INTRODUCTION

According to international recommendations, healthy pregnant women should exercise moderately for 30 minutes or more per day to obtain the health benefits of physical activity. Studies suggest that exercise during pregnancy is associated with a lower risk of gestational diabetes, preeclampsia and low back pain as well as a more optimal pregnancy weight gain, fewer symptoms of depression after pregnancy, and a decreased risk of cesarean delivery. Furthermore, regular exercise during pregnancy seems to reduce the risk of macrosomia without increasing the risk of low birth weight. Intelligence is an advanced integrated neurodevelopmental measure of human brain function and childhood...
intelligence has also been shown to be associated with future morbidity and mortality.\textsuperscript{12-14} Knowledge about the association between exercise during pregnancy and long-term neurodevelopmental consequences in the offspring is very sparse.\textsuperscript{15-18} A few studies of exercise during pregnancy and offspring neurodevelopment indicate that women who exercise may give birth to children with more favorable neurodevelopmental outcomes compared with sedentary women,\textsuperscript{15-17} whereas one study did not find an association.\textsuperscript{18} However, the studies are small with short-term follow-up.

Any beneficial (or detrimental) effects of physical activity during pregnancy on offspring neurodevelopment is of major public health importance. We therefore set out to further study the association between regular maternal exercise during pregnancy and offspring intelligence in a large population of mothers of Danish young male conscripts.

2 | METHODS

We used information from women enrolled in the Aarhus Birth Cohort (ABC).\textsuperscript{19} All pregnant women who attend routine antenatal care at the Obstetrics Department, Aarhus University Hospital, Denmark, have been invited to participate in ABC since 1989. In Denmark, more than 97\% of all women attend the antenatal care program,\textsuperscript{20} which is free of charge.\textsuperscript{19}

Only women who speak Danish were included in the ABC. The pregnant women were asked to complete two questionnaires during the first trimester.\textsuperscript{20} The first questionnaire provided information on women's height, age, pre-pregnancy weight, alcohol consumption, cigarette smoking, and medical and reproductive history. The second questionnaire provided information on social class, education and occupation, and working conditions. The attending midwife at the delivery also collected information on gestational age at birth, parity, and weight and length of the child at birth.

Dedicated questions regarding leisure-time activities and sports were asked from July 1989 through November 1991 only. The women were asked to provide details on how many hours per week they participated in sports as well as their level of leisure-time physical activity according to the following four categories: sedentary activity (eg, reading and watching television), light activity (eg, light level of gardening more than 3 hours a week and table tennis), moderate activity (sports or heavy leisure-time activities for more than 3 hours a week, for instance running, swimming, and playing tennis), or heavy activity (competitive sports several times a week). Few women participated in competitive sports, and therefore, the two highest categories were merged. Thus, the leisure-time physical activities were categorized as sedentary, light, and moderate to heavy. The questions concerning leisure-time physical activity were developed by Saltin and Grimby in 1968\textsuperscript{21} and further validated by Saltin in 1977.\textsuperscript{22} These questions have been widely used in studies of physical activity, especially during the last decades.\textsuperscript{23}

The research protocol for the Aarhus Birth Cohort was approved by the regional committee for ethics and science (no. 1991/2060) and the Danish Data Protection Agency (no. 2012-41-1084). Informed consent was obtained from all participants. The follow-up of the sons was approved by the Danish Data Protection Agency (no 2014-41-2851).

2.1 | Intelligence data

The Børge Priens test is an intelligence test used at conscription in Denmark since the 1950s. All healthy Danish men must complete this test as part of a number of tests to evaluate their suitability for military service during the year they turn 18 years.\textsuperscript{24} About 10\% of Danish men are exempted, mainly because of medical documentation for various physical conditions. The test contains 78 items divided into four subtests; letter matrices, verbal analogies, number series, and geometric figures combined to a total score. The Børge Priens test takes around 45 minutes to complete and does not contain multiple-choices. The total score ranges from 0 to 78 points.\textsuperscript{24}

Data from eligible mothers from the ABC were linked to their sons’ information from the Danish Conscription Registry and the Børge Priens test scores using the unique personal identifier assigned to all Danish citizens at birth.

2.2 | Outcome

The primary outcome for this study was the Børge Priens test score which was analyzed as a continuous variable as well as a categorical variable; with low intelligence being defined as a low score defined as less than 10\% of the population score.

2.3 | Statistics

The association between maternal level of physical activity and male offsprings’ Børge Priens test score as a continuous variable was analyzed by linear regression analysis and as a categorical variable by logistic regression analysis. The reference group was women who reported a sedentary level of activity for leisure-time physical activity and women who reported no sports (corresponding to 0 hours of sports per week) for the variable of hours of sports activity per week. Missing information on physical activity, sons’ Børge Priens test score, and the covariates; maternal years in school, tobacco consumption, and alcohol consumption were imputed\textsuperscript{25} based on all valid variables in the dataset (Stata command \textit{mi impute}). Imputation was performed by chained equations with number of imputations set at 50.

Analyses were adjusted for maternal body mass index, maternal years in school, and smoking. These potential
confounders were chosen on the basis of a directed acyclic graph (Figure S1) relying on the knowledge about the association between the outcome and exposure of interest from the literature. The potential confounders were included as categorical variables (see Table 1 for categories used).

We performed sensitivity analyses including (a) complete case analyses for the total population, (b) restricted analyses based on mothers who delivered their sons at 37 weeks gestation or later, (c) restricted analyses based on sons who had a birth weight appropriate for gestational age at delivery,26 and (d) restricted analyses based on women who reported no smoking during pregnancy. Finally, we stratified analyses by mothers’ years of schooling categorized as less than 12 years and 12 years or more. For the latter analyses, we tested interaction by using a
likelihood ratio test that compared the main factor model with a model also including a two-factor interaction-term.

Point estimates from linear regression analyses are presented as mean differences with 95% confidence intervals (CI) and from logistic regression analyses as odds ratios (OR) with 95% CI. Statistical significance was defined as a two-sided $P$-value less than .05.

We used Stata version 15.0 software (StataCorp) for all statistical analyses.

3 | RESULTS

A total of 9053 women were included at Aarhus University Hospital between July 1989 and November 1991, and 8038 of these completed the questionnaires. These women gave birth to 4141 liveborn male infants, who were assessed for availability of intelligence data (Figure S2). A total of 4008 were registered at conscription, of these 3469 sons had a Børge Priens test score and 539 (13%) had the score imputed. A total of 3309 mothers had valid information on their level of physical activity, whereas maternal level of physical activity was imputed for 699 (17%) mothers. The total population comprised 4008 mothers and sons after multiple imputation (Figure S2).

Figure 1 shows the distribution of the Børge Priens test scores in the 3469 male conscripts. The median score was 44 points and the 10th percentile was equivalent to a score of 31 points. Pre-pregnancy body mass index, parity, years of schooling, alcohol intake, and smoking were associated with

### Table 2

<table>
<thead>
<tr>
<th>Leisure-time physical activity</th>
<th>Predicted distribution after MI (%)</th>
<th>Mean difference (points) intelligence score (95% CI)</th>
<th>Adjusted$^a$ mean difference (points) intelligence score (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sedentary</td>
<td>43</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Light</td>
<td>50</td>
<td>1.7 (0.9; 2.5)</td>
<td>1.1 (0.3; 1.8)</td>
</tr>
<tr>
<td>Moderate to heavy</td>
<td>7</td>
<td>3.2 (1.8; 4.6)</td>
<td>2.0 (0.7; 3.3)</td>
</tr>
<tr>
<td>Sports, h/wk</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>72</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>1-2</td>
<td>18</td>
<td>2.7 (1.8; 3.7)</td>
<td>1.5 (0.6; 2.5)</td>
</tr>
<tr>
<td>≥3</td>
<td>10</td>
<td>3.4 (2.1; 4.7)</td>
<td>1.8 (0.6; 3.1)</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; MI, multiple imputation.
$^a$Multivariable adjustment included maternal body mass index, years in school (<12 years vs. ≥ 12 years), and smoking (yes vs. no). All estimates were statistically significant with $P \leq .005$. 
both maternal leisure-time physical activity and weekly hours of sports during the first trimester (Table 1).

The unadjusted and adjusted association between maternal level of physical activity and their sons’ intelligence score is shown in Table 2. Adjusted linear regression analyses showed that women with a light and a moderate to heavy level of leisure-time physical activity had sons with a higher Børge Priens test score compared with sons of inactive women; mean difference in points 1.1 (95% CI 0.3; 1.8) and 2.0 (95% CI 0.7; 3.3), respectively, (test for trend $P < .01$). In addition, we found an association between hours of sports during pregnancy and the sons’ Børge Priens test scores: adjusted mean difference for sons of women who spent 1-2 h/wk on sports was 1.5 points (95% CI 0.24; 0.65) and for ≥3 h/wk 1.8 points (95% CI 0.24; 0.75) compared to sons of mothers with no sports activity during the week (test for trend $P < .01$). Results were similar in the complete case analyses (Table S1).

The unadjusted and adjusted association between maternal level of physical activity and their sons’ risk of having an intelligence score below the 10th percentile is shown in Table 3. Women with a higher level of leisure-time physical activity had sons with a lower risk of having a Børge Priens test score below the 10th percentile (Table 3). The adjusted odds ratio (aOR) for a low score was 0.66 (95% CI 0.49; 0.88) for light and 0.46 (95% CI 0.23; 0.93) for moderate to heavy compared with sedentary leisure-time physical activity (test for trend $P < .01$). The aOR for a low Børge Priens test score was 0.50 (95% CI 0.30; 0.83) and 0.62 (95% CI 0.35; 1.10) for sons of women who spent 1-2 and ≥3 hours on sports per week compared to women with no weekly sports activity (test for trend $P < .01$). Estimates were similar in the complete case analyses (Table S2).

Results from analyses restricted to women who delivered at 37 weeks’ gestation or later (Table S3), to sons who had a birth weight appropriate for gestational age at delivery (Table S4), and to women who reported no smoking during pregnancy (Tables S5) were similar to results of the primary analyses. We found no evidence of an interaction between maternal years in school and level of physical activity on sons’ intelligence score (Table S6).

### DISCUSSION

Compared to sons of physically inactive women, we found that a higher level of leisure-time physical activity as well as more weekly hours of sports during pregnancy was associated with a significantly higher intelligence score in early adulthood in sons. Moreover, sons of physically active women had a significantly lower risk of a low intelligence score (less than the 10th percentile for this population) compared with sons of physically inactive women.

Our study results are supported by previous studies of children until the age of 5 years. Clapp et al. found that exercise during pregnancy was associated with a better score on the Wechsler Preschool and Primary Scale of Intelligence and improved oral language skills in 5-year-olds compared with offspring of women not exercising during pregnancy. In contrast, a study by Hellenes et al. found no significant differences in neurodevelopmental outcomes at 18 months of age in offspring assessed by Bayles Scales of Infant Development.

Our results are biologically plausible. Pregnant women who exercise seem to develop a placenta with a higher villous and intervillous space volume.
exercise increases cardiac output, and exercise has been proposed to stimulate angiogenesis through an increase in the proangiogenic Vascular Endothelial Growth Factor and Placental Growth Factor and a reduction in the anti-angiogenic soluble fms-like tyrosine kinase-1. In combination, these changes suggest that the pregnant women who exercise may have an increased placental blood flow at rest. Thus, exercise would increase oxygen and nutritional supply to the placenta which in turn may provide more favorable conditions for fetal organ growth including cerebral growth. This might eventually lead to an improvement in neurodevelopment, including a higher intelligence in adolescence and early adulthood.

Another biological explanation would be a more direct effect from maternal exercise during pregnancy on fetal brain development; a study performed on pregnant mice effect from maternal exercise during pregnancy on fetal neurodevelopment, including a higher intelligence in adulthood. This might eventually lead to an improvement in neurodevelopment, including a higher intelligence in adolescence and early adulthood.

The strengths of our current study include the large sample size of more than 4000 women and their sons. The Børge Priens test has a high correlation with the full-scale Wechsler Adult Intelligence Scale (WAIS), indicating that the test is a good measure of intelligence. The test is not publicly available in Denmark, and it is therefore impossible to study the test questions in advance. However, the young men’s motivation for aiming at good test results may be biased by the aim for being selected for military service. However, it seems unlikely that this aim would be associated with the mother’s physical activity level during pregnancy, and any bias would most likely be non-differential, that is biased toward the null hypothesis of no association.

Data on maternal physical activity were collected during pregnancy in 1989-1991 before any national recommendations to encourage pregnant women to exercise. Thus, the validity of the self-reported levels of physical activity was not compromised by women reporting according to recommendations rather than to the actual level of physical activity. Furthermore, the recall of physical activity was independent of the intelligence of the sons, since the information was provided during pregnancy. Our exposure consisted of two items thought to be measures of physical activity. The questions related to leisure-time physical activity have been validated previously and were found to correlate to maximal oxygen uptake, although validation was carried out in a non-pregnant population.

Some information on physical activity, potential confounders, and the Børge Priens test score were missing. We used imputation in order to not have selection bias from lack of cases with one or more missing variables. Women without information on physical activity had a higher body mass index, and they were more likely to be smokers compared with the women who provided the information. Both these factors have been shown to be associated with a lower level of education. Accordingly, our data may not be missing entirely at random and this requirement for multiple imputation may be violated to a certain extent. However, results from the complete case analyses were similar to those from the primary results based on the imputed dataset.

Some residual confounding may also exist. Maternal intelligence has been shown to correlate strongly with offspring intelligence, and if maternal intelligence is also associated with physical activity during pregnancy our results may be confounded due to lack of appropriate control for this variable. We adjusted for maternal schooling which may be considered as a proxy variable for intelligence. Overall, the evidence of an association between a higher level of physical activity and intelligence in adults is ambiguous.

The Aarhus Birth Cohort only included non-Hispanic, white pregnant women, and therefore, the results of the study may not be applicable to other or mixed populations of pregnant women. Furthermore, we are unable to generalize results to daughters since we only had access to data on male conscripts. In addition, some young men do not attend conscription based on their medical conditions. This may hamper the generalizability of our results, which may only apply to sons who are at good health as young men. Information on characteristics previously suggested to be associated with intelligence, such as breastfeeding and early-life stimulation unfortunately was unavailable in the cohort, and our analyses could therefore not be adjusted for these variables.

In conclusion, we found that a higher level of physical activity during early pregnancy was associated with a higher intelligence score in early adulthood in sons and with a lower risk of having intelligence below the 10th percentile for the population studied.

5 | PERSPECTIVES

We found that sons of women who were physically active during the first trimester of pregnancy were less likely to have a low intelligence score compared with sons of physically inactive women. These results, which are based on follow-up until the age of 17-20 years, are supported by previous observational studies with follow-up of the offspring until early childhood. Although these findings might add to
the notion that women should be advised to continue exercising during pregnancy, evidence of a possible cause-effect relationship is needed. Therefore, to pursue a clarification of the potential causal relation between sports in pregnancy and intelligence in the offspring, longer-term follow-up of a clinical trial randomizing more sedentary women to do various sports during pregnancy is warranted before women can be advised to continue exercising during pregnancy to improve neurodevelopment in their offspring.

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