Are Twins and Singletons Comparable? A Study of Disease-related and Lifestyle Characteristics in Adult Women

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The classic twin study is sometimes described as "the perfect natural experiment" for the investigation of the aetiology of complex disease, but assumptions of the twin design need to be empirically tested if their results are to be considered unbiased and representative of singleton populations. In this study comparisons of disease and prevalence of lifestyle characteristics have been made between twin participants in the St Thomas' Hospital UK adult twin registry, the largest twin volunteer register in the UK for the study of diseases of ageing, and a parallel population-based study of singleton women. The only differences found were for weight, where monozygotic (MZ) twins were lighter and had a smaller variance than dizygotic (DZ) twins and singletons. For the other variables studied, volunteer twins were not found to differ from age-matched singleton women in distribution or prevalence of: bone mineral density, osteoarthritis, blood pressure, hypertensive drug use, height, history of hysterectomy and ovariectomy, menopausal status and current alcohol and overall tobacco consumption. We conclude that the results of twin studies can be generalised to singleton populations for these measures and disease outcomes.

The classic twin study provides an efficient research design for the study of genetic and environmental influences, including the search for individual genes, underlying complex traits and disease (MacGregor, Snieder & Spector, 2000; Martin et al., 1997).

Nevertheless, the twin study design rests upon assumptions that need to be empirically tested if results are to be extrapolated to singleton populations (Kendler et al., 1993; Kyvik, 2000). Twin studies themselves must be adequately conducted so that the twin sample is representative of twin populations (Kaprio et al., 2000; Strachan, 2000). In addition, the possibility of significant differences between twins and singletons also needs to be considered (Phillips, 1993). Studies based in the UK, where no population register of adult twins currently exists, depend upon volunteers (Boomsma, 1998) and are susceptible to a number of well-documented biases. The recruitment of volunteer twins is known to be influenced by youth, gender, zygosity, health and education. With care, the extent of bias can be quantified (Lykken et al., 1988; Lykken et al., 1978; Mack et al., 2000). However, opportunities to compare attributes of disease in detail between volunteer twins and population-based singletons are rare. Although studies have addressed the representativeness of twins compared to the population of twins from which they were sampled (Lykken et al., 1978; Mack et al., 2000), there has been no extensive or systematic comparison of twins with singletons for disease and disease-related measures.

In the last decade, we have conducted two large parallel studies of age-related disease: the first in a national UK-based twin volunteer population (the St Thomas' UK Adult Twin Registry), the second in a community-based study of women residing in Chingford, London, England. In both, disease has been assessed and data collected using similar protocols. Here we address the representativeness of the twins by undertaking detailed comparisons between these two study populations.

Materials and Methods

Sources of Data

St Thomas' Study. The St Thomas' UK adult twin registry is a volunteer registry consisting of over 4,000 same sex twin pairs ranging from 18 to 76 years of age at first interview (Boomsma, 1998). The registry was initiated in 1992. Twins were recruited through a series of media campaigns asking for volunteers willing to participate in research investigating age-related diseases. Participating twins were unaware of the specific hypotheses tested and informed consent was obtained from all subjects.

Initially, only middle-aged women were recruited to the registry. From 1995 onwards men and women over 18 years were also invited to participate. As a result, 84 percent of the registry is female. The registry currently contains 45 percent monozygotic (MZ) and 55 percent dizygotic (DZ) twins.

To date 600 MZ and 1,400 DZ pairs from the twin registry have been interviewed and clinically assessed (Table 1 shows individuals aged 45–65). A higher proportion of DZ compared to MZ twins have been called for interview, as a recent focus has been to obtain genotype data for association and linkage studies. For the purposes of this investigation only Caucasian female twins were used for sample comparisons.

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Chingford Study. A population of 1,003 Caucasian women aged between 45 to 65 years were interviewed and clinically assessed between 1989 and 1991 (Table 1). The subjects were ascertained using an age-sex register at a six-partner general practice in the London suburb of Chingford, which covers a population of 11,000 people (Spector et al., 1993). All women aged between 45–65 years were sent an invitation for a screening examination at Chingford Hospital and a response rate of 77 percent was achieved. Their height, weight, smoking and alcohol intake, exercise patterns and body mass index (BMI) were similar to those found in national surveys at the time (see Tables 2–4; Bridgwood et al., 1998; Knight & Eldridge, 1984; ONS, 1991; Spector et al., 1993; White, 1991).

Clinical Data. The present analysis considers the following clinical data relating to chronic diseases measured in the two study populations, reflecting the Research Unit's interest in osteoarthritis (MacGregor, Snieder & Spector, 2000; Spector et al., 1996), osteoporosis (Arden & Spector, 1997; MacGregor, Snieder & Spector, 2000) and coronary heart disease (Poulter et al., 1999; Snieder et al., 2000). In addition to disease related variables, lifestyle and anthropomorphic variables that are known to influence disease are also considered.

1. Height measured in cm with a stadiometer; Weight in kg measured on scales to the nearest gram with the subject wearing light clothes and no shoes; Body mass index (BMI) calculated as kg/m^2.

Table 1

Age Distribution of Twin and Singleton Samples Compared to Census Figures for Women in England in 1991

	Sample						England Census 1991	
	MZ		DZ		Chingford			
Age	%	*n*	%	*n*	%	*n*	%	*n*
45–49	16.1	106	33.2	498	28.3	284	28.3	1,470,459
50–54	31.0	204	31.6	474	25.0	251	24.5	1,276,766
55–59	24.9	164	21.9	328	21.4	215	23.4	1,216,554
60–64	28.1	185	13.4	201	25.2	253	23.8	1,239,418
All	100	659	100	1501	100	1003	100.0	5,203,197

Table 2

Height Distribution of Twin and Singleton Samples Compared to the 1991 Health Survey for Women in England, by Age Group

%	Ages 45–54				Ages 55–64			
Height (cm)	MZ	DZ	Chingford	HS 1991	MZ	DZ	Chingford	HS 1991
< 155	10	8	8	15	16	14	14	18
155–159	21	23	27	31	26	24	29	32
160–164	36	31	36	31	32	34	32	30
165–169	24	25	18	17	20	20	17	18
170 +	9	13	11	6	6	8	8	2
All	100	100	100	100	100	100	100	100
n	303	958	531	236	347	524	451	225

Table 3

Weight Distribution of Twin and Singleton Samples Compared to the 1991 Health Survey for Women in England in 1991, by Age Group

%	Ages 45–54				Ages 55–64			
Weight (kg)	MZ	DZ	Chingford	HS 1991	MZ	DZ	Chingford	HS 1991
< 5 0	6	3	4	6	4	3	3	5
50–59	32	28	26	22	27	26	23	21
60–69	37	39	33	35	44	36	36	31
70–79	16	19	24	22	17	23	23	22
80+	9	11	13	16	8	12	15	20
All	100	100	100	100	100	100	100	100
n	300	956	531	235	346	524	451	223

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Table 4

Prevalence of Smoking in Twin and Singleton Samples Compared to the General Household Survey for Women Living in Great Britain in 1994, Stratified by Age Group

	Sample						GHS 1994	
	MZ		DZ		Chingford			
Age	%	*n*	%	*n*	%	*n*	%	*n*
35–49 *	21	277	24	1061	28	284	28	2091
50–59	20	347	17	756	23	466	26	1211
60+	11	266	15	337	17	253	17	2247
All	19	1103	22	2582	23	1003	26	5549

* Chingford 45–49 years

2. Total bone mineral density (BMD) of the spine and hip (in g/cm^2). Bone mineral density for the lumbar spine (L1–L4) and the femoral neck were measured by DXA (hologic QDR/1000W). The same make of apparatus was used to measure bone mineral density in both samples, calibrated to the same standards.
3. Osteoarthritis (OA) at the knee, hip and hand. Radiographs at each site were taken and scored for features of OA using the Kellgren and Lawrence (K&L) classification (Burnett et al., 1994). This is a 4-point scale (0–3) that includes data on the presence of osteophytes and joint space narrowing. For the twin and singleton samples both the intra-observer and inter-observer reproducibility obtained a k statistic of over 0.68 for all sites and features in both samples and were comparable with other similar studies (Hart et al., 1993).

   Knee OA was defined as a K&L score of 2 or more (denoting, as a minimum, the presence of definite osteophytes in either the left or right knee). Hip OA was defined as having a minimum joint space of < 2.5mm. Hand OA was assessed in the distal interphalangeal (DIP) finger joint and carpo-metacarpal phalangeal (CMC) thumb joint. Distal interphalangeal OA was defined, as a minimum, as the presence of definite osteophytes (K&L graded 2 or more) in two or more DIP joints. CMC OA was defined as K&L graded 2 or more, in either thumb joint.
4. Blood pressure. The same clinical research nurse, under standardised conditions, measured the diastolic and systolic blood pressures in each twin pair, with the subjects seated. A standard mercury sphygmomanometer was used for the whole Chingford sample and in twins up until 1995. After that, the blood pressure of twins was measured using an automated cuff sphymomanometer (OMRON HEM713C, Tokyo).
5. The use of prescribed anti-hypertensive drugs was recorded, which included diuretics, beta-blockers, calcium channel blockers, ACE inhibitors and nitrates.
6. Reproductive history. Ascertained by questionnaire including menopausal status, history of hysterectomy and ovariectomy at first interview; and Hormone Replacement Therapy (HRT) status recorded at interview as current, past use or never used (Snieder et al., 1998).
7. Current alcohol consumption. Recorded for both samples using administered questionnaires, estimating the typical number of units of alcohol consumed each week over the last year. Intake was recorded on a 7 point scale, as 1–5, 6–10, 11–15, 16–20, 21–40 and > 40 units of alcohol per week. Where this was not possible, "social drinker" or "never" were recorded. The prevalence of those drinking more than 10 units per week was used as a comparison between samples, with "social drinker" being graded as ≤ 10 units per week.
8. Tobacco use. Recorded as current, past use and never used in both samples.
9. Social class. The UK General Registrar Classification system was used to compare the social class of twins and singletons in the categories of senior management or professional (A/B), skilled non-manual (C1), skilled manual (C2) and semi or unskilled worker (D/E). For the Chingford sample, a socio-economic profile was performed using the Acorn classification system which is based on each subject's postcode and residence and then subsequently mapped onto the UK General Registrar Classification (CACI International, London, UK). In effect, social class in Chingford was based upon household rather than female occupation and therefore every woman was successfully placed in one of the four categories. The social class of twins was identified using information recorded on their current and previous three occupations. Women who were not working or had retired at interview were classified according to the longest previous job held. The 5 percent of twins who remained classified as "economically inactive" (e.g., housewife, retired) were categorised as "other" and were excluded in test comparisons with the complete four category classification of singletons.

Analytical Approach

Analysis focused upon a comparison of sample mean, prevalence and variance for each variable between MZ, DZ and singleton groups. Analyses were conducted in 5-year age strata. The age overlap between the twins and singletons at first interview was not exact, which meant only MZ and DZ twins could be compared below the age of 45 and

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over the age 65. These twin age groups were retained for analysis, despite no age overlap with the singleton sample, since comparison of MZ and DZ variances were of interest to assess possible twin volunteer bias (Lykken et al., 1988; Sham, 1998). To facilitate use of all the data, analytic methods were used that account for non-independent observations within twin pairs.

Continuous Variables. Continuous variables such as weight, BMD and blood pressure, were all normally distributed and were analysed using path analysis implemented in the statistical package Mx (Neale, 1995). As a preliminary check, the means and variances for twin and co-twin members of the pairs were tested for equality in the MZ and DZ groups. As anticipated, with the arbitrary assignment of twin and co-twin categories, in all cases these attributes were found to be equal. Therefore, in the baseline (or full) model used to test for the equality of means and variances between groups, the co-twin group means and variances were set to be equal. Analysis proceeded in a model fitting approach by comparing the full model with sub-models of interest.

The full model estimated eight parameters (μ_{MZ}, μ_{DZ}, $\mu_{Chingford}$, V_{MZ}, V_{DZ} , $V_{Chingford}$, Cov_{MZ} , Cov_{DZ}) using 12 summary statistics (μ_{MZ1}, μ_{MZ2}, μ_{DZ1}, μ_{DZ2}, $\mu_{Chingford}$, V_{MZ1}, V_{MZ2}, V_{DZ1}, V_{DZ2}, $V_{Chingford}$, Cov_{MZ} , Cov_{DZ}) and the analysis was repeated for each age stratum separately. The majority of baseline models were non-significant, indicating a good correspondence between this model and the observed data. (These are presented in Tables 5, 6 and 9, under the column heading "Full Model", whereby a threshold $\chi^2_{(4)} < 9.48$ and $p > 0.05$ indicates a model that does not deviate significantly from the observed data.)

Four sub-models were explicitly tested by comparison with the full model: MZ and DZ means were equated (with the singleton mean and all three group variances freely estimated); the pooled twin mean was equated with singletons (with all three group variances freely estimated); MZ and DZ variances were equated (with the singleton variance and all three group means freely estimated); and the pooled twin variance was equated with singletons (with all three group means freely estimated). Parameters were retained, and the hypothesis of equality rejected, if the sub-model corresponded to the observed data less well than the full model, using a threshold change in χ^2 corresponding to $p < 0.05$. Although only 4 sub-models were of explicit interest (MZ vs DZ and twins vs singletons), for clarity of presentation a best-fit model, selected from a possible 8 sub-models, is also provided in tables for continuous variables.

Discontinuous Variables. For categorical data (such as presence or absence of osteoarthritis), unadjusted odds ratios were estimated comparing the prevalence of each attribute: (a) between MZ and DZ twins; and (b) between twins and singletons. As with continuous variables, twin and co-twin groups were checked for equality in prevalence. The few differences that were found disappeared when assignment of twin 1 and twin 2 were randomised. To account for the non-independence of the co-twins, the procedure was carried out using the generalised estimating equation (GEE), implemented in the statistical package Stata (StataCorp, 1997).

Results

The results are presented in Tables 5 to 15. In general, few or no differences were found. No systematic pattern across age strata or large individual differences were found in group means, prevalence or variances for height (Table 5); bone mineral density (BMD) in the hip (Table 6); osteoarthritis in the knee and hip (Table 7); systolic blood pressure (Table 9); anti-hypertensive drug use (Table 10); menopausal status, history of hysterectomy and ovariectomy (Table 11); and for overall tobacco and current alcohol consumption (Tables 13 & 14).

Differences were found in adult weight (and therefore BMI measured as kg/m^2, Table 5); spine BMD in DZ twins aged 45–54 (Table 6); osteoarthritis of the hand in the 60–65 age group (Table 8); diastolic blood pressure for some age groups (Table 9); HRT use (Table 12), smoking (Table 13) and social class (Table 15).

The mean weight for MZ twins was found to be consistently lower than both DZ and singletons across all ages (Table 5) and there was evidence that the mean weight for DZ twins was slightly less than that of singletons. For women aged 45–65, MZ twins (μ = 64.3kg) are on average 2kg (95 percent confidence interval: 0.7, 3.3) lighter than DZ twins (μ = 66.3kg) and 2.6kg (95 percent confidence interval: 1.34, 3.89) lighter than Chingford sample (μ = 66.9). Overall the mean estimated difference between the DZ and singletons is 0.63kg (95 percent confidence interval: –0.4, 1.6), rising to 1.05kg (95 percent confidence interval: 0.04 – 2.07) for three of the age strata. Variances in weight appear smaller in DZ twins compared to singletons under the age of 55 and larger in those 55 or above, but the figures are only significant in the 50–54 age group. For women aged 45–65, MZ variances in weight (SD 10.3kg) are consistently smaller than DZ (SD 11.6kg) and singletons (SD 11.8kg) across age strata, with 4 out of 6 of the age groups being statistically significant. A similar pattern was observed in BMI, reflecting differences between groups for weight, but not in height.

Some differences in BMD were observed (Table 6), in particular for DZ twins aged 50–54, in whom bone density was slightly higher compared to MZ and singletons in the spine (0.042 g/cm^2 difference, 95 percent confidence interval: 0.02, 0.06; equivalent to 4% increase) and less so at the hip (0.025 g/cm^2, 95 percent confidence interval: 0.007, 0.04; 3% increase). The latter reflects a reduced BMD in singletons aged 50–54.

There is evidence of a lower prevalence in DIP and CMC hand OA (Table 8) in twins compared to singletons for two age groups (45–49 and 60–65). However, no differences in prevalence were seen in hip and knee OA (Table 7). OA is one of the more difficult diseases to clinically diagnose in a consistent manner (Spector & Cooper, 1994), and overall, the prevalence of OA in the hand, hip and knee are similar in the twin and singleton samples.

The best fit model for diastolic BP indicates that DZ twins in their 50s appear to have a higher resting blood pressure than MZ twins and singletons, although the difference between the groups is relatively small (Table 9). There is a mean increase of 2.1mmHG (95 percent confidence interval:

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Table 5

Means and Variances for Height, Weight and Body Mass Index (BMI) in MZ, DZ Twins and Singletons, Stratified by Age Group

ML	STH Twin studies (1992/98)						Chingford (1989/91)			Test for equality of means & variances between twins & population									
	MZ			DZ			Singletons			Full model:		Means:				Variances:				Best fit model	
												Twins		All 3		Twins		All 3			
Charac-teristic	mean	var_{MZ}	*n*	mean	var_{DZ}	*n*	mean	var_{Chg}	*n*	μ_{MZ} ne μ_{DZ} ne μ_{Chg} V_{MZ} ne V_{DZ} ne V_{Chg} $\chi^2_{(4)}$	*p*	$(\mu_{MZ} = \mu_{DZ})$ ne μ_{Chg} V_{MZ} ne V_{DZ} ne V_{Chg} $\Delta\chi^2_{(1)}$	*p*	$(\mu_{MZ} = \mu_{DZ} = \mu_{Chg})$ V_{MZ} ne V_{DZ} ne V_{Chg} $\Delta\chi^2_{(2)}$	*p*	μ_{MZ} ne μ_{DZ} ne μ_{Chg} $(V_{MZ} = V_{DZ})$ ne V_{Chg} $\Delta\chi^2_{(1)}$	*p*	μ_{MZ} ne μ_{DZ} ne μ_{Chg} $(V_{MZ} = V_{DZ} = V_{Chg})$ $\Delta\chi^2_{(2)}$	*p*	mean	variance
Height, cm																					
<45	163.9	37.6	414	163.4	37.8	1065	—	—	—	4.0	0.41	1.20	0.27	—	—	0.01	0.92	—	—	$\mu_{MZ} = \mu_{DZ}$	$V_{MZ} = V_{DZ}$
45 – 49	163.0	29.1	98	162.7	32.7	491	162.4	36.0	284	5.3	0.26	0.13	0.72	0.57	0.75	0.29	0.59	1.21	0.55	$(\mu_{MZ} = \mu_{DZ} = \mu_{Chg})$	$V_{MZ} = V_{DZ} = V_{Chg}$
50 – 54	161.7	35.3	201	162.9	38.7	467	161.7	34.9	251	4.0	0.41	3.02	0.08	6.06	0.05	0.35	0.55	0.91	0.63	$(\mu_{MZ} = \mu_{Chg})$ ne μ_{DZ}	$V_{MZ} = V_{DZ} = V_{Chg}$
55 – 59	160.9	34.4	164	161.7	36.6	324	161.7	36.0	215	3.7	0.44	1.05	0.31	1.30	0.52	0.11	0.74	0.11	0.95	$(\mu_{MZ} = \mu_{DZ} = \mu_{Chg})$	$V_{MZ} = V_{DZ} = V_{Chg}$
60 – 65	160.7	33.4	183	160.6	36.0	198	160.5	31.6	253	2.1	0.72	0.02	0.89	0.03	0.99	0.19	0.66	0.78	0.68	$(\mu_{MZ} = \mu_{DZ} = \mu_{Chg})$	$V_{MZ} = V_{DZ} = V_{Chg}$
>65	159.8	41.6	90	159.5	35.7	157	—	—	—	1.6	0.80	0.49	0.48	—	—	1.74	0.19	—	—	$\mu_{MZ} = \mu_{DZ}$	$V_{MZ} = V_{DZ}$
Weight, kg																					
<45	63.2	129.8	414	65.4	182.4	1064	—	—	—	2.4	0.67	7.0	0.01	—	—	10.5	0.00	—	—	μ_{MZ} ne μ_{DZ}	V_{MZ} ne V_{DZ}
45 – 49	62.6	112.5	98	65.3	132.8	491	65.9	144.4	284	3.5	0.47	2.9	0.09	3.9	0.14	0.6	0.44	1.5	0.47	μ_{MZ} ne $(\mu_{DZ} = \mu_{Chg})$	$V_{MZ} = V_{DZ} = V_{Chg}$
50 – 54	65.0	126.9	199	66.7	130.5	465	67.6	166.8	251	2.0	0.74	1.8	0.18	3.7	0.46	0.03	0.85	5.6	0.06	μ_{MZ} ne $(\mu_{DZ} = \mu_{Chg})$	$(V_{MZ} = V_{DZ})$ ne V_{Chg}
55 – 59	64.8	90.7	163	67.6	146.0	324	67.6	128.3	215	2.4	0.66	4.5	0.03	5.7	0.06	7.8	0.01	7.847	0.02	μ_{MZ} ne $(\mu_{DZ} = \mu_{Chg})$	V_{MZ} ne $(V_{DZ} = V_{Chg})$
60 – 65	64.1	90.2	183	65.8	132.0	198	66.9	119.2	253	7.7	0.11	1.7	0.19	5.6	0.06	5.2	0.02	5.2	0.04	μ_{MZ} ne $(\mu_{DZ} = \mu_{Chg})$	V_{MZ} ne $(V_{DZ} = V_{Chg})$
>65	63.1	111.7	90	65.7	125.0	157	—	—	—	1.4	0.85	8.6	0.00	—	—	8.7	0.00	—	—	μ_{MZ} ne μ_{DZ}	V_{MZ} ne V_{DZ}
BMI, kg/m^2																					
<45	23.5	17.6	414	24.5	24.3	1064	—	—	—	6.9	0.14	8.36	0.00	—	—	9.86	0.00	—	—	μ_{MZ} ne μ_{DZ}	V_{MZ} ne V_{DZ}
45 – 49	23.5	12.4	98	24.7	17.0	489	25.0	19.2	284	2.1	0.72	4.43	0.04	6.50	0.04	2.23	0.14	4.26	0.12	μ_{MZ} ne $(\mu_{DZ} = \mu_{Chg})$	V_{MZ} ne $(V_{DZ} = V_{Chg})$
50 – 54	24.9	16.2	199	25.2	19.5	465	25.8	21.3	251	7.3	0.12	0.45	0.50	4.75	0.09	1.47	0.23	2.93	0.23	$(\mu_{MZ} = \mu_{DZ})$ ne μ_{Chg}	V_{MZ} ne $(V_{DZ} = V_{Chg})$
55 – 59	25.1	13.6	163	25.8	20.3	324	25.8	17.2	215	2.5	0.65	2.62	0.11	3.3	0.19	5.25	0.02	5.67	0.06	μ_{MZ} ne $(\mu_{DZ} = \mu_{Chg})$	V_{MZ} ne $(V_{DZ} = V_{Chg})$
60 – 65	24.8	12.8	183	25.6	20.8	198	25.9	15.6	253	3.4	0.49	2.06	0.15	6.66	0.04	8.34	0.00	9.28	0.01	μ_{MZ} ne $(\mu_{DZ} = \mu_{Chg})$	V_{MZ} ne V_{DZ} ne V_{Chg}
>65	24.7	15.3	90	25.8	19.8	156	—	—	—	1.0	0.91	2.60	0.11	—	—	0.45	0.50	—	—	$\mu_{MZ} = \mu_{DZ}$	$V_{MZ} = V_{DZ}$

Table 6

Means and Variances for Bone Mineral Density at the Spine and Hip in MZ, DZ Twins and Singletons, Stratified by Age Group

ML	STH Twin studies (1992/98)						Chingford (1989/91)			Test for equality of means & variances between twins & population										
	MZ			DZ			Singletons			Full model:		Means:				Variances:				Best fit model	
												Twins		All 3		Twins		All 3			
Charac-teristic	mean	var_{MZ}	*n*	mean	var_{DZ}	*n*	mean	var_{Chg}	*n*	μ_{MZ} ne μ_{DZ} ne μ_{Chg} V_{MZ} ne V_{DZ} ne V_{Chg} $\chi^2_{(4)}$	*p*	$(\mu_{MZ} = \mu_{DZ})$ ne μ_{Chg} V_{MZ} ne V_{DZ} ne V_{Chg} $\Delta\chi^2_{(1)}$	*p*	$(\mu_{MZ} = \mu_{DZ} = \mu_{Chg})$ V_{MZ} ne V_{DZ} ne V_{Chg} $\Delta\chi^2_{(2)}$	*p*	μ_{MZ} ne μ_{DZ} ne μ_{Chg} $(V_{MZ} = V_{DZ})$ ne V_{Chg} $\Delta\chi^2_{(1)}$	*p*	μ_{MZ} ne μ_{DZ} ne μ_{Chg} $(V_{MZ} = V_{DZ} = V_{Chg})$ $\Delta\chi^2_{(2)}$	*p*	mean	variance
Spine BMD																					
(L1–L4)		x10^{-4}			x10^{-4}			x10^{-4}													
< 45	1.027	117	392	1.04	136	1012	—	—	—	3.6	0.46	2.6	0.11	—	—	2.08	0.15	—	—	$\mu_{MZ} = \mu_{DZ}$	$V_{MZ} = V_{DZ}$
45 – 49	0.999	197	95	1.02	181	477	1.047	200	282	6.0	0.20	1.4	0.24	6.64	0.04	0.23	0.63	0.9	0.64	$(\mu_{MZ} = \mu_{DZ})$ ne μ_{Chg}	$V_{MZ} = V_{DZ} = V_{Chg}$
50 – 54	0.980	189	197	1.03	233	456	0.985	221	245	3.1	0.55	7.8	0.01	11.84	0.00	2.14	0.14	4.0	0.14	$(\mu_{MZ} = \mu_{Chg})$ ne μ_{DZ}	$V_{MZ} = V_{DZ} = V_{Chg}$
55 – 59	0.954	229	163	0.95	238	319	0.945	262	208	2.4	0.66	0.0	0.95	0.34	0.84	0.05	0.82	0.7	0.70	$\mu_{MZ} = \mu_{DZ} = \mu_{Chg}$	$V_{MZ} = V_{DZ} = V_{Chg}$
60 – 65	0.889	205	179	0.9	251	194	0.890	206	244	4.3	0.37	0.4	0.53	0.60	0.74	1.12	0.29	2.0	0.37	$\mu_{MZ} = \mu_{DZ} = \mu_{Chg}$	$V_{MZ} = V_{DZ} = V_{Chg}$
>65	0.888	187	88	0.91	249	157	—	—	—	3.9	0.42	1.1	0.29	—	—	1.31	0.25	—	—	$\mu_{MZ} = \mu_{DZ}$	$V_{MZ} = V_{DZ}$
Femoral neck																					
BMD		x10^{-4}			x10^{-4}			x10^{-4}													
<45	0.864	137	391	0.86	140	1007	—	—	—	2.8	0.59	0.002	0.96	—	—	0.06	0.81	—	—	$\mu_{MZ} = \mu_{DZ}$	$V_{MZ} = V_{DZ}$
45 – 49	0.801	167	92	0.82	131	475	0.81	142	278	4.7	0.31	1.73	0.19	1.80	0.41	1.64	0.20	2.02	0.36	$\mu_{MZ} = \mu_{DZ} = \mu_{Chg}$	$V_{MZ} = V_{DZ} = V_{Chg}$
50 – 54	0.794	139	192	0.81	155	454	0.77	148	237	2.5	0.65	0.94	0.33	9.36	0.01	0.34	0.56	0.36	0.84	$(\mu_{MZ} = \mu_{DZ})$ ne μ_{Chg}	$V_{MZ} = V_{DZ} = V_{Chg}$
55 – 59	0.768	136	162	0.76	119	314	0.75	128	177	1.2	0.88	0.07	0.79	1.42	0.49	0.73	0.39	0.80	0.67	$\mu_{MZ} = \mu_{DZ} = \mu_{Chg}$	$V_{MZ} = V_{DZ} = V_{Chg}$
60 – 65	0.705	118	177	0.71	116	190	0.69	150	204	4.5	0.34	0.44	0.51	2.73	0.26	0.17	0.68	4.74	0.09	$\mu_{MZ} = \mu_{DZ} = \mu_{Chg}$	$V_{MZ} = V_{DZ} = V_{Chg}$
>65	0.699	113	87	0.69	126	156	—	—	—	8.0	0.09	0.01	0.92	—	—	0.24	0.62	—	—	$\mu_{MZ} = \mu_{DZ}$	$V_{MZ} = V_{DZ}$

Table 7

Prevalence for Osteoarthritis at the Knee and Hip in MZ, DZ Twins and Singletons, Stratified by Age Group

General estimating equation	STH Twin studies (1992/98)				Chingford (1989/91)		Odd ratios			
	MZ		DZ		Singletons					
Characteristic	Prevalence	*n*	Prevalence	*n*	Prevalence	*n*	$OR_{DZ:MZ}$	*p*	$OR_{Chg:Twin}$	*p*
Knee OA										
K&L 2+ (Osteophytes)										
<45	0.00	39	0.02	172	—	—	—	—	—	—
45 – 49	0.05	44	0.03	213	0.02	281	0.75	0.74	0.68	0.46
50 – 54	0.03	138	0.04	291	0.05	248	1.57	0.43	1.34	0.44
55 – 59	0.07	124	0.06	200	0.09	212	0.82	0.67	1.51	0.22
60 – 65	0.10	139	0.15	118	0.14	246	1.61	0.26	1.14	0.64
>65	0.22	65	0.22	103	—	—	1.04	0.92	—	—
Hip OA										
K&L 2+ (mjs)										
<45	0.00	40	0.05	168	—	—	—	—	—	—
45 – 49	0.10	30	0.03	204	0.06	264	0.3	0.12	1.54	0.31
50 – 54	0.07	94	0.05	240	0.06	233	0.7	0.51	1.08	0.83
55 – 59	0.06	72	0.13	152	0.11	199	2.6	0.10	0.98	0.96
60 – 65	0.10	73	0.17	95	0.09	232	1.9	0.21	0.63	0.16
>65	0.21	33	0.27	78	—	—	1.4	0.56	—	—

Table 8

Prevalence for Osteoarthritis in the Hand for MZ, DZ Twins and Singletons, Stratified by Age Group

General estimating equation	STH Twin studies (1992/98)				Chingford (1989/91)		Odd ratios			
	MZ		DZ		Singletons					
Characteristic	Prevalence	*n*	Prevalence	*n*	Prevalence	*n*	$OR_{DZ:MZ}$	*p*	$OR_{Chg:Twin}$	*p*
Hand DIP OA (K&L2+)										
<45	0.00	42	0.01	195	—	—	—	—	—	—
45 – 49	0.02	61	0.01	258	0.04	247	0.71	0.76	2.98	0.07
50 – 54	0.08	154	0.06	341	0.07	188	0.81	0.60	1.10	0.79
55 – 59	0.18	141	0.18	238	0.20	148	0.95	0.87	1.12	0.67
60 – 65	0.28	157	0.39	151	0.50	176	1.63	0.09	1.96	0.00
>65	0.39	85	0.48	120	—	—	1.43	0.26	—	—
Hand CMC OA (K&L2+)										
<45	0	42	0.02	193	—	—	—	—	—	—
45 – 49	0.03	61	0.04	255	0.06	252	1.33	0.75	1.39	0.44
50 – 54	0.17	151	0.11	339	0.12	197	0.62	0.13	0.88	0.64
55 – 59	0.35	140	0.25	236	0.26	160	0.60	0.05	0.87	0.53
60 – 65	0.37	155	0.30	151	0.48	170	0.76	0.32	1.84	0.00
>65	0.46	85	0.47	118	—	—	1.06	0.86	—	—

0.8, 3.4) for these twins, but this is not true for the remaining 4 out of 6 age groups, where DZ diastolic blood pressure is the same as other groups. There are no clear differences between any of the groups for systolic BP, apart for a lower blood pressure in singletons aged 45–49 (systolic 117mmHG in singletons compared to 121mmHG for twins).

The results for current and past HRT use differ between the three groups (Table 12). HRT use also differs by age and by year of interview. The prevalence of HRT use at first interview is lower among singletons for all age groups in comparison to MZ and DZ twins in this sample. For 45–65 years, the mean prevalence of HRT use at first interview was 24 percent for MZ twins, 30 percent for DZ and 7 percent for singletons. The prevalence for the combination of current or past use of HRT was also higher in twins than for singletons (for those 45–65 years: MZ: 40

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Table 9

Means and Variances for Diastolic and Systolic BP in MZ, DZ Twins and Singletons, Stratified by Age Group

ML	STH Twin studies (1992/98)						Chingford (1989/91)			Test for equality of means & variances between twins & population										
	MZ			DZ			Singletons			Full model:		Means:				Variances:				Best fit model	
												Twins		All 3		Twins		All 3			
Charac-teristic	mean	var_{MZ}	*n*	mean	var_{DZ}	*n*	mean	var_{Chg}	*n*	μ_{MZ} ne μ_{DZ} ne μ_{Chg} V_{MZ} ne V_{DZ} ne V_{Chg} $\chi^2_{(4)}$	*p*	$(\mu_{MZ} = \mu_{DZ})$ ne μ_{Chg} V_{MZ} ne V_{DZ} ne V_{Chg} $\Delta\chi^2_{(1)}$	*p*	$(\mu_{MZ} = \mu_{DZ} = \mu_{Chg})$ V_{MZ} ne V_{DZ} ne V_{Chg} $\Delta\chi^2_{(2)}$	*p*	μ_{MZ} ne μ_{DZ} ne μ_{Chg} $(V_{MZ} = V_{DZ})$ ne V_{Chg} $\Delta\chi^2_{(1)}$	*p*	μ_{MZ} ne μ_{DZ} ne μ_{Chg} $(V_{MZ} = V_{DZ} = V_{Chg})$ $\Delta\chi^2_{(2)}$	*p*	mean	variance
Diastolic BP																					
<45	71.4	111	387	73.9	119.2	1004	—	—	—	13.7	0.01	10.8	0.00	—	—	0.390	0.53	—	—	μ_{MZ} ne μ_{DZ}	$V_{MZ} = V_{DZ}$
45 – 49	78.5	118	88	76.8	111.7	405	72.9	85.0	255	5.2	0.27	1.3	0.25	28.9	0.00	0.14	0.71	3.1	0.22	$(\mu_{MZ} = \mu_{DZ})$ ne μ_{Chg}	$V_{MZ} = V_{DZ} = V_{Chg}$
50 – 54	78.4	135	180	80.2	144.1	380	78.0	116.6	229	4.3	0.37	1.9	0.17	4.7	0.09	0.94	0.33	2.1	0.34	$(\mu_{MZ} = \mu_{Chg})$ ne μ_{DZ}	$V_{MZ} = V_{DZ} = V_{Chg}$
55 – 59	78.3	113	144	81.3	109.9	247	79.3	109.4	185	8.4	0.08	4.6	0.03	5.6	0.06	0.07	0.79	0.1	0.96	$(\mu_{MZ} = \mu_{Chg})$ ne μ_{DZ}	$V_{MZ} = V_{DZ} = V_{Chg}$
60 – 65	83.2	147	164	80.3	112.6	156	81.1	124.4	208	1.2	0.87	3.3	0.07	3.4	0.18	1.76	0.18	2.5	0.28	$(\mu_{MZ} = \mu_{DZ} = \mu_{Chg})$	$V_{MZ} = V_{DZ} = V_{Chg}$
>65	83.0	162	73	83.9	122.4	114	—	—	—	1.6	0.81	0.1	0.74	—	—	2.39	0.12	—	—	$\mu_{MZ} = \mu_{DZ}$	$V_{MZ} = V_{DZ}$
Systolic BP																					
<45	113.2	176	387	115	193.9	1005	—	—	—	4.2	0.39	6.2	0.01	—	—	0.944	0.33	—	—	μ_{MZ} ne μ_{DZ}	$V_{MZ} = V_{DZ}$
45 – 49	123.5	313	88	120	234.5	405	116.7	207.7	255	5.9	0.21	0.0	0.96	8.3	0.02	0.04	0.85	0.1	0.97	$(\mu_{MZ} = \mu_{DZ})$ ne μ_{Chg}	$V_{MZ} = V_{DZ} = V_{Chg}$
50 – 54	125.2	324	180	126	323.2	379	126.3	362.6	229	1.7	0.79	0.3	0.57	0.5	0.78	0.00	0.96	2.5	0.29	$(\mu_{MZ} = \mu_{DZ} = \mu_{Chg})$	$V_{MZ} = V_{DZ} = V_{Chg}$
55 – 59	126.5	311	144	130	308.0	247	129.7	356.4	185	2.2	0.70	2.0	0.16	2.0	0.36	0.05	0.83	1.5	0.47	$(\mu_{MZ} = \mu_{DZ} = \mu_{Chg})$	$V_{MZ} = V_{DZ} = V_{Chg}$
60 – 65	139.0	479	164	132	376.3	156	136.5	380.3	208	10.2	0.04	3.2	0.07	3.5	0.17	0.66	0.42	1.5	0.47	μ_{MZ} ne $(\mu_{DZ} = \mu_{Chg})$	$V_{MZ} = V_{DZ} = V_{Chg}$
>65	147.1	415	73	142	382.1	114	—	—	—	2.9	0.58	0.9	0.34	—	—	0.01	0.92	—	—	$(\mu_{MZ} = \mu_{DZ} = \mu_{Chg})$	$V_{MZ} = V_{DZ} = V_{Chg}$

Table 10

Prevalence of Taking Anti-hypertensive Drugs in MZ, DZ Twins and Singletons, Stratified by Age Group

General estimating equation	STH Twin studies (1992/98)				Chingford (1989/91)		Odd ratios			
	MZ		DZ		Singletons					
Characteristic	Prevalence	*n*	Prevalence	*n*	Prevalence	*n*	$OR_{DZ:MZ}$	*p*	$OR_{Chg:Twin}$	*p*
Hypertension morbidity										
<45	0.03	395	0.03	1025	—	—	1.32	0.48	—	—
45 – 49	0.08	84	0.08	426	0.07	274	0.96	0.93	0.86	0.61
50 – 54	0.07	179	0.11	410	0.08	248	1.60	0.16	0.74	0.28
55 – 59	0.09	148	0.22	304	0.13	213	2.81	0.00	0.68	0.11
60 – 65	0.12	160	0.21	182	0.17	250	2.09	0.04	0.98	0.92
>65	0.23	80	0.28	144	—	—	1.34	0.40	—	—

Table 11

Menopausal Status, History of Hysterectomy and Ovariectomy in MZ, DZ Twins and Singleton Women, Stratified by Age Group

General estimating equation	STH Twin studies (1992/98)				Chingford (1989/91)		Odd ratios			
	MZ		DZ		Singletons					
Characteristic	Prevalence	*n*	Prevalence	*n*	Prevalence	*n*	$OR_{DZ:MZ}$	*p*	$OR_{Chg:Twin}$	*p*
Menopausal status										
<45	0.02	386	0.04	1003	—	—	2.10	0.09	—	—
45 – 49	0.43	93	0.33	452	0.31	284	0.76	0.07	0.84	0.29
50 – 54	0.81	170	0.80	405	0.84	251	0.98	0.73	1.34	0.18
55 – 59	0.99	143	1	268	1	215	—	—	1.00	0.67
60 – 65	1	185	1	201	1	253	—	—	—	—
>65	1	94	1	168	—	—	—	—	—	—
Hysterectomy										
<45	0.04	382	0.05	1007	—	—	1.40	0.33	—	—
45 – 49	0.21	102	0.22	471	0.18	284	1.07	0.82	0.78	0.19
50 – 54	0.27	193	0.25	436	0.29	251	0.89	0.62	1.18	0.34
55 – 59	0.21	164	0.29	318	0.23	215	1.50	0.10	0.83	0.33
60 – 65	0.31	183	0.25	192	0.23	253	0.76	0.27	0.79	0.23
>65	0.22	88	0.27	148	—	—	1.35	0.36	—	—
Ovary removed (1 or both)										
<45	0.01	377	0.04	966	—	—	3.21	0.03	—	—
45 – 49	0.11	93	0.10	463	0.04	284	0.99	0.98	0.43	0.01
50 – 54	0.15	188	0.12	426	0.12	251	0.74	0.24	0.95	0.81
55 – 59	0.09	160	0.14	304	0.10	215	1.69	0.13	0.78	0.38
60 – 65	0.17	176	0.11	183	0.13	253	0.64	0.17	0.93	0.78
>65	0.16	82	0.17	143	—	—	1.07	0.87	—	—

percent; DZ: 44 percent; singletons: 24 percent). The prevalence of HRT use rises with age, peaks for women in their fifties and then declines.

The prevalence of HRT use increased for both twins and singletons with the passage of time. Between 1992 and 1999 HRT prevalence steadily increased in twins aged over 50, from 25 per cent to 36 percent. The comparable figures for singletons between 1989 and 1991 were seven, eight and nine percent, respectively. The odds ratio for current HRT use in twins compared to singletons aged 45–65 years is reduced by about one third after adjusting for the observed cohort effect (crude OR 5.0; 3.8, 6.7. adjusted OR 3.4; 2, 4.8).

The twins smoked slightly less than singletons at first interview (Table 13). The difference in prevalence was small and when current and past figures are pooled, the prevalence of ever having smoked is the same for MZ, DZ and singletons for all age strata. In effect, more twins reported having given up smoking at interview than singletons.

The distribution of social class was comparable for twins and the Chingford sample, except for the categories of skilled white-collar (C1) and skilled manual worker (C2) for the 45–49 and 55–59 age groups (Table 15). In Chingford there were relatively more C2s in the 45–49 age group and fewer C1s for both age groups compared to twins. When the data are pooled across age groups, the

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Table 12

Prevalence of Hormone Replacement Treatment (HRT) for MZ, DZ Twins and Singletons, Stratified by Age Group

General estimating equation	STH Twin studies (1992/98)				Chingford (1989/91)		Odd ratios			
	MZ		DZ		Singletons					
Characteristic	Prevalence	*n*	Prevalence	*n*	Prevalence	*n*	$OR_{DZ:MZ}$	*p*	$OR_{Chg:Twin}$	*p*
HRT current										
<45	0.02	379	0.03	985	—	—	1.56	0.28	—	—
45 — 49	0.15	98	0.24	470	0.05	284	1.61	0.08	0.22	0.00
50 — 54	0.36	193	0.42	439	0.13	251	1.15	0.27	0.32	0.00
55 — 59	0.24	164	0.26	318	0.08	215	1.11	0.57	0.33	0.00
60 — 65	0.14	183	0.22	189	0.03	253	1.54	0.10	0.17	0.00
>65	0.05	88	0.14	147	—	—	2.99	0.08	—	—
HRT past										
<45	0.01	379	0.02	985	—	—	2.95	0.08	—	—
45 — 49	0.05	98	0.09	470	0.16	284	1.80	0.23	1.92	0.00
50 — 54	0.15	193	0.14	439	0.17	251	0.94	0.80	1.23	0.24
55 — 59	0.24	164	0.18	318	0.16	215	0.75	0.13	0.80	0.22
60 — 65	0.17	183	0.19	189	0.17	253	1.16	0.52	0.91	0.59
>65	0.10	88	0.14	147	—	—	1.33	0.49	—	—
Ever HRT (current/past)										
<45	0.03	379	0.06	985	—	—	1.94	0.05	—	—
45 — 49	0.20	98	0.34	470	0.21	284	1.65	0.03	0.67	0.00
50 — 54	0.51	193	0.55	439	0.30	251	1.09	0.35	0.55	0.00
55 — 59	0.48	164	0.45	318	0.25	215	0.93	0.48	0.54	0.00
60 — 65	0.31	183	0.41	189	0.20	253	1.34	0.07	0.54	0.00
>65	0.15	88	0.27	147	—	—	1.84	0.06	—	—

Table 13

Prevalence of Smoking in MZ, DZ Twins and Singletons, Stratified by Age Group

General estimating equation	STH Twin studies (1992/98)				Chingford (1989/91)		Odd ratios			
	MZ		DZ		Singletons					
Characteristic	Prevalence	*n*	Prevalence	*n*	Prevalence	*n*	$OR_{DZ:MZ}$	*p*	$OR_{Chg:Twin}$	*p*
current Smoker										
<45	0.23	388	0.28	1014	—	—	1.31	0.09	—	—
45 – 49	0.18	102	0.22	475	0.28	284	1.26	0.48	1.41	0.05
50 – 54	0.20	187	0.19	439	0.22	251	0.97	0.92	1.19	0.36
55 – 59	0.19	160	0.14	317	0.23	215	0.69	0.19	1.60	0.03
60 – 65	0.12	179	0.14	190	0.17	253	1.19	0.61	1.37	0.19
>65	0.08	86	0.15	147	—	—	1.92	0.19	—	—
past Smoker										
<45	0.19	388	0.19	1012	—	—	1.05	0.78	—	—
45 – 49	0.24	98	0.29	475	0.23	284	1.20	0.52	0.73	0.08
50 – 54	0.28	187	0.28	439	0.19	251	1.00	0.99	0.60	0.01
55 – 59	0.26	160	0.31	317	0.22	215	1.26	0.36	0.69	0.07
60 – 65	0.32	179	0.27	188	0.30	253	0.78	0.31	0.99	0.96
>65	0.39	84	0.26	148	—	—	0.56	0.07	—	—
ever Smoker										
<45	0.42	388	0.48	1014	—	—	1.14	0.11	—	—
45 – 49	0.43	102	0.51	475	0.50	284	1.19	0.21	1.01	0.87
50 – 54	0.48	187	0.47	439	0.41	251	0.99	0.94	0.87	0.12
55 – 59	0.46	160	0.45	317	0.46	215	0.99	0.92	1.01	0.94
60 – 65	0.45	179	0.42	190	0.47	253	0.92	0.56	1.09	0.36
>65	0.47	86	0.41	147	—	—	0.88	0.46	—	—

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Table 14

Prevalence of Drinking More than 10 Units of Alcohol per Week at Interview for MZ, DZ Twins and Singletons, Stratified by Age Group

General estimating equation	STH Twin studies (1992/98)				Chingford (1989/91)		Odd ratios			
	MZ		DZ		Singletons					
Characteristic	Prevalence	*n*	Prevalence	*n*	Prevalence	*n*	$OR_{MZ:DZ}$	*p*	$OR_{Twin:Chg}$	*p*
current Alcohol (10 > u.p.w)										
<45	0.22	390	0.17	1016	—	—	0.77	0.05	—	—
45 – 49	0.14	102	0.17	473	0.11	152	1.25	0.46	0.59	0.07
50 – 54	0.10	174	0.12	425	0.07	127	1.24	0.46	0.58	0.15
55 – 59	0.07	152	0.12	304	0.09	138	1.76	0.14	0.94	0.87
60 – 65	0.11	169	0.08	184	0.05	155	0.71	0.37	0.55	0.15
>65	0.15	82	0.13	144	—	—	0.90	0.78	—	—

Table 15

Distribution of Social Class [a] for MZ, DZ Twins and Singletons, Stratified by Age. Figures presented are for all twins [b]

Social class :		A / B	C1	C2	D / E	Other	Total		
		%	%	%	%	%	*n*	$\chi^2_{(3)}$	*p*
MZ vs DZ									
<45	MZ	31	48	7	3	12	372	7.9	0.09
	DZ	33	43	10	5	8	961		
45 – 49	MZ	34	54	9	4	0	82	0.9	0.92
	DZ	32	49	7	6	6	367		
50 – 54	MZ	29	45	16	9	2	128	2.8	0.59
	DZ	30	47	14	5	4	296		
55 – 59	MZ	20	62	11	5	1	92	3.9	0.41
	DZ	28	48	13	5	6	178		
60 – 65	MZ	28	51	12	8	2	99	4.9	0.30
	DZ	33	42	14	3	7	136		
>65	MZ	16	60	8	2	14	43	2.5	0.64
	DZ	27	53	9	4	6	89		
All (45 – 65)	MZ	28	52	12	7	1	419	3.2	0.52
	DZ	30	47	11	5	6	1018		
Twin vs Chingford									
45 – 49	Twin	32	50	7	6	5	449	29.0	0.00
	Chg	31	40	20	10	0	283		
50 – 54	Twin	29	46	14	6	4	424	2.2	0.70
	Chg	35	43	14	8	0	250		
55 – 59	Twin	25	53	12	5	5	283	12.0	0.02
	Chg	39	40	15	7	0	212		
60 – 65	Twin	31	46	13	5	5	248	7.1	0.13
	Chg	25	47	20	8	0	253		
All (45 – 65)	Twin	30	49	12	6	5	1437	25.0	0.00
	Chg	32	42	17	8	0	998		

[a] Twins who were retired or economically inactive at interview were classified according to the longest life-time employment based upon previous 3 jobs held. Those remaining unclassified as A–E on the General Registrar Classification have been classified as "other" for the purposes of comparision with the Chingford sample.

[b] Inclusion of both co-twins inflates the χ^2 statistic and possible Type I errors, but for this table the same results are obtained using only 1 co-twin. Reported χ^2 tests exclude the category "other"and utilise all twins.

distribution of social class was similar for twins and singletons aged 45–65 years. The proportion of twins and singletons in the General Registrar Classification categories were: senior management/ professional A/B (30 percent and 32 percent, respectively), skilled non-manual C1 (49 percent and 42 percent), skilled manual C2 (12 percent and 17 percent), and semi or unskilled work D/E (6 percent and 8 percent).

For the age strata in which group differences were observed, we investigated some possible causes. The mean

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differences observed between MZ, DZ twins and singletons for weight, spine BMD and diastolic BP were not found to vary by categories of social class, HRT or smoking. Neither could the observed differences in spine BMD, diastolic BP or hand OA be explained by weight. The prevalence of DIP and CMC hand OA was actually found to increase with HRT use in twins aged 60–65 and this is subject to further study. However, HRT use did not account for the lower prevalence in hand OA observed in twins for some age groups.

Tests were carried out using GEE (StataCorp, 1997) with MZ, DZ and singleton groups nested within categories of social class, HRT, smoking status and weight, in separate analyses. A post-estimation Wald test was used to test if differences between groups differed between categories. For example, lower MZ mean weight compared to DZ twins and singletons (–2.3kg 95 percent confidence interval: –1.1, –3.5) did not alter significantly by category of social class ($\chi^2_{(3)} = 1.5$, $p = 0.69$), although tests for social class may have been under-powered due to small numbers of MZ twins in classes C2 and D/E.

Discussion

Data on the similarity of twin and singleton populations for disease and disease related traits are sparse (Simmons et al., 1997). Our analysis is the first systematic comparison of twins and singletons to include a range of adult age groups for variables assessed using similar clinical methods. We have shown that for 19 clinical, anthropometric and lifestyle variables measured in the female population, only weight shows a small but consistent difference between MZ twins, DZ twins and singletons. The weight differences were not observed to influence the traits studied here, but this might not be true for other weight-related traits such as coronary heart disease. We found some difference in prevalence for HRT use and current smoking between twins and singletons and also — in certain age groups — differences were observed in BMD, diastolic blood pressure and prevalence of hand OA. However, it is possible the differences in diastolic blood pressure and prevalence of hand OA could be the result of measurement artefacts between samples. Overall, the similarity between the twin and singleton populations is striking, given the well-documented biases that may affect volunteer-based studies and the widely voiced concerns about the unusual birth history of twins.

Most of the differences found were not systematic across age groups and did not appear to have any obvious explanation. Group differences observed for specific age strata in weight, BMD, diastolic blood pressure and hand OA could not be accounted for by the differences in prevalence of smoking, social class and HRT status. Weight itself did not account for observed differences in spine BMD, diastolic blood pressure or hand OA. Differences in BMD were confined to two age groups — mean spine BMD is higher for singletons compared to twins aged 45–49 and lower in hip BMD for those aged 50–54. In addition, DZ twins aged 50–54 had higher spine BMD compared to MZ and singleton groups.

One explanation for differences observed in diastolic blood pressure might be a technical one. More accurate automated cuff measurements of blood pressure were introduced for twin studies in 1995. This may explain raised mean diastolic blood pressure in DZ twins, compared to MZ twins and singletons. A greater number of DZ twins have been clinically assessed from this time compared to MZ twins and singletons and automated measures are likely to be more accurate for diastolic blood pressure.

For OA, the prevalence of DIP and CMC hand OA was higher in singletons aged 60–65 and in MZ twins aged 55–59 for CMC OA. The reason for this is unclear, but one explanation could be inter-rater inconsistencies between samples.

The potential for bias in twin studies is well documented and a continuing source of concern in the interpretation of their results (Spector et al., 2000). Common twin biases can arise through the use of volunteers (Kyvik, 2000; Strachan, 2000), conducting studies in occupational groups (McMichael, 1976), selecting subjects from specific geographical locations (Romanov et al., 1990) and from the method of twin ascertainment itself (Hodge, 1998). In volunteer studies, Lykken et al. (1978) have suggested that DZ and male twins are likely to be less representative of their respective populations than are the female and MZ pairs, given their reduced willingness to participate. Their conclusions were based on an analysis of 11 international volunteer twin studies conducted between 1928 and 1977. If response rates are associated with traits, DZ and male twins will tend to be more homogeneous with smaller between pair trait variances. Such a bias would result in an underestimate of the true intraclass correlation in the population of DZ twins (Sham, 1998) and hence in an overestimate of heritability of the trait under study (a frequent criticism of twin studies). The authors recommended that all twin studies should include a test of means and variances to guard against the possibility of bias.

In our data we found no evidence for a reduction in DZ trait variances compared to MZ twins for all ages between 18–76 years, indicating the type of volunteer bias described by Lykken et al. (1978) does not appear to be an important influence in this study. This might be due to the fact that St Thomas' Hospital UK adult twin registry has recruited healthy volunteers, rather than selected by disease as was the case in the studies examined by Lykken et al. (1978). These twins are a motivated, healthy population of women who are more likely at first visit to use HRT and to have given up smoking compared to singletons. The higher prevalence of HRT use in twins could, in part, be accounted for by an observed cohort effect. Twins were ascertained later than the singletons and during the nineties there was an increased recognition of the health benefits of HRT to menopausal women. However, the cohort effect only partly accounts for the observed difference — the twins are still more likely to use HRT than singletons, even after having adjusted for cohort effects.

Out of 19 traits investigated in this study, the only trait to show consistent differences between groups across all age strata was adult weight. It seems unlikely that an unobserved healthy volunteer bias could account for the differences in weight between MZ twins, DZ twins and singletons, given the absence of differences observed for other variables. A more plausible explanation for these dif-

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ferences is that they may be related to differences in birth weight between twins and singletons, given the documented association between birth weight and adult weight observed in twin and singleton populations (Doyle et al., 1999; Lucas et al., 1999; Whitaker & Dietz, 1998). One of the major criticisms of the twin design stems from the lower birth weight of twins and the assertion that there is an association between fetal under-nutrition in middle to late gestation and the development of adult disease (Barker, 1995; Phillips, 1993). Twins experience considerable retardation in intrauterine growth and are on average 900g lighter than single children at birth (MacGillivray et al., 1988). An association with low birth weight has been reported for Type II diabetes mellitus, cardiovascular diseases and hypertension (Barker, 1992; Barker et al., 1993) and the association with blood pressure has been demonstrated in the St Thomas' twins among co-twins with extreme differences in birth weight (Poulter et al., 1999).

However, our results suggest that the birth weight differences between twins and singletons are not sufficiently large to translate into important differences in the prevalence of disease or in the distribution of disease related traits between these groups for the 19 variables studied here. Further, studies of monochorionic compared with dichorionic twins show no differences in the prevalence of adult disease (Duffy, 1993; Holm, 1983). (Monochorionic twins are exclusively monozygotic, comprise approximately two thirds of all MZ twins, and tend to have a lower birth weight than dichorionic twins (MacGillivray et al., 1988; Rama-Arroyo et al., 1988)). Mortality rates in twins have been shown not to differ from those in singleton populations (Christensen et al., 1995; Vagero & Leon, 1994) and twinning is not associated with raised blood pressure at the ages of 9 or 18 (Williams & Poulton, 1999). The association between birth weight and adult disease in an individual raises interesting questions concerning aetiology. However, there is nothing to suggest that this hypothesis cannot be studied with equal validity in both twin and singleton populations.

This study has involved multiple comparisons and p values have not been adjusted to correct for multiple testing, in favour of looking for consistent trends across age strata and considering the magnitude of effect size. As a result, out of the approximate 340 tests conducted, at α = 0.05, about 17 positive results might be expected to be due to Type I errors. We found 52 significant results at α = 0.05, 33 of which were due to differences in weight, BMI, HRT use and smoking. Hence it is possible that the remaining results could be statistical artefacts.

In terms of sample numbers and ability to detect differences between twins and the population, depending upon the effect size, our power is estimated to be high, while for MZ:DZ comparisons, power is more variable. For example, 12 out of the 19 variables examined were binomial, with average sample sizes within each age stratum of about 160 individuals for MZ twins, 370 for DZ and 250 for the population sample. Assuming a moderately large effect size, with mean prevalence of 10 percent in one sample and 20 percent in another, the power to detect differences between MZ and DZ twins would be 79 percent and a power of 95 percent would be obtained in comparisons between twins and singletons. As a result, assuming unbiased samples, we can be confident that this study will have detected moderate to large differences between twins and singletons, which was the main objective. False negative (Type II) rates are likely to be no higher than false positives (Type I) for twin: population comparisons, but false negatives are likely to occur at a higher rate for MZ:DZ twin comparisons.

Conclusion

We recognise that the Chingford study is not a national sample and the St Thomas UK adult twin register is not birth record-based — the representativeness of each for their respective populations cannot be estimated. However, based on a large sample of female volunteer twins aged 45–65, we have shown that twins do not differ from age-matched singleton women in terms of increased morbidity for bone mineral density, osteoarthritis, blood pressure, use of hypertensive medication, height, alcohol consumption and menopausal, hysterectomy and ovariectomy status. This result is of importance in supporting claims that twins are representative of singleton populations and confirm studies of twins to be a valid epidemiological tool.

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