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### Research Funding for Male Reproductive Health and Infertility in the UK and USA [2016 – 2019]

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### **Research Funding for Male Reproductive Health and Infertility in the UK and USA [2016 – 2019]**

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26 **Abstract:**

27

28 **Title:** Research Funding for Male Reproductive Health and Infertility in the UK and USA [2016 – 2019]

29 **Study question:** What is the research funding for male reproductive health and infertility in the UK  
30 and US between 2016 to 2019?

31 **Summary answer:** The average funding for a research project in male reproductive health and  
32 infertility was not significantly different to that for female-based projects (£653,733 in the UK and  
33 \$779,707 in the US). However, only 0.07% and 0.83% of government funds from NIHR (UK) and NICHD  
34 (USA) was granted for male reproductive health, respectively.

35 **What is known already:** There is a marked paucity of data on research funding for male reproductive  
36 health.

37 **Study design, size, duration:** Examined government databases over a total 4-year period from January  
38 2016 to December 2019.

39 **Participants/materials, setting, methods:** Information on the funding provided to male-based and  
40 female-based research was collected using public accessed web-databases from the UKRI-GTR, the  
41 NIHR's Open Data Summary, and the US' NIH RePORT. Funded projects that began research activity  
42 between January 2016 to December 2019 were recorded, along with their grant and project details.  
43 Strict inclusion-exclusion criteria were followed for both UK and US data with a primary research focus  
44 of male infertility, reproductive health and disorders, and contraception development. Funding  
45 support was divided into three research groups: male-based, female-based, and not-specified  
46 research. Between the 4-year period, the UK is divided into 5 funding periods, starting from 2015/16  
47 to 2019/20, and the US is divided into 5 fiscal years, from 2016 to 2020.

48 **Main results and the role of chance:** Between January 2016 to December 2019, UK agencies awarded  
49 a total of £11,767,190 to 18 projects for male-based research and £29,850,945 to 40 projects for

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50 female-based research. There was no statistically significant difference in funding average between

51 the two research groups ( $P=0.56$ ,  $W=392$ ). The US NIH funded 76 projects totaling \$59,257,746 for

52 male-based research and 99 projects totaling \$83,272,898 for female-based research. There was no

53 statistically significant difference in funding average between the two groups ( $P=0.83$ ,  $W=3834$ ).

54 **Limitations, reasons for caution:** The findings of this study cannot be used to generalize and reflect

55 global funding trends towards infertility and reproductive health as the data collected followed a

56 narrow funding timeframe from government agencies and only two countries. Other funding sources

57 such as charities, industry and major philanthropic organizations were not evaluated.

58 **Wider implications of the findings:** This is the first study examining funding granted by main

59 government research agencies from the UK and US for male reproductive health. This study should

60 stimulate further discussion of the challenges of tackling male infertility and reproductive health

61 disorders and formulate appropriate investment strategies.

62 **Study funding/competing interest(s):** CLRB is Editor for RBMO and has received lecturing fees from

63 Merck, Pharmasure, and Ferring. His laboratory is funded by Bill and Melinda Gates Foundation, CSO,

64 Genus. No other authors declare a conflict of interest.

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66

### Introduction.

67 Several recent studies have highlighted considerable research gaps in the understanding of male  
68 infertility encompassing critical areas such as basic science research, clinical diagnostics, non-  
69 Medically Assisted Reproduction (MAR) treatment options, and the impact of damage to the male  
70 genome on the health of the next generation (Barratt *et al.*, 2017, Barratt *et al.*, 2018, De Jonge and  
71 Barratt 2019, Barratt *et al.*, 2021, Schlegel *et al.*, 2021a,b). One general conclusion that can be drawn  
72 from these analyses is that significant funding is required to address the research questions (Barratt  
73 *et al.*, 2017, Barratt *et al.*, 2018). For any discipline, including reproductive medicine, an important  
74 aspect of assessing and formulating future funding requirements is to ascertain current funding. This  
75 knowledge can then be used to facilitate an objective needs analysis.

76 Surprisingly, there is a paucity of data on funding levels for male infertility and male reproductive  
77 health research (Barratt *et al.*, 2018, Barratt *et al.*, 2021). To date, only one study has specifically  
78 documented funding for male reproductive health research. Liao and colleagues (Liao *et al.*, 2020)  
79 assessed funding by the National Natural Science Foundation of China (NNSFC) for male infertility and  
80 reproductive health research between 1998-2018. The authors split this 20-year period into 3 funding  
81 phases beginning from 1998. By the third phase (2010-2018), a substantial increase of funding was  
82 awarded for male reproductive health (MRH) basic research by the NNSFC. However, there was  
83 minimal detail on the exact funding values. Barratt and colleagues provided a snapshot of funding for  
84 Male Reproductive Health in several countries that suggested overall funding levels were low, but no  
85 other details were provided (Barratt *et al.*, 2021).

86 In this study, we investigated government funded support of male reproductive health research. We  
87 examined research funded between January 2016 to December 2019 from the UK and US agencies.  
88 To provide context, we included funding for female-based reproductive health research and examined  
89 the proportion of research funding for reproductive health research and compared to the total  
90 research funding.

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91

## Materials and Methods.

### 92 Experimental Design:

93 Publicly accessible UK Research and Innovation (UKRI), National Institute for Health Research (NIHR),  
94 and National Institutes of Health (NIH) funding agency databases covering awards from January 2016  
95 to December 2019 were examined (see Supplementary Table I). Following the inclusion and exclusion  
96 criteria outlined within Supplementary Tables II and III, funding data were collected on research  
97 proposals investigating infertility and reproductive health. For simplicity, these are referred to  
98 collectively as ‘infertility research’. As the primary focus of this research is on infertility, the data were  
99 divided into three main groups: male-based, female-based, and not-specified (Supplementary Table  
100 II). The first two groups covered projects whose primary aim, based on the information presented in  
101 the research abstracts, timeline summaries and/or impact statements, was male- or female-focused.  
102 “Not-specified” includes research projects that have either not specified a primary focus towards  
103 either male or female or have explicitly stated a focus on both. The process was conducted and  
104 reviewed by E.G. with C.L.R.B. Total funding for all three groups, funding over time, and comparison  
105 with overall funding for a particular agency was examined.

### 106 UK Data Collection:

107 Starting in April 2018, the UK research councils, Innovate UK, and Research England were combined  
108 reporting under one organization, the UKRI (UKRI, 2019). The councils, such as the Medical Research  
109 Council (MRC), Biotechnology and Biological Sciences Research Council (BBSRC), Engineering and  
110 Physical Sciences Research Council (EPSRC), and Natural Environment Research Council (NERC),  
111 independently fund research projects according to their respective visions and missions; however,  
112 from 2018/19, their annual funding expenditures were reported under the UKRI’s annual reports and  
113 budgets. The UKRI’s Gateway to Research (UKRI-GTR) web-database allows users to analyse  
114 information provided on taxpayer-funded research. Relevant search terms such as “male infertility”  
115 or “female reproductive health” (see Supplementary Table II) were applied with appropriate database

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116 filters (Supplementary Table I). The project award relevance was determined by assessing the  
117 objectives in project abstracts, timeline summaries, and planned impacts. Supplementary Tables I, II  
118 and III provide the search filters and the reference criteria for inclusion/exclusion utilized for analysis.  
119 The UKRI-GTR provides the total funding amount granted to the projects within a designated period.  
120 The Open Data Summary View dataset from the NIHR was used as it provided details on funded  
121 projects, grants, summary abstracts, and project dates. Like the UKRI data, the NIHR excel datasheet  
122 had specific search terms and filters applied to exclude irrelevant projects (Supplementary Tables I, II,  
123 and III).  
124 The UKRI councils and NIHR report their annual expenditure and budgets for 1st April to 31st March.  
125 Thus, the selected projects will fall under the funding period of when their research activities begin,  
126 e.g. if a research project is started between May 20th, 2017, to March 20th, 2019, the project will be  
127 categorized under the funding period 2017/18. The projects assessed would begin their investigations  
128 between January 2016 to December 2019, therefore 5 consecutive funding periods were examined  
129 (2015/16, 2016/17, 2017/18, 2018/19, and 2019/20).

### 130 US Data Collection:

131 The NIH has a research portfolio online operating tools site (RePORT) providing access to their  
132 research activities, such as previously funded research, actively funded research projects, and  
133 information on NIH's annual expenditures. The RePORT-Query database has similar features as the  
134 UKRI-GTR and NIHR such as providing information on project abstracts, research impact, start- and  
135 end-dates, funding grants, and type of research. The same inclusion-exclusion criteria were applied as  
136 for the UK data collection, (see Supplementary Tables I, II, and III).

137 In contrast to the UK funding agencies, the NIH's fiscal year (FY) funding follows a calendar period  
138 from October 1st to September 30<sup>th</sup>, *i.e.*, FY2016 comprises funding activity from October 1st, 2015,  
139 to September 30th, 2016. Projects running over one calendar period are reported several times under

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140 consecutive fiscal years and the funds are divided according to the annual period of the project's  
141 activity.

142 During data collection, 74 projects were found as active with incomplete funding sums as the NIH  
143 divides the grants according to the budgeting period of every FY. The NIH are in the process of granting  
144 funds for the FY2021, so projects ending in FY2020 or FY2021 have provided a complete funding sum.  
145 For the active projects ending after 2021, incomplete funding data is shown. It is assumed the funding  
146 will increase in value by the time the research project ends in the future. To remain consistent with  
147 the UK data, projects granted funding are totalled as one figure and recorded under the FY the project  
148 first began research, whether they are active or completed. Thus, the US funding is referred to as  
149 “Current Total Funding”. For the US, the initial data collection period ran between October 2020 to  
150 December 2020 but then restarted for a brief period in January 2021 to complete the remaining  
151 funding values for several of the active research projects.

#### 152 Data Analysis:

153 The data were divided into the three groups and organized into the funding period or FY during which  
154 the project was first awarded. R-Studio (Version 1.3.1093) was utilized for the data analysis. Box-and-  
155 whisker plots are presented with rounded *P*-values. Kruskal-Wallis and Wilcoxon Rank Sum tests were  
156 generated to assess any statistical significance. The data were independently collected and do not  
157 assume a normal distribution, so rank-based, non-parametric tests such as the Kruskal-Wallis and  
158 Wilcoxon Rank-Sum were used. The Kruskal-Wallis test was used between more than 2 groups, with  
159 the *P*-values and Chi-Squared ( $\chi^2$ ) values provided. The Wilcoxon test was used between two groups  
160 with the *P*-value and the Wilcoxon test statistic, *W*, included. *P*-values <0.05 were considered  
161 statistically significant.

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164

Results.165 Total and Median Funding:166 *UK Data:*

167 Total funding for infertility from the UK funding agencies and the summary statistics of the UK data  
168 are presented in Tables I and II. Table III details the proportion of funding by the MRC and NIHR from  
169 2015/16 to 2018/19. Between 2016 to 2019, 76 studies were awarded funding by 4 UKRI councils and  
170 the NIHR investigating infertility and reproductive health. The MRC, BBSRC, and NIHR were the top 3  
171 awarding agencies, having funded 29, 23, and 15 projects, respectively. The UK agencies have awarded  
172 18 projects for male-based, 40 for female-based, and 18 projects for the non-specified group (Table  
173 I). For NIHR funding, there were only 2 awards for the male group compared to 11 for female group.  
174 Figure 1 presents a distribution of funding for the three groups. There was more spread for the female  
175 group, however there was no statistically significant difference between the mean values of the 3  
176 groups ( $P=0.69$ , Kruskal-Wallis,  $\chi^2 = 0.72$ ). There was no significant difference between male-based  
177 versus female-based funding ( $P=0.56$ ,  $W=392$ ).

178 *USA Data:*

179 The US total funding for infertility and summary statistics are presented in Tables IV and V. The funding  
180 amounts presented in Table IV includes research grants, program grants, and fellowships and contains  
181 the respective annual spending of each NIH institute. The NIH have awarded 76 projects for male-  
182 based, 99 for female-based, and 31 projects for the non-specified group. The National Institute of  
183 Child Health and Human Development (NICHD), Environmental Health Sciences (NIEHS), and General  
184 Medical Sciences (NIGMS) have awarded the most for infertility research out of 14 institutes, funding  
185 138, 27, and 26 projects, respectively.

186 The spread of funding is not largely different between the male-based and female-based groups  
187 (Figure 2), but more projects appeared to localize at the lower end of the scale for the female-based

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188 group. However, there was no statistical difference between the mean values of the 3 groups ( $P=0.16$ ,  
189 Kruskal Wallis  $\chi^2= 4.1$ ). There were no significant differences between male- and female-based  
190 research ( $P=0.83$ ,  $W=3834$ ).

191

#### 192 Funding over the years:

193 Funding over 4 consecutive years is presented in Supplementary Tables IV and V for the UK and US,  
194 respectively. The total funding, mean funding amount over the respective funding periods, and the  
195 distribution of data are presented in Supplementary Figures 1 and 2. There were no statistical  
196 significant difference in the funding over time within each of the 3 groups ( $P>0.05$ , Kruskal-Wallis), for  
197 both the UK and US.

198

#### 199 Proportion of Funding for Infertility and Reproductive Health Research in UK and USA:

200 The proportion of funding allocated to male and female infertility research is presented in Table III for  
201 UK and Table VI for US. The MRC fund research for reproduction and infertility and the NIHR have a  
202 dedicated research specialty for Reproductive Health and Childbirth (NIHR, 2021). When examining  
203 funding allocated directly for infertility research by the MRC, the proportion of total funding peaks at  
204 1.58% in 2016/17 (Table III). For the NIHR, the largest proportion of funding allocated to infertility  
205 research was in 2019/20 with 2.31% of the year's total awards. When examining total funding by the  
206 NIHR between 2015/16 and 2019/20, the proportion of funding for male-based infertility research  
207 was 0.07% and 0.79% for female-based research.

208 In the USA, of the 27 NIH institutes and research centres, the NICHD is a primary funder for furthering  
209 research on human development, improvement for reproductive health, and enhancing the lives of  
210 children and young adults (NIH, 2021). This also encompasses research for infertility and  
211 contraception development. The NICHD's annual funding for research between fiscal years 2011 and

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212 2020 was between \$873 million to \$1.1 billion (REPORT, 2021). In the FY2016, NICHD funded  
213 \$1,021,132,045 for research grants and fellowships, but only 1.63% or \$16,684,751 was for infertility  
214 research (as defined by the eligibility criteria in this study; Table VI). The funding proportion for the  
215 male-based research group was 0.48%, which was similar to the female-based funding proportion,  
216 0.51%. The proportion of total funding provided by the NICHD between 2016 and 2019 that was  
217 allocated to infertility research was estimated at 2.56%, with male-based receiving 0.83% and female-  
218 based receiving 1.32%.

219

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220

Discussion.

221 This study provides details of UK and US government funding for male infertility and male reproductive  
222 health covering the period 2016-2019. The information will be instructive for different stakeholders,  
223 *e.g.* workers in the discipline, grant organisations, commercial companies, and policy makers. This will  
224 enable the development of evidence-based informed decisions for future funding strategies This is  
225 critical as male infertility poses a global health risk for many millions of men yet research funding is  
226 not concomitant with the prevalence or impact of the disease.

227 We analysed public-accessible databases for UKRI, NIHR (UK) and US (NIH) covering the period of  
228 awards from January 2016 to December 2019. The primary objective was to determine funding for  
229 male reproductive health and infertility research. To provide context, we assessed 3 groups based on  
230 the primary focus of the research in reproductive biology/medicine: male-based, female-based, and  
231 not-specified (Supplementary Table II). Information from the aims, research abstracts, timeline  
232 summaries, and/or impact statements, was used to determine if a study was included and, if so, to  
233 which group it was assigned. This is necessarily a subjective process, therefore we provide our search  
234 and entry/exclusion criteria (Supplementary Tables I, II, and III), as well as a supplementary table of  
235 the research projects' titles from the UK and US (Supplementary Tables VI and VII). Whilst  
236 incorporation of different terms may produce different answers, the results are robust. For example,  
237 the application of data extraction is consistent between countries as the inclusion/exclusion criteria  
238 were the same. We were focused on infertility and associated links to infertility and reproductive  
239 disorders. No analysis was made to assess if there is bias in funding research for female reproduction  
240 versus male reproduction. Moreover, we do not examine submission numbers, triage, rejection rates,  
241 etc. and thus prioritization of research cannot be assessed.

242 Although the number of awards for female-based research is generally higher than for the male group  
243 (ratio of ~2:1 in UK, and 1.3:1 in USA), the average amount awarded per project was not significantly

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244 different in either country (see Tables II and IV, Figures 1 and 2), indicating that funding per project is  
245 not different between male and female reproductive health.

246 An important question to answer is, what is the proportion of funding for reproduction/male  
247 reproductive health compared to general research funding? There are several approaches to address  
248 this question. For both the UK and USA data, one method is to examine the total funding for research  
249 by the main funding agency and compare this to the data for male- and female-based research.  
250 Reproductive health research is primarily supported by the MRC and NIHR in the UK, and by the NICHD  
251 in the USA. In the funding periods 2015/16 to 2017/18, the total infertility research funding by MRC  
252 ranged from 0.87% to 1.58% of the total budget (Table III). Infertility research funding from NIHR  
253 ranged from 0.08% to 2.31% (2015/16 to 2019/20, Table III). For the US, the maximum infertility  
254 research funding by the NICHD was 3.39% of its total budget (Table VI).

255 Another approach was to assess the proportion of funding compared between research disciplines, or  
256 research categories, in the UK and USA, respectively. Within the UK data, we specifically examined  
257 research disciplines funded by the NIHR. From the April 1<sup>st</sup>, 2011 to present, the NIHR awarded over  
258 £216 million for Reproductive Health and Childbirth research, their 7th largest funding category.  
259 Mental Health, Cancer, and Cardiovascular Diseases were within the top 5 most funded categories  
260 (Supplementary Table VIII). NIHR awarded £21 million in 2017/18 for Reproductive Health and  
261 Childbirth research (NIHR, 2021), yet surprisingly there was minimal support towards male-based  
262 research as between 2016 to 2019 only two projects were funded (Table I, Supplementary Table VI).  
263 The small number of projects in male reproductive health funded by the NIHR was unexpected as NIHR  
264 are the largest UK funders for health care and clinical research (NIHR, 2021). NIHR supported 302  
265 studies for reproductive health with 94 of them being newly funded projects for 2019/20. However,  
266 using our criteria for study inclusion we only identified 4 projects focusing on infertility over the whole  
267 period (Table I, Supplementary Table IV). While we do not know the reason for the low funding rate,  
268 a plausible explanation is that, as NIHR fund a significant number of clinical trials, there may not have

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269 been sufficient high quality candidates for either diagnostic and/or treatment trials to be developed  
270 in male reproductive health (Barratt *et al.*, 2021).

271 To compare different research categories for the USA data, we did not use our collected data to  
272 provide estimated funding. Instead, we used the NIH's *Research Portfolio Online Reporting Tools*  
273 estimates of funding for various Research Condition and Disease Categories (RCDC)  
274 (<https://report.nih.gov/funding/categorical-spending#/>) and the NIH's annual research grants  
275 ([https://report.nih.gov/funding/nih-budget-and-spending-data-past-fiscal-years/budget-and-](https://report.nih.gov/funding/nih-budget-and-spending-data-past-fiscal-years/budget-and-spending)  
276 [spending](https://report.nih.gov/funding/nih-budget-and-spending-data-past-fiscal-years/budget-and-spending)). For the NIH, the values presented for the 299 RCDCs are not mutually exclusive because a  
277 project can fall under several categories. We examined research categories similar to those at the  
278 NIHR. For NIH these included: Contraception/Reproduction, Infertility, Obesity, and Mental Health  
279 (Supplementary Table IX). By estimating the proportion of funding for these categories from the NIH's  
280 Total Research Funding, we can see those categories such as Obesity and Mental Health were highly  
281 funded in comparison to Contraception/Reproduction and Infertility.

282 NICHD has funded under 1% of their annual research grants for male-based research for 3 out of 4  
283 consecutive fiscal years (Table VI). NICHD are primary funders for reproduction, infertility, and  
284 contraceptive development, therefore, it was unexpected to observe such low funding proportions. A  
285 possible factor for why our calculated funding proportion values by the NICHD are low may be due to  
286 our strict eligibility criteria during data collection. However, we applied our eligibility and exclusion  
287 criteria equally across all funding agencies, for the UK and US.

288 Two pertinent points arise from our study. Firstly, compared to the prevalence of the disease where  
289 1:7 couples are infertile (Boivin *et al.*, 2007, NICE, 2013), the proportion of research funding for male  
290 reproductive health is small (less than 1%, see Tables III and VI) compared to other diseases in the UK  
291 and US (Supplementary Table IX). This is surprising especially because MAR is a multi-billion-dollar  
292 global industry. Secondly, although the number of awards for female-based research is generally  
293 higher than for the male group (ratio of ~2:1 in the UK and 1.3:1 in the USA), the average funding

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294 awarded per project is not significantly different in either UK or USA (see Tables II and IV; Figures 1  
295 and 2). Whilst there are many challenges in comparing research funding between disciplines, the  
296 present findings directly imply a significant gap between impact of disease prevalence and research  
297 funding to investigate the disease, e.g., diagnosis and treatment. This apparent gap requires further  
298 detailed analysis and should include a comprehensive assessments of the health economic impact of  
299 male reproductive health.

300

301 There are several limitations to our study. Firstly, these findings cannot be generalized to reflect  
302 funding trends towards infertility and reproductive health worldwide. The data were collected from  
303 governmental agencies of two countries and over a narrow funding period. Further, the funding  
304 priorities of UK and US governmental agencies may not be a 'good fit model' for the funding priorities  
305 of government research agencies in other countries. Secondly, only government funding was  
306 investigated. We did not examine funding from non-governmental organizations (NGO's), e.g.  
307 Wellcome Trust, industry, Bill and Melinda Gates Foundation, and other major philanthropic  
308 organisations. As the UKRI, NIHR, and NIH are governmental agencies, their prioritization to providing  
309 fellowships, research grants, program centre grants, and others may not be similar to other charities  
310 and international organizations. Detailed analysis of funding from these other agencies would be  
311 instructive and assist in a more comprehensive analysis. Future work should include data from more  
312 countries, NGO's and include longer funding timeframes to accurately estimate total funding  
313 supporting for male infertility and male reproductive health and for more comprehensive assessment  
314 of funding trends.

315

316 In summary, we present recent government funding for male-based infertility and reproductive  
317 health, and by extension, funding towards female-based research. The information provided in this  
318 study should be useful for a variety of stakeholders as discussed earlier. A sentinel message is that

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319 whilst male infertility poses a global health risk for many millions of men, research funding to develop

320 better diagnostic tools and treatment regimens is not on par. The data analysis presented herein

321 should stimulate discussions for a strategic development of male reproductive health care

322 investments.

323



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Research Funding for Male Reproductive Health and Infertility in UK and USA [2016 – 2019]

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330 **Conflicts of Interests:**

331 CLRB is Editor for RBMO and has received lecturing fees (2019) from Merck, Pharmasure, and Ferring.

332 His laboratory is funded by Bill and Melinda Gates Foundation, CSO, Genus. No other authors declare

333 a conflict of interest.

334 **Authors Roles:**

335 The experimental design, primary data collection, and initial statistical analysis was performed by EG

336 as part of her undergraduate BSc honours research project. The initial draft of the manuscript was

337 written by EG and CB following discussions with CJD. All authors contributed to writing and editing the

338 manuscript and approving the final version.

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340 No specific funding was provided for data collection and/or analysis for this study. Whilst undertaking

341 this work EG was a BSc Biomedical Sciences honours student at University of Dundee, School of Life

342 Sciences, Dundee. ESHRE have provided funds to facilitate meetings and interactions of the MRHI

343 Working Group.

344 **Data Availability Statements:**

345 *The data underlying this article are available in the Dryad Digital Repository at*

346 <https://doi.org/10.5061/dryad.v9s4mw6wc>.

347

348

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**Main Figures**

390

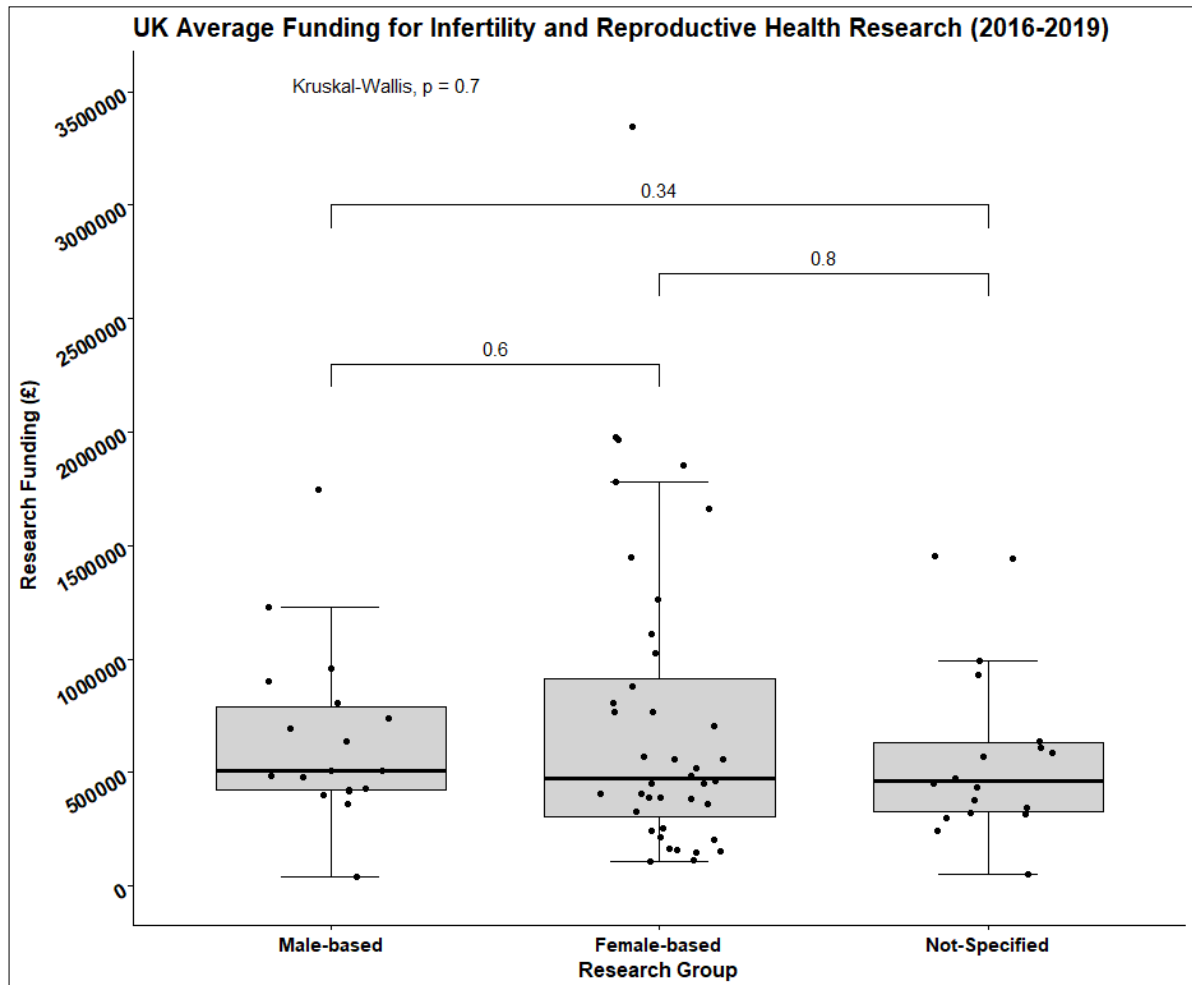
391

392 **Figure 1:** Box-and-whisker plot with a 95% confidence interval (CI) of awards for UK infertility and reproductive

393 health research under the three research categories: male-based, female-based, and not-specified. 18 projects

394 were funded for male-based research, 40 projects for female-based, and 18 for not-specified by the UKRI and

395 NIHR.



396

397

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## Research Funding for Male Reproductive Health and Infertility in UK and USA (2016 – 2019)

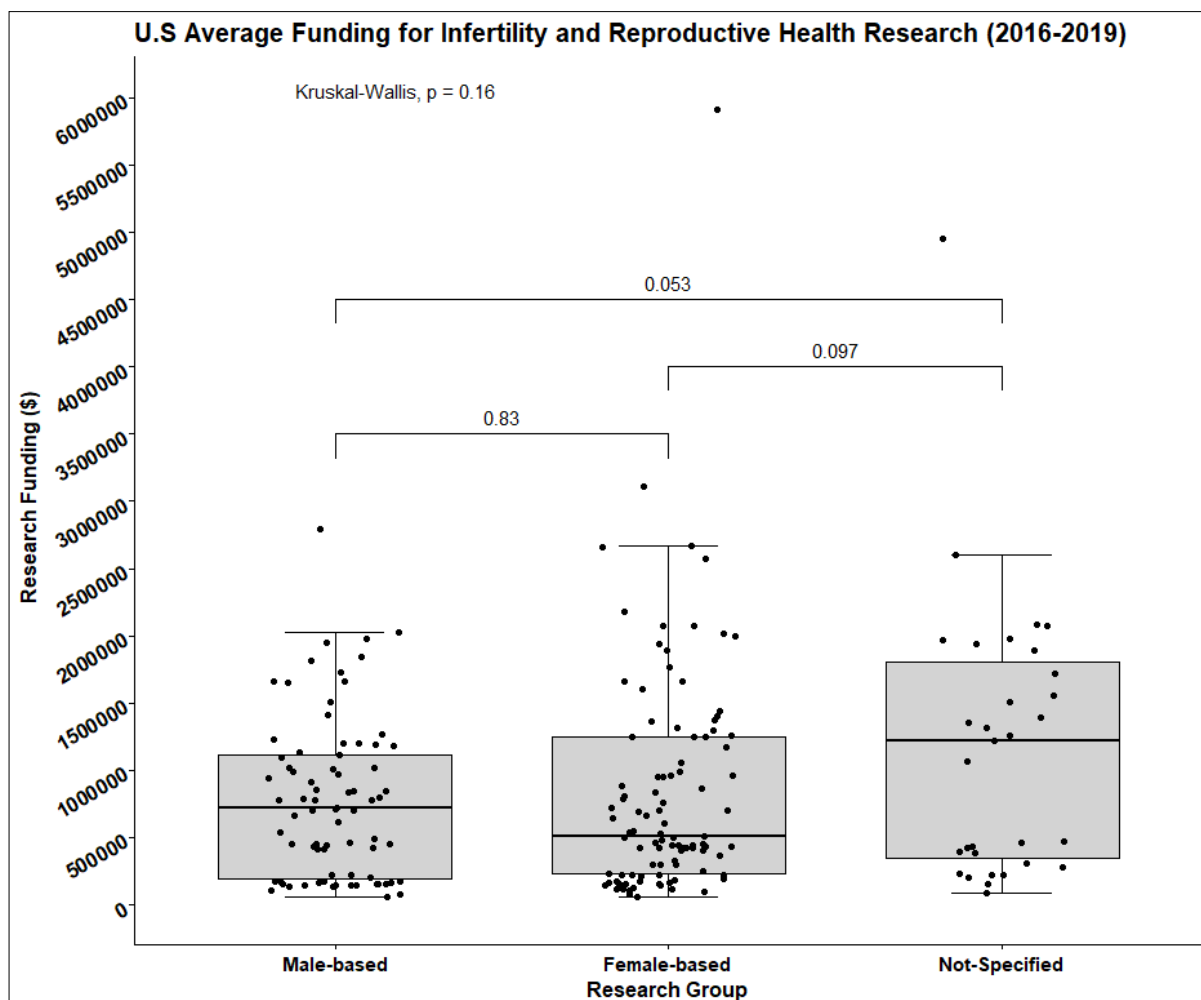
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398

399 **Figure 2:** Box-and-whisker plot has a 95% CI of the funding collected for US infertility and reproductive health

400 research under the three research focus categories: male-based, female-based, and not-specified. 76 projects

401 were funded for male-based, 99 projects for female-based, and 31 for not-specified group by the NIH agencies.



402

403

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Research Funding for Male Reproductive Health and Infertility in UK and USA [2016 – 2019]

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404

**Abbreviations List:**

405

| <b>Abbreviations for Funding Agencies/Institutes, Research Councils, and Databases</b> |  |
|--|--|
| BBSRC  | Biotechnology and Biological Sciences Research Council           |
| EPSRC  | Engineering and Physical Sciences Research Council               |
| HRCS   | Health Research Classification System                            |
| MRC  | Medical Research Council   |
| NCCIH  | National Centre for Complementary and Integrative Health         |
| NERC   | Natural Environment Research Council                             |
| NIA  | National Institute of Aging                                      |
| NIAAA  | National Institute on Alcohol Abuse and Alcoholism               |
| NIAID  | National Institute of Allergy and Infectious Diseases            |
| NIBIB  | National Institute of Biomedical Imaging and Bioengineering      |
| NICHD  | National Institute of Child Health and Health Development        |
| NIDDK  | National Institute of Diabetes and Digestive and Kidney Diseases |
| NIEHS  | National Institutes of Environmental Health Sciences             |
| NIGMS  | National Institute of General Medical Sciences                   |
| NHBLI  | National Heart, Blood, Lung Institute                            |
| NIH  | National Institutes of Health                                    |
| NIHR   | National Institute of Health and Research                        |
| NINR   | National Institute of Nursing Research                           |
| NIOSH  | National Institute for Occupational Safety and Health            |
| OD   | NIH's Offices of the Director                                    |
| RCDC   | Research, Conditions and Diseases Categories                     |
| RePORT   | Research Portfolio Online Reporting Tools                        |
| UKRI   | UK Research and Innovation                                       |
| UKRI-GTR   | UK Research and Innovation – Gateway to Research                 |

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**Main Tables**

**Research Funding for Male Infertility and Male Reproductive Health in the UK and USA [2016 – 2019]**

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### MAIN TABLES

**Table I: Total funding awarded by the UKRI and NIHR agencies for infertility research groups along with annual allocated funding.**

| Funding Period           | Funding Agency | Total Funding for Research Grants and Fellowships (£000)* | Research Groups        |                        |                        |
|--------------------------|----------------|---|------------------------|------------------------|------------------------|
|                          |                |   | Male-based (£) [N]     | Female-based (£) [N]   | Not-Specified (£) [N]  |
| 2015/16                  | BBSRC          | 330,473   | 0                      | 0                      | 0                      |
|                          | EPSRC          | 691,280   | 0                      | 0                      | 0                      |
|                          | MRC            | 487,157   | 1,748,922 [1]          | 3,346,448 [1]          | 0                      |
|                          | NIHR           | 268,000   | 0                      | 214,625 [1]            | 0                      |
|                          |                |   |                        |                        |                        |
| 2016/17                  | BBSRC          | 331,062   | 1,328,455 [3]          | 0                      | 695,839 [2]            |
|                          | EPSRC          | 733,188   | 958,032 [1]            | 0                      | 0                      |
|                          | MRC            | 341,630   | 676,826 [2]            | 3,259,734 [6]          | 1,444,459 [1]          |
|                          | NERC           | 190,519   | 0                      | 0                      | 51,390 [1]             |
|                          | NIHR           | 263,300   | 0                      | 1,027,318 [1]          | 0                      |
| 2017/18                  | BBSRC          | 348,808   | 359,758 [1]            | 359,772 [1]            | 1,042,358 [2]          |
|                          | EPSRC          | 844,134   | 694,461 [1]            | 0                      | 244,593 [1]            |
|                          | MRC            | 325,164   | 903,026 [1]            | 1,287,441 [2]          | 636,510 [1]            |
|                          | NERC           | 220,618   | 0                      | 0                      | 0                      |
|                          | NIHR           | 274,000   | 477,541 [1]            | 2,140,292 [3]          | 0                      |
| 2018/19                  | BBSRC          | 1,439,505**   | 934,840 [2]            | 1,719,275 [4]          | 2,276,094 [4]          |
|                          | EPSRC/UKRI     |   | 0                      | 252,693 [1]            | 0                      |
|                          | MRC            |   | 0                      | 5,535,724 [7]          | 437,695 [1]            |
|                          | NIHR           | 269,600   | 507,909 [1]            | 165,595 [1]            | 1,333,890 [2]          |
| 2019/20                  | BBSRC          | 1,401,130**   | 1,139,195 [2]          | 779,165 [2]            | 0                      |
|                          | EPSRC/UKRI     |   | 1,230,976 [1]          | 766,542 [1]            | 1,455,327 [1]          |
|                          | MRC            |   | 807,249 [1]            | 1,564,917 [4]          | 323,754 [1]            |
|                          | NERC           |   | 0                      | 0                      | 611,514 [1]            |
|                          | NIHR           | 321,200   | 0                      | 7,431,405 [5]          | 0                      |
| <b>Total Funding (£)</b> |                |   | <b>11,767,190 [18]</b> | <b>29,850,945 [40]</b> | <b>10,553,423 [18]</b> |

Table I Values collected are rounded to the nearest £ Sterling pound. [N] refers to the number of projects awarded. \*Total funding for research grants and fellowships (in millions) by the respective UKRI councils and NIHR were determined by consulting their public annual budgeting reports; \*\*As of the funding period 2018/19 and onwards, all UKRI councils report their annual expenditures as one, therefore the annual expenditure for research and innovation were obtained from the UKRI's annual reports.



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**Table II: Summary of the UK Awarded Research by the UKRI and NIHR**

|                         | Research Group               |                              |                              |
|-------------------------|------------------------------|------------------------------|------------------------------|
|                         | Male-based<br>[N=18]         | Female-based<br>[N=40]       | Not-Specified<br>[N=18]      |
| <b>Total (£)</b>        | 11,767,190                   | 29,850,945                   | 10,553,423                   |
| <b>Mean<br/>(SD)</b>    | 653,733<br>(384,131)         | 746,274<br>(690,065)         | 586,301<br>(387,951)         |
| <b>Median<br/>(IQR)</b> | 507,197<br>(423,630-789,793) | 476,163<br>(308,001-914,762) | 463,394<br>(328,457-630,261) |

Table II: All values are rounded to the nearest £ Sterling pound. SD, standard deviation of the data group; IQR, interquartile range which encompasses 50% of the data group.

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**Table III: The UK Proportion of Funding for Infertility Research**

| <b>Funding Period</b> | <b>UK Agency</b> | <b>Total Research Grants and Fellowships (£)</b> | <b>Total Funding Proportion for Infertility Research (%)</b> | <b>Male-based Funding Proportion (%)</b> | <b>Female-based Funding Proportion (%)</b> | <b>Not-Specified Funding Proportion (%)</b> |
|-----------------------|------------------|--|--|--|--|---|
| <b>2015/16</b>        | MRC              | 487,157,000                                      | 1.05   | 0.36                                     | 0.69                                       | 0   |
|                       | NIHR             | 268,000,000                                      | 0.08   | 0  | 0.08                                       | 0   |
| <b>2016/17</b>        | MRC              | 341,630,000                                      | 1.58   | 0.2                                      | 0.95                                       | 0.42  |
|                       | NIHR             | 263,300,000                                      | 0.39   | 0  | 0.39                                       | 0   |
| <b>2017/18</b>        | MRC              | 325,164,000                                      | 0.87   | 0.28                                     | 0.4  | 0.19  |
|                       | NIHR             | 274,000,000                                      | 0.96   | 0.17                                     | 0.78                                       | 0   |
| <b>2018/19</b>        | NIHR             | 269,600,000                                      | 0.74   | 0.19                                     | 0.06                                       | 0.49  |
| <b>2019/20</b>        | NIHR             | 321,200,000                                      | 2.31   | 0  | 2.31                                       | 0   |
| <b>Total</b>          | NIHR             | 1,396,100,000                                    | 0.87   | 0.07                                     | 0.79                                       | 0.1   |

Table III: The estimated proportion of funding for the UK was calculated using the data collected from Table 1. The proportions are rounded two 2 decimal points. The total research grants and fellowship values were obtained from the respective UK agency's annual reports and budgets. The MRC total research grants and fellowships from 2018/19 – 2019/20 were excluded as they are part of the UKRI and report their annual expenditures under one with other research councils, therefore the exact sum for research grants and fellowships for MRC was not available. The total funding proportion is only looking at NIHR funding from 2015/16 to 2019/20.

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**Table IV: Current Total Funding for Infertility Research Awarded by the NIH's funding institutes and the respective fiscal years.**

| Fiscal Year | NIH's Funding Institutes & Centres | Total Funding for Research Grants (\$)* | Research Groups     |                       |                        |
|-------------|------------------------------------|---|---------------------|-----------------------|------------------------|
|             |                                    |   | Male-based (\$) [N] | Female-based (\$) [N] | Not-Specified (\$) [N] |
| 2016        | NCCIH                              | 107,447,348                             | 0                   | 1,439,100 [1]         | 0                      |
|             | NIAID                              | 2,983,260,567                           | 0                   | 2,219,320 [2]         | 0                      |
|             | NICHD                              | 1,021,132,045                           | 4,927,677 [7]       | 5,183,197 [8]         | 6,573,877 [4]          |
|             | NIDDK                              | 1,580,485,601                           | 0                   | 95,610 [1]            | 0                      |
|             | NIEHS                              | 407,288,463                             | 1,784,198 [4]       | 3,890,638 [6]         | 233,712 [1]            |
|             | NIGMS                              | 2,231,411,724                           | 4,822,891 [3]       | 0                     | 8,085,074 [5]          |
| 2017        | NHBLI                              | 2,463,498,743                           | 0                   | 2,568,489 [1]         | 0                      |
|             | NIA                                | 1,708,012,380                           | 536,946 [1]         | 0                     | 0                      |
|             | NIAAA                              | 342,212,488                             | 0                   | 0                     | 398,788 [1]            |
|             | NICHD                              | 967,265,488                             | 12,430,159 [15]     | 13,078,769 [14]       | 7,325,909 [5]          |
|             | NIEHS                              | 1,638,513,361                           | 1,841,716 [1]       | 2,076,388 [1]         | 1,829,137 [2]          |
|             | NIGMS                              | 411,526,579                             | 2,831,714 [3]       | 3,105,261 [1]         | 2,776,900 [2]          |
| 2018        | NIA                                | 2,053,235,620                           | 0                   | 118,485 [1]           | 0                      |
|             | NIAID                              | 3,339,613,240                           | 0                   | 868,774 [1]           | 0                      |
|             | NICHD                              | 1,028,491,002                           | 8,755,795 [13]      | 17,441,843 [19]       | 2,396,625 [5]          |
|             | NIDDK                              | 1,613,382,619                           | 0                   | 0                     | 85,224 [1]             |
|             | NIEHS                              | 458,275,648                             | 4,412,912 [3]       | 3,443,045 [4]         | 1,943,533 [1]          |
|             | NIGMS                              | 2,506,055,218                           | 2,537,197 [3]       | 3,231,516 [3]         | 1,971,230 [1]          |
|             | NIOSH                              | Unavailable**                           | 169,500 [1]         | 0                     | 0                      |
| 2019        | NIAID                              | 3,496,548,418                           | 0                   | 2,668,689 [1]         | 0                      |
|             | NIBIB                              | 381,987,928                             | 0                   | 0                     | 1,259,032 [1]          |
|             | NICHD                              | 1,099,202,749                           | 8,395,362 [16]      | 18,668,208 [31]       | 0                      |
|             | NIEHS                              | 454,787,252                             | 1,095,907 [1]       | 1,792,109 [2]         | 0                      |
|             | NIGMS                              | 2,558,317,976                           | 2,364,252 [3]       | 888,154 [1]           | 1,064,618 [1]          |
|             | NINR                               | 129,862,737                             | 0                   | 495,303 [1]           | 0                      |
|             | OD                                 | 594,535,751                             | 1,505,963 [1]       | 0                     | 0                      |
| 2020        | NICHD                              | 1,133,572,974                           | 0                   | 0                     | 218,250 [1]            |
|             | NIEHS                              | 466,088,243                             | 845,557             | 0                     | 0                      |

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|                                   |                    |                    |                    |
|-----------------------------------|--------------------|--------------------|--------------------|
| <b>Current Total Funding (\$)</b> | 59,257,746<br>[76] | 83,272,898<br>[99] | 36,161,909<br>[31] |
|-----------------------------------|--------------------|--------------------|--------------------|

Table IV: Values collected are rounded to the nearest US \$ dollar. [N] refers to the number of projects awarded. From the start of data collection to the analysis, 7 projects changed their statuses from active to completed, making 138 projects out of 206 as active running. 67 of the 138 projects do not provide complete funding sums by the NIH, therefore, the funds were totalled up to their most recent awarding FY. \*The values for the annual spending of research grants by the NIH (in millions) was found in the NIH's RePORT Funding site: The Research Grants: Awards and Total Funding, by type and Institute/Centre. \*\*The values were not made available by the NIH.

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**Table V: Summary Statistics of the US Awarded Research by the NIH**

|                           | Research Group                 |                                |                                  |
|---------------------------|--------------------------------|--------------------------------|----------------------------------|
|                           | Male-based<br>[N=76]           | Female-based<br>[N=99]         | Not-Specified<br>[N=31]          |
| <b>Current Total (\$)</b> | 59,257,746                     | 83,272,898                     | 36,161,909                       |
| <b>Mean<br/>(SD)</b>      | 779,707<br>(594,203)           | 841,140<br>(862,707)           | 1,194,687<br>(1,046,679)         |
| <b>Median<br/>(IQR)</b>   | 718,541<br>(193,449-1,117,370) | 511,781<br>(227,847-1,246,408) | 1,223,600<br>(388,397-1,891,778) |

Table V: All values presented are rounded to the nearest US dollar and produced using RStudio.

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**Table VI: The Current Total NICHD Proportion of Funding for Infertility Research**

| Fiscal Year  | NIH Agency | Total Research Grants and Fellowships (\$) | Total Funding Proportion for Infertility Research (%) | Male-based Funding Proportion (%) | Female-based Funding Proportion (%) | Not-Specified Funding Proportion (%) |
|--------------|------------|--|---|-----------------------------------|-------------------------------------|--------------------------------------|
| 2016         | NICHD      | 1,021,132,045                              | 1.63  | 0.48                              | 0.51                                | 0.64                                 |
| 2017         | NICHD      | 967,265,488                                | 3.39  | 1.29                              | 1.35                                | 0.75                                 |
| 2018         | NICHD      | 1,028,491,002                              | 2.78  | 0.85                              | 1.7                                 | 0.23                                 |
| 2019         | NICHD      | 1,099,202,749                              | 2.46  | 0.76                              | 1.7                                 | 0                                    |
| <b>Total</b> | NICHD      | 4,116,091,284                              | 2.56  | 0.83                              | 1.32                                | 0.4                                  |

Table VI: The estimated proportion of funding for the US was calculated using the data collected from Table 4. FY2020 was excluded as only one project was awarded between 1<sup>st</sup> October to 31<sup>st</sup> December 2019 and would be unreflective of the funding proportion for this year. The total proportion looks at the total funding provided by the NICHD for infertility research from 2016 to 2019 and the total research funding granted by the NICHD. The annual research grants and fellowship values were obtained from the NIH's RePORT Budget and Spending site: The Research Grants: *Awards and Total Funding, by type and Institute/Centre*.

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### Supplementary Materials

## **Research Funding for Male Reproductive Health and Infertility in the UK and USA [2016 – 2019]**

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**Supplementary Tables:**

| <b>Supplementary Table I: Search filters used for respective databases</b> |                                 |                                 |   |
|--|---------------------------------|---------------------------------|---|
| <b>Search Filters</b>  | <b>UKRI – GTR</b>               | <b>NIHR – Open Data</b>         | <b>NIH – RePORT Query</b>   |
| <b>Project Start Year/Date</b>   | 2016;<br>2017;<br>2018;<br>2019 | 2016;<br>2017;<br>2018;<br>2019 | >=01/01/2016  |
| <b>Research Type<br/>Or Program Type</b>                                   | Research Grants;<br>Fellowships | Research;<br>Training           | Research Projects<br>Grants;<br>Training, Individual;<br>Training, Institutional* |
| <b>Limit Project search<br/>to**</b>                                       | N/A                             | N/A                             | Project Title<br>Project Terms<br>Project Abstracts                               |
| <b>Fiscal Year (FY)</b>  | N/A                             | N/A                             | No FY was selected  |
| <b>Funder<br/>Or<br/>Agency/Institute/Centre</b>                           | None Chosen                     | N/A                             | Check All   |

Supplementary Table I - N/A – not applicable to the database used or not an available search filter. \*Training, institutional is the support of research training programs within the research areas and priorities supported by the Institute to train predoctoral and/or postdoctoral fellows of an institution. \*\* 'Limit Project search to' is a feature of the NIH RePORTER Query system that searches the inputted search terms at the following options: project title, terms, and abstracts.



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**Supplementary Table II: Inclusion criteria for type of projects included into the data collection.**

| <b>Male-focused infertility research</b>   | <b>Female-focused infertility research</b>  | <b>Not-specified infertility research</b>   |
|--|---|---|
| Spermatogenesis research   | Oogenesis research  | Gametogenesis and infertility   |
| Sperm maturation, motility, and quality analysis research  | Menstruation/menstrual cycle abnormalities  | EDCs impacting general fertility  |
| Sperm dysfunction/disorders research   | Uterine and Ovarian disorders ( <i>e.g., Endometriosis, Polycystic Ovarian Syndrome, and Uterine Fibroids</i> ) | Underpinning the aetiology of infertility ( <i>not specifying the focus group</i> )   |
| Testicular and Prostate health (not cancer) research   | Female contraception research development   | Contraception development in conjunction with HIV/STI prevention  |
| Male contraception research development  | Maternal factors associated with ART outcomes   | Studies using animal and insect models to further the understanding of <b>human</b> infertility and contraception development |
| Paternal factors associated with ART outcomes  | EDCs association with female infertility  | Hormonal dysregulation  |
| Paternal association with fetus health/development (i.e., male infertility affecting fetus health/development) | Underpinning the aetiology of female infertility  | Cell/embryonic development dysregulation giving rise to infertility   |
| EDCs giving rise to male infertility   | Hormonal dysregulation and female infertility   |   |
| Underpinning the aetiology of male infertility   |   |   |
| Hormonal dysregulation and male infertility  |   |   |

Supplementary Table II – The inclusion criteria for the 3-research groups after examining abstracts, research impacts and public health relevance statements. Under each heading are the topics or field of research of reproductive health and infertility research.

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**Supplementary Table III: Type of projects that would be excluded from the data collection if the following were indicated as the primary research focus detailed in their abstracts and impacts, and example of few exceptions to include.**

| <b>Primary Research Focus</b>  | <b>Reasons for Exclusion</b>  | <b>Exceptions to include</b>   |
|--|---|--|
| <b>Research focusing on reproductive cancers (e.g., ovarian, prostate, testicular, uterine...) or other cancers</b>              | People who have cancers and are undergoing cancer treatments can negatively impact their fertility. Funding for cancer research goes away from focusing on infertility funding                            | If the project is investigating a concern that affected human fertility in addition to potentially causing cancers, they would be included.  |
| <b>Research focusing on STIs (e.g., <i>Chlamydia trachomatis</i> or <i>Gonorrhea</i>)</b>  | STIs are known to affect human fertility, but are usually funded under the category of infectious diseases rather than reproduction and infertility   | A study focusing on STIs would be included only if it is contraceptive development in conjunction to STI prevention  |
| <b>Research focusing on HIV and/or AIDs</b>  | HIV/AIDs are known to affect human fertility, but are usually funded under the category of infectious diseases and impact the immune system   | A study researching HIV or AIDs would be included only if it is contraceptive development in conjunction to HIV/AIDs prevention  |
| <b>Pregnancy/gestation; pregnancy health. Placental development Childbirth and Labor.</b>  |   | A study focusing on this area of research would be included if it were investigating a paternal contribution to implantation and clinical pregnancy outcomes   |
| <b>Research focusing on fetus health or development</b>  | These areas were not included as comparison was primarily aimed at examining male infertility. Work on pregnancy and fetus are more tangential to work on infertility research and creates a wider scope. | A study focusing on this area of research would be included if it were investigating a paternal or maternal contribution to the fetus' health, development, or future reproductive health, with or without the usage of ART. |
| <b>Research focusing on miscarriages</b>   |   | A study focusing on miscarriages would be included if it were investigating an association between miscarriages and paternal or maternal infertility, with or without the usage of ART.                                      |
| <b>Research focusing on the sociological, policy or economic studies for infertility, or a public intervention program study</b> |   |  |
| <b>Research focusing on animal, insect or plant infertility that are not used as model for human infertility research</b>        | These research areas stray away from research focusing primarily on human infertility and reproductive health.  |  |

Supplementary Table III - Type of projects that would be excluded from the data collection if the following were indicated as the primary research focus detailed in their abstracts and impacts, and few exceptions to include them.

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**Supplementary Table IV: UK funding awarded across the funding periods from January 2016 to December 2019**

| Funding Period | Research Groups          |                            |                             |
|----------------|--------------------------|----------------------------|-----------------------------|
|                | Male-based (£)<br>[mean] | Female-based (£)<br>[mean] | Not-Specified (£)<br>[mean] |
| 2015/16        | 1,748,922*               | 3,561,073<br>[1,780,534]   | 0                           |
| 2016/17        | 2,963,313<br>[522,539]   | 4,287,052<br>[562,710]     | 2,191,688<br>[547,922]      |
| 2017/18        | 2,434,786<br>[580,108]   | 3,787,505<br>[631,251]     | 1,923,461<br>[480,865]      |
| 2018/19        | 1,442,749<br>[480,917]   | 7,673,287<br>[590,253]     | 4,047,679<br>[578,240]      |
| 2019/20        | 3,177,420<br>[794,355]   | 10,542,029<br>[878,502]    | 2,390,595<br>[796,865]      |
| <b>Total</b>   | 11,767,190               | 29,850,945                 | 10,553,423                  |

Supplementary Table IV – The UK funding across the 5 consecutive funding periods awarded between January 2016 to December 2019. The values are rounded to the nearest Sterling pound. \*Value belongs to a single project awarded, thus, no mean was produced.

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**Supplementary Table V: US Current Funding across the 5 fiscal years from January 2016 to December 2019**

| Fiscal Year          | Research Groups         |                           |                           |
|----------------------|-------------------------|---------------------------|---------------------------|
|                      | Male-based (\$) [mean]  | Female-based (\$) [mean]  | Not-Specified (\$) [mean] |
| <b>2016</b>          | 11,534,766<br>[823,912] | 12,827,865<br>[712,659]   | 14,892,663<br>[1,489,266] |
| <b>2017</b>          | 17,640,535<br>[882,027] | 20,828,907<br>[1,225,230] | 12,330,734<br>[1,233,073] |
| <b>2018</b>          | 15,875,404<br>[793,770] | 25,103,663<br>[896,559]   | 6,396,612<br>[799,574]    |
| <b>2019</b>          | 13,361,484<br>[636,261] | 24,512,463<br>[680,902]   | 2,323,650<br>[1,161,825]  |
| <b>2020*</b>         | 845,557                 | 0                         | 218,250                   |
| <b>Current Total</b> | 59,257,746              | 83,272,898                | 36,161,909                |

Supplementary Table V – The US current funding for projects awarded funding beginning between January 2016 to December 2019. The values are rounded to the nearest US dollar. \*For 2020, male-based and not-specified groups were each awarded 1 project since the beginning of the FY (October 1<sup>st</sup> to December 31<sup>st</sup>, 2019), thus, no mean or median was produced.

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**Supplementary Table VI – Research Project Titles from UK Funding Agencies**

| Research Group | Project Reference | Research Study Title   |
|----------------|-------------------|--|
| Female-based   | PB-PG-0815-20009  | A mixed methods evaluation of online provision of oral contraceptives to measure: validity of self-reported biometric data; essential information transfer and user experience of self-measurement and submission of biometric data. |
| Not-Specified  | BB/S001255/1      | A novel mechanism underlying GnRH pulse generation by KNDy neurones  |
| Not-Specified  | BB/S000550/1      | A novel mechanism underlying GnRH pulse generation by KNDy neurones  |
| Female-based   | 15/113/01         | A randomised controlled trial to determine the effectiveness of bridging from emergency to regular contraception: The 'Bridge-it' study  |
| Female-based   | II-LB-0715-20003  | A trial of egg recovery rates for IVF using a collection chamber that provides environmental control: Eggcell Trial.   |
| Female-based   | MR/N024524/1      | Androgens and women's health: developing new therapies to treat endometrial disorders  |
| Male-based     | MR/N002970/1      | Androgens: unlocking the key drivers of male health and wellbeing  |
| Female-based   | EP/R041407/1      | Born Slippery: A Tribological Discourse on Hysterosalpingography as a Therapeutic Treatment for Infertile Women  |
| Male-based     | BB/S000801/1      | Building a molecular machine: analysis of co-chaperones for assembly of ciliary dynein motor complexes   |
| Not-Specified  | BB/P022065/1      | Can histone code-like 'switches' govern the multi-functionality of RNA-binding proteins?   |
| Female-based   | MR/N023692/1      | Can norethisterone enanthate (NET-EN) reduce the risk of recurrent bacterial vaginosis in women at high risk for HIV infection?  |
| Female-based   | MR/S036350/1      | Cell atlas of the human female reproductive system across the lifespan   |
| Female-based   | 17/60/22          | Chronic Endometritis and Recurrent Miscarriage - The CERM trial  |
| Female-based   | PB-PG-0817-20046  | Chronic endometritis and unexplained recurrent miscarriage: the role of the endometrial microbiome.  |
| Female-based   | MR/N011147/1      | Community pharmacist provision of contraception services for women receiving opiate substitution treatment   |
| Female-based   | BB/P003435/1      | Co-ordinated regulation of ovarian follicle assembly by Activin A and FoxL2  |
| Female-based   | PB-PG-0317-20018  | CRESCENDO Creating a Clinical Prediction Model to predict Surgical Success in Endometriosis  |
| Not-Specified  | MR/S023712/1      | Crowdsourcing with adolescents in Senegal to address social norms limiting their access to sexual and reproductive health services   |
| Not-Specified  | BB/N006933/1      | Cytoplasmic dynein and KASH5: partners in fertility  |
| Female-based   | BB/R015961/1      | Decoding the role of follicle stimulating hormone in ovarian ageing  |
| Female-based   | BB/R015961/2      | Decoding the role of follicle stimulating hormone in ovarian ageing  |
| Male-based     | BB/R003556/1      | Defining the impact of paternal nutrition on fetal growth regulation   |
| Not-Specified  | EP/R041814/1      | Engineering Novel Imaging Technologies for Reproductive Health: Transforming IVF outcomes  |
| Not-Specified  | NE/P010911/1      | Environmental determinants of IVF treatment  |
| Female-based   | MR/S000437/1      | Epigenome patterning in oocytes and its legacies in the embryo   |

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|               |                    |  |
|---------------|--------------------|--|
| Female-based  | MR/R003246/1       | Exploration of the oogenic potential of putative germ line stem cells isolated from the ovaries of girls and adult women   |
| Male-based    | BB/N009886/1       | FSTL3: A Crucial Regulator of Sertoli Cell Proliferation   |
| Male-based    | BB/S007407/1       | Function and structure of specialised ribosomes in the testis  |
| Female-based  | MR/S025235/1       | Gonadotropin action in the polycystic ovary  |
| Female-based  | MR/S037608/1       | Harnessing cross-country administrative data to evaluate national policy impacts on maternal, infant and child health and health inequalities-MatCHNet                       |
| Male-based    | BB/N007026/1       | How does pituitary androgen signalling support lifelong health and wellbeing? An integrated transgenic and systems biology approach  |
| Male-based    | MR/P009948/1       | Human germline in vitro models for development and the epigenetic program  |
| Female-based  | BB/R015635/1       | Identification of human-specific regulatory mechanisms in female germ cell development   |
| Female-based  | MR/S002456/1       | Identifying disease promoting macrophages and tissue-identity in endometriosis   |
| Female-based  | MR/S002456/2       | Identifying disease promoting macrophages and tissue-identity in endometriosis   |
| Male-based    | BB/P006612/1       | Identifying the functions of a family of nuclear RNA binding proteins that switch expression between somatic and meiotic cells   |
| Male-based    | MR/P02419X/1       | IMPC: Importance of PABPs in mammalian reproduction and physiology   |
| Female-based  | MR/P011454/1       | Improving adolescent access to contraception and safe abortion in sub-Saharan Africa: health system pathways   |
| Not-Specified | CS-2018-18-ST2-002 | Improving the evaluation and treatment of patients with reproductive disorders using kisspeptin  |
| Not-Specified | BB/R002703/1       | Interrogating the potential of mouse primordial germ cells in vivo   |
| Female-based  | II-LB-0715-20002   | Intra-Uterine SENSing using a battery-less, wireless intrauterine platform (U-SENSE)   |
| Not-Specified | MC_EX_MR/S015930/1 | Investigating retrotransposon-driven gene expression programmes in early development   |
| Female-based  | 17/116/01          | Letrozole or Clomifene, with or without metformin, for ovulation induction in women with polycystic ovary syndrome: a 2x2 factorial design randomised trial (The LOCI trial) |
| Female-based  | 15/143/01          | Medical treatment of heavy menstrual bleeding in primary care: Long term follow up of ECLIPSE trial cohort   |
| Female-based  | MR/P020283/1       | Menstrual health interventions and school attendance in Uganda (MENISCU-2)   |
| Female-based  | MR/P00265X/1       | MICA: CB2 agonists as a novel treatment for women with endometriosis-associated pain   |
| Male-based    | EP/P013651/1       | Modelling sperm-mucus interactions across scales   |
| Male-based    | MR/S021248/1       | MOLECULAR MECHANISMS OF MEIOTIC RECOMBINATION  |
| Not-Specified | MR/N022556/1       | MRC Centre for Reproductive Health at the University of Edinburgh  |
| Female-based  | MR/M009238/2       | Neuroinflammation in endometriosis: macrophages behaving badly?  |
| Female-based  | MR/R013454/1       | Novel methods for optimising health systems payment for performance interventions to improve maternal and child health in low-resource settings                              |
| Male-based    | BB/P001564/1       | Nucleosome positioning and transcriptional regulation in Drosophila differentiated cells   |

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|               |                 |   |
|---------------|-----------------|---|
| Male-based    | MR/P011799/1    | Paternal obesity-associated DNA methylation: an investigation into its reproducibility, reversibility and association with fetal growth restriction   |
| Female-based  | EP/S031561/1    | Peptide-mimetic hydrogels as a long-acting multipurpose drug delivery platform for combined contraception and HIV prevention  |
| Female-based  | MR/N006089/1    | Point-of-care testing and treatment of sexually transmitted infections to improve pregnancy outcomes in resource-limited, high-burden settings  |
| Male-based    | MR/S017151/1    | Protecting spermatogonial stem cells from chemotherapy-induced damage for fertility preservation in childhood cancer  |
| Female-based  | MR/R022194/1    | Puberty health interventions to improve menstrual health and School attendance among Gambian adolescents (MEGAMBO).   |
| Male-based    | EP/N021096/1    | Rapid Sperm Capture   |
| Female-based  | NIHR127280      | Recurrence of Endometriosis: a randomised controlled trial of clinical and cost effectiveness of Gonadotrophin Releasing Hormone Analogues with add back hormone replacement therapy versus repeat Laparoscopic surgery (REGAL trial)                       |
| Female-based  | MR/R008574/1    | Regulation of meiotic chromosome segregation by post-translational modifications  |
| Not-Specified | 16/95/01        | REMEDY: Randomised Evaluation of Management of sExual DYsfunction   |
| Not-Specified | BB/N018680/1    | Sex-determining mechanisms in the chick   |
| Not-Specified | BB/N018672/1    | Sex-determining mechanisms in the chick   |
| Not-Specified | MR/P011535/1    | Sex-specific disease aetiology from developmental steroid insults: mechanistic understanding and biomarker development towards disease prevention.  |
| Female-based  | NIHR128137      | STOP-OHSS (Shaping and Trialling Outpatient Protocols for Ovarian Hyper-Stimulation Syndrome): A feasibility study and randomised controlled trial, with internal pilot, to assess the clinical and cost-effectiveness of earlier active management of OHSS |
| Not-Specified | MR/N000188/1    | Structures and mechanism of BRCA2 in meiotic recombination  |
| Male-based    | PDF-2017-10-098 | Targeted caloric restriction to improve sperm quality in obese men with infertility   |
| Male-based    | 17/68/01        | Testosterone Effects and Safety in Men with Low Testosterone levels (TESTES): An evidence synthesis and economic evaluation   |
| Not-Specified | BB/S003681/1    | The Flux Capacitor: How mitochondria modulate metabolic flux and gene expression  |
| Female-based  | BB/T001542/1    | Understanding hyaluronan crosslinking mechanisms in ovulation and inflammation: CryoEM structural and interaction analysis of HC-HA/PTX3 complexes  |
| Female-based  | BB/T001631/1    | Understanding hyaluronan crosslinking mechanisms in ovulation and inflammation: CryoEM structural and interaction analysis of HC-HA/PTX3 complexes  |
| Not-Specified | NE/S011188/1    | Understanding the role of selection at the gametic level in adaptation to changing environments   |
| Female-based  | BB/S002995/1    | Unravelling the causes of declining uterine function with age   |
| Male-based    | BB/S008039/1    | Why is the highly conserved splicing regulator protein Tra2b essential for spermatogenesis?   |
| Female-based  | MR/N015177/1    | Women's reproductive health and its relation to diabetes and cardiovascular health.   |
| Female-based  | MR/N015177/2    | Women's reproductive health and its relation to diabetes and cardiovascular health.   |

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|               |                  |  |
|---------------|------------------|--|
| Female-based  | PB-PG-0815-20009 | A mixed methods evaluation of online provision of oral contraceptives to measure: validity of self-reported biometric data; essential information transfer and user experience of self-measurement and submission of biometric data. |
| Not-Specified | BB/S001255/1     | A novel mechanism underlying GnRH pulse generation by KNDy neurones  |
| Not-Specified | BB/S000550/1     | A novel mechanism underlying GnRH pulse generation by KNDy neurones  |
| Female-based  | 15/113/01        | A randomised controlled trial to determine the effectiveness of bridging from emergency to regular contraception: The 'Bridge-it' study  |

Supplementary Table VI – Research project titles from the UKRI and NIHR (UK) funding agencies. Some projects titles are repeated; however they would have separate grants awarded with different project IDs. Further information on each research project can be found in the UKRI and NIHR Dataset\_EG\_CDJ\_CLRB.



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**Supplementary Table VII – Research Project Titles from US Funding Agencies**

| Research Group | Project Reference          | Research Study Title  |
|----------------|----------------------------|---|
| Female-based   | 1R01HD100318-01            | 3/4: Pre-IVF Treatment with GNRH Antagonist in Women with Endometriosis - A prospective double blind placebo controlled trial (PREGNANT)                                      |
| Male-based     | 1R03HD087429-01A1          | A genome-wide drosophila RNA1 screen for regulators of centrosome reduction   |
| Male-based     | 1R21HD092828-01            | A home-based, rapid, sensitive semen analyser   |
| Female-based   | 1R01ES026964-01            | A longitudinal study of endocrine disrupter mixtures and reproductive aging   |
| Female-based   | 1R21HD090242-01            | A mouse model to demonstrate the impact of myometrial FSHR on fertility   |
| Female-based   | 1R01ES028923-01A1          | A preconception cohort study of air pollution, fertility, and miscarriage   |
| Not-Specified  | 1F32HD095620-01            | A role for hypothalamic melanocortin 3 receptors in integrating energy state with reproductive physiology   |
| Male-based     | 5R01HD091068-03            | A system for culturing mammalian spermatogonial cells   |
| Male-based     | 1R01HD095841-01            | Accumulation, storage, and release of sperm in the oviduct  |
| Male-based     | 1R01HD098039-01            | ALDH1A/A2 inhibitors for male contraception   |
| Male-based     | 1R61HD099743-01            | Allosteric cdk2 inhibitor discovery and development for male contraception  |
| Female-based   | 1F32HD090854-01A1          | An ovary-on-a-chip for understanding early folliculogenesis and reproductive toxicology in a large mammalian model  |
| Female-based   | 1U54HD096957-01            | Antibody-based contraceptive MPTS: preclinical and clinical research  |
| Male-based     | 1F31HD089693-01A1          | Assessing microenvironment and endothelial cell instruction of testis function  |
| Female-based   | 1R01HD096266-01            | Biological role of uterine glands in pregnancy  |
| Not-Specified  | 275201500002I-4-27500002-1 | Biological testing facility - maintenance of existing non-human primate colony  |
| Female-based   | 1R01AT008824-01A1          | Botanicals derived progestins and their impact on women's health  |
| Male-based     | 1R01HD096745-01A1          | Calcium signaling nanodomains in sperm motility and fertility   |
| Not-Specified  | 1R44HD097063-01            | Capsule-intravaginal ring for sustained release of antibodies for non-hormonal contraception and vaginal protection against HIV   |
| Not-Specified  | 1R35GM118066-01            | Causes and consequences of aneuploidy   |
| Female-based   | 1R01HD092550-01            | Causes and consequences of mitochondrial dysfunction in oocytes and cumulus cells   |
| Female-based   | 275201300019I-0-27500005-1 | CCTN-pharmacokinetic/pharmacodynamic evaluation of levonorgestrel butanoate for female contraception  |
| Male-based     | 1R15HD096759-01A1          | Cell-type specific inactivation of sumoylation during mouse spermatogenesis   |
| Male-based     | 1F32HD086986-01            | Chromatin dynamics, transcriptional activators and repressors in transition from proliferating progenitors to terminal differentiation during adult stem cell differentiation |
| Female-based   | 1R01GM123048-01A1          | Chromatin expulsion by the DNA replication licensing factor orc4 during asymmetric cell division in meiosis and differentiation   |
| Male-based     | 1R01GM123643-01            | Circumventing the blood-testis barrier  |
| Female-based   | 1F30HD085652-01A1          | Compartmental adrenomedullin signalling in the uterus during implantation   |

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|               |                           |   |
|---------------|---------------------------|---|
| Male-based    | 1R21HD090371-01A1         | Comprehensive mapping of mouse testis cell types and spermatogenic stages by single-cell rna sequencing                         |
| Male-based    | 1R01GM127379-01A1         | Control of spermatogonial stem cell formation   |
| Female-based  | 1R61HD099750-01           | Copper intravaginal contraception   |
| Not-Specified | 1R21HD098621-01A1         | Correction of endocrine disruptor-induced transgenerational epimutations by CRISPR-DCAS9  |
| Male-based    | 1P01HD087157-01A1<br>8120 | Crispr/cas9 and Small Molecules for Targeting Sperm Function and Fertilization  |
| Male-based    | 1R01GM123512-01A1         | Deciphering Pachytene piRNA Function  |
| Male-based    | 1R03HD093990-01A1         | Defining Mechanisms of Pp1 Phosphatase Specificity and Function Required for Male Fertility                                     |
| Female-based  | 1F31HD097830-01           | Defining the Neurophysiologic Mechanisms Engaged by Estradiol Feedback in Regulating Reproductive Neuroendocrine Function       |
| Not-Specified | 1R15HD084253-01A1         | Defining the Novel Role for the Rna Binding Protein Etr-1 in C.elegans Gametogenesis  |
| Male-based    | 1R01OD028223-01           | Derivation of Functional Spermatogonia Stem Cells From Rhesus Macaque Ipscs   |
| Male-based    | 1R01ES030942-01           | Determining How Preconception Exposure to Phthalates Impacts Sperm Function, the  |
| Female-based  | 1R21ES026454-01A1         | Detrimental Effects on Female Reproduction of in Utero and Neonatal Exposure to Common Phthalates DEHP and Its Replacement DINP |
| Male-based    | 1R21HD092700-01           | Developing an Animal Model to Identify the Role of the Sperm Centriole in Fertility   |
| Female-based  | 1R61HD099742-01           | Developing Modulators of the Sperm-specific Potassium Channel Slo3 for Contraception  |
| Female-based  | 1R43HD094454-01A1         | Development of a Biologic for Non-hormonal Contraception  |
| Male-based    | 1R21HD083616-01A1         | Development of a Zebrafish Model for Selenoprotein Synthesis and Function   |
| Male-based    | 1R61HD099720-01           | Development of Allosteric Hipk4 Inhibitors as Non-hormonal Male Contraceptives  |
| Female-based  | 1R21HD092739-01           | Development of New Therapeutic Strategies for Endometriosis   |
| Not-Specified | 1R56HD095629-01           | Development of Novel Sperm-binding Antibodies   |
| Not-Specified | 1R01HD084380-01A1         | Developmental Epidemiological Study of Children Born Through Reproductive Technology (Descrt)                                   |
| Not-Specified | 1R21ES024854-01A1         | Dioxin and Estradiol Regulation of Proteins Through Cugbp2  |
| Not-Specified | 1R01GM121688-01           | Dissecting the Origins of a Complex Reproductive Trait: Nematode Self Fertility   |
| Male-based    | 1R43HD097820-01           | Drug Interactions in Vitro for Ep055: a Non-hormonal Male Contraceptive   |
| Female-based  | 1R01HD091848-01A1         | Dynamic Regulation of the Ovarian Reserve   |
| Male-based    | 1F32GM130006-01           | Elucidating the Role of Small Rna Pathways in Heat-stress Induced DNA Damage During Spermatogenesis                             |
| Male-based    | 1F30HD097961-01           | Elucidating the Role of Tcf21+ Mesenchymal Cells in Testis Tissue Homeostasis and Regeneration                                  |
| Male-based    | 1R21ES026778-01A1         | Embryonic Inheritance of Sperm Methylome After Adult Exposure to Phthalates   |
| Female-based  | 1R01ES026998-01A1         | Environmentally Relevant Phthalate Exposures and Ovarian Function   |
| Male-based    | 1R01GM122776-01A1         | Epigenetic Regulation of Gene Expression During Spermatogenesis   |
| Male-based    | 1F32HD086939-01A1         | Epigenetic Regulation of Histone Eviction in Spermatogenesis  |

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|               |                   |   |
|---------------|-------------------|---|
| Female-based  | 1F32HD095618-01   | Epithelial Regeneration in the Adult Oviduct  |
| Male-based    | 1F32HD097932-01A1 | Examining the Androgenic and Progestational Effects of Novel Androgens for Male Contraception               |
| Male-based    | 1R01HD094698-01A1 | Exploring Vascular-mesenchymal Interactions in the Stem Cell Niche  |
| Not-Specified | 1R01HD089932-01A1 | Fa DDR Pathway in Germ Line Integrity   |
| Male-based    | 1R21HD094322-01   | Feasibility of in-home Semen Testing in a North American Preconception Cohort Study                         |
| Female-based  | 1R03HD097262-01   | Fertility Preservation in Women With Cystic Fibrosis Pre-lung Transplantation                               |
| Female-based  | 1R56HD086054-01A1 | FSH and IGF1R Signaling Crosstalk in Ovarian GCS  |
| Male-based    | 1R15GM126458-01   | Functional Analysis of MicroRNAs in C.elegans Spermatogenesis   |
| Male-based    | 1R01HD088412-01   | Functional Analysis of Novel Testis-expressed Secreted and Transmembrane Proteins                           |
| Female-based  | 1R01ES029464-01A1 | Functional and Epigenetic Effects of Preconceptional EDCs on the Female HPG Axis                            |
| Not-Specified | 1P01HD087157-01A1 | Functional Genomics and Dec-tec to Identify Germ Cell-specific Contraceptives                               |
| Male-based    | 1R01HD095341-01   | Functional Genomics and Proteomics to Reveal Reproductive-tract Specific Proteins                           |
| Not-Specified | 1R01GM117155-01   | Functions of Polo-like Kinases During Mammalian Meiosis   |
| Male-based    | 1R01ES030722-01A1 | Genetic and Epigenetic Mechanisms of Infertility Caused by Endocrine Disrupting Chemicals                   |
| Female-based  | 1R01HD086175-01A1 | Genetic Interrogation of Conserved Follicular Factors for Matrix Metalloproteinase Regulation and Ovulation |
| Female-based  | 1R21HD087427-01A1 | Genetic Studies of the Kit Receptor Tyrosine Kinase in Primordial Follicle Activation                       |
| Female-based  | 1R01HD093778-01   | Genetics and Genomics of the Ovarian Reserve and Female Fertility   |
| Female-based  | 1R21HD087973-01   | Genome-wide Identification of Genes Required for Decidualization  |
| Female-based  | 1F31HD088053-01   | Genotoxic Effects of L1 Retrotransposition Trigger Oocyte Elimination During MPI                            |
| Not-Specified | 1R21AA024889-01A1 | Germ Cell Mediated Epigenetic Memory of Ethanol Exposure  |
| Female-based  | 4R00HD080742-03   | Greb1 Action in Endometrial Function and Dysfunction  |
| Male-based    | 1R21ES027117-01   | Histone Lysine Crotonylation in Paternal Epigenetic Inheritance   |
| Female-based  | 1R01HD093726-01   | Homeostatic to Reactive Hyaluronan Matrices in Ovarian Reproductive Aging                                   |
| Male-based    | 1R01ES025066-01A1 | Human Pesticide Exposure and Epigenetic Changes in Sperm DNA  |
| Male-based    | 1R03HD097433-01   | Identification of Genetic Factors Contributing to Germline Stem Cell Maintenance                            |
| Male-based    | 1R21HD086839-01A1 | Identification of Phospho-proteins Regulating Sperm Function  |
| Not-Specified | 1R01ES027921-01A1 | Identity, Mechanisms and Early Life Impacts of Transporter Interfering Compounds                            |
| Not-Specified | 1F32HD094500-01   | Improving Bovine Cloning Efficiency by Enhancing Reprogramming During Embryonic Genome Activation (EGA)     |
| Female-based  | 1R01HD089957-01   | Improving Emergency Contraceptive Effectiveness in Obese Women  |
| Male-based    | 1R01HD092084-01   | Improving Fertility Preservation in Boys With Cancer  |
| Not-Specified | 1R01EB027099-01   | In Vivo Analysis of Mammalian Fertilization   |

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|               |                           |   |
|---------------|---------------------------|---|
| Female-based  | 1R61AI136008-01           | Ind-enabling Preclinical Development of a Multipurpose Intravaginal Ring for the Prevention of Herpes, HIV and Unintended Pregnancy   |
| Female-based  | 2R44AI124815-02A1         | Ind-enabling Preclinical Development of a System for the Multipurpose Prevention of HIV and Unintended Pregnancy  |
| Female-based  | 4R00NR017191-02           | Influence of Diet, Iron Stores, and Toxic Metals on Uptakes and Effects on Uterine Fibroid Risk in African American Women   |
| Female-based  | 1R41HD100190-01           | Innovative 3d Printed Intravaginal Ring Anelleo-pro, the First Single Administration of Progesterone for Infertility  |
| Female-based  | 1R21HD097601-01           | Integrative Metabolism of Oocyte Development and Its Modulation by Maternal Diet  |
| Female-based  | 1R21ES026282-01A1         | Investigating Modes of Action of Glyphosate-induced Ovotoxicity   |
| Male-based    | 1F31GM117971-01           | Investigating the Functional Role of Zinc Fluxes During Sperm Activation  |
| Female-based  | 5F31HD096838-01           | Investigating the Role of an FSHB Enhancer in FSHB Expression and Polycystic Ovary Syndrome   |
| Male-based    | 3R01HD091068-03S1         | IPSC-derived Organoids to Study Testis Function   |
| Male-based    | 1R03HD094046-01           | Isolation of Viable Human Sperm From Failed Microsurgical Testicular Biopsies   |
| Male-based    | 1R03HD099412-01           | L1 Retrotansposition During Spermatogenic Failure   |
| Female-based  | 1R01HD093671-01           | Large-scale Studies in Emerge to Discover the Genetic Determinants of Uterine Fibroids  |
| Male-based    | 1R03HD090315-01           | Lifestyle and Psychosocial Determinants of Male Subfertility: a Prospective Study   |
| Male-based    | 1R01HD084353-01A1         | Linking Fertility-associated Gene Polymorphisms to Aberrant Sperm Phenotypes  |
| Female-based  | 1R61AI142687-01           | Long Acting Film Technology for Contraception and HIV Prevention (Latch)  |
| Male-based    | 1R44HD099040-01           | Low Cost, Automated Smartphone Based Assay for Semen Analysis   |
| Male-based    | 1R44HD093493-01           | Low-cost, Portable and Automated Semen Analysis Using Computational Microscopy for Home-based Testing of Male Wellness and Fertility  |
| Male-based    | 1R35GM119458-01           | Macrophage Regulation of the Spermatogonial Stem Cell Niche   |
| Male-based    | 1R01ES028214-01           | Male Preconception Phthalates and Offspring Embryo and Sperm Allele-specific Methylome Programming  |
| Male-based    | 1P01HD087157-01A1<br>8121 | Manipulation of Sperm-specific Proteases Using Genetic and Chemical Approaches  |
| Female-based  | 1R35GM131810-01           | Maternal Control of Germline Development  |
| Not-Specified | 1R35GM118092-01           | Mechanism and Regulation of Meiotic Recombination   |
| Not-Specified | 3R01DK047320-22S2         | Mechanism of Selenoprotein Synthesis  |
| Female-based  | 1R01GM124519-01A1         | Mechanisms Driving the Transition From Oocyte to Embryo: the Role of the mRNA Decay Activator Zfp3612   |
| Female-based  | 1F30HD100126-01           | Mechanisms Linking Global Transcriptional Silencing and Zygotic Gene Activation During the Oocyte-to-embryo Transition in Mammals   |
| Male-based    | 4R00HD081204-02           | Mechanisms of a Novel Actin Related Protein in Male Gametes Ensuring Fertility  |
| Not-Specified | 1R01ES027487-01           | Mechanisms of Memory of Environmental Exposure: Determining the Role of Histone Modifications in Regulating Transgenerational Behavior Effects Caused by Environmental Chemical Exposure. |

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|               |                   |   |
|---------------|-------------------|---|
| Not-Specified | 1R15HD095735-01   | Mechanisms Underlying Telomere Function in Germ Cell Development  |
| Female-based  | 1R03HD087528-01A1 | Membrane Estrogen Receptor 1 Mediation of Epigenetic Effects of Estrogen  |
| Male-based    | 1R01HD093827-01A1 | Membrane Lipid Regulation of Calcium Channels in Sperm.   |
| Female-based  | 1R01HD087402-01A1 | Metabolic Events Controlling Ovarian Steroidogenesis  |
| Female-based  | 1R01HD092263-01   | Metabolic Regulators of Corpus Luteum Function  |
| Male-based    | 1R01GM132490-01   | Mitochondria-anchored Protein Complexes in piRNA Biogenesis and Function  |
| Female-based  | 1F32HD095550-01   | Modelling Human Embryonic Aneuploidy Using Pre-implantation Bovine Embryos  |
| Female-based  | 1F30AG058387-01A1 | Modelling Ovarian Ageing Phenotype in Mechanically Tuned 3d Matrices  |
| Female-based  | 5F30DK108561-02   | Molecular and Cellular Changes in the Peritoneal Surface Mesothelium During Adhesion Formation  |
| Female-based  | 1R21HD094096-01   | Molecular Identity of Maternal Regulators of the Egg to Embryo Transition   |
| Male-based    | 1R03HD098314-01A1 | Molecular Marker for Centriole Remodelling in Human Reproduction  |
| Female-based  | 1R35GM122580-01   | Molecular Mechanisms of the Maternal to Zygotic Transition  |
| Female-based  | 1R43HD097720-01   | Multi-center Prospective Study Assessing a Panel of MicroRNAs as a Non-invasive Test for Endometriosis  |
| Female-based  | 1R01HD086100-01A1 | Neuroendocrine Regulation of Reproduction by Glucocorticoids  |
| Female-based  | 1R01HD097675-01A1 | Neurotensin: a Novel Mediator of Ovulation  |
| Female-based  | 1R61HD099747-01   | Nonhormonal Contraceptive Intravaginal Ring Based on High Valency Anti-Sperm Antibody Constructs  |
| Female-based  | 1R43HD097941-01   | Non-hormonal Contraception Based on Vaginal Delivery of Multimeric Sperm-binding Antibodies   |
| Female-based  | 1R03HD098441-01   | Novel Reverse Genetics Approach to Probe Cytoskeletal Functions in Mammalian Oocytes  |
| Male-based    | 1R01HD090007-01   | Origin and Functional Significance of the Spermatogonial Stem Cell Transcriptome Barcode  |
| Female-based  | 1R21HD094983-01   | Oxygen as a Potential Regulator of Follicle Quiescence in the Primate Ovary   |
| Female-based  | 1R03HD090624-01A1 | P21-activated Kinase as Regulator of Actin and Microtubules in Mammalian Oocytes  |
| Female-based  | 6R21HD080148-02   | Parous Mouse: a Unique Model to Define Uterine Receptivity Versus Nonreceptivity  |
| Male-based    | 1R01ES028298-01A1 | Paternal Preconception Phthalates and Reproductive Health - Potential Mediation Through Sperm DNA Methylation   |
| Female-based  | 1F32HD097939-01   | Paxillin as a Mediator of Non-classical Androgen Receptor Actions in Ovarian Follicles  |
| Not-Specified | 5R01HD086478-03   | Phenotyping Early Embryonic Lethal Knockout Mice to Identify Essential Genes With Previously Uncharacterized Roles in Pre-implantation Development, Gastrulation, Turning, and Placentation |
| Female-based  | 1K99ES028748-01   | Phthalate-induced Ovulatory Dysfunction in Women  |
| Female-based  | 4R00ES028748-03   | Phthalate-induced Ovulatory Dysfunction in Women  |
| Female-based  | 1R56ES025147-01A1 | Phthalates and Ovarian Toxicity   |
| Female-based  | 1R01ES028661-01A1 | Phthalates and Ovarian Toxicity   |
| Female-based  | 1R56ES025728-01A1 | Placental Molecule Secretions Measured in Early Pregnancy Are Targets of Endocrine Disruption and Are Indicators of Sex-specific Fetal Development  |



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|               |                   |  |
|---------------|-------------------|--|
| Female-based  | 1R43HD097944-01   | Plant-derived Molecular Condom as an on-demand Nonhormonal Female Contraceptive  |
| Not-Specified | 1R01HD083260-01A1 | Postnatal Plasticity in the GNRH System  |
| Female-based  | 1R43AI124815-01   | Preclinical Development of a Multipurpose Intravaginal Ring for the Prevention of HIV and Unintended Pregnancy   |
| Female-based  | 1R01HD100336-01   | Pre-IVF Treatment With a GNRH Antagonist in Women With Endometriosis - a Prospective Double Blind Placebo Controlled Trial (Pregnant) - Application 1/4                  |
| Female-based  | 1R01HD100329-01   | Pre-IVF Treatment With a GNRH Antagonist in Women With Endometriosis - a Prospective Double Blind Placebo Controlled Trial (Pregnant) - Application 4/4                  |
| Female-based  | 1R01HD100343-01   | Pre-IVF Treatment With a GNRH Antagonist in Women With Endometriosis - a Prospective Double Blind Placebo Controlled Trial 2/3   |
| Female-based  | 1R01HD099487-01   | Primary Ovarian Insufficiency: Etiology and Comorbid Disease   |
| Male-based    | 1R01HD095631-01   | Project One: Development and Testing of Hca Ivr  |
| Male-based    | 5R01HD095630-02   | Project Three: Assessing Effects of Anti-CD52G MABS on STD Pathogens in Semen  |
| Female-based  | 1R21HD091337-01   | Prospective Randomized Trial of Tranexamic Acid Versus Levonorgestrel Intrauterine System for the Treatment of Heavy Menstrual Bleeding in Women With Uterine Fibroids   |
| Female-based  | 1R01HD092499-01A1 | Regulation of Ca <sup>2+</sup> Influx in Mouse Oocytes and Eggs During Maturation and Fertilization to Improve Assisted Reproductive Technologies and Modulate Fertility |
| Not-Specified | 1R01GM123556-01A1 | Regulation of Developmental Potency by the Transposon Line1  |
| Male-based    | 1R35GM118052-01   | Regulation of Meiosis in Mice  |
| Female-based  | 1R15HD099859-01   | Regulation of Oocyte Development by Steroid Hormones   |
| Not-Specified | 1R01GM113001-01A1 | Regulation of Sex-specific Gonad Stem Cell Niche Development by Doublesex  |
| Male-based    | 1R03HD096176-01   | Regulation of Sperm Metabolism and Fertility by Calcineurin and Gsk3   |
| Male-based    | 1F31HD097928-01A1 | Replication-independent DNA Methylation Dynamics During Post-Testicular Sperm Maturation   |
| Male-based    | 1R01GM124024-01   | Requirements for Cytosolic Chaperones in the De Novo Folding of Septin Proteins  |
| Male-based    | 4R00ES025231-03   | Retinoic Acid Signaling Disruption by Phthalates in Human and Rodent Fetal Testis  |
| Male-based    | 1K99ES025231-01A1 | Retinoic Acid Signaling Disruption by Phthalates in Human and Rodent Fetal Testis  |
| Female-based  | 1R01HD098200-01   | Reversible Contraception by Selective Silencing of GNRH-II   |
| Female-based  | 1R01HD084478-01A1 | Risk Factors for Early Pregnancy Loss  |
| Male-based    | 1R01HD094546-01A1 | Rna Pol II Pausing Is Critical for Spermatogenesis and Male Fertility  |
| Not-Specified | 1R01GM125800-01   | Role of Chromosomally Tethered Proteasome in Chromosome Pairing and Meiotic Recombination  |
| Not-Specified | 1R01GM127569-01A1 | Role of GCNA in Preserving Genome Integrity and Fertility  |
| Female-based  | 1R01HD089495-01A1 | Role of Neuroestradiol in Regulation of the GNRH Surge   |
| Female-based  | 1R56HD093383-01A1 | Role of the DNA Helicase LSH in Female Meiosis   |
| Male-based    | 1R01HD093703-01A1 | Role of the Extracellular Matrix During Wolffian/epididymal Duct Morphogenesis   |
| Male-based    | 1R01HD094736-01A1 | Roles of X- and Y-palindromic Genes in Mammalian Fertility   |
| Female-based  | 1R44HD095724-01   | Safety, and Acceptability of a Non-hormonal Vaginal Ring   |
| Female-based  | 1R01HD097202-01A1 | Salt-inducible Kinase Regulation of Ovarian Granulosa Cells  |

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|               |                           |   |
|---------------|---------------------------|---|
| Female-based  | 1R01GM129478-01           | Sexual Identity Maintenance in <i>Drosophila</i> Female Germ Cells  |
| Female-based  | 1R44HD097750-01           | Sirt1 and Bcl6: Dual Biomarkers of Endometriosis and Endometrial Receptivity  |
| Not-Specified | 1R01HD095628-01           | Slo3 K Channel: a Novel Target for Contraception  |
| Female-based  | 1R61HD099748-01           | Smart Polymer Fibers for Tampon-like Nonsteroidal Contraceptive Devices   |
| Not-Specified | 1R15GM117548-01           | Specification of Meiotic Cohesin Function by Divergent Alpha-kleisin Subunits   |
| Male-based    | 1R44HD095355-01           | Sperm Sample Preparation for Point of Care Applications   |
| Female-based  | 1R21HD092009-01           | Stem Cell-derived GnRH Neurons: Optimization and Characterization   |
| Female-based  | 1R01HD088638-01           | Study of Ovarian Aging and Reserve in Young Women (Soar)  |
| Female-based  | 1R61HD099745-01           | Synthetic mRNA-mediated Reversible Immunocontraception  |
| Not-Specified | 1K99ES025280-01A1         | Systems Approach to Define AHR Ligand Toxicity on Reproductive System Development   |
| Male-based    | 1P01HD087157-01A1<br>8119 | Targeting Sperm-specific Proteins During Meiosis and Sperm Morphogenesis  |
| Male-based    | 1R61HD099722-01           | Targeting Testis-specific Ubiquitin-proteasome Pathways for Male Contraception  |
| Female-based  | 1R01HL134840-01           | Telomeres and Fecundity   |
| Female-based  | 1R01HD097087-01           | The Actions of Steroid Hormones on Oviduct Function   |
| Male-based    | 1R01ES028712-01           | The Effects of Environmental Exposures on Semen Quality and the Sperm Epigenome   |
| Female-based  | 1R03HD095098-01           | The Function of Progesterone Receptor in Human Ovarian Follicles  |
| Female-based  | 1F32HD098805-01           | The Homeodomain Transcription Factors, Six6 and Six3, in the Circadian Regulation of Reproduction                                   |
| Not-Specified | 7R21HD088792-02           | the Impact of Piwi Associated Transcripts in <i>Xenopus</i> Germ Cell Development   |
| Female-based  | 1R15HD087911-01           | The Interaction Between Nat2 Acetylase Status and Exposure to Tobacco Smoke on Ovarian Reserve and in Vitro Fertilization Outcomes. |
| Female-based  | 1R01HD091117-01A1         | The Oocyte's Progression Through Meiosis: Involvement of a Heart Disease-associated Protein   |
| Female-based  | 1R01HD096077-01A1         | The Role of FOS in the Ovary  |
| Male-based    | 1R03HD090306-01           | the Role of Transcription Factor S-sox5 in Male Fertility and Sperm Flagella Formation  |
| Female-based  | 1R21HD094293-01A1         | Timing Endometrial Receptivity  |
| Female-based  | 1R01HD098278-01           | Towards a Preclinical Model for Overcoming Infertility With Induced Pluripotent Stem Cells  |
| Female-based  | 3R01ES027051-02S1         | Transdisciplinary Approach to Rapidly Identify Reproductive Toxics in Pregnant Women and Newborns                                   |
| Male-based    | 1R03OH011540-01           | Transgenerational Work Exposures, EDCs and Male Fertility   |
| Male-based    | 1R44HD100256-01           | Translational Feasibility of an Oral, Non-hormonal, Male Contraceptive Pill   |
| Male-based    | 1R56AG052581-01A1         | Tumor Suppressors Mediate a Reduction in Male Gamete Quality With Aging   |
| Female-based  | 1R21ES028963-01A1         | Water Disinfection by-products and Female Fertility   |
| Male-based    | 1R01GM130691-01           | Y Chromosome Evolution  |

Supplementary Table VII - Research project titles from the NIH (US) funding agencies. Some projects titles are repeated; however they would have separate grants awarded under different project IDs. Further information on each research project can be found in NIH Dataset\_EG\_CDJ\_CLRB.

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**Supplementary Table VIII: The NIHR's Sum of Funding Awarded for the HRCS Health Categories**

| <b>HRCS Health Categories</b>             | <b>Total Funding Awarded (£)</b> |
|---|----------------------------------|
| <b>Mental Health</b>                      | 493,552,549                      |
| <b>Generic Health Relevance</b>           | 484,950,225                      |
| <b>Cancer and Neoplasms</b>               | 347,947,217                      |
| <b>Infection</b>                          | 275,265,348                      |
| <b>Cardiovascular</b>                     | 224,898,509                      |
| <b>Neurological</b>                       | 222,002,645                      |
| <b>Reproductive Health and Childbirth</b> | 216,618,019                      |
| <b>Oral and Gastrointestinal</b>          | 164,146,703                      |
| <b>Respiratory</b>                        | 146,665,215                      |
| <b>Metabolic and Endocrine</b>            | 129,821,105                      |
| <b>Musculoskeletal</b>                    | 126,596,631                      |
| <b>Stroke</b>                             | 121,450,341                      |
| <b>Injuries and Accidents</b>             | 119,415,772                      |
| <b>Renal and Urogenital</b>               | 108,827,444                      |
| <b>Skin</b>                               | 66,127,071                       |
| <b>Eye</b>                                | 63,433,235                       |
| <b>Inflammatory and Immune System</b>     | 54,122,033                       |
| <b>Blood</b>                              | 29,836,676                       |
| <b>Disputed etiology and other</b>        | 23,847,721                       |
| <b>Congenital Disorders</b>               | 18,740,901                       |
| <b>Ear</b>                                | 11,238,128                       |

Supplementary Table VIII - The NIHR's Total Funding Awarded for the 21 health categories of research and specialties as of April 1<sup>st</sup>, 2011. The present data is extracted from the NIHR's Open Data.



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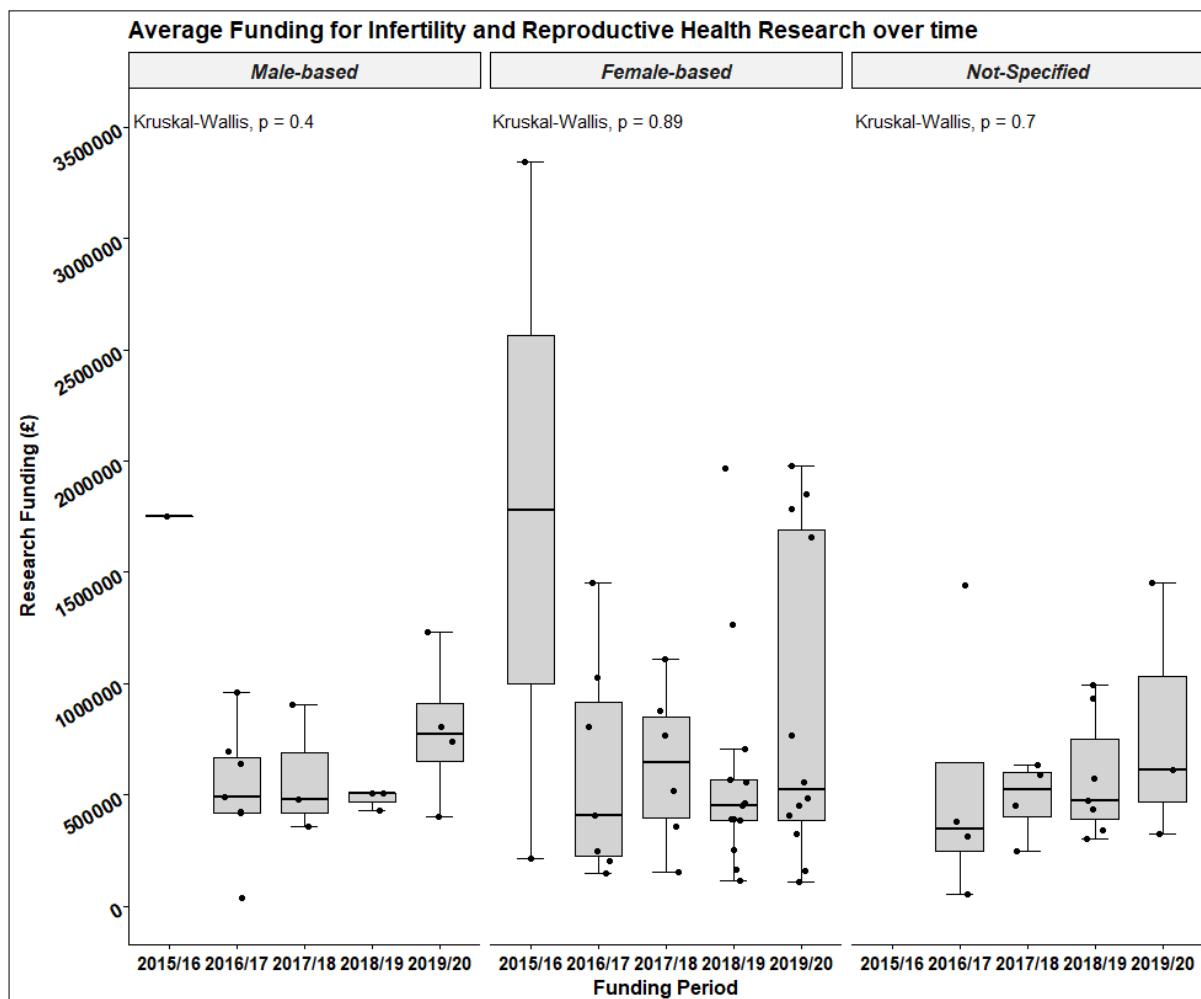
**Supplementary Table IX : Estimated Proportion of Funding to RCDC by the NIH against the NIH's Total Budget**

| RCDC                                   |               | Fiscal Years   |                |                |                |
|--|---------------|----------------|----------------|----------------|----------------|
|  |               | 2016           | 2017           | 2018           | 2019           |
| <b>Contraception/<br/>Reproduction</b> | Value (\$000) | 419,000        | 437,000        | 496,000        | 547,000        |
|  | (%)           | 1.85           | 1.82           | 1.91           | 1.94           |
| <b>Infertility</b>                     | Value (\$000) | 86,000         | 94,000         | 120,000        | 151,000        |
|  | (%)           | 0.38           | 0.39           | 0.46           | 0.54           |
| <b>Obesity</b>                         | Value (\$000) | 965,000        | 999,000        | 1,055,000      | 1,109,000      |
|  | (%)           | 4.26           | 4.16           | 4.07           | 3.94           |
| <b>Mental Health</b>                   | Value (\$000) | 2,454,000      | 2,717,000      | 3,010,000      | 3,296,000      |
|  | (%)           | 10.83          | 11.31          | 11.62          | 11.71          |
| <b>Total NIH Research Funding (\$)</b> |               | 22,649,752,290 | 24,031,670,764 | 25,906,788,735 | 28,143,252,479 |

Supplementary Table IX: The NIH fund 299 various research, conditions, and diseases categories (RCDC) and a project can fall under multiple RCDCs as the NIH does not budget research per category NIH, 2021). The estimated proportion of funding for the chosen categories of contraception/ reproduction, infertility, obesity, and mental health against the annual NIH total research grant funding between FY2016 to FY2019. The FY2020 was excluded from this table as only 2 projects were collected and would be incomparable. Value (\$000) refers to the estimated funding by the NIH RCDC Categorical Spending in millions. (%) is the calculated funding percentage or proportion for the RCDCs from the annual NIH Total Research Funding

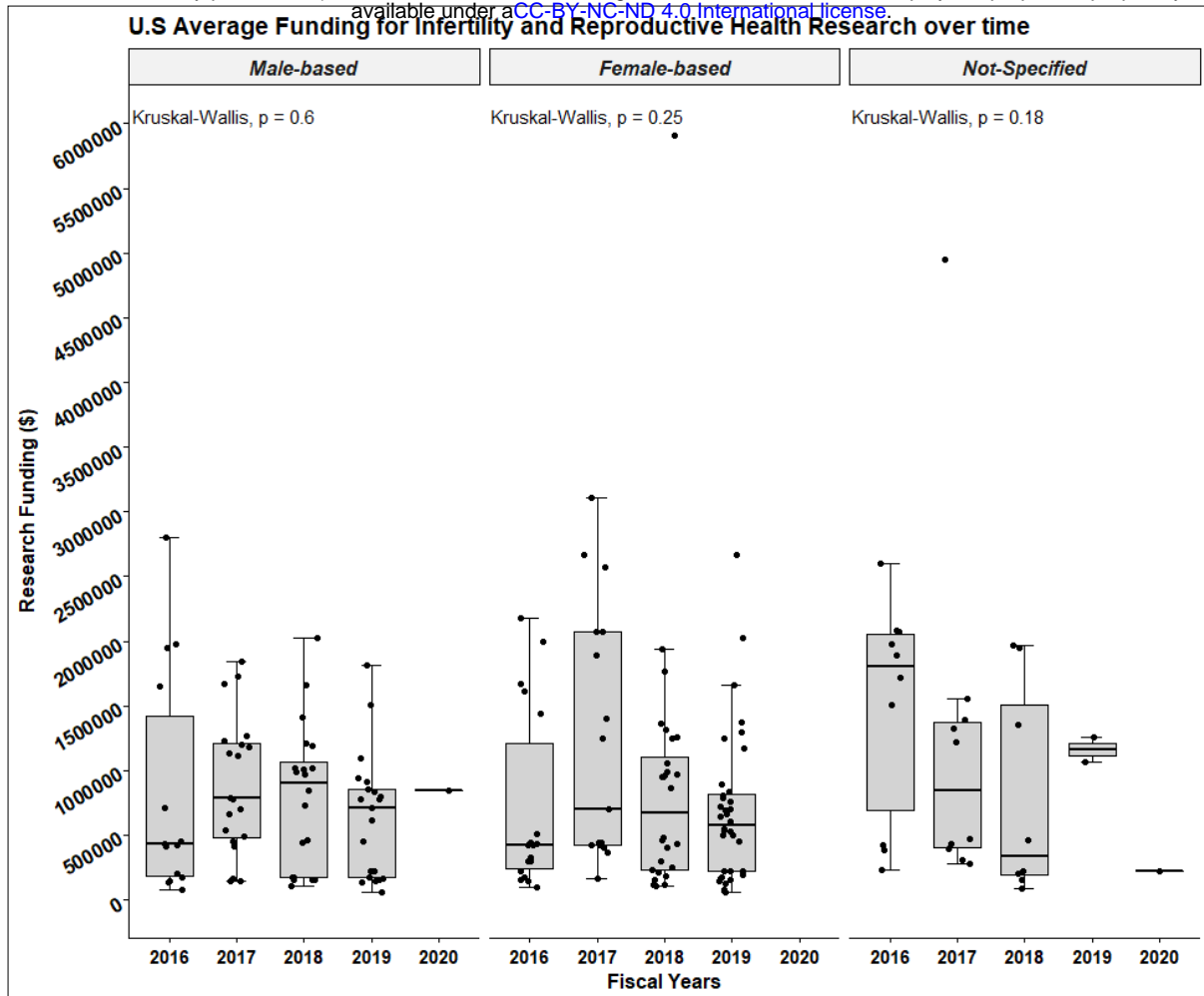
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### Supplementary Figures:



Supplementary Figure 1: The UK average funding across consecutive funding periods box-and-whisker plot with a 95% CI. 3 projects were collected between January 1<sup>st</sup> to March 31<sup>st</sup>, 2016, for the 2015/16 funding period, therefore many projects were not expected to be awarded funding. No statistically significant differences of funding variation were observed by the Kruskal-Wallis test over the consecutive funding periods of each research group. In the male-based group,  $P=0.39$  and  $\chi^2=4.08$  with 4 degrees of freedom. For the female-based group,  $P=0.89$  and  $\chi^2=1.1$  with 4 degrees of freedom. In the not-specified group,  $P=0.7$  and  $\chi^2=1.41$  with 3 degrees of freedom.

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Supplementary Figure 2: Box-and-whisker plot has a 95% CI for the funding awarded across the five consecutive FYs by the NIH institutes. In the FY2020, 2 projects were awarded funding between 1<sup>st</sup> October to 31<sup>st</sup> December 2019. The Kruskal-Wallis did not observe statistically significant differences of funding variation over the consecutive FYs of each research group. For the male-based group,  $P=0.59$  and  $\chi^2=2.76$  with 4 degrees of freedom. In the female-based group,  $P=0.25$  and  $\chi^2=4.12$  with 3 degrees of freedom. In the not-specified group,  $P=0.18$  and  $\chi^2=6.28$  with 4 degrees of freedom.