Objective To evaluate the effect of ethnicity of women on the outcome of in vitro fertilisation (IVF) or intracytoplasmic sperm injection (ICSI) treatment.

Design Observational cohort study.

Setting UK National Database.

Population Data from 2000 to 2010 involving 38,709 women undergoing their first IVF/ICSI cycle were analysed.

Methods Anonymous data were obtained from the Human Fertilization and Embryology Authority (HFEA), the statutory regulator of IVF and ICSI treatment in the UK. Data analysis was performed by regression analysis with adjustment for age, cause and type of infertility and treatment type (IVF or ICSI) to express results as odds ratio (OR) and 95% confidence intervals (95% CI).

Methods Live birth rate per cycle of IVF or ICSI treatment.

Results While white Irish (OR 0.73; 95% CI 0.60–0.90), Indian (0.85; 0.73–0.97), Bangladeshi (0.53; 0.33–0.85), Pakistani (0.68; 0.58–0.80), Black African (0.60; 0.51–0.72), and other non-Caucasian Asian (0.86; 0.73–0.99) had a significantly lower odds of live birth rates per fresh IVF/ICSI cycle than White British women, ethnic groups of White European (1.04; 0.96–1.13), Chinese (1.12; 0.77–1.64), Black Caribbean (0.76; 0.51–1.13), Middle Eastern (0.73; 0.51–1.04), Mediterranean European (1.18; 0.83–1.70) and Mixed race population (0.94; 0.73–1.19) had live birth rates that did not differ significantly. The cumulative live birth rates showed similar patterns across different ethnic groups.

Conclusion Ethnicity is a major determinant of IVF/ICSI treatment outcome as indicated by significantly lower live birth rates in some of the ethnic minority groups compared with white British women.

Keywords Assisted conception, embryo, ethnicity, in vitro fertilisation, infertility, intracytoplasmic sperm injection, live birth.

Tweetable abstract Ethnicity affects IVF outcome with lower live birth rates in some ethnic groups more than in white British.

Linked article This article is commented on by M Aboulghar, p. 911 in this issue. To view this mini commentary visit http://onlinelibrary.wiley.com/doi/10.1111/1471-0528.14313/full.
woman. Further, most treatment protocols devised are based on research studies conducted in the Caucasian population of Europe and North America with extrapolation of the resulting data and application of the practices to populations worldwide representing various ethnicities and races.

There are a few published studies highlighting ethnicity as a determining factor of importance in IVF/ICSI treatment outcome. However, most studies are based on small sample size and subjects described are of selected ethnicities and races and not representative of a general population sample, whereas larger published studies are based on the population of the USA. Another major issue of most published data is the pooling of different ethnicities under single wider categories such as Asians, which can include women from China, Japan, Korea, India, Bangladesh or Pakistan, who are significantly different racially and ethnically among each other. Further, most studies, especially those with smaller sample sizes, were from a single fertility unit, and a number of ethnic groups were under-represented to generate a valid conclusion.

We, therefore, accessed a large anonymised patient register held by the Human and Fertilisation and Embryology Authority (HFEA) of the UK with an overall objective to evaluate the effect of ethnicity of women on the clinical outcome of IVF or ICSI treatment in a large population. The HFEA regulates fertility clinics in the UK, and as part of its role, it requires that all clinics submit the baseline data for each treatment cycle, which also include the ethnicity of women.

**Methods**

This cohort study is carried out in the UK by reviewing the anonymised data obtained from the HFEA registry covering the period 2000–10. Only women undergoing their first cycle of IVF/ICSI treatment were included and this was done to ensure that the data were truly unbiased (see Figure S1). Approval for the study was granted by the National Health Service Research Ethics Committee and the Nottingham University NHS Trust Research and Development Department. The process of extracting data was in keeping with the rules governing data protection.

The variables extracted include women’s age, ethnicity, cause and type of infertility, duration of infertility, IVF or ICSI, number of embryos transferred, and day of embryo transfer. Outcomes included number of oocytes retrieved, number of oocytes fertilised by IVF or ICSI, number of embryos created, fertilisation rate (number of oocytes fertilised per number of oocytes inseminated), clinical pregnancy rate (number of pregnancies with positive heart beat on ultrasound per number of women starting IVF treatment), implantation rate (number of clinical pregnancies per number of embryos transferred), whereas live birth rate (proportion of cycles started that resulted in a live birth) was the main outcome measure in this study. Ethnicity was self-reported then categorised using recently recommended guidelines by the Office for National Statistics.

Data analysis was carried out using STATA 8.1. Univariate analysis using the available variables was performed first to assess the differences in baseline characteristics between White British women and those from other ethnic groups. Based on the distribution, bivariate analysis of continuous data was done with the Student’s t test or Mann–Whitney U test. The relationship between two categorical variables was analysed by performing unadjusted odds ratio (OR) with 95% confidence interval (95% CI), chi-square test and Fisher exact test. When the confidence interval around the odds ratio did not include 1.00, the difference was considered to be statistically significant in all statistical tests. Logistic regression models were used to assess the effects of ethnicity on the study outcomes controlling for confounding variables. The White British ethnic group was taken as reference group in the model given that it is the largest ethnic group in the data set. To estimate the independent contribution of ethnic minority group to treatment outcomes (relative to the White British reference group), multivariate logistic regression analyses were performed. Potential confounding factors found to be statistically significant in univariate analyses and variables regarded as clinically significant were included in the models. For continuous data, a multivariate linear regression model was used controlling for the same confounders in the logistic models.

**Results**

**Demographic information and prevalence of causes of infertility in women of different ethnic background**

Women undergoing their first cycle of treatment were analysed in this study (Figure 1). A cohort of 38 709 distributed as White British—28 408 (73.39%), White Irish—635 (1.64%), White European—3201 (8.27%), South-Asian Indian—1226 (3.17%), South-Asian Bangladeshi—105 (0.27%), South-Asian Pakistani—878 (2.27%), Chinese—135 (0.35%), Black British—168 (0.43%), Black African—879 (2.27%), Black Caribbean—1495 (3.86%), Mediterranean European—144 (0.37%), Middle-Eastern—171 (0.44%), Mixed Race—366 (0.95%) and Other Asian—898 (2.32%).

The mean age of women ranged from 29.7 years to 35.8 years (Table 1). Women from South-Asian Indian, South-Asian Pakistani, Black Caribbean and Middle-Eastern backgrounds were significantly younger than the White British women, and White Irish, White European and Black British women were significantly older than the reference ethnic group ($P < 0.05$). The causes of infertility vary between ethnic groups as shown in Table 1 (and see Figure S2).
Effects of ethnicity of women on ovarian response and clinical pregnancy rates

After adjusting for all variables, including age of patient at time of treatment, cause of female or male infertility, and type of treatment (ICSI versus IVF) South Asian Bangladeshi, South Asian Pakistani, Black African, Middle Eastern and Other Asian women have a significantly lower number of eggs collected than White British women (Table 2). Women of a mixed race also demonstrated a significantly lower number of eggs collected per treatment cycle. On the other hand, White Europeans had significantly higher numbers of eggs collected ($P < 0.0001$). There were no significant differences in the method of fertilisation (IVF or ICSI) used between women of different ethnicities. The data on number of embryos transferred, cryopreserved and the day of embryo transfer are shown in Table 2. South Asian Indian, South Asian Bangladeshi, South Asian Pakistani, Black British, Black African, Black Caribbean and Middle Eastern women were at higher risk of not reaching embryo transfer stage (cycle cancellation before embryo transfer after treatment started) (Table 2). The reported ovarian hyperstimulation syndrome rates have been generally similar across all the ethnic groups except for higher incidence reported at egg collection in Black British and Black Caribbean women.

White Irish, South Asian Indian, South Asian Bangladeshi, South Asian Pakistani, Black African, and Other Asian groups had a significantly lower odds of clinical pregnancy than White British women after adjusting for age, cause of subfertility and type of treatment (Table 3). In contrast, White Europeans had significantly higher odds (OR 1.09; 95% CI 1.01–1.18) after adjusting for the aforementioned characteristics. Other Ethnicities had comparable outcome to that of White British women.

Discussion

Main findings

The data from this large UK national database (HFEA) suggests that ethnicity is a major independent factor determining the chances of IVF or ICSI treatment success. Live birth rates following IVF or ICSI treatment were significantly lower in some of the ethnic groups (White Irish, South Asian Indian, Black British, Pakistani, Black African and Other Asian) compared with White British women, which suggests that ethnicity is a major determinant of live birth following IVF or ICSI treatment. Although the reason for this association is difficult to explain, the potential factors could be the observed differences in cause of infertility, ovarian response, fertilisation rates and implantation rates, which are all independent predictors of IVF success.

Strengths and limitations

Although there are a number of similar studies, this study is unique in the sub-categorising of ethnicities to represent more homogeneous subgroups of racial, cultural and lifestyle similarities: for example, Asian ethnicity clearly...
Table 1. Baseline characteristics of the women according to their ethnic group, expressed as OR 95% CI

| Ethnic Group                  | Sample Size (n) | Mean Age (SD) | Cause of Infertility (%), n | | |
|------------------------------|----------------|---------------|----------------------------|---|
| White                        | 28,408         | 34.4          | Tubal 4687 (80)             |   |
| Asian                         | 4,032          | 36.9          | Uterine 134 (0.8)           |   |
| South Asian                   | 2,997          | 34.5          | Ovulatory 3,359 (59)        |   |
| South Asian                   | 2,283          | 34.3          | Endometriosis 2,302 (8.1)   |   |
| Black British                 | 1,050          | 34.4          | Male factor 1,432 (0.9)     |   |
| Black African                 | 690            | 34.7          | Male factor 1,432 (0.9)     |   |
| Black African                 | 98             | 34.7          | Male factor 1,432 (0.9)     |   |
| Mediterranean                 | 7,734          | 34.9          | Male factor 1,432 (0.9)     |   |
| Middle Eastern                | 5,096          | 34.7          | Male factor 1,432 (0.9)     |   |
| Mixed Race                    | 628            | 34.9          | Male factor 1,432 (0.9)     |   |
| Other Asian                   | 1,782          | 34.7          | Male factor 1,432 (0.9)     |   |
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| Mixed Race                    | 628            | 34.9          | Male factor 1,432 (0.9)     |   |
| Other Asian                   | 1,782          | 34.7          | Male factor 1,432 (0.9)     |   |

Significantly lower (*P < 0.05, **P < 0.005, ***P < 0.0005)
Table 2. Treatment and outcome characteristics of the women according to their ethnic group

|                           | White British | White Irish | White European | South Asian Indian | South Asian Bangladeshi | South Asian Pakistani | Chinese | Black British | Black African | Black Caribbean | Mediterranean European | Middle Eastern | Mixed Race | Other Asian |
|---------------------------|---------------|-------------|----------------|-------------------|------------------------|-----------------------|---------|---------------|---------------|---------------------|-----------------------------|---------------|------------|------------|
| **Sample size, n (%)**    | 28 408 (76.1) | 635 (1.7)   | 3201 (8.6)     | 1226 (3.3)        | 105 (0.3)              | 878 (2.4)             | 135 (0.4)| 168 (0.5)     | 879 (2.4)     | 1495 (0.4)        | 144 (0.4)                  | 171 (0.5)     | 366 (1.0) | 898 (2.4)  |
| **IVF cycles, n (%)**    | 15 450 (54.6) | 334 (52.8)  | 1644 (51.7)**  | 656 (53.8)        | 85 (62.9)              | 102 (60.7)            | 343 (59.5) | 343 (59.5)     | 75 (50.3)     | 80 (46.6)**        | 198 (54.4)                 | 500 (56.0)    |            |            |
| **Mean no. of eggs / C6**| 9.5 ± 6.5     | 8.6 ± 6.2** | 10.1 ± 6.8***  | 9.9 ± 6.9***      | 8.7 ± 7.1              | 9.9 ± 6.8             | 8.9 ± 7.3 | 8.9 ± 7.4**   | 10.4 ± 7.9    | 9.5 ± 6.3           | 8.9 ± 6.7                   | 8.9 ± 6.2     | 9.1 ± 6.3 |            |
| **Mean fertilisation rate / C6** | 0.59 ± 0.26   | 0.59 ± 0.26 | 0.59 ± 0.25    | 0.55 ± 0.25**     | 0.53 ± 0.27**        | 0.60 ± 0.28           | 0.47 ± 0.29** | 0.51 ± 0.27** | 0.52 ± 0.27** | 0.54 ± 0.25        | 0.52 ± 0.29**                | 0.57 ± 0.26   | 0.55 ± 0.26** |          |
| **Mean no. of embryos created / C6** | 5.5 ± 4.4     | 5.0 ± 4.1   | 5.9 ± 4.6***   | 5.5 ± 4.5         | 4.7 ± 4.5             | 5.1 ± 4.3*            | 4.1 ± 3.8 | 4.2 ± 4.1**   | 4.6 ± 4.6**   | 5.4 ± 4.9           | 5.3 ± 4.3                   | 4.4 ± 4.0**   | 4.9 ± 4.1** |          |
| **Mean no. of embryos stored / C6** | 1.39 ± 3.02   | 1.07 ± 2.66*| 1.36 ± 2.86   | 1.48 ± 3.00       | 1.25 ± 2.97           | 1.30 ± 3.04           | 0.75 ± 1.86** | 0.67 ± 2.19** | 0.91 ± 2.31** | 1.26 ± 3.04**      | 0.78 ± 1.54                 | 0.88 ± 2.43** | 1.17 ± 2.50** | 0.99 ± 2.27** |
| **No. of embryos transferred / C6** | 42.6 (15.0)   | 95 (15.0)   | 489 (14.0)     | 216 (17.6)**      | 24 (22.9)**           | 175 (19.7)            | 22 (16.3) | 7 (0.7)       | 6 (0.7)       | 6 (0.7)            | 6 (0.7)                     | 6 (0.7)       | 6 (0.7)    | 6 (0.7)    |
| **OHSS reported**        | 173 (0.6)     | 3 (0.5)     | 20 (0.6)       | 11 (0.9)          | 2 (0.9)               | 7 (0.8)               | 0 (0.0)  | 6 (0.9)       | 6 (0.7)       | 6 (0.7)            | 6 (0.7)                     | 6 (0.7)       | 6 (0.7)    | 6 (0.7)    |
| **Implantation rate / C6**| 63.2 (2.2)    | 17 (2.7)    | 67 (2.1)       | 30 (2.5)          | 4 (0.8)               | 24 (2.7)              | 2 (1.5)  | 3 (1.8)       | 15 (1.7)      | 4 (2.7)            | 3 (2.1)                     | 4 (2.3)       | 6 (1.6)    | 14 (1.6)   |
| **Clinical pregnancy / C6** | 22 (2.4)      | 507 (17.6)* | 2539 (25.0)    | 932 (25.2)        | 75 (20.8)             | 649 (23.6)            | 104 (24.9) | 109 (24.8)    | 615 (17.7)*   | 108 (24.1)         | 102 (10.6)                  | 121 (24.8)    | 291 (22.7) | 675 (23.0) |
| **Live birth / C6**      | 75 (0.6)      | 122 (17.2)* | 948 (26.5)     | 313 (25.5)        | 22 (21.0)             | 208 (23.7)            | 38 (28.1) | 37 (22.0)     | 153 (7.4)*    | 32 (21.5)          | 45 (3.1)                    | 40 (23.4)     | 90 (24.5)  | 22.1 (24.6)

Significantly lower (*P < 0.05, **P < 0.01)
Significantly higher (***P < 0.05, ****P < 0.001)
Table 3. Multivariate analysis for number of eggs collected (coefficient and 95% CI), clinical pregnancy rate and live birth rate (OR and 95% CI); adjusted for age, cause of infertility and treatment type (IVF or ICSI)

| Ethnicity          | No. of eggs collected | Clinical pregnancy rate | Live birth rate |
|--------------------|-----------------------|-------------------------|-----------------|
| White British      | 0.81 (0.68-0.97)*     | 1.09 (1.01-1.18)**     | 1.04 (0.96-1.13) |
| White Irish        | -0.25 (-0.75 to 0.29) | -0.18 (-1.73 to 1.41)**| 0.85 (0.75-0.97)* |
| White European     | 0.67 (0.54-0.80)      | -2.63 (-3.85 to 0.17)   | 0.85 (0.75-0.97)* |
| White Indian       | -0.02 (-0.38 to 0.34) | -0.81 (-1.17 to -0.45)  | 0.85 (0.75-0.97)* |
| White Pakistani    | -1.32 (-1.73 to -0.91) | -0.80 (-1.07 to -0.53)  | 0.85 (0.75-0.97)* |
| South Asian        | -0.39 (-1.04 to 0.27) | -1.47 (-1.85 to -1.09) | 0.85 (0.75-0.97)* |
| South Asian Pakistani | -0.40 (-0.71 to 0.09) | -1.11 (-1.39 to -0.83) | 0.85 (0.75-0.97)* |
| Chinese            | -0.40 (-0.71 to 0.09) | 0.38 (-0.67 to 0.18)   | 0.85 (0.75-0.97)* |
| Black British      | -0.40 (-0.71 to 0.09) | 0.38 (-0.67 to 0.18)   | 0.85 (0.75-0.97)* |
| Black African      | -0.40 (-0.71 to 0.09) | 0.38 (-0.67 to 0.18)   | 0.85 (0.75-0.97)* |
| Black Caribbean    | -0.40 (-0.71 to 0.09) | 0.38 (-0.67 to 0.18)   | 0.85 (0.75-0.97)* |
| Mediterranean      | -0.40 (-0.71 to 0.09) | 0.38 (-0.67 to 0.18)   | 0.85 (0.75-0.97)* |
| European           | -0.40 (-0.71 to 0.09) | 0.38 (-0.67 to 0.18)   | 0.85 (0.75-0.97)* |
| Asian Pakistani    | -0.40 (-0.71 to 0.09) | 0.38 (-0.67 to 0.18)   | 0.85 (0.75-0.97)* |
| Middle Eastern     | -0.40 (-0.71 to 0.09) | 0.38 (-0.67 to 0.18)   | 0.85 (0.75-0.97)* |
| Mixed Race         | -0.40 (-0.71 to 0.09) | 0.38 (-0.67 to 0.18)   | 0.85 (0.75-0.97)* |
| Other Asian        | -0.40 (-0.71 to 0.09) | 0.38 (-0.67 to 0.18)   | 0.85 (0.75-0.97)* |

*<p><sup>.05</sup>
**<p><sup>.01</sup>

Significantly lower (**<p><sup>.001</sup>)

Significantly higher (***<p><sup>.001</sup>)

Conclusion

Live birth rates following IVF treatment were significantly lower in some of the ethnic groups compared with white British women, which suggests that ethnicity is a major independent variable affecting IVF treatment success. Although the prevalence of various causes of infertility varies in different ethnic groups, the ethnicity of the woman is independently correlated with success rates of IVF treatment cycle after controlling for age and causes of infertility. This study is just a cross-sectional study and therefore ethnicity should be considered when counselling women and couples about their realistic chances of IVF success. This study is just a demonstration factor. Medications in clinical practice as a major determinant of IVF outcome should incorporate ethnicity as a major determinant factor. Medications in clinical practice as a major determinant factor. Medications in clinical practice as a major determinant factor.
first step and further research is needed to understand the mechanisms leading to this variation in treatment outcome between ethnic groups and move towards tailoring tangible protocols specifically suited to each ethnic group to maximise their IVF/ICSI success without compromising their safety.

Disclosure of interests
None declared. Completed disclosure of interests form available to view online as supporting information.

Contribution to authorship
W.M.(1) and K.J. conceived the project, interpreted the results, and wrote the article. W.M.(2) analysed the data, B.C. critically appraised and edited the article. All authors read and approved the final version of the article.

Details of ethics approval
Approval for this study of the relationship between ethnic background and clinical outcome after ART was obtained on 18 June 2012 from the Research Ethics Committee of the East Midlands, UK (ref. no. 12/EM/0202).

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Supporting Information
Additional Supporting Information may be found in the online version of this article:
Figure S1. Flowchart demonstrating data filtering for inclusion and exclusion from the study.
Figure S2. Causes of infertility among various ethnic groups; reference group (White British) in green, significantly higher or lower odds in purple or orange respectively, and no statistical difference to the reference group in black.

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