

- 3 Reynolds TM, Nix AB, Dunstan FD, Dawson AJ. Age specific detection and false-positive rate: an aid to counselling in Down's syndrome. *Obstet Gynecol* 1993;81:447-50.
- 4 Wald NJ, Cuckle HS. Biochemical screening. In: Brock DJH, Rodeck CH, Ferguson-Smith MA, eds. *Prenatal diagnosis and screening*. Edinburgh: Churchill Livingstone, 1992:563-77.

conclusion that it may be advisable to plan to offer screening only to women aged over 30.

T M REYNOLDS

Consultant chemical pathologist

Clinical Chemistry Department,
Burton Hospitals NHS Trust,
Burton upon Trent,
Staffordshire DE13 0RB

- 1 Fletcher J, Hicks NR, Kay JDS, Boyd PA. Using decision analysis to compare policies for antenatal screening for Down's syndrome. *BMJ* 1995;311:351-6. (5 August.)
- 2 Reynolds T, John R, Spencer K. The use of unconjugated estriol in Down syndrome screening is unproven. *Clin Chem* 1993;39:2023-5.
- 3 Spencer K, Coombes E, Mallard A, Milford-Ward A. Free beta human chorionogonadotropin in Down's syndrome screening: a multicentre study of its role compared with other biochemical markers. *Ann Clin Biochem* 1992;29:506-18.
- 4 Dawson A, Jones G, Matharu M, Reynolds T, Penney M, John R, et al. Serum screening for Down's syndrome: a summary of one year's experience in south Wales. *Br J Obstet Gynaecol* 1993;100:875-7.
- 5 Reynolds T, Nix B, Dunstan F, Dawson A. Age related detection rates in Down screening: an aid to counselling. *Obstet Gynecol* 1993;81:447-50.

Costs were overestimated

EDITOR,—J Fletcher and colleagues' paper on using decision analysis to evaluate screening for Down's syndrome is valuable, but several extra factors need to be considered.¹ The authors state that screening causes anxiety but fail to mention the reassurance that it gives to many women. In addition, they based their study on use of the triple test despite the considerable body of evidence showing that a double test is as effective.^{2,3} Indeed, the national external quality assurance scheme's reports on Down's screening show that a double test is the option favoured by most laboratories. Abandoning the excess assay would save roughly £15 000 (assuming £2 per oestriol assay).

The prospective trial of screening in south Wales (the first routine screening programme for Down's syndrome to be offered for NHS patients), which evaluated all pregnancies referred to the participating hospitals, showed an 85% uptake of screening (those who were not screened either refused or presented too late) and that 85% of those in whom screening gave a positive result opted for amniocentesis.⁴ These figures are similar to those of Fletcher and colleagues (80% and 95% respectively), but because they give a lower rate of amniocentesis they may result in a lower economic estimate.

Furthermore, because the false positive rate in younger women is lower, Fletcher *et al* have overestimated the cost of detecting a case of Down's syndrome, which I estimate to be nearer to £40 000. Overall, Fletcher and colleagues' paper shows the power of this method of making rational decisions, which could be used for a variety of screening scenarios. Interpretation of the findings will vary: £40 000 to prevent the birth of a baby with Down's syndrome to a woman under 30 may be perceived as expensive but is low compared with the costs of caring for someone with the syndrome. Furthermore, we must not forget the feelings of the women: what could we say to a 29 year old woman who gave birth to a baby with the syndrome after being refused screening? It is also helpful to learn from history. When screening for Down's syndrome was introduced in Cardiff it was offered only to women aged 26 and over, for reasons similar to those quoted by Fletcher and colleagues. Within six months "consumer pressure" resulted in it being made available for all women irrespective of age. I therefore strongly disagree with the

Testing should be in all women

EDITOR,—The paper by J Fletcher and colleagues¹ was incorrect to conclude that restricting serum screening for Down's syndrome to women aged 30 or over is preferable to screening all women. Firstly, using a 58% detection rate and a 5% false positive rate for all pregnant women instead of estimates applicable to women aged 30 or over (72% and 12%²), and, secondly, not comparing screening policies appropriately introduces important errors.

Screening tests involve a trade off between detection rate and false positive rate. To compare screening policies, cut off levels must be set such that among all pregnancies in a community either the detection rate is held constant and the false positive rates compared or the false positive rate is held constant and the detection rates compared. Fewer miscarriages are induced by amniocentesis for each case of Down's syndrome detected if serum is tested in all women than if it is tested only in women aged 30 or over (0.30 or 0.41 *v* 0.46 respectively) (table).

Testing all women increases the cost of serum testing, whereas testing only older women means that more amniocenteses are performed per case detected, increasing this cost. At a detection rate of 51%—as achieved by the policy proposed by Fletcher and colleagues in 1000 women (table)—there would be 1000 serum tests and 31 amniocenteses if all women were tested or 410 serum tests and 47 amniocentesis tests if only women aged 30 or over were tested. On the basis of estimates of cost and uptake of amniocentesis cited in the paper, testing all women could cost about 25% more than testing only women aged 30 or over—a

smaller difference than reported in the paper and one that is acceptable for the added safety of the policy.

If the cost of serum screening for Down's syndrome and testing for α fetoprotein were less than the authors' generous estimate of £13.70 per woman screened then the difference in cost between the two policies would be reduced; if it were £6 or less (a realistic sum, given that screening for neural tube defects and Down's syndrome can be provided for about £15), serum testing all women would be less expensive than testing only those aged 30 or over.

Testing only women aged 30 or over introduces inequity by denying testing to younger women. Some women aged 30 or over with a high risk of having a child with Down's syndrome determined by a serum test will be offered an amniocentesis, but younger women, who could be at even higher risk, will not.

Offering serum screening to all women is the safest and most effective method of screening, maximising the detection rate for a given false positive rate. For this reason, and on grounds of fairness, it is the screening policy of choice.

NICHOLAS J WALD
Professor

ANNE KENNARD
Lecturer

HILARY WATT
Statistician

Department of Environmental and Preventive Medicine,
Wolfson Institute of Preventive Medicine,
Medical College of St Bartholomew's Hospital,
London EC1M 6BQ

JAMES E HADDOW
Medical director

GLENN E PALOMAKI
Director of biometry

GEORGE J KNIGHT
Laboratory director

Foundation for Blood Research,
PO Box 190,
Scarborough,
ME 04074,
USA

JACOB A CANICK
Professor

Department of Pathology and Laboratory Medicine,
Women and Infants Hospital of Rhode Island,
Providence,
RI 02905,
USA

- 1 Fletcher J, Hicks NR, Kay JDS, Boyd PA. Using decision analysis to compare policies for antenatal screening for Down's syndrome. *BMJ* 1995;311:351-6. (5 August.)
- 2 Wald NJ, Densem JW, Smith D, Klee GG. Four-marker serum screening for Down's syndrome. *Prenat Diagn* 1994;14:707-16.
- 3 Office of Population Censuses and Surveys. *Birth statistics—England and Wales*. London: HMSO, 1995. (Series FM1, No 22.)

Authors' reply

EDITOR,—One of the advantages of using decision analysis as a tool for considering the consequences of different screening policies is that the assumptions and numerical values on which the model's predictions are based are explicit. If there is debate about the assumptions or the numbers that should be used in the calculations it is easy to recalculate the model with the new numbers.

David Murray and Barry Tension suggest that our estimate of 75% for the uptake of amniocentesis in women aged 35 and over is too high. If their suggested figure of 45% is used the number of cases of Down's syndrome detected in Oxfordshire by a policy of offering amniocentesis to women aged 35 and over drops from 4.7 to 2.8/year, the number of miscarriages induced by amniocentesis from 6.6 to 4.0, and the total cost of the programme from £170 000 to £100 000. The cost per case detected and the number of pregnancies lost per case detected remain unchanged. Our conclusion that serum testing improves on testing based on age alone remains unchanged.

T M Reynolds and Kevin Spencer point out that the specificity and sensitivity of serum testing for Down's syndrome vary with maternal age. They are concerned that our decision to simplify the

Comparison of policies of screening for Down's syndrome with estimates of gestational age based on last menstrual period (estimates based on published estimates for performance of screening² with distribution of maternal age in Oxford in 1993³)

Screening policy	Risk cut off	Detection rate (%)	False positive rate (%)	No of miscarriages induced by amniocentesis per case of Down's syndrome detected*	
				Reported by Fletcher and colleagues ¹	Corrected
Triple test for all women	1:250	63	6.5	0.45	0.50
Triple test for only women aged 30 and over (A)	1:250	51†	4.7‡	0.25	0.44
Triple test for all women using cut off level to achieve:					
Same detection rate as A	1:130	51	3.1	§	0.29
Same false positive rate as A	1:190	58	4.7	§	0.39

*These estimates include cases of Down's syndrome that would be detected but would subsequently miscarry. If they were excluded the estimates would be about 33% higher.

†Proportion of all cases of Down's syndrome detected in whole community: 71% of babies with Down's syndrome are born to women aged ≥ 30 , in 72% of whom triple test will give positive result with risk cut off of 1:250—71% \times 72%=51%.

‡Proportion of amniocenteses among all pregnancies (women of all ages): 41% of unaffected births occur in women aged ≥ 30 , in 11.6% of whom triple test will give positive result—41% \times 11.6%=4.7%.

§Not specified.