M, Leoni F, Cucinelli F, et al. (2005) Assessment of insulin sensitivity from measurements in the fasting state and during an oral glucose tolerance test in polycystic ovary syndrome and menopausal patients. J Clin Endocrinol Metab 90: 1398-1406
21. Cleland SJ, Petrie JR, Morris AD, Ueda S, Dorrian CA, Connell JM (1996) FIRI: a fair insulin resistance index? Lancet 347: 770
22. Cohen O, Epstein GS, Weisz B, Homko CJ, Sivan E (2006) Longitudinal assessment of insulin sensitivity in pregnancy. Validation of the homeostasis model assessment. Clin Endocrinol (Oxf) 64: 640-644
23. Dagogo-Jack S, Askari H, Tykodi G (2009) Glucoregulatory physiology in subjects with low-normal, high-normal, or impaired fasting glucose. J Clin Endocrinol Metab 94: 2031-2036
24. DeFronzo R, Deibert D, Hendler R, Felig P, Soman V (1979) Insulin sensitivity and insulin binding to monocytes in maturity-onset diabetes. J Clin Invest 63: 939-946
25. de Rooij SR, Dekker JM, Kozakova M, et al. (2009) Fasting insulin has a stronger association with an adverse cardiometabolic risk profile than insulin resistance: the RISC study. Eur J Endocrinol 161: 223-230
26. Diamanti-Kandarakis E, Kouli C, Alexandraki K, Spina G (2004) Failure of mathematical indices to accurately assess insulin resistance in lean, overweight, or obese women with polycystic ovary syndrome. J Clin Endocrinol Metab 89: 1273-1276
27. Disse E, Bastard JP, Bonnet F, et al. (2008) A lipid-parameter-based index for estimating insulin sensitivity and identifying insulin resistance in a healthy population. Diabetes Metab 34: 457-463
28. Donahue RP, Prineas RJ, Donahue RD, et al. (1999) Is fasting leptin associated with insulin resistance among nondiabetic individuals? The Miami Community Health Study. Diabetes Care 22: 1092-1096
29. Ducluzeau PH, Cousin P, Malvoisin E, et al. (2003) Glucose-to-insulin ratio rather than sex hormone-binding globulin and adiponectin levels is the best predictor of insulin resistance in nonobese women with polycystic ovary syndrome. J Clin Endocrinol Metab 88: 3626-3631

30. Eliasson B, Attvall S, Taskinen MR, Smith U (1994) The insulin resistance syndrome in smokers is related to smoking habits. Arterioscler Thromb 14: 1946-1950
31. Emoto M, Nishizawa Y, Maekawa K, et al. (1999) Homeostasis model assessment as a clinical index of insulin resistance in type 2 diabetic patients treated with sulfonylureas. Diabetes Care 22: 818-822
32. Falkner B, Hulman S, Kushner H (1993) Insulin-stimulated glucose utilization and borderline hypertension in young adult blacks. Hypertension 22: 18-25
33. Ferrannini E, Balkau B, Coppack SW, et al. (2007) Insulin resistance, insulin response, and obesity as indicators of metabolic risk. J Clin Endocrinol Metab 92: 2885-2892
34. Ferrara CM, Goldberg AP (2001) Limited value of the homeostasis model assessment to predict insulin resistance in older men with impaired glucose tolerance. Diabetes Care 24: 245-249
35. Fink RI, Kolterman OG, Griffin J, Olefsky JM (1983) Mechanisms of insulin resistance in aging. J Clin Invest 71: 1523-1535
36. Finucane FM, Luan J, Wareham NJ, et al. (2009) Correlation of the leptin:adiponectin ratio with measures of insulin resistance in non-diabetic individuals. Diabetologia 52: 2345-2349
37. Furuhashi M, Ura N, Higashiura K, Murakami H, Shimamoto K (2003) Circulating resistin levels in essential hypertension. Clin Endocrinol (Oxf) 59: 507-510
38. Furuhashi M, Ura N, Higashiura K, et al. (2005) Low adiponectin level in young normotensive men with a family history of essential hypertension. Hypertens Res 28: 141-146
39. Galgani JE, de Jonge L, Rood JC, Smith SR, Young AA, Ravussin E (2010) Urinary C-peptide excretion: a novel alternate measure of insulin sensitivity in physiological conditions. Obesity (Silver Spring) 18: 1852-1857
40. Garg A, Helderman JH, Koffler M, Ayuso R, Rosenstock J, Raskin P (1988) Relationship between lipoprotein levels and in vivo insulin action in normal young white men. Metabolism 37: 982-987
41. Gastaldelli A, Ferrannini E, Miyazaki Y, Matsuda M, DeFronzo RA (2004) Beta-cell dysfunction and glucose intolerance: results from the San Antonio metabolism (SAM) study. Diabetologia 47: 31-39
42. Geloneze B, Pereira JA, Pareja JC, et al. (2009) Overcoming metabolic syndrome in severe obesity: adiponectin as a marker of insulin sensitivity and HDL-cholesterol improvements after gastric bypass. Arq Bras Endocrinol Metabol 53: 293-300
43. Goodarzi MO, Cui J, Chen YD, Hsueh WA, Guo X, Rotter JI (2011) Fasting insulin reflects heterogeneous physiological processes: role of insulin clearance. Am J Physiol Endocrinol Metab 301: E402-408
44. Guerrero-Romero F, Simental-Mendia LE, Gonzalez-Ortiz M, et al. (2010) The product of triglycerides and glucose, a simple measure of insulin sensitivity. Comparison with the euglycemic-hyperinsulinemic clamp. J Clin Endocrinol Metab 95: 3347-3351
45. Gutt M, Davis CL, Spitzer SB, et al. (2000) Validation of the insulin sensitivity index (ISI(0,120)): comparison with other measures. Diabetes Res Clin Pract 47: 177-184

46. Hanson RL, Pratley RE, Bogardus C, et al. (2000) Evaluation of simple indices of insulin sensitivity and insulin secretion for use in epidemiologic studies. Am J Epidemiol 151: 190-198
47. Hays NP, Starling RD, Sullivan DH, Fluckey JD, Coker RH, Evans WJ (2006) Comparison of insulin sensitivity assessment indices with euglycemic-hyperinsulinemic clamp data after a dietary and exercise intervention in older adults. Metabolism 55: 525-532
48. Heliovaara MK, Teppo AM, Karonen SL, Tuominen JA, Ebeling P (2005) Plasma IL-6 concentration is inversely related to insulin sensitivity, and acute-phase proteins associate with glucose and lipid metabolism in healthy subjects. Diabetes Obes Metab 7: 729-736
49. Hollenbeck CB, Chen N, Chen YD, Reaven GM (1984) Relationship between the plasma insulin response to oral glucose and insulin-stimulated glucose utilization in normal subjects. Diabetes 33: 460-463
50. Ijzerman RG, Stehouwer CD, Serne EH, et al. (2009) Incorporation of the fasting free fatty acid concentration into quantitative insulin sensitivity check index improves its association with insulin sensitivity in adults, but not in children. Eur J Endocrinol 160: 59-64
51. Ikeda Y, Suehiro T, Nakamura T, Kumon Y, Hashimoto K (2001) Clinical significance of the insulin resistance index as assessed by homeostasis model assessment. Endocr J 48: 81-86
52. Jenkins AB, Samaras K, Carey DG, Kelly P, Campbell LV (2000) Improved indices of insulin resistance and insulin secretion for use in genetic and population studies of type 2 diabetes mellitus. Twin Res 3: 148-151
53. Kanauchi M, Tsujimoto N, Hashimoto T (2002) Validation of simple indices to assess insulin sensitivity based on the oral glucose tolerance test in the Japanese population. Diabetes Res Clin Pract 55: 229-235
54. Kanauchi M (2003) Validation of the oral glucose insulin sensitivity index to assess insulin sensitivity in Japanese subjects for use in clinical practice. Eur J Clin Invest 33: 1022-1023
55. Kang ES, Yun YS, Park SW, et al. (2005) Limitation of the validity of the homeostasis model assessment as an index of insulin resistance in Korea. Metabolism 54: 206-211
56. Karelis AD, Pasternyk SM, Messier L, et al. (2007) Relationship between insulin sensitivity and the triglyceride-HDL-C ratio in overweight and obese postmenopausal women: a MONET study. Appl Physiol Nutr Metab 32: 1089-1096
57. Katsuki A, Sumida Y, Gabazza EC, et al. (2002) QUICKI is useful for following improvements in insulin sensitivity after therapy in patients with type 2 diabetes mellitus. J Clin Endocrinol Metab 87: 2906-2908
58. Katsuki A, Sumida Y, Urakawa H, et al. (2002) Neither homeostasis model assessment nor quantitative insulin sensitivity check index can predict insulin resistance in elderly patients with poorly controlled type 2 diabetes mellitus. J Clin Endocrinol Metab 87: 5332-5335
59. Katsuki A, Urakawa H, Gabazza EC, et al. (2005) Quantitative insulin sensitivity check index is a useful indicator of insulin resistance in Japanese metabolically obese, normal-weight subjects with normal glucose tolerance. Endocr J 52: 253-257

60. Katz A, Nambi SS, Mather K, et al. (2000) Quantitative insulin sensitivity check index: a simple, accurate method for assessing insulin sensitivity in humans. J Clin Endocrinol Metab 85: 2402-2410
61. Kirwan JP, Huston-Presley L, Kalhan SC, Catalano PM (2001) Clinically useful estimates of insulin sensitivity during pregnancy: validation studies in women with normal glucose tolerance and gestational diabetes mellitus. Diabetes Care 24: 1602-1607
62. Kolterman OG, Gray RS, Griffin J, et al. (1981) Receptor and postreceptor defects contribute to the insulin resistance in noninsulin-dependent diabetes mellitus. J Clin Invest 68: 957-969
63. Kotronen A, Vehkavaara S, Seppala-Lindroos A, Bergholm R, Yki-Jarvinen H (2007) Effect of liver fat on insulin clearance. Am J Physiol Endocrinol Metab 293: E1709-1715
64. Laakso M (1993) How good a marker is insulin level for insulin resistance? Am J Epidemiol 137: 959-965
65. Lansang MC, Williams GH, Carroll JS (2001) Correlation between the glucose clamp technique and the homeostasis model assessment in hypertension. Am J Hypertens 14: 51-53
66. Leonetti F, Iacobellis G, Zappaterreno A, et al. (2004) Insulin sensitivity assessment in uncomplicated obese women: comparison of indices from fasting and oral glucose load with euglycemic hyperinsulinemic clamp. Nutr Metab Cardiovasc Dis 14: 366-372
67. Lewanczuk RZ, Paty BW, Toth EL (2004) Comparison of the [13C]glucose breath test to the hyperinsulinemic-euglycemic clamp when determining insulin resistance. Diabetes Care 27: 441-447
68. Li G, Pan X (1995) A new insulin-sensitivity index for epidemiological study. Chin Med J (Engl) 108: 55-56
69. Liao Y, Kwon S, Shaughnessy S, et al. (2004) Critical evaluation of adult treatment panel III criteria in identifying insulin resistance with dyslipidemia. Diabetes Care 27: 978-983
70. Lind L, Lithell H, Pollare T, Ljunghall S (1994) On the interplay between insulin secretion and sensitivity as determinants of glucose tolerance. Acta Diabetol 31: 26-30
71. Lindmark S, Buren J, Eriksson JW (2006) Insulin resistance, endocrine function and adipokines in type 2 diabetes patients at different glycaemic levels: potential impact for glucotoxicity in vivo. Clin Endocrinol (Oxf) 65: 301-309
72. Lorenzo C, Haffner SM, Stancakova A, Laakso M (2010) Relation of direct and surrogate measures of insulin resistance to cardiovascular risk factors in nondiabetic finnish offspring of type 2 diabetic individuals. J Clin Endocrinol Metab 95: 5082-5090
73. Ludvik B, Nolan JJ, Baloga J, Sacks D, Olefsky J (1995) Effect of obesity on insulin resistance in normal subjects and patients with NIDDM. Diabetes 44: 1121-1125
74. Malita FM, Karelis AD, St-Pierre DH, et al. (2006) Surrogate indexes vs. euglycaemic-hyperinsulinemic clamp as an indicator of insulin resistance and cardiovascular risk factors in overweight and obese postmenopausal women. Diabetes Metab 32: 251-255
75. Malita FM, Messier V, Lavoie JM, Bastard JP, Rabasa-Lhoret R, Karelis AD (2010) Comparison between several insulin sensitivity indices and metabolic risk factors in overweight and obese postmenopausal women: a MONET study. Nutr Metab Cardiovasc Dis 20: 173-179

76. Malminiemi K (1995) Association between serum lipids, glucose tolerance, and insulin sensitivity during 12 months of celiprolol treatment. Cardiovasc Drugs Ther 9: 295-304
77. Marchesini G, Bianchi GP, Forlani G, et al. (1987) Insulin resistance is the main determinant of impaired glucose tolerance in patients with liver cirrhosis. Dig Dis Sci 32: 1118-1124
78. Mari A, Pacini G, Murphy E, Ludvik B, Nolan JJ (2001) A model-based method for assessing insulin sensitivity from the oral glucose tolerance test. Diabetes Care 24: 539-548
79. Mari A, Pacini G, Brazzale AR, Ahren B (2005) Comparative evaluation of simple insulin sensitivity methods based on the oral glucose tolerance test. Diabetologia 48: 748-751
80. Mari A, Manco M, Guidone C, et al. (2006) Restoration of normal glucose tolerance in severely obese patients after bilio-pancreatic diversion: role of insulin sensitivity and beta cell function. Diabetologia 49: 2136-2143
81. Mather KJ, Hunt AE, Steinberg HO, et al. (2001) Repeatability characteristics of simple indices of insulin resistance: implications for research applications. J Clin Endocrinol Metab 86: 5457-5464
82. Matsuda M, DeFronzo RA (1999) Insulin sensitivity indices obtained from oral glucose tolerance testing: comparison with the euglycemic insulin clamp. Diabetes Care 22: 1462-1470
83. Matsuhisa M, Yamasaki Y, Emoto M, et al. (2007) A novel index of insulin resistance determined from the homeostasis model assessment index and adiponectin levels in Japanese subjects. Diabetes Res Clin Pract 77: 151-154
84. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC (1985) Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia 28: 412-419
85. Mayorov AY, Naumenkova IV, Antsiferov MB, Dedov, II (2005) Influence of insulin treatment on insulin sensitivity in insulin requiring type 2 diabetes patients. Diabetes Res Clin Pract 68 Suppl1: S54-59
86. McAuley KA, Williams SM, Mann JI, et al. (2001) Diagnosing insulin resistance in the general population. Diabetes Care 24: 460-464
87. McCall JL, Tuckey JA, Parry BR (1992) Serum tumour necrosis factor alpha and insulin resistance in gastrointestinal cancer. Br J Surg 79: 1361-1363
88. Miyamoto I, Miyakoshi H, Nagai Y, et al. (1992) Characterization of the insulin resistance in liver cirrhosis: a comparison with non-insulin dependent diabetes mellitus. Endocrinol Jpn 39: 421-429
89. Muniyappa R, Irving BA, Unni US, et al. (2010) Limited predictive ability of surrogate indices of insulin sensitivity/resistance in Asian-Indian men. Am J Physiol Endocrinol Metab 299: E1106-1112
90. Natali A, Toschi E, Camastra S, Gastaldelli A, Groop L, Ferrannini E (2000) Determinants of postabsorptive endogenous glucose output in non-diabetic subjects. European Group for the Study of Insulin Resistance (EGIR). Diabetologia 43: 1266-1272

91. Ntyintyane L, Panz V, Raal F, Gill G (2010) Comparison between surrogate indices of insulin sensitivity and resistance, and the hyperinsulinaemic euglycaemic glucose clamp in urban South African blacks with and without coronary artery disease. Diab Vasc Dis Res 7: 151-157
92. Okamoto M, Okamoto M, Nishimura H, et al. (1991) Insulin-stimulated glucose uptake and fasting blood glucose. Endocrinol Jpn 38: 421-427
93. Ouwens DM, Bekaert M, Lapauw B, et al. (2012) Chemerin as biomarker for insulin sensitivity in males without typical characteristics of metabolic syndrome. Arch Physiol Biochem 118: 135-138
94. Perseghin G, Caumo A, Caloni M, Testolin G, Luzi L (2001) Incorporation of the fasting plasma FFA concentration into QUICKI improves its association with insulin sensitivity in nonobese individuals. J Clin Endocrinol Metab 86: 4776-4781
95. Petrie JR, Morris AD, Dorrian CA, Small M, Connell JM (1997) Specific insulin assays, insulin sensitivity and blood pressure. QJM 90: 465-475
96. Piche ME, Lemieux S, Corneau L, Nadeau A, Bergeron J, Weisnagel SJ (2007) Measuring insulin sensitivity in postmenopausal women covering a range of glucose tolerance: comparison of indices derived from the oral glucose tolerance test with the euglycemic-hyperinsulinemic clamp. Metabolism 56: 1159-1166
97. Pigeon E, Riou ME, St-Onge J, et al. (2009) Validation of a simple index (SIisOGTT) of insulin sensitivity in a population of sedentary men. Diabetes Metab 35: 398-403
98. Rabasa-Lhoret R, Bastard JP, Jan V, et al. (2003) Modified quantitative insulin sensitivity check index is better correlated to hyperinsulinemic glucose clamp than other fasting-based index of insulin sensitivity in different insulin-resistant states. J Clin Endocrinol Metab 88: 4917-4923
99. Raji A, Seely EW, Arky RA, Simonson DC (2001) Body fat distribution and insulin resistance in healthy Asian Indians and Caucasians. J Clin Endocrinol Metab 86: 5366-5371
100. Ramakrishnan G, Unni US, Raj T, Thomas T, Vaz M, Kurpad AV (2009) A pilot study on hyperinsulinaemic euglycaemic clamp based insulin sensitivity in young adult Indian males with low body mass index. Indian J Med Res 129: 409-417
101. Rasmussen-Torvik LJ, Pankow JS, Jacobs DR, et al. (2007) Heritability and genetic correlations of insulin sensitivity measured by the euglycaemic clamp. Diabet Med 24: 1286-1289
102. Reaven GM, Moore J, Greenfield M (1983) Quantification of insulin secretion and in vivo insulin action in nonobese and moderately obese individuals with normal glucose tolerance. Diabetes 32: 600-604
103. Ruige JB, Mertens IL, Bartholomeeusen E, Dirinck E, Ferrannini E, Van Gaal LF (2006) Fasting-based estimates of insulin sensitivity in overweight and obesity: a critical appraisal. Obesity (Silver Spring) 14: 1250-1256
104. Sabelis LW, Senden PJ, Zonderland ML, et al. (2003) Determinants of insulin sensitivity in chronic heart failure. Eur J Heart Fail 5: 759-765

105. Sindelka G, Skrha J, Prazny M, Haas T (2002) Association of obesity, diabetes, serum lipids and blood pressure regulates insulin action. Physiol Res 51: 85-91
106. Skrha J, Haas T, Sindelka G, et al. (2004) Comparison of the insulin action parameters from hyperinsulinemic clamps with homeostasis model assessment and QUICKI indexes in subjects with different endocrine disorders. J Clin Endocrinol Metab 89: 135-141
107. Soonthornpun S, Setasuban W, Thamprasit A, Chayanunnukul W, Rattarasarn C, Geater A (2003) Novel insulin sensitivity index derived from oral glucose tolerance test. J Clin Endocrinol Metab 88: 1019-1023
108. Soonthornpun S, Setasuban W, Thamprasit A (2007) Correlation between change in serum homocysteine levels during hyperinsulinemia and insulin sensitivity. J Med Assoc Thai 90: 1506-1511
109. Stanicka S, Vondra K, Pelikanova T, Vlcek P, Hill M, Zamrazil V (2005) Insulin sensitivity and counter-regulatory hormones in hypothyroidism and during thyroid hormone replacement therapy. Clin Chem Lab Med 43: 715-720
110. Straczkowski M, Kowalska I, Stepien A, et al. (2003) Insulin resistance in the first-degree relatives of persons with type 2 diabetes. Med Sci Monit 9: CR186-190
111. Straczkowski M, Stepien A, Kowalska I, Kinalska I (2004) Comparison of simple indices of insulin sensitivity using the euglycemic hyperinsulinemic clamp technique. Med Sci Monit 10: CR480-484
112. Stumvoll M, Mitrakou A, Pimenta W, et al. (2000) Use of the oral glucose tolerance test to assess insulin release and insulin sensitivity. Diabetes Care 23: 295-301
113. Syvertsen C, Halse J, Hoivik HO, et al. (2007) The effect of 6 months supplementation with conjugated linoleic acid on insulin resistance in overweight and obese. Int J Obes (Lond) 31: 1148-1154
114. Takanashi K, Inukai T (2000) Insulin resistance and changes in the blood coagulation-fibrinolysis system after a glucose clamp technique in patients with type 2 diabetes mellitus. J Med 31: 45-62
115. Wasada T, Arii H, Kuroki H, et al. (1995) The relationship between insulin resistance and insulin secretion in Japanese subjects with borderline glucose intolerance. Diabetes Res Clin Pract 30: 53-57
116. Yamasaki Y, Kawamori R, Wasada T, et al. (1997) Pioglitazone (AD-4833) ameliorates insulin resistance in patients with NIDDM. AD-4833 Glucose Clamp Study Group, Japan. Tohoku J Exp Med 183: 173-183
117. Yang S, Li Q, Song Y, et al. (2011) Serum complement C3 has a stronger association with insulin resistance than high-sensitivity C-reactive protein in women with polycystic ovary syndrome. Fertil Steril 95: 1749-1753
118. Yokoyama H, Emoto M, Fujiwara S, et al. (2003) Quantitative insulin sensitivity check index and the reciprocal index of homeostasis model assessment in normal range weight and moderately obese type 2 diabetic patients. Diabetes Care 26: 2426-2432
119. Yu Y, Suo L, Yu H, Wang C, Tang H (2004) Insulin resistance and endothelial dysfunction in type 2 diabetes patients with or without microalbuminuria. Diabetes Res Clin Pract 65: 95-104

120. Zaletel J, Barlovic DP, Prezelj J (2010) Adiponectin-leptin ratio: a useful estimate of insulin resistance in patients with Type 2 diabetes. J Endocrinol Invest 33: 514-518

ESM Table 2 Correlation coefficients between OGTT-based surrogate measures of insulin sensitivity and the hyperinsulinaemic euglycaemic clamp (reported in < 5 studies, either as a pooled correlation coefficient from a meta-analysis or if reported in only one study as a single correlation coefficient)

Name of surrogate measure	Pooled correlation (95% CI) or correlation coefficient reported in one study	Number of included studies [references]
AUC glucose	-0.40 (-0.55 to -0.23)	4 [1-4]
AUC glucose / AUC insulin	-0.17 (-0.64 to 0.38)	3 [5-7]
AUC $insulin_{180}$	-0.60	1 [8]
AUC $insulin_{240}$	-0.63 (-0.73 to -0.50)	1 [7]
AUC insulin / AUC glucose	-0.29	1 [9]
Avignon	0.70 (0.56 to 0.80)	3 [7, 10, 11]
Avignon (C-peptide)	0.60 (0.30 to 0.79)	1 [7]
Avignon (Si120)[a]	0.59 (0.30 to 0.78)	1 [7]
Bastard	0.69	1 [12]
CIR_{30} [b]	-0.05	1 [13]
CIR_{120} [c]	-0.17	1 [13]
$dG/dt \div I$ [d]	0.78	1 [14]
G_{30}	-0.28	1 [3]
G_{60}	-0.38	1 [3]
G_{90}	-0.51	1 [3]
Glucose change (%)	-0.40	1 [15]
I_{30}	-0.35 (-0.46 to -0.23)	4 [3, 13, 16, 17]
I_{60}	-0.49 (-0.57 to -0.40)	4 [2, 3, 16, 18]
I_{90}	-0.62	1 [3]
I_{180}	-0.51	1 [16]
$I_{30} - I_0$	-0.30	1 [19]
I_{30} / I_0	0.36	1 [13]
I_{120} / I_0	-0.06	1 [13]
$I_{60} * G_{60}$	-0.39	1 [20]
I_{30} / G_{30}	-0.23	1 [13]
$10000 / (I_{30} * G_{30})$	0.34	1 [13]
$(I_{30}-I_0) / (G_{30}-G_0)$	-0.22 (-0.42 to 0.01)	2 [13, 21]
$(I_{120} - I_0) / (G_{120} - G_0)$	-0.22	1 [13]
$I_{120} * G_{120}$	-0.57	1 [19]
$10000 / (I_{120} * G_{120})$	0.61 (0.52 to 0.69)	2 [11, 13]
I_{120} / G_{120}	-0.59 (-0.73 to -0.40)	2 [11, 13]
Ins_{index} [e]	-0.28	1 [19]
Malminiemi	0.83	1 [2]
Mean glucose	-0.65	1 [9]
$OGIS_{180}$ [f]	0.77	1 [22]
$SI_{is}OGTT$[g]	0.74 (0.60 to 0.83)	3 [11, 23, 24]

ESM Table 2 (continued)

Name of surrogate measure	Pooled correlation (95% CI) or correlation coefficient reported in one study	Number of included studies
Stumvoll ISI[h] (0, 30 min)	0.62	1 [25]
Stumvoll ISI[h] (0, 120 min)	0.70 (0.65 to 0.75)	2 [11, 25]
Stumvoll ISI[h] (0, 30, 60 min)	0.65	1 [25]
Stumvoll ISI[h] (0, 60, 120 min)	0.69	1 [25]
Stumvoll ISI DEM[i] (0, 30 min)	0.75	1 [25]
Stumvoll ISI DEM[i] (0, 120 min)	0.73 (0.58 to 0.83)	2 [11, 25]
Stumvoll ISI DEM[i] (0, 30, 60 min)	0.78	1 [25]
Stumvoll ISI DEM[i] (0, 60, 120 min)	0.79	1 [25]
Stumvoll MCR[j] (0, 30 min)	0.59	1 [25]
Stumvoll MCR[j] (0, 120 min)	0.68	1 [25]
Stumvoll MCR[j] (0, 30, 60 min)	0.62	1 [25]
Stumvoll MCR[j] (0, 60, 120 min)	0.68	1 [25]
Stumvoll MCR DEM[k] (0, 30 min)	0.75	1 [25]
Stumvoll MCR DEM[k] (0, 120 min)	0.79	1 [25]
Stumvoll MCR DEM[k] (0, 30, 60 min)	0.77	1 [25]
Stumvoll MCR DEM[k] (0,60,120 min)	0.79	1 [25]
Summed glucose	-0.42 (-0.49 to -0.34)	4 [10, 15, 16, 26]
Summed insulin	-0.63 (-0.68 to -0.58)	4 [10, 15, 16, 27]
Summed insulin / summed glucose	-0.52	1 [15]

All Spearman's rank correlation coefficients are converted to Pearson's r according to Rupinski & Dunlap to be able to compare correlation coefficients. [a] insulin sensitivity index at 120 min. [b] corrected insulin response (30 min). [c] corrected insulin response (120 min). [d] rate of decline in plasma glucose concentration / insulin concentration. [e] insulinogenic index. [f] oral glucose insulin sensitivity index (180 min). [g] simple index of insulin sensitivity (OGTT). [h] insulin sensitivity index. [i] insulin sensitivity index with demographic parameters. [j] metabolic clearance rate of glucose. [k] metabolic clearance rate of glucose with demographic parameters.

References

1. Yki-Jarvinen H, Helve E, Koivisto VA (1986) Relationship between oral glucose tolerance and insulin sensitivity in healthy man and type 1 diabetic patients. Acta Endocrinol (Copenh) 112: 355-360
2. Malminiemi K (1995) Association between serum lipids, glucose tolerance, and insulin sensitivity during 12 months of celiprolol treatment. Cardiovasc Drugs Ther 9: 295-304
3. Stumvoll M, Mitrakou A, Pimenta W, et al. (2000) Use of the oral glucose tolerance test to assess insulin release and insulin sensitivity. Diabetes Care 23: 295-301
4. Hays NP, Starling RD, Sullivan DH, Fluckey JD, Coker RH, Evans WJ (2006) Comparison of insulin sensitivity assessment indices with euglycemic-hyperinsulinemic clamp data after a dietary and exercise intervention in older adults. Metabolism 55: 525-532

5. Ducluzeau PH, Cousin P, Malvoisin E, et al. (2003) Glucose-to-insulin ratio rather than sex hormone-binding globulin and adiponectin levels is the best predictor of insulin resistance in nonobese women with polycystic ovary syndrome. J Clin Endocrinol Metab 88: 3626-3631
6. Leonetti F, Iacobellis G, Zappaterreno A, et al. (2004) Insulin sensitivity assessment in uncomplicated obese women: comparison of indices from fasting and oral glucose load with euglycemic hyperinsulinemic clamp. Nutr Metab Cardiovasc Dis 14: 366-372
7. Ciampelli M, Leoni F, Cucinelli F, et al. (2005) Assessment of insulin sensitivity from measurements in the fasting state and during an oral glucose tolerance test in polycystic ovary syndrome and menopausal patients. J Clin Endocrinol Metab 90: 1398-1406
8. Hollenbeck C, Reaven GM (1987) Variations in insulin-stimulated glucose uptake in healthy individuals with normal glucose tolerance. J Clin Endocrinol Metab 64: 1169-1173
9. Mari A, Pacini G, Brazzale AR, Ahren B (2005) Comparative evaluation of simple insulin sensitivity methods based on the oral glucose tolerance test. Diabetologia 48: 748-751
10. Bastard JP, Vandernotte JM, Faraj M, et al. (2007) Relationship between the hyperinsulinemic-euglycaemic clamp and a new simple index assessing insulin sensitivity in overweight and obese postmenopausal women. Diabetes Metab 33: 261-268
11. Lorenzo C, Haffner SM, Stancakova A, Laakso M (2010) Relation of direct and surrogate measures of insulin resistance to cardiovascular risk factors in nondiabetic finnish offspring of type 2 diabetic individuals. J Clin Endocrinol Metab 95: 5082-5090
12. Malita FM, Messier V, Lavoie JM, Bastard JP, Rabasa-Lhoret R, Karelis AD (2010) Comparison between several insulin sensitivity indices and metabolic risk factors in overweight and obese postmenopausal women: a MONET study. Nutr Metab Cardiovasc Dis 20: 173-179
13. Hanson RL, Pratley RE, Bogardus C, et al. (2000) Evaluation of simple indices of insulin sensitivity and insulin secretion for use in epidemiologic studies. Am J Epidemiol 151: 190-198
14. Abdul-Ghani MA, Matsuda M, Balas B, DeFronzo RA (2007) Muscle and liver insulin resistance indexes derived from the oral glucose tolerance test. Diabetes Care 30: 89-94
15. Cheng C, Campbell KL, Kushner H, Falkner BE (2004) Correlation of oral glucose tolerance test-derived estimates of insulin sensitivity with insulin clamp measurements in an African-American cohort. Metabolism 53: 1107-1112
16. Hollenbeck CB, Chen N, Chen YD, Reaven GM (1984) Relationship between the plasma insulin response to oral glucose and insulin-stimulated glucose utilization in normal subjects. Diabetes 33: 460-463
17. Petrie JR, Morris AD, Dorrian CA, Small M, Connell JM (1997) Specific insulin assays, insulin sensitivity and blood pressure. QJM 90: 465-475
18. Laakso M (1993) How good a marker is insulin level for insulin resistance? Am J Epidemiol 137: 959-965
19. Ahren B, Larsson H (2002) Quantification of insulin secretion in relation to insulin sensitivity in nondiabetic postmenopausal women. Diabetes 51 Suppl 1: S202-211

20. Gutt M, Davis CL, Spitzer SB, et al. (2000) Validation of the insulin sensitivity index (ISI(0,120)): comparison with other measures. Diabetes Res Clin Pract 47: 177-184
21. Wasada T, Arii H, Kuroki H, et al. (1995) The relationship between insulin resistance and insulin secretion in Japanese subjects with borderline glucose intolerance. Diabetes Res Clin Pract 30: 53-57
22. Mari A, Pacini G, Murphy E, Ludvik B, Nolan JJ (2001) A model-based method for assessing insulin sensitivity from the oral glucose tolerance test. Diabetes Care 24: 539-548
23. Pigeon E, Riou ME, St-Onge J, et al. (2009) Validation of a simple index (SIisOGTT) of insulin sensitivity in a population of sedentary men. Diabetes Metab 35: 398-403
24. Bastard JP, Lavoie ME, Messier V, Prud'homme D, Rabasa-Lhoret R (2012) Evaluation of two new surrogate indices including parameters not using insulin to assess insulin sensitivity/resistance in non-diabetic postmenopausal women: a MONET group study. Diabetes Metab 38: 258-263
25. Stumvoll M, Van Haeften T, Fritsche A, Gerich J (2001) Oral glucose tolerance test indexes for insulin sensitivity and secretion based on various availabilities of sampling times. Diabetes Care 24: 796-797
26. Miyamoto I, Miyakoshi H, Nagai Y, et al. (1992) Characterization of the insulin resistance in liver cirrhosis: a comparison with non-insulin dependent diabetes mellitus. Endocrinol Jpn 39: 421-429
27. Straczkowski M, Stepien A, Kowalska I, Kinalska I (2004) Comparison of simple indices of insulin sensitivity using the euglycemic hyperinsulinemic clamp technique. Med Sci Monit 10: CR480-484

ESM Table 3 Correlation coefficients between fasting surrogate measures of insulin sensitivity and the hyperinsulinaemic euglycaemic clamp (reported in < 5 studies, either as a pooled correlation coefficients from a meta-analysis or if reported in only one study as a single correlation coefficient)

Name of surrogate measure	Pooled correlation (95% CI) or correlation coefficient reported in one study	Number of included studies
Avignon (Sib[a])	0.62 (0.38 to 0.78)	1 [1]
Avignon (Sib[a], C-peptide)	0.67 (0.36 to 0.84)	1 [1]
Bennett	0.62 (0.32 to 0.81)	2 [2, 3]
Disse	0.73 (0.51 to 0.86)	2 [4, 5]
Fasting Belfiore	0.59 (0.39 to 0.73)	3 [3, 6, 7]
Fasting Belfiore (C-peptide)	0.59 (0.40 to 0.73)	1 [1]
Belfiore FFA[b]	0.57	1 [7]
HOMA-AD[c]	-0.64	1 [8]
HOMA-%B[d]	-0.62	1 [9]
HOMA β-cell function	-0.40 (-0.61 to -0.15)	4 [9-12]
HOMA (C-peptide)	-0.59 (-0.73 to -0.40)	1 [1]
HOMA-IR[e]	-0.33 (-0.57 to -0.03)	2 [9, 13]
HOMA (modified)	-0.49	1 [14]
Huang	0.28	1 [6]
IAI[f]	-0.82	1 [15]
I_0*G_0	-0.56	1 [11]
10000 / (I_0*G_0)	0.47 (0.09 to 0.74)	2 [10, 16]
- (log I_0 + log G_0)	-0.82	1 [15]
Raynaud	0.09 (-0.80 to 0.85)	3 [3, 6, 17]
QUICKI-glycerol	0.74 (0.50 to 0.88)	1 [18]
TyG index[g]	-0.68	1 [19]

All Spearman's rank correlation coefficients are converted to Pearson's r according to Rupinski & Dunlap to be able to compare correlation coefficients. [a] insulin sensitivity basal index. [b] Fasting Belfiore index including free fatty acids. [c] HOMA index including adiponectin. [d] computer-based model for β-cell function. [e] computer-based model for insulin resistance. [f] insulin activity index (The calculation of IAI is very similar to the calculation of HOMA-IR and both should perform similarly compared with the HEC.) [g] triglycerides and glucose index.

References

1. Ciampelli M, Leoni F, Cucinelli F, et al. (2005) Assessment of insulin sensitivity from measurements in the fasting state and during an oral glucose tolerance test in polycystic ovary syndrome and menopausal patients. J Clin Endocrinol Metab 90: 1398-1406
2. McAuley KA, Williams SM, Mann JI, et al. (2001) Diagnosing insulin resistance in the general population. Diabetes Care 24: 460-464
3. Lorenzo C, Haffner SM, Stancakova A, Laakso M (2010) Relation of direct and surrogate measures of insulin resistance to cardiovascular risk factors in nondiabetic finnish offspring of type 2 diabetic individuals. J Clin Endocrinol Metab 95: 5082-5090

4. Disse E, Bastard JP, Bonnet F, et al. (2008) A lipid-parameter-based index for estimating insulin sensitivity and identifying insulin resistance in a healthy population. Diabetes Metab 34: 457-463
5. Antuna-Puente B, Disse E, Faraj M, et al. (2009) Evaluation of insulin sensitivity with a new lipid-based index in non-diabetic postmenopausal overweight and obese women before and after a weight loss intervention. Eur J Endocrinol 161: 51-56
6. Leonetti F, Iacobellis G, Zappaterreno A, et al. (2004) Insulin sensitivity assessment in uncomplicated obese women: comparison of indices from fasting and oral glucose load with euglycemic hyperinsulinemic clamp. Nutr Metab Cardiovasc Dis 14: 366-372
7. Ruige JB, Mertens IL, Bartholomeeusen E, Dirinck E, Ferrannini E, Van Gaal LF (2006) Fasting-based estimates of insulin sensitivity in overweight and obesity: a critical appraisal. Obesity (Silver Spring) 14: 1250-1256
8. Matsuhisa M, Yamasaki Y, Emoto M, et al. (2007) A novel index of insulin resistance determined from the homeostasis model assessment index and adiponectin levels in Japanese subjects. Diabetes Res Clin Pract 77: 151-154
9. Ramakrishnan G, Unni US, Raj T, Thomas T, Vaz M, Kurpad AV (2009) A pilot study on hyperinsulinaemic euglycaemic clamp based insulin sensitivity in young adult Indian males with low body mass index. Indian J Med Res 129: 409-417
10. Hanson RL, Pratley RE, Bogardus C, et al. (2000) Evaluation of simple indices of insulin sensitivity and insulin secretion for use in epidemiologic studies. Am J Epidemiol 151: 190-198
11. Ahren B, Larsson H (2002) Quantification of insulin secretion in relation to insulin sensitivity in nondiabetic postmenopausal women. Diabetes 51 Suppl 1: S202-211
12. Kang ES, Yun YS, Park SW, et al. (2005) Limitation of the validity of the homeostasis model assessment as an index of insulin resistance in Korea. Metabolism 54: 206-211
13. Muniyappa R, Irving BA, Unni US, et al. (2010) Limited predictive ability of surrogate indices of insulin sensitivity/resistance in Asian-Indian men. Am J Physiol Endocrinol Metab 299: E1106-1112
14. Jenkins AB, Samaras K, Carey DG, Kelly P, Campbell LV (2000) Improved indices of insulin resistance and insulin secretion for use in genetic and population studies of type 2 diabetes mellitus. Twin Res 3: 148-151
15. Li G, Pan X (1995) A new insulin-sensitivity index for epidemiological study. Chin Med J (Engl) 108: 55-56
16. Kanauchi M (2003) Validation of the oral glucose insulin sensitivity index to assess insulin sensitivity in Japanese subjects for use in clinical practice. Eur J Clin Invest 33: 1022-1023
17. Bastard JP, Rabasa-Lhoret R, Maachi M, et al. (2003) What kind of simple fasting index should be used to estimate insulin sensitivity in humans? Diabetes Metab 29: 285-288
18. Rabasa-Lhoret R, Bastard JP, Jan V, et al. (2003) Modified quantitative insulin sensitivity check index is better correlated to hyperinsulinemic glucose clamp than other fasting-based index of insulin sensitivity in different insulin-resistant states. J Clin Endocrinol Metab 88: 4917-4923
19. Guerrero-Romero F, Simental-Mendia LE, Gonzalez-Ortiz M, et al. (2010) The product of triglycerides and glucose, a simple measure of insulin sensitivity.

Comparison with the euglycemic-hyperinsulinemic clamp. J Clin Endocrinol Metab 95: 3347-3351

ESM Table 4 Pooled correlation coefficients between surrogate measures of insulin sensitivity and the hyperinsulinaemic euglycaemic clamp in subgroups NGT, IGT and type 2 diabetes

	NGT		IGT		Type 2 diabetes	
Name of surrogate measure [references]	r (95% CI)	n	r (95% CI)	n	r (95% CI)	n
OGTT-based indices						
AUC insulin [1-7]	-0.65 (-0.72 to -0.55)	5	-0.59 (-0.72 to -0.41)	3	-0.30 (-0.49 to -0.08)	2
Belfiore [3, 6, 8-11]	0.63 (0.56 to 0.69)	5	0.71 (0.58 to 0.81)	3	0.48	1
Matsuda [3, 6, 8-14]	0.63 (0.54 to 0.71)	8	0.75 (0.67 to 0.81)	5	0.51 (0.13 to 0.76)	4
OGIS [6, 9, 14]	0.57 (0.43 to 0.68)	2	0.41	1	0.50	1
Stumvoll MCR [8, 12, 14]	0.56 (0.47 to 0.63)	3	0.75 (0.65 to 0.82)	3	0.29 (-0.39 to 0.77)	2
Stumvoll ISI [6, 8, 10, 12]	0.55 (0.46 to 0.63)	3	0.74 (0.65 to 0.81)	3	0.60	1
Cederholm [6, 9-12]	0.47 (0.31 to 0.61)	4	0.45 (0.26 to 0.61)	3	0.59 (0.33 to 0.76)	2
Insulin (30 min) [7, 15, 16]	-0.35 (-0.44 to -0.25)	2	-0.26	1	-0.29	1
Insulin (60 min) [4, 15]	-0.55 (-0.67 to -0.41)	2	-0.50	1	-0.27	1
Insulin (120 min) [4, 7-9, 12, 15, 16]	-0.56 (-0.63 to -0.48)	6	-0.58 (-0.70 to -0.41)	4	-0.21 (-0.40 to -0.01)	3
Fasting indices						
IAI[a] [17]	-0.78	1	-0.71	1	-0.71	1
Revised QUICKI [18, 19]	0.70 (0.29 to 0.90)	1	0.82	1	0.63 (0.18 to 0.86)	2
McAuley [8, 19, 20]	0.64	1	0.69	1	0.39 (0.16 to 0.57)	2
QUICKI [6, 8-10, 18-29]	0.53 (0.41 to 0.63)	9	0.60 (0.39 to 0.75)	4	0.61 (0.47 to 0.73)	8
HOMA [3, 6-12, 14, 16, 18-21, 23-27, 30-35]	-0.53 (-0.61 to -0.43)	12	-0.55 (-0.65 to -0.42)	8	-0.59 (-0.67 to -0.50)	15
Fasting Belfiore [8, 9, 19]	0.49 (-0.03 to 0.81)	2	0.74	1	0.37	1
Fasting insulin [3, 4, 7-9, 12, 14-17, 19, 21, 24, 26, 27, 32, 34, 36-43]	-0.57 (-0.65 to -0.48)	13	-0.55 (-0.68 to -0.39)	8	-0.52 (-0.59 to -0.44)	13
I_0 / G_0 [8, 9, 16, 19]	-0.40 (-0.71 to 0.04)	3	-0.65 (-0.81 to -0.40)	2	-0.29	1
G_0 / I_0 [3, 17, 19, 20]	0.37 (-0.41 to 0.81)	2	0.75	1	0.28 (0.10 to 0.44)	3
Fasting glucose [7, 8, 41, 43-46]	-0.25	1	-0.18	1	-0.21 (-0.53 to 0.16)	6

[a] insulin activity index (The calculation of IAI is very similar to the calculation of HOMA-IR and both should perform similarly compared with the HEC.) Abbreviations: NGT, normal glucose tolerance; IGT, impaired glucose tolerance; r, pooled correlation coefficient; n, number of studies included in the meta-analysis; OGIS, oral glucose insulin sensitivity index; MCR, metabolic clearance rate of glucose; ISI, insulin sensitivity index; I_0, fasting insulin; G_0, fasting glucose;

References

1. Ferrara CM, Goldberg AP (2001) Limited value of the homeostasis model assessment to predict insulin resistance in older men with impaired glucose tolerance. Diabetes Care 24: 245-249
2. Reaven GM, Moore J, Greenfield M (1983) Quantification of insulin secretion and in vivo insulin action in nonobese and moderately obese individuals with normal glucose tolerance. Diabetes 32: 600-604

3. Ciampelli M, Leoni F, Cucinelli F, et al. (2005) Assessment of insulin sensitivity from measurements in the fasting state and during an oral glucose tolerance test in polycystic ovary syndrome and menopausal patients. J Clin Endocrinol Metab 90: 1398-1406
4. Laakso M (1993) How good a marker is insulin level for insulin resistance? Am J Epidemiol 137: 959-965
5. Cleland SJ, Petrie JR, Morris AD, Ueda S, Dorrian CA, Connell JM (1996) FIRI: a fair insulin resistance index? Lancet 347: 770
6. Hays NP, Starling RD, Sullivan DH, Fluckey JD, Coker RH, Evans WJ (2006) Comparison of insulin sensitivity assessment indices with euglycemic-hyperinsulinemic clamp data after a dietary and exercise intervention in older adults. Metabolism 55: 525-532
7. Petrie JR, Morris AD, Dorrian CA, Small M, Connell JM (1997) Specific insulin assays, insulin sensitivity and blood pressure. QJM 90: 465-475
8. Lorenzo C, Haffner SM, Stancakova A, Laakso M (2010) Relation of direct and surrogate measures of insulin resistance to cardiovascular risk factors in nondiabetic finnish offspring of type 2 diabetic individuals. J Clin Endocrinol Metab 95: 5082-5090
9. Leonetti F, Iacobellis G, Zappaterreno A, et al. (2004) Insulin sensitivity assessment in uncomplicated obese women: comparison of indices from fasting and oral glucose load with euglycemic hyperinsulinemic clamp. Nutr Metab Cardiovasc Dis 14: 366-372
10. Soonthornpun S, Setasuban W, Thamprasit A, Chayanunnukul W, Rattarasarn C, Geater A (2003) Novel insulin sensitivity index derived from oral glucose tolerance test. J Clin Endocrinol Metab 88: 1019-1023
11. Matsuda M, DeFronzo RA (1999) Insulin sensitivity indices obtained from oral glucose tolerance testing: comparison with the euglycemic insulin clamp. Diabetes Care 22: 1462-1470
12. Piche ME, Lemieux S, Corneau L, Nadeau A, Bergeron J, Weisnagel SJ (2007) Measuring insulin sensitivity in postmenopausal women covering a range of glucose tolerance: comparison of indices derived from the oral glucose tolerance test with the euglycemic-hyperinsulinemic clamp. Metabolism 56: 1159-1166
13. Kirwan JP, Huston-Presley L, Kalhan SC, Catalano PM (2001) Clinically useful estimates of insulin sensitivity during pregnancy: validation studies in women with normal glucose tolerance and gestational diabetes mellitus. Diabetes Care 24: 1602-1607
14. Mari A, Pacini G, Murphy E, Ludvik B, Nolan JJ (2001) A model-based method for assessing insulin sensitivity from the oral glucose tolerance test. Diabetes Care 24: 539-548
15. Hollenbeck CB, Chen N, Chen YD, Reaven GM (1984) Relationship between the plasma insulin response to oral glucose and insulin-stimulated glucose utilization in normal subjects. Diabetes 33: 460-463
16. Hanson RL, Pratley RE, Bogardus C, et al. (2000) Evaluation of simple indices of insulin sensitivity and insulin secretion for use in epidemiologic studies. Am J Epidemiol 151: 190-198
17. Li G, Pan X (1995) A new insulin-sensitivity index for epidemiological study. Chin Med J (Engl) 108: 55-56
18. Rabasa-Lhoret R, Bastard JP, Jan V, et al. (2003) Modified quantitative insulin sensitivity check index is better correlated to hyperinsulinemic glucose clamp than other fasting-based index of insulin sensitivity in different insulin-resistant states. J Clin Endocrinol Metab 88: 4917-4923
19. Ruige JB, Mertens IL, Bartholomeeusen E, Dirinck E, Ferrannini E, Van Gaal LF (2006) Fasting-based estimates of insulin sensitivity in overweight and obesity: a critical appraisal. Obesity (Silver Spring) 14: 1250-1256
20. Zaletel J, Barlovic DP, Prezelj J (2010) Adiponectin-leptin ratio: a useful estimate of insulin resistance in patients with Type 2 diabetes. J Endocrinol Invest 33: 514-518
21. Straczkowski M, Stepien A, Kowalska I, Kinalska I (2004) Comparison of simple indices of insulin sensitivity using the euglycemic hyperinsulinemic clamp technique. Med Sci Monit 10: CR480-484
22. Skrha J, Haas T, Sindelka G, et al. (2004) Comparison of the insulin action parameters from hyperinsulinemic clamps with homeostasis model assessment and QUICKI indexes in subjects with different endocrine disorders. J Clin Endocrinol Metab 89: 135-141
23. Ntyintyane L, Panz V, Raal F, Gill G (2010) Comparison between surrogate indices of insulin sensitivity and resistance, and the hyperinsulinaemic euglycaemic glucose clamp in urban South African blacks with and without coronary artery disease. Diab Vasc Dis Res 7: 151-157

24. Katsuki A, Urakawa H, Gabazza EC, et al. (2005) Quantitative insulin sensitivity check index is a useful indicator of insulin resistance in Japanese metabolically obese, normal-weight subjects with normal glucose tolerance. Endocr J 52: 253-257
25. Diamanti-Kandarakis E, Kouli C, Alexandraki K, Spina G (2004) Failure of mathematical indices to accurately assess insulin resistance in lean, overweight, or obese women with polycystic ovary syndrome. J Clin Endocrinol Metab 89: 1273-1276
26. Yokoyama H, Emoto M, Fujiwara S, et al. (2003) Quantitative insulin sensitivity check index and the reciprocal index of homeostasis model assessment in normal range weight and moderately obese type 2 diabetic patients. Diabetes Care 26: 2426-2432
27. Mather KJ, Hunt AE, Steinberg HO, et al. (2001) Repeatability characteristics of simple indices of insulin resistance: implications for research applications. J Clin Endocrinol Metab 86: 5457-5464
28. Katz A, Nambi SS, Mather K, et al. (2000) Quantitative insulin sensitivity check index: a simple, accurate method for assessing insulin sensitivity in humans. J Clin Endocrinol Metab 85: 2402-2410
29. Katsuki A, Sumida Y, Gabazza EC, et al. (2002) QUICKI is useful for following improvements in insulin sensitivity after therapy in patients with type 2 diabetes mellitus. J Clin Endocrinol Metab 87: 2906-2908
30. Kang ES, Yun YS, Park SW, et al. (2005) Limitation of the validity of the homeostasis model assessment as an index of insulin resistance in Korea. Metabolism 54: 206-211
31. Bonora E, Targher G, Alberiche M, et al. (2000) Homeostasis model assessment closely mirrors the glucose clamp technique in the assessment of insulin sensitivity: studies in subjects with various degrees of glucose tolerance and insulin sensitivity. Diabetes Care 23: 57-63
32. Emoto M, Nishizawa Y, Maekawa K, et al. (1999) Homeostasis model assessment as a clinical index of insulin resistance in type 2 diabetic patients treated with sulfonylureas. Diabetes Care 22: 818-822
33. Ikeda Y, Suehiro T, Nakamura T, Kumon Y, Hashimoto K (2001) Clinical significance of the insulin resistance index as assessed by homeostasis model assessment. Endocr J 48: 81-86
34. Katsuki A, Sumida Y, Urakawa H, et al. (2002) Neither homeostasis model assessment nor quantitative insulin sensitivity check index can predict insulin resistance in elderly patients with poorly controlled type 2 diabetes mellitus. J Clin Endocrinol Metab 87: 5332-5335
35. Matsuhisa M, Yamasaki Y, Emoto M, et al. (2007) A novel index of insulin resistance determined from the homeostasis model assessment index and adiponectin levels in Japanese subjects. Diabetes Res Clin Pract 77: 151-154
36. Geloneze B, Pereira JA, Pareja JC, et al. (2009) Overcoming metabolic syndrome in severe obesity: adiponectin as a marker of insulin sensitivity and HDL-cholesterol improvements after gastric bypass. Arq Bras Endocrinol Metabol 53: 293-300
37. Natali A, Toschi E, Camastra S, Gastaldelli A, Groop L, Ferrannini E (2000) Determinants of postabsorptive endogenous glucose output in non-diabetic subjects. European Group for the Study of Insulin Resistance (EGIR). Diabetologia 43: 1266-1272
38. Straczkowski M, Kowalska I, Stepien A, et al. (2003) Insulin resistance in the first-degree relatives of persons with type 2 diabetes. Med Sci Monit 9: CR186-190
39. Wasada T, Arii H, Kuroki H, et al. (1995) The relationship between insulin resistance and insulin secretion in Japanese subjects with borderline glucose intolerance. Diabetes Res Clin Pract 30: 53-57
40. Blonk MC, Jacobs MA, Friedberg CE, et al. (1994) Determinants of insulin sensitivity and consequences for lipoproteins and blood pressure in subjects with non-insulin-dependent diabetes mellitus. Metabolism 43: 501-508
41. Ludvik B, Nolan JJ, Baloga J, Sacks D, Olefsky J (1995) Effect of obesity on insulin resistance in normal subjects and patients with NIDDM. Diabetes 44: 1121-1125
42. Takanashi K, Inukai T (2000) Insulin resistance and changes in the blood coagulation-fibrinolysis system after a glucose clamp technique in patients with type 2 diabetes mellitus. J Med 31: 45-62
43. Yamasaki Y, Kawamori R, Wasada T, et al. (1997) Pioglitazone (AD-4833) ameliorates insulin resistance in patients with NIDDM. AD-4833 Glucose Clamp Study Group, Japan. Tohoku J Exp Med 183: 173-183
44. DeFronzo R, Deibert D, Hendler R, Felig P, Soman V (1979) Insulin sensitivity and insulin binding to monocytes in maturity-onset diabetes. J Clin Invest 63: 939-946

45. Kolterman OG, Gray RS, Griffin J, et al. (1981) Receptor and postreceptor defects contribute to the insulin resistance in noninsulin-dependent diabetes mellitus. J Clin Invest 68: 957-969
46. Mayorov AY, Naumenkova IV, Antsiferov MB, Dedov, II (2005) Influence of insulin treatment on insulin sensitivity in insulin requiring type 2 diabetes patients. Diabetes Res Clin Pract 68 Suppl1: S54-59