

Uptake and acceptability of antenatal HIV testing: randomised controlled trial of different methods of offering the test

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Abstract

Objective: To determine the uptake and acceptability of different methods of a universal offer of voluntary HIV testing to pregnant women.

Design: Randomised controlled trial involving four combinations of written and verbal communication, followed by the direct offer of a test. The control group received no information and no direct offer of a test, although testing was available on request.

Setting: Hospital antenatal clinic covering most of the population of the city of Edinburgh.

Subjects: 3024 pregnant women booking at the clinic over a 10 month period.

Main outcome measures: Uptake of HIV testing and women's knowledge, satisfaction, and anxiety.

Results: Uptake rates were 6% for those in the control group and 35% for those directly offered the test. Neither the style of leaflet nor the length of discussion had an effect on uptake. Significant independent predictors of uptake were a direct test offer; the midwife seen; and being unmarried, previously tested, and younger age. Knowledge of the specific benefits of testing increased with the amount of information given, but neither satisfaction nor anxiety was affected by the type of offer.

Conclusions: The universal offer of HIV testing is not intrusive and is acceptable to pregnant women. A policy of offering the HIV test to all women resulted in higher uptake and did not increase anxiety or dissatisfaction. Uptake depends more on the midwife than the method of offering the test. Low uptake rates and inadequate detection of HIV infection point to the need to assess a more routine approach to testing.

Introduction

With increasing optimism about the benefits of antenatal HIV testing in terms of measures that can greatly reduce the chance of the baby being infected,^{1,3} there is a demand for effective, acceptable programmes of testing and appropriate patient information.⁴ This study was designed to respond to this demand by comparing different ways of offering voluntary testing to all pregnant women in a randomised, controlled trial.

Currently, antenatal testing policies, practices, and uptake rates vary,⁵⁻⁸ and this has encouraged debate about how testing should be offered: to all women (universal policy), selectively (for those with recognised risk factors), or on a "request only" basis. Another conflict of opinion has been whether the test should be offered with comprehensive information, as would be done in an HIV testing clinic, or whether it should be offered more in line with the other antenatal blood tests, with minimal information. Minimal information may be more likely to achieve high uptake.⁷⁻⁹ Compre-

hensive information aims to ensure informed choice but may result in high costs in midwives' time and increased anxiety.¹⁰ Studies have examined the outcomes of the different policies,⁴⁻¹¹ but the different methods have not been compared systematically, with an evaluation of the direct impact on women. Although most women are at low risk, the offer of the test may itself cause anxiety, as has been found with other antenatal tests,¹² and feelings of resentment about being offered the test may reduce satisfaction with the care provided.

The prevalence of HIV infection in Edinburgh (1:660 deliveries 1990-5) has fallen since its peak of 1:250 deliveries in 1986 but remains high in comparison to many centres.¹³ Before this trial, there was no universal testing policy in Edinburgh and only a small percentage of women attending antenatal clinics were selectively offered the test, most commonly because of a history of intravenous drug use. In the years immediately preceding the study, less than 1% of women seen antenatally had an HIV test during pregnancy. Because of this relatively high prevalence and the lack of a universal testing policy, Edinburgh was ideally suited for this randomised controlled trial.

The study aimed to determine whether different methods of offering the test would lead to significantly different uptake rates and to assess the impact of the different methods on the woman's response in terms of her satisfaction, anxiety, and knowledge. Demographic and situational factors were examined to determine their effect on uptake. The goal was to have sufficient information to define the most effective and acceptable approach to testing. The methodology was approved by Lothian Reproductive Medicine Ethics Committee.

Methods

Design, setting, and subjects

The study was a randomised controlled trial in the main maternity hospital in the city of Edinburgh (about 5000 deliveries a year). The randomly allocated interventions (table 1) were different presentations of an offer of voluntary named HIV testing to all pregnant women attending the antenatal clinic for their first (booking) visit to the hospital during a 10 month period from May 1996 to February 1997.

Women in the four intervention groups were directly offered the test by a midwife (universal policy). Women in the control group were not routinely offered a test and were not, individually, given any information about the test, either verbally or in print, unless they asked. This was the clinical situation before the study.¹⁴ However, testing was advertised by poster, and the information letter about the study made it clear to women in this group that the test was available

and that they could ask for a test if they wanted it (request policy). This was done because we believed that current acceptable practice had to include easy availability of HIV testing.

Key outcomes were uptake of testing and women's knowledge of HIV, satisfaction with consultation, and anxiety.

Procedure

All women for whom a postal booking appointment was made during the 10 months of the study were randomised. In response to referral from the general practitioner, each patient was assigned an antenatal number generated by the hospital computer. This marked the point of formal entry to the trial, and each woman was randomly assigned by a computer programme to one of five groups. Within blocks of 24 successive women, eight were allocated to the control group and four to each of the intervention groups.

An information letter was sent to all women with the booking information package, explaining the nature and purpose of the study. It explained that she could choose whether or not she wanted an HIV test and that the questionnaire was voluntary. An information leaflet, if applicable, was enclosed within the posted information. Later, at the booking clinic, each woman was approached by the research midwife and was given the opportunity to opt out of participating in the study. A coded sticker inside the patient's notes showed the midwives which discussion protocol to use during the consultation. Women were excluded if they were known to be HIV positive and if there was language difficulty and no interpreter was available, but this information was available only after randomisation and after the study information had been sent, so exclusions were made at time of booking; in these cases the midwife did not discuss HIV testing.

Most bookings were carried out by 10 midwives who all received training in offering the test by using the two discussion protocols designed for the study. The training involved role play and information sharing between the midwives, the research team, and a specialist HIV counsellor. The two protocols were introduced and the importance of the distinction between them was emphasised. Throughout the study, occasional meetings provided support and continued emphasis on the distinction between the two protocols. A researcher also periodically monitored all midwives' consultations to ensure that the protocols were being followed.

If the woman decided to take the test, she was required to sign a consent form. In this event, the blood sample which was used to test for syphilis was also tested for HIV.

Immediately after the consultation with the midwife, women were asked to complete the questionnaire, which assessed their knowledge, satisfaction, and anxiety.

To determine HIV prevalence among childbearing women in Scotland, unlinked anonymous HIV testing of dried blood spots from Guthrie cards obtained from neonates has been performed since January 1990. Guthrie cards corresponding to all pregnant women included in the study were coded to establish if the women had belonged to either the control or the intervention group. This enabled the investigators to deter-

mine how many women in the study population who did not have an HIV test were antibody positive

Materials

Leaflets—Two types of leaflet were developed with professional help and piloted with pregnant women. The "HIV specific" leaflet (Flesch score 65, indicating good readability¹⁵) explained in some detail the benefits of offering testing, with particular reference to treatment with zidovudine (AZT) and avoidance of breast feeding. It also explained what the test is and what the results mean; stated the disadvantages of testing; and gave information about insurance and about HIV transmission. It explained that the midwife would offer the test and what it would involve and it emphasised that testing was the woman's choice. The "blood tests" leaflet (Flesch score 66) contained a short summary of the "HIV specific" leaflet as part of information about all the blood tests that were available, with the aim of normalising HIV testing. This leaflet noted that testing could benefit the baby but did not provide specific details.

Pretest discussion protocols—The two discussion protocols were printed on card and were placed in each consulting room for the midwives' reference. The "comprehensive" protocol (two pages of A4 paper), developed with professional help and with reference to guidelines,^{16,17} covered the main information points included in the "HIV specific" leaflet, re-emphasising the benefits of testing for the baby. Personal risk, the possibility of a positive result, and the support available were also discussed if a woman decided to take the test. The "minimal" protocol (half a page of A4 paper) was a short check that the woman had read and understood the leaflet and that she knew what both a positive and negative result implied. If she decided to take the test she was given information about what the test involved.

Questionnaire—The questionnaire contained a standardised scale to measure anxiety (six item form of the Spielberger state trait anxiety inventory¹⁸) and specific questions and scales developed for this particular study, based on measures reported in various previous papers. Internal consistencies of the main outcome scales were high: knowledge of HIV (11 items, Cronbach's $\alpha = 0.91$); satisfaction (5 items, Cronbach's $\alpha = 0.91$); and anxiety (6 items, Cronbach's $\alpha = 0.89$).

Midwives' checklist—The midwives noted uptake, which was checked with the laboratory reports. They also noted time taken for discussing HIV, any previous HIV testing, whether the woman or her partner was an intravenous drug user, and nationality.

Table 1 Characteristics of study groups

Group	Leaflet	Discussion with midwife	Offered testing	No (%) completing questionnaire*
1	None	None	No†	882/994 (89)
2	All blood tests	Minimal	Yes	441/495 (89)
3	All blood tests	Comprehensive	Yes	478/521 (92)
4	HIV specific	Minimal	Yes	453/495 (92)
5	HIV specific	Comprehensive	Yes	450/519 (87)

*Denominators represent women who were randomised and participated in the trial; all were included in the primary end point (uptake rate).

†HIV testing was available on request for this group and was advertised in a letter about the study sent to all women and by poster in the clinic.

Table 2 Characteristics of women in intervention groups

Characteristic	Group					Significance
	1	2	3	4	5	
Mean (SD) age (years)	29.3 (5.4)	29.4 (5.3)	29.8 (5.5)	29.6 (5.5)	29.6 (5.5)	$F_{(4,3009)}=0.89, P=0.47$
No (%) married	661/974 (67.9)	357/487 (73.3)	372/512 (72.6)	355/491 (72.3)	350/504 (69.4)	$\chi^2=7.3, df=4, P=0.12$
No (%) primiparous	516/990 (52.1)	236/492 (48.0)	232/518 (44.8)	241/494 (48.8)	249/516 (48.2)	$\chi^2=7.9, df=4, P=0.10$
No (%) unemployed	64/835 (7.7)	29/409 (7.1)	29/448 (6.5)	26/422 (6.2)	31/432 (7.2)	$\chi^2=1.2, df=4, P=0.87$
Area risk code (No (%) at lower risk)*	404/966 (41.8)	190/477 (39.8)	213/506 (42.1)	199/475 (41.9)	211/498 (42.4)	$\chi^2=0.8, df=4, P=0.94$
Social deprivation score (% affluent)†	481/848 (56.7)	227/419 (54.2)	231/448 (51.6)	224/409 (54.8)	238/436 (54.6)	$\chi^2=3.2, df=4, P=0.52$

*Split into two groups: lower risk group includes groups 1 and 2 of the five categories.

†Split into two groups: affluent group contains groups 1, 2, and 3 of the seven categories.

Demographic variables—Demographic variables were collected by the midwife at the time of the booking visit and were later downloaded from the hospital computer. The known HIV prevalence in the area of Edinburgh in which the women lived was used as an indirect measure of risk: a five point “area risk” code (1 = no HIV cases in area; 5 = > 1 case per 1000) was derived on the basis of the number of people identified as being infected with HIV who were alive in each postcode area to the end of 1996 (excluding homosexual and bisexual men).¹⁹ A seven point social deprivation score was also derived from postcodes (1 = highly affluent; 7 = very deprived).²⁰ As data from the hospital computer were incomplete, data for the demographic variables were missing for some women.

Statistical methods

The target sample size of 3000 was chosen to have approximately 90% power to show a significant change ($P < 0.05$) in uptake from 70% to 80% between intervention groups.

Statistical analysis was done using SPSS; all analyses were by intention to treat. Proportions of women taking the test were compared with the χ^2 test, using the Mantel-Haenszel trend test for ordinal variables. Logistic regression methods were used to determine the significant independent predictors of uptake. Knowledge was analysed with the χ^2 test, comparing the proportion who made the correct response with those who made an incorrect or “don’t know” response for each item separately. A satisfaction score was devised as the sum of all five items and was compared across groups by using non-parametric analysis of variance (Kruskal-Wallis) because of the positively skewed distribution. The anxiety score (sum of all six items, pro-rated to be comparable to the original 20 item scale) was compared across groups by using one way analyses of variance.

Results

Sample

In all, 3505 pregnant women were randomised over the 10 month period; 3024 women participated. One woman was excluded because she was known to be HIV positive and six because of language difficulty (two were Pakistani, two Chinese, one Russian, and one Italian). A total of 311 women did not participate because of miscarriages or terminations before booking; 33 did not receive information about the study through the post; 119 never attended the clinic; and 11 refused to participate. Characteristics in the five study groups did not differ (table 2).

Thirty five women were defined as high risk because either they or their partner were intravenous drug users. These women were all randomised into the study, but they were treated as they would have been before the study began. Regardless of intervention group, there was a policy of selective testing for all women at high risk.

Uptake

Table 3 shows uptake rates for each of the five study groups. The average uptake for all women offered the test (excluding the control group) was 35%. Each of the methods of directly offering the test resulted in a higher uptake than in the control group (6% uptake) ($\chi^2 = 308.5, df = 4, P < 0.0001$). However, there was no significant difference between the four methods of directly offering the test ($\chi^2 = 3.9, df = 3, P = 0.27$).

Of the 760 women tested, one woman was newly identified as HIV positive. One woman previously known to be HIV positive was included in the sample. Three HIV infected women were not detected during

Table 3 Effect of intervention on uptake of HIV testing

	Group					Significance
	1	2	3	4	5	
No (%) tested	55/994 (5.5)	179/495 (36.2)	193/521 (37.0)	171/495 (34.5)	164/519 (31.6)	$\chi^2=308.5, P < 0.001$

Table 4 The effect of demographic factors and previous testing on uptake of HIV testing. Values are numbers (percentages) of women taking test

Variable	No (%) taking test	χ^2	P value
Age:			
Older (≥ 30 years)	367/1579 (23.2)	6.97	$P < 0.01$
Younger (< 30 years)	393/1433 (27.4)		
Marital status:			
Married	468/2095 (22.3)	28.9	$P < 0.001$
Single	277/873 (31.7)		
Parity:			
Multiparous	377/1536 (24.5)	0.75	$P > 0.05$
Primiparous	382/1474 (25.9)		
Employed in or outside the home:			
Yes	574/2367 (24.2)	15.3	$P < 0.001$
No	67/179 (37.4)		
Previous test:			
Yes	131/298 (43.9)	49.4	$P < 0.001$
No	596/2402 (24.8)		

Table 5 Effect of risk of HIV (derived from postcode area) on uptake of HIV testing by women attending antenatal clinics

Area	1	2	3	4	5	Significance
No (%) taking test	48/173 (28)	158/692 (23)	87/352 (25)	261/954 (27)	184/751 (25)	Mantel-Haenszel $\chi^2=0.32, P > 0.05$

Group 1 has no HIV cases; group 5 has >1 case per 1000 population.

the 10 month trial; two of the three had been randomised to the control group.

What predicts uptake?

Tables 4-8 show that the best independent predictor of uptake was being directly offered the test, followed, in order, by which midwife offered the test, not being married, having had a previous test, and being younger. Although deprivation score (table 6) and employment status (table 4) were related to uptake, they were not significant independent predictors.

Acceptability of testing

Overall, 89% (2703/3024) responded to the questionnaire (table 1), and 88% of women (2362/2699) responded positively to the question, "Are you in favour of an HIV test being available to all pregnant women?" When they were asked to choose the best of five methods of offering the test, only 210 (9%) reported that it should be left up to the woman to request the test from the midwife.

Knowledge of HIV

General knowledge of HIV was good and did not differ significantly by method of offering testing (data not shown). Specific knowledge about vertical transmission and the effects of zidovudine and breast feeding, which was provided only in the "HIV specific" leaflet and the comprehensive discussion protocol, was much poorer.

Intervention had a significant effect on specific HIV knowledge (table 9). Knowledge was greatest when the information was repeated in both the leaflet and the discussion (group 5).

Satisfaction

In general, satisfaction with the consultation was high (mean (SD) score 21.5 (3.4), maximum possible = 25). Satisfaction was not affected by the method of offering testing (Kruskal-Wallis $\chi^2 = 2.23$, $df = 4$, $P = 0.69$) (data not shown).

Anxiety

The anxiety level of the entire sample (pro-rated mean 36.7 (11.0), maximum possible = 80) was similar to that found previously in a group of 200 pregnant women and lower than in women who had received an α foeto-protein screening result showing the fetus was at high risk (47.7 (15.8), maximum = 80).¹⁸ Anxiety was not affected by method of offering testing ($F_{(4, 2568)} = 1.38$, $P = 0.24$) (data not shown).

Time taken for discussion

The average time taken for the comprehensive protocol was 7 minutes 40 seconds (SD = 4 minutes 30 seconds) and for the minimal protocol, 4 minutes 30 seconds (3 minutes 5 seconds).

Table 6 Effect of social deprivation on uptake of HIV testing by women attending antenatal clinics

Social deprivation score	1	2	3	4	5	6	7	Significance
No (%) of women taking test	108/490 (22)	112/509 (22)	98/402 (24)	208/828 (25)	33/144 (23)	28/94 (30)	33/93 (35)	Mantel-Haenszel $\chi^2 = 7.8$, $P < 0.01$

Derived from postcode area; 1=highly affluent; 7=very deprived.²⁰

Table 7 Effect of midwife on uptake of HIV testing by women attending antenatal clinics

Midwife	A	B	C	D*	E	F	G	H	I	J	K	Significance
No (%) of women taking test	52/353 (15)	21/134 (16)	55/316 (17)	63/291 (22)	68/312 (22)	41/170 (24)	138/492 (28)	78/263 (30)	61/188 (32)	119/361 (33)	66/138 (48)	$\chi^2 = 100.2$, $P < 0.001$

*The 10 midwives in this group were not analysed individually as they each did <63 bookings; each of the other 10 midwives did >130 bookings.

Table 8 Significant predictors of uptake of HIV testing found with logistic regression analyses (forward conditional method)

Factor	Measures			
	Wald χ^2	df	P value	Odds ratio (95% CI)
Offer of testing (offered testing directly v being in the control group)	186.8	1	<0.0001	8.4 (6.2 to 11.5)
Midwife*	84.3	10	<0.0001	—
Marital status (married v being single)	20.9	1	<0.0001	0.59 (0.46 to 0.74)
Previous test (yes v no)	11.5	1	0.0007	1.6 (1.2 to 2.1)
Age (increase in age, fitted as continuous variable)	6.6	1	0.01	0.98 (0.96 to 0.99)

*Single odds ratio cannot be calculated for overall effect of all midwives.

Table 9 Specific knowledge about HIV by method of offering the test

Group	Leaflet	Discussion with midwife	No (%) giving correct answer	
			Breast feeding*	Zidovudine†
1	None	None	263/865 (30)	128/865 (15)
2	All blood tests	Minimal	128/435 (29)	87/438 (20)
3	All blood tests	Comprehensive	284/468 (61)	190/470 (40)
4	HIV specific	Minimal	202/448 (45)	171/448 (38)
5	HIV specific	Comprehensive	309/446 (69)	243/446 (54)
Significance			$\chi^2 = 267.4$, $df = 4$, $P < 0.001$	$\chi^2 = 277.8$, $df = 4$, $P < 0.001$

**A pregnant woman who has HIV can infect her baby through breast feeding."

†A pregnant woman who has HIV can reduce the chance of her baby becoming infected by taking zidovudine (AZT)."

Discussion

The antenatal booking visit is a sensitive time: much information is being exchanged, and it is important that the introduction of a new screening test will not adversely affect the experience. This, added to the controversy surrounding HIV testing, has led to particular concern among health professionals about the introduction of HIV testing into antenatal care. Our data show that this apprehension is unfounded. Women were willing to discuss their attitudes to HIV testing and were positive about the availability of testing. Moreover, the universal offer of testing did not seem to be intrusive to the booking visit or to cause anxiety, and it was not inappropriately time consuming.

Methodological considerations

The control group was necessary for methodological reasons, but raised important ethical issues. For the study to be acceptable to the ethical committee and to the patient representative groups we contacted, we had to make it clear to the control group that the trial was taking place and that they could ask for an HIV test. In response to this, there was an increase in testing from less than 1% in the previous year to 6%, and thus more women in this group had testing than would otherwise have been the case.

Although uptake was much lower than expected for the sample size calculation, the power to detect a difference of 10% between groups is unchanged. The expected uptake rate was based on the findings of a study in Edinburgh that found an uptake rate of 71%.²¹ This large difference in uptake rate between the two studies is perhaps a reflection of the way the test was presented. While the previous study emphasised the research purpose of determining HIV prevalence, the present study was geared towards women's choice rather than deliberately aiming to increase testing rates.

Types of offer

Offering the test to all women compared to "on request" availability (as in the control group) resulted in significantly higher uptake but did not increase the women's anxiety or dissatisfaction. No one method of offering the test emerged as the most acceptable. Neither anxiety nor dissatisfaction increased with the amount of information given, lending no support to previous suggestions that comprehensive discussion may have an adverse impact.¹⁰ Nor did one method of offering the test emerge as the most effective, as shown by uptake, suggesting that the extent of information given is irrelevant. Previous research on prenatal testing for cystic fibrosis has shown that more information results in lower uptake,⁹ but this is not supported by our findings.

However, knowledge of specific benefits of testing increased with the amount of information given. This is an important indication that the midwives followed the discussion protocols and that the interventions were systematically different. It also shows that providing specific information can increase women's informed choice, which is a desirable outcome. So, although prolonged discussion along the lines of the HIV testing clinic model is not necessary, specific benefits should be highlighted.

Recommendations

- In areas where unlinked anonymous HIV testing indicates appreciable levels of undetected HIV infection in childbearing women, all women attending antenatal clinics should be offered the test and midwives should be required to keep a record of the offer
- Leaflets specifically about HIV infection and about all blood tests both have advantages. We recommend a leaflet containing information about all blood tests, but including more information about HIV, specifying clearly the benefits of testing during pregnancy
- A minimal approach to discussion is advised as it will cost less in terms of midwives' time, but it should contain specific information on the benefits of testing
- Midwives play an important role in affecting uptake, and research should focus on differences between midwives that may affect uptake rates
- In an attempt to increase uptake and detection rates, a routine approach to testing should be assessed systematically

Factors affecting uptake

Being unmarried and younger were independent demographic predictors suggesting that women were making the decision to take the test on the basis of personal risk assessment. The univariate finding that uptake increased with extent of social deprivation supports this assertion. However, there was no effect of risk area on uptake, suggesting that women at higher risk in terms of possible local exposure to the virus were no more likely to take the test than women at very low risk.

The midwife had a very important effect on uptake. This supports the findings of a smaller study ($n = 448$) which recorded much wider differences between 12 midwives (3%-82%).²² In this study we found that even though we provided the midwives with the same information during training and gave them clear, written protocols to work from, their uptake rates were significantly different. This challenges the prevalent assumption that the behaviour of health professionals is based solely on the extent of their medical knowledge. Marteau and Johnston have argued that psychological models used to predict patients' behaviour should also be applied to health professionals, implying that midwives' attitudes should be taken into account when considering uptake of testing.²³

Benefits of routine offer

Our study focused on women's choice and assessed opinion, satisfaction, and anxiety. Nevertheless the main point of offering HIV testing is to enable infected women to take steps to prevent vertical transmission. The prevalence of HIV infection shown by anonymised testing was similar to that in previous years (1 in 600 deliveries). What was unexpected and quite out of keeping with past experience¹³ was the high proportion of infected women in whom seropositivity was unknown. During the study, one HIV positive woman was detected out of two who were offered the test. Two unknown positive women in the control group did not request testing, which reinforces the necessity for the test to be offered to pregnant women rather than simply be available on request. Whether

Key messages

- HIV testing in pregnancy is beneficial, but uptake rates are not high
- Offering the test to women attending antenatal clinics increases uptake without increasing anxiety or dissatisfaction
- The extent of information given is not important in terms of whether women take the test and whether they find the procedure acceptable
- Uptake depends more on the midwife than the method of offering the test
- Low uptake rates and inadequate detection of HIV infection point to the need to assess a more routine approach to testing

another voluntary system would be more effective is not certain. Out of 35 women selectively offered testing because of a history of injecting drug use (self or partner), 14 declined HIV testing.

In London, where there is a higher prevalence of HIV infection in pregnancy, testing policies are failing to detect most HIV positive women before they give birth.¹¹ There is therefore an urgent need to define the factors that will increase uptake rates. The results of this study show that requiring the midwives to offer the test and documenting that offer results in a 35% uptake rate, which is higher than in most units in London,⁵ where practice is inconsistent and few have written protocols.¹¹ Moreover, women found the test acceptable, no matter how it was presented, and the most frequent reason given for taking the test was "It's a good idea to have as a routine test." In the light of this evidence, and in support of the recent assertion that "the time has come to bring HIV antibody testing alongside other diagnostic screening tests,"²⁴ we propose assessing the acceptability of a routine approach to testing, in which concise but specific information and discussion is provided and the test is done automatically unless the woman chooses not to be tested.

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codesigner of the study protocol and materials, discussed core ideas, helped to interpret the data, and contributed to the paper. RJP gave advice on the original study design and on the analyses of data, supervised data analyses, and edited the paper. WMS and FDJ are guarantors for the paper.

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Endpiece

Hypothesis and fact

The great tragedy of Science—the slaying of a beautiful hypothesis by an ugly fact.

Thomas Henry Huxley, *Collected Essays* (1893-4),
"Biogenesis and Abiogenesis"