Hypertension in pregnancy

Construction and characterisation of a longitudinal clinical blood pressure database for epidemiological studies of hypertension in pregnancy

Mary Lou Thompson[a], Raymond S. Miller[c] and Michelle A. Williams[b,c]

Departments of [a]Biostatistics and [b]Epidemiology, University of Washington School of Public Health and Community Medicine, and [c]Center for Perinatal Studies, Swedish Medical Center, Seattle, WA, USA

Correspondence:
Dr Michelle A. Williams, Department of Epidemiology, Center for Perinatal Studies, Swedish Medical Center, 1124 Columbia Street, Suite 750, Seattle, WA 98104, USA.
E-mail: mwilliam@u.washington.edu

Summary

Thompson ML, Miller RS, Williams MA. Construction and characterisation of a longitudinal clinical blood pressure database for epidemiological studies of hypertension in pregnancy. *Paediatric and Perinatal Epidemiology* 2007; **21:** 477–486.

Blood pressure measurement plays a central role in the screening and management of hypertension during pregnancy. Although descriptions of changes in blood pressure patterns of normotensive and hypertensive pregnancies are plentiful, relatively little is known about how modifiable environmental and lifestyle characteristics, including maternal diet and physical activity, influence blood pressure levels in pregnancy. In this paper we provide a detailed description of the first 2000 subjects enrolled in the Omega Prospective Cohort Study. Our intention is to characterise the cohort and to establish a rigorous data framework that will form the basis for future analyses of the association between blood pressure patterns in pregnancy and modifiable risk factors. We describe the construction of a representative longitudinal blood pressure analysis database drawn from routinely collected measurements. In doing this, we explore possible over- and under-representation of patients and evaluate ways of modifying the database to address areas of possible bias. In addition, we consider questions of data quality which are specific to blood pressure measurements. In an accompanying paper, we use this database to explore the influence of maternal pre-pregnancy adiposity on blood pressure levels across gestation.

Keywords: *blood pressure measurements*, *longitudinal*, *bias*, *pregnancy*, *serial measures*.

Introduction

Improved understanding of the determinants of blood pressure changes during pregnancy, and the application of that understanding towards the prevention and control of hypertensive disorders of pregnancy, is essential for decreasing the morbidity and mortality borne by women and their families worldwide. Cardiovascular changes known to take place in pregnancy include generalised reductions in vascular tone resulting from systemic vasorelaxation, as well as increased blood volume, heart rate and cardiac output. These changes, considered physiological in uncomplicated pregnancies, are altered in women who develop pre-eclampsia and other hypertensive disorders of pregnancy.

Importantly, clinical blood pressure measurement plays a central role in the screening and management of hypertension during pregnancy.[1,2] Although descriptions of changes in blood pressure patterns of normotensive and hypertensive pregnancies are plentiful, relatively little is known about how modifiable environmental and lifestyle characteristics, including maternal diet and physical activity, influence blood pressure levels during pregnancy. While data from cross-sectional observational studies indicate, for instance, that maternal dietary antioxidants and

pregestational adiposity may influence the occurrence of pre-eclampsia, the absence of prospective data that characterise maternal blood pressure changes (a marker of maternal adaptation to the haemodynamic demands of the uteroplacental unit) precludes examination of the nature and magnitude of the effect of such factors.

In this paper we provide a detailed description of the blood pressure substudy of the Omega Cohort Study and of the construction and characterisation of the associated longitudinal database. In an observational study with longitudinal records such as this, evaluation of whether there is balanced representation of subjects across the study is more complex than when there is only a single measurement per individual. We explore longitudinal representation in a variety of ways and modify the database to address some areas of possible bias. In doing this, we illustrate a general approach to determining the validity of a set of longitudinal measurements (here consisting of clinically generated blood pressures) as a research database. In addition, we consider questions of data quality which are specific to blood pressure measurements.

This paper is intended to serve as a foundation and reference for future analyses of the association between modifiable risk factors and blood pressure during pregnancy. In an accompanying paper, we report findings from analyses with aims that were twofold. First, we sought to corroborate earlier reports indicating the influence of maternal pre-pregnancy adiposity on blood pressure levels across gestation. Second, in the process of completing our first aim, we sought to provide evidence suggestive of the 'face validity' of routinely measured ambulatory blood pressure from clinically diverse settings.

Methods

Study design and population

The Omega Study is an ongoing prospective study examining the metabolic and dietary predictors of pre-eclampsia, gestational diabetes and other pregnancy outcomes.[3,4] The study population was drawn from women attending prenatal care at clinics affiliated with the Swedish Medical Center and Tacoma General Hospital in Seattle and Tacoma, WA. Recruiting began in December 1996, and we present here the results from the first 2000 women enrolled by September 2002. Women were ineligible if they were younger than 18 years old, did not speak and read English, did not plan to carry the pregnancy to term or deliver at either of the two research hospitals, and/or were past 20 weeks' gestation. All women were enrolled in the study for only one pregnancy.

The procedures used in this study were in agreement with the protocols approved by the Institutional Review Boards of the Swedish Medical Center and Tacoma General Hospital. All participants provided written informed consent.

Analytical population

The analytical population is derived from participants who enrolled in the Omega Study between December 1996 and September 2002. During this period, 2556 eligible women were approached and 2000 (78%) agreed to participate. We excluded 19 women whose pregnancy ended (miscarriage $n = 14$; induced abortion $n = 5$) prior to the clinical recording of at least one antepartum blood pressure; 56 women for whom we could not locate a clinic or medical record; and 5 women with a gestational age of first prenatal care visit greater than 20 weeks. Hence, 1920 women remained and these subjects comprised the core study cohort.

Data collection and blood pressure records

We used primarily clinical blood pressures taken and recorded during routine antepartum visits. All systolic and diastolic blood pressure measurements, along with the date and gestational age when the reading was taken, were abstracted retrospectively from participants' clinical records. Blood pressures taken upon admission for inpatient observation or to the emergency room were considered only when blood pressure from an expected antepartum visit was unavailable. In the final database, this augmentation was necessary for less than 10% of women and augmented records constituted 1.5% of total blood pressure records in this database. Blood pressures taken during active labour or during the postpartum period were not considered. During the study period, many different healthcare providers made blood pressure readings part of routine clinical practice. Therefore, we cannot be certain that all blood pressure readings were consistently determined using the fifth Krotkoff sound. Although the measures are not strictly standardised as they would be in a clinical trial, blood pressures were

taken using standard mercury sphygmomanometers scaled to even numbers and patients were seated during evaluation.

Throughout, we will use the term 'blood pressure record' to simultaneously denote systolic and diastolic blood pressure records. Mean arterial pressure, considered an integrated parameter of blood pressure, is known to be more reproducible than individual systolic and diastolic blood pressures.[5] We therefore also computed mean arterial pressure for each subject according to the following formula:

$$\text{mean arterial pressure} = \tfrac{2}{3}\text{diastolic} + \tfrac{1}{3}\text{systolic}$$

Relevant covariates

At the time of enrolment in the Omega Study, a 45- to 60-min structured questionnaire was administered by a trained interviewer. Information on medical and reproductive histories and sociodemographic and lifestyle characteristics was collected. We also obtained (self-reported) information regarding maternal educational attainment, annual household income, prenatal vitamin supplement use and smoking during pregnancy. Maternal age was determined at the time of the interview and was expressed in years. Parity was reported as the number of previous pregnancies lasting beyond 20 weeks' gestation. Gestational age of pregnancy was determined using maternal self-report of the last normal menstrual period, and this date was confirmed by ultrasound examination completed prior to 20 weeks' gestation. Non-fasting blood and urine specimens were collected, processed and stored during early pregnancy. Detailed information about maternal habitual dietary intake during the periconceptional period and early pregnancy was ascertained using a self-administered, 121-item semiquantitative food frequency questionnaire.[6] Food composition values were obtained from the University of Minnesota Nutrition Coding Center nutrient database.[7] Antepartum characteristics and pregnancy outcome information were abstracted from clinic and hospital labour and delivery medical records after the estimated delivery date.

Evaluating participants' longitudinal representation

Longitudinal data collected from routine measurements are subject to many potential biases. In our setting, women may be over- or under-represented in the records for reasons that are related to the outcome (here blood pressure) and possibly to covariates of interest. This over- or under- representation may vary across stages of pregnancy. For instance, some women enrolled at an earlier gestational age than others, and some women delivered earlier. Additionally, there may be 'confounding by indication', in that women who have higher blood pressure levels may be over-represented and may also have different characteristics on covariates of interest. We emphasise that hypothesis testing was undertaken not to assess risk factor associations, but rather to evaluate possible biases in this routinely collected longitudinal data set.

Hypothesis tests comparing characteristics of different groups within the sample were based on chi-squared tests for categorical variables and *t*-tests or *F*-tests for continuous variables. Where repeated measures on the same individual were used, estimation was based on generalised estimating equations with an assumption of exchangeable correlation and using robust estimates of variance. The level of significance was set at 0.05. Analyses were carried out using STATA version 9.2.[8]

We addressed the issue of representation over the duration of pregnancy in a number of ways. We first examined the distribution of gestational age at first prenatal visit and compared selected characteristics of participating women according to whether their gestational age at first visit was <7, 7–10 or >10 weeks. This analysis evaluates one possible source of bias: whether women whose records commenced later in pregnancy differ from those whose records commenced earlier.

Once prenatal visits have commenced, pregnant women are expected to keep to a regular schedule of prenatal clinic visits, and the expected number of visits varies across gestation. We defined 'early', 'middle' and 'late' pregnancy to coincide with, respectively, gestational age <27 completed weeks, when antepartum visits are expected to occur every 4 weeks; gestational age 27–35 completed weeks, when antepartum visits are expected to occur every 2 weeks; and ≥36 completed weeks gestation, when antepartum visits are expected to take place weekly until delivery.[9] Within each of these pregnancy periods, after adjusting for time of first prenatal visit and delivery date, we identified women who had had two or more fewer blood pressure records than expected, and two or more records in excess of expected. We then compared selected characteristics of these women with those of women who were appropriately represented accord-

ing to the prescribed regimen. This analysis allowed us to identify factors which are associated with the extent of use of prenatal care, and hence which might also represent a source of bias. All of the above analyses were based on the 'source' data, namely the full clinic longitudinal database, which includes all available clinic blood pressure records for each woman in the study, without augmentation by hospital records.

The recommended prenatal visit regimen results in more records later in pregnancy than in early pregnancy. To address the problem of possible over-representation of individual women and to ensure that different periods in pregnancy were equally represented, the final 'analysis' database was constructed based on 11 pregnancy intervals, each of 4 weeks, with the exception of the last interval, which was of 2 weeks. For each woman in the study, a single record (if available) was randomly selected from the source data for each of the intervals 1–4, 5–8, 9–12, 13–16, 17–20, 21–24, 25–28, 29–32, 33–36, 37–40 and 41–42 weeks. Intervals with no blood pressure records were supplemented with hospital records, when available. This constituted the final analysis database.

For this final database, as an assessment of possible remaining bias, we examined the distribution of the number of blood pressure records per woman and compared the characteristics of women who had ≥ 7 records (out of a possible 11) with those who had <7 records. As a separate descriptive exercise, we examined the distribution of systolic, diastolic and mean arterial blood pressures in each of the above 11 pregnancy intervals.

In summary, we evaluated possible sources of bias in the 'source' longitudinal data set by comparing groups of women defined by date of enrolment and by number of visits during three stages of pregnancy. We addressed possible over-representation of individual women and of stages of pregnancy by random selection from the longitudinal record of each woman. We then also compared characteristics of women according to their total number of visits in the final analysis database.

Assessing data quality

Two particular data quality problems are recognised as potentially arising with blood pressure measurements: the possibility of identical successive measurements and of last digit preference.[10–12] We determined the prevalence in the original source data of identical successive measurements for systolic and diastolic blood pressure. We also examined the distribution of the last digit of systolic and diastolic blood pressure records in the analysis database. We evaluated the impact of digit preference by conducting preliminary analyses, comparing mean blood pressure levels across trimesters of pregnancy, with and without random reassignment of digit-preferred readings.

Results

The source data set contained 23 296 systolic and 23 288 diastolic blood pressure records from 1920 women. The median gestational age at first prenatal visit was 8 weeks (range 2–20 weeks). Eight per cent of participants had their first prenatal visit by week 6 of pregnancy, and 85.2% by week 10. Table 1 shows the distribution of selected population characteristics according to gestational age at first prenatal visit. Importantly, trimester-specific mean blood pressure values did not differ significantly across the three groups.

The mean number of prenatal visits for women in the study was 12.2 (median = 13, interquartile range: 11–14 visits). Not surprisingly, for all three defined periods of pregnancy ('early', 'middle', 'late'), we noted that women who had more prenatal care visits (and more recorded antenatal blood pressure values) in the 'source' data, as compared with their counterparts with the expected number of visits, were more likely to have a diagnosis of pre-eclampsia (data not shown). In 'early' and 'middle' pregnancy, women with more records than expected were more likely to have experienced gestational diabetes during the index pregnancy, and to have delivered at an earlier gestational age. Mean trimester-specific blood pressures were also significantly elevated relative to women who adhered to the prescribed regimen (data not shown). In weeks 36–42 of pregnancy (i.e. the 'late' period), third-trimester mean blood pressure differed significantly across the groups, being highest in the group who were over-represented in late pregnancy and lowest in the women who were under-represented (data not shown). These comparisons serve to illustrate the kind of biases that can arise if the issue of longitudinal representation across the cohort is not evaluated.

The next steps in constructing the analysis database were intended to ensure, to the extent possible, that there was no over-representation of participants in any period of pregnancy, and also no over-representation of any period of pregnancy.

Table 1. Characteristics of the study cohort according to categories of gestational age at first prenatal care visit, Seattle and Tacoma, WA, 1996–2002

Characteristics	Gestational age of first prenatal care visit			
	<7 weeks (n = 153) %	7–10 weeks (n = 1242) %	>10 weeks (n = 525) %	P-value
Maternal age (years)				0.010
<20	0.7	0.5	1.6	
20–34	72.3	71.4	65.3	
35+	26.5	28.2	33.1	
Unmarried	13.5	7.7	14.1	<0.0005
Multiparous	25.0	34.8	29.2	0.010
Maternal race/ethnicity				0.437
Non-Hispanic white	87.2	84.7	85.1	
African American	0.7	1.8	3.0	
Asian	5.4	7.9	6.8	
Other	6.8	5.6	5.2	
Annual household income (US$)				0.001
<30 000	3.5	3.2	7.5	
30 000–70 000	32.4	24.9	24.5	
70 000+	64.1	72.0	68.0	
Less than 12 years' education	4.1	4.2	6.6	0.109
Pre-pregnancy body mass index (kg/m^2)				0.242
<20.0	18.2	19.1	22.3	
20.0–24.9	53.4	57.3	52.8	
25.0–29.9	16.2	15.1	13.8	
≥30.0	12.2	8.5	11.2	
Gestational age at delivery (weeks)				0.057
<28	9.2	4.3	5.3	
28–36	10.5	9.3	12.2	
37–40	67.3	72.1	70.9	
41–42	13.1	14.3	11.6	
Pre-eclampsia	6.6	5.3	6.0	0.724
Gestational diabetes	4.6	3.9	5.4	0.353
	Mean (SE)	Mean (SE)	Mean (SE)	
First trimester				
Systolic blood pressure	114.01 (0.88)	113.88 (0.28)	113.72 (0.52)	0.947
Diastolic blood pressure	70.14 (0.55)	70.68 (0.20)	70.25 (0.36)	0.439
Mean arterial pressure	84.76 (0.63)	85.07 (0.21)	84.72 (0.38)	0.674
Second trimester				
Systolic blood pressure	114.26 (0.86)	114.72 (0.25)	115.53 (0.41)	0.178
Diastolic blood pressure	69.11 (0.56)	69.59 (0.18)	69.74 (0.28)	0.604
Mean arterial pressure	84.15 (0.62)	84.57 (0.19)	84.94 (0.31)	0.421
Third trimester				
Systolic blood pressure	116.29 (0.84)	117.30 (0.26)	117.27 (0.43)	0.514
Diastolic blood pressure	72.64 (0.61)	72.59 (0.20)	72.76 (0.30)	0.894
Mean arterial pressure	86.81 (0.64)	87.19 (0.20)	87.31 (0.33)	0.779

Our final analysis database contained a total of 14 229 systolic blood pressure records and 14 225 diastolic blood pressure records from 1920 women. These records were randomly selected from those available in the source data, so that each woman contributed (a maximum of) one blood pressure record per 4-week period from the start of pregnancy until week 40 and (a maximum of) one record thereafter. Consequently each woman had at most 11 records in the final analysis database. In the process of constructing this final analysis database, we used 216 blood pressure readings that were recorded for 187 women (representing 1.5% of

Table 2. Comparison of study subjects with less than 7 recorded blood pressure values vs. those with at least 7 recorded values in the analysis database, Seattle and Tacoma, WA, 1996–2002

	<7 records (N^a = 341)		≥7 records (N^a = 1579)		
Characteristics	*n*	%	*n*	%	*P*-value
Maternal age (years)					0.015
<20	6	1.9	7	0.5	
20–34	216	66.9	1085	70.8	
35+	101	31.3	448	29.1	
Unmarried	42	13.0	141	9.2	0.035
Multiparous	95	29.4	510	33.1	0.196
Maternal race/ethnicity					0.006
Non-Hispanic white	275	85.4	1303	84.7	
African American	13	4.0	25	1.6	
Asian	14	4.4	123	8.0	
Other	20	6.2	87	5.7	
Less than 12 years' education	21	6.7	69	4.6	0.115
Annual household income (US$)					0.001
<30 000	26	8.3	57	3.8	
30 000–69 999	88	28.0	371	24.8	
70 000+	200	63.7	1070	71.4	
Pre-pregnancy body mass index (kg/m^2)					0.320
<20	66	20.4	302	19.6	
20.0–24.9	166	51.4	865	56.2	
25.0–29.9	57	17.7	217	14.1	
≥30.0	34	10.5	156	10.1	
Gestational age at delivery (weeks)					<0.0005
<28	95	27.9	0	0.0	
28–36	88	25.8	108	6.8	
37–40	145	42.5	1225	77.6	
>40	13	3.8	246	15.6	
Pre-eclampsia	15	6.1	86	5.5	0.708
Gestational diabetes	11	4.5	67	4.3	0.913
	Mean (SE)		Mean (SE)		
First trimester					
Systolic blood pressure	114.70 (0.67)		113.53 (0.26)		0.103
Diastolic blood pressure	70.82 (0.45)		70.45 (0.19)		0.441
Mean arterial pressure	85.45 (0.48)		84.80 (0.19)		0.205
Second trimester					
Systolic blood pressure	115.74 (0.59)		114.62 (0.23)		0.074
Diastolic blood pressure	69.91 (0.43)		69.48 (0.16)		0.347
Mean arterial pressure	85.18 (0.45)		84.53 (0.17)		0.171
Third trimester					
Systolic blood pressure	118.14 (0.83)		117.02 (0.24)		0.199
Diastolic blood pressure	71.95 (0.60)		72.52 (0.17)		0.361
Mean arterial pressure	87.34 (0.63)		87.35 (0.18)		0.987

[a]Individual characteristic totals may vary due to missing observations.

the final database) who were hospital inpatients during the antepartum period and, therefore, missed a regularly scheduled prenatal care appointment.

We evaluated the extent of internal under-representation in our analysis database, and whether women who were under-represented differed from those who were adequately represented. We noted that 82% of women had ≥ 7 systolic blood pressure records (out of a maximum possible 11) in our database. Table 2 compares the characteristics of these women with those who had fewer records. Women with more complete records were younger, were more likely to be married and had higher income, and there was a higher representation of women of Asian race. Not

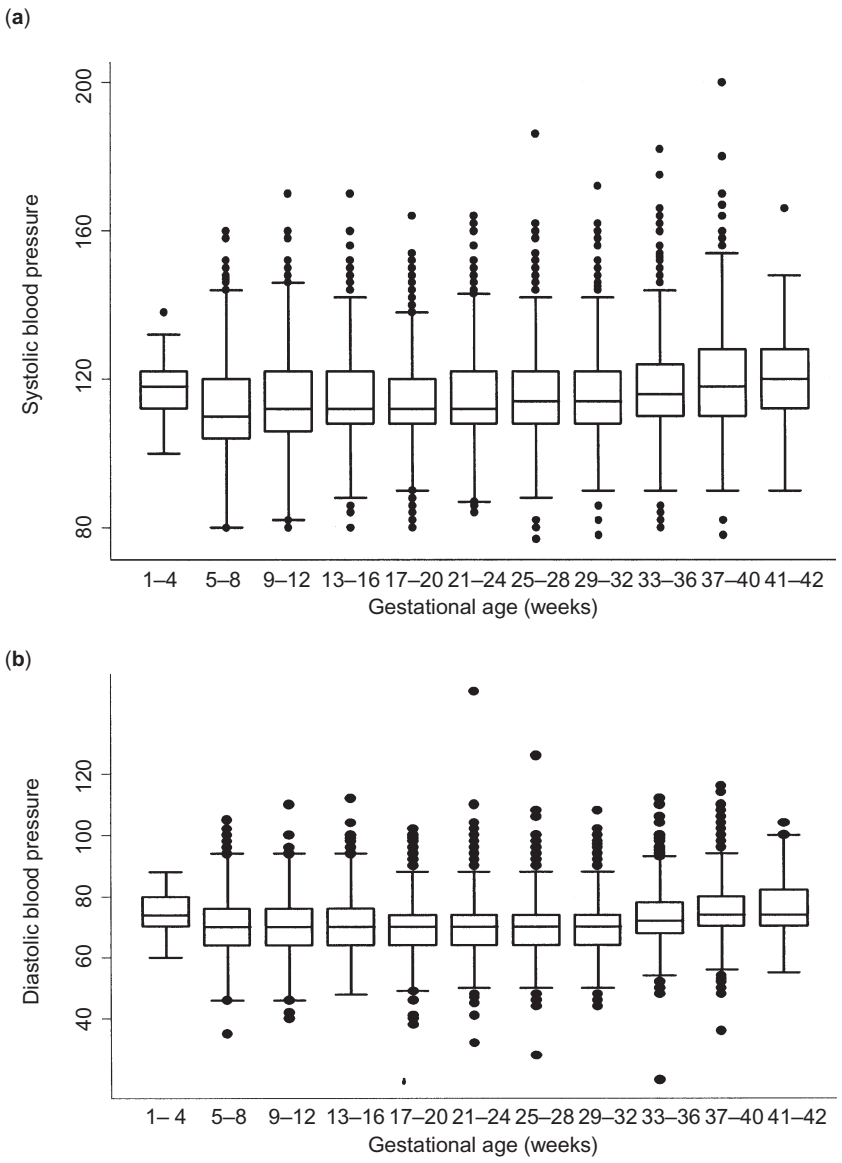

Figure 1. Longitudinal distribution of systolic (a) and diastolic (b) blood pressure in the analysis database. The boxes extend from the 25th to the 75th percentile, with the line within the box being at the median. The 'whiskers' extend to the smallest/largest observation, not an outlier. Outliers are shown individually.

surprisingly, the two groups differed by gestational age at delivery, with women with fewer records having delivered earlier. Importantly, however, there were no differences of note in mean blood pressure values across the two groups.

Figure 1 shows the distribution of systolic and diastolic blood pressure records for each of the 11 pregnancy intervals considered in the final analysis database. The longitudinal characteristics of these figures will be explored in more depth in our companion paper[13] and subsequent papers.

Two aspects of data quality of particular relevance to blood pressure measurements were also evaluated. First, we considered the extent to which successive identical blood pressure readings were present in the source database. From these analyses we noted that 62% of women had one or more successive systolic blood pressure readings that were identical. Approximately 78% of women had one or more successive identical diastolic blood pressure readings. Second, we evaluated the extent to which digit preference was evident in available blood pressure records. In the analysis database, odd digit measurements occurred rarely, constituting 1.2% of systolic and 0.9% of diastolic blood pressure readings. Figure 2 shows the frequency of individual blood pressure readings, restricted to even digits. There was evidence of a preference for the digit zero, which would be expected to

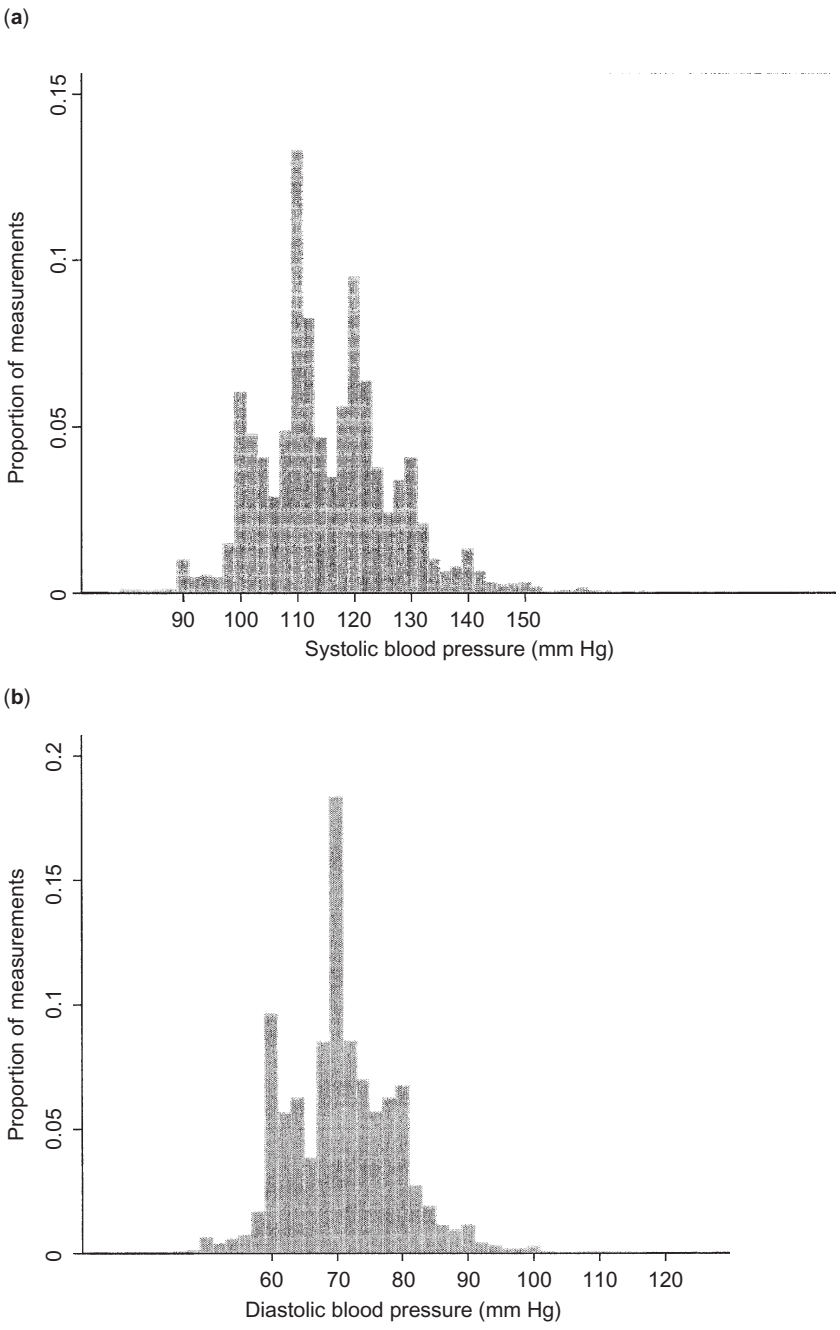

Figure 2. Distribution of systolic (a) and diastolic (b) blood pressure in the analysis database (restricted to even digits).

occur in 20% of readings, if readings were restricted to even digits. However, 35.3% of systolic and 36.5% of diastolic readings end in zero.

A comparison of trimester-specific mean systolic and diastolic blood pressures was carried out, with and without random reassignment of the systolic blood pressure readings ending in zero, where the reassigned readings are randomly assigned to the even digits. This random reassignment effectively recreates the blood pressure readings without zero preference, under the assumption that there is no upward or downward bias in the observed rounding to zero (so that, for instance, measurements of systolic blood pressure of 122 and 118 are equally likely to have been recorded as 120). As would be expected, estimates of mean blood pressure were essentially unchanged (data not shown). However, standard errors of these estimates were slightly increased after the random reassignment, although not to a degree that had any impact on hypothesis tests. In summary, it appears that

observed preference for the digit zero resulted in reduced variability in blood pressure readings but not of a magnitude that would impact hypothesis testing.

Discussion

In this study, we explored the extent to which the characteristics of the first 2000 women enrolled in the Omega Cohort Study differed according to their use of prenatal care. We note the relative homogeneity of the Omega cohort, where Caucasian, higher-income, well-educated women predominate. Overall, the use of prenatal care in the cohort was good, with high adherence to the prescribed visit regimen throughout the first 35 weeks of gestation. However, as would be expected, the characteristics of women who were over-represented in their number of available blood pressure records differed from those who were adequately represented. Namely, differences in the distributions of maternal sociodemographic characteristics, mean trimester-specific systolic, diastolic and mean arterial blood pressures, as well as in the cumulative incidence of pre-eclampsia and gestational diabetes, were noted.

From the source database, we constructed an analysis database which is a balanced subset of the original source data. The analysis database was designed to address problems such as the bias which may have been induced by the over-representation, throughout pregnancy, of women with higher levels of systolic and diastolic blood pressures. In the analysis database, trimester-specific mean systolic, diastolic and arterial pressures did not vary according to number of records per subject, and it appeared reasonable to assume that cross-sectional and longitudinal blood pressure summaries may be interpreted as being representative of those in the population of pregnant women from which this cohort is drawn. We have presented an approach to determining the validity of a particular set of longitudinal measurements (here consisting of clinically generated blood pressures) as a research database. While it may not be possible in all settings to adjust for the types of biases that we have considered here, we believe that the method that we have described may be generally useful in evaluating the validity of other series of longitudinal measurements.

The high frequency of successive identical repeat blood pressure readings in the source data is consistent with other findings reported in the literature. In the context of repeated measurements that are at least 5 min apart, Bennett[14] and Hense *et al*.[11] report on multicentre studies where the proportion of identical duplicate measurements ranged from 4% to 70%. The issue of identical repeat measurements does not, however, arise in our analysis database, which is based on a longitudinal subset of the source data. A preference for the digit zero is also a characteristic of the blood pressure measurements in other studies of blood pressure. In simulation studies, Bennett[14] and Hense *et al*.[11] showed that digit preference did not influence means and standard deviations, but that percentiles and proportions above certain thresholds were affected. Preference for the digit zero remains a feature of the analysis data for our cohort. Our preliminary assessment of the impact of this feature of the data suggests that this zero digit preference will not affect conclusions of the analyses in our companion paper.[13]

As in any observational study that depends on medical records, the accuracy and completeness of recorded data are dependent on parameters beyond the control of investigators. However, results from our evaluation of collected blood pressure data, and findings summarised in the companion paper which evaluated trimester-specific blood pressure values according to maternal pre-pregnancy adiposity,[13] suggest that blood pressure data collected routinely during pregnancy may be used in epidemiological studies. Conduct of analytical studies that carefully integrate these databases and that create analytical databases designed to quantify, describe and possibly mitigate sources of bias may help improve our understanding of determinants of blood pressure changes during pregnancy.

Acknowledgements

This research was supported in part by an award from the National Institutes of Health (R01-HD/HL 32562). The authors are indebted to the participants of the Omega Study for their cooperation. They are also grateful for the technical expertise of the Center for Perinatal Studies staff, and to the Editors and two anonymous reviewers for helpful comments, which have improved the clarity of the manuscript.

References

1 Bergel E, Carroli G, Althabe F. Ambulatory vs. conventional methods of monitoring blood pressure during pregnancy. *Cochrane Database of Systematic Reviews* 2002; **2**: CD001231.

2 Hermida RC, Ayala DE, Iglesias M. Differences in circadian pattern of ambulatory pulse pressure between healthy and complicated pregnancies. *Hypertension* 2004; **44**:316–321.
3 Zhang C, Williams MA, Sorensen TK, King IB, Kestin MM, Thompson ML, *et al.* Maternal plasma ascorbic acid (vitamin C) concentrations and risk of gestational diabetes mellitus. *Epidemiology* 2004; **15**:597–604.
4 Williams MA, Qiu CF, Muy-Rivera M, Vadachkoria S, Song T, Luthy DA. Plasma adiponectin concentrations in early pregnancy and subsequent risk of gestational diabetes mellitus. *Journal of Clinical Endocrinology and Metabolism* 2004; **17**:574–581.
5 Darvoic GO. *Haemodynamic Monitoring*. Philadelphia, PA: W.B. Saunders, 2002.
6 Patterson RE, Kristal AR, Tinker LF, Carter RA, Bolton MP, Agurs-Collins T, *et al.* Measurement characteristics of the Women's Health Initiative food frequency questionnaire. *Annals of Epidemiology* 1999; **9**:178–187.
7 Schakel SF, Sievert YA, Buzzard IM. Sources of data for developing and maintaining a nutrient database. *Journal of the American Dietetics Association* 1988; **88**:1268–1271.
8 Stata Corp. *Stata Statistical Software*, release 9.2. College Station, TX: Stata Corporation, 2004.
9 American Academy of Pediatrics/American College of Obstetricians and Gynecologists. *Guidelines for Prenatal Care*, 3rd edn. Washington, DC: American Academy of Pediatrics/American College of Obstetricians and Gynecologists, 1992.
10 Hessel PA. Terminal digit preference in blood pressure measurements: effects on epidemiological associations. *International Journal of Epidemiology* 1986; **15**:122–125.
11 Hense HW, Kuulasmaa K, Zaborskis A, Kupsc W, Tuomilehto J. Quality assessment of blood pressure measurements in epidemiological surveys. The impact of last digit preference and the proportions of identical duplicate measurements. *Revae d'Epidémiologie et de Santé Publique* 1990; **38**:463–468.
12 de Lusignan S, Belsey J, Hague N, Dzregah B. End-digit preference in blood pressure recordings of patients with ischaemic heart disease in primary care. *Journal of Human Hypertension* 2004; **18**:261–265.
13 Miller RS, Thompson ML, Williams MA. Trimester-specific blood pressure levels in relation to maternal pre-pregnancy body mass index. *Paediatric and Perinatal Epidemiology* 2007; **21**:487–494.
14 Bennett S. Blood pressure measurement error: its effect on cross-sectional and trend analyses. *Journal of Clinical Epidemiology* 1994; **47**:293–301.

Did you spot?

Outcome of pregnancy

Gestational age shortening in single births at term. Italy 1990–1998. *European Journal of Epidemiology* 2007; 22:263–265.
Italy: Gestational length among term births of over 2 million singletons in 1990–98 showed a decrease.

Spontaneous preterm birth of liveborn infants in women at low risk in Australia over 10 years: a population-based study. *BJOG* 2007; 114:731–735.
Australia: 1994–2003. Rate of preterm delivery increased, particularly the rate with spontaneous onset of labour; the increase in multiparae was twice as high as the increase in primiparae.

Differential parental weight and height contributions to offspring birthweight and weight gain in infancy. *International Journal of Epidemiology* 2007; 36:104–107.
UK: Millennium cohort. A total of 6811 term white infants; birthweight and weight gain to 9 months. Weights of each parent were independently associated with child's weight gain, but birthweight was much more associated with maternal than paternal weight.

Iron supplements in pregnancy

A randomised placebo-controlled trial to determine the effect of iron supplementation on pregnancy outcome in pregnant women with haemoglobin ≥13.2 g/dL. *BJOG* 2007; 114:684–688.
Iran: Randomised controlled trial of iron supplements or placebo to women with high haemoglobin early in second trimester. Supplemented women were more likely to develop hypertension and to have infants who were small-for-gestational-age.

