	ApoE phenotype group			Age
	E2/E2+E3/E2	E3/E3	E4/E3+E4/E4	
Dutch twin families (fathers)	n = 23	n = 86	n = 45	48·1 (6·3)
Systolic BP (mm Hg)	129·6 (11·3)	127·9 (9·7)	128·9 (12·2)	
Diastolic BP (mm Hg)	82·5 (8·8)	80·4 (7·4)	81·3 (8·7)	
Dutch twin families (mothers)	n = 27	n = 94	n = 27	45·6 (5·9)
Systolic BP (mm Hg)	125·8 (10·3)	126·7 (14·7)	123 8 (14·9)	
Diastolic BP (mm Hg)	79·9 (7·0)	77·3 (10·4)	77·4 (11·1)	
Zutphen Study (men only)	n = 47	n = 359	n = 126	75·0 (4·6)
Systolic BP (mm Hg)	149·4 (19·8)	150·0 (21·3)	150·7 (22·4)	
Diastolic BP (mm Hg)	83·1 (10·7)	81·5 (11·6)	82·3 (12·4)	
Greenland Inuit (men)	n = 2	n = 37	n = 23	30–35
Systolic BP (mm Hg)	112·0 (0·0)	116·9 (10·5)	121·4 (14·7)	
Diastolic BP (mm Hg)	61·0 (9·9)	72·5 (11·6)	73·1 (11·2)	
Greenland Inuit (women)	n = 1	n = 36	n = 37	30–35
Systolic BP (mm Hg)	109	111·8 (13·7)	103·1 (16·0)*	
Diastolic BP (mm Hg)	73	73·4 (10·8)	66·9 (15·2)	

Analysis of variance (to compare three apoE groups in Dutch population samples) or *t* test (to compare only E3/E3 and E4/E4+E4/E3 Inuit groups) were used to compare unadjusted pressure levels. Only significant p-values (<0·05) are shown *p = 0·014. BP = blood pressure.

Table: **Mean (SD) age, systolic and diastolic blood pressure, and apoE phenotype in Dutch and Greenland Inuit population samples**

Detailed descriptions of these populations have been published elsewhere.[2-4] Blood pressure was measured with standardised protocols. ApoE phenotype was determined as described previously.[5] Individuals with the E4/E2 phenotype were excluded from analyses, because of the opposite effects of these two alleles on lipid metabolism. Analyses were done on unadjusted blood pressure values. Since men have a significantly higher systolic pressure than women, the association was studied in the sexes separately. In the Dutch population samples, we were unable to find a significant influence of apoE phenotype on systolic blood pressure (table). In the Inuit, because of the small population size, the E2/E2+E3/E2 group was excluded from statistical analysis. Inuit women with the E3/E3 phenotype showed a significantly higher systolic pressure than APOE*4 allele carriers, whereas in Inuit men such an effect could not be established.

In these population samples of different ethnic origin, with different age and gender composition and not selected for plasma cholesterol concentrations, no consistent influence of apoE gene variability on systolic blood pressure could be found. Application of selection criteria for cholesterol concentrations similar to those used by Uusitupa and co-workers, and statistical analyses adjusting for age, body mass index, and use of anti-hypertensive drugs did not change the results in any of our three populations (results not shown). Thus although the apoE polymorphism affects plasma cholesterol in most populations, the hypothesis that apoE polymorphism affects blood pressure through its effect on low-density lipoprotein cholesterol, as suggested by Uusitupa and co-workers, is not sustained by our results.

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1 Uusitupa M, Sarkkinen E, Kervinen K, Antero Kesäniemi Y. Apolipoprotein E phenotype and blood pressure. *Lancet* 1994; **343:** 57.

2 Boomsma DI, Orlebeke JF, Martin NG, et al. Alpha-1-antitrypsin and blood pressure. *Lancet* 1991; **337:** 1547.

3 Hertog MGL, Feskens JM, Hollman PCH, et al. Dietary flavanoids and the risk of coronary heart disease: the Zutphen Elderly Study. *Lancet* 1993; **343:** 1007-11.

Apolipoprotein E phenotype and blood pressure

SIR—Uusitupa and colleagues[1] showed that in a selected Finnish population sample (n=159), individuals with either the apolipoprotein (apo) E4/E4 or E4/E3 phenotype had a significantly higher (8 mm Hg) systolic blood pressure than individuals with other apoE phenotypes. Intrigued by this association we analysed blood pressure in three independent populations for which apoE phenotypes were also available: (i) 302 fathers and mothers in 160 Dutch twin families; (ii) 532 elderly men participating in the Zutphen Study; and (iii) 136 Greenland Inuit men and women.

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5 Havekes LM, de Knijff P, Beisiegel U, et al. A rapid micro-method for apolipoprotein E phenotyping directly in serum. *J Lipid Res* 1987; **28:** 445-63.

Follow-up of children in the Italian Study of Aspirin in Pregnancy

Sir—The CLASP study (March 12 p 623) results do not lend support to routine prophylactic or therapeutic administration of aspirin in pregnancy to all women at increased risk of pre-eclampsia or intrauterine growth retardation, but suggest that low-dose aspirin treatment is justified in women judged liable to early-onset severe pre-eclampsia. The use of low-dose aspirin in pregnancy, however, has raised concerns about safety. We have now concluded 18 months' follow-up of children born from women recruited in the Italian Study of Aspirin in Pregnancy (ISAP)[1], and report the results with respect to the safety of chronic use of 50 mg of aspirin in pregnancy.

We undertook a postal questionnaire study 18 months after delivery. We asked about the child's vital status, height, weight, malformations, respiratory, hearing, and vision problems, and other major disorders. The other questions were derived from Sonnander's questionnaire,[2] in which there was agreement between parents and professionals on the gross and fine motor and language development of the child. The questions had age-related norms:[2] if a child was not able to perform a function that at least 90% of 18-month-old babies could, he or she was judged to have gross or fine motor or language difficulties. This questionnaire was derived from that used in the paediatric follow-up of children of the CLASP study. We posted a reminder to non-responders after 40 days. Both mailings included a cover letter, the questionnaire, and a preprinted prepaid envelope. If no reply was received, we telephoned the parents three times, at different times of the day and of the week.

The follow-up started in October, 1990. Thus, 41 babies born before February, 1989, were not included. After exclusion of stillbirths and infants who died within the first week of life, a total of 1393 questionnaires were mailed (700 to the women allocated to aspirin, including 108 twins, and 693 to the no treatment group, including 114 twins). Information was obtained for 827 children (72·4%) for the aspirin and 761 (73·2%) for the no-treatment group. General characteristics (maternal age, parity, education, criteria for trial entry, and weeks of gestation at randomisation) and pregnancy outcome (pregnancy-induced hypertension, duration of gestation, weight at birth, mode of delivery) did not differ among responders to the postal questionnaire and women who were contacted by phone or lost to follow-up (data not shown). No significant differences emerged between the two groups with respect to indicators of development and health status (table). Malformations, diseases, and other health problems showed no specific patterns and were much the same in the two groups.

A weakness of this study is the percentage of non-responders. However, the results did not differ when the analysis compared information obtained by postal questionnaire with that obtained by telephone. The questionnaire asked the parents to indicate all the child's main problems; thus abnormalities and diseases were based on the parents' perception of their severity. It is unlikely that the allocation to aspirin or no-treatment affected the reporting, and, if anything, treated women should tend to be more accurate in recalling and reporting malformations or problems.

	Aspirin (827) No. (%)	No treatment (761) No. (%)
Causes of death (0-6 day; 7-28 day; 29 day-1 month; 2-6 mo)		
Prematurity	1	—
Pulmonary diseases	—	1
Respiratory distress syndrome	1	—
Malformations*	7	8
Diseases†	9	9
Height <10th percentile‡	20 (8·4)	18 (12·1)
Weight <10th percentile§	75 (12·7)	83 (14·9)
Health problems		
Respiratory	59 (12·1)	52 (8·9)
Gross/fine motor	13 (3·0)	28 (7·2)
Hearing	1	0
Sight	3 (1·0)	3 (1·0)
Language	65 (12·3)	47 (11·1)

*Atrial septal defect, cataract defect, cleft palate, club foot, congenital ptosis, Down's syndrome, echocardiac, oesophageal atresia, multicystic kidney, hypospadias, spina bifida, torticollis, valgus foot.
†Major eczema, cardiomegaly, coeliac disease, cerebral palsy, epilepsy, growth failure, haemangioma, hypothyroidism, herpes, Schönlein-Henoch purpura, tuberculosis, synovitis.
‡According to ref 4.

Table: **Results of follow-up according to treatment allocation in the Italian Study of Aspirin in Pregnancy**

With these caveats, our findings suggest that the use of low-dose aspirin in pregnancy is safe with respect to the risks of malformation and of major impairment in development at 18 months of age.

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Evaluation of urine by turbidimetry

Sir—Tremblay and Labbe (Feb 18, p 478) report the augmentation of dipstick testing with an assessment of urine clarity for the screening of samples for paediatric urinary tract infections. With one modification (the addition of acetic acid to clear phosphate-related turbidity) Rawal's method of turbidimetric determination is essentially that used by physicians since the Middle Ages.

The ability to distinguish borderline cases of crystal clear from not crystal clear in a consistent and reproducible manner probably imposes performance limits on such a test. With this in mind I did turbidimetric urine analysis on 258 randomly selected samples from all sources. Only catheter specimens were excluded. All requests were for microscopy

	Threshold values (WCC)			
	10·0	10·5	20·7	21·0
Sensitivity (%)	100	99·1	94·1	92·2
Specificity (%)	53·5	63·8	88·1	91·5
PPV* (%)	24·7	40·2	67·8	83·8
NPV* (%)	100	98·5	97·8	97·3

*PPV, positive predictive value; NPV, negative predictive value.

Table: **Sensitivity, specificity, and predictive values**