whole screened population the number of babies with Down's syndrome was 25. With Wald and colleagues' screening test, the number of Down's syndrome babies detected was 12. With screening by maternal age ≥ 37 years alone, the number detected could have been 7 out of 25. These proportions are not significantly different (Fisher's exact test p=0·24; odds ratio 2·37; 95% confidence interval 0·73 to 7·68). Even with the different uptake of amniocentesis in the two groups—that is, 75% for all ages and 63% for those ≥ 37 years—there was still no significant difference in the result (p=0·2; odds ratio 2·95 (0·77 to 11·3)).

Only 4·9% of women were aged ≥ 37 years; the confidential enquiries into maternal deaths in the United Kingdom 1985-7 reported that 8% of pregnant women were over 35[2] and in our hospital in 1991 the proportion ≥ 37 years was 9·2%. This proportion is likely to rise as women delay their families for personal and financial reasons, and as this proportion rises the detection rates from the triple test and from maternal age alone will become even more similar.

In any particular district the cost of introducing this programme will depend on the proportion of women ≥ 37 years; in addition, many authorities (including our own) have now abandoned α fetoprotein testing, relying for neural tube defect screening on ultrasonography alone, and the cost of reintroducing this test would need to be accounted for in the calculations.

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1 Wald NJ, Kennard A, Densem JW, Cuckle HS, Chard T, Butler L. Antenatal maternal serum screening for Down's syndrome: results of a demonstration project. *BMJ* 1992;**305**:391-4. (15 August.)
2 Department of Health, Welsh Office, Scottish Home and Health Department. *Report on the Confidential Enquiries into Maternal deaths in the United Kingdom 1985-1987.* London: HMSO, 1991:18.

EDITOR,—Nicholas J Wald and colleagues describe a demonstration project for Down's syndrome screening in which the detection rate achieved was 48% (12/25 cases) at a 4·1% false positive rate.[1] They used three biochemical tests (α fetoprotein, total human chorionic gonadotropin, and unconjugated oestriol) along with maternal age in the so called triple test.

Our screening programme has used only α fetoprotein (and maternal age) in combination with the marker free β human chorionic gonadotrophin. In our large retrospective study free β human chorionic gonadotrophin was shown to be the biochemical marker with the greatest predictive value for Down's syndrome.[2] Studies with 90 cases of Down's syndrome and 2862 unaffected controls showed that the combination of α fetoprotein and free β human chorionic gonadotrophin detected more cases of Down's syndrome than did the triple test approach. This study confirmed previous findings in which detection rates of 75-80% were achieved in the early gestational period (14-16 weeks).[3-5]

In prospective studies using the free β protocol we have achieved detection rates for Down's syndrome of 73% (11/15) with a 5·5% false positive rate. Unlike Wald *et al*'s study, which detected only 20% more cases than would have been detected by a policy of screening according to advanced maternal age, our programme detected an additional 53% of cases. These results, in which α fetoprotein and free β human chorionic gonadotrophin detect more cases of Down's syndrome in younger women, confirmed observations in our retrospective study, in which this combination detected 100% more cases in women under 30 than did the triple test.

Observations that concentrations of free β human chorionic gonadotrophin are raised in the first trimester in Down's syndrome pregnancies[6] add further weight to our argument that free β human chorionic gonadotrophin is the marker of choice for Down's syndrome screening. The benefit of additional tests such as unconjugated oestriol is at best unproved and at worst widens the error in the risk estimate,[7 8] may add to the false positive rate,[2 9 10] and adds to the laboratory screening costs.

The scientific and medical community is best served by a balanced argument of the facts, rather than the exaggerated media reports of recent publications. Health authorities should be aware of the cost implications of making decisions in which suboptimal screening programmes are suggested. The general public and patients are not best served by an oversimplification of the facts that in turn grab headlines. Fortunately the scientific and medical community is capable of seeing through the "hype" and is able to make its own balanced judgments. At least as many laboratories in the United Kingdom are now using the free β human chorionic gonadotrophin protocol as are offering the triple test. The benefit of an increased detection rate and improved screening efficiency with the use of technologically advanced analytical procedures[11] will ensure that those benefits become available to all health authorities.

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1 Wald NJ, Kennard A, Densem JW, Cuckle HS, Chaud T, Butler L. Antenatal maternal serum screening for Down's syndrome: results of a demonstration project. *BMJ* 1992; **305**:391-4. (15 August.)
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EDITOR,—We have carried out with others a similar study to that by Nicholas J Wald and colleagues,[1] offering screening for Down's syndrome to 10 000 pregnant women in south Wales. This was submitted to the Welsh Office in February 1992. We would like to comment on the findings of Wald and colleagues.

In the population studied by Wald and colleagues 5·5% of women were aged over 37 years; in these women the detection rate was 71%. The detection rate in younger women was only 39%. This is important because the overall detection rate in a predominantly younger population would be decreased. Our population has only 2·8% of pregnancies in women aged over 37.

The initial screen positive rate found by Wald and colleagues was 5·7%, whereas our study had an initial screen positive rate of 3·5%. They used the triple test (α fetoprotein, human chorionic gonadotrophin, and unconjugated oestriol, whereas we used a double test (α fetoprotein and human chorionic gonadotrophin). The detection rates in the two studies were almost identical: Wald and colleagues found 48% and we found 50%.

Our detection rate was effectively identical to that of Wald and colleagues but we had an initial screen positive rate that was 40% lower. We used only two analytes, consistent with reports that using unconjugated oestriol in screening is of minimal benefit,[2 3] increases the false positive rate,[4] and greatly increases the imprecision of risk estimates.[5]

Thus, although Wald and colleagues' study shows that Down's syndrome screening is a useful addition to antenatal care, it does not show that the triple test has any advantages over a double test.

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1 Wald N, Kennard A, Densem J, Cuckle HS, Chard T, Butler L. Antenatal maternal serum screening for Down's syndrome: results of a demonstration project. *BMJ* 1992;**305**:391-4. (15 August.)
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EDITOR,—Although we congratulate Nicholas J Wald and colleagues on their demonstration project,[1] three points deserve comment.

Firstly, we are surprised that 25% (129/526) of the women who proved positive on screening subsequently declined the offer of amniocentesis despite access to individual counselling. We speculate that many of these women did not understand the nature of the initial screening test and that the knowledge that they were at increased risk of having a Down's syndrome baby could have been a source of stress for the remainder of their pregnancy.

Secondly, the authors discuss the advantage of performing a dating ultrasound examination on all women at the time of screening to avoid the need to later reassess positive results after a revision of gestational age. Another advantage is in avoiding possible costly litigation by women with false negative results, where it might be argued that dating by clinical methods alone is negligent. Had a scan been performed, the screening test would have been interpreted differently and amniocentesis offered.

Finally, to assess the population impact of the screening programme it is necessary to know how many Down's syndrome babies were born to the 26% of mothers who declined screening.

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1 Wald NJ, Kennard A, Densem JW, Cuckle HS, Chard T, Butler L. Antenatal maternal serum screening for Down's syndrome: results of a demonstration project. *BMJ* 1992;**305**: 391-4. (15 August.)

EDITOR,—Nicholas J Wald and colleagues claim that antenatal serum screening for Down's

syndrome is effective in practice and can be readily integrated into routine antenatal care.[1] They do not, however, deal with the thorny issue of informed consent. This is a crucial point because under common law patients have the right to receive sufficient information, in a way that they can understand, about the screening programme, including any substantial risks, so that they can make a balanced judgment.[2]

According to an editorial in the *BMJ*, "women should be told what the test is for and its false positive and false negative rates. The consequences of a positive result must be explained... these can be serious resulting in the loss of a normal infant because of a complication of the diagnostic procedure."[3]

To make such an informed choice on whether or not to enter this screening programme, a woman would therefore need a careful explanation of the screening test and its implications before having her blood sample taken. For example, she should understand that the purpose of the programme is to terminate Down's syndrome pregnancies. She should also understand that after the blood test she may be told that there is a 1 in 250 chance that the baby she is carrying has Down's syndrome, and she must know that if she decides to submit to amniocentesis that there is a chance of 1 in 100 or 200 of losing a normal baby. In other words, the concept of risk needs to be explained. The level of explanation requires detailed counselling, which will take a great deal of time. It cannot be provided by a leaflet alone. Wald and colleagues, however, have not mentioned the cost of the professional time needed to obtain informed consent. This is puzzling because this is probably the major cost associated with the screening programme. Those health authorities that have introduced the screening programme, or are contemplating doing so, should be aware that in the opinion of P J Edwards and D M B Hall "failure to obtain informed consent for a screening programme is not only ethically unacceptable but also exposes the health authority to the risk of litigation."[3]

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1 Wald NJ, Kennard A, Densem JW, Cuckle HS, Chard T, Butler L. Antenatal maternal serum screening for Down's syndrome: results of a demonstration project. *BMJ* 1992;**305**: 391-4. (15 August.)
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3 Edwards PJ, Hall DMB. Screening, ethics, and the law. *BMJ* 1992;**305**:267-8. (1 August.)

EDITOR,—Assessing a screening programme extended to 12 603 women, Nicholas J Wald and colleagues concluded that "antenatal serum screening for Down's syndrome is effective and acceptable in practice."[1] The findings were extensively reported in the media, alongside calls for this type of screening to be made nationally available on the NHS.[2]

Any screening test that improves individual risk estimates is to be welcomed. In evaluating any programme, however, it is important not to confuse community cost-benefits with cost-benefits to the pregnant woman. The gulf between these two viewpoints is perhaps best illustrated by comparing the detection rate of the triple test at a population level (overall efficiency 48%, rising to 71% for women 37 and over) with the reliability experienced at an individual level (56 out of every 57 women under 37 who "screened positive" proved after amniocentesis to have unaffected pregnancies).

It is also important that uncritical acceptance in the media should not pre-empt the normal process of scientific evaluation, particularly when only limited NHS resources are likely to be made available for screening and only one programme is likely to be implemented. The following information is needed before the implications of the current report can be fully assessed: demographic data (including maternal age distributions and previous Down's syndrome births) for screened and unscreened samples; number of Down's syndrome births detected in relation to total number of Down's syndrome births within the four regions over the period of the study (to determine programme efficiency as opposed to test efficiency); number of miscarriages after amniocentesis; and data on the nature and extent of counselling needs of different client groups, on the perceived value of counselling, and on its proportional contribution to programme costs. Given the small numbers of affected pregnancies on which detection rates inevitably had to be calculated and the likely mobility of women in these age groups, it is to be assumed that a direct method of ascertaining outcome in screened cases was used. A more precise measure of uptake than one based only on number of pregnancies screened and number of deliveries would have been helpful.

At this stage the triple test should perhaps be described to prospective parents as a prescreening test rather than as a screening test. Confirmatory diagnosis requires amniocentesis, and impact on incidence depends totally on affected pregnancies being terminated. Decisions on termination cannot be made until around 20 weeks' gestation. This introduces several other considerations into any cost-benefit analysis, not least of which are maternal anxiety experienced before, during, and after screening and the stress associated with amniocentesis and late termination; the negative effects of false positive results on maternal attitudes towards the baby, both before and after delivery[3 4]; and the unknown effects of maternal stress and amniocentesis on fetal development.

Wald's team has expressed concern that the triple test is not yet widely available and in some regions is being made available only to older women.[5] Certainly women of all ages should have access to the best available test. Given the efficiency of the triple test observed in the United Kingdom, however, it is important that its predictive value is not overstated by the media.[6] To suggest that "the wide confidence limits on the observed detection rate (28%-69%) mean that predicted results are a better guide to expected performance than the observed results"[1] is not necessarily helpful at this stage, nor are cost comparisons based on expected (16/26) rather than observed (12/25) detection rates.

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1 Wald NJ, Kennard A, Densem JW, Cuckle HS, Chard T, Butler L. Antenatal maternal serum screening for Down's syndrome: results of a demonstration project. *BMJ* 1992;**305**: 391-4. (15 August.)
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EDITOR,—Nicholas J Wald and colleagues conclude that maternal serum screening for Down's syndrome is cost effective and performs better than selection for amniocentesis on the basis of maternal age alone.[1] We can confirm the basis of his conclusions when applied to a district. We conducted a cost effectiveness exercise and evaluated its implications for purchasing in the City and Hackney Health Authority.

City and Hackney is an inner city district with a population of 196 000 and 3900 births per year, 10% of which are to women aged 36 and over.[2] In the absence of screening, five babies with Down's syndrome would be born each year (1·3/1000[3]).

Antenatal screening using the triple test, as outlined by Wald and colleagues, followed by amniocentesis in the 5% of pregnant women at highest risk, can detect over 60% of cases[3] and with termination of affected pregnancies would prevent three of the five cases of Down's syndrome born in Hackney each year (assuming a 100% uptake rate).

The alternative policy of offering screening to all pregnant women aged 36 and over, known to be at a higher risk of Down's syndrome, would result in a higher amniocentesis rate, since 10% of all pregnancies in Hackney are in women aged 36 and over. Screening by age alone (assuming 100% uptake) detects only 32% of Down's syndrome pregnancies,[4]—1·5 per year in Hackney.

At existing uptake rates the costs of the two types of screening programmes compare as in the table. The cost per case detected is similar in the two types of screening. Although the triple test screening programme costs £36 200 more per year, for the extra cost the district gets a test that covers the whole population; a test that doubles the detection rate of Down's syndrome; and a screening programme that requires 30% fewer amniocenteses. In addition, there are extra potential savings in paediatric surgery and medicine and in social and institutional care.

Costs of screening for Down's syndrome

	Screening with triple test	Amniocentesis on all women aged ⩾36
Cost of triple test (including counselling)	£45 200	
Cost of amniocentesis	£20 250	£29 250
Down's syndrome cases detected per year	1·78	0·78
Total cost	£65 450	£29 250
Cost per case detected	£36 769	£37 500

It can also be argued that triple test screening is more equitable and humane than a screening programme based on maternal age. Although the risk to mothers under 36 is less, the number of births is much greater and thus about 70% of all Down's syndrome births are to women in this age group.[5] In addition, although a 100% amniocentesis uptake would detect 32% of all pregnancies with Down's syndrome, the uptake rate for amniocentesis has actually been only 50% or so, resulting in a detection rate of under 15%.[4] This in part accounts for why screening based on maternal age alone has not reduced the incidence of Down's syndrome. It has also been shown that women value information about their pregnancy that reduces uncertainty, even if they do not wish to avoid the birth of a handicapped child.[6]

We recommended that City and Hackney District Health Authority purchase the triple test screening programme. This has been implemented in the current contractual year.

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1 Wald NJ, Kennard A, Densem JW, Cuckle HS, Chard T, Butler L. Antenatal maternal screening for Down's syndrome: results of a demonstration project. *BMJ* 1992;**305**:391-4. (15 August.)
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