PATHOPHYSIOLOGICAL DOMAINS UNDERLYING THE
METABOLIC SYNDROME: AN ALTERNATIVE FACTOR
ANALYTIC STRATEGY

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Abstract. Factor analysis (FA) has become part and parcel in metabolic syndrome (MBS) research. Both exploration- and confirmation-driven factor analyzes are rampant. However, factor analytic results on MBS differ widely. A situation that is at least in part attributable to misapplication of FA. Here, our purpose is (i) to review factor analytic efforts in the study of MBS with emphasis on misusage of the FA model and (ii) to propose an alternative factor analytic strategy.

Methods: The proposed factor analytic strategy consists of four steps and confronts weaknesses in application of the FA model. At its heart lies the explicit separation of dimensionality and pattern selection as well as the direct evaluation of competing inequality-constrained loading patterns. A high-profile MBS data set with anthropometric measurements on overweight children and adolescents is reanalyzed using this strategy.

Results: The reanalysis implied a more parsimonious constellation of pathophysiological domains underlying phenotypic expressions of MBS than the original analysis (and many other analyzes). The results emphasize correlated factors of impaired glucose metabolism and impaired lipid metabolism.

Conclusions: Pathophysiological domains underlying phenotypic expressions of MBS included in the analysis are driven by multiple interrelated metabolic impairments. These findings indirectly point to the possible existence of a multifactorial aetiology.

Key words: Factor analysis; Metabolic syndrome

Abbreviations: AACE = American Academy of Clinical Endocrinologists; BMI = body mass index; CFA = confirmatory factor analysis; CVD = cardiovascular disease; DBP = diastolic blood pressure; DM = diabetes mellitus; EFA = exploratory factor analysis; EGIR = European Group for study of Insulin Resistance; FA = factor analysis; G2 = blood glucose level two hours after oral glucose intake; GB = blood glucose level at (fasting) baseline; HDL chol. = high density lipoprotein cholesterol; HOMA = homeostatic model assessment; IR = insulin resistance; MBS = metabolic syndrome; NCEP ATPIII = National Cholesterol Education Program - Adult Treatment Panel III; PCA = principal components analysis; SBP = systolic blood pressure; trig. = triglycerides; UCFM = unrestricted confirmatory factor model; WHO = World Health Organization

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1. Introduction

Certain risk factors for type 2 diabetes mellitus (DM) and atherosclerotic cardiovascular disease (CVD) have long been observed to cluster together in the individual [1, 2]. This clustering has rendered renewed interest with Reaven’s contention [3, 4] that insulin resistance forms its basis. Today, the complex of interrelated risk factors of metabolic origin is known as the ‘metabolic syndrome’ (MBS) [5, 6]. It is considered to be a major threat to current and future public health, especially as MBS might result from maladaptive human metabolism in the face of food energy abundance in combination with a sedentary lifestyle [7, 8].

Recently, the MBS concept has been hotly debated [9–18]. A number of interrelated reasons are at the heart of the debate. The aetiology of the syndrome is largely unknown as to date it is unclear if a single pathogenetic process promotes the syndrome, or if multiple different pathogenetic processes need to concur in order for the syndrome to express itself. Notwithstanding the unknown aetiology, a number of expert groups, among which the World Health Organization (WHO) [19] and the National Cholesterol Education Program - Adult Treatment Panel III (NCEP ATPIII) [20], have published (slightly) different definitions of MBS intended for clinical diagnosis. However, clinical evidence on whether MBS is a better predictor of CVD and DM risk than its individual components, is equivocal [10, 21].

The stance on the MBS concept taken here is the following. The aetiology does not have to be known for the existence of a condition to be accepted [17], as is the case with, for example, type 2 DM. Current knowledge is however limited, such that MBS is not considered a clinical entity, but rather as defining a state of heightened risk for DM and CVD. The syndromic approach taken is epidemiological rather than clinical. In the sense that MBS is deemed to provide a conceptual framework for the clustering of metabolic risk factors. An important step in furthering epidemiologic understanding of the syndrome is then an assessment of the pathophysiological constellation of what are deemed to be phenotypic expressions of MBS. A constellation we believe to be driven, not by insulin resistance [3, 4], but by multiple interrelated metabolic impairments [22].

Factor analysis (FA) has become an oft-used tool for evaluations of phenotypic domains underlying MBS [23]. FA is a multivariate technique that may reveal a pattern of reduced dimensionality among a larger set of intercorrelated variables [24]. FA, however, is often poorly understood while being routinely executed [25], leading to diffuse findings and possibly confusing efforts in understanding MBS. This paper aims to review factor analytic efforts in the study of MBS, with emphasis on misusage of FA. An alternative factor analytic strategy is proposed that confronts weaknesses in the application of FA. A high-profile MBS data set with anthropometric measurements on overweight and obese children and adolescents is reanalyzed using the alternative strategy. The findings may give renewed cachet to both FA and its connection to MBS research.

2. Assessing Factor Analytic Efforts in MBS Research

2.1. The Factor Analytic Model. FA has come to be heavily utilized in the MBS research community since its seminal usage by Edwards, et al. [26]. An important question thrusting the FA efforts in MBS research is if a unifying physiology dominated by insulin resistance underlies the clustering of metabolic risk variables, or if there are multiple underlying physiologic phenotypes.
The common factor analytic model assumes that a random $p$-dimensional vector of observed variables can be grouped by their covariances or correlations into a lower-dimensional linear combination of latent variables:

$$
(z_i = \mu + \Lambda \xi_i + \epsilon_i)
$$

In (1) $z_i$ denotes the (possibly standardized) observed variable of dimension $p$ for person $i$, $\mu$ denotes the intercept, $\epsilon_i$ denotes the error measurements for person $i$, and $\Lambda$ is a $(p \times m)$-dimensional matrix of factor loadings in which each element $\lambda_{jk}$ is the loading of the $j$th variable on the $k$th factor, $j = 1, \ldots, p$, $k = 1, \ldots, m$. Then $\xi_i$ represents a latent variable of dimension $m$, with $m < p$, whose elements are referred to as common factors. In effect, FA represents a method of identifying or specifying latent factors that account for the (co)variances among observed variables by partitioning observed variance into common variance (attributable to the underlying latent common factors) and unique variance (among which are error components) [24]. In the standard model the random variables $z_i$, $\xi_i$, and $\epsilon_i$ are assumed to have Gaussian distributions, although the development of robust estimation procedures (e.g., [27, 28]) have somewhat softened the necessity of this assumption. (See Appendix ‘Basics of Factor Analysis’ for a more detailed overview of the FA model). The model can have both explorative and confirmative thrusts. Before assessing these thrusts some general remarks on FA are made.

A first general comment on the utilization of FA by the MBS research community is that basic model assumptions are seldom assessed. The model boasts several implicit assumptions such as a nonsingular sample covariance matrix and a reasonable proportion of variance among the observed variables being common variance. The appropriateness of these assumptions is easily [29] but rarely assessed. Moreover, the explicit distributional assumptions imply usage of observed variables of continuous metric and disqualifies the common FA model for binary and categorical observed data. Many MBS studies, however, employ standard FA on variables of non-continuous metric. In such situations extensions of the standard FA model are needed [30,31].

A second general comment concerns interpretational overextension. The FA model cannot determine existence of MBS nor assess clinical importance of MBS as a concept [25]. What FA can do is, through the latent factors (when adhering to a realist ontology [32]), give indications of pathophysiological domains that underlie phenotypic expressions of MBS.

### 2.2. Comments on Exploratory Efforts.

In exploratory FA (EFA) both $m$ and the meaning of latent factors are unknown. In the exploratory sense, FA is a theory-generating technique used for the identification of meaningful latent factors. Most MBS studies utilize FA in the exploratory sense [33-43]. Many deployments of EFA are however suboptimal.

EFA is often confused with principal components analysis (PCA). PCA is a data-reductional technique, seeking to identify components. It resembles the model in (1) without inclusion of error measurements, leading the components to differ conceptually and mathematically from latent factors in EFA [44]. Components are weighted linear combinations of observed variables seeking to efficiently explain observed variance in the data [45], leaving the explanation of observed covariance
secondary [44]. Many MBS studies employing FA, however, seek to obtain an explanation of the observables’ covariation through a small number of explanatory factors. Also, a phenotype is just an expression of genotype or pathophysiology, indicating the necessity of including measurement error. As such, employing common EFA would be more appropriate.

An important decision in EFA is determining the number of factors to retain. Many methods are heuristic, relying on subjective judgments or arbitrary cut-off values. The Guttman-Kaiser rule [46, 47] is the most popular rule of thumb. It states that one should retain at most those factors associated with eigenvalues whose magnitude exceeds the average eigenvalue (the average eigenvalue being 1 when using standardized data). This criterion, as well as many other heuristic factor retention criteria, are prone to under- (retaining too few factors) and overfactoring (retaining too many factors) [48, 49].

Given the above it is disconcerting that factor analytic efforts in MBS research are usually based on what has been termed ‘Little jiffy’ [29]: Employment of PCA, retainment of components based on the Guttman-Kaiser rule followed by a Varimax rotation [50], and the subsequent interpretation of rotated components as if they were common factors. Such mechanical use of EFA stunts learning and interpretation [51], and is (in part) responsible for the widely differing results obtained with EFA in MBS research. See the online supplement to this paper for an overview of the disparate results obtained with EFA as well as confirmatory FA (next subsection).

2.3. Comments on Confirmatory Efforts. Confirmatory FA (CFA) is a theory-testing technique. An a priori factor structure is assumed, with given \( m \), with a pre-specified loadings matrix in which exclusion constraints indicate which variables are indicators of which latent factor(s), and with possibly correlated factors and error variances. The model or models stated then remain to be tested. CFA studies are gaining interest in MBS research [52–58]. Standard CFA however, can also be misapplied.

The evaluation of model fit in CFA is essentially the evaluation of a diffuse hypothesis as it is unclear in case of misspecification if the pattern of loadings or the factor dimensionality is to blame [59]. Moreover, specifying a pattern of factor loadings through exclusion restrictions implies a loss of information in the sense that more exclusion restrictions are applied than is usually necessary for identification of the FA model. Additionally, exclusion restrictions may amount to errors of omission, may make the unrealistic assumption that items are factorially pure (in the population), and may induce bias in estimates of the free parameters [60, 61]. These issues are intricately connected to the well-known and widespread situation of exploratively obtained factor structures not being confirmed by CFA [60].

Some recent CFA studies in MBS research claim to provide evidence that a single latent factor underlies MBS [53, 55, 58]. These studies include four observed variables, some of which are functions of several variables usually employed as separate phenotypic items. This practice (called parceling) is justified by the claim that utilization of multiple measures for what is believed to be a trait will lead to a model with multiple factors, thus clouding efforts to establish a single latent factor underlying MBS. However, the inclusion of multiple sets of correlated measures does not irrevocably lead to a model with more than one latent factor,
unless some measures would identify a doublet factor (see Section ‘Step 1: Dimensionality Selection’ below). Also, the mentioned CFA efforts may actually provide evidence for a hierarchical latent factor [52] rather than a single pathophysiological domain underlying MBS, as the usage of functions of variables implies a (partial) pre-compression of the data. Parceling changes the nature of the data, may mask model misspecification and thus may inflate goodness-of-fit (indices) [62] (cf. [63]). Indeed, “it is possible to argue (inappropriately) that a single factor solution provides a good fit to the data under apparently benign parceling strategies” [62]. Moreover, while a two-factor model can be modeled on four variables, such a model would not be meaningful given that the observables were constructed to represent a single factor; implying that the one-factor model is the only model to be meaningfully fitted on the four observed variables. The possibility to assess if there are multiple (related) pathophysiological domains underlying phenotypic expressions of MBS is then denied. A meaningful scientific method, however, allows for multiple competing theories to be tested [64], as single hypotheses suffer from confirmation bias.

3. AN ALTERNATIVE FACTOR ANALYTIC STRATEGY

An alternative confirmatory factor analytic strategy is proposed that aims to confront the weaknesses in the application of FA. In a sense the strategy seeks to bridge the EFA – CFA divide so as to increase the inferential power of a factor analysis. This strategy is embedded within the Bayesian model selection approach, whose analytical advantages have been well documented [65]. The main Bayesian model selection criterion is the Bayes factor. This quantity incorporates model fit as well as model complexity and expresses “the evidence provided by the data in favor of one scientific theory, represented by a statistical model, as opposed to another” [66]. It can be used to compare any two models. Using Bayes factors, one can compute posterior model probabilities, which, assuming a uniform prior on the model space, are normalized Bayes factors. These quantities express model (un)certainty, in the sense that posterior model probabilities can be interpreted as the relative amounts of support in the data for the models under consideration. See Appendix ‘A Primer on Bayesian Statistics’ for more information on the Bayes factor and posterior model probabilities.

The strategy proposed consists of the following steps:

**Step 1:** Determine formally the (intrinsic) number of common factors based on a weighing of model fit and model complexity. For example along the lines specified in Peeters [67], who uses a Bayesian EFA model for selecting the optimal dimension $m$;

**Step 2:** Whence settled on latent factor dimensionality $m$, specify an unrestricted confirmatory factor model (UCFM). An UCFM is a FA model that corresponds to EFA in the sense that only minimal restrictions are placed on the factor loadings matrix and the factor covariance matrix for achieving global rotational uniqueness of the factor solution. However, the restrictions are to be chosen such that they convey preconceived theoretical meaning and thus render unnecessary post-hoc rotation of the solution for interpretation purposes. Peeters [68] gives minimal conditions for specifying a UCFM;
Step 3: Formulate, using the UCFM obtained in Step 2 as a base model, competing inequality constrained factor structures making use of inequality constraints on and between the free parameters in the loadings matrix. Substantive theory is then not represented by exclusion restrictions to express a pre-specified factor loading pattern, but by the imposition of inequality constraints; 

Step 4: Compute the posterior model probability for each constrained model under consideration and determine the constrained model most supported by the data.

The strategy explicitly encourages the formulation of competing inequality constrained theories for (statistical) scrutiny. When used in full, the thrust of the sequence is confirmatory, with the explicit separation of dimensionality and pattern selection in order to avoid embarking on diffuse hypotheses.

4. Reanalysis of Data by Weiss et al. [69]

4.1. Data. The data have been described elsewhere [69]. It considers a multietnic, multiracial cohort of 464 nondiabetic obese and overweight children and adolescents. The data contain measurements on the body mass index (BMI), blood glucose level at (fasting) baseline (GB) and two hours after (G2) oral glucose intake (both in mg/dl), fasting levels of triglycerides (trig.; mg/dl) and high-density lipoprotein (HDL) cholesterol (mg/dl), systolic and diastolic blood pressure (SBP, DBP; both in mm Hg), and insulin resistance (IR). IR was measured through homeostatic model assessment (HOMA). For more information on the data, see Weiss et al. [69].

Consideration of pediatric samples is important as current prevalence of MBS among youngsters may give indications of the future burden of DM and CVD. The measurements are in line with the American Academy of Clinical Endocrinologists (AACE) position on MBS [70], which emphasizes the epidemiologic pathophysiological perspective. The inclusion of IR makes it possible to test theories regarding the importance of IR in the MBS construct.

The little jiffy approach was the original factor analytic strategy for analyzing the data [69]. Here, the alternative strategy will be utilized for reanalysis. As in Weiss et al. [69], the natural logarithm was taken of the glucose, insulin resistance and triglycerides measurements to abide the normality assumption. The data were standardized such that a case of modeling the correlation matrix is considered. The sample correlation matrix is nonsingular and the Kaiser-Meyer-Olkin test [29] indicates that a reasonable proportion of variance among the variables might be common variance.

4.2. Step 1: Dimensionality Selection. Posterior model probabilities are computed for each model allowed by the condition \((p-m)^2 - p - m \geq 0\). This inequality simply states that the number of nonredundant elements in the sample covariance matrix must be greater than or equal to the number of freely estimable parameters in the model, which places an upper bound on \(m\). The data have eight measured variables \(p = 8\), giving that the maximum number of factors that can be extracted equals \(m = 4\). The computation strategy couples the candidate estimator method for computing Bayes factors [71] with the use of training samples [72]. This practice allows one to obtain determinate Bayes factors and subsequent posterior model probabilities using standard diffuse conjugate or noninformative priors [73].
computation strategy is embedded within a search strategy too weed out models suffering from rank deficiency in $\Lambda$ as this is a direct indicator for overfactoring (see [6] in Appendix ‘Basics of Factor Analysis’). This search excludes the $m = 4$ model. The following posterior model probabilities are obtained when assuming that each model is equally likely a priori: $P(m = 1|Z) = 0$; $P(m = 2|Z) = 1$; and $P(m = 3|Z) = 0$. The data thus support the two-factor model.

These results differ from Weiss et al. [69] and several other factor analytic efforts in which a three-factor (or higher) solution was found. A first reason for the retention of more latent factors in these studies is the tendency of heuristic factor-selection rules to overfactor [48,49]. More formal selection procedures, such as the likelihood ratio test in maximum likelihood EFA and the assessment of information criteria, do not escape this tendency [74,75].

Another reason for the higher factor solution in other studies might be the existence of doublet factors. Doublet factors are factors that arise as the result of common variance due to correlation between just two variables [24]. Doublet factors are considered to be conceptually weak factors and the assignment of an independent latent construct to a doublet factor is contentious. SBP and DBP are variables that, within the battery of measurements on phenotypic expressions of MBS, usually correlate only with each other resulting in a doublet factor to be extracted (usually termed ‘hypertension’). The strategy employed here sees past the doublet factor and indicates the more parsimonious model with two factors as optimal.

4.3. **Step 2: Base Model Formulation.** A UCFM for $m = 2$ will be formulated for confirmatory efforts. Abiding conditions given by Peeters [68], the following minimal restrictions on $\Lambda$ are chosen for global rotational uniqueness:

$$
\Lambda_0 = \begin{bmatrix}
\lambda_{11} & \lambda_{12} \\
\lambda_{21} & \lambda_{22} \\
\lambda_{31} = 0 & \lambda_{32} > 0 \\
\lambda_{41} & \lambda_{42} \\
\lambda_{51} > 0 & \lambda_{52} = 0 \\
\lambda_{61} & \lambda_{62} \\
\lambda_{71} & \lambda_{72} \\
\lambda_{81} & \lambda_{82}
\end{bmatrix}
\begin{bmatrix}
\text{BMI} \\
\log_e\{\text{trig.}\} \\
\text{HDL chol.} \\
\log_e\{\text{IR}\} \\
\log_e\{\text{GB}\} \\
\text{log}_e\{\text{G2}\} \\
\text{SBP} \\
\text{DBP}
\end{bmatrix}
$$

The exclusion restrictions $\{\lambda_{31}, \lambda_{52}\} = 0$ identify the model up to polarity reversals in the columns. The polarity truncations $\{\lambda_{32}, \lambda_{51}\} > 0$ then ensure global rotational uniqueness of the model. These constraints are chosen for the following reasons. First, from prior knowledge and previous analyzes a two-factor solution is deemed to consist of a glucose and a lipid factor. HDL chol. is then believed to have a large loading on a lipid (second) factor while having a small loading on the first factor, and $\log_e\{\text{GB}\}$ is believed to have a large loading on a glucose (first) factor while having a small loading on the second factor. These variables then serve as an indicator of the respective factors. It is thus reasonable to specify $\{\lambda_{31}, \lambda_{52}\} = 0$ and $\{\lambda_{32}, \lambda_{51}\} > 0$. Second, the chosen minimal restrictions comply with all competing inequality constrained formulations of factor structure to be assessed.

4.4. **Step 3: Formulating Competing Constrained Factor Structures.** Factor structure for confirmatory efforts is not represented using exclusion restrictions
but by imposing inequality constraints on and between the parameters left free in the UCFM. The following inequality constrained competing factor structures are formulated:

\[
\Lambda_1 = \begin{bmatrix}
\lambda_{11} & > & |\lambda_{12}| \\
|\lambda_{21}| & < & -\lambda_{22} \\
\lambda_{31} & = & 0 \\
\lambda_{41} & > & |\lambda_{42}| \\
\lambda_{51} & > & 0 \\
\lambda_{61} & > & |\lambda_{62}| \\
\lambda_{71} & > & |\lambda_{72}| \\
|\lambda_{81}| & < & -\lambda_{82}
\end{bmatrix}
\begin{array}{l}
\text{BMI} \\
\log_{e}\{\text{trig.}\} \\
\log_{e}\{\text{IR}\} \\
\log_{e}\{\text{GB}\} \\
\log_{e}\{G2\} \\
\text{SBP} \\
\text{DBP}
\end{array}
\]

\[
\Lambda_2 = \begin{bmatrix}
|\lambda_{11}| & < & -\lambda_{12} \\
|\lambda_{21}| & < & -\lambda_{22} \\
\lambda_{31} & = & 0 \\
\lambda_{41} & > & .4 \\
\lambda_{51} & > & 0 \\
\lambda_{61} & > & |\lambda_{62}| \\
\lambda_{71} & > & -\lambda_{72} \\
\lambda_{81} & < & -\lambda_{82}
\end{bmatrix}
\begin{array}{l}
\text{BMI} \\
\log_{e}\{\text{trig.}\} \\
\log_{e}\{\text{IR}\} \\
\log_{e}\{\text{GB}\} \\
\log_{e}\{G2\} \\
\text{SBP} \\
\text{DBP}
\end{array}
\]

\[
\Lambda_3 = \begin{bmatrix}
\lambda_{11} & > & |\lambda_{12}| \\
|\lambda_{21}| & < & -\lambda_{22} \\
\lambda_{31} & = & 0 \\
\lambda_{41} & > & |\lambda_{42}| \\
\lambda_{51} & > & 0 \\
\lambda_{61} & > & |\lambda_{62}| \\
|\lambda_{71}| & < & .3 \\
|\lambda_{81}| & < & .3
\end{bmatrix}
\begin{array}{l}
\text{BMI} \\
\log_{e}\{\text{trig.}\} \\
\log_{e}\{\text{IR}\} \\
\log_{e}\{\text{GB}\} \\
\log_{e}\{G2\} \\
\text{SBP} \\
\text{DBP}
\end{array}
\]

A formulation like \(\lambda_{71} < -\lambda_{72}\) states that the negative of \(\lambda_{72}\) is believed to be larger than \(\lambda_{71}\). Note that this is a much more informative formulation than the more usual strategy of setting \(\lambda_{71} = 0\) and letting \(\lambda_{72}\) be free to be estimated in order to express the belief that SBP is an indicator for the second latent factor rather than the first one. In the same respect, a formulation like

\[
\lambda_{61} > |\lambda_{62}| \Rightarrow \begin{cases} 
\lambda_{61} - \lambda_{62} > 0 \\
\lambda_{61} + \lambda_{62} > 0 
\end{cases}
\]

indicates the belief that \(\lambda_{61}\) is larger than \(\lambda_{62}\), irrespective of the latter’s sign. A statement like

\[
|\lambda_{82}| < .3 \Rightarrow -3 < \lambda_{82} < .3
\]

indicates the belief that \(\lambda_{82}\) takes a value in the interval \([-3, .3]\).

In all models insulin resistance, blood glucose level at baseline and two hours after glucose intake are mainly related to the glucose factor, while fasting levels of triglycerides and HDL cholesterol form the base of the lipid factor. Note that for the lipid factor polarity fixation is brought about by demanding \(\lambda_{32} > 0\). HDL cholesterol is generally regarded as ‘good’ cholesterol, meaning that the choice \(\lambda_{32} > 0\) amounts to modeling a factor denoting unimpaired lipid metabolism. Hence
formulations like $|\lambda_{21}| < -\lambda_{22}$, as under given polarity truncation the triglycerides item is believed to be strongly negatively related to a lipid factor.

Model 1 adds detail to the base model and the basic factors by stating that BMI and systolic blood pressure are linked to the glucose factor ($\lambda_{11} > |\lambda_{12}|$, $\lambda_{71} > |\lambda_{72}|$), while diastolic blood pressure is believed to be linked to the lipid factor ($|\lambda_{81}| < -\lambda_{82}$). Model 2 states the hypothesis that BMI is an indicator for the lipid rather than the glucose factor ($|\lambda_{11}| < -\lambda_{12}$). Also, in this model both systolic and diastolic blood pressure are related to the lipid rather than the glucose factor, with the additional belief that both blood pressure measures will load positively on the latter ($\lambda_{71} < -\lambda_{72}$, $\lambda_{81} < -\lambda_{82}$). Moreover, the second model states that insulin resistance may be the measure tying MBS together. In a multifactor model this would imply that the insulin resistance measure achieves a large or dominant loading on both the glucose and lipid factor ($\lambda_{41} > .4$, $\lambda_{42} < -.4$). Model 3 resembles the first model, but states that the association of systolic and diastolic blood pressure with the factors is rather loose.

4.5. **Step 4: Constrained-Model Selection and Interpretation.** Bayes factors for models under inequality constraints are easily computed [76]. Again, standard (diffuse) conjugate and noninformative priors are utilized. Assuming a uniform prior on the model space the following posterior model probabilities are obtained for the constrained two-factor models under consideration: $P(M_1|Z) = .0004$; $P(M_2|Z) = 0$; and $P(M_3|Z) = .9996$. Conditioned on the data, the third model receives almost all support.

The third constrained model connects trig. and HDL chol. to a lipid metabolism factor and IR, GB, and G2 to a glucose metabolism factor. Moreover, the model states that BMI is related to the glucose metabolism factor rather than the lipid metabolism factor. The finding that blood pressure is not an independent pathophysiological factor is consistent with epidemiologic evidence that insulin resistance and lipid metabolism play a role in the pathogenesis of hypertension rather than hypertension being a physiologic phenotype [22].

**Table 1. Posterior Means and 95% Credible Intervals for $\Lambda_0$**

| Parameter | Factor 1 | 95% CI  | Factor 2 | 95% CI  | Item           |
|-----------|----------|---------|----------|---------|----------------|
| $\lambda_{11}$ | .324     | [.207, .440] | $\lambda_{12}$ | -.068   | [-.191, .055]  | BMI             |
| $\lambda_{21}$ | -.006    | [-.303, .215] | $\lambda_{22}$ | -.653   | [-.956, -.379] | log$_e$ {trig.} |
| $\lambda_{31}$ | -        | -       | $\lambda_{32}$ | .706    | [.442, .940]  | HDL chol.       |
| $\lambda_{41}$ | .767     | [.613, .921] | $\lambda_{42}$ | -.179   | [-.343, -.022] | log$_e$ {IR}   |
| $\lambda_{51}$ | .470     | [.360, .585] | $\lambda_{52}$ | -       | -              | log$_e$ {GB}   |
| $\lambda_{61}$ | .355     | [.205, .492] | $\lambda_{62}$ | -.124   | [-.289, .036]  | log$_e$ {G2}   |
| $\lambda_{71}$ | .274     | [.136, .416] | $\lambda_{72}$ | .029    | [-.118, .171]  | SBP             |
| $\lambda_{81}$ | .202     | [.069, .347] | $\lambda_{82}$ | .139    | [-.017, .292]  | DBP             |

The estimates of the UCFM given in Table 1 also lend support to model 3. (Confer Appendix ‘Results Factor Analytic Approach Weiss et al. [69]’ to see, in contrast, the parameter estimates obtained with the little jiffy approach of the original study [69]). The table contains posterior means and credible intervals. A
credible interval is a posterior probability interval. For example, the posterior probability that $\lambda_{11}$ lies in the interval $[0.207, 0.440]$ is .95. (See Appendix ‘Reproduced Correlation Structure’ for an indication of the success of the two-factor UCFM in retrieving the sample correlation matrix).

The estimates indicate that the hypertension variables seem to be relatively weak in their association with the respective factors. The credibility intervals indicate that these variables are mostly related to the glucose metabolism factor, which would be in line with the hypothesis that hypertension is related to insulin resistance and impaired glucose metabolism [3, 4]. Regarding the contention that insulin resistance is the basis for MBS: IR is related to both the glucose and lipid factors. However, the posterior mean of the loading tying IR to the lipid metabolism factor is relatively small and the upper bound of its credibility interval approaches zero. The second inequality constrained model is thus rightly not supported by the data.

The two latent factors are appreciably correlated with a posterior mean of $\rho = -0.277$ and a 95% credible interval of $[-0.417, -0.137]$. Note that, as stated in Section ‘Step 3: Formulating Competing Constrained Factor Structures’, the second factor models unimpaired lipid metabolism. Thus, the selected model indicates that, given the data and measurements, impaired glucose metabolism and impaired lipid metabolism are positively related pathophysiological domains. Moreover, the two factors connect to two main hypotheses regarding syndrome aetiology, stating that the risk-factor associations are due to abnormality of the insulin/glucose metabolism and/or abnormality of the lipid metabolism [22].

5. Discussion

Applications of FA in MBS research were evaluated. Lacunae in both EFA and CFA were discussed. It is argued that the mechanical use of EFA and misunderstandings of CFA are, at least in part, responsible for the widely differing results obtained with FA on data with phenotypic expressions of MBS.

An alternative factor analytic strategy is proposed. The strategy consists of four steps and aims to confront the weaknesses in application of the FA model, by: (i) Formally assessing optimal choice of factor dimensionality; (ii) Canceling the need for post-hoc rotation of the factor solution; (iii) Allowing to express a confirmatory factor structure through informative inequality constraints rather than through rigid exclusion restrictions; (iv) Encouraging the formulation of competing inequality constrained theory-based expressions of factor structure, in order to avoid confirmation bias.

The alternative strategy was utilized in reanalyzing a high-profile data set on which factor analyzes were previously employed. The data consider eight variables as phenotypic expressions of MBS in a cohort of nondiabetic overweight and obese children and adolescents [69]. The reanalysis based on the alternative strategy implied a more parsimonious constellation of pathophysiological domains underlying phenotypic expressions of MBS than the original analysis (and many other analyzes). The selected two-factor solution stresses correlated factors of impaired glucose metabolism and impaired lipid metabolism. This solution does not assign hypertension a separate factor which is consistent with epidemiologic evidence that insulin resistance and lipid metabolism play a role in the pathogenesis of hypertension rather than hypertension being a physiologic phenotype [22]. Moreover, there
is no strong evidence of insulin resistance being dominant in both the glucose and lipid domains.

Several limitations of this study should be considered. First, the data consider a multiethnic cohort while MBS may express itself differently across ethnic groups and gender. Note, however, that the specification of a factor model through inequality constraints would also be helpful in assessing measurement (factorial) invariance across groups. Second, MBS may develop with age and with the advent of DM and CVD, implying that the data might represent a snap-shot of phenotypic expressions related to MBS. Third, the proposed factor analytic strategy is more involved than routine uses of EFA and regular CFA in the sense that it requires more computation time and puts higher cognitive demands on the researcher. Nevertheless, these drawbacks are felt to be outweighed by the advantages of the strategy and the proposed steps are deemed to form a viable analytic alternative for other studies seeking to use FA.

The findings suggest that there are two correlated pathophysiological domains underlying the phenotypic expressions of MBS included in the analysis. These domains are characterized by impaired glucose metabolism and impaired lipid metabolism, respectively. These findings indirectly point to the possibility that several different pathogenic processes need to coincide in order to be able to identify a MBS construct. It might be timely to postulate the possible existence of a multifactorial aetiology.

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Appendix: Basics of Factor Analysis

The unrestricted factor model is considered. Let $Z^T ≡ [z_1, \ldots, z_n]$ define (standardized) $p$-variate observation vectors on $i = 1, \ldots, n$ subjects, such that $z_i^T \equiv [z_{i1}, \ldots, z_{ip}] \in \mathbb{R}^p$ denotes a realization of the random vector $Z_i^T ≡ [Z_{i1}, \ldots, Z_{ip}] \in \mathbb{R}^p$. Also, let $\Xi^T ≡ [\xi_1, \ldots, \xi_n]$ define $m$-variate vectors of latent factor scores on $n$ subjects with $\xi_i^T ≡ [\xi_{i1}, \ldots, \xi_{im}] \in \mathbb{R}^m$.

The model $\{\}$ maintains the following assumptions: (i) $z_i \perp \perp z_{i'}$, $\forall i \neq i'$; (ii) $\text{rank}(\Lambda) = m$; (iii) $\epsilon_i \sim \mathcal{N}(0, \Psi)$, with $\Psi \equiv \text{diag}(\psi_{11}, \ldots, \psi_{pp})$, and $\psi_{jj} > 0$; (iv) $\xi_i \sim \mathcal{N}_m(0, \Phi)$; and (v) $\xi_i \perp \perp \epsilon_{i'}, \forall i, i'$. The likelihood for the observations conditional on the realization of $\Xi$ can then be expressed as:

$$L(\mu, \Lambda, \Xi, \Psi, \Phi; Z) = \prod_{i=1}^{n} f(z_i | \mu, \Lambda, \xi_i, \Psi, \Phi)$$

$$= \prod_{i=1}^{n} \left(2\pi\right)^{-\frac{p}{2}} |\Psi|^{-\frac{1}{2}} \exp\left\{-\frac{1}{2} \epsilon_i^T \Psi^{-1} \epsilon_i\right\},$$

(2)
where $\epsilon_i = \mathbf{z}_i - \mu - \Lambda \xi_i$. Marginalizing over $\xi_i$ the likelihood of the observed data can be obtained:

$$L(\mu, \Lambda, \Psi, \Phi; \mathbf{Z}) = \prod_{i=1}^{n} \int f(z_i | \mu, \Lambda, \xi_i, \Psi, \Phi) g(\xi_i | \Phi) \, d\xi_i$$

$$= \prod_{i=1}^{n} (2\pi)^{-\frac{p}{2}} |\Lambda \Phi \Lambda^T + \Psi|^{-\frac{1}{2}}$$

$$\times \exp \left\{ -\frac{1}{2}(z_i - \mu)^T (\Lambda \Phi \Lambda^T + \Psi)^{-1} (z_i - \mu) \right\},$$

(3)

giving that the factor decomposition constrains the covariance structure of the $\mathbf{z}_i$ to

$$\Sigma = \Lambda \Phi \Lambda^T + \Psi.$$  

(4)

Then, for existence (vi), generally $(p - m)^2 - p - m \geq 0$, simply stating that the number of nonredundant elements in the sample correlation matrix $S$ must be greater than or equal to the number of freely estimable parameters in $\Sigma$, which places an upper bound on $m$.

Now, $\Phi \in \mathbb{R}^{m \times m}$ denotes the factor covariance matrix, giving that $\Phi$ represents an oblique model in which the latents may share covariation. Note that, for positive definite $\Phi$, we may always find $\mathbf{V} \in \mathbb{R}^{m \times m}$ such that $\Phi = \mathbf{V} \mathbf{V}^T$, and

$$\Sigma = \Lambda \Phi \Lambda^T + \Psi = (\Lambda \mathbf{V}) (\mathbf{V}^{-1} \Phi (\mathbf{V}^{-1})^T) (\Lambda \mathbf{V})^T + \Psi = (\Lambda \mathbf{V}) (\Lambda \mathbf{V})^T + \Psi.$$  

(5)

Equation (5) implies that any oblique representation has equivalent orthogonal representations. The orthogonal representation makes the following statements on identification less involved.

It is well known that for given $\Lambda$ and $\Psi$, theformer is defined uniquely only up to rotation. Correspondingly the FA literature has focussed mainly on identification of $\Psi$. The main result of which is that if assumption (vi) holds, $\Psi$ is almost surely identified $[77]$. This result is however contingent upon the rank of $\Lambda$. The implications of a failure to abide model assumption (ii) were explored by Anderson and Rubin $[78]$ and Geweke and Singleton $[79]$. Suppose that $\operatorname{rank}(\Lambda) = r < m$. Then there exists a matrix $\mathbf{Q} \in \mathbb{R}^{m \times (m-r)}$ for which $(\Lambda \mathbf{V}) \mathbf{Q} = \mathbf{0}$ and $\mathbf{Q}^T \mathbf{Q} = \mathbf{I}_{m-r}$, such that for any $\mathbf{M} \in \mathbb{R}^{p \times (m-r)}$ with mutually orthogonal rows

$$\Sigma = (\Lambda \mathbf{V}) (\Lambda \mathbf{V})^T + \Psi = (\Lambda \mathbf{V} + \mathbf{M} \mathbf{Q}^T) (\Lambda \mathbf{V} + \mathbf{M} \mathbf{Q}^T)^T + (\Psi - \mathbf{M} \mathbf{M}^T).$$  

(6)

Equation (6) implies that no consistent estimator of $\Psi$ exists if $\Lambda$ fails to be of full column rank. This may induce corresponding multimodalities in the densities of $\Psi$ and $\Lambda$ $[74]$, and is related to the choice of factor dimensionality and the possibility of retaining too many factors.

The FA model also copes with an inherent indeterminacy of the parameters, being: Rotational indeterminacy of the factor solution. Assume that $\mathbf{R} \in \mathbb{R}^{m \times m}$ is an arbitrary nonsingular matrix. Returning to the implied covariance structure of the observed data, we then have

$$\Sigma = \Lambda \Phi \Lambda^T + \Psi = (\mathbf{A} \mathbf{R}) (\mathbf{R}^{-1} \Phi (\mathbf{R}^{-1})^T) (\mathbf{A} \mathbf{R})^T + \Psi,$$

(7)

implying that there is an infinite number of alternative matrices $\Lambda^\dagger = \mathbf{A} \mathbf{R}$ and $\Phi^\dagger = \mathbf{R}^{-1} \Phi (\mathbf{R}^{-1})^T$ that generate the same covariance structure $\Sigma$. The operation $\Lambda \mapsto \mathbf{A} \mathbf{R}$ is termed ‘rotation’. Thus, in any solution, $\Lambda$ can be made to satisfy $m^2$
additional conditions, which is naturally equivalent to the number of independent elements of $R$.

From the above it is clear that any method of estimation requires at a minimum $m^2$ restrictions on $\Lambda$ and $\Phi$. The EFA tradition usually achieves this by requiring that $\Phi = I_m$ and $\Lambda^T \Psi^{-1} \Lambda$ be diagonal accompanied by an order condition on the diagonal elements. These restrictions are arbitrary such that whence estimation is settled EFA traditionally endeavors on applying a rotation that satisfies certain criteria for interpretation purposes. Peeters [68] has given minimal conditions for the formulation of a rotationally unique confirmatory unrestricted factor model that cancels the need for post-hoc rotation.

APPENDIX: A PRIMER ON BAYESIAN STATISTICS

The Bayesian viewpoint is distinct from the classical approach to statistics. Let $\Theta$ denote a model-specific collection of unknown parameters of continuous metric. The frequentist approach solely utilizes the likelihood of the observed data $L(\Theta; X)$, in that a retrospective evaluation is made of a certain statistic used to estimate $\Theta$ over all possible $X$ values conditional on the true unknown $\Theta$ which is deemed fixed. The Bayesian approach views $\Theta$ as random. This allows for probability statements about $\pi(\Theta|X)$, the distribution of model parameters conditioned on the observed data. To provide the mentioned conditional probabilities, a joint probability function for $\Theta$ and $X$ must be provided for. To this purpose a prior distribution $\pi(\Theta)$ must be specified, which reflects the formalized knowledge or uncertainty about the parameters before observation of the data. Using a basic property of conditional probability known as Bayes’ rule [80, 81], one obtains the posterior distribution as:

$$
\pi(\Theta|X) = \frac{L(\Theta; X)\pi(\Theta)}{\int L(\Theta; X)\pi(\Theta) \partial \Theta}.
$$

Expression (8) encapsulates the core machinery of Bayesian statistics, whose flexibility has proven to extend to complex problems (consult, for example [82, 83]). The denominator in (8) is called the prior predictive density or marginal likelihood and is key in Bayesian model selection.

Let us shortly review Bayesian model selection for latent variable models. Let $\vartheta$ denote latent data. For the factor model described in Section ‘The Factor Analytic Model’, $\Theta = \{\mu, \Lambda, \Psi, \Phi\}$ and $\vartheta = \Xi$. Now, let $g(\vartheta|\Theta)$ denote the density of latent data $\vartheta$ given $\Theta$ and assume that the complete data likelihood consists of $L(\Theta, \vartheta; X)g(\vartheta|\Theta)$. Suppose also that the prior $\pi(\Theta)$ is available for the unknown model parameters $\Theta$. The marginal likelihood is then expressed as:

$$
m(X) = \int L(\Theta, \vartheta; X)\pi(\Theta)g(\vartheta|\Theta) \partial(\Theta, \vartheta).
$$

The marginal likelihood expresses the likelihood of the data conditional on the model entertained. This quantity is of import in the construction of the Bayes factor, the main Bayesian model selection criterion. Suppose that $S$ competing models $M_s$ are under consideration, for $s = 1, \ldots, S$. The Bayes factor of $M_s$ to
\( M_s \) is then expressed as \([84,85]\):

\[
(10) \quad B_{ss'} = \frac{m_s(X)}{m_{ss'}(X)} = \frac{\int L_s(\Theta_s, \vartheta_s; X) \pi_s(\Theta_s) g_s(\vartheta_s|\Theta_s) \, \partial(\Theta_s, \vartheta_s)}{\int L_{ss'}(\Theta_{ss'}, \vartheta_{ss'}; X) \pi_{ss'}(\Theta_{ss'}) g_{ss'}(\vartheta_{ss'}|\Theta_{ss'}) \, \partial(\Theta_{ss'}, \vartheta_{ss'})}.
\]

The Bayes factor embodies the ratio of posterior odds to prior odds for the models under consideration. The expression in (10) resembles a likelihood ratio. But instead of evaluating the respective likelihoods at the maximum likelihood estimates, the parameters are integrated out with respect to the priors. The BF thus can be viewed as representing a ‘weighted’ likelihood ratio that provides a measure “of the evidence provided by the data in favor of one scientific theory, represented by a statistical model, as opposed to another” \([66]\). The Bayes factor behaves like a natural Occam’s razor, as model fit and complexity are accounted for in the marginal likelihood \([86,87]\). For interpretation the quantity (10) can be referred to half-units on the \( \log_{10} \) scale (Appendix B of \([85]\)) or one can consider \( 2 \log_e B_{ss'} \) \([66]\), which is on the same scale as likelihood ratio statistics. Another interpretational aid might be the posterior model probability, defined as \([72]\):

\[
(11) \quad P(M_{ss'}|X) = \left( \sum_{s=1}^{S} p_s \cdot B_{ss'} \right)^{-1}.
\]

In (11) \( p_s \) denotes the prior probability one assigns to model \( M_s \) being best, \( \sum_{s=1}^{S} p_s = 1 \). The posterior model probability \( P(M_{ss'}|X) \) gives the posterior probability, given the batch of models under consideration, that model \( M_{ss'} \) is the correct model for the data at hand. A normalization of the Bayes factor ensues when letting \( p_s = S^{-1} \) \( \forall s \).

The Bayes factor as a model selection criterion has several advantages (cf., \([66,73]\): (i) It provides both a measure of evidence against a competing model and a measure of support for the alternative model; (ii) It will not by default favor the alternative model in (very) large samples; (iii) It allows one to take model uncertainty into account, thus providing a consistent quantity for the comparison of a multitude of competing models; (iv) It can handle the comparison of both nested and nonnested models. For an introduction to Bayesian statistics see \([82,83]\). For Bayesian factor analysis see \([73,88]\). For inequality-constrained-model selection for Bayesian FA as well as Bayesian treatments of both EFA and CFA, see \([67]\).

**Appendix: Results Factor Analytic Approach Weiss et al. \([69]\)**

Table 2 contains the results of the little jiffy approach to the data as given in the original study (Table 3 in \([69]\)). A three-component solution was obtained in which the first component was interpreted as ‘obesity and glucose metabolism’, the second as ‘dyslipidemia’, and the third as ‘blood pressure’.

**Appendix: Reproduced Correlation Structure**

Table 3 contains the sample correlations, the correlations reproduced by the factor analysis, and the residual correlations (sample correlation minus reproduced correlation).
Table 2. Results little jiffy analysis on the data

| Components | 1  | 2  | 3   | Item          |
|------------|----|----|-----|---------------|
|            | .44| .13| .06 | BMI           |
|            | .09| .83| .04 | logₑ {trig.}  |
|            | -.13|-.82|.06 | HDL chol.     |
|            | .76|.27|.15 | logₑ {IR}     |
|            | .72|-.14|.07 | logₑ {GB}     |
|            | .67|.10|-.06| logₑ {G2}     |
|            | .15|.09|.79 | SBP           |
|            | .01|.09|.83 | DBP           |

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Table 3. Matrix containing observed (Pearson), reproduced, and residual correlations

|       | 1   | 2   | 3   | 4   | 5   | 6   | 7   | 8   |
|-------|-----|-----|-----|-----|-----|-----|-----|-----|
| BMI   |     |     |     |     |     |     |     |     |
| observed | 1.000 |     |     |     |     |     |     |     |
| reproduced | 1.002 |     |     |     |     |     |     |     |
| residual | -.002 |     |     |     |     |     |     |     |
| log₂{trig.} |     |     |     |     |     |     |     |     |
| observed | .041 | 1.000 |     |     |     |     |     |     |
| reproduced | .101 | .984 |     |     |     |     |     |     |
| residual | -.060 | .016 |     |     |     |     |     |     |
| HDL chol. |     |     |     |     |     |     |     |     |
| observed | -.143 | -.423 | 1.000 |     |     |     |     |     |
| reproduced | -.111 | -.459 | .998 |     |     |     |     |     |
| residual | -.032 | .036 | .002 |     |     |     |     |     |
| log₂{IR} |     |     |     |     |     |     |     |     |
| observed | .314 | .259 | -.254 | 1.000 |     |     |     |     |
| reproduced | .291 | .250 | -.276 | 1.006 |     |     |     |     |
| residual | .023 | .009 | .022 | -.006 |     |     |     |     |
| log₂{GB} |     |     |     |     |     |     |     |     |
| observed | .071 | .051 | -.066 | .387 | 1.000 |     |     |     |
| reproduced | .161 | .082 | -.092 | .384 | 1.004 |     |     |     |
| residual | -.090 | -.031 | .026 | .003 | -.004 |     |     |     |
| log₂{G2} |     |     |     |     |     |     |     |     |
| observed | .121 | .197 | -.105 | .336 | .233 | 1.000 |     |     |
| reproduced | .141 | .143 | -.157 | .338 | .183 | .999 |     |     |
| residual | -.020 | .054 | .052 | -.002 | .050 | .001 |     |     |
| SBP   |     |     |     |     |     |     |     |     |
| observed | .132 | .065 | -.028 | .190 | .104 | .084 | 1.000 |     |
| reproduced | .089 | .029 | -.033 | .212 | .125 | .100 | .999 |     |
| residual | .043 | .036 | .005 | -.022 | -.021 | -.016 | .001 |     |
| DBP   |     |     |     |     |     |     |     |     |
| observed | -.013 | -.016 | .084 | .093 | .095 | -.010 | .332 | 1.000 |
| reproduced | .047 | -.056 | .059 | .111 | .077 | .048 | .047 | .999 |
| residual | -.060 | .004 | .025 | -.018 | .018 | -.058 | .275 | .001 |

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SUPPLEMENTARY MATERIAL

Tables S1 and S2 below list overviews of published studies on the MBS employing factor analytic techniques. Table S1 lists studies among the child and adolescent cohort. Table S2 lists studies among subjects other than children and adolescents. Studies were found using the PubMed search engine by pairing the search term “factor analysis” with each in {“metabolic syndrome”, “insulin resistance syndrome”, and “syndrome X”} (the names that are regularly used to refer to the MBS). By usage of these terms English-language publications were sought with (online) publication dates from 1994 (year of publication of the seminal article by [26]) to January 2014. See [90, 91] and the online supplement to [53] for additional (complementary) overview tables. Please consider the remarks below for full understanding of Tables S1 and S2.

Eligibility criteria. Included studies focus their factor analytic efforts, as in the main text, on variables of a metabolic nature. Studies that focus mainly on hemostatic, inflammatory, lifestyle, or diet variables were excluded. Studies that provided no information on their factor analytic procedure (extraction, retention, and rotation) were also excluded. In addition, studies that considered binary or categorical variables in standard factor models were also not considered.

Data extraction. If a study that focuses on the mentioned variables for exclusion in addition ran a factor analytic procedure on the traditional metabolic variables, then only the results of the analysis on the metabolic variables are reported. When study and validation cohorts were available in a certain study, only the study cohort is reported when results comply. Also, when FA was performed on various (sub)sets of variables, we chose to report the FA on the combination of items most in concurrence with the data (re-)analyzed in this study.

When representing EFA efforts (including PCA) the description of the factors is based on the loading cut-offs chosen by the authors of the original studies. When representing CFA efforts in the tables below, we focus on the factor structure, not on other model details such as correlated error variables. When a higher-order factor model is utilized in a certain study only the first-order factors are described (the second-order factor is always termed ‘MBS’). It is however explicitly indicated when a higher-order model is fitted. In addition, we only report final models when describing CFA efforts. Details such as usage of modification indices can be found in the studies themselves.

The assessment of the stability of the factor analytic model is generally known as the issue of ‘measurement invariance’. This issue arises in longitudinal data (is the model stable over the measured time-points) or when the total sample is considered to consist of subgroups (is the model stable over all subgroups that make up the total sample). Invariance can be studied on the level of the model structure (number of factors and factor structure) or, given a certain model structure, on the level of the parameter values. A formal approach would be to perform multiple group analyses, possibly paired with a hierarchy of invariance tests (see e.g., [92]). This formal approach is strongly tied to CFA. An informal approach, usually performed in EFA-type analyses, would be to perform separate EFA’s (or PCA’s) on the data from the respective subgroups or time-points and to assess loosely if the model is...
stable. In the tables below we use ‘assessment of measurement invariance’ to refer to the more formal approach while we use ‘subgroup analyzes’ to refer to the more informal approach. In the tables below it is explicitly indicated if, within a certain study, factor analytic results differ over the various subgroups or time-points. If the model structure is considered invariant (in the original study) this will be designated with ‘structure considered invariant’. If model structure and parameter values are considered invariant (in the original study) this will be designated with ‘model considered invariant’.

Reading the tables. In the tables below ‘approach’ refers to the factor analytic approach taken and ‘factors’ refers to either common factors (in the case of a true factor analytic approach) or principal components (in case of a PCA approach). The sample size given is the size of the sample included in the factor analytic efforts. Characteristics refer to the characteristics of the sample included in the FA.

Note that in the description of factors the ordering is of import in the PCA approach and in an EFA approach with certain rotation criteria. The factors then can be understood as being in descending order of (percent of) variance explained (in the observed variables). In a CFA approach, the stated ordering of factors is arbitrary. The numbering in this latter case is solely to convey the number of factors modelled.

The reported studies are ordered according to year of publication. While the metabolic variables may at first seem to differ widely between the included studies, one may note that in many cases surrogate measures are used. For example, often the apolipoproteins B and A-I are used as surrogates for the LDL and HDL cholesterol fractions, respectively. Note also that the measures for insulin resistance can vary over studies, e.g., fasting and postload insulin, HOMA-IR, or the intravenous glucose tolerance test are some of the measures that are oft-used. In addition, the tables use ‘/’ to designate a ratio, e.g., trig./HDL chol. indicates the triglycerides over HDL cholesterol ratio.

The tables utilize, next to the abbreviations used in the main text, the following additional abbreviations:

: %BF = percent body fat; 17HP = 17-hydroxyprogesterone; Adi = adiponectin; Apo A-I = apolipoprotein A-I; Apo B = apolipoprotein B; AST = abdominal skinfold thickness; BW = body weight; CASPIAN = Childhood and Adolescence Surveillance and Prevention of Adult Non-Communicable Disease; FFFA = fasting free fatty acids; FG = fasting glucose; FI = fasting insulin; fib. = fibrinogen; FT = free testosterone; HbA1c = glycated hemoglobin; HC = hip circumference; HDL$_2$ = high density lipoprotein 2 cholesterol; HDL tot. = total high density lipoprotein cholesterol; IAF = (CT-measured) intra-abdominal fat area; IAI = Instituto Auxologico Italiano; IMGD = insulin-mediated glucose disposal; IS = insulin sensitivity; IVGTT = intravenous glucose tolerance test; LDL chol. = high density lipoprotein cholesterol; LDL-PPD = low-density lipoprotein peak particle diameter; LR = likelihood ratio; MAP = mean arterial pressure; ML = maximum likelihood; NFG = non fasting glucose; NHLBI = National Heart, Lung, and Blood Institute; NO$_x$ = nitric oxide metabolites; PAI-1 = plasminogen activator inhibitor-1; PAL = physical activity level
(minutes/week); PCDD/Fs = polychlorinated dibenzo-p-dioxin, dibenzofurans persistent organic pollutants; PFFA = postload free fatty acids; PG = postload glucose; PI = postload insulin; PIn = ponderal index; RA = renin activity; SSK = subscapular skinfold; SSPG = steady state plasma glucose; S:T = subscapular to triceps; SuRFNCD = Surveys of Risk Factors of Non-Communicable Diseases; TC = total cholesterol; TER = trunk extremity ratio; TFM = trunk fat mass; tria. = triacylglycerols; TSI = Torres Strait Islander; TTTS = trunk-to-total skinfolds; UA = uric acid; U:C = urinary albumin - creatinine ratio; WBC = white blood cell count; WC = waist circumference; WHR = waist-to-hip ratio.
Table S1: Factor analyzes of the MBS in the child and adolescent cohort

| Study                  | Characterization                                                                 | Approach                                                                 | Description factors                                                                 |
|------------------------|----------------------------------------------------------------------------------|--------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
| Chen et al. [93]       | - Bogalusa Heart Study                                                          | Little jiffy                                                             | 1. trig., HDL chol., FG, PI, PIn                                                     |
|                        | - Biracial (black/white) community-based population                             |                                                                          | 2. SBP, DBP, PI                                                                      |
|                        | - n ≥ 4, 522 children, adolescents, and young adults                            |                                                                          |                                                                                     |
| Chen et al. [94]       | - Bogalusa Heart Study                                                          | Little jiffy, ethnic                                                    | Whites                                                                               |
|                        | - Biracial (black/white) community-based population                             | subgroup analyzes                                                       | 1. %BF, SBP, DBP                                                                     |
|                        | - n ≥ 264 (132 whites, 132 African Americans)                                    |                                                                          | 2. %BF, HDL chol., trig.                                                             |
|                        |                                                                                |                                                                          | 3. %BF, IR                                                                            |
|                        |                                                                                |                                                                          | African Americans                                                                    |
|                        |                                                                                |                                                                          |                                                                                     |
| Dwyer et al. [95]      | - Tasmanian Infant Health Study                                                 | EFA, factor retention based                                             | Non-obese                                                                            |
|                        | - Children from 1989 singleton births, Tasmania                                  | on LR testing, extraction by                                              | 1. SBP, DBP                                                                          |
|                        | - n ≥ 298 8-year-olds                                                           | principal axis factoring,                                               | 2. PI, FG                                                                            |
|                        |                                                                                | Harris-Kaiser rotation (oblique)                                        | 3. trig., HDL chol., LDL chol.                                                       |
| Moreno et al. [96]     | - Schoolchildren, Zaragoza, Spain                                               | Little jiffy, obesity                                                  | Obese                                                                                |
|                        | - n ≥ 142 (74 non-obese, 68 obese)                                              | subgroup analyzes                                                       | 1. BMI, WC, Leptin, DBP                                                              |
|                        |                                                                                |                                                                          | 2. DBP, SBP                                                                          |
|                        |                                                                                |                                                                          | 3. trig., HDL chol., Leptin, UA                                                       |
|                        |                                                                                |                                                                          | 4. PI, FG                                                                            |
| Lambert et al. [95]    | - Quebec Child and Adolescent Health and Social Survey                           | Little jiffy, with                                                      | Boys                                                                                 |
|                        | - Quebecian youth aged 9, 13, and 16                                            | relaxed Guttman-Kaiser                                                 | 1. BMI, %BF, WC, LDL chol., trig., Leptin                                             |
|                        | - n ≥ 2, 223 (706 9-y-olds, 716 13-y-olds, 817 16-y-olds)                       | rule, age subgroup analyzes                                           | 2. SBP, DBP                                                                          |
|                        |                                                                                |                                                                          | 3. SBP, DBP                                                                          |
|                        |                                                                                |                                                                          | 15-y and 16-y-olds                                                                   |
|                        |                                                                                |                                                                          | 1. BMI, PI, trig., HDL chol.                                                          |
|                        |                                                                                |                                                                          | 2. SBP, DBP                                                                          |
|                        |                                                                                |                                                                          | 3. PI, FG                                                                            |
| Park et al. [97]       | - School-going volunteers, urban South Korea                                     | PCA, Guttman-Kaiser rule, un speculated orthogonal                      | Girls                                                                                |
|                        | - Middle and high-school students aged 13-18                                     | rotation, gender subgroup analyzes                                    | 1. BMI, %BF, WC, Leptin, FG                                                           |
|                        | - n ≥ 148 (68 boys, 80 girls)                                                    |                                                                          | 2. SBP, DBP                                                                          |
|                        |                                                                                |                                                                          | 3. LDL chol., HDL chol.                                                               |
| Study                          | Characterization                                                                 | Approach         | Description factors |
|-------------------------------|----------------------------------------------------------------------------------|------------------|---------------------|
| Weiss et al. [69]             | Multiethnic, multiracial cohort                                                   | Little jiffy     | BMI, HOMA-IR, FG, PG |
|                               | Nondiabetic overweight children and adolescents                                  |                  | trig., HDL chol.    |
|                               | - n = 464                                                                        |                  | SBP, DBP            |
| Goodman et al. [98]           | Princeton School District Study                                                  | Little jiffy     | FG, WC, BMI; fib.   |
|                               | School-based study, Cincinnati, Ohio, USA                                         |                  | LDL chol. TC        |
|                               | Nondiabetic 7th to 12th graders                                                   |                  | SBP, DBP            |
| Retnakaran et al. [99]        | Sandy Lake Health and Diabetes Project                                           | EFA, factor retention based | WC, %BF, BMI, trig., FI |
|                               | Nondiabetic children aged 10-19                                                   | on scree plot, extraction by | trig., HDL chol., FG, PG, FI |
|                               | - n = 212 (subsample with BP measurements)                                         | oblique rotation (Promax) | SBP, DBP            |
| Ghosh [100]                   | Calculcutta, India                                                               | Little jiffy, gender | Boys                |
|                               | Apparently healthy Asian Indian adolescents                                       | subgroup analyzes | WC                  |
|                               | - n = 400 (200 boys, 200 girls)                                                  |                  | S-T, trig. FG       |
|                               |                                                                                |                  | SBP, DBP, MAP       |
| Goodman et al. [101]          | Princeton School District Study                                                  | Little jiffy, baseline | Girls              |
|                               | School-based study, Cincinnati, Ohio, USA                                         | and 3-year follow-up | WC                  |
|                               | - n = 1,098                                                                      | subgroup analyzes | S-T, trig. FG       |
|                               |                                                                                |                  | SBP, DBP            |
| Kelishadi et al. [102]        | CASPFIAN Study                                                                  | Little jiffy, subgroup | Non-MBS             |
|                               | Subjects from 6 provinces in Iran, aged 6 to 18                                   | analysis by age and | TC, LDL chol.       |
|                               | - n = 4,811 (678 ATPIII MBS, 4,133 non-MBS)                                      | MBS-designation   | trig., HDL chol., FG|
|                               |                                                                                |                  | WC, BMI              |
|                               |                                                                                |                  | SBP, SBP            |
| Li et al. [103]               | National Health and Nutrition Examination Survey                                  | CFA, ML estimation, | Non-MBS             |
|                               | Adolescents aged 12-17                                                           | assessment measurement | 1. WC, trig., FI, SBP |
|                               | - n = 1,262                                                                      | invariance across sex and | (Model considered invariant) |
| Study          | Characterization                                                                 | Approach                                                                 | Description factors                                                                 |
|---------------|---------------------------------------------------------------------------------|--------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
| Ng et al. [104]| - Hong-Kong Chinese adolescents  
- Aged 12-19  
- $n = 2,192$ (958 boys, 1,144 girls) | Little jiffy, gender subgroup analyzes                                   | Boys  
1. BW, WC, BMI  
2. SBP, DBP  
3. trig., HDL chol., LDL chol.  
4. FG  
Girls  
1. BW, WC, BMI  
2. SBP, DBP, FG  
3. trig., HDL chol.  
4. LDL chol. |
| Ramachandran et al. [105]| - School-based survey, Chennai, India  
- Children aged 12-19  
- $n = 2,640$ (1,323 boys, 1,317 girls) | PCA, component retention and rotation (orthogonal) subgroup analyzes | Boys  
1. WC, SBP, DBP  
2. trig., WC, PG, FI  
3. HDL chol., trig., PG  
Girls  
1. WC, SBP, DBP, FI  
2. HDL chol., trig., WC, FI  
3. PG, FI |
| Goodman et al. [56]| - Fels Longitudinal Study  
- Focus on developmental puberty stages  
- $n = 442$ | CFA, assessment invariance of 3 alternative models (1-factor model, 4-factor model, 2nd-order factor model) across developmental puberty stages | None of the models gave (consistent) adequate fit (across developmental puberty stages) |
| Mayer-Davis et al. [106]| - SEARCH for Diabetes in Youth Study  
- Type 1 and Type 2 diabetics, aged 10-22  
- $n = 1,293$ (1,198 Type 1, 95 Type 2) | CFA, ML estimation, assessment various CFA models (1-3 factors), assessment measurement invariance across diabetes type | Boys  
1. BMI, WC  
2. trig., HDL chol.  
3. DBP, SBP  
(Model considered invariant) |
| Noto et al. [107]| - Primary and secondary schools, Serre Calabre Montane, Italy  
- Schoolchildren aged 7-14  
- $n = 1,629$ (859 boys, 770 girls) | Little jiffy, gender subgroup analyzes                                   | Boys  
1. WC, BMI, age, SBP  
2. HDL chol, trig.  
3. SBP, DBP  
4. FG  
(Model considered invariant) |
| Ghasemi et al. [108]| - Tehran Lipid and Glucose Study  
- District 13 of Tehran, Iran  
- $n = 851$ (88 with MBS, 236 overweight) | Little jiffy, subgroup analysis w.r.t. MBS-designation and weight | Boys  
1. SBP, DBP, WC, BMI  
2. trig., HDL chol, WC, BMI  
3. FG, NO$_2$  
4. MBS  
Girls  
1. WC, BMI  
2. trig., HDL chol.  
3. SBP, DBP  
4. FG, NO$_2$    |
### Table S1 (Continued)

| Study                                | Characterization                                                                 | Approach                                                                 | Description Details                                                                 |
|--------------------------------------|---------------------------------------------------------------------------------|--------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
| Martínez-Vizcaíno et al. [109]       | - Children from 20 schools in Cuenca, Spain
- Children aged 10-13
- n = 1,020 | CFA, usage of parceling, assessment measurement
invariance across gender and physical activity | 1. WC, trig./HDL chol., F1, MAP
(Model considered invariant) |
| Khader et al. [110]                   | - Household sample from 12 governorates, Jordan
- Children and adolescents
- n = 655 | Little jiffy, subgroup analyses w.r.t. gender and age | 1. BMI, WC
2. DBP, SBP
3. HDL chol., trig.
4. FG
(Structure considered invariant) |
| Martinez-Vizcaíno et al. [111]       | - European Youth Heart Study
- 6-year follow-up study
- Swedish and Estonian children aged 9 at start
- n = 634 (174 Swedish, 460 Estonian) | CFA, ML estimation, usage of parceling, assessment measurement
invariance across ethnicity and time | 1. WC, trig./HDL chol., F1, MAP
(Model considered invariant) |
| Olza et al. [112]                     | - Children from 3 regions of Spain
- Obese Caucasian children aged 5-14
- n = 478 | Little jiffy | 1. SBP, PG, HOMA-IR
2. HDL chol., trig.
3. BMI, SBP |
| Gurka et al. [112]                    | - National Health and Nutrition Examination Survey
- Non-Hispanic blacks, whites, and Hispanics aged 12-19
- n = 4,147 | CFA, ML estimation, assessment measurement
invariance across sex-ethnicity combinations | 1. BMI, SBP, HDL chol., trig., FG
(Structure considered invariant) |
| Hong et al. [113]                     | - Ho Chi Minh City, Vietnam
- Urban high-school students
- n = 617 (284 boys, 333 girls) | Little jiffy, gender subgroup analyzes | Boys
1. BMI, WC
2. SBP, DBP, LDL chol
3. trig., HDL chol. |
| Girls                                | 1. BMI, WC
2. SBP, DBP, LDL chol. 
3. trig., HDL chol. |
| Suchday et al. [114]                  | - Students liberal arts college, Mumbai, India
- Students aged 15-23
- n = 112 | Little jiffy | 1. SBP, WHR, DBP, BMI, FI
2. TC, trig.
3. FG, BMI, FI |
| Wang et al. [115]                     | - Beijing Child and Adolescent Metabolic Syndrome Study
- Schoolchildren aged 6 to 18 | Little jiffy, gender subgroup analysis | Non-parceling, boys
1. WC, trig., HDL chol., HOMA-IR, FI, Leptin, Adi |
| Pecora et al. [116]                   | - Children from 3 regions of Italy
- Louisiana children aged 10-12
- n = 4,86 | Little jiffy | 1. SBP, DBP, WC
2. trig., HDL chol., WC |
| Suchday et al. [117]                  | - Students liberal arts college, Mumbai, India
- Students aged 15-23
- n = 112 | Little jiffy | 1. SBP, WHR, DBP, BMI, FI
2. TC, trig.
3. FG, BMI, FI |
| Wang et al. [118]                     | - Beijing Child and Adolescent Metabolic Syndrome Study
- Schoolchildren aged 6 to 18 | Little jiffy, gender subgroup analysis | Non-parceling, boys
1. WC, trig., HDL chol., HOMA-IR, FI, Leptin, Adi |

*Table S1 (Continued)*
Table S1 (Continued)

| Study                  | Characterization                        | Approach               | Description factors                                                                 |
|------------------------|-----------------------------------------|------------------------|--------------------------------------------------------------------------------------|
|                        | - n = 3,373 (1,717 boys, 1,656 girls)  | followed by parceling  | 2. WC, SBP, DBP                                                                      |
|                        |                                         |                        | 3. FG, HOMA-IR, FI                                                                   |
|                        |                                         |                        | Non-parceling, girls                                                                 |
|                        |                                         |                        | 1. WC, FG, HOMA-IR, FI, Leptin                                                       |
|                        |                                         |                        | 2. WC, trig., HDL chol., Leptin, Adi                                                  |
|                        |                                         |                        | 3. WC, SBP, DBP                                                                      |
|                        |                                         |                        | Usage of parceling                                                                   |
|                        |                                         |                        | 1. WC, MAP, trig./HDL chol., Leptin/Adi                                               |

Table S2: Factor analyses of the MBs in additional cohorts

| Study                  | Characterization                                      | Approach               | Description factors                                                                 |
|------------------------|-------------------------------------------------------|------------------------|--------------------------------------------------------------------------------------|
| Edwards et al. [26,116]| - Kaiser-Permanente Women Twins Study                | Little jiffy           | 1. BW, WC, FI, FG                                                                    |
|                        | - Unrelated, nondiabetic women                        |                        | 2. FI, PI, FG, PG, SBP                                                                |
|                        | - n = 284                                             |                        | 3. trig., HDL chol., LDL-PPD                                                          |
| Donahue et al. [117]   | - Miami Community Health Study                       | Little jiffy           | 1. UA, SBP, DBP, HDL chol., trig., WC, IMGD                                           |
|                        | - Nondiabetic African-Americans and non-Hispanic whites |                      | 2. FI, PG, DBP, IMGD                                                                 |
|                        | - n = 50                                              |                        |                                                                                      |
| Meigs et al. [118]     | - Framingham Offspring Study                         | Little jiffy, gender   | 1. FI, PI, BMI, WBR, HDL chol., trig.                                                  |
|                        | - Nondiabetic men and women                          | subgroup analyzes      | 2. GB, G2, FI, PI                                                                    |
|                        | - n = 2,458 (1,150 men and 1,308 women)              |                        | 3. BMI, SBP, DBP                                                                     |
|                        |                                                       |                        | (Structure considered invariant)                                                     |
| Edwards et al. [119]   | - Honolulu Heart Program                             | Little jiffy, subgroup | Nondiabetic                                                                           |
|                        | - Nondiabetic elderly Japanese-American men          | analyses by gender to  | 1. BW, WC                                                                            |
|                        | - n = 3,159 (2,760 nondiabetic and 399 diabetic)     | diabetic status         | 2. SBP, DBP                                                                          |
|                        |                                                       |                        | 3. trig., HDL chol.                                                                  |
|                        |                                                       |                        | 4. FG, FI                                                                            |
|                        |                                                       |                        | Diabetic                                                                              |
|                        |                                                       |                        | 1. SBP, WC                                                                           |
|                        |                                                       |                        | 2. SBP, DBP                                                                          |
|                        |                                                       |                        | 3. trig., HDL chol., FG                                                               |
|                        |                                                       |                        | 4. FG, FI                                                                            |
| Gray et al. [120]      | - Strong Heart Study                                 | Little jiffy, subgroup | Nondiabetic males                                                                     |
|                        | - American Indians                                   | analyses by gender and  | 1. BMI, FI                                                                            |
|                        | - n = 4,228 (975 and 1,202 nondiabetic men and women,| diabetic status         | 2. SBP, DBP                                                                          |
|                        | 783 and 1,268 diabetic men and women)                |                        | 3. HDL chol., trig., FI                                                               |
|                        |                                                       |                        | Nondiabetic females                                                                   |
|                        |                                                       |                        | 1. BMI, FI                                                                            |
|                        |                                                       |                        | 2. SBP, DBP                                                                          |
|                        |                                                       |                        | 3. HDL chol., trig.                                                                  |
|                        |                                                       |                        | Diabetic males                                                                        |
|                        |                                                       |                        | 1. SBP, DBP                                                                          |
|                        |                                                       |                        | 2. HDL chol., trig., FG                                                               |
| Study                        | Characterization                                                                 | Approach                          | Description factors                                                                 |
|-----------------------------|----------------------------------------------------------------------------------|-----------------------------------|--------------------------------------------------------------------------------------|
| Leyva et al. [121]          | - RISC-2 Study                                                                  | Little jiffy                      | 1. IR, FG, PI, Leptin                                                                |
|                             | - Nondiabetic men                                                               |                                    | 2. Leptin, IVGTT, S/T, UA, SBP, BMI                                                  |
|                             | - n = 74                                                                        |                                    | 3. HDL chol., trig.                                                                  |
| Chen et al. [122]           | - Nondiabetic residents Kinmen Taiwan                                           | Little jiffy, gender subgroup analyzes | 1. SBP, DBP                                                                         |
|                             | - n = 8, 437 (3,659 men and 4,778 women)                                       |                                    | 2. FI, BMI, WHR, HDL chol., trig.                                                    |
|                             |                                                                                  |                                    | 3. PG                                                                               |
| Sakkinen et al. [123]       | - Cardiovascular Health Study                                                   | Little jiffy                      | 1. BW, WC, PI, FG                                                                    |
|                             | - Elderly nondiabetics                                                          |                                    | 2. PI, PG                                                                           |
|                             | - n = 322                                                                       |                                    | 3. SBP, DBP                                                                         |
|                             |                                                                                  |                                    | 4. trig., HDL chol.                                                                  |
| Snehalatha et al. [124]     | - Urban cluster survey, Madras, India                                            | PCA, component retention          | 1. BMI, FG, PI, HOMA-IR                                                              |
|                             | - Nondiabetic adults                                                            | Varimax rotation, gender subgroup analyzes | 2. BMI, SBP, DBP                                                                    |
|                             | - n = 654 (396 men and 258 women)                                               |                                    | 3. BMI, WHR, chol., trig.                                                            |
|                             |                                                                                  |                                    | 4. BMI, WHR, HOMA-IR                                                                 |
| Anderson et al. [125]       | - Chinese men and women                                                          | EFA, factor retention             | 1. FI, FG, BMI, WC, IS                                                               |
|                             | - n = 145                                                                       | Varimax rotation                   | 2. BMI, MAP, WC                                                                     |
|                             |                                                                                  |                                    | 3. HDL chol., WC, trig.                                                              |
| Hodge et al. [126]          | - Island of Mauritius                                                           | Little jiffy, gender subgroup analyzes | 1. WHR, BMI, Leptin, trig., HDL chol., FA, PI                                      |
|                             | - Nondiabetic adults                                                            |                                    | 2. UA, SBP, DBP                                                                     |
|                             | - n = 3, 068 (1,414 men and 1,654 women)                                        |                                    | 3. PI, FG, PG                                                                        |

**Table S2 (Continued)**
| Study                        | Characterization                                                                 | Approach                          | Description factors                                                                 |
|-----------------------------|----------------------------------------------------------------------------------|-----------------------------------|--------------------------------------------------------------------------------------|
| Shmulewitz et al.           | - Pacific island of Kosrae, Micronesia<br>- Nondiabetic adults<br>- n = 628      | PCA, component retention and rotation (orthogonal) unspecified                   | 1. BW, WHR, Leptin, FI<br>2. TC, trig., Apo B<br>3. FG, SBP, DBP<br>4. Leptin, trig., Apo A-I |
| Adami et al.                | - Obese Italian adults<br>- n = 163                                              | Little jiffy                       | 1. trig., HDL chol., SBP, DBP<br>2. FI, HOMA-IR<br>3. BMI, Leptin, FG                  |
| Arya et al.                 | - San Antonio Family Diabetes Study<br>- Nondiabetic Mexican-Americans<br>- n = 261 | Little jiffy                       | 1. BMI, Leptin, FI<br>2. DBP, SBP<br>3. HDL chol., trig.                            |
| Hanley et al.               | - Insulin Resistance Atherosclerosis Study<br>- Nondiabetic adults<br>- n = 1,087 | Little jiffy                       | 1. BMI, WC, FG, PG, HOMA-IR, trig., HDL chol.<br>2. DBP, SBP<br>(See [33] for subgroup analyzes) |
| Hanson et al.               | - Gila River Indian Community, Arizona, USA<br>- Adult Pima Indians<br>- n = 1,448 (1,918 nondiabetics, 470 diabetics) | Little jiffy, usage of parceling, subgroup analyzes by diabetic status          | Non-diabetics<br>1. F1 x PG, F1 x FG, F1 / FG, PI / PG<br>2. BW, WC<br>3. DBP, SBP<br>4. HDL chol., trig. |
| Kue Young et al.            | - Sample survey 3 contiguous regions of Canada<br>- Adult Indians, Inuit, and non-Aboriginal Canadians<br>- n = 3,930 (875 Indians, 387 Inuit, 2,670 non-Aboriginals) | Little jiffy                       | Non-Diabetics<br>1. F1 x PG, F1 x FG, F1 / FG, PI / PG<br>2. BW, WC<br>3. DBP, SBP<br>4. HDL chol., trig., F1 x FG |
| O’Dea et al.                | - Aboriginal and Torres Strait Islander People, Australia<br>- Community-based risk factor survey<br>- n = 863 (643 Aborigines and 220 Islanders) | Little jiffy, subgroup analyzes by gender and ethnicity                         | Tall, males<br>1. FG, PG, FI, trig., HDL chol., WHR<br>2. FI, SBP, DBP, BMI, WHR<br>Tall, females<br>1. FG, PG, FI, trig., HDL chol., BMI, WHR<br>2. FI, SBP, DBP<br>Aboriginals, males<br>1. SBP, DBP, BMI, WHR<br>2. FG, PG, BMI, WHR<br>3. FI, trig., HDL chol., BMI<br>Aboriginals, females<br>1. SBP, DBP<br>2. FG, PG<br>3. FI, trig., HDL chol., BMI, WHR |
| Study                        | Characterization                                                                 | Approach                      | Description factors                                                                 |
|-----------------------------|----------------------------------------------------------------------------------|-------------------------------|--------------------------------------------------------------------------------------|
| Choi et al. [132]           | - The South-West Seoul Study                                                      | Little jiffy, gender subgroup analyses | Males: 1. BMI, WHR, HDL chol., trig., PI, FI  
                                         | - Urban elderly non-diabetic Koreans                                              |                               | 2. SBP, DBP  
                                         | - \( n = 1,314 \) (249 men, 1,065 women)                                         |                               | 3. PI, PG  
                                         | Females: 1. BMI, HDL chol.                                                      |                               | 4. PI, PG  
                                         | Females: 2. SBP, DBP                                                           |                               | 5. BMI, WHR, PI, FG                                                           |
| Ford [35]                   | - National Health and Nutrition Examination Survey                                | Little jiffy, subgroup analyses by gender, ethnicity and age | Males: 1. HDL chol., trig., PI, WC, BMI, WHR, UA  
                                         | \( n = 6,868 \) (3,410 men, 3,458 women)                                         |                               | 2. SBP, DBP  
                                         | Females: 1. PI, WC, BMI, WHR, UA                                               |                               | 3. FG, U-C  
                                         | Females: 2. SBP, DBP                                                           |                               | 4. BMI, WHR, PI, FG                                                           |
| Hanley et al. [133]         | - Sandy Lake Health and Diabetes Project                                          | EFA, retention based on (no)   | 1. FI, WC, %BF  
                                         | - Nondiabetic adult native Canadians                                             | scree plot, factor extraction by principal axis factoring, Varimax rotation | 2. FI, WC, trig., HDL chol., Adi  
                                         | - \( n = 728 \) (305 men, 423 women)                                           |                               | 3. FI, FG, PG  
                                         | (See [35] for other subgroup analyses)                                         |                               |                                                                   |
| Howard et al. [134]         | - Women's Health Initiative                                                       | Little jiffy, ethnicity subgroup analyses | White: 1. BMI, HC, WC, HOMA-IR, FI, FG  
                                         | - Nondiabetic postmenopausal female adults                                       |                               | 2. HOMA-IR, FI, HDL chol., trig., HDL2/HDL tot.  
                                         | - \( n = 3,083 \) (1,635 White, 802 Black, 390 Latino, 256 Asian/Pacific Islander) |                               | 3. TC, LDL chol.  
                                         | (Structure similar in other ethnic subgroups)                                  |                               | 4. SBP, DBP  
                                         |                                                                   |                               |                                                                   |
| Novak et al. [135]          | - Göteborg, Sweden                                                                | CFA, ML estimation             | 1. SBP, DBP  
                                         | - Middle-aged Caucasian males                                                    |                               | 2. BMI, WHR  
                                         | - \( n = 284 \)                                                               |                               | 3. FI, FG  
                                         |                                                                   |                               | 4. trig., HDL chol.  
| Shen et al. [52]            | - Normative Aging Study                                                           | CFA, robust ML estimation, second-order factor taken to reflect MBS, measurement invariance over cardiovascular disease and age groupings | 1. FI, PI, FG, PG  
                                         | - Male participants                                                            |                               | 2. BMI, WHR  
                                         | - \( n = 847 \)                                                               |                               | 3. trig., HDL chol.  
                                         |                                                                   |                               | 4. SBP, DBP  
                                         | (Structure deemed invariant)                                                  |                               |                                                                   |
| Tang et al. [136]           | - NHLBI Family Heart Study                                                        | EFA, factor retention based on on Gottman-Kaiser rule, factor extraction by ML estimation, rotation unspecified | 1. BMI, WHR, SSK, trig., HDL chol., HOMA-IR, PAI-1, UA  
                                         | - Probands' family members                                                       |                               | 2. trig., LDL chol., TC  
                                         | - \( n = 2,831 \)                                                             |                               | 3. BMI, SSK  
                                         |                                                                   |                               | 4. trig., LDL chol.  
                                         |                                                                   |                               |                                                                   |
| Study                        | Characterization                                                                 | Approach                                      | Description factors                                      |
|-----------------------------|----------------------------------------------------------------------------------|-----------------------------------------------|----------------------------------------------------------|
| Cai et al. [137]            | - San Antonio Family Heart Study                                                 | Little jiffy                                  | 1. BW, BMI, WC, HC, %BF, FI, AST                         |
|                             | - Nondiabetic Mexican-Americans                                                  |                                               | 2. PG, PG, FI                                             |
|                             | - n = 566                                                                        |                                               | 3. SBP, DBP                                               |
|                             |                                                                                  |                                               | 4. HDL chol., trig.                                       |
| Jones et al. [138]          | - Spinal cord-injured men                                                         | Little jiffy                                  | 1. %BF, PAL, TFM, PG, PI                                 |
|                             | - n = 20                                                                         |                                               | 2. PAL, TC/HDL chol., HDL chol., PI                       |
|                             |                                                                                  |                                               | 3. PG, FI                                                 |
| Nelson et al. [139]         | - Swedish Adoption/Twin Study of Aging                                            | CFA, further approach                         | 1. IS, MAP, WRR, TC/HDL chol.                            |
|                             | - n = 1, 944                                                                     | unspecified, usage of parceling               |                                                          |
| Oh et al. [177]             | - Mokdong Study of Diabetes Prevalence                                           | PCA, component retention                      |                                                          |
|                             | - Urban Korean adults                                                            | unspecified, Varimax rotation,               |                                                          |
|                             | - n = 655 (206 men, 449 women)                                                   | gender subgroup analyses                      |                                                          |
| Wang et al. [140]           | - National Diabetes Survey China                                                  | Little jiffy, gender and diabetic status     |                                                          |
|                             | - Nondiabetic Chinese adults                                                     | subgroup analyzes                            |                                                          |
|                             | - n = 934 (449 and 485 nondiabetic men and women, 132 and 173 diabetic men and women) |                                               |                                                          |
|                             |                                                                                  | Nondiabetic males                             |                                                          |
|                             |                                                                                  | 1. BMI, WRR, FI, FG                           |                                                          |
|                             |                                                                                  | 2. SBP, DBP                                   |                                                          |
|                             |                                                                                  | 3. PI, PG, FG                                 |                                                          |
|                             |                                                                                  | 4. TC, trig.                                  |                                                          |
|                             |                                                                                  | Nondiabetic females                           |                                                          |
|                             |                                                                                  | 1. BMI, WRR, FI                               |                                                          |
|                             |                                                                                  | 2. SBP, DBP                                   |                                                          |
|                             |                                                                                  | 3. PI, PG, FG                                 |                                                          |
|                             |                                                                                  | 4. TC, FI, PI                                 |                                                          |
|                             |                                                                                  | Diabetic males                                |                                                          |
|                             |                                                                                  | 1. SBP, DBP                                   |                                                          |
|                             |                                                                                  | 2. UA, trig., FG, PG                          |                                                          |
|                             |                                                                                  | 3. BMI, WRR, trig., FI                       |                                                          |
|                             |                                                                                  | 4. TC, FI, PI                                 |                                                          |
|                             |                                                                                  | Diabetic females                              |                                                          |
|                             |                                                                                  | 1. SBP, DBP                                   |                                                          |
|                             |                                                                                  | 2. UA, PG, FG                                 |                                                          |
|                             |                                                                                  | 3. BMI, WRR, trig., FI                       |                                                          |
|                             |                                                                                  | 4. TC, FI, PI                                 |                                                          |
| Ang et al. [178]            | - Singapore National Health Survey                                               | Little jiffy, subgroup analyzes w.r.t. gender and ethnicity | Chinese males and females, Malay males                  |
|                             | - Nondiabetic Chinese, Malay, and Asian Indian adults                           |                                               | 1. HOMA-IR, BMI, WHR, HDL chol., trig.                   |
|                             | - n = 4, 265 (1,671 Chinese, 281 Malay, 158 Indian)                             |                                               | 2. PG, PG, HOMA-IR                                       |
| Study | Characterization | Approach | Description factors |
|-------|------------------|----------|----------------------|
| Ghosh [39] | - Employees Eastern Railway Government, India - Middle-aged Bengalee Hindu men - n = 212 | Little jiffy | 1. WHR |
| Lin et al. [41] | - Northern Manhattan Family Study - Subjects from Caribbean-Hispanic families - n = 803 | Little jiffy | 1. trig., HDL chol., FG, WC 2. SBP, DBP |
| Mohan et al. [42] | - Chennai Urban Rural Epidemiology Study - Adult diabetic from Chennai, India - n = 100 | Little jiffy, component retention not specified | 1. trig., HDL chol., HOMA-IR, Adi, WC 2. WC, SBP, DBP |
| Lion et al. [43] | - Taipei Veterans General Hospital - Cross-sectional studies from Spain, Mauritius, and USA - n = 393 | Little jiffy | 1. BMI, WC, FG, trig., HDL chol., UA 2. SBP, DBP |
| Pladevall et al. [53] | - CFA study using previously collected data - Nondiabetic middle-aged Chinese men - n = 4,318 | CFA, ML estimation, usage of parceling | 1. WC, HOMA-IR, trig./HDL chol., MAP |
| Shah et al. [54] | - Insulin Resistance-Atherosclerosis Study - Data as used in [33] | CFA, ML estimation | 1. SBP, DBP 2. HDL chol., trig. 3. FG, PG, FG 4. WC, BMI |
| Shen et al. [44] | - Miami Community Health Study - Nondiabetic Caucasians, African and Cuban-Americans - n = 517 | CFA, ML estimation, second-order factor taken to reflect MBS, assessment measurement invariance over gender, ethnicity and age groupings | 1. PG, FG 2. BMI, WC 3. trig., HDL chol. 4. SBP, DBP (Structure deemed invariant) |
| Study                        | Characterization                                                                 | Approach                      | Description factors                                                                 |
|-----------------------------|----------------------------------------------------------------------------------|-------------------------------|-------------------------------------------------------------------------------------|
| Zanolin et al [145]         | Outpatients, Verona, Italy                                                       | Little jiffy                  | 1. BMI, DBP, HDL chol., trig., UA                                                   |
|                             | Caucasian nondiabetic hyperandrogenic women                                       |                               | 2. BMI, DBP, SBP, FT                                                              |
|                             | - n = 255                                                                         |                               | 3. FG, PG, PI, trig., FT                                                           |
|                             | 2. BMI, DBP, SBP, FT                                                             |                               | 4. PI, FT, 17HP                                                                   |
| Chien et al [146]           | Chin-Shan Community Family Study                                                  | Little jiffy                  | 1. SBP, DBP, WC, BMI                                                              |
|                             | Adolescent probands and relatives, China                                          |                               | 2. TC, LDL chol.                                                                  |
|                             | - n = 1, 227                                                                     |                               | 3. HOMA-IR, FG, HDL chol., trig.                                                   |
| Razak et al [147]           | Study of Health Assessment and Risk in Ethnic Groups                             | PCA, retention and            | 1. FG, PG, PI, HOMA-IR, HbA1c, FFFA, FFFA                                          |
|                             | Subjects from 4 ethnic groups from 4 regions, Canada                              | rotation criteria             | 2. PI, HOMA-IR, LDL chol., HDL chol., trig., FFFA                                  |
|                             | - n = 1, 078                                                                     | unspecified                   | 3. SBP, DBP                                                                       |
| Ghosh [148]                 | Nondiabetic pre and postmenopausal Bengalee women                                | Little jiffy, menopausal      | Prenopausal                                                                        |
|                             | - n = 200 (100 pre and 100 postmenopausal)                                       | subgroup analyzes             | 1. WC, WHR                                                                        |
|                             |                                                                               |                               | 2. TC, trig., HDL chol., LDL chol., FG                                              |
|                             |                                                                               |                               | 3. SBP, DBP                                                                       |
|                             |                                                                               |                               | Postmenopausal                                                                     |
|                             |                                                                               |                               | 1. WC, WHR                                                                        |
|                             |                                                                               |                               | 2. WC, WHR, FG                                                                    |
|                             |                                                                               |                               | 3. TC, trig., HDL chol., LDL chol., FG                                              |
|                             |                                                                               |                               | 4. SBP, DBP                                                                       |
| Lafortuna et al [149]       | Patients IAI, Piancavallo, Italy                                                 | Little jiffy                  | Rural                                                                              |
|                             | Adult obese women                                                                |                               | 1. BMI, WC, PI, HDL chol.                                                         |
|                             | - n = 552                                                                         |                               | 2. SBP, DBP, PI                                                                  |
|                             |                                                                               |                               | 3. trig., UA                                                                       |
|                             |                                                                               |                               | 4. FG, PG, HDL chol.                                                              |
| Reimann et al [150]         | Transition and Health during Urbanization Study                                  | Little jiffy, subgroup        | Suburban                                                                           |
|                             | Rural, semurban, and urban Black South Africans                                   | analyses w.r.t.               | 1. BMI, WC, trig.                                                                 |
|                             | - n = 448 (140 rural, 118 semurban, 190 urban)                                   | urbanization                  | 2. SBP, DBP, PI                                                                  |
|                             |                                                                               |                               | 3. FG, PI                                                                         |
|                             |                                                                               |                               | 4. FG, HDL chol.                                                                  |
|                             |                                                                               |                               | 5. trig., UA                                                                      |
| Wu et al [151]              | Patients enrolled in a General Hospital, Taipei, Taiwan                           | Little jiffy, glucose         | Urban                                                                             |
|                             | Participates in routine health check                                             | tolerance subgroup            | 1. BMI, WC, HDL chol.                                                            |
|                             |                                                                               |                               | 2. FG, PI, trig.                                                                  |
|                             |                                                                               |                               | 3. SBP, DBP                                                                       |
|                             |                                                                               |                               | 4. FG, PG, HDL chol.                                                              |
|                             |                                                                               |                               | Normal glucose tolerance                                                          |
|                             |                                                                               |                               | 1. SBP, DBP                                                                       |
| Study | Characterization | Approach | Description factors |
|-------|-----------------|----------|---------------------|
| Boronat et al. [57] | Telde Study - Non diabetic adult Canadians - \( n = 902 \) | CFA, ML estimation, usage of parceling, assessment measurement invariance across gender | 1. WC, trig./HDL chol., HOMA-IR, MAP (Structure deemed invariant) |
| Leone et al. [152] | Paris Investigations Préventives et Cliniques Center - Subjects underwent health examination - \( n = 121,965 \) | PCA, retention based on scree plot, Varimax rotation | 1. HDL chol., trig. 2. SBP, FG 3. WC |
| Öhrvik et al. [153] | 75 year olds from Västerås, Sweden - \( n = 401 \) (198 males, 203 females) | EFA, factor extraction by principal axis factoring, factor retention based on scree plot, Varimax rotation, gender subgroup analyses | 1. WC, HDL chol., trig., FG 2. SBP, DBP (Structure deemed invariant) |
| Chang et al. [154] | Nondiabetic dioxin-exposed Taiwanese - \( n = 1,409 \) | Little jiffy, gender subgroup analyses | Males 1. WC, HOMA-IR, SBP, Leptin 2. trig., HDL chol. Females 1. WC, SBP, Leptin 2. trig., HDL chol. |
| Esteghamati et al. [155] | SuRFNCD 2007, Iran - Iranian adults - \( n = 3,601 \) (1,483 males, 1,518 females) | Little jiffy, gender subgroup analyses | Males 1. WC, HOMA-IR, SBP, Leptin 2. trig., HDL chol. Females 1. WC, SBP, Leptin 2. trig., HDL chol. |
| Marsland et al. [156,157] | University of Pittsburgh Adult Health and behavior Project - Non-hispanic White and African American subjects - \( n = 645 \) middle-aged community volunteers | CFA, robust ML estimation, second-order factor taken to reflect MBS | 1. SBP, DBP 2. F1, FG 3. BMI, WC 4. HDL chol., trig. |
| Barbosa-Leiker et al. [158] | Spokane Heart Study - \( n = 604 \) | CFA, robust ML estimation, assessment measurement invariance over time points | 1. BMI, DBP, FG, HDL chol., trig. (Model considered stable across time) |
| Meshkani et al. [159] | Unrelated Iranian adults - Normal and impaired glucose tolerant subjects - \( n = 501 \) (266 males, 235 females) | Little jiffy, gender subgroup analyses | Males 1. BMI, WC, F1, UA 2. SBP, DBP 3. FG, trig., HDL chol. Females 1. WC, SBP, Leptin 2. trig., HDL chol. |
| Study                  | Characterization                                                                 | Approach                                                                 | Description factors                                                                 |
|-----------------------|---------------------------------------------------------------------------------|--------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
| Solera-Martínez et al. | - First-year university students  
- Universidad de Castilla-La Mancha, Spain  
- n = 683 | CFA, ML estimation, usage of parceling, assessment measurement invariance over gender | Females  
1. SBP, DBP  
2. BMI, WC, FL  
3. FG, trig., HDL chol., UA |
| Azimi-Nezhad et al.   | - Stanislas cohort (France) and Kharasan province (Iran)  
- France: n = 1,386 (678 men, 708 women)  
- Iran: n = 1,194 (569 men, 605 women) | Extraction method unspecified, retention based on scree plot, usage Varimax rotation, subgroup analyses w.r.t. gender and ethnicity | Iranian males and females, French males  
1. SBP, DBP, WC  
2. trig., WC, FG, HDL chol.  
French females  
1. SBP, DBP, WC, FG  
2. trig., WC, HDL chol. |
| Esteghamati et al.    | - Outpatient clinic, Vali-Azer hospital, Iran  
- Iranian adults  
- n = 894 (327 nondiabetics, 567 diabetics) | Little jiffy, subgroup analyses according to diabetic status | Nondiabetics  
1. WC, HOMA-IR, trig., SBP, Apo B  
2. HDL chol., Apo A-I  
Diabetes  
1. WC, HOMA-IR, SBP  
2. HDL chol., Apo A-I  
3. trig., Apo B |
| Stevenson et al.      | - Spokane Heart Study  
- Non-clinical healthy volunteers  
- n = 434 | CFA, robust ML estimation | 1. BMI, FG, HDL chol., trig., SBP |
| Chirino et al.        | - Peruvian Study of Cardiovascular Disease Prevention  
- Andean Hispanic adults  
- n = 2,513 | CFA, ML estimation, assessment measurement invariance over gender | 1. WC, SBP, DBP, trig., FG  
(Structure considered invariant) |
| Dusseault-Belanger et al. | - Centre Hospitalier Universitaire de Sherbrooke, Canada  
- Cohort with diverse medical histories  
- n = 7,213 | PCA, component retention  
rotation unspecified | 1. BW, MAP, FG, HDL chol., trig.  
2. MAP, FG |
| Gómez-Marcos et al.   | - EVIDENT study  
- Spanish adults  
- n = 636 (258 men, 378 women) | CFA, ML estimation, usage of parceling, assessment measurement invariance across gender | Males  
1. BMI, trig./HDL chol., HOMA-IR, MAP  
Females  
1. WC, trig./HDL chol., HOMA-IR, MAP |
| Gurka et al.          | - National Health and Nutrition Examination Survey  
- Nondiabetic whites, blacks, and Hispanics  
- n = 6,870 | CFA, ML estimation, assessment measurement invariance across gender and ethnicity | 1. WC, SBP, HDL chol., trig., FG  
(Structure considered invariant) |
| Study          | Characterization                                                                 | Approach                                                                 | Description factors                          |
|---------------|---------------------------------------------------------------------------------|--------------------------------------------------------------------------|----------------------------------------------|
| Huo et al.    | Residents Beijing, China - $n = 7,472$                                           | CFA, ML estimation, usage of parceling, assessment measurement invariance across gender and age groups | Middle-aged men  
Women / Young and senior men  
1. WC, trig./HDL chol., FG, MAP  
2. WC, FG, SBP |
| Nilsson et al. | 75 year olds from Västerås, Sweden - $n = 396$ (196 men, 200 women)            | PCA, retention based on Guttman-Kaiser rule, variability eigenvalues assessed by bootstrapping, gender subgroup analyses | Males  
1. FG, HDL chol., trig., WC  
2. DBP, SBP  
3. FG, WBC  
Females  
1. FG, HDL chol., trig., WC, WBC  
2. DBP, SBP |
| Sabanayagam et al. | Asian ethnic groups in Singapore - Middle-aged to elderly subjects  
- $n = 9,477$ (3,167 Chinese, 3,082 Malays, 3,228 Indians) | Little jiffy                                                                 | Chinese  
1. NFG, HbA1c  
2. trig., HDL chol., BMI  
3. SBP, DBP  
Malay  
1. NFG, HbA1c  
2. SBP, DBP  
3. trig., HDL chol.  
Indian  
1. NFG, HbA1c  
2. SBP, DBP  
3. trig., HDL chol.  
4. BMI |
| Smits et al.  | Subjects recruited by public advertisement - Nondiabetic individuals from Greater Seattle community - $n = 134$ | CFA, ML estimation                                                         | 1. trig., HDL chol., IS, SBP, DBP, IAP, PAI-1 |

### Notes
- CFA: Confirmatory Factor Analysis  
- ML: Maximum Likelihood  
- NFG: Normative Fasting Glucose  
- HbA1c: Hemoglobin A1c  
- IS: Insulin Sensitivity  
- HDL chol.: High-Density Lipoprotein Cholesterol  
- BMI: Body Mass Index  
- WC: Waist Circumference  
- SBP: Systolic Blood Pressure  
- DBP: Diastolic Blood Pressure  
- FG: Fasting Glucose  
- IS: Insulin Sensitivity  
- HDL chol.: High-Density Lipoprotein Cholesterol  
- BMI: Body Mass Index  
- WC: Waist Circumference  
- SBP: Systolic Blood Pressure  
- DBP: Diastolic Blood Pressure  
- FG: Fasting Glucose  
- MAP: Mean Arterial Pressure.