Maternal body fat and infant body weight influence human milk intake by the infant: A causal inference approach

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Abstract

Background: Several scholars have found an association between maternal body composition and her breast milk output. But, in order to obtain the desired unconfounded effect estimates for this association, knowledge of the underlying causal relationships is necessary, taking into account all possible confounding background variables.

Objective: To explore the causal relationships underlying the association between maternal body composition and breast milk output.

Methods: Data for this study were obtained from a database in which milk intake data was pooled together (188 mother-infant pairs). All studies used the dose-to-the-mother deuterium-oxide turnover method for measuring breast milk transfer from mother to infant. Causal inference search algorithms were used to determine which causal graphs were compatible with the given data.

Results: This exploratory study identified several confounders in the association between maternal body composition and breast milk output, like parity, smoking and education. When decomposing body mass index (BMI) into fat mass index (FMI) and fat free mass index (FFMI), we found that the effect of body composition on milk output is affected by maternal fat mass rather than the mothers' lean mass. In addition, we found that infants with higher body weight consume more milk rather than the other way around.

Conclusion: The use of causal inference techniques on milk intake data revealed that the effect of BMI on milk output is through maternal fat mass. Furthermore, our findings suggest that the infant exercises control over milk output through its body weight rather than that the mother's milk output drives infant growth.

Keywords: Dose-to-the-mother, stable isotope, body composition, breast milk output, causal inference

Introduction

Breast milk intake is highly variable between infants (1). Drivers of milk intake are primarily an infant's lean mass and rate of energy expenditure (2), whether supplemental feedings are given (3-5), and sex (1). In addition to these child-level factors, several maternal factors are underlying this variability (6,7). Findings on the association between maternal overweight and breast milk output have been inconsistent. Analyzing population-mean values from 41 populations, no association was detected between maternal body mass index (BMI) and breast-milk transfer from mother to infant (8). However, individual populations varied as to whether maternal BMI was correlated or not with milk fat content, and several individual studies also reported an association between high levels of maternal fat and decreased breast milk transfer (9,10). Therefore, we still lack understanding of how maternal body composition is associated with breast-milk transfer at the individual level.

The effect of obesity on breastfeeding initiation is through a lower prolactin response to suckling at 48 h post-partum (11) and an apparent delay in lactogenesis II (12). Besides maternal body composition, parity has been associated with breast milk transfer (7,13,14), as well as behavioral and socioeconomic factors such as smoking and educational level (15-18). Some of the above mentioned variables are also known to be associated with maternal body composition. For example, the prevalence of overweight and obesity is considerably higher among people with low socioeconomic status than among people from high socioeconomic background, mainly because of different dietary patterns (19).

To be able to identify the correct set of confounding variables for which correction should take place in order to obtain the desired unconfounded effect estimates for the association between maternal body composition and breast milk intake, knowledge of the underlying causal relationships is necessary, taking into account all possible confounding background variables (20,21). The statistical associations found so far in milk intake studies do not necessarily reflect causal connections, although biological mechanisms help to understand the directions of causation (22). Though not the primary scope of this paper, the analysis also allows for an understanding of the direction of the association between weight of the infant and its milk intake, an association that is still disputed. Do heavier infants drink more milk, or do infants who consume more milk become heavier? In other words, the issue of reverse causality has remained unsolved.

The aim of this study is to explore the causal relationships that underlie the association between maternal body composition and breast milk intake using causal inference search algorithms. Not only can the causal effects between exposure and outcome variables be investigated, but the effect of background variables on both exposure and outcome variables can also be explored, at the same time offering the possibility to distinguish between direct and indirect effects and to detect mediation patterns (23). To our knowledge, the method of causal inference search algorithms combined with structural equation modelling has not been used before in the context of maternal body composition and breast milk intake.

Methods

Data

We used the Milk Intake Meta-Analysis (MIMA) database (1) as a starting point for our analysis and identified relevant variables. The MIMA database consists of pooled milk intake data from 16 studies, all assessing breast milk intake volume by using the deuterium oxide turnover method dose-to-the mother technique. This method has been described previously by Coward et al. (1982) (24) and Haisma et al. (2003) (3). Mother-infants dyads were selected for the current study if data were available for specific maternal and child infant background variables, the independent variables BMI, fat mass index (FMI, i.e. FM normalized for height), fat free mass index (FFMI, i.e. FFM normalised for height), height, and human milk intake as the outcome variable (**table 1**). In the MIMA database, these variables were available from two studies from Brazil (3,25) and one from the UK. We added data from a new study from Colombia (26).

Causal inference search algorithms need a complete case analysis. This resulted in the deletion of 16 cases with missing data points. The final dataset consisted of 188 mother-infant dyads of which 137 were from Brazil, 33 from the UK and 18 from Colombia **(table 2**). Due to methodological requirements, the country variable was transformed into a dichotomous variable in which Brazil and Colombia are combined as one category. We found no difference (at $p<0.05$ level) between these two countries for the variables under study, except for maternal height and smoking.

Causal inference search algorithms

To explore causal relationships between the variables under study, causal inference search algorithms were used in combination with structural equation modelling. Causal inference search algorithms are statistical tools for exploring causal mechanisms based on the theory of causal graphs (23). Causal graphs represent the causal relationship between variables in a model, with vertices denoting variables that are connected with undirected or directed edges (arrows). Search algorithms are used to determine which (classes of) causal graphs are compatible with the given data (27). A short introduction to the theory and concepts of causal graphs and an illustration of the principles of the used algorithms with use of our own data can be found as supplemental material.

To explore the potential causal relationships between the variables, different search algorithms were applied to the data. We used the algorithms CPC (Conservative Peter Clark), JCPC (Joseph Conservative Peter Clark) CFCI (Conservative Fast Causal Inference) and GES (Greedy Equivalent Search) (28). These algorithms differ in the search strategies they use for finding the most plausible causal graphs and on the assumptions they make regarding the data. Similarities found in the graphs resulting from the different algorithms and resulting from varying the measure of strictness with which edges are removed from the searches (alpha levels in the case of CPC, JCPC and CFCI and penalty discounts for GES) underline our confidence in the specific results. By adding background information to the models, the number of possible graphs given by the search algorithms can be limited. Certain effects are ruled out before applying the search algorithms: due to time chronology constraints, infant variables like sex, birth weight, age and weight at the start of the study could not have had - or be highly unlikely - an effect on maternal variables like age, parity, smoking, years of education and body composition. We have also forbidden effects from maternal variables to child variables that are highly unlikely: none of the maternal variables could have an effect on the infant's sex or age.

All mentioned search algorithms were applied to each of the measures of body composition (BMI, FMI, and FFMI) and for height as a measure for maternal somatic capital. The analyses involving search algorithms were done with use of the freeware program TETRAD version 5.1.0-6. Model fit was determined by using the Bayesian information criterion (BIC) score, with the model with the lowest score being indicated as the model having the best fit with the data. This resulted in a best fitting model for each measure of body composition. For these models, structural equation modelling (SEM) was applied to find the values of the regression coefficients and for further investigating of model fit by reporting $\chi2$/df, root mean square error of approximation (RMSEA) and Bentlers comparative fit index (CFI). For this, we used the 'sem' (structural equation models) library in R (29). In general, $\chi2/df < 2$ indicates a good fitting model, as does a root mean square error of approximation (RMSEA) value lower than 0.08 (and preferably lower than 0.05) and a Bentler comparative fit index (CFI) value exceeding 0.9. The null hypothesis tested by the chi-square test states that the population covariance matrix over the measured variables is equal to the covariance matrix of the model.

Results

Model fit

The best model (i.e. the model with the lowest BIC-score) for each of the four measures for maternal body composition (BMI, FMI, FFMI and height) was found by the GES algorithm with penalty discount 0.2. This algorithm assumes among others the true underlying causal graph to be acyclic, all variables involved to be continuous with a joint normal distribution and all causal effects to be linear. Model fit parameters RMSEA and CFI indicate only moderate fit, with best results for the models for height and FFMI. According to $\chi2$/df scores the generated models do not have a good fit with the data. Model fit results are not surprising, as we most likely could not meet all data assumptions (see appendix). However, the algorithms tend to work well for unimodal symmetrical distributions, a criterion which is met by most of our variables.

Body composition and human milk intake

In the BMI model (**figure 1**), we found a direct negative effect of maternal BMI on milk intake. When decomposing BMI into FMI and FFMI, it is found that the direct (negative) effect of body composition on milk intake is only present in the FMI model (**figure 2**). None of the search algorithms that were applied to the data found a direct effect of FFMI on milk intake (**figure 3**), indicating that the direct inverse effect of body composition on milk intake is caused only by the fat mass of the mother, and not by her lean mass. The height of the mother has an indirect effect on human milk intake through several variables (**figure 4**). Firstly, maternal height is positively related to birth weight, which in turn is related to a higher infant weight at the start of the milk intake study. A higher weight of the infant results in a higher chance of being exclusively breastfed during the study period, leading to more breast milk intake.

Smoking and education in relation to human milk intake

In all four models, a direct effect of smoking on milk intake by the infant was found. Infants of mothers who smoke tended to have a significant lower milk intake than infants from non-smoking mothers. Maternal BMI is a mediating factor in the effect of smoking on milk intake. However, the effect of smoking on body composition was found to be reversed in the FMI model and not present at all in the FFMI model. None of the four models showed a direct effect of smoking on whether the infant is exclusively or partially breastfed.

Education of the mother was included in the models as a proxy for socio-economic status and was found to have a confounding effect in the association between maternal body composition (BMI, FMI and FFMI) and breast milk intake by the infant. The effect of education on maternal body composition was mediated through parity: more years of education led to lower parity, which in turn led to lower BMI and FMI. Maternal education also influenced milk intake through a direct negative effect on smoking.

Effect of parity on body composition

A direct effect of parity on body composition was found in the models for BMI, FMI and FFMI. For each of these measures a positive effect of parity was found. Thus, higher parity is associated with higher BMI, resulting from both higher fat mass as well as higher fat free mass. Maternal height was selected as a measure of somatic capital. Height remains fairly fixed over the reproductive lifespan with limited potential to be influenced by prior childbearing or current pregnancy. This is also supported by our findings: no effect of parity on height was found.

Causality between birth weight and milk intake

Results of the causal inference approach can also be derived from comparing the graphs that resulted from different search algorithms with different alpha levels and penalty discounts. Overlapping patterns between the graphs indicate a more prominent and consistent relationship. The patterns that appeared in all our models, regardless of search algorithm, alpha level or penalty discount are effects that have been earlier described in literature. For example, in all models we found a direct negative effect of education on smoking, as well as a negative effect of education on parity. The age of the infant was found to have a direct negative effect on feeding pattern, meaning that the older the infant, the more likely it was to receive partial breastfeeding instead of exclusive breastfeeding. In the overlapping patterns we also found direct effects that were expected, like the positive effect of maternal age on parity and the positive effect of infant age on their weight.

With the 12 variables under study, a hypothetical total of 52 effects in the causal graphs (edges) could have been found taking into account the forbidden effects given to the search algorithms. None of the graphs found by the algorithms showed more than 20 edges, meaning that 32 edges are consistently missing. These missing edges can give an indication of no direct causal effect. This is particularly interesting with regard to the issue of reverse causality in the association between the infant's weight and its milk intake. In this study no direct effect of human milk intake on infant weight was found. In all models in which an association between human milk intake and weight was indicated, the reverse effect was found, indicating a stronger causal effect of infant weight on milk intake than the other way around. We did not find a direct association between maternal BMI, FMI, or FFMI and birth weight indicating that the direct association between birth weight and breast milk intake is not a continuation in infancy of a tendency of heavier mothers to have larger offspring.

Examination of the graphs that have been generated by the CFCI search algorithm can give an indication of the possibility of underlying latent variables. For different p-values, the CFCI algorithm indicates the possibility of the existence of a latent variable having an effect on both maternal BMI/FMI and smoking.

Discussion

This study is the first to explore causal pathways between maternal body composition, human milk intake by the infant and related maternal and infant variables. Even though the generated models have only moderate fit with the data according to the RMSEA and CFI scores, comparing the models can still give valuable insights in exploring the causal associations between body composition and breast milk intake. The four models with the best data fit generated for BMI, FMI, FFMI and height suggest that the effect of maternal body composition on human milk intake is caused by the fat mass of the mother, and not by her lean mass. This result is in line with earlier findings. Rasmussen (30) proposed that having a high fat mass after pregnancy may lead to hormonal abnormalities, resulting in low milk volume. Other studies have linked maternal adiposity with breast-milk fat content (31), hence if the milk were more energy-dense, then a lower volume would be required through a mechanism of self-regulation by the infant (32). Our findings are consistent with a recent review (33) showing that maternal lean mass is the primary predictor of offspring birth weight, whereas declines in maternal skinfolds during lactation indicate fat mass as the primary non-dietary source of breast-milk energy content. The effect of maternal fat mass on milk intake could be due to more practical issues as well. The lower initiation and duration rate of breastfeeding among overweight woman (34) may be due to mechanical problems related with large adipose tissue (35). Poor body image is also mentioned as a risk factor for low breastfeeding rates (36).

The direct negative effect of smoking on milk intake suggests that smoking causes a lower human intake by the infant. According to Hopkinson (37) this negative effect of smoking on breast milk transfer is partly due to lower prolactin levels that are present in smoking women during pregnancy. These hormones are necessary for the initiation of milk production. Additionally, smoking is associated with earlier weaning (17) suggesting that smokers have a certain lifestyle in which the practice of breastfeeding is impeded in several ways. However, in our study we found no clear evidence that smoking causes partial breastfeeding instead of exclusive breastfeeding.

One major advantage of using a causal inference approach is that the directions of associations can be explored. This is particularly interesting when looking at the associations between weight of the infant and milk intake. The association between weight of the infant and the amount of milk intake has been found in several studies, but it is questioned whether higher weight leads to more milk intake, or the other way around (reverse causality). A recent analysis found that both infant lean mass and energy expenditure, but not infant fat mass, were associated with milk intake at 12 weeks, indicating that higher rates of energy utilisation in the infant stimulate appetite for milk (2). Similarly, the direction of the association between weight and milk intake in our models leads consistently from weight to milk intake, either directly or being mediated through feeding pattern. Our findings support the suggestion by Kramer et al (38) as well. Infants who grow more rapidly, thus heavier babies, tend to cry more often from hunger, and will therefore get breastfed more often leading to more milk intake. This fits in the parent-offspring conflict theory as suggested by Wells (39). He explored crying in relation to mother-infant signaling. Since crying costs a lot of calories (40), infants with colic should be thin, or should stop crying to stop being thin. But, colicky babies tend to be plump, indicative of their spare calories that can be spent on crying without damaging their weight gain.

In this exploratory study using a causal inference approach, we identified several confounders in the association between maternal body composition and breast milk output, including parity, smoking and education. When decomposing BMI into FMI and FFMI, we found that the effect of body composition on milk output is likely to be caused by maternal fat mas and not by the mothers' lean mass. We also were able to shed light on the direction of the association between infant weight and breast milk volume and found that infants with higher body weight consume more milk rather than the other way around.

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Figure legends

Figure 1

The causal graph with the best model fit for the association between BMI and breast milk intake. The graph represents the equivalence class of causal models found as a result of the GES search algorithm with penalty discount of 0.2. Each arrow is accompanied by a number, representing the estimated regression weight. These numbers reflect the (positive or negative) size of the causal effect per unit change.

Figure 2

The causal graph with the best model fit for the association between FMI and breast milk intake. The graph represents the equivalence class of causal models found as a result of the GES search algorithm with penalty discount of 0.2. Each arrow is accompanied by a number, representing the estimated regression weight. These numbers reflect the (positive or negative) size of the causal effect per unit change.

Figure 3

The causal graph with the best model fit for the association between FFMI and breast milk intake. The graph represents the equivalence class of causal models found as a result of the GES search algorithm with penalty discount of 0.2. Each arrow is accompanied by a number, representing the estimated regression weight. These numbers reflect the (positive or negative) size of the causal effect per unit change.

Figure 4

The causal graph with the best model fit for the association between maternal height and breast milk intake. The graph represents the equivalence class of causal models found as a result of the GES search algorithm with penalty discount of 0.2. Each arrow is accompanied by a number, representing the estimated regression weight. These numbers reflect the (positive or negative) size of the causal effect per unit change.

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Statement of authors' contributions to manuscript

FH and HH designed the study; SE, MF, HH GOV and JW provided data; TC constructed the MIMA database; SBG and FH performed statistical analyses and interpreted results; FH, HH and SBG wrote the paper. JW, TC, MF, SE and GOV provided feedback on the draft paper. HH and SBG have primary responsibility for its final content. All authors have read and approved the final manuscript.

Data availability

Data are stored at the file-protected data repository of the Faculty of Spatial Sciences; additional data are available on reasonable request.

Conflict of interest

The authors have no conflict of interest to declare.

Figures

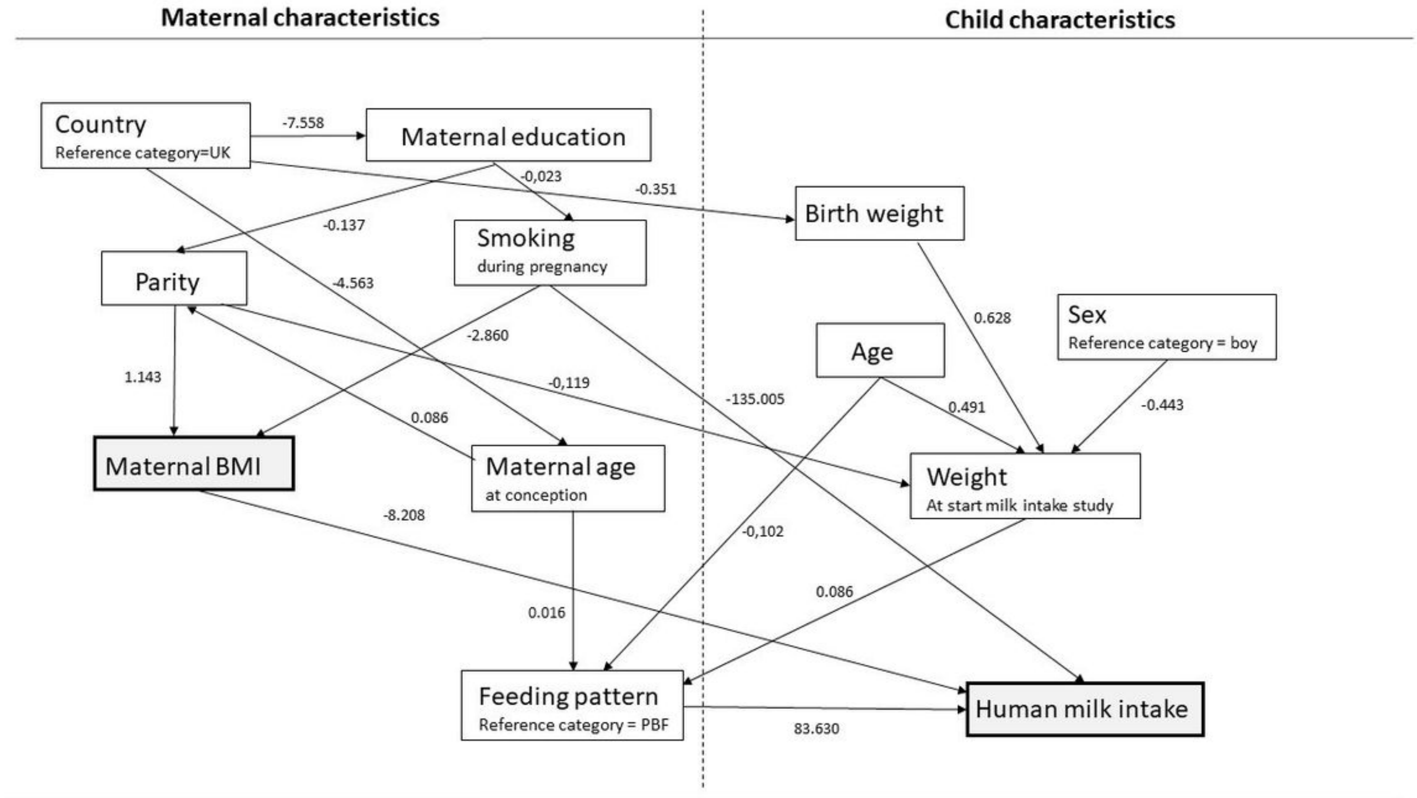

Figure 1

The causal graph with the best model fit for the association between BMI and breast milk intake. The graph represents the equivalence class of causal models found as a result of the GES search algorithm with penalty discount of 0.2. Each arrow is accompanied by a number, representing the estimated regression weight. These numbers reflect the (positive or negative) size of the causal effect per unit change.

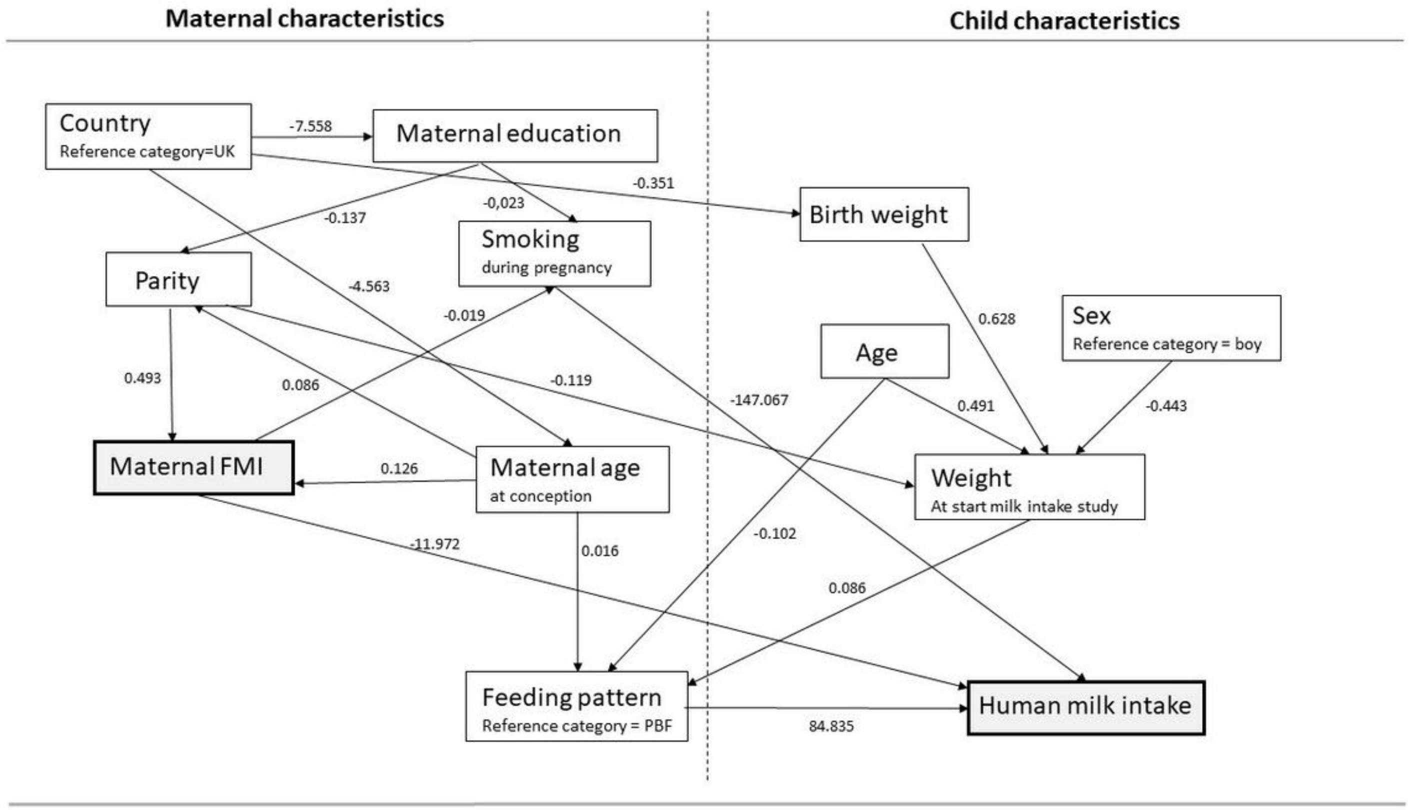

Figure 2

The causal graph with the best model fit for the association between FMI and breast milk intake. The graph represents the equivalence class of causal models found as a result of the GES search algorithm with penalty discount of 0.2. Each arrow is accompanied by a number, representing the estimated regression weight. These numbers reflect the (positive or negative) size of the causal effect per unit change.

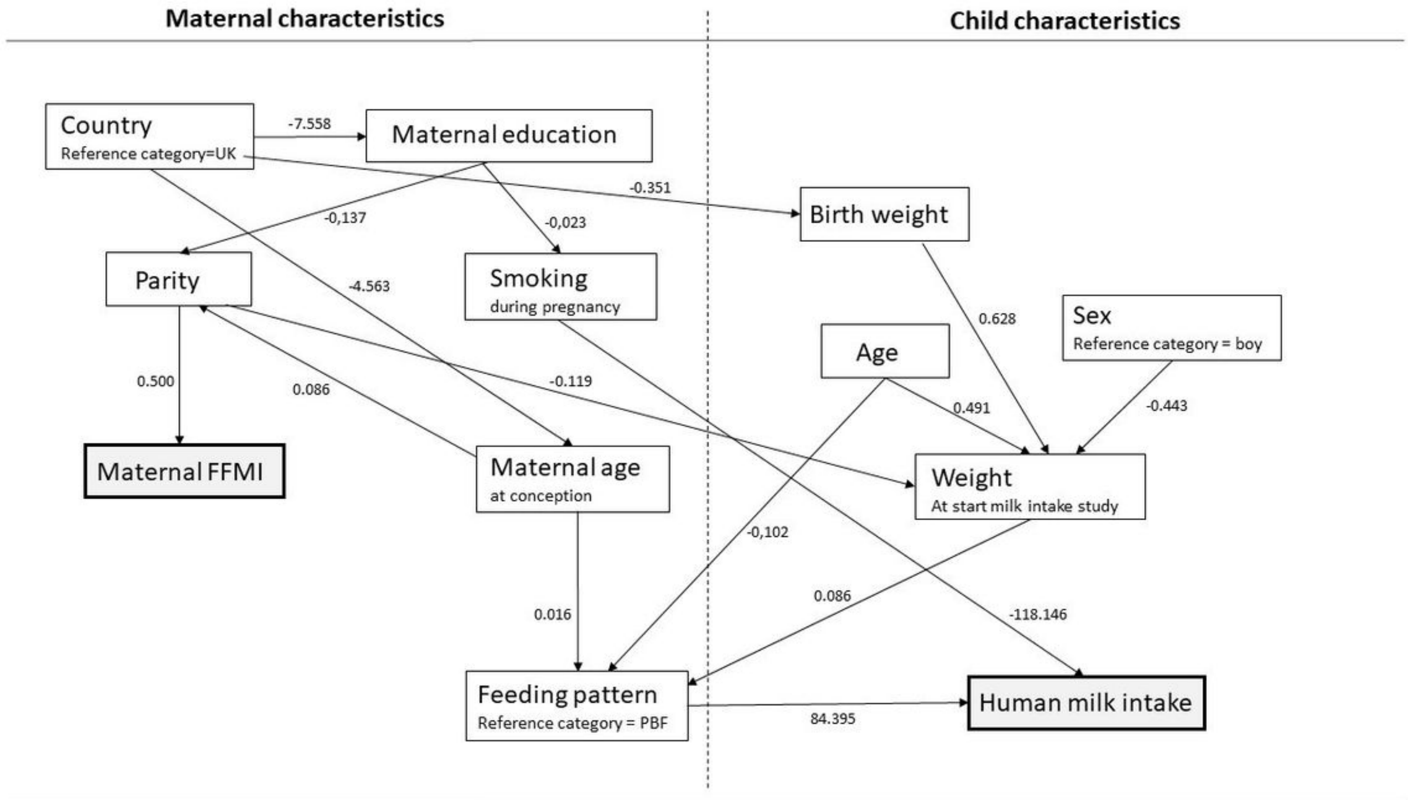

Figure 3

The causal graph with the best model fit for the association between FFMI and breast milk intake. The graph represents the equivalence class of causal models found as a result of the GES search algorithm with penalty discount of 0.2. Each arrow is accompanied by a number, representing the estimated regression weight. These numbers reflect the (positive or negative) size of the causal effect per unit change.

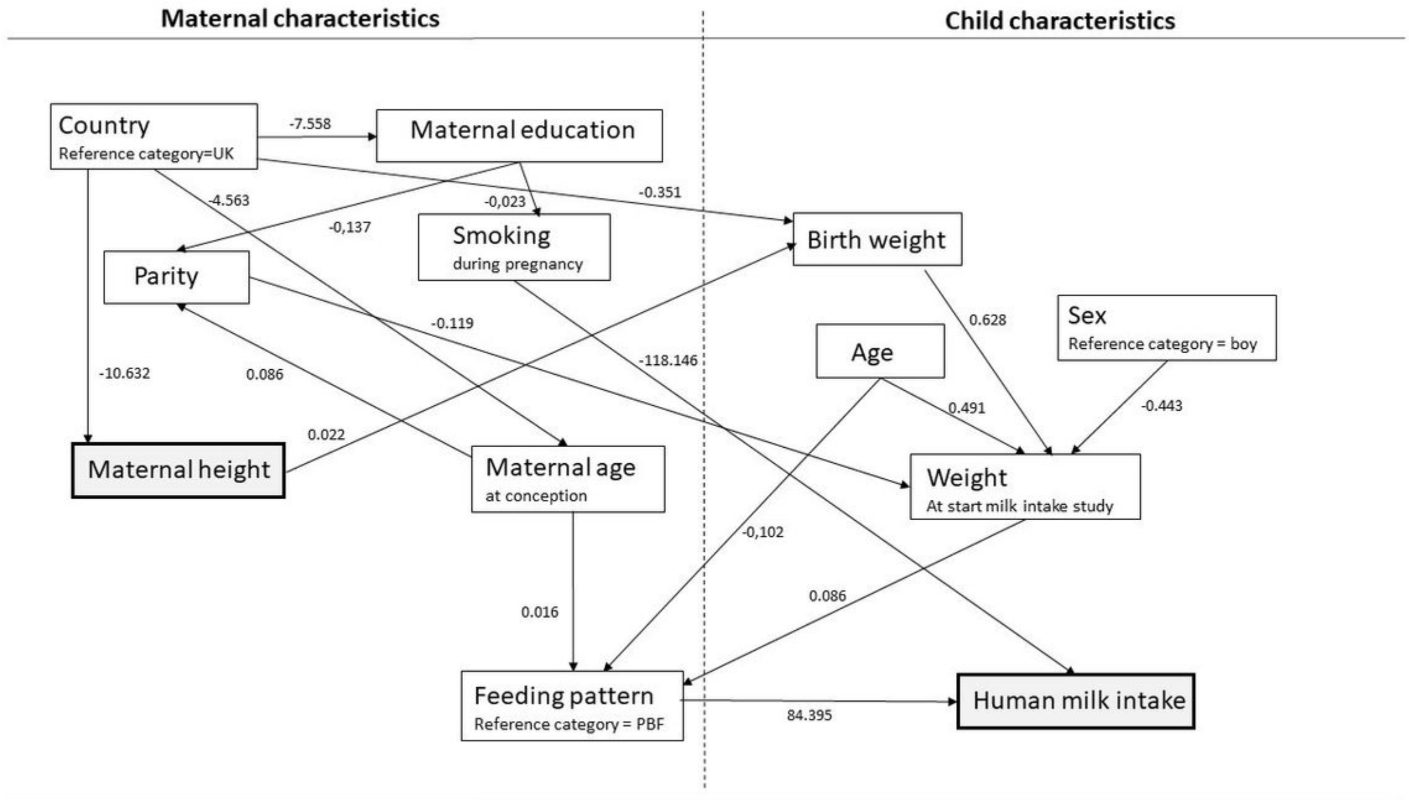

Figure 4

The causal graph with the best model fit for the association between maternal height and breast milk intake. The graph represents the equivalence class of causal models found as a result of the GES search algorithm with penalty discount of 0.2. Each arrow is accompanied by a number, representing the estimated regression weight. These numbers reflect the (positive or negative) size of the causal effect per unit change.