Use and Abuse of HOMA Modeling

Tara M. Wallace, MD
Jonathan C. Levy, MD
David R. Matthews, MD

Homeostatic model assessment (HOMA) is a method for assessing β-cell function and insulin resistance (IR) from basal (fasting) glucose and insulin or C-peptide concentrations. It has been reported in >500 publications, 20 times more frequently for the estimation of IR than β-cell function.

This article summarizes the physiological basis of HOMA, a structural model of steady-state insulin and glucose domains, constructed from physiological dose responses of glucose uptake and insulin production. Hepatic and peripheral glucose efflux and uptake were modeled to be dependent on plasma glucose and insulin concentrations. Decreases in β-cell function were modeled by changing the β-cell response to plasma glucose concentrations. The original HOMA model was described in 1985 with a formula for approximate estimation. The computer model is available but has not been as widely used as the approximation formulae. HOMA has been validated against a variety of physiological methods.

We review the use and reporting of HOMA in the literature and give guidance on its appropriate use (e.g., cohort and epidemiological studies) and inappropriate use (e.g., measuring β-cell function in isolation). The HOMA model compares favorably with other models and has the advantage of requiring only a single plasma sample assayed for insulin and glucose.

In conclusion, the HOMA model has become a widely used clinical and epidemiological tool and, when used appropriately, it can yield valuable data. However, as with all models, the primary input data need to be robust, and the data need to be interpreted carefully.

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Homeostatic model assessment (HOMA) of β-cell function and insulin resistance (IR) was first described in 1985 (1). The technique is a method for assessing β-cell function and IR from basal glucose and insulin or C-peptide concentrations. The model has been widely used since it was first published, and we present here an overview of the model and its appropriate use and limitations in clinical science.

Types of model

In contrast to curve fitting or "minimal models," such as that described by Bergman and Cobelli (2), HOMA is one of a family of "paradigm models." The two types of model are constructed on a dif-ferent basis, and their use requires markedly different sampling. Minimal models take individual dynamic data and use curve-fitting equations to determine an optimal (though not always unique) mathematical solution to describe the data (i.e., computation is required for each dataset). Paradigm models are physiologically based structural models with theoretical solutions adjusted to the population norms; thus, data from individuals can be used to yield estimates of β-cell function and insulin sensitivity from the solution without further computation.

Bergman and Cobelli's minimal model, which uses curve-fitting equations limited to a small number of variables, requires a significant time series of data

from a glucose tolerance test plus an additional stimulus from tolbutamide or insulin to yield a unique solution. By contrast, the HOMA model is derived from a mathematical assessment of the interaction between β-cell function and IR in an idealized model that is then used to compute steady-state insulin and glucose concentrations. The output of the model is calibrated to give normal β-cell function of 100% and normal IR of 1. Once this interrelationship is calculated, one can estimate β-cell function and IR for any pair of plasma glucose and insulin concentrations without having to refit the model.

The physiological basis for the HOMA model

The HOMA model is used to yield an estimate of insulin sensitivity and β-cell function from fasting plasma insulin and glucose concentrations (1). The relationship between glucose and insulin in the basal state reflects the balance between hepatic glucose output and insulin secretion, which is maintained by a feedback loop between the liver and β-cells (3). The predictions used in the model arise from experimental data in humans and animals. The β-cell response curve (Fig. 1A) was originally constructed on the basis of a basal production rate of 10 mU/min (74 pmol/min) (4) at a plasma glucose level of 4 mmol/l, into an insulin space of 13 l with a plasma insulin half-life of 4 min (5). Hepatic glucose efflux and uptake are modeled to be dependent on plasma glucose and insulin concentrations (Fig. 1B) (6). Insulin is modeled to decay with a half-life of 3.8 min with an additional slower component (5,7); the insulin concentration controls glucose uptake in fat and muscle (Fig. 1C and D). The basal glucose efflux of 0.8 mmol/min (8,9) is assumed to enter a space of 17 l (9,10). In normal humans, 50% of the basal glucose turnover is to the nervous system, and this is a glucose-dependent process (Fig. 1E) (11). The remainder of glucose uptake by muscle (12–14) and fat is both glucose and insulin dependent (Fig. 1C and D) (15).
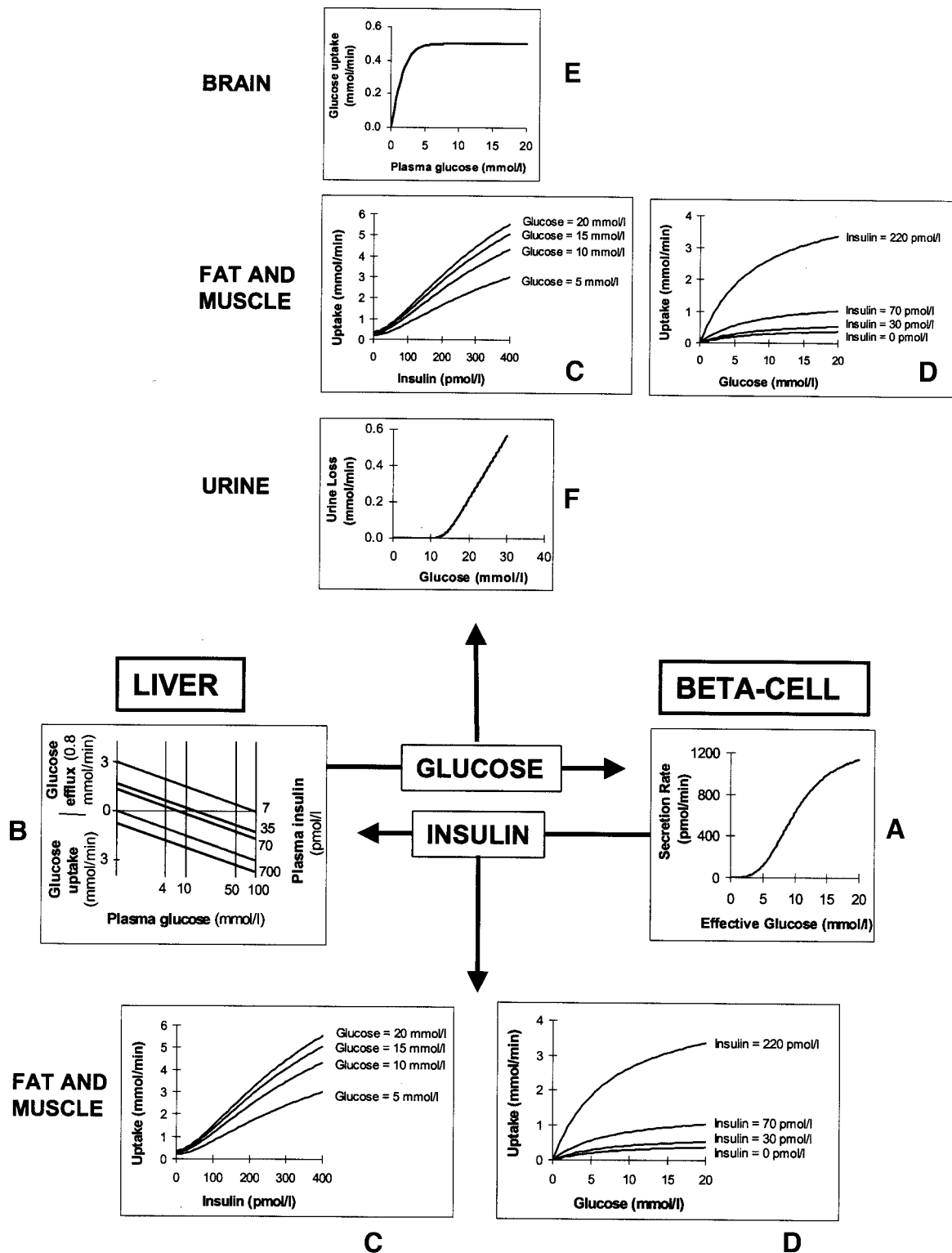
Decreases in β-cell function were modeled by changing the β-cell response to plasma glucose concentrations. Insulin sensitivity was modeled by proportion-

Figure 1—*The underlying physiological basis of the HOMA model. The feedback loop between the liver and the β-cell is central to the model. Plasma glucose concentration in the basal state is regulated by hepatic glucose output, which is insulin dependent (B). Insulin concentration is dependent on β-cell response to glucose (A). Insulin signals glucose uptake in fat and muscle (C and D). Glucose disposal is modeled in brain (E) and kidney (F) as being dependent only on glucose, and in fat and muscle as being dependent on glucose and insulin concentrations (C and D).*

ately decreasing the effect of plasma insulin concentrations at both the liver and the periphery (3). In either situation, the glucose turnover in the model remains constant. No distinction is made between hepatic insulin sensitivity and peripheral insulin sensitivity.

HOMA1: the original HOMA model

HOMA1, the original model from Matthews et al. (1) (Fig. 2*A*), contained a simple mathematical approximation of the original nonlinear solution to the iterative equations (this is the explanation for the exponential functions, which are cancelled out, in that article). The equations are widely used and simplify to:

HOMA1-IR = (FPI × FPG)/22.5
HOMA1-%B = (20 × FPI)/(FPG − 3.5)

for IR and β-cell function, respectively, where FPI is fasting plasma insulin concentration (mU/l) and FPG is fasting plasma glucose (mmol/l).

HOMA2: the updated HOMA model (i.e., the computer model)

HOMA2, the correctly solved computer model (16), has nonlinear solutions (Fig. 2*B*), and these should be used when HOMA is compared with other models (e.g., the minimal model). In addition, the updated (1996) version of the HOMA model accounts for variations in hepatic and peripheral glucose resistance (i.e, the reduction in the suppression of hepatic glucose output [by hyperglycemia] and the reduction of peripheral glucose-stimulated glucose uptake) (Fig. 1*B*) (17). The insulin secretion curve has been modified to allow for an increase in insulin secretion in response to a plasma glucose concentration of >10 mmol/l (Fig. 1*A*). This version incorporates an estimate of proinsulin secretion into the model and thus allows the use of either total (radioimmunoassay [RIA]) or specific insulin assays. Renal glucose losses have also been included in the model, thus allowing its use in hyperglycemic subjects (Fig. 1*F*). (The HOMA2 model is available from www.OCDEM.ox.ac.uk or from J.C.L. or D.R.M.)

The computer model can be used to determine insulin sensitivity (%S) and β-cell function (%B) from paired fasting plasma glucose and RIA insulin, specific insulin, or C-peptide concentrations across a range of 1–2,200 pmol/l for insu-
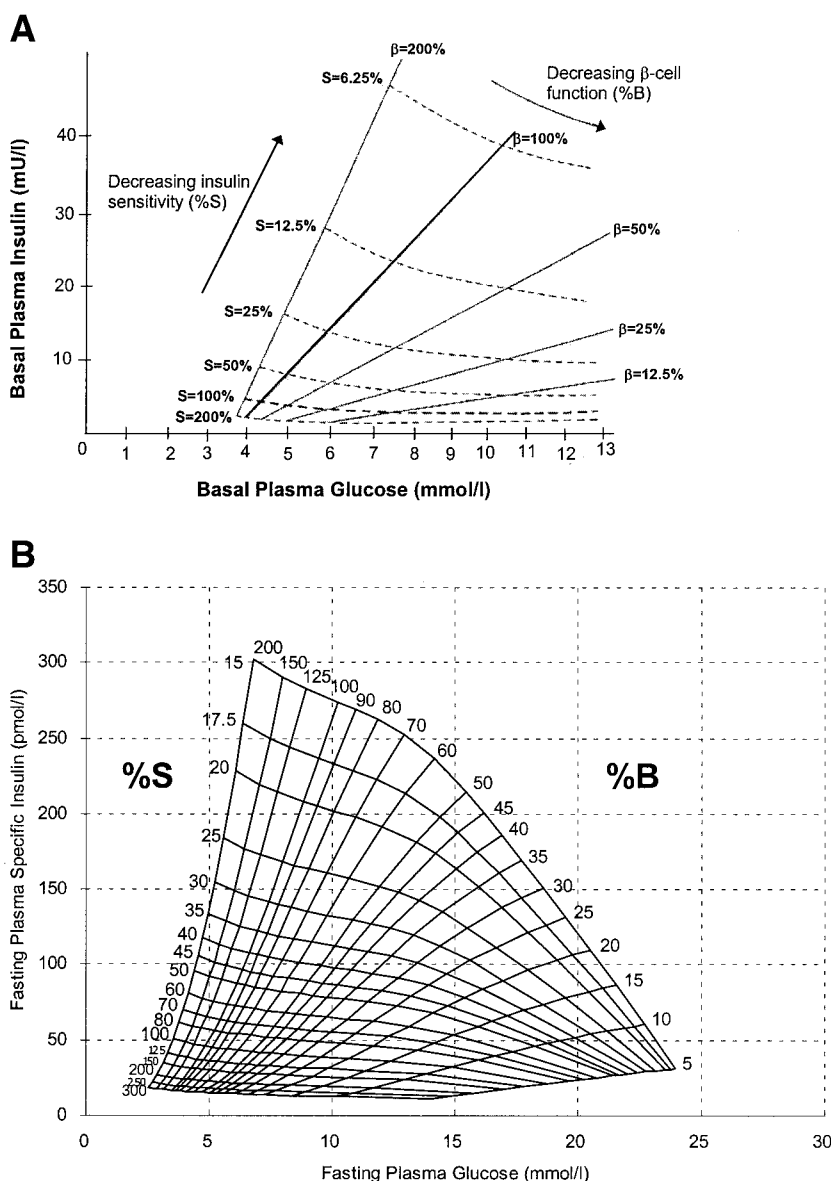
Figure 2— *The 1985 HOMA model (A), redrawn from ref. 1, and the 1996 HOMA model (B).*

lin and 1–25 mmol/l for glucose. Clinical judgment is required when entering data: for example, a plasma glucose of <2.5 mmol/l either represents hypoglycemia, which is a non–steady-state situation, or an assay problem. In either case, it is clear that such values should not be used in the model. If both C-peptide and insulin data are available, there is a logic for using C-peptide data to calculate β-cell function (since C-peptide is a marker of secretion) and for using insulin data to calculate %S (since HOMA-%S is derived from glucose disposal as a function of insulin concentration). However, in practice, insulin and glucose have usually been used to yield

both functions, as the theoretical advantage of using C-peptide has to be offset against the additional cost and the practicalities of analyzing and storing the additional C-peptide samples.

The equations give estimates of HOMA1-IR and HOMA1-%B that can be used between populations (with the proviso that the insulin and glucose assays are comparable) or for examination of longitudinal changes. However, the equations were based on the 1985 HOMA1 model, which was calibrated to an insulin assay used in the 1970s, and systematically underestimate %S and consequently overestimate %B when compared with

Table 1—*Correlations of HOMA against other methods*

Insulin sensitivity method	Correlation with HOMA-%S	Comments	HOMA model	Ref.	*P*
Euglycemic clamp	$R_s = 0.88$	NGT ($n = 12$), diabetes ($n = 11$)	Equation	1	0.0001
Euglycemic clamp	$R_s = 0.82$	NGT ($n = 62$), diabetes ($n = 53$)	Equation	21	0.0001
Euglycemic clamp	$r = 0.73$	Diabetes ($n = 80$)	Equation	22	0.0001
Euglycemic clamp	$r = 0.73$	Diabetes ($n = 55$)	Equation	30	0.0001
Euglycemic clamp	$r = 0.58$	NGT ($n = 104$)	Equation	31	0.0005
Euglycemic clamp	$r = 0.78$	Diabetes ($n = 30$)	Computer	18	0.0001
Minimal model	$r = 0.7$	NGT ($n = 87$)	Equation	23	0.001
Minimal model	$r = 0.88$	NGT ($n = 7$), IGT ($n = 5$), diabetes ($n = 1$)	Computer	32	

β-Cell function method	Correlation with HOMA-%β	Comments	HOMA model	Ref.	*P*
Hyperglycemic clamp	$R_S = 0.69$	NGT ($n = 10$), diabetes ($n = 11$)	Equation	1	0.001
Hyperglycemic clamp	$r = 0.62$	NGT ($n = 104$)	Equation	31	0.0005
Hyperglycemic clamp	$R_S = 0.9$	NGT ($n = 36$), diabetes ($n = 21$)	Computer	33	0.001
Hyperglycemic clamp	$r = 0.87$	Diabetes ($n = 30$)	Computer	18	0.0001
AIR (IVGTT)	$r = 0.73$	NGT ($n = 7$), IGT ($n = 8$), diabetes ($n = 9$)	Computer	25	
CIGMA	$r = 0.88$	NGT ($n = 7$), IGT ($n = 8$), diabetes ($n = 9$)	Computer	25	
CIGMA	$R_S = 0.87$	NGT ($n = 11$), diabetes ($n = 12$)	Equation	1	0.0001

AIR, acute insulin response.

newer assays. Thus, the equations function well in assessing relative change; that is, the percentage change or difference in one model will reflect as a similar percentage change or difference in the other. However, in assessing absolute resistance or β-cell function, the corrected nonlinear (computer) model should be used, as this has been recalibrated in line with current insulin assays and extended to allow the use of C-peptide if required. The equations are currently being adjusted for use with newer assays. The computer model gives a value for insulin sensitivity expressed as HOMA2-%S (where 100% is normal), which is simply the reciprocal of HOMA2-IR.

Sampling
Because insulin secretion is pulsatile, the use of the mean of three samples taken at 5-min intervals to compute HOMA is theoretically better than a single sample (1). However, in practice a single sample is often taken, and if population estimates are sought, this is an acceptable compromise and yields a similar result in large datasets. Data from 30 subjects with diet-treated type 2 diabetes (18) show near-perfect correlations between HOMA2-%B and HOMA2-%S computed from the mean of three basal samples at 5-min intervals and from a single basal sample ($r = 0.99$, $P < 0.0001$). However, when HOMA is used to determine β-cell func-

tion and insulin sensitivity in individuals, the use of a single sample gives intrasubject coefficients of variation (CVs) of 10.3% for HOMA-%S and 7.7% for HOMA-%B (18) compared with 5.8 and 4.4%, respectively, when three samples are taken; in these circumstances, the use of the mean insulin concentration from three samples is advisable.

C-peptide, a measure of insulin secretion, can be used in HOMA modeling of both β-cell function and IR. C-peptide is a robust measure of insulin secretion but not of insulin action, and the concept of the model is that %S is a function of glucose metabolism driven by the action of insulin. It is therefore more appropriate to use fasting insulin concentrations for the determination of %S if these are available. The use of two assays, C-peptide and insulin, to determine β-cell function and insulin sensitivity, respectively, reduces bias. Careful handling of the samples is essential because hemolysis results in the degradation of insulin and freezing samples results in degradation of C-peptide. In addition to these potential problems, insulin interassay variation can be large, and in the past, values have varied considerably between different laboratories (19). These problems may reduce when international standardization of insulin assays is implemented.

Validation of the HOMA model
HOMA has been compared with a number of well-validated methods used to measure IR and β-cell function (Table 1). Although the hyperinsulinemic-euglycemic clamp and the hyperglycemic clamp are often referred to as the "gold standard" tests, one should of course be very cautious of this terminology since it has implications that the result from such a test might be "better" or indeed "correct." Results from dynamic tests are likely to be systematically different from steady-state basal tests: clamps are complex stress tests with insulin and glucose concentrations and flux well outside the normal range. There is no justification for the view that one test is yielding indexes that are superior to another—they give information about different aspects of β-cell function or IR. Although data about reproducibility (inter- and intrasubject CVs) may sway the investigator in favor of one test or another, it is also true that discrimination between pathological states may be superior in some models despite apparently larger CVs (20). There is good correlation between estimates of IR derived from HOMA and from the euglycemic clamp ($R_s = 0.88$, $P < 0.0001$ [1]; $R_s = 0.85$, $P < 0.0001$ [21]; and $r = 0.73$, $P < 0.0001$ [22]) and between HOMA and the minimal model ($r = 0.7$, $P < 0.001$) (23). Estimates of β-cell function using HOMA have been shown to corre-

Table 2—*Some examples of the use of the HOMA model*

Type of study	Glycemic category	Example refs.	Findings
Physiology: comparison of methods	Diabetes IGT Normal	30, 22, 21, 1, 25, 33 25 21, 1, 25, 31, 33	There is good correlation between estimates of IR derived from HOMA and from the euglycemic clamp in normal and diabetic subjects: $R_s = 0.88$ ($P < 0.0001$) (1), $R_s = 0.85$ ($P < 0.0001$) (21), $r = 0.73$ (22), and $r = 0.73$ (30). Estimates of β-cell function using HOMA have been shown to correlate well with estimates using CIGMA ($R_s = 0.88$) (25), hyperglycemic clamps ($R_s = 0.61$; $P < 0.01$ [1]; $R_s = 0.9$, $P < 0.001$ [33]; $r = 0.62$, $P < 0.005$ [31]), and with the acute insulin response from the IVGTT ($R_s = 0.63$) (25).
Epidemiology: one-off	Diabetes IGT/IFG Normal	34, 35 34, 35 34, 37, 35, 36	In the San Antonio Heart Study, cross-sectional analysis of 2,465 subjects with varying degrees of glucose tolerance showed that Mexican-Americans were significantly more insulin resistant and had higher insulin secretion than non-Hispanic whites at all levels of glucose tolerance (34). Matsumoto et al. (35) assessed insulin resistance cross-sectionally in 756 Japanese subjects and showed that subjects with diabetes had significantly increased IR compared with subjects with IGT, but there was no significant difference in IR between subjects with NGT and IGT. HOMA has also been used to investigate the relationship between various genetic polymorphisms and insulin resistance in cross-sectional studies (36).
Longitudinal measurement	Diabetes IGT Normal	26, 38 27 27	The UKPDS examined the effects of sulphonylureas, metformin, and diet on %B and %S over 6 years (26). There was an initial increase in %B (from 46 to 78%) at 1 year in subjects on sulphonylureas, followed by a steady decline in function to 52% at 6 years. Subjects on diet only ($n = 486$) exhibited a gradual decline in β-cell function of about 4% per year. In metformin-treated subjects ($n = 159$), %S increased from 51 to 62% at 1 year, remaining at 62% at 6 years. The Belfast study also examined changes in HOMA-%B and HOMA-%S over a 6-year period in 432 patients with type 2 diabetes on diet only or oral agents (38). In the Mexico City Study, %B and %S were measured in 1,449 Mexican subjects with NGT or IGT. After 3.5 years, 4.4% of subjects with NGT and 23.4% with IGT had progressed to diabetes: the development of diabetes was associated with lower %S at baseline (27).
Assess response to treatment	Diabetes	39	Pioglitazone was shown to increase %B and %S compared with placebo in a 23-week study of 197 subjects with type 2 diabetes (39).
Assess risk of developing diabetes	Normal	40	Costa et al. (40) studied 205 first-degree relatives of patients with diabetes, 10.2% were found to have diabetes and 30.7% IGT. %S was reduced in normal subjects with a first-degree relative with type 2 diabetes compared with control subjects (40).
Rodents		41, 42	HOMA has not been validated for animal studies.

IFG, impaired fasting glucose.

late well with estimates using continuous infusion glucose model assessment (CIGMA) (24) (another paradigm model) ($R_s = 0.88$) (25), hyperglycemic clamps ($R_s = 0.61$, $P < 0.01$) (1), and the acute insulin response from the intravenous glucose tolerance test (IVGTT) ($R_s = 0.63$) (25).

REVIEW OF THE PUBLISHED USE OF THE HOMA MODEL — A literature search using Medline found that the use of the HOMA model has been reported in 572 published

works. In ~75% of them, the model is used in the assessment of IR as a one-off measure in epidemiological or genetic studies. The model is used 20 times more frequently for the estimation of IR than β-cell function. In >50% of reports, the model is used in nondiabetic populations. Examples of the use of HOMA are shown in Table 2.

GENERAL USE OF THE HOMA MODEL — The choice of method used to assess IR and β-cell function depends on the size and type of study

to be undertaken. Although clamps are useful techniques for intensive physiological studies on relatively small numbers of subjects, a simpler tool such as HOMA may be more appropriate for use in large epidemiological studies.

Cohort changes in β-cell function and IR
HOMA can be used to assess longitudinal changes in β-cell function and IR in patients with diabetes in order to examine the natural history of diabetes and to assess the effects of treatment. For example,

the model was used in the U.K. Prospective Diabetes Study (UKPDS) to demonstrate the effects of sulfonylureas and metformin on IR and β-cell function, compared with diet, over a 6-year period (26). The study showed an initial increase in β-cell function (from 46 to 78%) at 1 year in subjects on a sulfonylurea, followed by a steady decline in function to 52% at 6 years. Subjects on diet only ($n = 486$) exhibited a gradual decline in β-cell function of ~4% per year. Insulin sensitivity only changed in subjects on metformin ($n = 159$), increasing from 51 to 62% at 1 year and remaining at 62% at 6 years.

Epidemiology: cross-sectional studies

HOMA has been used to assess IR and β-cell function as a one-off measure in >150 epidemiological studies examining subjects of various ethnic origins with varying degrees of glucose tolerance. For example, in the Mexico City Study, β-cell function and IR were assessed cross-sectionally using HOMA in 1,449 Mexicans with normal or impaired glucose tolerance (IGT) (27). Subjects were followed up for 3.5 years in order to ascertain the incidence of diabetes and to examine any possible relationship with baseline β-cell function and IR. By 3.5 years, 4.4% of subjects with normal glucose tolerance (NGT) and 23.4% with IGT had progressed to diabetes. The development of diabetes was associated with higher HOMA-IR at baseline. This study used the HOMA1 equations and single glucose/insulin pairs rather than the mean of three samples at 5-min intervals.

The use of HOMA in the normal population

Although it has been argued that HOMA is no better than fasting insulin concentrations for the estimation of insulin sensitivity in normal individuals, there are several reasons why the use of HOMA in normal subjects is worthwhile. The use of HOMA to quantify insulin sensitivity and β-cell function can be helpful in normal populations as it allows *1*) comparisons of β-cell function and insulin sensitivity to be made with subjects with abnormal glucose tolerance and *2*) the collection of longitudinal data in subjects who go on to develop abnormal glucose tolerance.

Physiological studies

HOMA can also be used in physiological studies to measure insulin sensitivity and β-cell function in addition to stimulated estimates derived from more complex tests such as clamps and IVGTTs (18). Combining data from these tests gives information about insulin sensitivity or β-cell function across the dose-response curve. HOMA and clamps yield steady-state measures of insulin secretion and insulin sensitivity in the basal and maximally stimulated states, respectively. HOMA measures basal function at the nadir of the dose-response curve, whereas clamps are an assessment of the stimulated extreme (i.e., V_{max}). The IVGTT and oral glucose tolerance test (OGTT) yield measures of dynamic (non–steady-state) insulin secretion and insulin sensitivity over the middle of the physiological range.

HOMA-%S in individuals

HOMA can be used to track changes in insulin sensitivity and β-cell function longitudinally in individuals. The model can also be used in individuals to indicate whether reduced insulin sensitivity or β-cell failure predominates. When used in individuals, triplicate insulin samples should be used to improve the CV.

CAVEATS

Cross-cultural comparisons

Cross-cultural reports using HOMA are appropriate, but one should not necessarily conclude that any population has a defect compared with another simply on the basis of finding a HOMA-%S that is lower. One would need to establish the prevailing normal HOMA-%S from a normoglycemic population in each comparative group. For example, subjects with IGT from the Mexico City Diabetes Study ($n = 260$) (27) have reduced insulin sensitivity (geometic mean 45.1%-S, SEM 43.3–47.0%) compared with 352 subjects from the Insulin Resistance Atherosclerosis Study (IRAS) (28) (56.7%-S, 54.8–58.6%) (ANOVA $P < 0.001$). Taken in isolation, this might imply that IR plays a greater part in the pathophysiology of IGT in the subjects from Mexico City than in those studied in IRAS. But when insulin sensitivity is examined in the two populations in subjects with NGT, a similar difference is found (66.2%, 65.0–67.4%) in 1,634 subjects from Mexico City com-

pared with 652 subjects from IRAS (78.0%, 76.2–79.8%) (ANOVA $P < 0.001$). Although insulin sensitivity is <100% in subjects with NGT in both of these populations, one cannot conclude that there is necessarily a metabolic defect, although it would not exclude the possibility. Collateral evidence, such as the finding that the metabolic syndrome was closely associated with the resistant groups, would give credence to the supposition that reduced insulin sensitivity was a marker of risk.

Assessment of HOMA-%S in subjects on insulin

It is possible to use HOMA to assess insulin sensitivity in subjects treated with insulin, but it is imperative to ensure that samples are taken when glucose and insulin concentrations are in a steady state. For example, it would be meaningless to measure HOMA-%S following the administration of a short-acting insulin analog when the glucose level will be falling rapidly. An additional problem is that subcutaneously administered insulin enters into the peripheral circulation and is therefore not subject to the same degree of first-pass metabolism as endogenous insulin secreted into the portal circulation. Thus, the assumptions about hepatic extraction included in the model do not apply when a subject is being treated with exogenous insulin. The use of HOMA in subjects on insulin needs further validation, and studies to examine the use of HOMA in these circumstances are in progress.

Measurement of HOMA-%B in subjects on insulin

The insulin-glucose HOMA model cannot be used to assess β-cell function in those taking exogenous insulin. Under such circumstances, the C-peptide HOMA model, which uses plasma C-peptide concentrations to reflect endogenous insulin secretion, could be used, but the use of the model in this situation has not been verified.

Measurement of HOMA-%B in subjects on secretagogues

HOMA-%B is a measure of β-cell activity, not of β-cell health or pathology. HOMA can be used in subjects on insulin secretagogues, but the results need to be interpreted with caution. For example, data from the UKPDS showed an initial in-

crease in β-cell function (from 46 to 78%) at 1 year in subjects on a sulfonylurea, followed by a steady decline in function to 52% at 6 years (26). The apparent improvement in β-cell function in the first year simply reflects the secretagogue mechanism of action of sulfonylureas, and the following decline of ~5% per year over 5 years is in line with that of the diet-only group (4% per year), showing that there has been no amelioration of the rate of β-cell failure with treatment. These data illustrate that the HOMA model of β-cell function reflects insulin secretion rather than β-cell "health."

INAPPROPRIATE USE OF HOMA

To report β-cell function in isolation
HOMA apportions the basal state of insulin and glucose in terms of resistance and β-cell function. It can be seen from the model that for individuals with normal glucose levels, HOMA solutions might indicate 100% β-cell function and 100% insulin sensitivity, or, in the case of a thin, fit individual with high sensitivity, 50% β-cell function and 200% insulin sensitivity. Within the context of reporting both results, these are appropriate solutions—sensitivity is doubled, so the β-cells are functioning at 50% of normal. However, if the β-cell data are reported in isolation, one might conclude erroneously that the subject had failing β-cells, as opposed to appropriately low secretion, because the sensitivity of the body was high.

The assessment of IR and β-cell function in animal studies
The HOMA model has not been validated for use in rodents or any other animals, and such use violates the assumptions of the model.

STATISTICAL AND MATHEMATICAL ASPECTS OF HOMA

Reproducibility
There are issues relating to reproducibility (both within subject and between subject) inherent in all methods of assessment. The CV for HOMA was initially reported as 31% (1) using immunoreactive insulin assays, but more recent studies, using specific insulin assays and many more subjects, have demonstrated CVs between 7.8% (21) and 11.7% (22).

The use of the percentage scale
A potential source of confusion is that of terminology: when using the equations, normal IR is defined as 1, but when using the computer model, normal insulin sensitivity is defined as 100%. But scales of percentages raise their own problems, since statements describing a percentage change can be ambiguous—a change on the scale from 50 to 60% is a 10% change in units but a 20% relative change. Authors need to be clear about this when reporting their data.

The HOMA model versus other models
HOMA may yield a different estimate of β-cell function or IR from the minimal model. It should be recognized that HOMA is a measure of basal insulin sensitivity and β-cell function and, in contrast to clamps, is not intended to give information about the stimulated state.

Correct reporting of HOMA
HOMA estimates of β-cell function and insulin sensitivity are usually not normally distributed. The data should be tested for normality, and if they are found to not be normal, they should be logarithmically transformed and reported as geometric means with appropriate measures of dispersion.

Variations of HOMA equations: QUICKI
The Quantitative Insulin Sensitivity Check Index (QUICKI) (29) is identical to the simple equation form of the HOMA model in all comparative respects, except that QUICKI uses a log transform of the insulin glucose product.

$$\text{HOMA-IR} = 22.5/(\text{FPI} \times \text{FPG}) = \text{constant}/(\text{FPI} \times \text{FPG})$$

$$\text{QUICKI} = 1/[\log(\text{FPI}) + \log(\text{FPG})] = 1/[\log(\text{FPI} \times \text{FPG})]$$

QUICKI is thus not a new model and should be recognized as simply being log HOMA-IR, which explains the near-perfect correlation with HOMA. It has the same disadvantage/limitations as the use of the HOMA equations compared with the computer model.

CONCLUSIONS — The HOMA model has proved be a robust clinical and epidemiological tool in descriptions of the pathophysiology of diabetes. Already quoted in >500 publications, it has become one of the standard tools in the armamentarium of the clinical physiologist.

HOMA analysis allows assessment of inherent β-cell function and insulin sensitivity and can characterize the pathophysiology in those with abnormal glucose tolerance. Longitudinal data in normal subjects who go on to develop abnormal glucose tolerance is particularly informative. The use of HOMA to make comparisons across ethnic groups is valid, but the baseline HOMA-%S from a normoglycemic population in each comparative group should be established first in order to determine whether a difference in insulin sensitivity between groups simply reflects a different baseline.

Although longitudinal changes in HOMA-%B in subjects on insulin secretagogues can be useful in determining β-cell function over time, it must be remembered that any initial increase in HOMA-%B following initiation of treatment simply reflects the mechanism of action of the drug. β-Cell function cannot be interpreted in the absence of a measure of insulin sensitivity, and therefore HOMA-%S should always be reported alongside HOMA-%B. The use of HOMA to assess insulin sensitivity in subjects treated with insulin has many potential problems and needs further validation.

Clarity is needed in reporting HOMA due to the problems of describing changes in percentages. HOMA values are rarely normally distributed and should therefore be logarithmically transformed and reported as geometric means with appropriate measures of dispersion. When used appropriately, HOMA can yield valuable data, but as is common with all models, the primary input data need to be robust and the data should be interpreted carefully.

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