ESC European Society of Cardiology

European Heart Journal (2018) **39**, 993–998
doi:10.1093/eurheartj/ehx687

**CLINICAL RESEARCH**
*Congenital heart disease*

# Long-term mortality in patients with atrial septal defect: a nationwide cohort-study

**Camilla Nyboe[1]*, Zarmiga Karunanithi[1], Jens Erik Nielsen-Kudsk[2], and Vibeke E. Hjortdal[1]**

[1]Department of Cardiothoracic Surgery, Aarhus University Hospital, Palle Juul-Jensens Boulevard 99, 8200 Aarhus N, Denmark; and [2]Department of Cardiology, Aarhus University Hospital, Palle Juul-Jensens Boulevard 99, 8200 Aarhus N, Denmark

*Received 6 March 2017; revised 22 May 2017; editorial decision 3 November 2017; accepted 8 November 2017; online publish-ahead-of-print 2 December 2017*

**See page 999 for the editorial comment on this article (doi: 10.1093/eurheartj/ehx633)**

**Aims** In this nationwide cohort of atrial septal defect (ASD) patients, the largest to date, we report the longest follow-up time with and without closure in childhood and adulthood compared with a general population cohort.

**Methods and results** Using population-based registries, we included Danish individuals born before 1994 who received an ASD diagnosis between 1959 and 2013. All diagnoses were subsequently validated ($n = 2277$). Using the Kaplan–Meier estimates and Cox proportional hazards regression adjusted for sex, birth year, and a modified Charlson Comorbidity Index, we compared the mortality of ASD patients with that of a birth year and sex matched general population cohort. The median follow-up from ASD diagnosis was 18.1 years (range 1–53 years). Patients with ASD had a higher mortality [adjusted hazard ratio (HR): 1.7; 95% confidence interval (CI): 1.5–1.9] compared with the general population cohort. The adjusted HR 30 days after closure was 1.4 (95% CI: 1.2–1.7), and it was 2.4 (95% CI: 2.0–2.9) for patients without closure.

**Conclusion** Overall, ASD patients had a higher long-term mortality than a general population cohort matched on birth year and gender. Our data indicate a lower relative mortality of those ASD patients undergoing closure than the ASD patients not undergoing closure.

**Keywords** Heart septal defect • Mortality • Heart defects • Congenital • Epidemiology

## Introduction

Half a century ago, the life expectancy of ASD patients was reported to be less than 50–60 years;[2] however, later studies have demonstrated higher survival rates.[3–5] Murphy *et al.*[1] reported that closure before the age of 24 years normalized the mortality risk compared with the expected survival of the background population, whereas patients with closure after the age of 24 had an increased mortality risk. Cuypers *et al.*[6] investigated 139 patients with surgical closure before the age of 15 and found low morbidity and mortality rates 35 years after closure. Similar results were found by Roos-Hesselink *et al.*[7] in a study including 135 patients with up to 26 years of follow-up. However, none of these studies were directly compared with a matched background population.

In adulthood, it is unclear whether ASD closure changes the natural course. Closure has been reported to reduce the 10-year mortality rate in some studies[5] and had no impact in others.[3,8] John Sutton *et al.*[4] found that patients with ASD closure had a survival rate comparable with those with no ASD after 5 and 10 years but with no follow-up beyond this time. Longer follow-up has shown reduced survival of ASD patients, regardless of closure, compared with matched controls,[1] but these data were collected more than 25 years ago and contemporary studies of large population with a long-term follow-up are lacking. Hence, evidence is needed to clarify whether a small ASD impact on survival and whether ASD patients normalize mortality risk after closure in either childhood or adulthood. We therefore aimed to estimate the long-term mortality of adult ASD patients with and without

* Corresponding author. Tel: +45 20959903, Fax: +45 78453079, Email: camilla@nyboe.nu

closure compared with a general population cohort in a nationwide cohort covering up to 53 years of follow-up.

# Materials and methods

## Study cohort and design

This nationwide cohort study was based on national medical registries in Denmark. Part of the study cohort has previously been used in investigations of the impact of an ASD on pneumonia,[9] atrial fibrillation, and stroke.[10,11] The unified Danish health care system is publicly funded with equal access for all Danes. Hospital data are gathered in nationwide public registries linked to a unique personal identification number (the CPR number) provided for all inhabitants since 1968. Information on the date of birth, date of immigration, and date of death was identified in the Danish Civil Registration System.[12]

Two data sources were used to identify ASD patients for this study. We used the Danish National Patient Registry (DNPR) established in 1977 to identify patients born before 1994 and diagnosed with an ASD[13] from 1977 to 2013. The DNPR contains information on all inpatient and outpatient hospital contacts in Denmark, dates of admission and discharge, surgical procedures, and discharge diagnoses coded according to the International Classification of Disease (ICD).[14] The 8th edition was used until 1993 after which the 10th version has been used. In Denmark, it is mandatory by law for all healthcare centres and hospitals to report to the register, and it is considered to be nearly complete.[13] Two independent doctors reviewed all hospital records to validate the diagnosis registered in the DNPR. The ASD closing procedure was likewise registered in the DNPR, and the date was confirmed in the review of hospital records. During this medical record review, we identified a small number of patients with ASD diagnosis dates and/or ASD closure dates recorded before the initiation of the DNRP. Thus, the dates of diagnoses of the included subjects ranged from 1959 to 1 January 2013. The second data source included patients diagnosed with ASD before the age of 15 years between 1963 and 1974. These patients are a subgroup of a cohort used in a previous study of patients with congenital heart defects.[15] The patients were identified by an experienced physician from 1970 to 1974 by review of inpatient and outpatient hospital records in all Danish medical and paediatric departments.[16] The CPR number of the patients alive in 1968 was manually identified, and their diagnoses were translated into ICD-10 codes. Patients who died before 1968 ($n = 5$), and therefore did not receive a CPR number, were excluded. We only included patients with an isolated ASD except those few ($n = 3$) who had a concomitant patent arterial duct, thought to be of no relevance in adulthood. Patients were excluded if the defect was described as a patent foramen ovale. Thus, only patients with an ASD diagnosis confirmed by medical record review were included in this study.

For every validated ASD patient, 10 people from the general population were matched on sex and birth year using the Danish Civil Registration System.

Baseline comorbidity was identified using the ICD diagnoses in the DNPR covering both inpatients and outpatient diagnoses before or at the time of the ASD diagnosis. Only comorbidities registered after 1977 were included in the baseline comorbidity due to the lack of information before this time. Comorbidity was indexed in the Charlson Comorbidity Index, which includes diagnoses of heart-, lung-, cerebral-, renal-, and liver disease, as well as cancer, Human Immune Deficiency Virus, and diabetes, for a total of 17 diagnoses. Patients were categorized into four groups depending on their score as follows: no coexisting comorbidity, mild, moderate, and severe comorbidity. We modified the index by excluding diagnoses that could be caused by the ASD in the intermediate step in the causal pathway between the ASD and mortality. Hence, we did not include comorbidities such as cerebrovascular disease (except neurological diseases), pulmonary heart disease and those of the hemiplegia/paraplegia diagnoses caused by stroke as adjustment in our analyses.[17,18]

## Mortality

Death was identified using data from the Civil Registration System. The causes of death were obtained from the Danish Register of Causes of Death. Mortalities in the period between 1959 and 1977 were identified in the hospital records and added separately. Patients without a CPR number in 1968 ($n = 5$) were unaccounted for in terms of death or emigration.

## Statistical analysis

Follow-up of ASD patients and the comparison cohort started on the date of diagnosis or closure (the index date for the matched comparison cohort members). Follow-up continued until death, emigration, or the end of Follow-up (1 January 2013), whichever came first. For patients with closure, 30 days of mortality after the procedure was computed both in total and in terms of closure before or after 1990 when catheter closure was introduced in Denmark. The Kaplan–Meier curves were computed with either age or time since diagnosis/closure as a time-scale.

We used Cox proportional hazards regression to compute hazard ratios (HR) of mortality for ASD patients, beginning at the time of diagnosis for those without closure and 30 days after closure for those with closure, and compared them with the general population cohort. Age was the underlying time scale. The patients were stratified by age at time of the closure, and the HR was adjusted for gender, Downs Syndrome, and the Charlson Comorbidity Index.[17,18]

In a separate analysis, we entered closure as a time varying exposure to compare mortality of ASD patients with and without closure. This analysis was done by adjustment for pulmonary arterial hypertension and Eisenmenger syndrome. We graphically verified the assumption of proportional hazards with log minus log plots. Analyses were performed using Stata 13 (StataCorp LP, College Station, TX, USA). This study was approved by The Danish Data Protection Agency (j.nr. 2010-41-4649) and by the National Board of Health (j.nr. 7-604-04-2/193/KWH).

# Results

The hospital records of all patients eligible for validation ($n = 4408$) diagnosed in one of 80 hospitals in Denmark since 1959 were reviewed. The majority of the patients (74%) were diagnosed in one of the four university hospitals in Denmark. Surgical closure was performed in five public hospitals and transcatheter closure in two public hospitals all with highly specialized teams. No ASD closures were performed in private institutions. Patients were excluded from the validation process if the ASD diagnosis was inadequate or missing in the hospital record or if a concomitant congenital heart disease was present. A total of 2277 patients met the inclusion criteria after validation.

## Baseline characteristics

Most of the ASD patients ($n = 1554$, 68%) had closure of their defect during follow-up. Median follow-up was 18.1 years (range 1–53.3 years) after diagnosis. The ASD patients, especially those without closure, had more baseline comorbidities than the comparison cohort at the time of diagnosis (*Table 1*).

**Table 1** Baseline characteristics at time of diagnosis

| | ASD total ($n = 2277$) | ASD closed ($n = 1554$) | ASD unclosed ($n = 723$) | Comparison cohort ($n = 22756$) |
|---|---|---|---|---|
| Female, *n* (%) | 1384 (61) | 979 (63) | 405 (56) | 13 834 (61) |
| Mean age, end of FU (years) | 45.4 ± 0.4 | 46.6 ± 0.5 | 43.0 ± 0.9 | 46.0 ± 0.1 |
| Chronic lung disease, *n* (%) | 181 (8) | 113 (7) | 68 (9) | 1024 (5) |
| Diabetes, *n* (%) | 116 (5) | 74 (5) | 42 (6) | 790 (3) |
| Pulmonary heart disease, *n* (%) | 123 (5) | 60 (4) | 63 (9) | 52 (0.02) |
| Hypertension, *n* (%) | 262 (12) | 188 (12) | 74 (10) | 1661 (7) |
| Ischaemic heart disease, *n* (%) | 325 (14) | 239 (15) | 86 (12) | 1212 (5) |
| Cerebrovascular events, *n* (%) | 180 (8) | 132 (8) | 48 (7) | 613 (3) |
| Arrhythmia, *n* (%) | 514 (23) | 396 (25) | 118 (16) | 715 (3) |

ASD, atrial septal defect.

## Mortality

The 30 days of mortality after closure was 0.9% ($n = 8$), of which five were after surgery, one was after transcatheter treatment, and two were after unknown procedures. Of the eight patients, six were adults (three were more than 65 years old), and two were children.

The ASD patients had an overall increased mortality risk (*Figure 1*) compared with the comparison cohort with an adjusted HR of 1.7 (95% CI: 1.5–1.9) (*Table 2*). The HR was higher [adjusted HR: 2.4 (95% CI: 2.0–2.9)] for those with no closure compared with those who had closure during follow-up [adjusted HR: 1.4 (95% CI: 1.2–1.7)]. Comparison of mortality for patients with ASD closure vs. those without closure showed an adjusted HR of 1.6 (95% CI: 1.3–2.1).

For patients with closure there was an increased mortality risk if closure was performed after the age of 18 years. The adjusted HR comparing the ASD patients with the general population was 1.6 (95% CI: 1.2–2.2) in the group of ASD patients who had closure performed between 18 and 50 years of age and the adjusted HR was 1.3 (95% CI: 1.02–1.6) in patients with closure after the age of 50 years. For those ASD patients with closure performed before the age of 18 years, the long-term mortality remained increased when adjusted for the modified Charlson comorbidity index, with a HR of 1.7 (95% CI: 1.03–2.9). When adjusted also for Down syndrome, the relative risk was the same, but no longer statistically significant [HR: 1.6 (95% CI: 0.9–2.7)]. In a direct comparison, there was a higher, but not statistically significant, mortality risk for males [adjusted HR: 1.2 (95% CI: 0.95–1.5)] compared to females.

## Causes of death

Patients with closure had significantly fewer cardiac deaths ($P < 0.01$) than those without closure where almost half the patients died from cardiac disease (*Table 3*). Heart failure in particular was a more frequent cause of death in the group of patients who had no ASD closure. In both groups, 14% and 15%, respectively, 'ASD' was reported as being the cause of death. It remains unknown to which extent this covers heart failure and pulmonary heart disease. There was a higher number of cancer-related deaths in the closure group but this was not statistically significant ($P = 0.064$). Patients who had closure by surgery did not have a higher risk of long-term mortality compared with those who had closure performed by catheter (HR 0.6, 95% CI: 0.2–1.8; $P = 0.39$).

# Discussion

This is the largest nationwide cohort study with the longest follow-up time including closed as well as unclosed ASD and including all ASDs closed by surgery as well as those closed by catheter. It shows, that mortality was higher for ASD patients than for the background population.

The 30 days of mortality found in this study is in concordance with most recent studies emphasizing the low risk of the closure procedures in ASD patients.[19] The long-term survival has; however, been a subject of debate. Recent studies primarily focus on the short- to medium-term outcome of single-centre study populations, often with good results within 5–8 years after closure.[20–23] Kutty *et al.* found that only 3% of ASD patients with closure had died at the end of follow-up (range 5–20 years), but only half of the patients were older than 20 years at time of closure, and with a 20% loss to follow-up the mortality could be underestimated. In contrast, Jeong *et al.* found much higher mortalities of 21% after closure and 27% with no closure with a mean follow-up of 6.8 years.[24] John Sutton *et al.*[4] found that adult patients with ASD closure did not have altered survival compared with a matched control group 5–10 years after closure. The very low long-term survival of 40% in patients with closure found by Murphy *et al.*[1] was not replicated in this study. We found that more than 80% were alive 30 years after closure and that the survival rate for the comparison cohort was similarly higher than the one found by Murphy *et al.*[1] This difference could be explained by general health improvements and increased life expectancy in the population over the last 50 years. The general life expectancy has improved by nearly 5 years since 1990[25] when the study by Murphy *et al.*[1] was published and much more since the 1950 s when the patients in the study by Murphy *et al.*[1] had surgery. Furthermore, the expanded knowledge in medical treatment, intensive care facilities, and improved treatment options for the patients could improve the overall life expectancy of the patients in this study.

The mortality risk for patients *without closure* in our study was increased compared to those who had closure during follow-up.

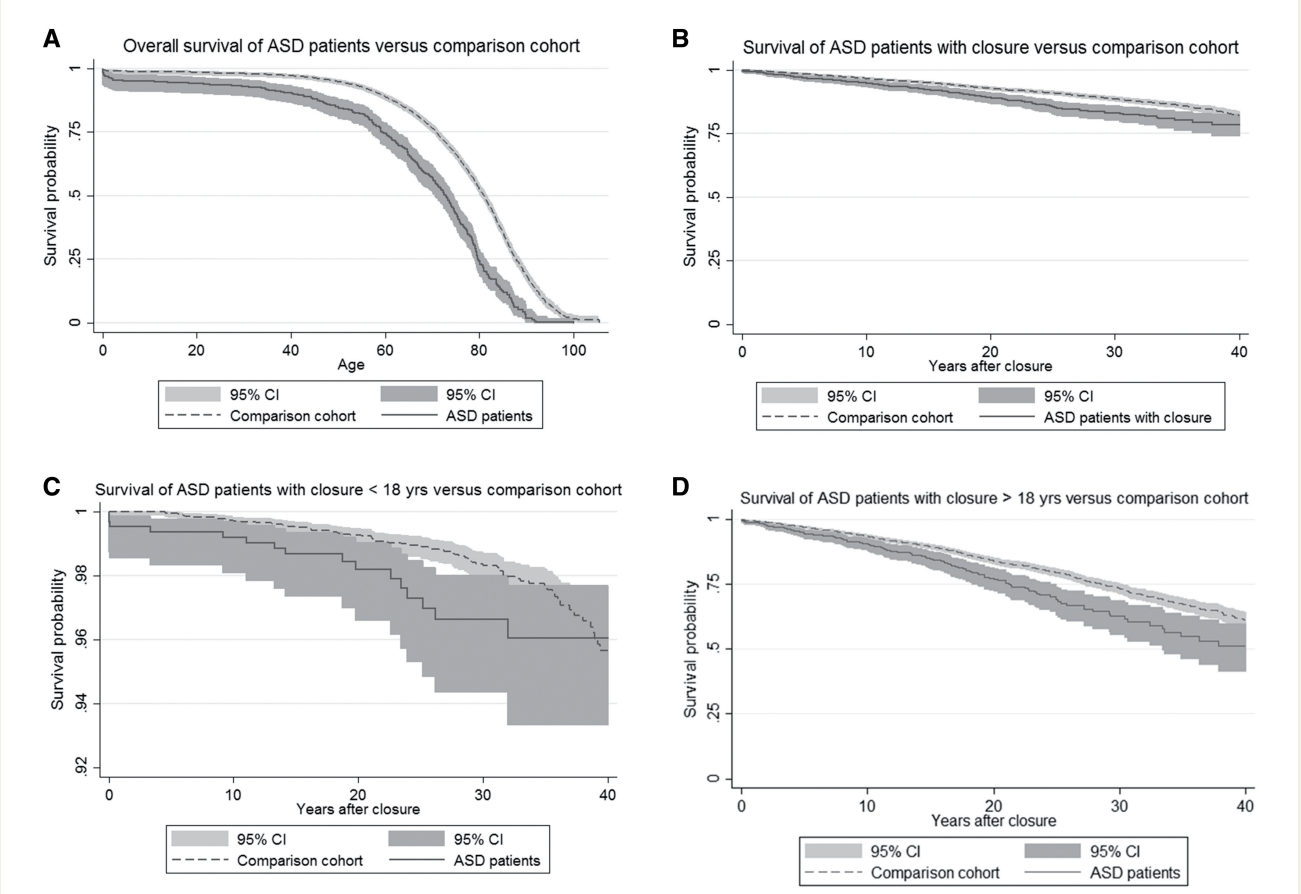


**Figure 1** (*A*) Survival in years in atrial septal defect (ASD) patients without closure compared with the comparison cohort with age as an underlying time scale. (*B*) Survival in ASD patients after closure compared with the comparison cohort with years after closure as an underlying time scale. (*C*) Survival in patients with closure before the age of 18 compared with the comparison cohorts with years after closure as an underlying timescale. (*D*) Survival in patients with closure after the age of 18 compared with the comparison cohorts with years after closure as an underlying timescale.

However, the patients without closure were far from comparable with those who had closure during follow-up. The patients without closure were older at the time of diagnosis and had more comorbidity. Six patients were not eligible for closure due to high pulmonary blood pressure or Eisenmenger syndrome. We excluded those patients in the direct comparison between treatment with or without closure well aware that these complications may possibly be a consequence of the ASD. Some of the differences in baseline comorbidity could be caused by the ASD, such as atrial fibrillation, stroke, and pulmonary heart disease. We excluded these diagnoses from the Charlson Comorbidity Index to avoid adjustment for intermediate steps between ASD and mortality that are potentially influenced by ASD closure. Hence, the present outcomes could result from a difference in ASD-related comorbidity, which was consequently not adjusted for, that is atrial fibrillation, stroke, and pulmonary infections, as these are intermediate steps between ASD and mortality. In Denmark, patients with no symptoms and no right ventricular enlargement or a $Q_p/Q_s$ ratio smaller than 1.5 are typically not offered closure. Those patients without closure are anticipated to have a completely normal life expectancy compared with the comparison cohort. However, with time the magnitude and importance of a shunt may increase due to age-related changes in the circulation and we may need to revisit the indication for closure in those patients as they age. This is supported by the fact that cardiac-related mortality is very high in this group. We do not know the number of patients with large shunts who have not been offered closure due to comorbidity or who declined further treatment. Further knowledge regarding survival and changes in indication of closure with increasing age of those with small and haemodynamically insignificant ASDs is warranted. Adult ASD patients without closure could possibly benefit from a medical re-examination including symptoms, shunt, and right ventricle dimensions. In patients without closure, it is also important to remember that there is a proportion of patients with a small defect, that are not yet diagnosed. These patients might not have had reason to consult the health care system, and their morbidity and mortality could possibly be lower than in patients diagnosed with a small ASD.

Closure of an ASD before the age of 18 years does not seem to normalize the mortality risk compared to the background population, although the increased risk does not reach significance. We know that the risk of arrhythmia, stroke, and pneumonia starts to increase after the 4th or 5th decade.[9,10] Most of the patients in our study and other similar research with closure in childhood have not reached

**Table 2 HR for mortality in patients with closed or unclosed atrial septal defect compared with a general population comparison cohort in different age groups and within two time intervals after diagnosis or closure**

| Hazard ratio (95% CI) | | | |
|---|---|---|---|
| | ASD closed[a] | ASD unclosed | ASD total |
| ASD all | 1.6 (1.4–1.9) | 3.1 (2.6–3.7) | 2.1 (1.8–2.3) |
| | 1.4 (1.2–1.7)[b] | 2.5 (2.1–3.0)[b] | 1.7 (1.5–1.9)[b] |
| | 1.4 (1.2–1.7)[c] | 2.4 (2.0–2.9)[c] | 1.7 (1.5–1.9)[c] |
| ASD closed | 1.7 (1.03–2.9) | | |
| <18 years | 1.7 (1.02–2.8)[b] | | |
| | 1.6 (0.9–2.6)[c] | | |
| ASD closed | 1.9 (1.4–2.5) | | |
| 18–50 years | 1.7 (1.3–2.3)[b] | | |
| | 1.7 (1.2–2.2)[c] | | |
| ASD closed | 1.5 (1.2–1.9) | | |
| >50 years | 1.3 (1.02–1.6)[b] | | |
| | 1.3 (1.02–1.6)[c] | | |

Adjusted mortality risk for ASD patient with closure, no closure during the follow-up period and the total cohort of ASD patients compared with the comparison cohort.
ASD, atrial septal defect.
[a]Mortality risk starting 30 days after closure.
[b]Adjusted for the modified Charlson Comorbidity Index and gender.
[c]Adjusted for the modified Charlson Comorbidity Index, gender, and Downs.

**Table 3 Causes of death for atrial septal defect patients**

| | No closure, *n* = 723 *n* (%) | After closure, *n* = 1554 *n* (%) |
|---|---|---|
| **Total deaths** | **156** | **159** |
| **Cause of death** | | |
| Cardiac, non-ischaemic | 49 (31) | 31 (19) |
| Heart failure | 19 | 4 |
| Atrial fibrillation | 2 | 4 |
| Mitral valve pathology | 4 | 2 |
| Other[a] | 24 | 21 |
| Cardiac, ischaemic | 24 (15) | 23 (14) |
| Ischaemic heart disease | 11 | 16 |
| AMI | 13 | 7 |
| Cardiac, total | 73 (47) | 54 (34) |
| Infection | 10 (6) | 10 (6) |
| Pneumonia | 8 (5) | 7 (4) |
| Stroke | 9 (6) | 11 (7) |
| Cancer | 22 (14) | 38 (24) |
| Diabetes/kidney disease | 8 (5) | 10 (6.3) |
| Chronic lunge disease | 7 (4) | 8 (5) |
| Downs | 9 (6) | 2 (1.3) |
| Other | 15 (10) | 16 (10) |
| Unknown | 3 (2) | 10 (6.3) |

Causes of deaths divided into categories. Percentages in each category is of the total number of deaths for patients either with or without closure.
ASD, atrial septal defect.
[a]Other cardiac disease includes those listed only as death caused by ASD, cardiomyopathy, and heart disease of no further specification.

this age yet. We can therefore only speculate about the possible increase in mortality risk in these patients in the years to come.

## Limitations

Certain limitations should be kept in mind while interpreting the registry-based data in this study. Information on the type of ASD and the shunt dimensions is not available in these registries, and the results of this study must be interpreted for the entire ASD population. Misclassification is possible although all hospital records were validated for the correct diagnosis, status, and date of closure.[9] Losses to follow-up could lead to selection bias if those lost to follow-up differ in outcome to those with full follow-up. The five patients with no CPR number are likely to have died before receiving a CPR number and thereby possibly caused an underestimation of the study results. However, the number of patients with no CPR number was small, and with the almost complete follow-up of the DNPR and Central Person Registry, bias due to loss of follow-up is not relevant in this study. The registration of the death dates in the Civil Registration System is considered to be practically without error.[26] Selection bias could be of importance in patients with an unclosed ASD. The majority of patients with an unclosed ASD have no symptoms and the diagnosis is therefore often given in relation to other hospital admittances with possibly significant disease. However, we have minimized the influence of comorbidities not related to the ASD by adjusting for the Charlson Comorbidity Index. Baseline comorbidity is not included in patients diagnosed before 1977 and their comparison cohort. This could underestimate the difference in baseline comorbidity between these two groups. Later occurrence of comorbidity used in the Charlson Comorbidity Index is; however, complete for all groups.

The causes of death registered in *The Danish Register of Causes of Death* are only as precise as what the doctor interpreting and entering the cause of death writes on the death certificate. In cases where no autopsy was performed, the cause can be registered as most likely, but ailments such as ASD, Downs, etc. are obviously not valid death causes and are likely to cover unknown causes of death.

# Conclusions

Patients with an ASD have increased mortality compared with the general population regardless of closure in childhood or adulthood. Closure—especially in childhood seems to improve survival in ASD patients. Our data indicate the importance of long-term medical follow-up of ASD patients, even with simple small defects. Adult patients with an unclosed ASD may need a re-evaluation 5–10 years after diagnosis, since symptoms, shunting, impact on cardiac function, and indication for closure may change over time.

## Acknowledgements

The authors would like to thank Anna Hjortdal for collecting the patient demographics for analyses in this study, and Jørgen Videbæk, MD and Henning Bækgaard, MD for collecting the hospital records from the period of 1963 to 1977.

## Funding

Aarhus University, The Central Denmark Region, and The Augustinus Foundation.

**Conflicts of interest**: none declared.

## References

1. Murphy JG, Gersh BJ, McGoon MD, Mair DD, Porter CJ, Ilstrup DM, McGoon DC, Puga FJ, Kirklin JW, Danielson GK. Long-term outcome after surgical repair of isolated atrial septal defect. Follow-up at 27 to 32 years. *N Engl J Med* 1990; **323**:1645–1650.
2. Campbell M. Natural history of atrial septal defect. *Br Heart J* 1970;**32**:820–826.
3. Shah D, Azhar M, Oakley CM, Cleland JG, Nihoyannopoulos P. Natural history of secundum atrial septal defect in adults after medical or surgical treatment: a historical prospective study. *Br Heart J* 1994;**71**:224–227; discussion 228.
4. John Sutton MG, Tajik AJ, McGoon DC. Atrial septal defect in patients ages 60 years or older: operative results and long-term postoperative follow-up. *Circulation* 1981;**64**:402–409.
5. Konstantinides S, Geibel A, Olschewski M, Gornandt L, Roskamm H, Spillner G, Just H, Kasper W. A comparison of surgical and medical therapy for atrial septal defect in adults. *N Engl J Med* 1995;**333**:469–473.
6. Cuypers JA, Opic P, Menting ME, Utens EM, Witsenburg M, Helbing WA, van den Bosch AE, Ouhlous M, van Domburg RT, Meijboom FJ, Bogers AJ, Roos-Hesselink JW. The unnatural history of an atrial septal defect: Longitudinal 35 year follow up after surgical closure at young age. *Heart* 2013; **99**:1346–1352.
7. Roos-Hesselink JW, Meijboom FJ, Spitaels SE, van DR, van REH, Utens EM, Bogers AJ, Simoons ML. Excellent survival and low incidence of arrhythmias, stroke and heart failure long-term after surgical asd closure at young age. A prospective follow-up study of 21-33 years. *Eur Heart J* 2003;**24**:190–197.
8. Attie F, Rosas M, Granados N, Zabal C, Buendia A, Calderon J. Surgical treatment for secundum atrial septal defects in patients >40 years old. A randomized clinical trial. *J Am Coll Cardiol* 2001;**38**:2035–2042.
9. Nyboe C, Olsen MS, Nielsen-Kudsk JE, Johnsen SP, Hjortdal VE. Risk of pneumonia in adults with closed versus unclosed atrial septal defect (from a nationwide cohort study). *Am J Cardiol* 2014;**114**:105–110.
10. Nyboe C, Olsen MS, Nielsen-Kudsk JE, Hjortdal VE. Atrial fibrillation and stroke in adult patients with atrial septal defect and the long-term effect of closure. *Heart* 2015;**101**:706–711.
11. Karunanithi Z, Nyboe C, Hjortdal VE. Long-term risk of atrial fibrillation and stroke in patients with atrial septal defect diagnosed in childhood. *Am J Cardiol* 2017;**119**:461–465.
12. Pedersen CB. The danish civil registration system. *Scand J Public Health* 2011;**39**: 22–25.
13. Schmidt M, Schmidt SA, Sandegaard JL, Ehrenstein V, Pedersen L, Sorensen HT. The danish national patient registry: A review of content, data quality, and research potential. *Clin Epidemiol* 2015;**7**:449–490.
14. Lynge E, Sandegaard JL, Rebolj M. The danish national patient register. *Scand J Public Health* 2011;**39**:30–33.
15. Videbaek J, Laursen HB, Olsen M, Hofsten DE, Johnsen SP. Long-term nationwide follow-up study of simple congenital heart disease diagnosed in otherwise healthy children. *Circulation* 2016;**133**:474–483.
16. Laursen HB. Some epidemiological aspects of congenital heart disease in denmark. *Acta Paediatr Scand* 1980;**69**:619–624.
17. Christensen S, Johansen MB, Christiansen CF, Jensen R, Lemeshow S. Comparison of charlson comorbidity index with saps and apache scores for prediction of mortality following intensive care. *Clin Epidemiol* 2011;**3**:203–211.
18. Quan H, Sundararajan V, Halfon P, Fong A, Burnand B, Luthi JC, Saunders LD, Beck CA, Feasby TE, Ghali WA. Coding algorithms for defining comorbidities in icd-9-cm and icd-10 administrative data. *Med Care* 2005;**43**:1130–1139.
19. Karamlou T, Diggs BS, Ungerleider RM, McCrindle BW, Welke KF. The rush to atrial septal defect closure: Is the introduction of percutaneous closure driving utilization? *Ann Thorac Surg* 2008;**86**:1584–1590; discussion 1590–1591.
20. Sadiq M, Kazmi T, Rehman AU, Latif F, Hyder N, Qureshi SA. Device closure of atrial septal defect: medium-term outcome with special reference to complications. *Cardiol Young* 2012;**22**:71–78.
21. Walters DL, Boga T, Burstow D, Scalia G, Hourigan LA, Aroney CN. Percutaneous asd closure in a large Australian series: short- and long-term outcomes. *Heart Lung Circ* 2012;**21**:572–575.
22. Guo JJ, Luo YK, Chen ZY, Cao H, Yan XP, Chen H, Peng YF, Lin CG, Chen LL. Long-term outcomes of device closure of very large secundum atrial septal defects: a comparison of transcatheter vs intraoperative approaches. *Clin Cardiol* 2012;**35**:626–631.
23. Ueda H, Yanagi S, Nakamura H, Ueno K, Gatayama R, Asou T, Yasui S. Device closure of atrial septal defect: immediate and mid-term results. *Circ J* 2012;**76**:1229–1234.
24. Jeong IS, Ahn BH, Kim SJ, Oh SG, Oh BS, Kim SH. Mid- to long-term results of surgical treatment of asd in patients over 60 years old. *Korean J Thorac Cardiovasc Surg* 2011;**44**:137–141.
25. Statistics Denmark. *Statistical 10-year review 2016*, p. 31, ISBN: 978-87-501-2224-1.
26. Frank L. Epidemiology. When an entire country is a cohort. *Science* 2000;**287**: 2398–2399.

## Corrigendum

doi:10.1093/eurheartj/ehw625
*Online publish-ahead-of-print 24 December 2016*

**Corrigendum to:** 'Randomized trial of switching from prescribed non-selective non-steroidal anti-inflammatory drugs to prescribed celecoxib: the Standard care vs. Celecoxib Outcome Trial (SCOT)' [Eur Heart J (2016) doi: 10.1093/eurheartj/ehw387]

The clinical trial registration number was missing from the above article's abstract as originally published.

Clinical Trial Registration: https://clinicaltrials.gov/show/NCT00447759 NCT00447759

The article has now been corrected online.