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Lower rate of selected congenital heart defects with better maternal diet quality: a population-based study

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ABSTRACT

Objective To evaluate whether better diet quality in mothers is associated with lower risk for major non-syndromic congenital heart defects in their children.

Design Multicentre population-based case–control study, the National Birth Defects Prevention Study.

Setting Ten sites in the USA.

Participants Mothers of babies with major non-syndromic congenital heart defects (n=9885) and mothers with unaffected babies (n=9468) with estimated date of delivery from 1997 to 2009.

Main outcome measures Adjusted ORs for specific major congenital heart defects by quartiles of maternal diet quality in the year before pregnancy, assessed by the Diet Quality Index for pregnancy (DQI-P) and the Mediterranean Diet Score. Quartile 1 (Q1) reflecting the worst diet quality and Q4 the best diet quality.

Results Better diet quality was associated with reduced risk for some conotruncal and atrial septal heart defects. For DQI-P, estimated risks reductions (Q4 vs Q1) for conotruncal defects were 37% for tetralogy of Fallot (OR 0.63, 95% CI 0.49 to 0.80) and 24% overall (OR 0.76, 95% CI 0.64 to 0.91); and for septal defects, 23% for atrial septal defects (OR 0.77, 95% CI 0.63 to 0.94) and 14% overall (OR 0.86, 95% CI 0.75 to 1.00). Risk reductions were weaker or minimal for most other major congenital heart defects.

Conclusions Better diet quality is associated with a reduced occurrence of some conotruncal and septal heart defects. This finding suggests that a reduction in certain cardiac malformations may be an additional benefit of improved maternal diet quality, reinforcing current preconception care recommendations.

What is already known on this topic

- Congenital heart defects are common, costly and critical, with few options for primary prevention.
- Some studies suggest that multivitamin supplementation could decrease the risk for congenital heart defects, but the data are not conclusive.
- Other studies have suggested that better diet quality might reduce the risk for some congenital anomalies, but data specifically on congenital heart defects are scarce.

What this study adds

- Better maternal diet is associated with a lower rate of some conotruncal and septal heart defects.
- A reduction in some congenital heart defects may be an additional benefit of improved maternal diet quality, reinforcing current preconception care recommendations.

INTRODUCTION

Congenital heart defects (CHDs) are common, costly and critical. They affect nearly 1% of newborns,[1–3] consume increasing resources[4 5] and are associated to nearly one in four infant deaths due to birth defects in the USA.[6] Finding common modifiable risk factors of CHDs has proven challenging. The discovery of folic acid as an effective preventive factor for neural tube defects has increased the attention on nutrition as a potential modifier of risk for other birth defects, including CHDs. Most studies on CHDs to date have focused on supplements (folic acid alone or a multivitamin mix). In some studies, but not all, the risk for selected CHDs was reduced in pregnancies of women who used multivitamin supplements before conception through early pregnancy.[7–12] However, in countries with folic acid fortification, a consistent decline in population rates of CHDs has not been reported.[3] These observations underscore the need to move beyond evaluating single nutrients and examine nutrition more holistically. Research into dietary patterns has proven useful in other health outcomes, including cardiovascular disease, hypertension, diabetes and some cancers, and has even led to successful dietary approaches to reduce disease risk (eg, the Dietary Approaches to Stop Hypertension diet to reduce the risk for hypertension). Dietary approaches have only recently been applied to birth defect risk, and scarce population-based data are available. Recently, investigators from the National Birth Defects Prevention Study (NBDPS) have reported reduced risk for some birth defects (neural tube defects and orofacial clefts)[13] but not others (hypospadias)[14] with better maternal diet quality, as estimated by the Mediterranean Diet Score (MDS) and the Diet Quality Index for Pregnancy (DQI-P). Here we expand this dietary pattern approach to major non-syndromic CHDs.

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METHODS

Study design

The NBDPS is a population-based, multicentre case–control study of modifiable risk factors for major birth defects. Because of this focus, the study excluded known chromosomal or genetic conditions, thus focusing on non-syndromic birth defects. This specific analysis includes pregnancies with estimated due dates from October 1997 through December 2009. The study is an approved activity of the Institutional Review Boards of the study centres and the Centers for Disease Control and Prevention (CDC). Detailed methods and descriptions of the 10 study sites (Arkansas, California, Georgia, Iowa, Massachusetts, North Carolina, New Jersey, New York, Utah, Texas) are published.[15] Seven sites included cases among live births, stillbirths (fetal deaths at ≥20 weeks' gestation) and elective pregnancy terminations; two included live births and stillbirth, and one live birth only. Each site randomly selected approximately 150 liveborn non-malformed controls per year from birth certificates or from birth hospitals to represent the population from which cases were derived. Because of high prevalence, muscular ventricular septal defects and ventricular septal defects 'not otherwise specified' were included for the initial project years only (up to 1998 births). Participation rates were 67% for case mothers and 65% for control mothers.

Case review and classification

Final eligibility was determined centrally by clinical geneticists. All CHD diagnoses were confirmed by echocardiography, catheterisation, surgery or autopsy. Each case was classified as isolated (CHD but no other major birth defect) or non-isolated (with other major unrelated birth defects). Cases were also assigned a CHD diagnosis centrally and systematically[16] by a team of clinicians with expertise in paediatric cardiology. Each CHD case was also classified as a simple, association or complex case.[16] Online supplementary table S1 summarises the CHD phenotypes by analytic group, with their codes.[16]

Diet quality evaluation

Maternal interviews were standardised, computer-based and conducted primarily by telephone in English or Spanish. Median time from delivery to interview was 13 months for cases and 9 months for controls. Interviews included a food frequency questionnaire (FFQ) focusing on the average consumption of foods in the year before pregnancy. The questionnaire, a shortened version of that developed by Willett and colleagues for the *Nurses Health Study,* included 58 food items.[17] Intake of food supplements, breakfast cereals, sodas, and caffeinated tea and coffee was assessed by questions focusing on the three months before pregnancy. The US Department of Agriculture nutrient database (V.19) was the source of nutrient data. Food supplements were not included in the analysis because there were rarely used by participants and incompletely represented in this database. Dietary folate intake was expressed as dietary folate equivalents to take into account the greater bioavailability of folic acid in fortified foods compared with natural folate. Consumption of food groups was measured as the sum of consumption of food items included in the group.

We used two a priori indices of diet quality: MDS and DQI-P. We chose these two indices because they were previously validated and reflected common recommended dietary guidelines. MDS increases the closer an individual's diet fits a typical Mediterranean diet;[18–20] six components are positively scored (legumes, grains, fruits and nuts, vegetables, fish, and the ratio of monounsaturated to saturated fatty acid intake) and three are negatively scored (dairy, meat and sweets).[18–20] The DQI-P modifies the Diet Quality Index (developed to reflect the 2000 Dietary Guidelines for Americans and the 1992 Food Guide Pyramid) to incorporate pregnancy-specific nutritional recommendations;[21] six components are positively scored (grains, vegetables, fruits, folate, iron and calcium) and two are negatively scored (per cent of calories from fat and sweets). Scores were computed as follows:[13] for each food-based component (eg, dairy), we took the estimated average amount consumed per day (combining the reported frequency of use with the food serving), assigned a decile score to each food component (based on the distribution among controls) and summed the scores. Analyses were based on quartiles and deciles of the summed scores computed among controls.

Interviews were conducted with 11 085 mothers of cases and 10 200 mothers of controls. To minimise bias and confounding, we made the following exclusions (figure 1): mothers reporting pregestational diabetes (a strong risk factor for CHD) or those with average daily energy intake <500 or >5000 kcal, or with missing data on two or more food items. The final sample included 9885 case mothers and 9468 control mothers.

Statistical methods

We used V.9 of the NBDPS analytic data set. For the statistical analyses, we used SAS software (SAS V.9.2, SAS Corporation, Cary, North Carolina, USA). We used Spearman's rank correlation to measure the correlation between the diet quality indices. We used logistic regression to estimate ORs and 95% CIs, with the lowest quartile (or decile, as appropriate) as reference. We used a simple model that adjusted only for energy intake, and more fully adjusted models that incorporated multiple potential confounders selected a priori based on the previous studies reporting their association with CHD risk: periconceptional use of folic acid-containing supplements (regular use, intermittent use in month preceding conception through second month of pregnancy, no use), maternal race/ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, Other), education (less than, equal to or greater than high school), body mass index (kg/m^2), smoking and study site (state). Because risk estimates were similar in the simple and adjusted models, we present the adjusted estimates. Interactions (in particular as relates to folic acid use) were examined both by

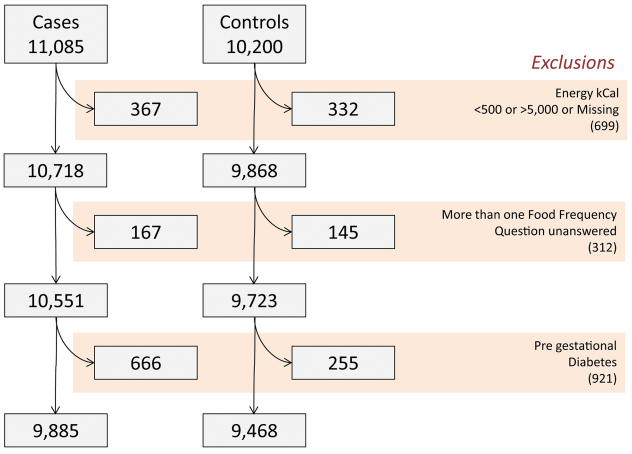

Figure 1 Flow diagram of exclusions in the study of maternal diet quality and risk for congenital heart defects, National Birth Defects Prevention Study, 1997–2009.

evaluating effect estimates in stratified analyses and by the significance of statistical interaction terms (multiplicative) in the logistic models. The primary focus of this study was on selected conotruncal and septal heart defects because of prior studies suggesting preventive benefits with multivitamin supplementation, but we secondarily evaluated also other major heart defects, for which few data are available in the literature.

RESULTS

Table 1 shows descriptive characteristics of the study sample. Of the control mothers, 18% smoked in early pregnancy, 38% were overweight or obese, and 76% reported using folic acid-containing supplements at some time in the periconceptional period (31% regularly). Missing values are typically <1% of the total (range 0–4%).

Diet quality among controls

We observed a correlation between the two diet score indices ($r=0.45$, $p<0.01$). Quartiles were uniformly distributed when stratified by maternal education, but with a trend of lower diet quality among overweight and obese women (data not shown).

Diet quality and CHDs

We observed inverse associations between better diet quality scores and risk for selected conotruncal and septal defects (table 2). For most other CHD types, except possibly for right-sided obstructive defects, we saw no consistent pattern of association (table 3). The inverse associations were typically stronger for DQI-P compared with MDS. The strongest association was between DQI-P and tetralogy of Fallot, with an OR for the highest versus lowest quartile of DQI-P of 0.63 (95% CI 0.49 to 0.80). Trends in ORs were evaluated using the Mantel–Haenszel χ^2 test. To examine diet quality through finer gradations, we also assessed risk by deciles of diet quality scores (figure 2). Overall, ORs decreased with increasing deciles, with greatest reductions typically observed in the top decile. For example, the OR for tetralogy of Fallot comparing 10th versus 1st decile (>90th centile vs <10th centile) was 0.55 (95% CI 0.38 to 0.79). We did not identify interactions with maternal folic acid use, body mass index or smoking (data not shown).

DISCUSSION

In this large population-based study, better maternal diet quality during the year before pregnancy was associated with a reduced

Table 1 Descriptive characteristics of study participants, National Birth Defects Prevention Study, 1997–2009

Characteristic	Controls		All CHD		Tetralogy of Fallot		dTGA		VSD pm		ASD2	
	N (n=9468)	%	N (n=9885)	%	N (n=947)	%	N (n=616)	%	N (n=898)	%	N (n=1525)	%
Maternal race/ethnicity												
Non-Hispanic white	5594	59.1	5904	59.7	540	57.0	412	66.9	525	58.5	805	52.8
Non-Hispanic black	1031	10.9	1078	10.9	115	12.1	35	5.7	143	15.9	184	12.1
Hispanic	2183	23.1	2217	22.4	219	23.1	117	19.0	173	19.3	437	28.7
Asian/Pacific Islander	271	2.9	269	2.7	37	3.9	24	3.9	28	3.1	38	2.5
American/Alaskan Native	49	0.5	40	0.4	6	0.6	1	0.2	5	0.6	10	0.7
Other	334	3.5	373	3.8	30	3.2	27	4.4	24	2.7	51	3.3
Maternal age												
<20 years	944	10.0	887	9.0	69	7.3	56	9.1	82	9.1	168	11.0
20–24	2161	22.8	2317	23.4	219	23.1	137	22.2	212	23.6	423	27.7
25–29	2639	27.9	2703	27.3	250	26.4	163	26.5	229	25.5	426	27.9
30–34	2424	25.6	2488	25.2	247	26.1	172	27.9	213	23.7	307	20.1
≥35	1300	13.7	1490	15.1	162	17.1	88	14.3	162	18.0	201	13.2
Maternal education												
≤12 years	3814	40.3	4153	42.0	380	40.1	228	37.0	380	42.3	709	46.5
>12 years	5604	59.2	5678	57.4	564	59.6	384	62.3	514	57.2	808	53.0
Smoking												
Yes	1708	18.0	1996	20.2	158	16.7	123	20.0	194	21.6	368	24.1
Folic acid use												
None	2110	22.3	2224	22.5	187	19.7	145	23.5	227	25.3	391	25.6
Intermittent	4300	45.4	4638	46.9	440	46.5	268	43.5	390	43.4	733	48.1
Regular	2938	31.0	2878	29.1	309	32.6	195	31.7	267	29.7	377	24.7
Maternal body mass index												
Underweight (<18.5)	498	5.3	515	5.2	41	4.3	27	4.4	48	5.3	92	6.0
Normal (18.5 to <25)	4937	52.1	4809	48.6	461	48.7	333	54.1	450	50.1	706	46.3
Overweight (25 to <30)	2086	22.0	2267	22.9	225	23.8	134	21.8	211	23.5	341	22.4
Obese (≥30)	1555	16.4	1880	19.0	185	19.5	103	16.7	157	17.5	312	20.5
Birth weight <2500 g	552	5.8	2140	21.6	215	22.7	51	8.3	220	24.5	536	35.1
Gestational age <37 weeks	869	9.2	2307	23.3	192	20.3	64	10.4	238	26.5	615	40.3

Because of missing values, percentages may not sum to 100 and categories to the total number of cases or controls. Missing values for controls ranged from 0% for maternal age to 4.1% for maternal body mass index. Percentages are calculated on the total number of cases or controls, including those with missing values.
Smoking, maternal reported smoking from 1 month before pregnancy through first trimester of pregnancy.
Folic acid use, supplement use (folic acid alone or folic acid containing supplement) from 1 month before pregnancy through second month of pregnancy.
ASD2, secundum atrial septal defect; CHD, congenital heart defects; dTGA, d-transposition of the great arteries; VSD pm, perimembranous ventricular septal defect.

Table 2 Association of selected conotruncal and septal heart defects with Diet Quality Index in Pregnancy (DQI-P) and Mediterranean Diet Score (MDS), National Birth Defects Prevention Study, 1997–2009

	All conotruncal defects (n=1938)			Tetralogy of Fallot (n=947)			d-TGA (n=616)		
	Cases	aOR	95% CI	Cases	aOR	95% CI	Cases	aOR	95% CI
DQI-P									
Quartile 1	614	1 (reference)		308	1 (reference)		199	1 (reference)	
Quartile 2	471	0.87	0.76 to 1.00	234	0.83	0.69 to 1.00	148	0.86	0.68 to 1.08
Quartile 3	455	0.83	0.72 to 0.97	225	0.78	0.63 to 0.95	142	0.82	0.64 to 1.05
Quartile 4	398	0.76	0.64 to 0.91	180	0.63	0.49 to 0.80	127	0.79	0.59 to 1.06
p for trend		**			**			*	
Decile 10 vs 1		0.66	0.50 to 0.87		0.55	0.38 to 0.79		0.58	0.36 to 0.93
MDS									
Quartile 1	508	1 (reference)		237	1 (reference)		180	1 (reference)	
Quartile 2	519	0.97	0.84 to 1.11	239	0.93	0.76 to 1.12	168	0.93	0.74 to 1.16
Quartile 3	458	0.93	0.80 to 1.07	238	0.98	0.80 to 1.19	128	0.76	0.59 to 0.97
Quartile 4	453	0.98	0.84 to 1.14	233	0.99	0.80 to 1.23	140	0.93	0.72 to 1.21
p for trend									
Decile 10 vs 1		0.80	0.63 to 0.87		0.92	0.67 to 1.26		0.58	0.39 to 0.85
	All septal defects (n=3315)			**VSD pm (n=898)**			**ASD2 (n=1525)**		
DQI-P									
Quartile 1	1010	1 (reference)		274	1 (reference)		472	1 (reference)	
Quartile 2	795	0.92	0.82 to 1.03	227	0.97	0.80 to 1.18	358	0.88	0.75 to 1.03
Quartile 3	743	0.84	0.74 to 0.95	203	0.84	0.68 to 1.04	343	0.78	0.66 to 0.93
Quartile 4	745	0.86	0.75 to 1.00	194	0.84	0.66 to 1.08	352	0.77	0.63 to 0.94
p for trend		**			*			*	
Decile 10 vs 1		0.82	0.65 to 1.02		0.96	0.65 to 1.41		0.59	0.43 to 0.81
MDS									
Quartile 1	1019	1 (reference)		267	1 (reference)		388	1 (reference)	
Quartile 2	1057	0.99	0.88 to 1.11	226	0.86	0.71 to 1.04	408	1.01	0.86 to 1.18
Quartile 3	1000	1.00	0.88 to 1.12	216	0.91	0.74 to 1.11	400	1.00	0.84 to 1.17
Quartile 4	903	0.93	0.82 to 1.06	189	0.86	0.69 to 1.07	329	0.83	0.69 to 0.99
p for trend					*				
Decile 10 vs 1		0.84	0.70 to 1.01		0.88	0.68 to 1.15		0.79	0.64 to 0.99

p value for trend: *0.01 <p<0.05; **p<0.01.
OR adjusted for maternal energy intake, race/ethnicity, folic acid supplement use smoking, maternal education, maternal body mass index, study centre (see methods for details).
Because of missing values, categories may not sum up to the total number of cases.
ASD2, secundum atrial septal defect; dTGA, d-transposition of the great arteries; VSD pm, perimembranous ventricular septal defect.

risk for selected non-syndromic CHDs. These CHDs were mostly specific subgroups of conotruncal and septal defects. No clear risk reduction was observed for several other CHDs. The risk reduction trended fairly smoothly throughout the range of diet quality scores (figure 2), with no obvious plateau until the highest decile of the distribution. These relations were not substantively influenced by maternal folic acid use, body mass index or smoking. Of note, the types of heart defects for which a risk reduction was observed (selected conotruncal and septal heart defects) were similar to those reported in studies of periconceptional multivitamin supplementation.[7–10]

These findings must be interpreted in the context of the study's methods and setting. The interview instrument is a shortened version of the Willett FFQ and includes 58 food items. We used the DQI-P and MDS scores with modifications (eg, DQI: excluded the meals/snacks pattern and included sweets component; MDS: excluded alcohol component and included sweets component); these changes were not specifically validated. Limitations of the study include the inability to validate reported dietary intakes, as well as the potential influence of residual confounding, selection and recall bias, and multiple comparisons. We adjusted for multiple potential confounders; the adjustments did not alter the results markedly, suggesting (but not excluding) that significant residual confounding or bias is unlikely. Diet quality can be associated with social class indicators, some of which (but not all) we were able to include in the adjusted analysis. Selection and recall biases are a constant concern in such observational and retrospective studies, particularly given the study's participation rates (which were, however, similar between cases and controls), and in part the time difference from delivery to interview between the two groups (also relatively small: median of 4 months). However, the diet score is based on multiple inputs, so it is unlikely that recall would be systematically biased for all of them. In general, studies that have evaluated the magnitude of recall bias in birth defect studies suggest that it is likely minimal in well-conducted studies.[22 23] Study strengths include the population-based setting, the completeness of interview (small number of missing values) and the centralised case review by clinical specialists.

Table 3 Association of selected major congenital heart defects with Diet Quality Index in Pregnancy (DQI-P) and Mediterranean Diet Score (MDS), National Birth Defects Prevention Study, 1997–2009

	LVOTO, all (n=1702)			Hypoplastic left heart (n=505)			Aortic stenosis (n=290)			Coarctation of the aorta (n=898)		
LVOTO group	**Cases**	**aOR**	**95% CI**	**Cases**	**aOR**	**95% CI**	**Cases**	**aOR**	**95% CI**	**Cases**	**aOR**	**95% CI**
DQI-P												
Quartile 1	491	1 (reference)		152	1 (reference)		91	1 (reference)		247	1 (reference)	
Quartile 2	452	1.05	0.90 to 1.21	128	0.92	0.71 to 1.19	87	1.17	0.85 to 1.60	229	1.04	0.85 to 1.27
Quartile 3	402	0.97	0.83 to 1.14	113	0.87	0.66 to 1.15	60	0.90	0.62 to 1.30	226	1.04	0.84 to 1.28
Quartile 4	357	0.93	0.77 to 1.12	112	0.86	0.62 to 1.19	52	0.90	0.58 to 1.41	187	0.94	0.73 to 1.21
Decile 10 vs 1		0.79	0.58 to 1.06		0.91	0.55 to 1.53		1.25	0.65 to 2.39		0.58	0.38 to 0.89
MDS												
Quartile 1	460	1 (reference)		147	1 (reference)		86	1 (reference)		224	1 (reference)	
Quartile 2	466	1.00	0.86 to 1.15	128	0.89	0.69 to 1.14	84	1.09	0.79 to 1.50	247	1.01	0.83 to 1.23
Quartile 3	394	0.96	0.82 to 1.12	115	0.91	0.70 to 1.19	70	1.10	0.79 to 1.55	205	0.95	0.77 to 1.17
Quartile 4	382	1.04	0.88 to 1.23	115	1.01	0.76 to 1.34	50	1.03	0.70 to 1.53	213	1.05	0.84 to 1.30
Decile 10 vs 1		0.88	0.68 to 1.23		0.69	0.44 to 1.06		0.86	0.46 to 1.59		0.98	0.70 to 1.36
	RVOTO, all (n=1627)			**Pulmonary atresia (n=159)**			**Pulmonary stenosis (n=1217)**			**Tricuspid atresia (n=133)**		
RVOTO group	**Cases**	**aOR**	**95% CI**	**Cases**	**aOR**	**95% CI**	**Cases**	**aOR**	**95% CI**	**Cases**	**aOR**	**95% CI**
DQI-P												
Quartile 1	529	1 (reference)		52	1 (reference)		406	1 (reference)		39	1 (reference)	
Quartile 2	383	0.84	0.72 to 0.98	37	0.78	0.50 to 1.21	281	0.83	0.70 to 0.98	32	0.79	0.48 to 1.30
Quartile 3	364	0.79	0.67 to 0.93	35	0.76	0.47 to 1.23	274	0.81	0.67 to 0.97	27	0.56	0.32 to 0.98
Quartile 4	351	0.79	0.65 to 0.96	35	0.72	0.41 to 1.26	256	0.82	0.66 to 1.02	35	0.67	0.37 to 1.24
Decile 10 vs 1		0.74	0.55 to 1.00		1.19	0.50 to 2.83		0.71	0.50 to 1.00		0.65	0.26 to 1.66
MDS												
Quartile 1	441	1 (reference)		52	1 (reference)		322	1 (reference)		31	1 (reference)	
Quartile 2	454	1.03	0.89 to 1.19	43	0.78	0.52 to 1.18	352	1.10	0.93 to 1.30	30	0.92	0.55 to 1.54
Quartile 3	415	1.05	0.90 to 1.23	38	0.66	0.42 to 1.04	311	1.14	0.95 to 1.36	34	0.97	0.57 to 1.63
Quartile 4	317	0.87	0.73 to 1.04	26	0.43	0.25 to 0.75	232	0.97	0.79 to 1.18	38	0.95	0.55 to 1.66
Decile 10 vs 1		0.86	0.66 to 1.11		0.39	0.17 to 0.93		0.94	0.69 to 1.27		1.25	0.58 to 2.72
	AVSD (n=233)			**TAPVR (n=227)**			**Single Ventricle (n=250)**			**Heterotaxy (n=253)**		
Other, or complex	**Cases**	**aOR**	**95% CI**	**Cases**	**aOR**	**95% CI**	**Cases**	**aOR**	**95% CI**	**Cases**	**aOR**	**95% CI**
DQI-P												
Quartile 1	84	1 (reference)		71	1 (reference)		80	1 (reference)		66	1 (reference)	
Quartile 2	61	0.83	0.58 to 1.19	46	0.72	0.48 to 1.08	63	0.97	0.68 to 1.39	68	1.19	0.83 to 1.71
Quartile 3	47	0.69	0.46 to 1.02	63	0.98	0.66 to 1.45	61	1.02	0.70 to 1.49	72	1.20	0.82 to 1.75
Quartile 4	41	0.65	0.41 to 1.05	47	0.63	0.38 to 1.03	46	0.73	0.45 to 1.18	47	0.67	0.41 to 1.08
Decile 10 vs 1		0.81	0.40 to 1.65		0.88	0.40 to 1.92		1.05	0.51 to 2.16		0.55	0.26 to 1.17

Continued

Table 3 Continued

LVOTO group	LVOTO, all (n=1702)			Hypoplastic left heart (n=505)			Aortic stenosis (n=290)			Coarctation of the aorta (n=898)		
	Cases	aOR	95% CI	Cases	aOR	95% CI	Cases	aOR	95% CI	Cases	aOR	95% CI
MDS												
Quartile 1	72	1 (reference)		51	1 (reference)		57	1 (reference)		65	1 (reference)	
Quartile 2	60	0.87	0.61 to 1.24	70	1.26	0.86 to 1.85	71	1.09	0.75 to 1.57	55	0.77	0.53 to 1.12
Quartile 3	61	1.03	0.72 to 1.48	50	0.90	0.59 to 1.38	64	1.10	0.75 to 1.62	71	1.01	0.70 to 1.45
Quartile 4	40	0.77	0.50 to 1.19	56	1.05	0.68 to 1.63	58	1.03	0.68 to 1.57	62	0.80	0.54 to 1.20
Decile 10 vs 1		0.65	0.33 to 1.28		0.57	0.30 to 1.11		0.90	0.47 to 1.69		0.66	0.38 to 1.16

ORs are adjusted for potential confounders (see text).Because of missing values, categories may not sum up to the total number of cases.
AVSD, atrioventricular septal defects (atrioventricular canal defects); LVOTO, left ventricular outflow tract obstruction; RVOTO, right ventricular outflow tract obstruction; TAPVR, total anomalous pulmonary venous return.

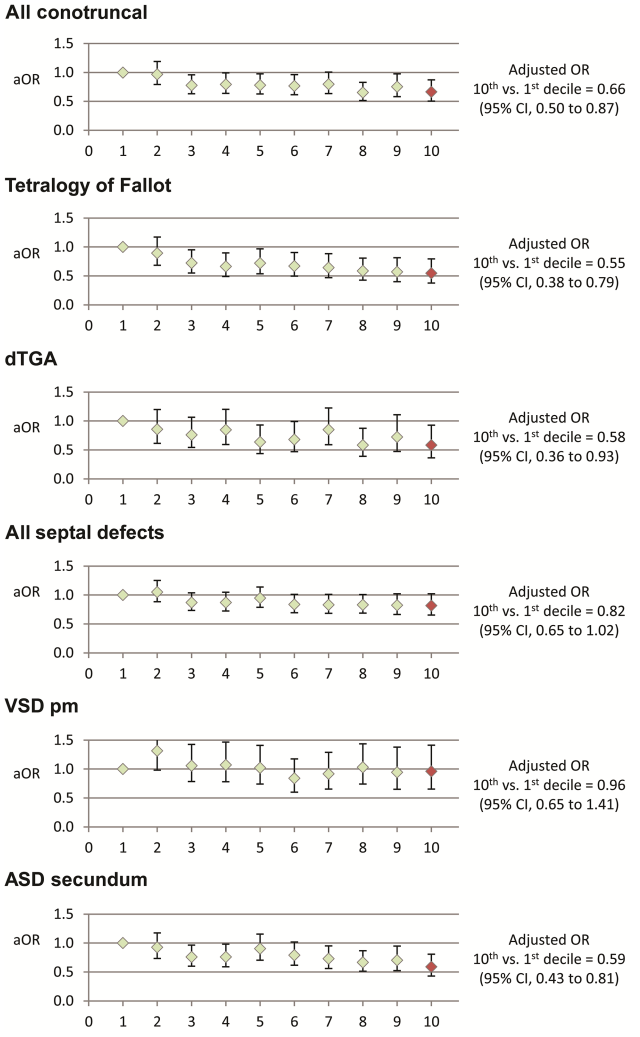

Figure 2 Estimated risks for conotruncal and septal heart defect, by deciles of Diet Quality Index in Pregnancy (DQI-P), National Birth Defects Prevention Study, 1997–2009. Deciles of DQI-P scores on horizontal axis, adjusted OR on vertical axis (reference stratum=first decile). ASD, secundum atrial septal defect; dTGA, d-transposition of the great arteries; VSD pm, perimembranous ventricular septal defect.

The findings of the study must also be interpreted in the context of the available knowledge on diet and cardiac risk factors. Some studies examined a priori diet quality indices in relation to the risk of birth defects,[13 14 24] but not of CHDs. The studies that used the DQI-P and MDS reported associations between increasing diet quality and reduced risk for some birth defects (neural tube defects and orofacial clefts[13]), but not others (microtia and hypospadias).[14 24] The magnitude of the risk reduction for CHDs in this study (table 2) is approximately similar, if slightly weaker, to that observed for neural tube defects and orofacial clefts with similar dietary indices.[13] Of note, risk reductions for neural tube defects and orofacial clefts tended to be more marked with the DQI-P than the MDS, a pattern similar to that observed in this study for the selected CHDs. In the prior study, the estimated risk reduction varied by phenotype (eg, apparently greater for anencephaly than for spina bifida); we noted marked variations also by CHD phenotype, between as well as within anatomical subgroups (eg, between tetralogy of Fallot and d-transposition of the great arteries, and between atrial and ventricular septal defects), which are not unexpected given the etiological and pathogenetic heterogeneity of CHDs.

Other studies evaluated CHD risk in relation not to a priori indices, but rather to dietary patterns generated through statistical analyses of the data. In one such study,[25] reduced rank regression (focusing on diets associated with high levels of one-carbon donors in plasma) characterised a diet rich in fish and seafood as being associated with reduced CHD risk. Because their case group (231 cases) included different types of CHDs and clinical presentations, including genetic syndromes, their results and ours are not directly comparable. Another study[26] used NBDPS data and statistically driven grouping (latent class analysis) to define four main dietary patterns; one of these ('prudent diet') was associated with reduced risks for neural tube and CHDs. This 'prudent diet' was higher in fruits, vegetables, whole wheat grains, reduced-fat dairy and fish compared with the other dietary patterns ('Western', 'low-calorie Western', 'Mexican'). Although the dataset used in that study overlapped with ours, the many methodological differences preclude direct comparisons of results. In our study, the analysis focused on a priori indices of diet quality, to be more easily reproducible and comparable to prior studies of other birth defects the in the NBDPS. In addition, the evaluation by quartiles or deciles allowed us to examine gradations of diet quality. Folic acid supplement use in the two studies was defined slightly differently; however, folic acid use in the few months before conception is stable among most women in our dataset, so the difference in timing is unlikely to be important analytically. Finally, an unresolved questions is why the strength of the inverse association between diet quality and CHD risk varied in the two a priori indices, though it is notable that also in previous evaluations of other birth defects[13] the inverse association between diet quality and birth defect risk was similarly stronger for DQI than MDS.

In summary, in this population-based study, we found that better maternal diet quality in the year before pregnancy, using two a priori diet indices, was associated with reduced risks for specific subgroups of CHDs, including tetralogy of Fallot. These results add to the accumulating evidence of the importance of diet quality for many health outcomes. There are very few known protective factors for CHDs; if better diet could help reduce the risk, it would represent a further benefit of the recommendations about optimal nutrition that are part of many preconception care initiatives.

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Disclaimer The findings and conclusions in this report are those of the author(s) and do not necessarily represent the views of the Centers for Disease Control and Prevention or of the California Department of Public Health.

Competing interests None declared.

Patient consent Obtained.

Ethics approval Approval for each study was obtained from the respective academic institutions at each site.

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Data sharing statement NBDPS is not permitted to release individual-level data or aggregated data with small cell sizes. The scientific protocol for this analysis is available on request.

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Lower rate of selected congenital heart defects with better maternal diet quality: a population-based study

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