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# Embryo utilisation rate and transferable embryo to oocyte ratio correlate positively with livebirth rate but negatively with oocyte number: analysis of 14,156 fresh IVF/ICSI cycles

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# **Abstract**

**Background** The live birth rates (LBRs) do not rise after a certain number of oocytes are collected in fresh IVF cycles. Although the detrimental effect of high ovarian response on the endometrium has been recognised, the effect of high oocyte yield on oocyte competency remains disputed. The purpose of this study was to examine whether high oocyte yield adversely affect the competency of oocytes or embryos. We retrospectively analysed UK's National database (published by Human Fertilisation and Embryology Authority (HFEA)- year 2015–2016) including couples who underwent first IVF treatment with single embryo transfer or had no available embryo, due to tubal or unexplained infertility among women aged < 40 years.

**Results** Retrospective analysis of 14,156 fresh IVF/ ICSI cycles that met the inclusion criteria revealed an inverse correlation between Embryo Utilisation Rate (EUR) and the oocyte yield (r= -0.250047, p < 0.0001). The Transferable Embryo to Oocyte Ratio (TEOR) also inversely correlated with the number of retrieved oocyte (r= -0.331431, p < 0.0001). The number of oocytes that did not produce transferable embryos had a stronger positive correlation with oocyte yield (r= 0.916676, p < 0.0001) than those produced transferable embryos (r= 0.569972, p < 0.0001). Both EUR (p= 0.01) and TEOR (p < 0.0001) correlated positively with the live birth except in the women age-group of 38–39 years. Although fertilisation rates remained similar, both EUR and TEOR declined steadily with the increasing number of oocytes until it reached a nadir at around 8–9 oocytes. At this point the LBR in fresh cycles reached its peak.

**Conclusion** The EUR and TEOR decline with increasing oocyte yield while both the ratios have a positive correlation with live birth. Despite declining EUR and TEOR, increasing oocyte yield can still boost fresh cycle LBR until the proportions of transferable embryos fall to a nadir. Thus, the focus needs to be on finding more efficient method for embryo selection and avoid generating too many wasteful oocytes that only pose more risk or raise cost without improving fresh cycle LBR.

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**Trial number** Being a retrospective study, prior registration of the trial was not required.

Clinical trial number Not applicable.

Keywords Embryo utilisation rate, Transferable embryo to oocyte ratio, Oocyte yield, Live birth rate, IVF

# **Background**

In conventional practice, the aim of multi-follicular development in an in-vitro fertilisation/intracytoplasmic sperm injection (IVF/ ICSI) cycle is to obtain as many oocytes as possible, particularly since the publication of several retrospective studies that demonstrate ever-rising cumulative live birth rate (LBR) with increasing oocyte yield [1-3]. However, studies over the last decade have indicated that the optimum oocyte yield to maximise LBR is around 15 (between 12 and 18 oocytes) [2]; LBRs in fresh embryo transfer (ET) cycles do not increase once the optimal number is reached [2, 4-9], or may even decline at a higher yield [10]. As a result, the number of oocytes can no longer predict the fresh cycle LBR once 15–20 oocytes are collected [6, 7]. In another study, the oocyte yield has been found to be only a weak predictor of livebirth, regardless of how many oocytes were retrieved [11].

Endometrial factors have been implicated to explain why fresh cycle pregnancy outcome is limited by high oocyte number. A concomitant rise in serum estradiol level [12] and or high serum progesterone level at the time of the ovulation trigger [13] in the event of high oocyte yield has been associated with impaired endometrial receptivity. A high stimulation dose has been shown to independently affect the endometrium adversely in fresh IVF cycles [14]. We hypothesised that deranged endometrial receptivity may not be the only reason to explain why fresh cycle LBR stops rising after the optimum of 15–18 oocytes. Oocyte and embryo competency in relation to ovarian response may also be associated with final pregnancy outcome. If this is the fact, eliminating the endometrial factor by freezing all embryos and subsequent frozen-thawed embryo transfer may not boost cumulative LBR to a large extent. Indeed, a stunted increment of cumulative LBR at a very high oocyte yield was observed in the studies that reported constantly increasing cumulative LBR [1, 3]. This is supported by laboratory-based studies that reported high oocyte yield to be associated with increased chromosomal error in the oocytes [15]; increasing intra-cytoplasmic dysmorphism [16] increasing number of an euploid (along with euploid) embryos [17] and an apparent decline in the ratio of euploid embryos to oocytes retrieved [18].

Two commonly used terms to measure intrinsic competency of individual oocytes are: 'baby to oocyte rate' which represents LBR in fresh plus subsequent frozen-thawed ET per oocyte retrieved [19], and 'oocyte

utilisation rate' (OUR) that stands for cumulative LBRs per mature oocyte retrieved [20]. Although cumulative LBRs do not stop rising with the increasing oocyte yield [1, 3], a series of studies have demonstrated decreasing cumulative LBRs per oocyte (baby to oocyte rate) as the number of retrieved oocytes increases [8, 19, 21, 22]. This can be explained by the study by Figueira R de C, et al. that showed the number of fetal heartbeats detected on the ultrasound scan per retrieved oocyte to be inversely related to the number of mature oocytes [16]. The OUR also has been shown to decline with increasing oocyte yield in women aged < 38 years [20]. There is some suggestion from the published data that the proportion of oocytes that produce transferable embryos declines with higher oocyte yield in autologous IVF/ ICSI cycles [16], as well as among the recipients of donor oocytes [23]. In absence of a highly efficient method of embryo selection, most competent embryos or euploid embryos may get diluted with larger cohort of incompetent or aneuploid embryos. This phenomenon, along with the fact that even transfer of a euploid embryo does not always result in live birth due to other factors e.g., suboptimal endometrial receptivity, cumulative LBR per oocyte declines with higher oocyte yield. Despite all the above evidence, more data from large population was required to substantiate the contribution of oocyte competency as a factor for declining fresh-cycle LBR.

We conducted a retrospective analysis of a large anonymised national database to investigate whether the competency of oocytes and embryos are possible factors behind static fresh-transfer LBRs with larger number of oocytes. To answer this question, we examined two important associations:

- 1. The correlation between Embryo Utilisation Rate (EUR) or Transferable Embryos to oocytes ratio (TEOR) and the oocyte yield. By taking the ratio of transferable embryos as an intermediate surrogate of LBR, any possible effect of endometrial factor on the assessment of oocyte competency was eliminated. The association of EUR and TEOR with the LBR has also been investigated as a justification for taking these two ratios as the surrogate of LBR.
- The relationship of EUR as well as TEOR with the aggregated fresh LBRs linked to the number of oocytes retrieved.

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#### Methods

### Design

This was a retrospective analysis of all stimulated IVF/ICSI cycles that met the inclusion criteria from the United Kingdom's national registry on assisted reproduction published online by Human Fertilisation and Embryology Authority (HFEA) over 2 years' time, between 1st January 2015 and 31st December 2016 [24]. More recent database published by HFEA does not give the exact number of oocytes and embryos, therefore previous years' database was used. Being a retrospective analysis of anonymised data published in a public domain; this study did not require Ethical Committee approval.

#### Inclusion and exclusion criteria

Only 1st IVF/ ICSI cycles that had oocyte retrieval followed by either a single embryo transfer (SET) or no available embryo for transfer, in couples with tubal and unexplained infertility within woman's age of 18 to 39 years were included. Thus, the relationship between the oocyte yield and embryo development or live birth was predominantly influenced by inherent oocyte competency, avoiding the possible effect of severe male factor, endometriosis, polycystic ovarian syndrome (PCOS) or advanced age of women on the laboratory or clinical outcomes. IVF treatment with donor sperm was included. Cycles where pre-implantation genetic testing (PGT) were excluded from the analysis. Cycles that were cancelled before oocyte retrieval were not included. It was not clear in the HFEA database whether no transferable embryo was obtained due to a policy of mandatory blastocyst culture, even with very few embryos, therefore only the cycles where at least one transferable embryo was obtained were taken for any analysis related to EUR.

# **Outcome measures**

Our primary outcome measure was the correlation between the EUR or TEOR and the oocyte yield. Secondary outcome measures determined the relationship of oocyte yield with the number of immature oocytes, the number of oocytes that produced or failed to produce transferable embryos and fertilisation rates (2 pronuclei, or 2PN). The trend of LBRs, EUR as well as the TEOR with each number of oocytes retrieved in a SET scenario were observed by plotting in a graph.

# **Definitions** used

'LBR' is defined as birth of a viable neonate according to HFEA (UK). 'EUR' is defined by the ratio of transferable embryos to total 2PN zygotes. 'TEOR' is defined as the proportion of transferable embryos out of all oocytes, while, OUR is LBR (fresh and frozen transfer cycle) out of all *mature* oocyte retrieved [20]. The number of transferable embryos is calculated by adding up the number

of fresh embryos transferred plus the number cryopreserved. Fertilisation rate is the number of 2 PN zygotes out of total oocytes. The determination as to which embryos were suitable for transfer was made according to each clinic's ET policy.

# Statistical analysis

The age of the women were divided into 3 groups as per HFEA: <35 years, 35-37 years and 38-39 years. Linear regression analysis was performed to find the association between two continuous variables and correlation coefficient for each was obtained. Multiple logistic regression model was employed to relate between a continuous (e.g., age, number of oocytes, oocytes that produced transferable embryos) and categorical dependent variable (e.g., live birth). The odds-ratio (OR) with 95% confidence intervals (CI) were presented after adjusting for other significant variables. A p value of < 0.05 has been considered statistically significant. The fertilisation rate, TEOR, EUR, fresh cycle LBR per oocyte as well as the total LBRs were plotted against each number of oocytes retrieved. Oocyte yield is represented as total number of oocytes retrieved, whilst analyses with the 'mature' oocytes (from ICSI cycles) have also been presented separately. Microsoft excel was used for graphic representation of the trend of EUR, TEOR, fertilisation rate and LBR in relation to the number of oocyte retrieved, the rest of the analysis including regression analysis was carried out in StatsDirect software (version 3.3.5, dated 22/03/2021) (https://www.statsdirect.com/).

# Results

In the study period, 14,156 IVF/ ICSI consecutive cycles fulfilled the inclusion criteria. No oocyte was collected in 1,063 cycles which were excluded in the analyses related to TEOR. ICSI was performed in 3,637 (27.8%) cycles. In 2,087 cycles, retrieved oocytes did not produce a transferable embryo and therefore excluded for analysis related to EUR. The cycles were grouped by woman's age < 35 years (n = 8154 cycles), 35–37 (n = 3,970) and 38–39 years (n = 2,032). Cycles with no suitable embryo for transfer were included in the multiple regression analysis. In the majority of the cycles (8,362/ 11,006, 76.0%) the embryos were transferred at blastocyst stage.

Linear regression analysis showed a moderate positive correlation between the number of immature oocytes and the oocyte yield in the ICSI cycles (correlation coefficient 0.547796, p < 0.0001) (data not shown in figure). There was a moderate positive correlation between the oocytes that generated a transferable embryo and oocyte yield (total oocytes: r = 0.569972, p < 0.0001, mature oocytes: r = 0.596334 (p < 0.0001) (Fig. 1).

However, the correlation was stronger between oocytes that failed to produce a transferable embryo and total Datta et al. Journal of Ovarian Research (2025) 18:112 Page 4 of 8

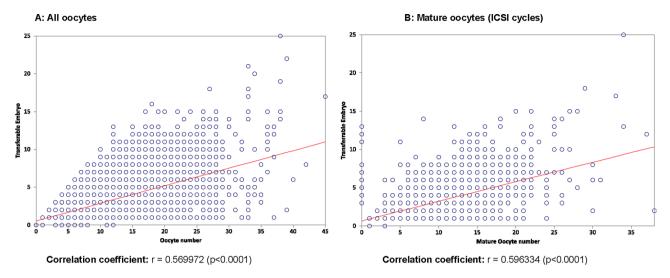


Fig. 1 Correlation between oocytes that resulted in a transferable embryo and oocyte yield (total and mature oocytes)

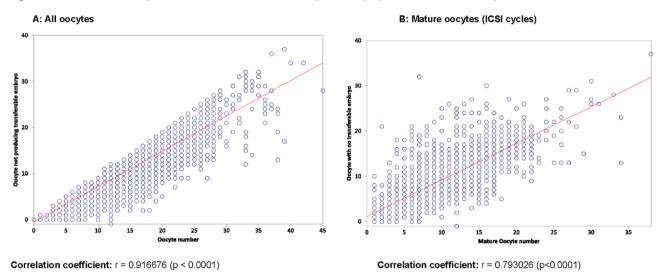


Fig. 2 Correlation between oocytes that did not result in a transferable embryo and oocyte yield (total and mature oocytes)

oocyte yield (total oocytes: r = 0.916676, p < 0.0001, mature oocytes: r = 0.793026 (p < 0.0001) (Fig. 2).

The TEOR had an inverse correlation with the oocyte yield (total oocytes: r = -0.3000, p < 0.0001; mature oocytes: r = -0.331431, p < 0.0001) (Fig. 3A and B) The EUR also correlated negatively with the oocyte yield (coefficient (r) = -0.250047, p < 0.0001) (Fig. 3C).

Among possible confounders, woman's age-groups (OR 0.9740, CI 0.973 to 0.975; p < 0.0001), the method of insemination (IVF or ICSI) (OR 0.450, CI 0.431 to 0.471; p < 0.0001) and the stage of transferred embryo (cleavage stage or blastocyst) (p < 0.0001) were found to have statistically significant correlation with live birth. Overall, TEOR was found to be positively correlated with live birth (p < 0.0001), after adjusting for woman's age, method of insemination, day and stage of ET (Table 1). EUR has also been found to have a positive correlation

with LBR (p = 0.01) after adjusting for the same variables in a multiple regression analysis (Table 1). However, when regression analysis was performed in different agegroups, both EUR and TEOR related directly with LBR in the age-groups of <35 years and 35–37 years, but not in women aged between 38 and 39 years (Table 1).

The proportion of 2 PN zygotes to all oocytes (i.e., fertilisation rate) remained unchanged with increasing oocyte yield (Fig. 4); while both EUR and TEOR declined steadily with the increasing number of oocytes until it reached a nadir (EUR at 44.9%, TEOR at 33.0%) at the oocyte number of 8–9 then plateaued (Fig. 4). This trend was observed regardless of whether the embryo was transferred at cleavage stage (day 2 or 3) or in blastocyst stage (day 5 or 6) or whether the denominator was total oocytes or mature oocytes (Fig. 4). The LBR, on the other hand, increased steadily with number of oocytes

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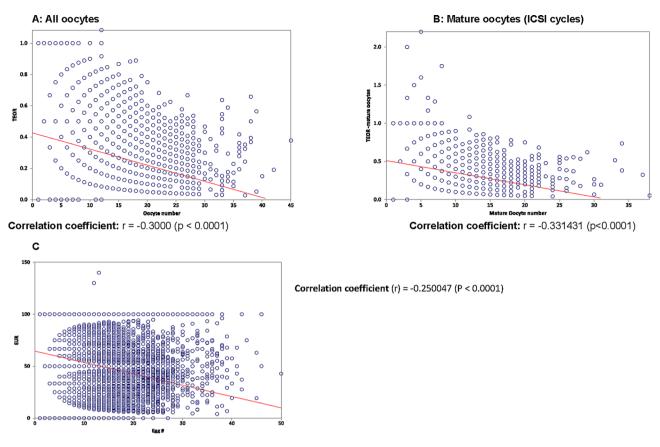


Fig. 3 Correlation between transferable embryo to cocyte ratio (TEOR) and the ooeyte yield

**Table 1** Embryo utilisation rate and transferable embryo to oocyte ratio as predictors of live birth stratified by Woman's agegroups

Age-groups of women (years)	EUR *OR <sup>1</sup> (95% CI)	TEOR ** OR <sup>2</sup> (95% CI)
Any age-group	<b>1.002</b> (1.001 to 1.004) $p = 0.01$	<b>1.006</b> (1.004 to 1.006) <i>p</i> < 0.0001
18-34	<b>1.002</b> (0.999–1.004) <i>p</i> = 0.05	<b>1.006</b> (1.003 to 1.009) <i>p</i> < 0.0001
35-37#	<b>1.003</b> (1.000- 1.006) $p = 0.04$	<b>1.007</b> (1.003 to 1.011) $p = 0.0003$
38-39#	<b>1.001</b> (0.996–1.006) <i>p</i> = 0.73	<b>1.006</b> (0.999 to 1.012) $p = 0.05$

<sup>\*</sup> EUR=embryo utilisation rate, \*\* TEOR=Transferable embryo to oocyte ratio, <sup>1</sup> adjusted for number of embryos (0 or 1) and stage of the transferred embryo (cleavage stage or blastocyst), <sup>2</sup> adjusted for method of insemination (IVF or ICSI), number of embryos (0 or 1) and stage of the transferred embryos (cleavage stage or blastocyst)

until 9 oocytes were retrieved before it plateaued. Thus, the around same oocyte number that was associated with plateauing of LBRs, was also associated with both the proportion of transferable embryos indices (TEOR as well as EUR) reaching the nadir (Fig. 4). The fresh cycle LBRs per oocyte also declined with the number of oocytes (Fig. 4).

### **Discussion**

Our retrospective analysis of a large national database shows a very strong positive correlation (r = 0.916676, p < 0.0001) between the number of oocytes that do not generate a transferable embryo and the oocyte yield (Fig. 2A, B). Consequently, TEOR or EUR have been found to have an inverse correlation with the number of oocytes (Fig. 3A, B). There is a weakly positive association between total oocyte yield and the number of oocytes that generated transferable embryos (Fig. 1); but the correlation is much stronger with the number of oocytes that fail to produce a transferable embryo even when immature oocytes are excluded (Fig. 2). This means, the more oocytes that are retrieved, the more incompetent oocytes are likely to be generated. As a result, the proportions of apparently 'competent embryos' out of total oocytes decline while the fertilisation rate (proportion of total embryos out of total oocytes) remains at a similar level (around 65% in our study) with increasing oocyte yield (Fig. 4). It indicates that the quality indicator (EUR or TEOR) is affected with the high oocyte yield, but not the quantity (fertilisation rate) when male factor and other oocyte related factors are excluded. Of note, the EUR which is not affected by the number of immature

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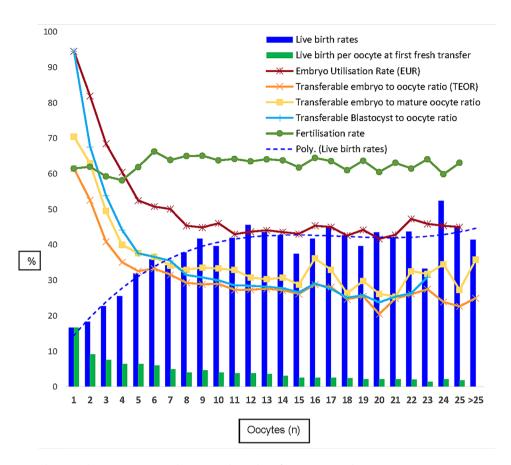


Fig. 4 EUR, TEOR, FR, crude LBR and LBR per oocyte in relation to each number of oocyte retrieved

oocytes generated or fertilisation potential of oocytes, also shows the similar trend as of TEOR.

The proportions of transferable embryos- both TEOR and EUR appeared to have a positive correlation with live birth confirming that both TEOR and EUR can be considered as a surrogate of pregnancy outcome while determining the competency of oocytes in relation to oocyte yield.

We have shown that the EUR and TEOR tend to be higher with fewer oocytes which is in agreement with a previous smaller study by Figueira R deC, et al. [16]. It also partly explains why previous studies found cumulative LBR per oocyte ('baby to oocyte ratio') [8, 21, 25] and OUR (cumulative LBR per *mature* oocyte) decline with increasing number of oocytes [20]. A declining proportion of usable embryos with high oocyte yield among the oocyte donors has been reported to result in a static cumulative LBR per 100 oocytes thawed for the recipients [23]. This study supports our study indicating that comprised pregnancy rates with high oocyte yield could be due to the oocyte or embryo potential independent of endometrial factor.

We found that both EUR and TEOR declined steadily with an increasing oocyte yield until 8 oocytes were retrieved and remained at this nadir thereafter (Fig. 4).

Simultaneously, the LBRs, rose steadily as the number of oocytes increased to a similar number of around 9 retrieved oocytes, after which it plateaued (Fig. 4). This could be a coincidence but may also indicate that efficiency per oocyte drops while the rise in the absolute number of transferable embryos (surrogate of potentially euploid embryos) still boosts the LBR until a saturation point is reached. After that, transfer of a single embryo may not be enough to keep the pregnancy rate rising due to the possibility of inadvertently selecting a potentially aneuploid embryo from a larger cohort of embryos. The saturation point for cumulative live birth, if any, is yet to be determined; there is some indication that increment in the cumulative slows down with very high oocyte yield [1, 3, 5]. Stoop et al. reported a falling cumulative LBR per mature oocyte (OUR) with increasing oocyte yield in younger women until the age of 38 years, then the OUR dropped rapidly with advancing age regardless of the number of mature oocytes obtained [20]. This can explain our findings of the direct correlation between TEOR/ EUR and live birth in the woman's age groups of <35 and 35–37 years, but not in 38–39 years age-group.

The evidence in support of our findings can be found in the studies that examined the ploidy status of embryos. The study by Labarta, et al., 2017 reported that the Datta et al. Journal of Ovarian Research (2025) 18:112 Page 7 of 8

absolute number of aneuploid embryos also rises with increasing oocyte number [17]. An RCT by Arce et al. showed a static (high-grade) blastocyst to oocyte ratio despite rising oocyte yield with increasing ovarian stimulation [26]. Another recent study observed a trend of decreasing euploid embryo to oocyte ratio with increasing oocyte number [18].

The findings of our study have raised question on generating too many oocytes while the proportion of transferable embryos remains small. It is well recognised that collecting oocytes over and above the optimum number is futile in fresh cycles. Although the cut-off number for optimising cumulative LBR has not been settled yet, a tailing-off cumulative LBR at a very high oocyte yield indicates that the same may be applicable in this scenario too. It is recognised that "Freeze all embryos" reduces the risk of ovarian hyperstimulation syndrome and eliminate detrimental effect of endometrial receptivity in presence of high response. However, our data confirm that high EUR and TEOR in younger women positively predict fresh cycle LBR, but not the oocyte yield. Future studies may explore whether this holds true for cumulative LBR at a higher optimum oocyte number. Future studies may also add evidence on the impact of other variables e.g., BMI or treatment protocols on this issue.

To our knowledge, this is the first large-scale study to investigate the relationship between the competency of the oocytes, reflected in the ratio of transferable embryos and the oocyte yield from a national database. To specifically evaluate the oocyte competency, we aimed to eliminate confounding factors such as, severe male factor, endometriosis, PCOS and women aged 40 years and above which might have had an impact on the oocyte/embryo quality and LBR [27]. Also, by including only the 1st IVF/ ICSI cycles with SET, we avoided the prognostic factors related to multiple failed cycles from any individual patient. The inclusion criteria may appear somewhat selective; however, the homogeneity of the population has increased the reliability of our primary outcome which was, oocyte competency.

The main limitation of this study is the absence of information on ovarian reserve and treatment protocols including stimulation dosages in an anonymised HFEA database available online. We believe, like other authors who have used the same national registry [7], that the study population is large enough for these variables not to have significant impact on the analysis. Thus, the findings of our study have been derived from a "real-world" scenario with all its variations in the protocols. The age of the woman was given in age-groups; hence we did multivariate (logistic) regression analysis separately under each age-group and separate regression analysis in each age-group.

Since individual patient data on subsequent frozenthawed cycles were not available, the outcome of subsequent frozen-thawed transfer cycles or cumulative outcomes and LBR per oocyte as a marker of oocyte competency could not be ascertained. However, LBR per oocyte in fresh SET in our study also declines in parallel with the TEOR (Fig. 4). The evidence of concomitant drop in cumulative (from fresh + frozen transfer) LBR per oocytes with higher oocyte yield in other studies [8, 19– 22] suggests that high proportion of transferable embryos with fewer retrieved oocytes may not be just due to small denominator. This decline in the LBR per oocytes as well as the observation that the increment in the cumulative LBR also slows down with very high oocyte yield [1, 3] indicate that our findings could be applicable for cumulative LBR as well. Besides, the findings of our study have answered our study question of whether the oocyte competency contributes to plateauing of fresh cycle LBR with higher oocyte yield.

There was a possibility of relaxing the selection for transferring when the oocyte yield is low. This may explain why the rate of decline in the EUR or TEOR was steeper with fewer oocytes, but the decline gradually lessened with increasing oocyte yield. However, a steady decline in the EUR and TEOR (without any fluctuation), regardless of whether blastocyst transfer or cleavagestage embryo transfer (Fig. 4) indicated that this decline was not merely due to embryologist's inclination for transferring otherwise non-transferable embryos when the yield is very low. The information on both embryograding system and ET policy of each IVF clinic were not available in the HFEA database. However, given the IVF laboratories in the UK tend to follow the embryo-grading system introduced by Academy of Clinical Embryologists (ACE) and the number of embryo transfer as guided by HFEA, certain level of uniformity in practice throughout the UK was maintained.

# Conclusion

Our study has demonstrated that the higher oocyte yield, the higher is the proportion of oocytes that do not generate transferable embryos. The diminishing proportion of transferable embryos could be one of the explanations for static LBR in fresh cycle after an optimum number of oocytes is retrieved. The attention should be to improve the oocyte competency and embryo selection methods in fresh transfer cycles rather than generating excess oocytes which only adds costs and health risks to women. Future research is needed to confirm if the findings of our study apply in relation to cumulative live birth rates.

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We acknowledge and thank the HFEA for publishing anonymised data online to enable us to access them for research purpose.

#### **Author contributions**

AKD: Conceptualised the idea, collected data, analysed, and wrote the first draft. GN: Approved and assisted in finalising the idea, prepared the final draft and signed off the final version. SC: Reviewed the idea, edited the terminologies, revised the title, abstract and prepared the final draft. MW: Checked the laboratory aspect of the study and edited the draft. SD: Expanded the idea adding age-wise stratification of live birth rate, edited the draft and approved.

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No funding required.

#### Data availability

https://www.hfea.gov.uk/about-us/data-research

#### **Declarations**

# Ethics approval and consent to participate

The study was a retrospective analysis of data collected from the anonymous registry of the Human Fertilisation and Embryology Authority, UK. The registry is available online for public. Therefore, Ethical Committee approval was not necessary.

#### Consent for publication

Not applicable.

#### **Competing interests**

The authors declare no competing interests.

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