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# Secundum atrial septal defect closure in adults in the UK

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## Aims

To examine determinants of access to treatment, outcomes, and hospital utilization in patients undergoing secundum atrial septal defect (ASD) closure in adulthood in England and Wales.

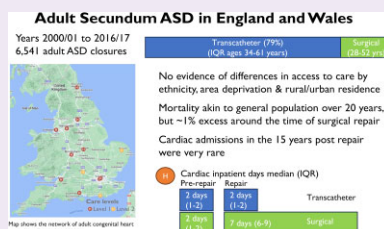
## Methods and results

Large retrospective cohort study of all adult patients undergoing secundum ASD closures in England and Wales between 2000/01 and 2016/17. Data were from population-based official data sets covering congenital heart disease procedures, hospital episodes, and death registries. Out of 6541 index closures, 79.4% were transcatheter [median age 47 years, interquartile range (IQR) 34–61] and 20.6% were surgical (40 years, 28–52). The study cohort was predominantly female (66%), with socioethnic profile similar to the general population. Mortality in hospital was 0.2% and at 1 year 1.0% [95% confidence interval (CI) 0.8–1.2%]. Risk of death was lower for transcatheter repairs, adjusting for age, sex, year of procedure, comorbidities, and cardiac risk factors [in-hospital adjusted odds ratio 0.09, 95% CI 0.02–0.46; 1-year adjusted hazard ratio 0.5, 95% CI 0.3–0.9]. There was excess mortality 1 year after ASD closure compared with matched population data. Median (IQR) peri-procedural length of stay was 1.8 (1.4–2.5) and 7.3 (6.2–9.2) days for transcatheter and surgical closures, respectively. Hospital resource use for cardiac reasons started the year before repair (median two inpatient and two outpatient-only days) and decreased post-repair (zero inpatient and one outpatient days during the first 2 years).

## Conclusion

This national study confirms that ASD closure in adults, by surgical or transcatheter methods, is provided independently of ethnic or socioeconomic differences, it is low (but not no) risk, and appears to reduce future cardiac hospitalization even in older ages.

## Graphical Abstract



## Keywords

Atrial Septal Defect (ASD) • Adult Congenital Heart Disease (ACHD) • Grown Up Congenital Heart (GUCH) • Mortality • Hospital utilization • Equal access to health care

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congenital cardiac surgery,<sup>19</sup> their data quality being acceptable from April 2009 onwards.

Age of death was primarily sourced from NCHDA and complemented with the linked ONS life status. The age at which a patient was most recently known to be alive was sourced from the linked ONS life status and, if not available (no linkage to ONS), the latest age from the most recent LAUNCHES QI record was used. Ages were available with four decimal places but in many cases had been derived assuming noon as time of the day, resulting in a 12-h ambiguity in ages. 'Spells' of care were defined as combinations of time-overlapping series of events, allowing up to 24-h gap between events due to many records using only dates and not times of day for admission and discharge.<sup>11</sup> Hospital utilization was available before, during, and after the repair spells, with different follow-ups for each patient and data source considered. Overall service utilization was averaged over yearly intervals pre- and post-repair spell, using all patients with data in the interval of interest to calculate its average. Inpatient spells were defined as those containing an inpatient admission, and outpatient spells were defined as those containing an attended outpatient appointment with no inpatient record. Total number of days spent at hospital was calculated, counting one full day for outpatient spells, and for visualization purposes rounding up inpatient spell length of stay (LoS) to the nearest integer. Cardiac service utilization was identified using the existence of any NCHDA records and information from the HES APC health research groups and the HES OP treatment speciality field. The identification method was detailed in a previous LAUNCHES-related publication (see 'Cardiac contacts' in [Supplementary material](#)).<sup>20</sup>

## Descriptive analysis

Baseline demographics are presented for the whole group and by type of repair. Categorical characteristics (sex, ethnicity, English deprivation quintile, and rural/urban residence) are described as counts and percentage by group. Comparisons to the demographics of the general population were possible on years when the National Census was run.<sup>16</sup> Age is aggregated in three age groups: 16–39 years, 40–64 years, and 65 years and older.

We use bar and line plots to represent: trends in adult ASD repair by era overall and by type of repair; age at repair; quintile of deprivation and association with type of repair and ages at repair; urban/rural residence compared with Census counts for England and Wales<sup>16</sup>; centre variation in numbers and type of repair (limiting the analysis to centres with at least 150 repairs over the period of study); and trends by era in type of repair by centre.

## Event analysis

Cumulative mortality over time [average and 95% confidence interval (CI)] was estimated using Kaplan–Meier (KM), separately by type of repair for all ages and by age groups. Comparisons of survival estimates between transcatheter and surgical repairs were performed using logistic regression (for in-hospital mortality) or Cox regression (for long-term mortality). Estimates were adjusted for age at repair, sex, year of repair, congenital comorbidities, and pre-operative acquired comorbidities and additional cardiac risk factors.<sup>19</sup> This was done directly or using a logistic regression propensity score in case of a low number of events; the number of propensity score matches was selected roughly as the sample proportion of transcatheter per surgical index repairs. The mortality results for each of the eight groups were compared with average mortality in the general population<sup>17</sup> by assessing the overlap between KM CI estimates and average mortality of the matched general population. These results adjusted for age, year of birth, and sex: ASD patients were matched to the general population data on those three variables. Details on length of survival follow-up are provided in the main text and numbers at risk over time are shown within the KM figures. Summary data underlying the figures and comparisons to the matched general population are given in the [Supplementary material](#). Hospital utilization pre-/peri-/post-repair

is shown using box and bar plots, by type of repair and age groups, distinguishing between inpatient/outpatient days and non-cardiac/cardiac reasons. Comparisons of median LoS at repair and 1 year before/after repair were performed using median regression adjusting for age at repair, sex, year of repair, congenital comorbidities, and pre-operative acquired comorbidities and additional cardiac risk factors. Follow-up time details are provided for hospital utilization in the main text and numbers supporting the main text and figures are found in the [Supplementary material](#).

All data analysis was carried out using Stata/MP version 17.0. This study meets all five of the CODE-EHR minimum framework standards for the use of structured health care data in clinical research, with four out of five standards meeting preferred criteria: <https://doi.org/10.1093/eurheartj/ehac426>.

## Results

### Cohort profile

Of a total of 96 041 patients who underwent an NCHDA-reported procedure between April 2000 and March 2017, we identified 6541 patients who underwent closure of a secundum ASD at age 16 or older (see [Supplementary material online, Table S3](#)). Surgical closure was performed in 1346 patients (20.6%) and transcatheter closure in 5195 patients (79.4%).

There were 228 patients (3.5%) with more than one repair recorded: 149 of these patients had a failed catheter procedure followed by a surgical repair; four had a partially dehiscenced surgical repair followed by catheter repair; 12 had more than one surgical repair; and 63 had more than one catheter repair.

Baseline demographics are given in [Table 1](#). Compared with census data of those aged 16 years and older in England and Wales,<sup>16</sup> patients who underwent a secundum ASD repair were younger, more likely to be female (consistent with previous literature<sup>21</sup>), and slightly more likely to be from an ethnic minority than the general population; there were no significant differences by area deprivation quintile, or by rural/urban classification of residence to the general population (see [Supplementary material](#) for details). Compared with those with transcatheter repair, patients with a surgical repair were more likely to have congenital comorbidities ( $\chi^2$  test  $P$  value of 0.004) and pre-repair risk factors ( $P = 0.001$ ); there was no statistical difference in the presence of acquired comorbidities pre-repair ( $P = 0.056$ ).

### Practice trends and variation across England and Wales

There was a rapid increase in the numbers of ASD closures reported between 2000 and 2005, but since then total numbers and the relative distribution of transcatheter vs. surgical closure have been static over time ([Figure 1](#)). Most of this early increase was due to a large rise in the numbers of reported transcatheter ASD closures in keeping with the development and distribution of transcatheter techniques in this era and also due to incomplete national case ascertainment in the earliest years of data collection.

Numbers of procedures by age were relatively similar between ages of 16 and 64 years, and then fell with only small numbers of procedures performed in those aged over 80 years ([Figure 2A](#)). Median age at surgical repair was 40 years [interquartile range (IQR) 28–52] and at transcatheter repair it was 47 years (IQR 34–61). Older patients were more likely to undergo transcatheter (and not surgical) closure than younger patients ([Figure 2A](#)).

There were marked variations in practice when surgical vs. catheter closure was examined by centre ([Figure 2B](#)), with a notable difference in the percentage of closures performed surgically vs. transcatheter in the different centres. Two large volume centres (H09 and H05) had a higher proportion of patients undergoing surgical closure than in

**Table 1** Demographic profile of cohort at index atrial septal defect closure: overall and by repair type

	All patients	Transcatheter repair	Surgical repair
Type of repair	6541	5195 (79.4%)	1346 (20.6%)
Age in years, median (IQR)	46 (33–60)	47 (34–61)	40 (28–52)
Sex			
Female	4297 (65.7%)	3418 (65.8%)	879 (65.4%)
Male	2242 (34.3%)	1776 (34.2%)	466 (34.6%)
Missing	2	1	1
Ethnicity			
White	5562 (87.4%)	4483 (88.6%)	1079 (82.7%)
Non-white	802 (12.6%)	577 (11.4%)	225 (17.3%)
NA ethnicity	177	135	42
Area of residence deprivation			
Deprived area	2317 (38.9%)	1782 (37.8%)	535 (43.4%)
IMD Q1 (most deprived)	1119 (18.8%)	849 (18.0%)	270 (21.9%)
IMD Q2	1198 (20.1%)	933 (19.8%)	265 (21.5%)
Non-deprived area	3633 (61.1%)	2935 (62.2%)	698 (56.6%)
IMD Q3	1230 (20.7%)	979 (20.8%)	251 (20.4%)
IMD Q4	1139 (19.1%)	926 (19.6%)	213 (17.3%)
IMD Q5 (least deprived)	1264 (21.2%)	1030 (21.8%)	234 (19.0%)
NA deprivation quintile	591	478	113
Rural/urban residence			
Rural	1140 (20.3%)	959 (21.5%)	181 (15.6%)
Urban	4485 (79.7%)	3504 (78.5%)	981 (84.4%)
NA rural/urban	916	732	184

Note: Unless otherwise stated, the numbers represent counts per group. Transcatheter vs. surgical comparisons: age median and IQR,  $P = 0.000$ ; sex,  $P = 0.755$ ; ethnicity,  $P = 0.000$ ; QIMD,  $P = 0.003$ ; and rural/urban,  $P = 0.000$ . IMD, index of multiple deprivation; NA, not applicable or missing/invalid field; Q, quintile.

other centres. When examined more closely, there appeared to be a more pronounced or delayed era effect in the uptake of transcatheter ASD closure in some centres (see [Supplementary material online, Figure S3](#)). H09 had very high rates of surgery in the earlier eras, but since 2008, the proportion of surgical cases reduced dramatically and was similar to other centres in the most recent period. However, in centre H05, the surgical vs. transcatheter ratio remained relatively unchanged over the period of the study.

There was no statistically significant difference between the total numbers of ASD closure by IMD quintile in England ( $P$  value 0.183) ([Figure 2C](#)). Those in the deprived areas (Q1 and Q2) were, however, more likely to undergo surgical rather than transcatheter closure than those from non-deprived areas (Q3, Q4, and Q5) (23.1% vs. 19.2%;  $P$  value  $<0.001$ ) and were more likely to undergo closure at an earlier age (4.7 and 2.8 years earlier, on average, for catheter and surgical repairs, respectively;  $P = 0.008$  and  $P = 0.004$ ) ([Figure 2D](#)).

## Mortality

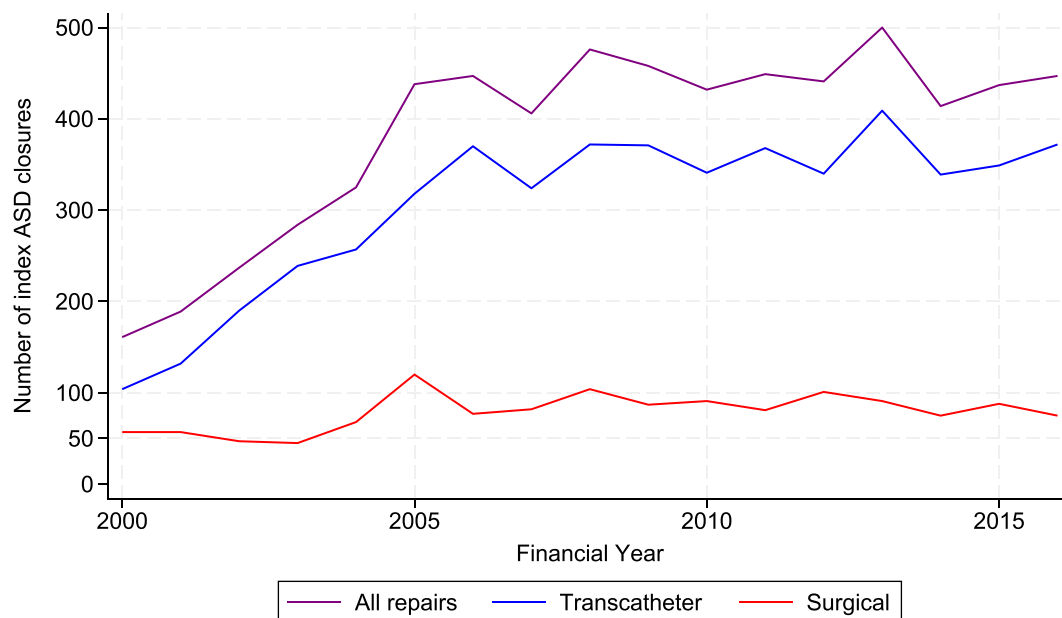
In-hospital mortality at index ASD closure was 0.2% overall (15 events in 6541 patients); 0.9% in surgical repairs; and 0.1% in catheter repairs ( $P$  value  $<0.001$ ). The in-hospital mortality risk was significantly lower for transcatheter repairs even after adjusting (using a logistic propensity score) for age, sex, year at index repair, congenital comorbidities, acquired comorbidities pre-repair, and additional cardiac risk factors pre-repair (adjusted odds ratio 0.09, 95% CI 0.02–0.46). For surgical repairs, in-hospital mortality was 0.5% for ages 16–39 years, 1.0% for ages 40–64 years, and 3.3% for older ages (65 years and more). Even for older ages, observed in-hospital mortality was low for transcatheter repairs (0.1%). Median (IQR) life status follow-up

from index ASD repair was 10.8 years (7.3–14.9), with a maximum available follow-up of 21.8 years (earliest procedure April 2000 and latest life status February 2022).

[Figure 3](#) shows the cumulative incidence of death (KM estimates) over the full follow-up period post-repair, split by type of repair and age groups (see [Supplementary material online, Figure S4](#) for full cohort, by repair type, and by age groups figures). Overall average 1-year mortality was 1.0% (95% CI 0.8–1.2%). When compared with mortality in an age, birth year, and sex-matched population in England and Wales,<sup>17</sup> there was slight excess mortality in catheter patients of all ages in the first year from repair [general population average mortality 0.6% vs. transcatheter closure 0.9% (0.7–1.2%)] but no cumulative mortality difference after the first year ([Figure 3](#), left column). In patients undergoing surgical closure, there is excess cumulative mortality up to 16 years post-procedure ([Figure 3](#), right column). This is mostly explained by the excess during the first year after repair [general population mortality 0.3% vs. surgical closure 1.2% (0.7–1.9%)] for the patients aged 40–64 years, a relatively small additional excess mortality persists around 8–13 years post-repair (maximum additional excess of 0.2%). The 1-year mortality excess was not significant once in-hospital mortality was taken into account, overall and by repair type. See the [Supplementary material](#) for further numerical results.

Surgical repairs had a higher mortality risk than transcatheter repairs only at 1 year [adjusted hazard ratio (HR) 2.0, 95% CI 1.1–3.7] and 2 years post-repair (adjusted HR 1.8, 95% CI 1.1–2.9) but not at later years post-repair or even at 2 years conditional on surviving to the first year post-repair ( $P = 0.559$ ). By age, these differences were found significant only for the age group of 40–65 years but not for ages 16–39 years or 65 years and more. Other factors significant for





**Figure 1** Total number of index atrial septal defect closures per year of data, overall and by type of repair.

the adjusted 1-year mortality risk were age (adjusted HR 1.1, 95% CI 1.0–1.1) and being male (adjusted HR 2.1, 95% CI 1.3–3.4).

## Hospital utilization

Length of stay for the index ASD closure spell was median (IQR) 1.8 (1.4–2.5) days for transcatheter closure and 7.3 (6.2–9.2) days for surgical repairs; the adjusted difference in LoS between transcatheter and surgical closures was 5.0 (95% CI 4.9–5.1) days in median (adjusting for age, gender, year of repair, comorbidities, and additional cardiac risk factors). Most of the hospital stay during the index ASD closure was post-operative: median (IQR) 1.0 (0.9–1.0) days for transcatheter repairs and 6.0 (5.0–7.0) days for surgical repairs. Peri-operative LoS increased with age (Figure 4).

Data on hospital utilization were available for a median of 11.7 years prior to the index ASD spell (IQR 8.1–15.3 years, maximum 19.0 years) and were non-zero and covering at least 2 years prior to index ASD spell for 5777 patients (with HES data at the index ASD spell). Median (IQR) follow-up for hospital utilization after the index ASD repair spell was 7.7 (4.3–11.4) years, with a maximum of 18.0 years, and was available for 5778 patients (with HES data at the index ASD spell).

In the first year after completion of their index ASD repair spell, patients spent a median (IQR) of 4 (2–8) days in or at hospital following transcatheter repair and 5 (3–11) days following surgical repair, with 2 (1–3) of those days [3 (2–5) if surgical repair] being cardiac admissions/visits (Figure 5, and see [Supplementary material online, Figure S5](#), showing only inpatient and outpatient days for clarity). Median LoS 1 year post-repair was significantly higher after surgical repairs, adjusting for age, sex, year of repair, comorbidities, and additional cardiac risk factors ( $P$  value <0.001). Hospital utilization decreased over the following years. In the year preceding the index ASD repair spell, patients spent 6 (4–11) days in hospital, with 4 (2–6) of those being for cardiac reasons. Utilization increased with age. See the [Supplementary material](#) for yearly tables (and additional counts of days in A&E).

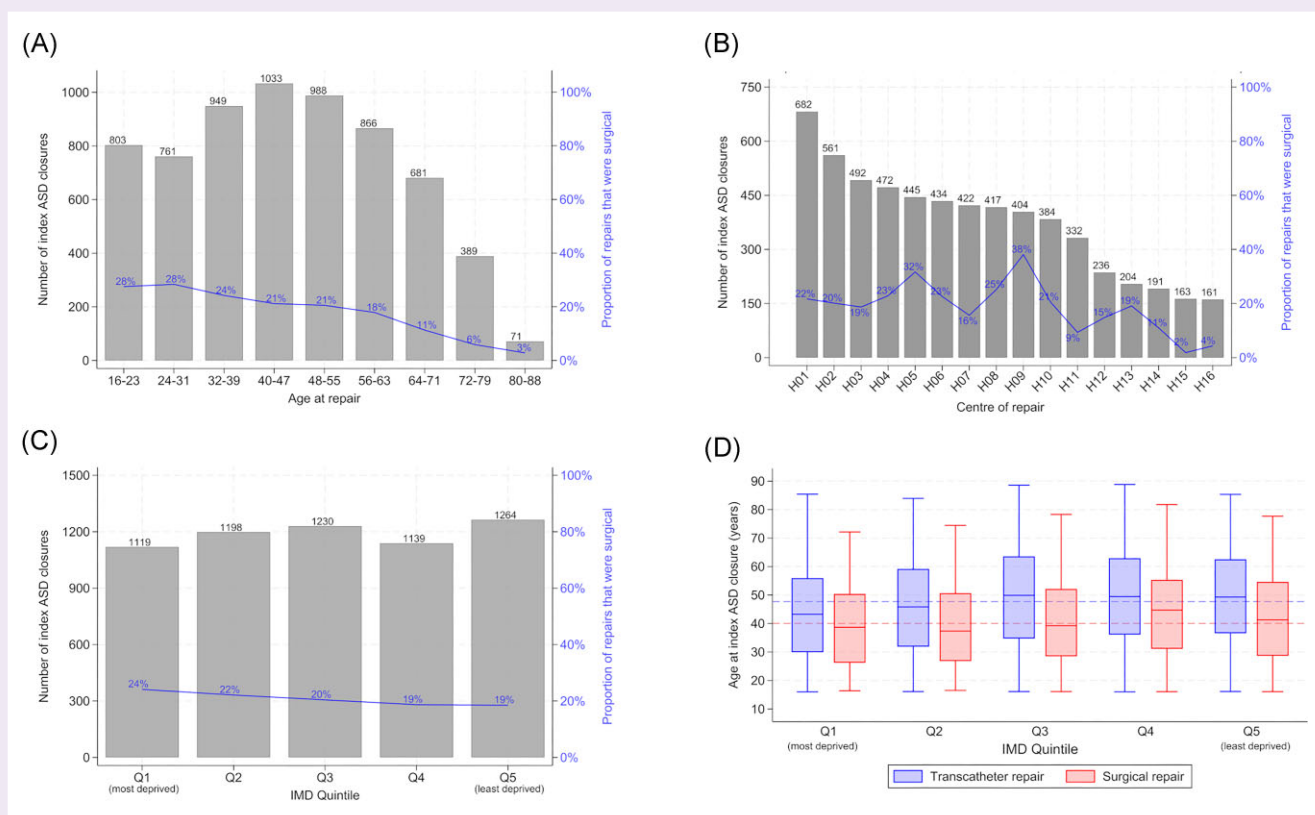
## Discussion

Our study is one of the largest reported cohorts examining outcomes and factors determining closure of secundum ASD in adults to date. Data collection for congenital heart procedures in the UK is robust, with mandatory, externally validated submission of all transcatheter intervention and surgical procedures for congenital heart disease to the NCHDA, such that this data set should give a near complete representation of the national cohort during most of this time period.

Over the study period, we saw a significant increase in the numbers of reported cases from the earliest era, followed by stabilization of both total numbers of cases performed and the proportion of cases closed surgically, since around 2005. This is likely to largely reflect improvements in data capture across the country, as it took a few years before all centres undertaking adult ASD closure began submitting to the audit.

There were significantly more women in our cohort, which is consistent with the known sex difference in incidence of ASD.<sup>21</sup>

We demonstrate a median age of closure in all comers of 46 years, with a clear preference to transcatheter repair in the older age groups. This may be because larger defects, which are less suitable for transcatheter repair, present at an earlier age due to the greater haemodynamic burden and therefore symptoms may prompt earlier presentation. Smaller defects, more suitable for transcatheter closure, are likely to be relatively asymptomatic and may only be picked up incidentally when patients are undergoing routine investigations, such as ECG, chest X-ray, or echocardiogram, which are more likely to be performed as patients get older. However, these data may also reflect a reluctance to refer for or to undertake cardiac surgery in older patients with ASD due to a perceived unfavourable risk–benefit analysis. There is an increasing body of evidence regarding the benefits of ASD closure even in older patients,<sup>22,23</sup> and given that our outcome data show that in those older than 65 years, there is no significant difference in mortality between transcatheter and surgical closure of ASD, a careful patient-by-patient assessment should be made by a specialist team regarding the risks and potential benefits of ASD



**Figure 2** (A) Age at index atrial septal defect closures: total number and type, by 8-year age periods. (B) Centre variation: total number and type of index atrial septal defect repairs, by centre. Note: a total of 15 centres with fewer than 150 repairs over the study period were excluded. (C) Total and type of index atrial septal defect closure by quintile of area deprivation (at the time of repair). (D) Age at repair by type of index atrial septal defect closure by quintile of area deprivation (at the time of repair). Note. The index of multiple deprivation was defined for patients with residence in England ( $N = 5950$ ). Age bars are interquartile range; extreme values not shown.

closure in older patients, particularly those with comorbidities. Our data also demonstrate that in the older cohort health care utilization for cardiac indications is remarkably low once their ASD is closed.

Variation by ethnicity, deprivation, and geography has been reported previously for health care utilization in the UK and access to services.<sup>24–26</sup> We noted a similar ethnic make-up of our treated cohort to that of contemporaneous population data reported in the Census for England and Wales.<sup>16</sup> There was no significant difference between IMD quintiles in the overall number of patients undergoing ASD closure and no significant differences in ASD closure rates in people living in rural vs. urban areas. Those in the most deprived areas did undergo closure at a slightly younger age and were more likely to undergo surgical rather than transcatheter closure than those from less deprived areas. The reasons for this are unclear, although there are higher proportions of younger adults and people in poor health living in deprived areas,<sup>18</sup> which might explain (at least partly) a higher occurrence of surgical repairs.

## Mortality and morbidity

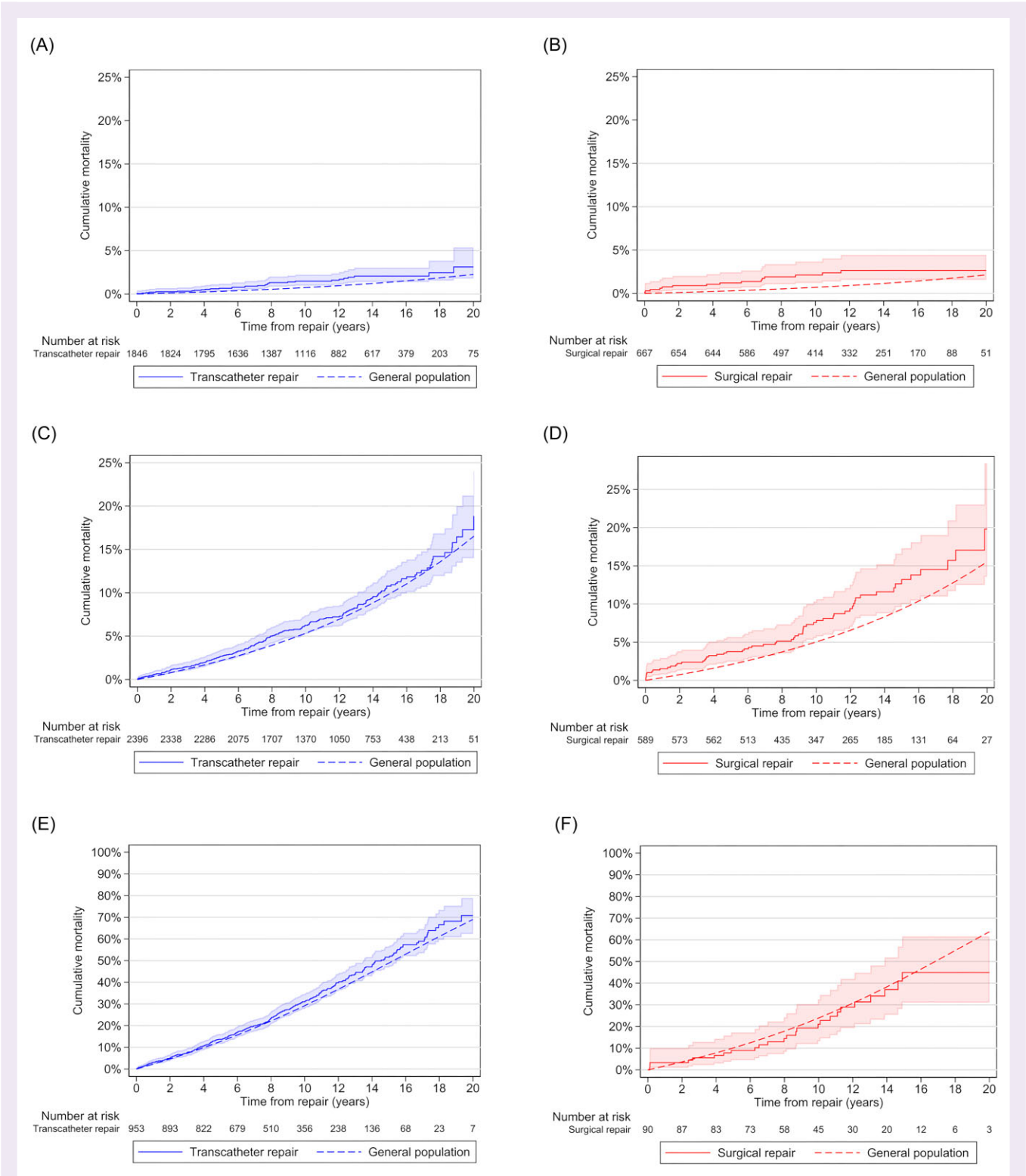
Our data show an excess 1-year mortality in patients who underwent ASD closure when compared with age, year of birth, and sex-matched population data. This is mainly explained by peri-procedural excess mortality, particularly in patients undergoing surgical procedures, in keeping with meta-analyses of smaller series.<sup>21</sup> In our series, in younger patients (16–39 years), there appears to be an excess ongoing cumulative mortality up to 17 years post-procedure, which is not

entirely explained by the peri-operative excess (albeit unexplained excess is small  $<0.2\%$ ). The reasons behind this are unclear but are similar to findings in a Danish cohort study with median follow-up of 18 years.<sup>27</sup> Interestingly in that study, patients with ASD who did not undergo closure had an even higher mortality than those who did.

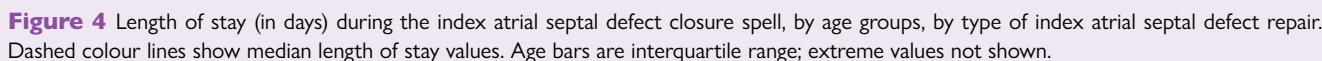
We have already postulated that it may be those patients with larger and therefore more haemodynamically significant ASDs who present earlier and therefore undergo earlier repair and are more likely to require surgical rather than transcatheter closure. Although we usually see good resolution of right-hand-side of the heart volume loading after ASD closure, in some patients with very large defects the right-hand-side of the heart never returns completely to normal size and therefore may continue to pre-dispose to arrhythmia, particularly atrial fibrillation with its associated stroke risk in later life. The Danish group demonstrated an increased incidence of late atrial fibrillation and stroke in their patients with ASD, which is only partially corrected by undergoing closure.<sup>28,29</sup> Despite ASD closure, a large cohort in Finland also showed an ongoing excess incidence of new atrial fibrillation compared with controls.<sup>30</sup>

Although the majority of patients with ASD have normal pulmonary vascular resistance, some patients with ASD develop pulmonary hypertension (PAH), possibly through a permissive genotype mechanism, and it is conceivable that these young patients undergoing surgical closure of large defects are pre-disposed to pulmonary vascular disease with its poorer prognosis. A rather small series from Belgium showed ongoing development of PAH particularly in older patients undergoing ASD closure.<sup>31</sup> The low cardiac hospital





**Figure 3** Post-repair mortality Kaplan–Meier estimates (average and 95% confidence band) by age at index closure (16–39 years on first row, 40–64 years on second row, and 65 or more years on third row) and type of repair (transcatheter on left column and surgical on right column), with added average mortality in England and Wales for the general population matched on age, year of birth, and sex.



post-procedure. The oldest cohort has ongoing cardiology outpatient attendances even up to 15 years post-procedure suggesting either ongoing issues related to later closure of their ASD or other cardiac comorbidity, which of course becomes more frequent with age.

## Strengths and weaknesses

This is a large cohort study, which, given the mandatory nature of procedure reporting to the NCHDA, should represent a near-complete picture of the national practice and gives a long follow-up time.

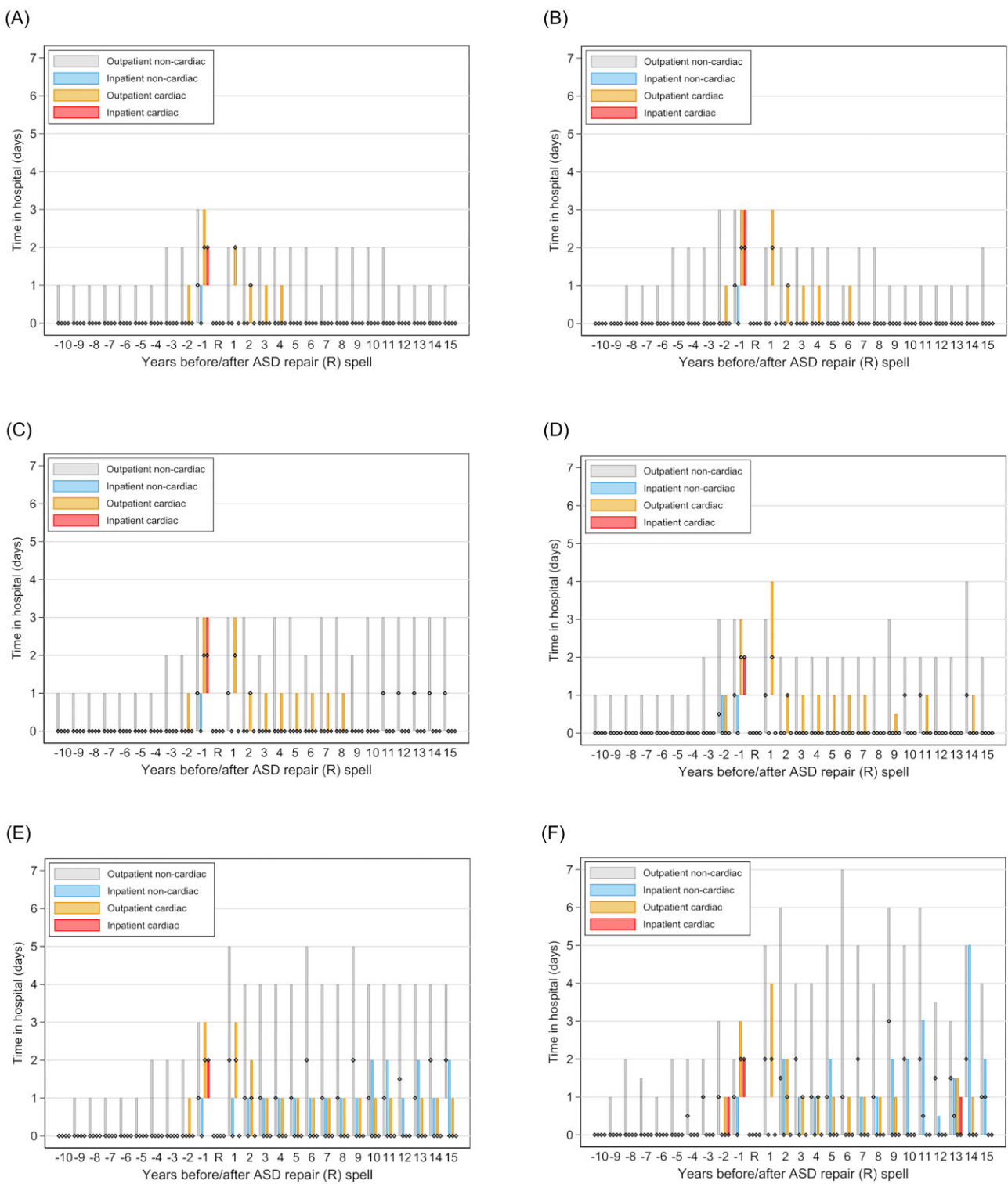
National Congenital Heart Disease Audit only receives data regarding patients who have had a cardiac procedure and does not include patients diagnosed with ASD but who did not undergo closure. Our data cannot show us how highly selected the age groups are, and whether patients, particularly older ones, were not undergoing, or not being considered for ASD closure, particularly surgical, on the basis of perceived risk. Our data cannot tell us whether there are significant inter-racial differences in the population prevalence of ASD.

Unfortunately, we did not have access to cause of death to help explain the excess mortality seen at one year post-repair. We also had little data on morbidity, other than being aware of ongoing outpatient and inpatient activity.

## Conclusion

Atrial septal defect is the commonest congenital cardiac lesion presenting in adulthood. Atrial septal defect closure carries a very small excess mortality risk over an age- and sex-matched cohort of the general population. Surgical closure is associated with a higher mortality risk than transcatheter closure. The excess mortality is largely procedural, and the risk returns to baseline in older age groups, whereas younger patients carry a very small cumulative excess mortality risk out to 17 years post-procedure. It is not known whether there is any excess mortality risk in patients with untreated ASD.

Atrial septal defect closure appears to reduce further cardiac hospitalization even in older age groups. We see fewer cardiac inpatient



**Figure 5** Days in hospital per year around the index atrial septal defect closure spell, by type of repair (transcatheter at the left or surgical at the right), by age groups. For each year we include all patients with Hospital Episode Statistics data in that year. *R* is the index procedure (repair) spell for which length of stay was omitted in this figure to avoid large values (see [Figure 4](#)). Median values are shown with a black diamond symbol. Bars are interquartile range. Extreme values not shown.



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