

1 **Consequences of prenatal geophagy on maternal prenatal health, risk of childhood geophagy and**  
2 **child psychomotor development**

3 Michael O Mireku<sup>1,2</sup>, Leslie L Davidson<sup>3</sup>, Romeo Zoumenou<sup>4</sup>, Achille Massougbdji<sup>4</sup>, Michel Cot<sup>2,5</sup>,  
4 Florence Bodeau-Livinec<sup>6,7</sup>

5 **Affiliations :** <sup>1</sup> University of Lincoln, School of Psychology, Lincoln, UK; <sup>2</sup> Institut de Recherche pour le  
6 Développement (IRD), Mère et Enfant Face aux Infections Tropicales, Paris, France; <sup>3</sup> Columbia  
7 University, Mailman School of Public Health and the College of Physicians and Surgeons, NY, USA;  
8 <sup>4</sup> Université d'Abomey-Calavi, Faculté des Sciences de la Santé, Cotonou, Bénin; <sup>5</sup> PRES Sorbonne Paris  
9 Cité, Université Paris Descartes, Faculté des Sciences Pharmaceutiques et Biologiques, Paris, France; <sup>6</sup>  
10 Ecole des Hautes Etudes en Santé Publique, Département Méthodes quantitatives en santé publique,  
11 Rennes, France; <sup>7</sup>Inserm UMR 1153, Obstetrical, Perinatal and Pediatric Epidemiology Research Team  
12 (Epopé), Center for Epidemiology and Statistics Sorbonne Paris Cité, DHU Risks in Pregnancy, Paris  
13 Descartes University, Paris, France.

14 **Address correspondence to:** Michael Osei Mireku, School of Psychology, University of Lincoln. Sarah  
15 Swift Building, Brayford Wharf East. Lincoln, LN5 7AY

16 Tel: +44 (0)1522 825807

17 Email: [mmireku@lincoln.ac.uk](mailto:mmireku@lincoln.ac.uk)

18 **Short title:** Prenatal geophagy, maternal health and child development

19 **Acknowledgements:** The authors sincerely thank the mothers and children who participated in this study.  
20 We also thank the staff of the three health centers (Allada, Atogon, Sékou), Dr. Smaila Ouédraogo, Dr.  
21 Manfred Accrombessi, Dr. Ghislain Koura and the entire *Tovi* and *MiPPAD* field personnel who were  
22 involved in data collection.

23 **Source of funding:** The Eunice Kennedy Shriver National Institute of Child Health & Human  
24 Development (NIH/NICHHD) funded The TOVI study, grant R21-HD060524. The MiPPAD trial  
25 (NCT00811421- <https://clinicaltrials.gov/ct2/show/NCT00811421>) was co-funded by the European and  
26 Developing Countries Clinical Trials Partnership (EDCTP- IP.07.31080.002). The opinions represented  
27 here are the sole responsibility of the authors and do not necessarily represent the official views of the  
28 funders.  
29

30 **Conflict of Interest Statement:** The authors have no conflict of interest to disclose.

31 Word count: Abstract - 246 Main body - 3205

32

33

34

35

36 **Abstract**

37 Objective: To investigate the relationship between prenatal geophagy, maternal prenatal haematological  
38 indices, malaria, helminth infections and cognitive and motor development among offspring.

39 Methods: At least a year after delivery, 552 out of 863 HIV-negative mothers with singleton births who  
40 completed a clinical trial comparing the efficacy of sulfadoxine-pyrimethamine and mefloquine during  
41 pregnancy in Allada, Benin, responded to a nutrition questionnaire including their geophagous habits  
42 during pregnancy. During the clinical trial, helminth infection, malaria, haemoglobin and ferritin  
43 concentrations were assessed at first and second antenatal care visits (ANV), and at delivery. After the first  
44 ANV, women were administered daily iron and folic acid supplements until three post-delivery. Singleton  
45 children were assessed for cognitive function at age one year using the Mullen Scales of Early Learning.

46 Results: The prevalence of geophagy during pregnancy was 31.9%. Pregnant women reporting geophagy  
47 were more likely to be anaemic (adjusted odds ratio, AOR= 1.9, 95% Confidence interval, CI [1.1, 3.4])  
48 at their first ANV if they reported geophagy at the first trimester. Overall, prenatal geophagy was not  
49 associated with maternal haematological indices, malaria or helminth infections, but geophagy during the  
50 third trimester and throughout pregnancy was associated with poor motor function (AOR= -3.8, 95% CI [-  
51 6.9, -0.6]) and increased odds of geophagous behaviour in early childhood, respectively.

52 Conclusions: Prenatal geophagy is not associated with haematological indices in the presence of  
53 micronutrient supplementation. However, it may be associated with poor child motor function and infant  
54 geophagy. Geophagy should be screened early in pregnancy.

55

56 Keywords: geophagy; pica; anaemia; pregnancy; iron deficiency; child development.

57

58

59

60

61

62

63

64

65

66

## 67 **Introduction**

68 Maternal, neonatal and child health has taken centre stage in the policies of several health  
69 systems around the world especially in developing countries where maternal and infant  
70 mortalities are highest [1]. In Africa, the drive towards improving maternal and child health has  
71 been steered by the millennium development goals (MDGs) 4 and 5: to reduce by two thirds,  
72 between 1990 and 2015, the under-five mortality rate and within this same period, to reduce by  
73 three quarters the maternal mortality ratio, respectively [2]. This agenda is currently being  
74 furthered by the Strategic Development Goals to reduce global maternal deaths to 70 per 100,000  
75 live births [3]. Notwithstanding the several interventions aimed at reducing maternal and child  
76 morbidity and eventual mortality, and the strides made by these interventions, very little  
77 attention has been paid to nutritional habits of pregnant women, particularly, pica practices, that  
78 could expose them and their offspring to adverse consequences.

79 Pica is the persistent craving and consumption of substances deemed non-nutritive by the  
80 consumer [4]. Common forms of pica include pagophagy (compulsive consumption of ice or  
81 freezer frosts), amylophagy (compulsive consumption of purified starch) and geophagy  
82 (compulsive consumption of earth, dirt or clay) [5]. The practice which has existed since the  
83 days of Hippocrates (460-370 BC) still persists in many parts of the world [6]. Geophagy in  
84 pregnancy has been reported even in some developed countries, mostly among minority groups  
85 in the United States [7]. The global prevalence of geophagy remains unknown but a recent meta-  
86 analysis estimated the global prevalence of prenatal maternal and postpartum pica to be 27.8%  
87 [8]. The Africa region was reported to have the highest prevalence of over 40% [8]. These  
88 regional and global estimates however only reflect the very limited studies on the subject and are  
89 likely to be an underestimation of the true prevalence.

90 Considering that geophagy and other forms of pica are common among pregnant women who are  
91 among the most vulnerable to environmental exposures, it is essential to understand the health  
92 and developmental consequences associated with the practice. The mystery surrounding  
93 geophagy in pregnancy is that even after millenniums of persistent practice, very little is  
94 understood on the causes and potential consequences on maternal health, immediate birth  
95 outcomes and later child health and development. Results from the few published studies on the  
96 subject report ambivalent findings with some reporting potential consequences due to mercury

97 poisoning [9], exposure to metals such as cadmium, copper, manganese, arsenic [10, 11], soil-  
98 transmitted helminth (STH) infections (*A. lumbricoides*) [12] and reduced haemoglobin and  
99 ferritin concentrations [13].

100 As a secondary data analysis to the *Tovi* study which sought to investigate the impact of prenatal  
101 maternal anaemia on early child cognitive development, this paper assesses the relationship  
102 between geophagy in pregnancy and maternal anaemia, iron deficiency (ID), malaria and  
103 helminth infections, birth outcomes and, in the child, geophagy practices and cognitive and  
104 motor development.

## 105 **Methods**

106 Approximately one year after their children were born, mothers in the *Tovi* study who had [14]  
107 singleton births in Allada, Benin, were asked to respond to a Supplementary Nutrition  
108 Questionnaire (SNQ) on their eating habits during pregnancy. The SNQ was initially designed to  
109 investigate the sources of high blood lead levels observed in some of the children and mothers  
110 and the details are explained elsewhere [15]. As part of the SNQ, mothers responded to questions  
111 on geophagy practices during pregnancy as well as the nutrition and geophageous behaviour of  
112 their children. Mothers were asked about consuming processed clay (*kalaba* or kaolin, both of  
113 which are kaolinite soils) or earth during pregnancy, which are three common soil-types  
114 consumed by pregnant women in the region. In addition mothers indicated, to the best of their  
115 knowledge, which trimester in pregnancy, they practiced geophagy. Women were said to be  
116 geophageous if they consumed any of these three soil types during pregnancy. Women were  
117 considered to practice *polygeophagy* if they consumed two or more of these soil types during  
118 pregnancy.

119 Mothers enrolled in this retrospective nutritional survey were HIV negative and had participated  
120 in a clinical trial during pregnancy, called *Malaria in Pregnancy Preventive Alternative Drugs*  
121 (MiPPAD) (NCT00811421), which compared the efficacy of two intermittent preventive  
122 treatments for malaria in pregnancy (IPTp). The pregnant women were recruited into the clinical  
123 trial if they were at most 28 weeks pregnant, HIV negative and attending antenatal care visit  
124 (ANV) for the first time. Inclusion criteria into the trial included no prior intake of iron, folic  
125 acid or vitamin B12 supplements during pregnancy. Detailed inclusion and exclusion criteria for  
126 the MiPPAD clinical trial have been published elsewhere [16].

127 At first ANV, sociodemographic and anthropometric data, and gravidity of pregnant women  
128 were recorded. Pre-pregnancy body mass index (BMI) in  $\text{kg/m}^2$  was calculated from BMI and  
129 gestational age at 1<sup>st</sup> ANV using the technique presented in an earlier publication [17]. At each  
130 of the three visits, blood and stool samples were taken for clinical assessments. Venous blood  
131 samples were taken for assessment of haemoglobin (Hb) concentration, serum ferritin  
132 concentration and plasmodium parasitemia. Stool samples were taken to determine the presence  
133 of helminth eggs using the Kato-Katz technique [18]. C-reactive protein (CRP) concentrations  
134 were measured to correct for high ferritin concentrations in participants with inflammations.

135 During the MiPPAD clinical trial, at the first ANV all women were administered anthelmintic if  
136 they were in the second trimester of pregnancy following the guidelines of the Beninese Ministry  
137 of Health. In addition, throughout pregnancy women were administered daily iron (200 mg oral  
138 ferrous sulphate) and folic acid (5 mg daily) supplements until three months after delivery.  
139 Women were treated when sick. Iron, folate and medicines for treating illness were provided to  
140 pregnant women free of charge. The direct intake of supplements was not monitored.

141 Anaemia was defined as Hb less than 110 g/l [19]. Helminth infection was defined as the  
142 presence of at least one egg of any intestinal helminth per gram of stool. Iron deficiency was  
143 defined as serum ferritin concentration less than  $12\mu\text{g/l}$  or serum ferritin between  $12\mu\text{g/l}$  and  $70$   
144  $\mu\text{g/l}$  when CRP concentration was greater than  $5\text{mg/L}$  [20].

145 Gender, weight and gestational age (using fundal height) of the new-born were determined at  
146 birth. Low birth weight (LBW) and preterm birth were defined as less than 2500 g and less than  
147 37 weeks of gestation, respectively. At age one year, cognitive and motor functions of the  
148 children were assessed by a trained nurse using the Mullen Scales of Early Learning (MSEL)[21]  
149 was adapted for this setting [22]. The MSEL consists of five scales: Gross Motor (GM) scale,  
150 Fine Motor (FM) scale, Receptive Language (RL) scale, Expressive Language (EL) scale and  
151 Visual Perception (VP) scale. Crude score for each MSEL scale was transformed into normalised  
152 scores called the *T*-scores by using a standardised table with the child's chronological age at  
153 assessment. The age-standardised *T*-scores of the FM, EL, RL and VP were combined to form  
154 the ELC score.

155 Within three days after the MSEL assessments, a different nurse conducted home visits during  
156 which mothers responded to questionnaires on family possessions, the home environment using

157 the Home Observatory Measurement of the Environment (HOME) inventory [23], postnatal  
158 depression using Edinburgh Postnatal Depression Scale [24] and maternal postnatal intelligent  
159 quotient (IQ) using Raven's Progressive Matrices test [25]. The second nurse was blind to the  
160 MSEL results of the child.

#### 161 *Ethical consideration*

162 Informed consent was sought from all women in the presence of a witness at recruitment into the  
163 clinical trial. Women provided thumbprints to confirm their agreement to participate in the study  
164 if they who could not read and write, after it has been explained to them in a local language. The  
165 *Tovi* study was approved by the institutional review boards of the University of Abomey-Calavi  
166 in Benin and New York University in USA and the Research Institute for Development's (IRD)  
167 Consultative Ethics Committee in France.

#### 168 *Statistical analyses*

169 First we compared and described maternal baseline characteristics during pregnancy and child  
170 characteristics at birth between mothers who responded to the SNQ and those who did not  
171 respond. We also described the prevalence of geophagy among pregnant women and their  
172 offspring. Then we assessed the relationship between mother-child sociodemographic  
173 characteristics and geophagy during pregnancy.

174 Using unconditional logistic regression, we compared the odds of the major maternal outcome  
175 variables of interest i.e. anaemia, ID, malaria and helminth infection, at baseline between women  
176 who practiced geophagy during the first trimester and those who were not geophageous at the  
177 first trimester. Next, since the major maternal outcome variables of interest were assessed  
178 repeatedly at different ANVs over the course of pregnancy, mixed effect models were used to  
179 explain the effect of geophagy on the proposed outcomes. Specifically, random intercept was  
180 applied at the individual level in all models. Then we compared the model with the random slope  
181 at gestational age and random intercept at the individual level to the model with the model with  
182 only the random intercept using the likelihood ratio (LR) test. Where the LR test showed  
183 significant difference between the models, the model with the random slope was used. Individual  
184 level predictors included in the model were level of education, pre-pregnancy BMI, maternal  
185 gestational age, gravidity, age at first ANV, family possession and maternal IQ.

186 In assessing the consequences of prenatal maternal geophagy on adverse birth outcomes and  
187 child development, unconditional logistic regression models were used. For continuous  
188 outcomes, multiple linear regressions were used. Stepwise removal of covariates was used to  
189 deselect covariates whose P-values were more than 0.05 in the adjusted model with the exception  
190 of ID at the period of follow-up.

191 All statistical analyses were conducted using Stata IC/14.1 (StataCorp Lp, College station, TX).

## 192 **Results**

193 Of the 828 eligible mothers-child pairs, 552 (66.7%) responded to the SNQ of the *Tovi* study  
194 (Figure 1). Mothers who responded to SNQ had at baseline entry into the clinical trial, lower  
195 BMI, lower prevalence of ID, high prevalence of malaria and were more likely to be housewives  
196 compared to non-respondents. Child characteristics at birth were similar among respondent and  
197 non-respondent mothers (Table 1).

198 The prevalence of geophagy in pregnancy (i.e. geophagy during at least one trimester) was  
199 31.9%. The majority of geophageous pregnant women preferred processed clay (*kalaba* or  
200 kaolin) to earth (Supplementary Table 1). The prevalence of geophagy was highest during  
201 second trimester (21.4%). Forty-five (54.2%) of the geophageous pregnant women at first  
202 trimester remained geophageous during second trimester. *Polygeophagy* was rare among  
203 pregnant women and no pregnant woman consumed all three soil-types. About half of one-year-  
204 old children were reported to be geophageous by their mothers, of whom 37.6% were  
205 geophageous during pregnancy.

206 Among pregnant women who practiced geophagy during the second trimester, the proportions of  
207 housewives were significantly higher compared to those who were employed (Supplementary  
208 Table 2). Pregnant women who practice geophagy during the first trimester were more likely to  
209 be anaemic, adjusted odds ratio (AOR) =1.9, 95% confidence interval, CI [1.1, 3.4], and less  
210 likely to have malaria, AOR = 0.4, 95% CI [0.2, 0.9] at their first ANV compared to those who  
211 did not practice geophagy during the first trimester (Table 2). Geophagy in pregnancy was not  
212 associated with maternal haematological indices, malaria or helminth infections during  
213 pregnancy in the multilevel analysis (Table 3).

214 As shown in Table 4, children were more likely to be geophageous at age one year if their  
215 mothers had practiced geophagy at any trimester during pregnancy ( $P$ -value<0.05). Children of  
216 mothers who practiced geophagy during the third trimester had 3.8 [95% CI: 0.6, 6.9] lower GM  
217 function at age one year compared to those whose mothers did not practice geophagy during the  
218 third trimester in the adjusted model (adjusted for gravidity, maternal education, HOME score,  
219 prenatal maternal ID at delivery).

## 220 **Discussion**

221 The findings of this study show that pregnant women who practiced geophagy during the first  
222 trimester were more likely to be anaemic at their first ANV compared to those who did not  
223 practice geophagy. Our study however does not show any later increased risk of anaemia, or risk  
224 of ID, malaria and helminth infection over the course of pregnancy between pregnant women  
225 who practiced geophagy and those who did not practice geophagy. The study further reveals that  
226 geophagy in pregnancy is associated with increased risk of geophagy in children, and poor child  
227 gross motor function (for geophagy in the third trimester).

228 The prevalence of geophagy during pregnancy in this study population is similar to that reported  
229 by Mensah et al [26] among pregnant women in Ghana (31.9%). Although geophagy is thought  
230 to be a practice common among people of low socioeconomic status, geophagy was not  
231 associated with socioeconomic factors of pregnant women in both the study in Ghana and in our  
232 study. Many other studies also found no association between the prevalence of geophagy and  
233 sociodemographic factors [12, 27].

234 The observed association between prenatal maternal geophagy and increased odds of anaemia  
235 and was associated with an increased risk of anaemia at the first ANV as shown by some cross-  
236 sectional studies [28, 29]. Although higher odds of ID at first ANV was observed among  
237 geophageous pregnant women, the association was not statistically significant. On the contrary,  
238 geophagy during the first trimester was associated with reduced odds of malaria at first ANV. A  
239 study among the same population in Benin showed that a high iron concentration in pregnancy is  
240 associated with an increased risk for malaria and plasmodium parasitaemia.[30] This may  
241 explain the reduced likelihood of malaria at first ANV among pregnant women who practiced  
242 geophagy during the first trimester although adjusting for ID did not change the strength of the  
243 association. We did not find an increased risk of anaemia and iron deficiency in any trimester

244 among geophageous pregnant women, similar to what has been reported in a study with similar  
245 longitudinal data [12]. The administration of IFA supplements, IPTp and anthelmintic following  
246 the first ANV may have reduced the impact that geophagy in itself had on maternal health  
247 outcomes. Daily iron supplementation beginning at first ANV did not attenuate the prevalence of  
248 geophagy among pregnant women during the second and third trimesters similar to what was  
249 found in randomized control trial in children in Zambia [31]. On the contrary, the prevalence of  
250 geophagy was highest during the second trimester with 18% of pregnant women who did not  
251 practice geophagy during the first trimester, becoming geophageous by the second trimester. In  
252 our study population, hookworms were the most prevalent species of soil-transmitted helminths  
253 [32]. The most common mode of transmission of hookworms in our population maybe likely to  
254 be by cutaneous penetration relative to ingestion and this might explain the lack of association  
255 observed between geophagy and helminth infection during pregnancy. In addition, pregnant  
256 women in Allada, Benin preferred processed and dried clay (*kalaba* or kaolin) to earth. The  
257 processed clay is usually cooked and dried to get rid of moisture hence it is less likely to contain  
258 helminth eggs compared to earth.

259 In terms of birth outcomes and child development, results from our study showed that geophagy,  
260 regardless of the trimester, was not associated with preterm birth similar to the findings of a  
261 study conducted in Texas [33]. Geophagy at specific trimesters were consistently not associated  
262 with increased risk of LBW similar to the results found by some studies that assessed geophagy  
263 or pica at only one time during pregnancy [33, 34]. Geophagy at all trimesters of pregnancy was  
264 associated with increased risk of geophagy in children. Although the biological mechanism for  
265 such an association is unknown, mothers who reported that they practiced geophagy may have  
266 been forthcoming reporting about geophagy practice by their children compared to those who  
267 concealed the practice. Also, children whose mothers practiced geophagy in the third trimester of  
268 pregnancy performed poorer on GM scales compared to those whose mothers did not practice  
269 geophagy in this trimester. The biological explanation for this observed relationship is unknown.  
270 Even though we have shown in previous research that low prenatal Hb levels is associated with  
271 poor GM function of children [14], in the current study, prenatal geophagy was not associated  
272 with increased risk of anaemia or ID during pregnancy. The observed mean difference in GM  
273 scores is approximately 80% of that observed between at-risk autistic and low-risk 14-month-old

274 children [35]. However, this represents 0.38 of the standard deviation of the population mean  
275 GM score and thus unlikely to be clinically significant.

276 The biological significance of geophagy remains controversial even though the practice of  
277 geophagy and other forms of pica during pregnancy appears to be common in sub-Saharan  
278 Africa. A recent comprehensive review on pica in pregnancy[36] acknowledges the controversy  
279 in the findings from existing published studies. This aforementioned review attributes the  
280 controversy to a number of problems including underreporting, inadequate study design (mainly,  
281 cross-sectional), and chanced discovery of geophagy by researchers. These problems inhibit the  
282 determination of temporality between geophagy and its risk factors or consequences.

283 To our knowledge, this study is the first to assess the consequences of prenatal maternal  
284 geophagy not only on maternal health and birth outcomes but also on child development and  
285 geophagy habits using a longitudinal data. Also, the use of multilevel analysis in assessing the  
286 association between geophagy and factors of maternal health allowed us to account for the intra-  
287 person variability due to the repeated measurements obtained over the course of pregnancy.

288 Our study is however limited in the retrospective assessment of geophagy in pregnancy which  
289 could have led to recall bias in the assessment of exposure among respondents. This also did not  
290 allow us to assess the quantity and frequency of soil consumption during the period of  
291 assessment as well as the physicochemical properties of the type of soil they consumed. Certain  
292 types of geophagous clay soils have been shown to have therapeutic effect particularly on the  
293 skin and the gastrointestinal tract due to their adsorptive properties and their ability to regulate  
294 the viscosity and flow of mucus in the intestinal tract [37, 38]. Considering the therapeutic  
295 properties of some geophagous soils, the ability to geochemically differentiate between *kalaba*  
296 or kaolin or earth could have added more information to this study. Also, the absence of data on  
297 the frequency of consumption did not permit the investigation of potential dose-response  
298 relationship between prenatal geophagy and the maternal and child health outcomes considered  
299 in this study. Further, maternal baseline characteristics were similar between mothers who  
300 responded to the SNQ and those who did not except for BMI, occupation, malaria and iron  
301 deficiency hence we cannot rule out the possibility of non-response bias in this study although it  
302 is unlikely that mothers refused participate in the study because of their BMI during their first

303 ANV. Housewives were however easier to find during follow-up data collection in the field  
304 compared to the employed mothers.

305

### 306 **Conclusion**

307 The findings of our study suggest that women who practice geophagy in pregnancy during the  
308 first trimester of pregnancy are more likely to be anaemic at their first ANV. However, geophagy  
309 in pregnancy is not associated with increased risk of malaria, helminth, ID or anaemia over the  
310 course of pregnancy. Further, geophagy in pregnancy increases the risk of geophagy in children  
311 and may lead to poor motor function of infants. Pregnant women should be informed about the  
312 potential consequences of geophagy in pregnancy. Also, health care providers should elucidate  
313 maternal geophagy early in pregnancy to prevent potential consequences.

### 314 **References**

315 [1] Partnership for Maternal, Newborn & Child Health and WHO. *Guide for Implementing*  
316 *Essential Interventions for Reproductive, Maternal, Newborn and Child Health (RMNCH): A*  
317 *Multisectoral Policy Compendium for RMNCH*. Geneva: World Health Organisation., 2014.

318 [2] United Nations. *The Millennium Development Goals Report 2015*. New York: United  
319 Nations, 2015.

320 [3] *Progress towards the Sustainable Development Goals*. Report of the Secretary - General  
321 E/2017/66, United Nations, 2017.

322 [4] World Health Organization. *The ICD-10 Classification of Mental and Behavioural*  
323 *Disorders: Clinical descriptions and diagnostic guidelines*. Geneva: World Health Organization,  
324 1992.

325 [5] Young SL. Pica in Pregnancy: New Ideas About an Old Condition. *Annu Rev Nutr* 2010;  
326 30: 403–422.

327 [6] Hippocrates, Littré MPE. *Oeuvres complètes d'Hippocrates*. Baillière, 1853.

328 [7] Lin JW, Temple L, Trujillo C, et al. Pica during pregnancy among Mexican-born women:  
329 a formative study. *Matern Child Nutr* 2015; 11: 550–558.

330 [8] Fawcett EJ, Fawcett JM, Mazmanian D. A meta- analysis of the worldwide prevalence of  
331 pica during pregnancy and the postpartum period. *Int J Gynecol Obstet* 2016; 133: 277–283.

- 332 [9] Rajae M, Long RN, Renne EP, et al. Mercury Exposure Assessment and Spatial  
333 Distribution in A Ghanaian Small-Scale Gold Mining Community. *Int J Environ Res Public*  
334 *Health* 2015; 12: 10755.
- 335 [10] Nyanza EC, Joseph M, Premji SS, et al. Geophagy practices and the content of chemical  
336 elements in the soil eaten by pregnant women in artisanal and small scale gold mining  
337 communities in Tanzania. *BMC Pregnancy Childbirth* 2014; 14: 144.
- 338 [11] Kutalek R, Wewalka G, Gundacker C, et al. Geophagy and potential health implications:  
339 geohelminths, microbes and heavy metals. *Trans R Soc Trop Med Hyg* 2010; 104: 787–795.
- 340 [12] Kawai K, Saathoff E, Antelman G, et al. Geophagy (Soil-eating) in Relation to Anemia  
341 and Helminth Infection among HIV–Infected Pregnant Women in Tanzania. *Am J Trop Med Hyg*  
342 2009; 80: 36–43.
- 343 [13] Geissler PW, Prince RJ, Levene M, et al. Perceptions of soil-eating and anaemia among  
344 pregnant women on the Kenyan coast. *Soc Sci Med* 1999; 48: 1069–1079.
- 345 [14] Mireku MO, Davidson LL, Koura GK, et al. Prenatal Hemoglobin Levels and Early  
346 Cognitive and Motor Functions of One-Year-Old Children. *Pediatrics* 2015; peds.2015-0491.
- 347 [15] Bodeau-Livinec F, Glorennec P, Cot M, et al. Elevated Blood Lead Levels in Infants and  
348 Mothers in Benin and Potential Sources of Exposure. *Int J Environ Res Public Health* 2016; 13:  
349 316.
- 350 [16] González R, Desai M, Macete E, et al. Intermittent Preventive Treatment of Malaria in  
351 Pregnancy with Mefloquine in HIV-Infected Women Receiving Cotrimoxazole Prophylaxis: A  
352 Multicenter Randomized Placebo-Controlled Trial. *PLoS Med* 2014; 11: e1001735.
- 353 [17] Ouédraogo S, Koura GK, Accrombessi MMK, et al. Maternal anemia at first antenatal  
354 visit: prevalence and risk factors in a malaria-endemic area in Benin. *Am J Trop Med Hyg* 2012;  
355 87: 418–424.
- 356 [18] Tarafder MR, Carabin H, Joseph L, et al. Estimating the sensitivity and specificity of  
357 Kato-Katz stool examination technique for detection of hookworms, *Ascaris lumbricoides* and  
358 *Trichuris trichiura* infections in humans in the absence of a ‘gold standard’. *Int J Parasitol* 2010;  
359 40: 399–404.
- 360 [19] *Worldwide prevalence of anaemia 1993–2005: WHO Global database on anaemia.*  
361 Geneva: World Health Organization, 2008.
- 362 [20] Ouédraogo S, Koura GK, Bodeau-Livinec F, et al. Maternal Anemia in Pregnancy:  
363 Assessing the Effect of Routine Preventive Measures in a Malaria-Endemic Area. *Am J Trop*  
364 *Med Hyg* 2013; 12-0195.
- 365 [21] Mullen EM. *Mullen Scales of Early Learning: AGS Edition.* Circle Pines, Minnesota:  
366 American Guidance Service, 1995.

- 367 [22] Koura KG, Boivin MJ, Davidson LL, et al. Usefulness of Child Development Assessments  
368 for Low-Resource Settings in Francophone Africa. *J Dev Behav Pediatr JDBP*. Epub ahead of  
369 print 29 July 2013. DOI: 10.1097/DBP.0b013e31829d211c.
- 370 [23] Caldwell BM, Bradley RH. *Home Inventory Administration Manual*. University of  
371 Arkansas for Medical Sciences, 2001.
- 372 [24] Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression. Development of the  
373 10-item Edinburgh Postnatal Depression Scale. *Br J Psychiatry J Ment Sci* 1987; 150: 782–786.
- 374 [25] Raven J. The Raven’s Progressive Matrices: Change and Stability over Culture and Time.  
375 *Cognit Psychol* 2000; 41: 1–48.
- 376 [26] Mensah FO, Twumasi P, Amenawonyo XK, et al. Pica practice among pregnant women in  
377 the Kumasi metropolis of Ghana. *Int Health* 2010; 2: 282–286.
- 378 [27] Luoba AI, Wenzel Geissler P, Estambale B, et al. Earth-eating and reinfection with  
379 intestinal helminths among pregnant and lactating women in western Kenya. *Trop Med Int*  
380 *Health* 2005; 10: 220–227.
- 381 [28] Thomson J. Anaemia in pregnant women in eastern Caprivi, Namibia. *South Afr Med J*  
382 *Suid-Afr Tydskr Vir Geneeskde* 1997; 87: 1544–1547.
- 383 [29] Young SL, Khalfan SS, Farag TH, et al. Association of Pica with Anemia and  
384 Gastrointestinal Distress among Pregnant Women in Zanzibar, Tanzania. *Am J Trop Med Hyg*  
385 2010; 83: 144–151.
- 386 [30] Moya-Alvarez V, Cottrell G, Ouédraogo S, et al. Does Iron Increase the Risk of Malaria in  
387 Pregnancy? *Open Forum Infect Dis* 2015; 2: ofv038.
- 388 [31] Nchito M, Geissler PW, Mubila L, et al. Effects of iron and multimicronutrient  
389 supplementation on geophagy: a two-by-two factorial study among Zambian schoolchildren in  
390 Lusaka. *Trans R Soc Trop Med Hyg* 2004; 98: 218–227.
- 391 [32] Mireku MO, Boivin MJ, Davidson LL, et al. Impact of Helminth Infection during  
392 Pregnancy on Cognitive and Motor Functions of One-Year-Old Children. *PLoS Negl Trop Dis*  
393 2015; 9: e0003463.
- 394 [33] Rainville AJ. Pica Practices of Pregnant Women are Associated with Lower Maternal  
395 Hemoglobin Level at Delivery. *J Am Diet Assoc* 1998; 98: 293–296.
- 396 [34] Patil CL. Appetite Sensations in Pregnancy among Agropastoral Women in Rural  
397 Tanzania. *Ecol Food Nutr* 2012; 51: 431–443.
- 398 [35] Ekberg TL, Falck-Ytter T, Bölte S, et al. Reduced Prospective Motor Control in 10-  
399 Month-Olds at Risk for Autism Spectrum Disorder. *Clin Psychol Sci* 2016; 4: 129–135.

- 400 [36] Young SL. Pica in pregnancy: new ideas about an old condition. *Annu Rev Nutr* 2010; 30:  
401 403–422.
- 402 [37] Williams LB, Haydel SE. Evaluation of the medicinal use of clay minerals as antibacterial  
403 agents. *Int Geol Rev* 2010; 52: 745–770.
- 404 [38] Droy-Lefaix MT, Tateo F. Chapter 11.6 Clays and Clay Minerals as Drugs. In: Faiza  
405 Bergaya BKG and GL (ed) *Developments in Clay Science*. Elsevier, pp. 743–752.
- 406

**Table 1.** Comparison of first ANV maternal baseline characteristics and infant birth outcomes among respondent and non-respondent mothers

Characteristics	Respondents (n=552)	Non-respondents (n=311)	P
<u>Mothers</u>			
Age at 1 <sup>st</sup> ANV (years) <sup>a</sup>	25.8 ± 0.3	25.9 ± 0.2	0.857
Gestational age at 1 <sup>st</sup> ANV (weeks) <sup>a</sup>	22.0 ± 0.2	22.4 ± 0.2	0.145
Prepregnancy BMI (kg/m <sup>2</sup> ) <sup>a</sup>	21.0 ± 3.2	22.0 ± 4.1	<0.001
Gravidity			
Primigravida	100 (18.1)	55 (17.7)	0.874
Multigravida	452 (81.9)	256 (82.3)	
Education			
Primary or more	177 (32.1)	112 (36.0)	0.238
Never schooled	375 (67.9)	199 (64.0)	
Occupation			
Housewives	291 (52.7)	129 (41.5)	0.002
Employed	261 (47.3)	182 (58.5)	
Malaria at 1 <sup>st</sup> ANV			
Negative	456 (82.6)	275 (88.4)	0.023
Positive	96 (17.4)	36 (11.6)	
Anemia at 1 <sup>st</sup> ANV (Hb<110 g/l)			
No anemia	176 (31.9)	102 (32.8)	0.783
Anemia	376 (68.1)	209 (67.2)	
Iron deficiency at 1 <sup>st</sup> ANV			
No iron deficiency	386 (69.9)	190 (61.1)	0.008
Iron deficiency	166 (30.1)	121 (38.9)	
Helminth infection at 1 <sup>st</sup> ANV			
Negative	473 (87.0)	280 (91.2)	0.062
Positive	71 (13.0)	27 (8.8)	
<u>Infants</u>			
Birthweight			
Low (< 2500 g)	51 (10.0)	33 (11.4)	0.542
Normal (≥ 2500 g)	457 (90.0)	256 (88.6)	
Gestational age at birth			
Preterm (<37 weeks)	34 (6.3)	26 (9.0)	0.149
Normal (≥37 weeks)	506 (93.7)	262 (91.0)	
Sex			
Boy	271 (49.1)	143 (46.0)	0.379
Girl	281 (50.9)	168 (54.0)	

Unless otherwise stated, values are presented as number (percentage)

<sup>a</sup> Presented as Mean ± SD

ANV- antenatal care visit; BMI-body mass index

**Table 2.** Unconditional logistic regression on the relationship between geophagy at first trimester and maternal health outcomes at baseline

	<u>Maternal health outcomes</u>			
	<u>Iron deficiency</u> AOR [95% CI]	<u>Anemia</u> AOR [95% CI]	<u>Malaria</u> AOR [95% CI]	<u>Helminth</u> AOR [95% CI]
Geophagy at 1 <sup>st</sup> trimester				
Yes	1.3 [0.8; 2.1]	1.9 [1.1; 3.4]*	0.4 [0.2; 0.9]*	1.0 [0.5; 2.0]
No [Reference)	1	1	1	1

AOR- Adjusted odds ratio; ANV-Antenatal care visit

All models were adjusted for gravidity, pre-pregnancy BMI, maternal IQ, gestational age at ANV1, maternal age, family possession, and maternal education

\* $P < 0.05$

**Table 3.** Multilevel models on the consequences of geophagy in pregnancy on maternal health

	<u>Iron deficiency (ID)</u> AOR [95% CI] <sup>a</sup>	<u>Malaria</u> AOR [95% CI] <sup>a</sup>	<u>Anemia</u> AOR [95% CI] <sup>b</sup>	<u>Helminth</u> AOR [95% CI] <sup>a</sup>
Geophagy in pregnancy				
Yes	1.1 [0.8, 1.6]	0.6 [0.4, 1.0]	1.2 [0.7, 1.8]	0.9 [0.5, 1.6]
No [Reference)	1	1	1	1

AOR- Adjusted odds ratio; CI- Confidence interval

<sup>a</sup> Random intercept at the individual level

<sup>b</sup> Random intercept at the individual level and random slope for gestational age.

All models adjusted for maternal gestational age, level of education, pre-pregnancy body mass index, gravidity, family possession score, age at first ANV, and maternal intelligent quotient.

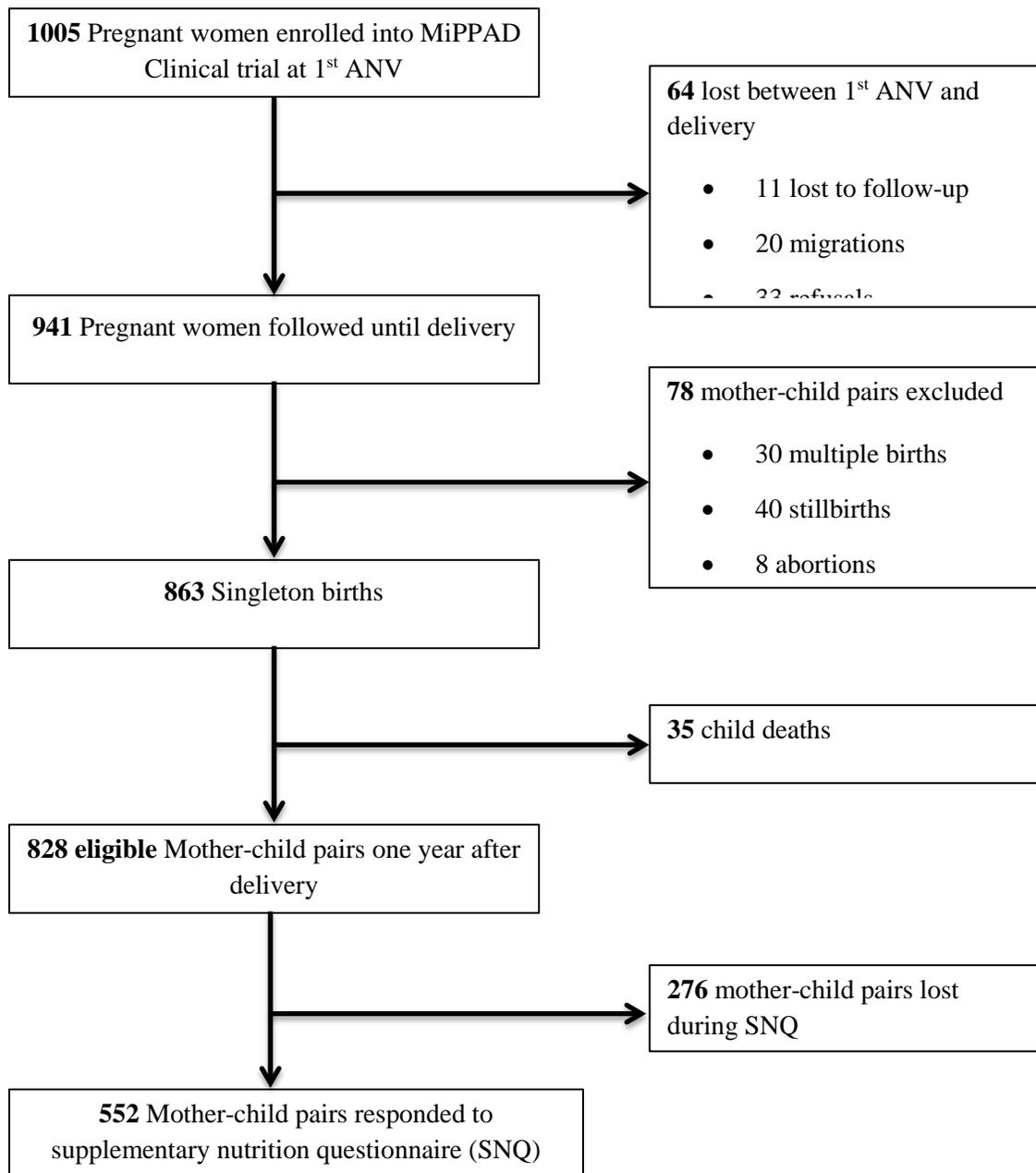
**Table 4.** Consequences of geophagy in pregnancy on birth outcomes and infant development

Geophagy in pregnancy	Birth outcomes		Age one year		
	Preterm AOR [95% CI] <sup>b</sup>	LBW AOR [95% CI] <sup>a</sup>	Geophagy AOR [95% CI] <sup>d</sup>	ELC score AMD [95% CI] <sup>h</sup>	GM score AMD [95% CI] <sup>i</sup>
Geophagy during 1 <sup>st</sup> trimester	1.4 [0.6, 3.6]	1.7 [0.8, 3.7]	0.6 [0.4, 1.0] <sup>e*</sup>	-0.1 [-3.3, 3.2]	0.4 [-2.8, 3.7]
Geophagy during 2 <sup>nd</sup> trimester	1.0 [0.4, 2.5]	1.2 [0.6, 2.4] <sup>c</sup>	2.8 [1.8, 4.3] <sup>f‡</sup>	-0.2 [-3.1, 2.6]	-1.5 [-4.3, 1.4]
Geophagy during 3 <sup>rd</sup> trimester	0.8 [0.3, 2.4]	1.0 [0.4, 2.3]	3.0 [1.8, 5.0] <sup>e‡</sup>	-2.0 [-5.2, 1.2]	-3.8 [-6.9, -0.6]*
Geophagy during at least one trimester	0.9 [0.4, 2.1]	1.6 [0.9, 3.1]	1.5 [1.0, 2.2] <sup>g*</sup>	-1.1 [-3.6, 1.5]	-1.4 [-3.4, 0.4] <sup>j</sup>

AOR- Adjusted odds ratio; CI- Confidence interval; AMD- Adjusted mean difference; LBW- Low birth weight; ELC- Early learning composite; GM- Gross motor; ID – Iron deficiency; BMI - Body mass index

\* $P < 0.05$ ; † $P < 0.001$

Adjusted for <sup>a</sup> gravity + prenatal ID at time of follow-up, <sup>b</sup> a + family possession score, <sup>c</sup> b + ID at 2<sup>nd</sup> ANV, <sup>d</sup> pre-pregnancy BMI + maternal IQ + prenatal ID at time of follow-up, <sup>e</sup> d + maternal education, <sup>f</sup> a+d+ malaria at 2<sup>nd</sup> ANV, <sup>g</sup> a+d+ malaria at 1<sup>st</sup> ANV, <sup>h</sup> pre-pregnancy BMI + maternal education + maternal occupation + HOME score+ prenatal ID at time of follow-up, <sup>i</sup> gravity + maternal education + HOME score+ prenatal ID at time of follow-up, <sup>j</sup> i + pre-pregnancy BMI + family possession score



**Figure 1.** Flowchart of the follow-up of pregnant women and children

**Supplementary Table 1.** Prevalence of geophagy and soil preference among pregnant women and infants

	N=552 number (%)
<u>Mothers</u>	
Geophagy (either kalaba or kaolin or earth)	
1 <sup>st</sup> trimester	83 (15.0)
2 <sup>nd</sup> trimester	118 (21.4)
3 <sup>rd</sup> trimester	92 (16.7)
Frequency of geophagy	
At least once during pregnancy	176 (31.9)
Never during pregnancy	376 (68.1)
Soil preference during pregnancy	
Kalaba	122 (22.1)
Kaolin	55 (10.0)
Earth	18 (3.3)
Polygeophagy	
Kalaba + kaolin	18 (3.3)
Kalaba + earth	1 (0.2)
Kaolin + earth	0 (0.0)
Kalaba + kaolin + earth	0 (0.0)
<u>Infants</u>	
Geophagous	271 (49.1)
Non-geophagous	281 (50.9)

**Supplementary Table 2.** Relationship between geophagy in pregnancy and maternal and infant sociodemographic characteristics

	Geophagy at 1 <sup>st</sup> trimester			Geophagy at 2 <sup>nd</sup> trimester			Geophagy at 3 <sup>rd</sup> trimester		
	Yes	No	<i>P</i>	Yes	No	<i>P</i>	Yes	No	<i>P</i>
Age at 1 <sup>st</sup> ANV (years)	26.1 ± 5.3	25.8 ± 5.6	0.636	25.6 ± 5.6	25.9 ± 5.6	0.629	25.6 ± 5.5	25.9 ± 5.6	0.632
Gestational age at 1 <sup>st</sup> ANV (weeks)	21.7 ± 3.9	22.0 ± 3.9	0.389	21.8 ± 4.0	22.0 ± 3.8	0.492	21.7 ± 4.0	22.1 ± 3.8	0.362
Prepregnancy BMI (kg/m <sup>2</sup> )	21.2 ± 2.9	21.0 ± 3.2	0.649	21.2 ± 3.1	21.0 ± 3.2	0.395	21.1 ± 2.8	21.0 ± 3.3	0.726
Family possession score	5.8 ± 2.9	5.5 ± 2.7	0.415	5.8 ± 2.8	5.5 ± 2.8	0.402	5.7 ± 2.8	5.5 ± 2.8	0.537
RAVEN Score	15.0 ± 3.1	15.3 ± 4.9	0.991	14.4 ± 3.1	15.5 ± 5.0	0.094	14.4 ± 3.3	15.5 ± 4.9	0.075
EPDS Score	7.4 ± 4.0	8.1 ± 4.1	0.200	8.4 ± 4.0	7.9 ± 4.1	0.199	8.6 ± 4.1	7.9 ± 4.0	0.063
HOME Score	26.9 ± 2.1	26.9 ± 2.3	0.558	27.0 ± 2.1	26.8 ± 2.4	0.654	27.1 ± 2.1	26.8 ± 2.3	0.303
Gravidity, n (%)									
Primigravida	12 (12.0)	88 (88.0)	0.348	23 (23.0)	77 (77.0)	0.662	18 (18.0)	82 (82.0)	0.693
Multigravida	71 (15.7)	381 (84.3)		95 (21.0)	357 (79.0)		74 (16.4)	378 (83.6)	
Education, n (%)									
Primary or more	25 (14.1)	152 (85.9)	0.680	50 (28.3)	127 (71.8)	0.007	37 (20.9)	140 (79.1)	0.066
Never schooled	58 (15.5)	317 (84.5)		68 (18.1)	307 (81.9)		55 (14.7)	320 (85.3)	
Occupation, n (%)									
Housewives	35 (13.4)	226 (86.6)	0.311	67 (25.7)	194 (74.3)	0.020	46 (17.6)	215 (82.4)	0.567
Employed	48 (16.5)	243 (83.5)		51 (17.5)	240 (82.5)		46 (15.8)	245 (84.2)	

Unless otherwise stated, values are presented as Mean ± SD

<sup>a</sup> Presented as number (percentage)

ANV- antenatal care visit; BMI-body mass index; HOME- home observation measurement of the environment; EPDS- Edinburgh postnatal depression scale