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1 **Epidemiology of Gestational Diabetes Mellitus according to IADPSG/WHO 2013**  
2 **criteria among Obese Pregnant Women in Europe**

3

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17

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21

1 **Abstract**

2 **Aims**

3 Accurate prevalence estimates for gestational diabetes mellitus (GDM) amongst pregnant  
4 women in Europe are lacking due to the use of a multitude of diagnostic criteria and screening  
5 strategies in both high-risk women and the general pregnant population. Our aims were to  
6 calculate the prevalence of GDM in early, mid and late gestation in a cohort of women with  
7 BMI  $\geq 29$  kg/m<sup>2</sup> across 11 centers in Europe using the IADPSG/WHO 2013 diagnostic criteria  
8 and to report pregnancy outcomes and important risk factors for GDM.

9

10 **Methods:**

11 Pregnant women (n=1023, 86.3% European ethnicity) with a body mass index (BMI)  
12  $\geq 29.0$  kg/m<sup>2</sup> enrolled into the DALI (Vitamin D And Lifestyle Intervention for GDM  
13 prevention) pilot, lifestyle and Vitamin D studies of this pan-European multi-center trial,  
14 attended for an oral glucose tolerance test (OGTT) in early, mid and late pregnancy.  
15 Demographic, anthropometric and metabolic information were obtained at enrolment and  
16 throughout pregnancy. GDM was diagnosed using IADPSG/WHO 2013 criteria. GDM  
17 treatment followed local policies.

18

19 **Results:**

20 Numbers recruited per country ranged from 80-217. Dropout (7.1%) was low. Overall, 39% of  
21 women developed GDM during pregnancy with no significant differences in prevalence across  
22 countries. Prevalence of GDM was high (24%; 242/1023) in early pregnancy. Despite the DALI  
23 interventions, a further 14% (94/672) developed GDM when tested at mid gestation (24-28  
24 weeks), and 13% (59/476) of the remaining cohort in late gestation (36 weeks). Demographics  
25 and lifestyle factors were similar at baseline between women with GDM and those who  
26 maintained normal glucose tolerance (NGT). Previous GDM (16.5% vs 7.9% p=0.002),  
27 congenital malformations (6.4% vs 3.3% p=0.045) and macrosomia (31.4% vs 17.9% p=0.001)  
28 were reported more frequently in those who developed GDM. Significant anthropometric and

1 metabolic differences were already present in early pregnancy between women developing  
2 GDM or not.

3

4 **Conclusions:**

5 The prevalence of GDM diagnosed by IADPSG/WHO 2013 GDM criteria in European  
6 pregnant women with a BMI  $\geq 29.0$  kg/m<sup>2</sup> is substantial, posing a significant health burden to  
7 these pregnancies and to the future health of the mother-offspring pair. Criteria for GDM in  
8 early pregnancy, supported by robust evidence of the benefits of treatment are urgently needed  
9 to guide modern GDM screening and treatment strategies.

10

11 **Keywords:**

- 12 Pregnancy
- 13 Weight regulation and obesity
- 14 Clinical Science and Care
- 15 Health care delivery
- 16 Clinical diabetes
- 17 Epidemiology

18

19

20 **Abbreviations**

21 ANOVA	Analysis of Variance
22	
23 BMI	Body Mass Index
24	
25 DALI	Vitamin D and Lifestyle Intervention for Gestational Diabetes Mellitus Prevention
26	
27	
28 EBCOG	European Board and College of Obstetrics and Gynaecology
29	
30 FIGO	International Federations of Gynecology and Obstetrics
31	
32 GDM	Gestational Diabetes Mellitus
33	
34 HAPO	Hyperglycemia and Adverse Pregnancy Outcomes
35	

1	IADPSG	International Association of the Diabetes and Pregnancy Study
2		Groups
3		
4	NGT	Normal Glucose Tolerance
5		
6	OGTT	Oral Glucose Tolerance Test
7		
8	RCT	Randomised Controlled Trial
9		
10	WHO	World Health Organisation
11		

1 **Introduction**

2  
3 Gestational diabetes mellitus (GDM) is defined as carbohydrate intolerance resulting in  
4 hyperglycaemia of variable severity with onset or first recognition during pregnancy, excluding  
5 those with diabetes in pregnancy likely to represent overt diabetes mellitus [1]. Women with  
6 GDM are more likely to suffer pregnancy complications and the diagnosis is associated with  
7 both immediate and long-term adverse consequences for their offspring [2, 3]. Furthermore,  
8 studies investigating postnatal maternal glucose function have shown the prevalence of type 2  
9 diabetes to be as high as 38% in the first year postpartum and as high as 60% in women followed  
10 for up to 16 years postpartum [4-6].

11  
12 The prevalence of GDM in Europe is reported to vary considerably and in certain populations  
13 is reported to occur in over 20% pregnancies [7, 8]. Unfortunately, accurate prevalence  
14 estimates in Europe are lacking due to highly inconsistent screening and diagnostic criteria both  
15 in high-risk women and the general pregnant population [9]. This makes pan-European surveys  
16 of GDM very difficult and limits the effects of large scale GDM prevention and treatment  
17 strategies. In 2008, the International Association of Diabetes and Pregnancy Study Groups  
18 (IADPSG) developed a consensus statement for a new strategy to diagnose GDM [3]. The  
19 chosen cut-off points for glucose on a 75-gram glucose tolerance test convey an odds ratio for  
20 adverse outcomes of at least 1.75 compared with women with mean glucose levels at 24-28  
21 weeks in the Hyperglycemia and Neonatal Outcomes (HAPO) study [3, 10]. In 2013 both the  
22 World Health Organisation (WHO) and the Endocrine Society revised their guidelines and now  
23 advise that the IADPSG criteria should be used for the diagnosis of GDM [1, 11]. The  
24 International Federation of Gynecology and Obstetrics (FIGO) also support this approach [12].  
25 Recently, the IADPSG has indicated that the criteria are not for use in early pregnancy [13] but  
26 have not provided criteria for up to 24 weeks gestation.

27  
28 The aim of this study was to use information collected during the Vitamin D and Lifestyle  
29 Intervention for gestational diabetes mellitus prevention (DALI) trial to determine the

1 prevalence of GDM in early, mid and late gestation among high risk obese women across 11  
2 centers in Europe using the IADPSG/WHO 2013 diagnostic thresholds. Risk factors and  
3 pregnancy outcomes were also evaluated.

4

5



1 **Research Design and Methods**

2 The DALI trial was a prospective multi-center, randomised controlled trial (RCT) comparing  
3 different lifestyle approaches that may prevent gestational diabetes mellitus (GDM)  
4 progression in overweight/obese ( $BMI \geq 29 \text{ kg/m}^2$ ) pregnant women recruited prior to 20 weeks  
5 gestation [7, 14, 15]. The presented analysis consists of women from the pilot, lifestyle and  
6 Vitamin D cohorts [14,15]. The study enrolled women from 11 centers in 9 European countries  
7 representing North, South, East and West areas of Europe [United Kingdom, Ireland, Austria,  
8 The Netherlands, Belgium, Denmark (2 sites), Italy (2 sites), Spain, Poland]. Each local  
9 research ethics committee approved the study and written informed consent was obtained from  
10 all participating subjects. The study was performed in accordance with the principles of the  
11 ‘Declaration of Helsinki’ and registered in ISRCTN registry (ISRCTN70595832). DALI was  
12 funded by the European Union 7th framework (FP7/ 2007–2013) under Grant Agreement  
13 no.242187.

14

15 **Patient involvement**

16 Representatives of the target group were interviewed in the developmental stage of the DALI  
17 trial about their preferences of intervention content, modality, frequency and location. Patients  
18 were not involved in the actual conduct of the study, but participants provided feedback on the  
19 burden of the intervention and their experiences with the study in general, as part of a process  
20 evaluation. Patient organisations are actively involved in the dissemination of the results to the  
21 lay public.

22

23 **Participants**

24 The main inclusion criteria were: age  $\geq 18$  years, singleton pregnancy up to and including 19+6  
25 weeks of gestation,  $BMI \geq 29 \text{ kg/m}^2$  before pregnancy, and ability to give informed consent.  
26 Exclusion criteria included pre-existing diabetes, the need for complex diets, inability to walk  
27  $\geq 100$  meters safely, and significant chronic medical condition or psychiatric disease.  
28 Consecutive consenting women undertook a 75g oral glucose tolerance test (OGTT)  $< 20$  weeks

1 gestation, with GDM diagnosed from venous samples using locally available laboratory  
2 methods according to the IADPSG/WHO 2013 criteria (fasting plasma glucose  $\geq$  5.1mmol/L,  
3 1 hour plasma glucose  $\geq$  10.0 mmol/L and 2 hour plasma glucose  $\geq$  8.5 mmol/L) (IADPSG).  
4 Women diagnosed with GDM at baseline were excluded from the RCT (Lifestyle and/or  
5 Vitamin D). The remaining cohort was re-tested in mid gestation (24-28 weeks), and if GDM  
6 was not diagnosed, they were retested again in late gestation (35-37 weeks) with further 75g  
7 OGTT using IADPSG/WHO 2013 criteria. Recruitment was conducted between January 2012  
8 and February 2014.

9

10 **Assessments**

11 Information regarding demographics, anthropometric and metabolic factors was obtained from  
12 all women at enrolment through anthropometric and metabolic measurements, and by  
13 completion of questionnaires (14). A 75g OGTT was performed with blood samples for glucose  
14 and insulin taken fasting and, 60, and 120 minutes after glucose ingestion. The homeostasis  
15 model assessment of insulin resistance (HOMA-IR) was calculated using glucose and insulin  
16 values [fasting plasma glucose level (mg/dL) x fasting insulin level (microunit/mL) / 405] [16].

17

18 **Data Analyses**

19 Data were entered into a bespoke web-based electronic database. Descriptive data analysis was  
20 performed for all parameters. Continuous variables were summarized by mean  $\pm$  standard  
21 deviation and categorical variables by counts and percentages. Comparisons between GDM and  
22 normal glucose tolerant (NGT) obese women were performed using t-Test and/or analysis of  
23 variance (ANOVA) for continuous data and Chi square tests for binary data. For non-normally  
24 distributed data, non-parametric tests were used to compare ranks between groups. Multivariate  
25 logistic regression models were applied to identify risk factors for GDM diagnosis at any time  
26 point adjusting for potential confounders. Variables significant in univariate analysis as well as  
27 those previously identified as risk factors in the literature were entered into the multivariate  
28 model. To avoid collinearity, highly correlated factors were entered in separate models (for

1 instance, BMI, weight, neck and waist circumference). The risk factor with the highest odds  
2 ratio was retained in these instances. Factors (at baseline) included age, weight, BMI,  
3 neck/waist circumference, marital status, education, parity, employment, alcohol consumption,  
4 smoking, (family) history of GDM and previous pregnancy risk factors (congenital  
5 malformation, macrosomic baby, previous pregnancy loss, PCOS, chronic hypertension).  
6 Statistical analysis was performed using SPSS 21.0 (SPSS Inc, Chicago, USA). A two-sided p-  
7 value <0.05 was considered statistically significant. No permutations were made for missing  
8 data.

9

10

11

1 **Results**

2 **DALI enrollment**

3 Enrollment occurred across 11 sites in 9 European countries. A total of 1023 women were  
4 enrolled (pilot, lifestyle and vitamin D trials) and 73 (7.1%) women dropped out or were lost  
5 to follow up across all sites. Enrollment rates (defined as percentage of eligible women enrolled  
6 per site) between countries ranged from 7.8 to 21.2% (average 11%) giving a wide spread  
7 across the European populations (Table 1).

8  
9

10 **Prevalence of GDM**

11 Table 2 outlines the GDM prevalence by period of gestation and country. DALI found a high  
12 prevalence of GDM of in early pregnancy (<20 weeks gestation) with 242/1023 (24%) women  
13 diagnosed. A total of 5 of these women met the criteria for overt diabetes in pregnancy. Of the  
14 242 women diagnosed in early pregnancy, 190 (78.5%) met the diagnostic criteria based on  
15 fasting glucose alone ( $\geq 5.1$ mmol/L). Women diagnosed in early pregnancy were not enrolled  
16 in the randomised controlled trial. There was a spread of prevalence from a low of 10-11% in  
17 the United Kingdom and Ireland to the highest in Denmark at 43%. In total, 672 women were  
18 re-tested at mid-gestation (24-26 weeks) and 94 (14%) had developed GDM despite the  
19 interventions of the trial. Once again there was a spread of prevalence from a low of 8% in  
20 Ireland to a maximum of 21% in Italy. Finally, 476 women previously categorized as NGT  
21 (without GDM at the OGTT at 24-26 weeks) completed the final OGTT at 36 weeks gestation  
22 of whom 59 (13%) developed GDM despite the diet and lifestyle interventions. There was a  
23 spread in prevalence from a low of 9% in Italy to a high of 16% in Belgium. Overall 395 (39%)  
24 women fulfilled the IADPSG/WHO 2013 GDM criteria at any point within the trials. The  
25 lowest overall total prevalence was in United Kingdom at 24% and the highest prevalence was  
26 in Denmark at 52%.

27

28 **Demographic and lifestyle factors:**

1 Table 3 outlines the demographic and lifestyle factors at baseline of all women enrolled in the  
2 randomised controlled trials according to glucose tolerance status (GDM at any time versus  
3 NGT). There was no significant difference in ethnicity between those who maintained normal  
4 glucose tolerance (NGT) and those that developed GDM during the trial. Over 50% reported  
5 attaining a high (university equivalent) education reflective of the university cities where  
6 recruitment occurred. Attaining a low level of education was similar in women with NGT and  
7 GDM at 12.0% and 12.8% respectively. In total 5.2% of mothers reported consuming alcohol  
8 during pregnancy. One third of fathers (33.8%) were active smokers, double the rate reported  
9 by mothers (16.2%) with no difference in active smoking between women with NGT and  
10 GDM. Nulliparous females accounted for 50.3% of the total cohort.

11

#### 12 **Maternal GDM Risk Factors:**

13 Maternal GDM risk factors at enrolment are displayed in table 4. There were no differences  
14 between women with GDM at any time and those with NGT in history of diabetes in a first-  
15 degree relative, polycystic ovary syndrome (PCOS), reported chronic hypertension or  
16 reported past history of a previous pregnancy loss. More women with GDM than NGT  
17 reported a previous history of GDM (7.9% vs 16.5%,  $p=0.002$ ), congenital malformations  
18 (3.3% vs 6.4%,  $p=0.045$ ) and a previous macrosomic baby (17.9% vs 31.4%,  $p=0.001$ ).

19

#### 20 **Anthropometric/metabolic characteristics pre-pregnancy and at first assessment**

21 Table 5 compares anthropometric and metabolic measurements among women with NGT and  
22 those with early and mid/late pregnancy GDM. Significant differences between women with  
23 NGT and GDM were observed. Reported pre-pregnancy and enrollment weight and BMI were  
24 significantly greater in women with GDM in early pregnancy. Waist circumference was  
25 significantly different between those with NGT (107.3cm), those with early GDM (114.4cm)  
26 and those with GDM in mid- or late-pregnancy (107.1cm) ( $p=0.009$ ). Significant differences  
27 were also noted between groups in terms of systolic blood pressure (SBP), diastolic blood  
28 pressure (DBP) and heart rate (HR) with higher measurements observed for those women with

1 GDM in early pregnancy. As expected, women with GDM in early pregnancy had higher  
2 fasting, one hour and two hour glucose levels but levels were also significantly higher in women  
3 who went on to develop GDM later compared to women with NGT. HOMA index of insulin  
4 resistance at first assessment was significantly higher in those with early (4.5) versus mid- or  
5 late-GDM (3.6) and those with NGT had the lowest level (3.0) ( $p<0.001$ ).

6  
7 **Risk of GDM development**

8 Table 6 outlines the results of a multivariate logistic regression analysis to evaluate the odds  
9 of GDM development. Independent risk factors for GDM development were nulliparity (OR  
10 1.6), neck circumference at initial visit (OR 1.1) and GDM in a previous pregnancy (OR 2.3)  
11 and a previous macrosomic baby (OR 1.7).

12  
13 **Pregnancy outcomes according to glucose tolerance.**

14 Table 7 shows pregnancy outcomes for all women enrolled in the study versus those with a  
15 diagnosis of GDM in mid and late pregnancy (as those with early GDM were excluded from  
16 enrollment) or NGT: no significant differences were found.

17  
18

1 **Discussion**

2 We found an overall prevalence of GDM of 39%, using IADPSG/WHO 2013 criteria across  
3 early, mid and late gestation among overweight/obese women who were evaluated for  
4 inclusion in the DALI trial. Participants were well distributed across 11 European centers, the  
5 largest cohort attending two sites in Denmark (21.2%). DALI allows for a meaningful  
6 interpretation of the European prevalence of GDM as identical screening was used in 11  
7 centers across 9 European states, using WHO 2013 criteria. A substantial proportion was  
8 found in early pregnancy (24%), and the other 15% diagnosed equally across mid and late  
9 pregnancy. The prevalence of GDM varied across countries, ranging from 52% in Denmark  
10 to 24% in the United Kingdom. These findings are in contrast to prior prevalence data that  
11 included women across all BMI categories and reported an overall prevalence of 2-6% with a  
12 lower prevalence towards the Northern Atlantic seaboard of Europe compared to the Southern  
13 Mediterranean seaboard [8]. This variance is likely to be due to lack of uniformity of  
14 screening in the aforementioned study, lower glucose cut-off points of IADPSG/ WHO 2013  
15 criteria compared to other guidelines and the inclusion of only those women with a BMI  
16  $\geq 29\text{kg/m}^2$  in the current study.

17  
18 Within this group of women at high risk for GDM, there was no variation in demographics or  
19 lifestyle factors according to glucose tolerance, and certain previously reported risk factors  
20 were associated with GDM in the logistic regression (prior GDM, prior macrosomia).  
21 However, other well-established risk factors for GDM, such as a diagnosis of PCOS and  
22 diabetes in a first-degree relative were not significant: this may be due to the overwhelming  
23 risk-effect of obesity. The significant risk of GDM observed among these obese women is of  
24 concern given the global rise in obesity and the knowledge that both obesity and GDM are  
25 independently associated with adverse maternal-fetal outcomes [10, 17]. Furthermore, 70% of  
26 obese women with GDM develop type 2 diabetes within 15 years of delivery, compared with  
27 30% of lean women with GDM [18, 19]. It is evident that effective policies to reduce obesity  
28 levels are necessary and this may result in both clinical and economic benefits [20]. Indeed,

1 an initial step may be to ensure universal BMI screening for women of reproductive age.  
2 Then, clinicians may be more likely to assist with weight loss and provide appropriate care to  
3 identify and reduce secondary complications of increasing BMI [21, 22].

4  
5 Among women with a BMI  $\geq 29.0$  kg/m<sup>2</sup>, women with GDM in early pregnancy had a  
6 significantly higher weight and BMI compared to those with NGT and those with GDM in  
7 mid/late pregnancy. It is an interesting observation that these differences were limited to  
8 women with early GDM, while women with GDM in mid/late pregnancy were not  
9 significantly different from those with NGT in terms of weight and BMI. Similar findings  
10 were observed for neck circumference and systolic and diastolic blood pressure. This is useful  
11 clinical information and could be used in a 'risk score' for early GDM, although we would  
12 recommend screening all of these women. The use of neck circumference is a novel measure  
13 and may overcome inaccuracies associated with measuring waist circumference [23]. After  
14 excluding women with early GDM, women who go on to develop GDM in mid/late  
15 pregnancy also have elevated glucose levels at baseline compared to those who continue with  
16 NGT. This trend is also evident when examining measures of insulin resistance. While there  
17 are limitations to indices such as HOMA-IR such as racial differences in mixed populations,  
18 they act as a reasonable surrogate for the gold standard euglycemic-hyperinsulinemic clamp  
19 [16, 24]. In this study, women with GDM in early pregnancy demonstrated significantly  
20 higher insulin resistance compared to those with GDM in later pregnancy or those with NGT  
21 as previously reported [25]. These findings support prior work characterizing women with  
22 early-onset GDM as having higher levels of insulin resistance and those with GDM in later  
23 pregnancy being more similar to women with NGT [26]. Higher BMIs of the women with  
24 early-onset GDM is felt to at least partially explain this phenomenon.

25  
26 Although screening practices vary, one commonly used approach is to screen the majority of  
27 women for GDM at 24-28 weeks gestation with earlier testing reserved for those with risk  
28 factors [27]. However, almost one quarter of our cohort was positive in early pregnancy (<20



1 weeks gestation). While the diagnostic cut off values for GDM in early pregnancy are  
2 controversial [9, 13], based on our findings there is some evidence that early screening in  
3 obese women may be warranted. As the majority of these women were captured using the  
4 fasting glucose alone, there may be a role for using this measure rather completing a full  
5 OGTT. Screening is of particular importance in the presence of the additional risk factors  
6 noted to be independently associated with GDM development at any stage of the study. On  
7 multivariate analysis, a history of GDM in a previous pregnancy was the strongest  
8 independent risk factor identified (odds ratio 2.3), followed by a history of a macrosomic  
9 baby (odds ratio 1.7). Additional independent risks included nulliparity (odds ratio 1.6) and  
10 larger neck circumference on initial evaluation (odds ratio 1.1). Women in this study were  
11 diagnosed according to the IADPSG/WHO 2013 criteria (1, 3). While international practices  
12 vary, this approach adapted by the DALI study is in keeping with recommendations from the  
13 European Board and College of Obstetrics and Gynaecology (EBCOG) and FIGO [9]. Due to  
14 a lower fasting glucose cutoff of 5.1mmol/L, use of the IADPSG/WHO 2013 criteria result in  
15 an increased prevalence of GDM compared to alternative diagnostic criteria, however their  
16 use is supported by data revealing that women with fasting plasma glucose levels of 5.1 –  
17 5.5mmol/L have an increased risk of adverse outcomes [27, 28]. It is hoped that there will be  
18 a move towards uniformity in the diagnosis of GDM across Europe in the future. This will  
19 stimulate research in the field of GDM and give the opportunity for more women to receive a  
20 timely diagnosis and appropriate treatment for GDM. It is clear that the criteria for diagnosing  
21 GDM in early pregnancy need urgent resolution and studies to delineate these criteria and  
22 quantify any benefits from treatment are urgently required.

23

24 Limitations of our findings include the fact that women were recruited and consented to  
25 partake in a randomised controlled trial which may have resulted in a selection bias. We do  
26 not address the optimal GDM prevention strategy as women received a variety of lifestyle  
27 modifications and vitamin D therapy during the trial and these are reviewed in the DALI pilot  
28 and lifestyle RCT outcomes papers [14, 15]. If there was an impact of the interventions on

1 individual women, the prevalence of GDM in mid-late pregnancy may be an under-estimate.  
2 On the other hand, as discussed in relation to early pregnancy, use of the IADPSG criteria to  
3 diagnose additional cases of GDM in late pregnancy is not validated and the justification for  
4 this requires further study. Finally, once diagnosed with GDM, women were managed  
5 according to local practice at each site and this could influence birth outcomes.  
6 Nevertheless, these women represent a wide spectrum of European countries and data were  
7 carefully collected, recorded and analysed to give an accurate overview of the patterns of  
8 GDM in this population. This work fills an important gap in the literature and highlights the  
9 high prevalence of GDM associated with obesity in a European population.

10

11 In conclusion, the overall prevalence of GDM diagnosed by the IADPSG/WHO 2013 GDM  
12 criteria in European pregnant women participating in the DALI study is 39% with a significant  
13 proportion (24%) diagnosed in early pregnancy. Criteria for GDM in early pregnancy,  
14 supported by robust evidence of the benefits of early and late treatment are urgently needed to  
15 inform pan-European GDM screening and treatment strategy. Such a high GDM prevalence in  
16 early pregnancy, and the difficulty in preventing GDM developing de novo, highlights the  
17 critical need for preventative interventions before pregnancy.

18

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21 who participated in this study.

22

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25 Agreement no.242187.

26

27 **Duality of Interest**

28 The authors declare no conflict of interest.

1

2 **Contribution Statement**

3

4 AME drafted the manuscript, AV completed the statistical analysis, FPD was the project  
5 supervisor and all authors revised the manuscript critically and approved the final version to be  
6 published.

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1 **Table 1: Enrollment of pregnant women in the DALI lifestyle and vitamin D studies by**  
 2 **country**

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Country	Number enrolled	Percentage of total trial population
Spain	99	9.7%
Austria	110	10.8%
Belgium	101	9.9%
Denmark (2 sites)	217	21.2%
Poland	91	8.9%
Italy (2 sites)	116	11.3%
Ireland	84	8.2%
Netherlands	80	7.8 %
United Kingdom	125	12.2%
<b>TOTAL</b>	<b>1023</b>	<b>100%</b>

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10 **Table 2: GDM prevalence according to gestation period and country**

Country	Number Enrolled	GDM Early pregnancy N (%)	GDM Mid pregnancy N (%)	GDM Late pregnancy N (%)	GDM Total
Spain	99	25/99 (25%)	10/65 (15%)	6/46 (13%)	41/99 (41%)
Austria	110	22/110 (20%)	12/72 (17%)	6/45 (13%)	40/110 (36%)
Belgium	101	21/101 (21%)	12/75 (16%)	10/61 (16%)	43/101 (43%)
Denmark	217	93/217 (43%)	11/106 (10%)	8/77 (10%)	112/217 (52%)
Poland	91	17/91 (19%)	12/68 (18%)	7/47 (15%)	36/91 (40%)
Italy	116	16/116 (14%)	18/85 (21%)	5/54 (9%)	39/116 (34%)
Ireland	84	9/84 (11%)	5/63 (8%)	7/47 (15%)	21/84 (25%)
Netherlands	80	27/80 (34%)	4/44(9%)	1/18 (5%)	32/81 (41%)
United Kingdom	125	12/125 (10%)	10/94 (11%)	9/74(12%)	31/125 (24%)
<b>TOTAL</b>	<b>1023</b>	<b>242/1023 (24%)</b>	<b>94/672 (14%)</b>	<b>59/476 (13%)</b>	<b>395/1023 (39%)</b>

11 GDM: gestational diabetes mellitus  
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1 **Table 3: Demographics/Lifestyle factors of participants at enrollment.**

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	All Women %	NGT %	GDM <sup>a</sup> %	P value
Ethnicity				
European	86.3%	86.4%	86.2%	ns
Non-European	13.7%	13.6%	13.8%	ns
Education				
High	55.2%	56.9%	52.4%	ns
Medium	32.5%	31.1%	34.3%	ns
Low	12.3%	12.0%	12.8%	ns
Living with a partner	93.4%	93.8%	91.8%	ns
Employment status				
Working	77.0%	77.1%	76.8%	ns
Not Working	14.3%	13.8%	15.0%	ns
Home Duties	8.7%	9.1%	8.2%	ns
Current maternal alcohol	5.2%	6.1%	3.8%	ns
Current maternal smoking	16.2%	16.7%	15.4%	ns
Current paternal smoking	33.8%	34.6%	32.6%	ns
Nulliparous	50.3%	48.7%	52.9%	ns

3 NGT: normal glucose tolerance. GDM: gestational diabetes mellitus. P-value for comparison  
4 of women with NGT versus GDM.

5 <sup>a</sup>Women who developed GDM at any time during pregnancy.

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**Table 4: Maternal risk factors for GDM development.**

	All Women %	NGT %	GDM <sup>a</sup> %	P-value
Diabetes in a first degree relative	24.6%	23.7%	27.7%	ns
Polycystic ovarian syndrome	10.4%	10.3%	10.7%	ns
Chronic hypertension	13.0%	12.8%	13.7%	ns
Previous GDM	9.8%	7.9%	16.5%	0.002
Previous congenital malformation	4.0%	3.3%	6.4%	0.045
Previous macrosomic baby	21.0%	17.9%	31.4%	0.001
Previous pregnancy loss	11.1%	10.2%	14.1%	ns

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GDM: gestational diabetes mellitus.

P-value for comparison of women with NGT versus GDM.

<sup>a</sup>Women who developed GDM at any time during pregnancy.



1 **Table 5: Anthropometric/metabolic factors pre-pregnancy and early pregnancy**  
 2 **according to glucose tolerance**

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	NGT	GDM Early Pregnancy	GDM mid- /late- pregnancy	P value comparison of 3 groups	P value comparison early versus mid-/late pregnancy
Age (years)	31.9(5.4)	32.7 (5.1)	32.0 (5.0)	ns	ns
Height (cm)	165.7 (6.7)	165.5 (6.1)	165.0 (7.4)	ns	ns
Pre-pregnancy weight (kg)	92.8 (13.5)	96.8 (16.1)	91.0 (14.9)	<0.001	<0.001
Pre-pregnancy BMI (kg/m <sup>2</sup> )	33.7 (4.2)	35.3 (5.4)	33.4 (4.7)	<0.001	<0.001
Weight at enrollment (kg)	94.8 (13.5)	99.3 (17.1)	93.5 (14.7)	<0.001	<0.001
BMI at enrollment (kg/m <sup>2</sup> )	34.5 (4.2)	36.2 (5.6)	34.2 (4.4)	<0.001	<0.001
Waist circumference (cm)	107.3 (10.1)	114.4 (60.9)	107.1 (10.1)	0.009	ns
Neck circumference (cm)	36.3 (2.1)	37.4 (4.9)	36.3 (2.2)	<0.001	0.008
Systolic blood pressure (mmHg)	116.4 (11.1)	118.5 (10.1)	115.9 (10.8)	0.03	0.019
Diastolic blood pressure (mmHg)	72.8 (8.5)	75.1 (8.5)	73.0 (11.8)	0.003	0.036 <sup>a</sup>
Heart rate (beats/minute)	79 (10.2)	82 (10.6)	81 (9.3)	0.001	ns
Fasting glucose (mmol/L)	4.5 (0.3)	5.2 (0.5)	4.6 (0.3)	<0.001	<0.001
1 hour glucose (mmol/L)	6.5 (1.4)	8.9 (2.0)	7.5 (1.4)	<0.001	<0.001
2 hour glucose (mmol/L)	5.7 (1.1)	7.3 (1.7)	6.2 (1.1)	<0.001	<0.001
HOMA Index	3.0 (2.6)	4.5 (2.7)	3.6 (3.6)	<0.001	0.007

4 Data expressed as mean (standard deviation). HOMA IR: homeostatic model assessment for  
 5 insulin resistance. NGT: normal glucose tolerance. GDM: gestational diabetes mellitus  
 6 <sup>a</sup> not significant when applying Bonferroni adjustment for multiple comparisons.

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 10 **Table 6: Logistic regression analysis evaluating risk of GDM (yes/no) at any stage of the**  
 11 **study.**

	Odds ratio	95% CI		p-value
		lower	upper	
Nulliparous	1.6	1.0	2.5	0.032
Neck circumference at initial evaluation (cm) <sup>a</sup>	1.1	1.0	1.2	0.011
GDM in previous pregnancy	2.3	1.3	4.0	0.004
Previous macrosomic baby	1.7	1.1	2.6	0.014

12 GDM: gestational diabetes mellitus.

13 <sup>a</sup>Continuous variable

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**Table 7: Pregnancy outcomes for women enrolled in the trial according to glucose status<sup>a</sup>**

	All Enrolled Women %	NGT %	GDM mid/late pregnancy %	P value %
Caesarean section	36.2%	34.1%	40.2%	ns
Pre-eclampsia	3.1%	2.8%	3.8%	ns
Pregnancy-induced hypertension	12.2%	11.3%	14.2%	ns
Birthweight ≥4 kg	16.4%	15.2%	18.5%	ns
Birthweight <2.5kg	3.9%	3.4%	4.8%	ns
Neonatal intensive care unit admission	9.0%	9.9%	6.6%	ns
Gestational at delivery (weeks)	39.6 (5.9)	39.5 (3.0)	39.8 (9.6)	ns
Birth weight (g)	3468 (578)	3456 (524)	3488 (657)	ns
Birth length (cm)	51.4 (3.5)	51.4 (3.3)	51.4 (3.8)	ns

NGT: normal glucose tolerance. GDM: gestational diabetes mellitus.

P-value for comparison of women with NGT versus GDM.

<sup>a</sup>Women with early GDM were excluded from the study therefore pregnancy outcomes are unavailable.