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Research Article

Patterns of Aortic Valve Replacement in Europe: Adoption by Age

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Short Title: AVR in Europe by Age

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Abstract

Introduction: The management of patients with severe aortic stenosis (AS) may differ according to patient age. The aim of this analysis was to describe patterns of aortic valve replacement (AVR) use in European countries stratified by age.

Methods: Procedure volume data for AVR, including surgical aortic valve replacement (sAVR) and transcatheter aortic valve implantation (TAVI), for the years 2015–2020 were obtained from national databases for twelve European countries (Austria, Czech Republic, Denmark, England, Finland, France, Germany, Norway, Poland, Spain, Sweden, and Switzerland). Procedure volumes were reported by patient age (<50 years, by five-year age groups between 50 and 85 years, and ≥85 years). Patients per million population (PPM) undergoing AVR each year were calculated using population estimates from Eurostat.

Results: AVR PPM varied widely between countries, from 508 PPM in Germany to 174 PPM in Poland in 2020. TAVI rates ranged from 61% in Switzerland and Finland to 25% in Poland. AVR PPM increased with age to a peak at 80–84 years, after which it decreased again. AVR procedures increased from 2015 to 2019 at an average annual rate of 3.9%. AVR increased more substantially in people aged ≥80 years than in younger age groups; these older age groups accounted for 30% of all AVR procedures in 2015 and 35% in 2019. TAVI accounted for an increasing proportion of all AVR procedures as patient age increased; an overall average of 96% of males and 98% of females aged ≥85 years received TAVI as the treatment modality, although adoption of TAVI differed between countries.

Conclusions: There is considerable variation in the rates of AVR use and the adoption of TAVI versus sAVR between European countries. The use of TAVI has increased in recent years, particularly for older patients.

Introduction

The prevalence of aortic stenosis (AS) increases with age, and the number of patients presenting with clinically significant AS is expected to increase in the future due to general population ageing [1-3].

In patients with severe AS, aortic valve replacement (AVR) is recommended (ESC GL 2021). ESC/EACTS guidelines recommend surgical AVR (sAVR) in patients <75 years being at low surgical risk, while transcatheter aortic valve implantation (TAVI) is recommended for patients >75 years [4] independent of surgical risk and in younger patients with intermediate to high surgical risk. In recent years, there has been a significant increase in the use of TAVI in elderly patients aged ≥80 years [5]. In addition to differences in treatment approaches between age groups, the management of patients with severe AS, including the rate of adoption of TAVI, varies between European countries [5-6]. This database analysis aimed to describe patterns of AVR (sAVR and TAVI) use stratified by age in different European countries, including an evaluation of changes over time.

Materials and Methods

Procedure volume data for surgical aortic valve replacement (sAVR) and transcatheter aortic valve implantation (TAVI) and TAVI+ PCI (percutaneous coronary intervention) combined were extracted from national statistical databases for 12 European countries, including Austria [7-9], Czech Republic [10, 11], Denmark [12,13], England [14-16], Finland [17], France [18, 19], Germany [20, 21], Norway [22-24], Poland [25-26], Spain [27, 28], Sweden [29, 30] and Switzerland [31, 32] (**Table 1** and **Supplementary Table 1**).

To compare changes in AVR over time, data were analysed for a 6-year period from 2015 to 2020 (except for England, where only data up to 2019 were available at the time of analysis).

The sAVR and TAVI codes used in the study are found in **Supplementary Table 2**. In each case, the data sources provided information on volumes of procedures by five-year age groups for patients between 50 and 85 years and by patient sex. Patients aged less than 50 were grouped together, as were those aged ≥85 years.

Due to privacy protection measures, Denmark and Norway do not provide numbers of patients for any combination of age and sex that comprises less than five patients, while in Spain, this applies when there are fewer than three patients; in these cases, values were imputed so that the sum of individual age and sex combinations added up to the total provided in the registry data. Procedure numbers are based on procedure type (sAVR or TAVI) and are not separated according to disease aetiology; therefore, the data include both aortic stenosis (AS) and aortic regurgitation (AR) procedures. Some countries report inpatient and outpatient activity, whereas others report only inpatient activity; for this analysis, it was assumed that all valve procedures took place on inpatients. It was also assumed that each database provides an almost complete picture of the sAVR and TAVI activity in the relevant country.

Patients per million population (PPM) undergoing AVR were calculated each year, using estimates of population by age and sex group published by Eurostat [33]. Data from the Office for National Statistics [34] were used for England because Eurostat does not publish estimates for that country.

Results

The average PPM undergoing AVR across all countries in 2020 was 339. The AVR PPM varied between countries, from 508 PPM in Germany to 174 PPM in Poland. Across all countries in 2020, 51% of the procedures were TAVI, and 49% were sAVR. TAVI rates ranged from 61% of all AVR in Switzerland and Finland to 25% in Poland.

There was a significant country-wise variation between PPM of AVR, especially in patients ≥80 years. Comparing PPM above and below the mean and there is a 5-fold difference between Denmark at 3,339 PPM and Poland at 664 PPM **(Shown in Fig. 1).**

In the 75–84-year age range, Austria, Denmark, Finland, France, Norway, and Switzerland exhibited high levels of AVR adoption. At the same time, the Czech Republic, England, Spain, and Sweden had a mid-level, and Poland had a lower level of adoption. In Poland, the proportion of the population treated peaked at 75–79 years, which was younger than in other countries. The significant country-specific variation persisted in the age group of very elderly (≥85 years). Overall, the treatment rates were lower in elderly patients than in those between 75 and 79 years, especially in Austria, Denmark, Finland, and Norway. Still, country-specific rates were similar to those in the younger cohort.

Aggregated data for 2015–2020 from all countries included in the study except England are presented in **Figure 2** by age and type of procedure. From 2015 to 2019, total AVR procedures grew at an average annual rate of 3.9%, with TAVI growing at an average annual rate of 16.0% and sAVR declining by 3.0%. By age group, AVR grew more substantially in people aged 80 years or older, with procedures increasing by an average of 10.8% per year in the ≥85-year age group and 6.9% per year in the 80–84-year age group compared with 1.8% in the groups below 80 years of age. This meant that over time the 80+ age groups accounted for an increasing proportion of the total (all ages combined) number of AVR performed, rising from 30% of all AVR in 2015 to 35% in 2019.

Consistent with the expansion of AVR in the elderly, the use of TAVI has increased to constitute a larger proportion of AVRs. In the age group of 75–79 years, TAVI accounted for 29% of AVR procedures in 2015 and grew to 58% in 2020. To a lesser extent, in the group aged <65 years, TAVI increased from 3% to 6% of AVR procedures between 2015 and 2019. The proportion of TAVI among total AVR procedures increased substantially with increasing age **(shown in Fig. 3).** However, the adoption of TAVI varied by country **(shown in supplementary Fig. 1).** Particularly in the age group 75-79 years, the ratio of TAVI to SAVR differed from 78% in Finland to 34% in England.

Discussion

Nearly 20 years ago, the Euro Heart Survey highlighted that the most frequently stated reason that patients did not undergo treatment for single valve disease was old age [35]. In recent years up to 2020, substantial growth in treating patients aged >80 years, which is likely to continue as the population ages, confirms that TAVI has given new options for patients suffering from aortic valve disease. The fact that the growth of AVR PPM in the elderly age groups continues upward suggests that many patients remain untreated.

Our analysis highlights the variation in AVR PPM across European countries and may identify the age-specific undertreatment. Differences in reimbursement systems between countries may account for some of this. However, the different AVR adoption rates also reflect the age demographics in different countries. For example, in Germany 11.5% of its population is 75 years or older. If we adjust for the age profile differences by calculating the overall AVR PPM rate as if every country had the same age profile, the difference in overall PPM between Germany and Norway changes from 157 to 42 **(shown in supplementary Fig. 2**).

Naturally, a question arises about whether the higher AVR adoption countries have seen a steeper reduction in the surgical approach than the low-adoption countries. To some extent, this can be observed, as relatively high use of sAVR remains in England's 80–84-year age group; likewise, sAVR adoption in Sweden is higher than in its Nordic neighbours. However, Germany, a country with a very high level of AVR adoption, and Spain, a country with comparably lower AVR adoption, have similar sAVR adoption rates in that age group. Likewise, in the 75-79-year age group, we can observe that France, Germany, and Austria have strong adoption of surgery, far higher than in countries with lower adoption of TAVI, such as England, Spain and Sweden. These observations suggest that sAVR implant levels are relatively independent of overall AVR adoption and that increased utilisation of TAVI is not at the cost of decreased SAVR (16% increase of TAVI and 3% decrease of SAVR) but rather reflects improved diagnosis and referral pathways.

Treatment of the very elderly (≥85 years)

The increase in the prevalence of AS with age is well documented. In a large study, Nkomo et al. [36] showed moderate to severe AS increasing from 0.2% in the general population in the age range 55–64 to 2.8% in the ≥75-years group. The AGES-Reykjavik found a prevalence of severe AS (diagnosed by AV area measured with echocardiography) of 2.4% at age 70–79 years, which increased steeply to 7.3% at age >80 years [37]. The Tromsø study reported the prevalence of mild, moderate, and severe AS (identified by a mean gradient) to be 3.7% at age 70–79 years and 10.3% at age 80–89 years [2].

The steep increase in the percentage of the population with AS is evident in the treatment data presented in this study. **Fig. 3** reveals a consistent relationship between age and PPM, reaching a peak in the 80–84-year age group. That peak involved 0.42% of the male population and around 0.27% of females in Germany in 2020. It is not difficult to imagine the increase in the proportion of individuals affected by AS continuing into the elderly population aged ≥85 years. Some countries treat a higher portion of the very elderly. France shows a relatively small difference of 10% between the peak treatment rates observed in the 80–84-year age group and in the ≥85-year age group (**shown in supplementary Fig. 3**). That compares favourably to Spain, where the older age group is treated far less than the 80–84-year group, with a 42% difference. We do not know the clinical condition of the very elderly patients behind these numbers, which could explain some of the differences between countries and sexes. Still, we can speculate that the advanced age and likely higher comorbidities of this population probably prevent their being referred for AVR or being treated once they are referred. Nevertheless, as prevalence rates probably increase in the ≥85-year age group, and treatment rates currently decrease in this age group in all countries, this indicates a degree of undertreatment that might be corrected by careful selection.

Outcomes/life expectancy for 85+ and nonagenarian patients

Patients aged >85 years can have excellent outcomes after TAVI. About half of the patients undergoing TAVI in the randomized PARTNER study [38] had an age of 83.6 and above, but randomized studies in nonagenarians are clearly missing. Other studies have generally found that rates of post-TAVI complications and 30-day and 1-year mortality in patients aged >85 years are similar to those in patients aged <85 [39-41]. However, studies specifically evaluating nonagenarians have produced conflicting results. Some registry studies have reported a higher rate of mortality in patients aged >90 years compared with younger patients at 30 days [42, 43] and one year [42] post-TAVI. In contrast, other studies have found that survival was similar between patients above and below 90 years at up to 4–5 years post-TAVI [44, 45]. One study found that mortality at 1-year post-TAVI was higher in nonagenarians compared with an age- and sex-matched general population cohort, but that after two years, the survival curves converged [46]. The Swiss-TAVI registry found a linear increase in post-TAVI complications and mortality with increasing age. Still, it noted that after 90 years of age, patients who underwent TAVI had similar mortality to a national reference population [47]. Age should not be the sole deciding factor when treating patients with AS; other factors, such as comorbidities and frailty, should be considered [48]. TAVI may be appropriate for fully selected nonagenarians [42, 46, 49].

sAVR conversion and 2021 Guidelines

The 2021 ESC/EACTS guidelines for managing valvular heart disease recommend sAVR for symptomatic AS patients aged <75 years who are low surgical risk and TAVI for patients aged ≥75 years or younger patients who are intermediate to high risk [4]. Our study gathered data before the publication of this update. In addition, we did not obtain information on the specific reasons for treatment choices in patients. However, we can make some general comments concerning the patient's age. In 2020, TAVI was used in the majority of patients aged ≥75 years in the overall analysis, although a substantial number of younger patients also received TAVI. There was considerable variation between countries, most notably in the 75–79-year age group, with less than half of patients in this age group receiving TAVI in several countries, including England and Spain. In the overall analysis, the use of TAVI increased in all age groups between 2015 and 2019, including in patients aged <65 years. This might suggest that in some European countries, real-world clinical practice differs from the latest guideline recommendations, something which has been noted previously in Europe and the USA

[50, 51]. However, there are various possible reasons for using TAVI in younger age groups, such as patients being high risk, patient preference, and an increasing level of surgical experience and availability of improved devices leading to younger high-risk patients being treated.

Limitations

Data were obtained for 12 European countries; efforts were made to identify data sources for other Western European countries, including Belgium, Ireland, Italy, Netherlands, and Portugal, but were unsuccessful. This analysis relied on information about procedure volumes from publicly available sources. We did not obtain data specifically for AS; therefore, AVR performed to treat AR is included in the procedure numbers. This study did not report clinical outcomes; however, clinical data on AS patients in France from the same PMSI database have been reported previously [52, 53]. Comparison of PMSI data for cases of AS with our dataset from the same source that included all etiologies suggests that in 2019, AR comprised 29% of sAVR cases (increasing from 24% in 2011) and 4% of TAVI cases (decreasing from 5% in 2011). The AR cases included in our analysis may affect the strength of the observations.

Conclusions

There is considerable variation in the rates of AVR use and the adoption of TAVI versus sAVR between European countries. Given that age-stratified prevalence rates appear similar across European countries, the data suggest that this variation may also be the results in differences in healthcare systems. Overall, it has been observed the use of TAVI has increased in recent years, particularly for older patients.

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None

Statement of Ethics

Ethical approval and consent were not required as this study was based on publicly available data.

Inform consent Statement

Ethical approval and consent were not required as this study was based on publicly available data.

Conflict of Interest Statement

Nathan Petersen and Jana Kurucova are employees of Edwards Lifesciences, a manufacturer of TAVI and sAVR valves. Peter Bramlage is a research consultant and received funding for performing clinical research into the safe use of aortic valves by Edwards Lifesciences. The other authors have held lectures and were part of advisory boards, which were held

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Author contributions

NP developed the idea for the manuscript, which was collectively discussed and refined in the group of authors (CA, VD, HE, CG, CH, WW, JK, PB), which was moderated and collated by TR and SB. NP collated the data and performed the statistical analyses. PB drafted the first version of the manuscript in close cooperation with TR and SB. The outcomes of the analysis and the manuscript draft subsequently underwent critical revision by all coauthors (CA, VD, HE, CG, CH, WW, NP, JK). PB then revised the manuscript based on the author's comments and submitted the manuscript. All authors approved the submission of the final manuscript version (TR, CA, VD, HE, CG, CH, WW, NP, JK, PB, SB).

Data Availability Statement

The data underlying this article is not publicly available due to ethical reasons. Further enquiries can be directed to the corresponding author.

References

1 Iung B, Delgado V, Rosenhek R, Price S, Prendergast B, Wendler O, et al.; EORP VHD II Investigators. Contemporary presentation and management of valvular heart disease: the EURObservational Research Programme Valvular Heart Disease II Survey. Circulation. 2019 Oct;140(14):1156-69.

2 Eveborn GW, Schirmer H, Heggelund G, Lunde P, Rasmussen K. The evolving epidemiology of valvular aortic stenosis. the Tromsø study. Heart. 2013 Mar;99(6):396-400.

3 Bonow RO, Greenland P. Population-wide trends in aortic stenosis incidence and outcomes. Circulation. 2015 Mar 17;131(11):969-71.

4 Vahanian A, Beyersdorf F, Praz F, Milojevic M, Baldus S, Bauersachs J, et al.; ESC/EACTS Scientific Document Group. 2021 ESC/EACTS Guidelines for the management of valvular heart disease. Eur J Cardiothorac Surg. 2021 Oct 22;60(4):727-800.

5 Eugène M, Duchnowski P, Prendergast B, Wendler O, Laroche C, Monin JL, et al.; EORP VHD II Registry Investigators Group. Contemporary management of severe symptomatic aortic stenosis. J Am Coll Cardiol. 2021 Nov 30;78(22):2131-43.

6 Lutz M, Messika-Zeitoun D, Rudolph TK, Schulz E, Thambyrajah J, Lloyd G, et al. Differences in the presentation and management of patients with severe aortic stenosis in different European centres. Open Heart. 2020 Sep;7(2):e001345.

7 Gesundheit Österreich [internet]. Österreichisches Gesundheitsinformationssystem – Auswertungen. [cited 2022 Jan 3]. Available from: https://goeg.at/OEGIS.

8 Statistics Austria [Internet]. Health information systems in Europe - Structures and processes. [cited 2022 Jan 3]. Available from: https://ec.europa.eu/health/ph_projects/2001/monitoring/fp_monitoring_2001_a1_frep_13_en.pdf.

9 Bundesministerium Soziales, Gesunheit, Pflege und Konsumentenschutz [Internet]. Leistungskatalog BMSGPK 2021. [cited 2022 Jan 3]. Available from: https://www.sozialministerium.at/dam/jcr:f2b8f869-146b-48a2-96aa-7fbc5c5a7b13/LEISTUNGSKATALOG%20BMSGPK%202021.pdf.

10 Institute of Health Information and Statistics of the Czech Republic. [Internet]. NRHZS. [cited 2022 Jan 3]. Available from: https://www.uzis.cz/index.php?pg=registry-sber-dat--narodni-registr-hrazenych-zdravotnich-sluzeb.

11 Institute of Health Information and Statistics of the Czech Republic [Internet]. NRKOI – Modul kardiochirurgických operací (NKR). [cited 2022 Apr 5]. Available from: https://www.uzis.cz/index.php?pg=registry-sber-dat--narodni-zdravotni-registry--narodni-registr-kardiovaskularnich-operaci-a-intervenci--modul-kardiochirurgickych-operaci.

12 eSundhed [Internet]. Dokumentation af register esundhed.dk [cited 2022 Jan 3]. Available from: https://www.esundhed.dk/Dokumentation/DocumentationExtended?id=5.

13 Sundhedsdatastyrelsen [Internet]. SKS-dumper, vers 1.06. [cited 2022 Jan 3]. Available from: https://medinfo.dk/sks/dump.php.

14 NHS Digital [Internet]. Hospital admitted patient care activity 2016-2019. [cited 2022 Jan 3]. Available from: https://digital.nhs.uk/data-and-information/publications/statistical/hospital-admitted-patient-care-activity.

15 NHS Digital [Internet]. NHS Digital's legal right to collect information. [cited 2022 Jan 3]. Available from: https://digital.nhs.uk/about-nhs-digital/our-work/keeping-patient-data-safe/how-we-look-after-your-health-and-care-information/nhs-digital-s-legal-right-to-collect-information.

16 NHS [Internet]. Classifications Browser OPCS-4.9. [cited 2022 Jan 4]. Available from: https://classbrowser.nhs.uk/#/book/OPCS-4.9/volume1-p2-1.html+PART_2.

17 Finnish Institute for Health and Welfare [Internet]. Primary health care. [cited 2022 Apr 5]. Available from: https://thl.fi/en/web/thlfi-en/statistics-and-data/data-and-services/quality-and-statistical-principles/quality-descriptions/primary-health-care.

18 Boudemaghe T, Belhadj I. Data Resource Profile: The French National Uniform Hospital Discharge Data Set Database (PMSI). Int J Epidemiol. 2017 Apr1;46(2):392-392d.

19 Sécurité Sociale l'Assurance Maladie [Internet]. CCAM en ligne. [cited 202 Jan 3]. Available from: https://www.ameli.fr/accueil-de-la-ccam/index.php.

20 Statistiches Bundesamt (DESTATIS) [Internet]. Case-based hospital statistics (DRG statistics) Operations and procedures for inpatients and patients in hospitals up to the encodable endpoint. 2016-2019. [cited 202 Jan 3]. Available from: https://www.destatis.de/DE/Home/_inhalt.html.

21 Federal Institute for Drugs and Medical Devices [Internet]. OPS. [cited 2022 Jan 3]. Available from: https://www.dimdi.de/dynamic/en/classifications/ops/index.html.

22 Lovdata [Internet]. Norwegian Patient Register Regulations. [cited 2022 Jan 3]. Available from: https://lovdata.no/dokument/SF/forskrift/2007-12-07-1389/KAPITTEL_1#%C2%A71-2.

23 Helsedirektoratet [Internet]. Datasett. helsedirektoratet.no. [cited 2022 Jan 3]. Available from: https://www.helsedirektoratet.no/tema/statistikk-registre-og-rapporter/helsedata-og-helseregistre/norsk-pasientregister-npr/datasett.

24 Direktoratet for e-helse [Internet]. Norsk klinisk prosedyrekodeverk. [cited 2022 Jan 3]. Available from: https://www.ehelse.no/kodeverk/prosedyrekodeverkene-kodeverk-for-medisinske-kirurgiske-og-radiologiske-prosedyrer-ncmp-ncsp-og-ncrp.

25 Zdrowia, Narodowy Fundusz [Internet]. Statystyki. NFZ Narodowy Fundusz Zdrowia. [cited 2022 May 5]. Available from: https://statystyki.nfz.gov.pl/.

26 Bartus K, Sadowski J, Litwinowicz R, Filip G, Jasinski M, Deja M, et al. Changing trends in aortic valve procedures over the past ten years-from mechanical prosthesis via stented bioprosthesis to TAVI procedures-analysis of 50,846 aortic valve cases based on a Polish National Cardiac Surgery Database. J Thorac Dis. 2019 Jun;11(6):2340-49.

27 Gobierno de España Ministerio de Sanidad [Internet]. Portal Estadistíco. [cited 2022 Jan 3]. Available from: https://pestadistico.inteligenciadegestion.mscbs.es/publicoSNS/S/rae-cmbd.

28 World Health Organization [Internet]. ICD-10 Version:2016. [cited 2022 Jan 3]. Available from: https://icd.who.int/browse10/2016/en.

29 Socialstyrelsen [Internet]. Om statistiken. [cited 2022 Jan 3]. Available from: https://www.socialstyrelsen.se/statistik-och-data/statistik/om-statistiken/.

30 NOMESCO [Internet]. NOMESCO Classification of Surgical Procedures. [cited 2022 Jan 3]. Available from: https://norden.diva-portal.org/smash/get/diva2:970547/FULLTEXT01.pdf.

31 Federal Office for Statistics Switzerland [Internet]. Health bfs.admin.ch. [cited 2022 May 5]. Available from: https://www.bfs.admin.ch/bfs/de/home/statistiken/gesundheit.html.

32 Federal Office for Statistics [Internet]. Swiss Operation Classification (CHOP). [cited 2022 May 5]. Available from: https://www.bfs.admin.ch/bfs/de/home/statistiken/kataloge-datenbanken/publikationen.assetdetail.9286150.html.

33 Eurostat [Internet]. Population on 1 January by age group, sex and citizenship. [cited 2022 Jan 3]. Available from: https://appsso.eurostat.ec.europa.eu/nui/show.do?dataset=migr_pop1ctz&lang=en.

34 Office for National Statistics [Internet]. Clinical Commissioning Groups (CCGs) population estimates by single year of age and sex, England: mid-2001 to mid-2019. [cited 2022 Jan 3]. Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationestimates/adhocs/12429clinicalcommissioninggroupsccgspopulationestimatesbysingleyearofageandsexenglandmid2001tomid2019.

35 Iung B, Baron G, Butchart EG, Delahaye F, Gohlke-Bärwolf C, Levang OW, et al. A prospective survey of patients with valvular heart disease in Europe: The Euro Heart Survey on Valvular Heart Disease. Eur Heart J. 2003 Jul;24(13):1231-43.

36 Nkomo VT, Gardin JM, Skelton TN, Gottdiener JS, Scott CG, Enriquez-Sarano M. Burden of valvular heart diseases: a population-based study. Lancet. 2006 Sep 16;368(9540):1005-11.

37 Danielsen R, Aspelund T, Harris TB, Gudnason V. The prevalence of aortic stenosis in the elderly in Iceland and predictions for the coming decades: the AGES-Reykjavík study. Int J Cardiol. 2014 Oct 20;176(3):916-22.

38 Leon MB, Smith CR, Mack M, Miller C, Moses JW, Svensson LG, et al. Transcatheter Aortic Valve Implantation for Aortic Stenosis in Patients Who Cannot Undergo Surgery. J Engl J Med. 2011; 363: 1597-1607.

39 van den Brink FS, Wijtsma I, Amrane H, Vossenberg TNE, Haenen J, Porta F, et al. Outcome of transcatheter aortic valve replacement in patients over 85 years of age versus patients aged 85 and younger. Neth Heart J. 2022 Oct;30(10):473-78.

40 Kara K, Kloppe A, Ewers A, Bösche L, Aweimer A, Erdogan H, et al. Outcomes after transcatheter aortic valve replacement in older patients. Herz. 2021 Sep;46(Suppl 2):222-27.

41 Dąbrowski M, Pyłko A, Chmielak Z, Kwieciński J, Kukuła K, Wysocki K, et al. Comparison of transcatheter aortic valve implantation outcomes in patients younger than 85 years and those aged 85 years or older: a single-center study. Pol Arch Intern Med. 2021 Feb 26;131(2):145-51.

42 Arsalan M, Szerlip M, Vemulapalli S, Holper EM, Arnold SV, Li Z, et al. Should transcatheter aortic valve replacement be performed in nonagenarians?: insights from the STS/ACC TVT Registry. J Am Coll Cardiol. 2016 Mar 29;67(12):1387-95.

43 Vlastra W, Chandrasekhar J, Vendrik J, Gutierrez-Ibanes E, Tchétché D, de Brito FS Jr, et al. Transfemoral TAVR in nonagenarians: from the CENTER Collaboration. JACC Cardiovasc Interv. 2019 May 27;12(10):911-20.

44 Vendrik J, van Mourik MS, van Kesteren F, Henstra MJ, Piek JJ, Henriques JPS, et al. Comparison of outcomes of transfemoral aortic valve implantation in patients <90 with those >90 years of age. Am J Cardiol. 2018 Jun 15;121(12):1581-86.

45 Habertheuer A, Aranda-Michel E, Schindler J, Gleason TG, Kilic A, Kliner D, et al. Longitudinal outcomes of nonagenarians undergoing transcatheter aortic valve replacement. Ann Thorac Surg. 2021 May;111(5):1520-28.

46 Barth S, Hautmann MB, Reents W, Zacher M, Griese DP, Kerber S, Diegeler A, Hamm K. Transcatheter aortic valve replacement for severe aortic stenosis can improve long-term survival of nonagenarians as compared to an age- and sex-matched general population. J Cardiol. 2020 Feb;75(2):134-9.

47 Attinger-Toller A, Ferrari E, Tueller D, Templin C, Muller O, Nietlispach F, et al. Age-related outcomes after transcatheter aortic valve replacement: insights from the SwissTAVI Registry. JACC Cardiovasc Interv. 2021 May10;14(9):952-60.

48 Adrichem R, Van Mieghem NM. Age is no factor in TAVI. Neth Heart J. 2022 Oct;30(10):447-8.

49 Galatas C, Afilalo J. Transcatheter aortic valve replacement over age 90: Risks vs benefits. Clin Cardiol. 2020 Feb;43(2):156-62.

50 Lauten A, Rudolph TK, Messika-Zeitoun D, Thambyrajah J, Serra A, Schulz E, et al. Management of patients with severe aortic stenosis in the TAVI-era: how recent recommendations are translated into clinical practice. Open Heart. 2021 Jan;8(1):e001485.

51 Sharma T, Tapales AJD, Ross CS, Malenka DJ, Flynn JM, Ferguson M, et al. Concordance of guideline-based risk stratification and selection of patients for transcatheter aortic valve implantation or surgical replacement. Am J Cardiol. 2022 Jun 15; 173:94-9.

52 Grave C, Juillière Y, Tuppin P, Weill A, Gabet A, Tribouilloy C, Olié V. Epidemiological features of aortic stenosis in a French nationwide study: 10-year trends and new challenges. J Am Heart Assoc. 2020 Dec;9(23):e017588.

53 Nguyen V, Willner N, Eltchaninoff H, Burwash IG, Michel M, Durand E, et al. Trends in aortic valve replacement for aortic stenosis: a French nationwide study. Eur Heart J. 2022 Feb 12;43(7):666-79.

TABLES

Table 1. Sources of data by country

Legend: sAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation

FIGURES

Fig. 1. Patients per million undergoing AVR procedures by age group, for both sexes combined for each country

Legend: AVR, aortic valve replacement

Fig. 2. Trends in absolute numbers of AVR by age and therapy type for all countries included in the study except England. Average annual growth rates for 2015–2019 for A) TAVI and B) sAVR.

Legend: AVR, aortic valve replacement; sAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation

Fig. 3. Average patients per million by age and therapy in 2020 (England 2019) for all countries combined (overall population)

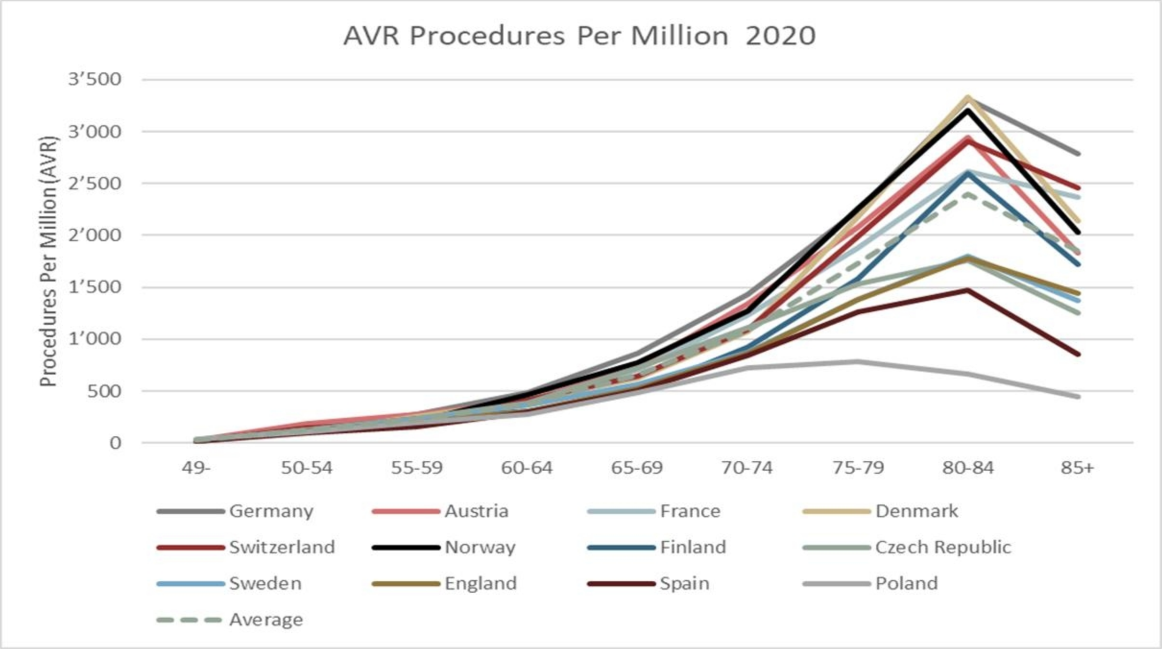
Legend: AVR, aortic valve replacement; PPM, patients per million; TAVI, transcatheter aortic valve implantation

Table 1. Sources of data by country

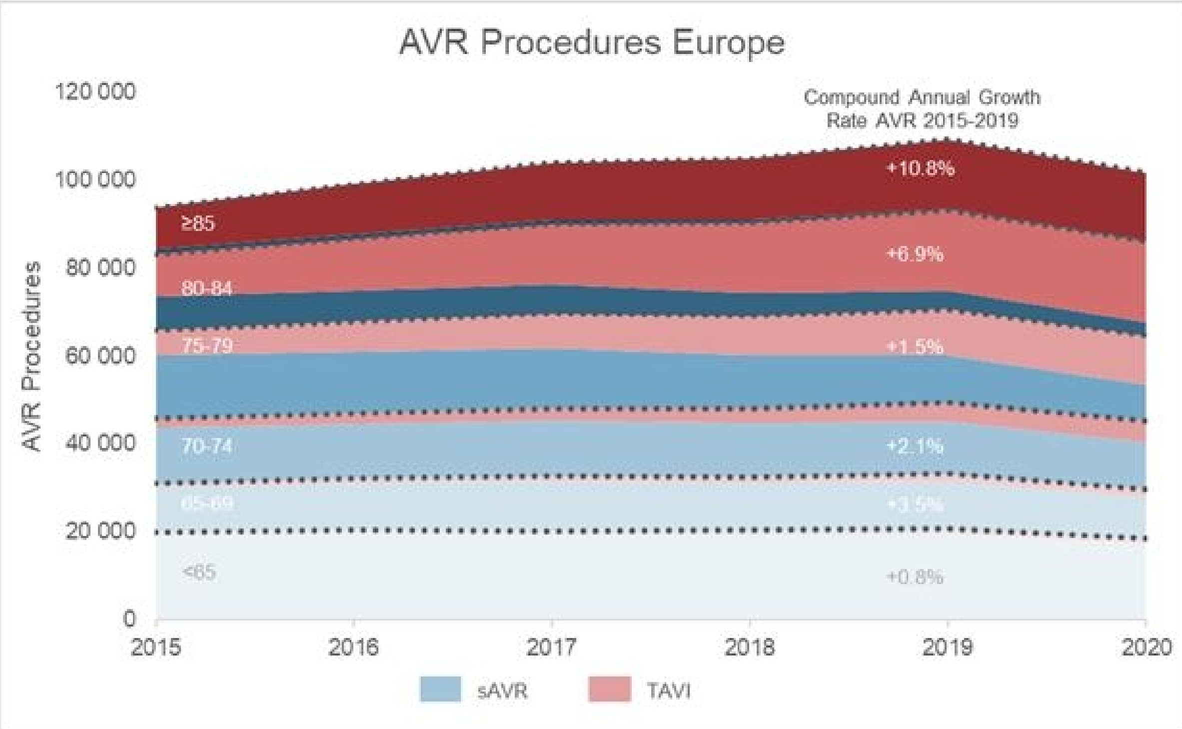
Country	Source
Austria	ÖGIS (Austrian Health Information System) [7-9] Data were requested directly from the authority
Czech Republic	UZIS (Institute of Health Information and Statistics) [10, 11] Data were requested directly from the authority
Denmark	National Patient Register [12, 13] Data available online through to 2018, and requested directly from the National Patient Register for 2019 and 2020
England	NHS Digital (National Health Service) [14-16] Total AVR data available online; codes distinguishing sAVR from TAVI were requested directly from NHS Digital
Finland	THL (Institute of Health and Welfare) [17] Data were requested directly from the authority
France	PMSI (Programme de Médicalisation des Systèmes d'Information) [18, 19] Data were requested directly from the authority
Germany	DESTATIS (German Federal Office of Statistics) [20, 21] Data were requested directly from the authority
Norway	National Patient Register [22-24] Total AVR data available online; codes distinguishing sAVR from TAVI were requested directly from the Norwegian Directorate of Health
Poland	NFZ (National Health Fund) [25, 26] Data were requested directly from the authority
Spain	RAE-CMBD (Registry of Specialized Health Activity [27, 28] Data available online
Sweden	National Board of Health and Welfare [29, 30] Data available online

Switzerland	BFS (Federal Statistics Office) [31, 32] TAVI and sAVR data available online; specific data splits by sex and five-year age groupings were requested directly from the Federal Statistics Office

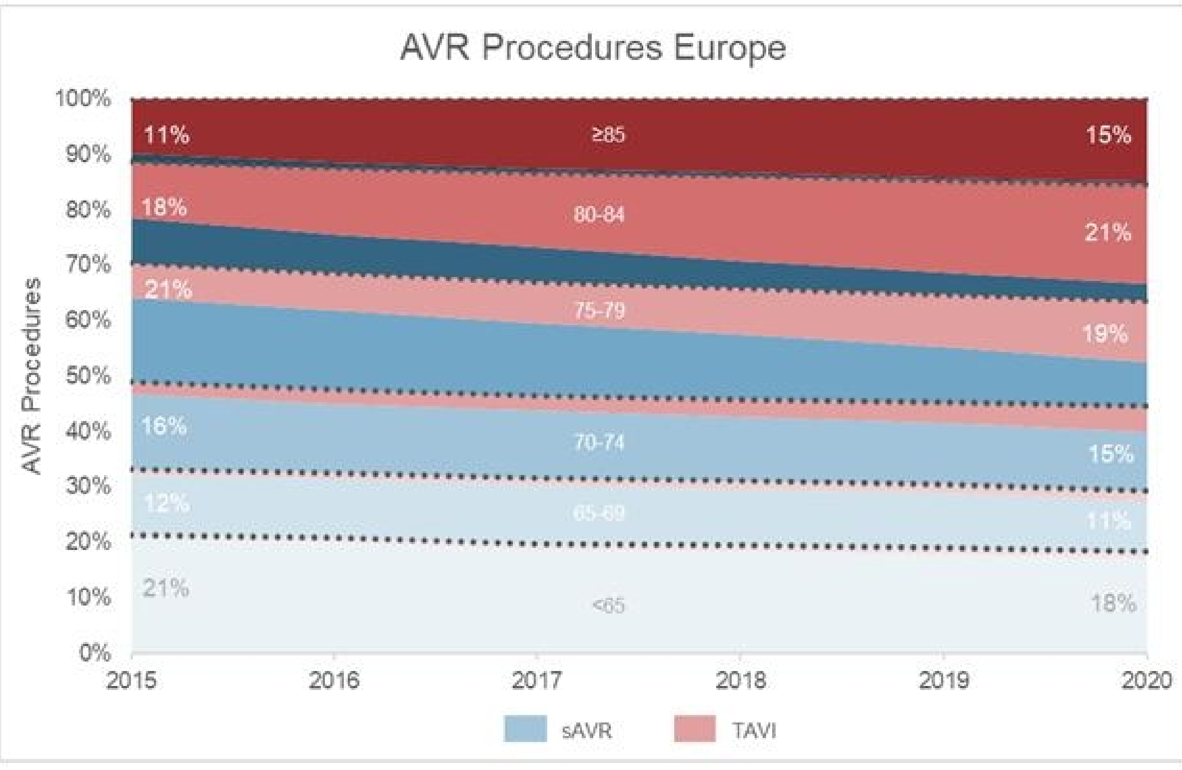
Legend: sAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation



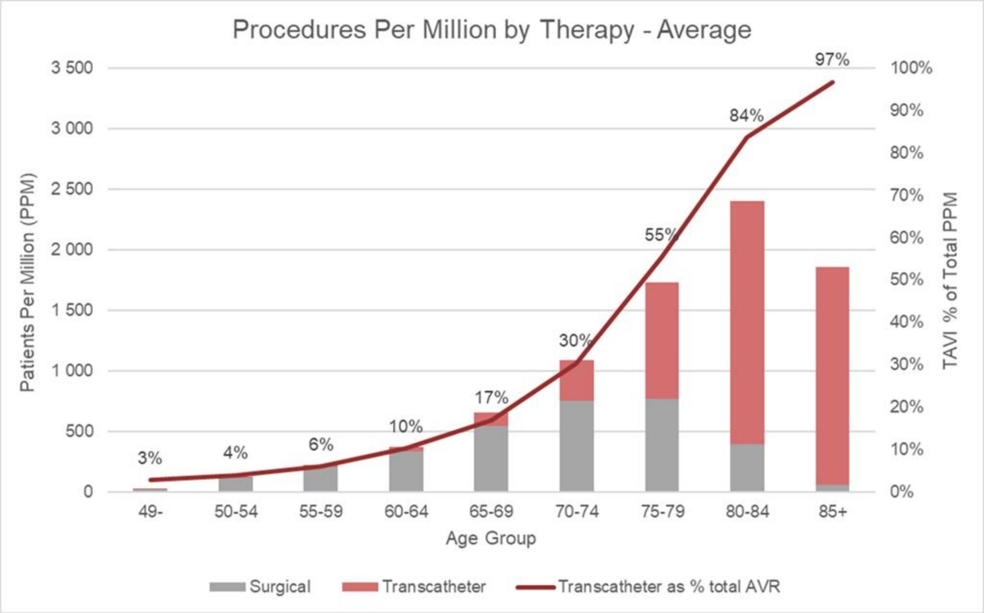
AVR Procedures Per Million 2020
Procedures Per Million (AVR)
3’500
3’000
2’500
2’000
1’500
1’000
500
0
49-
50-54
55-59
60-64
65-69
70-74
75-79
80-84
85+
Germany
Austria
France
Denmark
Switzerland
Norway
Finland
Czech Republic
Sweden
England
Spain
Poland
Average



AVR Procedures Europe
Compound Annual Growth Rate AVR 2015-2019
120 000
100 000
80 000
60 000
40 000
20 000
0
AVR Procedures
≥85
80-84
75-79
70-74
65-69
<65
+10.8%
+6.9%
+1.5%
+2.1%
+3.5%
+0.8%
2015
2016
2017
2018
2019
2020
sAVR
TAVI



AVR Procedures Europe
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
AVR Procedures
11%
≥85
15%
18%
80-84
21%
21%
75-79
19%
16%
70-74
15%
12%
65-69
11%
21%
<65
18%
2015
2016
2017
2018
2019
2020
sAVR
TAVI



Procedures Per Million by Therapy - Average
Patients Per Million (PPM)
3 500
3 000
2 500
2 000
1 500
1 000
500
0
TAVI % of Total PPM
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
3%
4%
6%
10%
17%
30%
55%
84%
97%
49-
50-54
55-59
60-64
65-69
70-74
75-79
80-84
85+
Age Group
Surgical
Transcatheter
Transcatheter as % total AVR

Supplementary material Legends

Supplementary Table 1 Sources of data by country

Legend: sAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation

Supplementary Table 2 Procedure classification system and procedure codes for sAVR and TAVI used in the study

Legend: sAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation

Supplementary Fig. 1. Average patients per million by age and therapy for individual countries in 2020 (except England, 2019)

Legend: AVR, aortic valve replacement; PPM, patients per million; TAVI, transcatheter aortic valve implantation

Supplementary Fig. 2. Impact of the age profile of individual countries: aortic valve replacement (AVR) patients per million population (PPM), unadjusted and adjusted for age profile calculated as if the age profile of each country corresponded to the average of all countries

Legend: PPM = patients per million population.

Supplementary Fig. 3. Difference in aortic valve replacement implants per million from the 80–84-year age group to the ≥85-year age group, expressed as a positive number

Legend: PPM = patients per million population

Supplementary Table 1 Sources of data by country

Country	Source
Austria	ÖGIS (Austrian Health Information System) ÖGIS is maintained by Health Austria (GÖG). Data are sourced from individual hospitals and consolidated at the federal level by GÖG [7]. Individual hospitals are required to report the medical procedures by the Documentation in Health Care Act (No. 745/1996 §1)[8]. Procedure coding with a MEL code is required for reimbursement in the diagnosis-related group (DRG) system [9].
Czech Republic	UZIS (Institute of health information and statistics) Data for the Czech Republic come from UZIS and a combination of two sources: TAVI data were sourced from the NRHZS or National Register of Paid Health Services and sAVR data from the NKR or Cardiac Surgery Module. Data for the NRHZS is reported by insurers and contains all reported and recognized procedures provided by a healthcare provider in the Czech Republic [10]. The NKR is a registry that records all cardiac surgeries performed and each cardiac surgery center in the Czech Republic is required to report surgery data to the registry [11]. In each registry, a unique patient identifier is used, and duplicates are removed from the report obtained from UZIS. TAVI codes are provided in **Supplementary Table 1**. UZIS reported that sAVR was identified in the NKR as surgical replacements of aortic valves.
Denmark	National Patient Register The National Patient Register in Denmark is maintained by the Danish Health and Medicines Authority [12]. The legal basis for the register is provided by the Health Act LBK no 1188. The register includes all procedures taking place in public hospitals and in private hospitals paid for by public funds; because of the DRG system in Denmark, private hospitals are not paid for publicly funded procedures without the episode being recorded in the register. Activity relating to self-pay or insurance pay procedures may be incomplete, but we assumed most valve replacement procedures in Denmark were public pay. In Nordic countries, procedures are classified according to the NOMESCO (Nordic Medico-Statistical Committee) coding; in Denmark a slightly different NOMESCO coding is used, called SKS coding [13].
England	NHS Digital (National Health Service) Procedures in England are published by the NHS Digital organization in the Hospital Episodes Statistics (HES) data warehouse [14]. NHS Digital is given legal right to collect healthcare information by the Health and Social Care Act 2012 [15]. The database contains all admissions to NHS hospitals as well as NHS commissioned activity in non-NHS hospitals. Patient stays are recorded as Finished

	Consultant Episodes (FCEs) and are defined as a period of care for a patient under a single physician at a single hospital. Activity taking place in the rest of the United Kingdom (Scotland, Wales, and Northern Ireland) are not recorded in the NHS England Digital database. A year in the database is defined as the period between April 1 and March 31 of the following calendar year; for simplicity, we matched the NHS data to the calendar year where most of the overlap occurs. For example, the NHS England year 2018/2019 is matched to calendar year 2018. Procedures in England are coded with an OPCS number, specific to the NHS system [16].
Finland	THL (Institute of Health and Welfare) In Finland, maintenance of healthcare statistics is the responsibility of the THL, and inpatient hospital stays are reported by the mandate of several legal acts [17]. Individual municipalities who are responsible for healthcare submit data on inpatient stays yearly to THL, who engage in data quality checks and aggregate the data at the national level. THL procedure codes are a variation on the Nordics NOMESCO coding system and are specific to Finland.
France	PMSI (Programme de Médicalisation des Systèmes d'Information) The PMSI is an administrative database comprising all procedures taking place in France in both public and private hospitals. The purpose of the database is primarily to facilitate the reimbursement of procedures in the French Prospective Payment System (PPS) [18]. Procedures are coded according to a common classification scheme for France, the CCAM [19].
Germany	DESTATIS (German Federal Office of Statistics) For Germany, we used case-based hospital statistics published by the German Federal Office of Statistics [20]. The dataset includes all inpatient procedures in hospitals that are reimbursed by health insurers through the country's DRG reimbursement system by application of §1 of the Hospital Remuneration Act (KHEntgG). Data are grouped according to an operation and procedure code (OPS) specific to the German healthcare system [21].
Norway	National Patient Register The Norwegian Directorate of Health maintains a Patient Register for the purposes of administration and quality assurance of the specialist health services in the country. The legal basis for the register is determined by Royal Decree no. 7 from December 2007 and relates to the Ministry of Health and Care Services [22]. The Norwegian Patient Register contains both procedures funded through the DRG system in the country and activity with other funding [23]. Coding of procedures is accomplished using an NCSP number [24], using the NOMESCO system as a basis.
Poland	NFZ (National Health Fund)

	The NFZ maintains data relating to numbers of procedures paid for by the NFZ [25]. We assumed all procedures in Poland are paid for by the NFZ. Specific to the sAVR codes, there is some ambiguity in the definition of the surgical procedure codes. The code descriptions reference a particular surgical procedure, but the descriptions also include procedures that cost similar amounts as the referenced procedure. It is possible the data overstate the number of sAVRs if procedures of a similar cost but not representing an AVR are recorded using the same codes. We compared the 2015 NFZ surgical data to a recent publication of the mandatory Polish National Cardiac Surgery Database[26]. That study excluded patient records that were less than 90% complete and patients younger than 18 years of age and would therefore logically be lower than those reported by NFZ. Indeed, we found the NFZ numbers to be about 23% higher than the cardiac surgery database (7504 versus 6101), highlighting the potential overstatement of the NFZ numbers.
Spain	RAE-CMBD (Registry of Specialized Health Activity) The RAE-CMBD from the Spanish Ministry of Heath combines administrative and clinical information on patients treated in Spain. Updated rules for RAE-CMBD were introduced by royal decree 69/2015 in 2015, and since 2016 the registry reports data on procedures occurring in both public and private hospitals [27]. ICD-10 procedure codes [28] have been used as the basis of the RAE-CMBD procedure registry from 2016 onwards; prior to that year, ICD-9 codes were used.
Sweden	National Board of Health and Welfare The Swedish National Board of Health and Welfare has been appointed by the government to be responsible for, and publish statistics related to, healthcare, and is regulated by law (2001: 99) on official statistics [29]. Data related to sAVR and TAVI can be found in the National Patient Registry of specialist care. The statistics reported are inpatient care and outpatient specialist care visits. Hospitals in Sweden use the NOMESCO (Nordic Medico-Statistical Committee) classification of surgical procedures for recording procedure numbers in the database [30].
Switzerland	BFS (Federal Statistics office) In Switzerland, hospital medical statistics are collected by the BFS. The data are collected from every hospital in Switzerland on a yearly basis. The legal basis is provided by Federal Statistics Law of October 1, 1992 (BStatG) and the Federal Health Insurance Act of March 18, 1994 (KVG) [31]. In Switzerland, CHOP codes are used for classifying procedures and the coding is unique to Switzerland [32].

Legend: sAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation

Supplementary Table 2 Procedure classification system and procedure codes for sAVR and TAVI used in study

Country	Classification System	Procedure Code	Description	Procedure Type
Austria	MEL	DB070	Replacement of the aortic valve with a stentless valve	sAVR
Austria	MEL	DB080	Replacement of the aortic valve with a stented valve	sAVR
Austria	MEL	DB082	Replacement of the aortic valve with an artificial mechanical valve	sAVR
Austria	MEL	DG090	Reconstruction of the ascending aorta with aortic valve replacement	sAVR
Austria	MEL	DG100	Reconstruction of the ascending aorta with aortic valve replacement in cardiac arrest	sAVR
Austria	MEL	DB025	Replacement of the aortic valve - catheter-supported, transapical	TAVI
Austria	MEL	DB026	Replacement of the aortic valve - catheter-supported, transvascular	TAVI
Czech Republic		7035	(DRG) Transapical transcatheter aortic valve implantation	TAVI
Czech Republic		17697	Catheter implantation of the valve	TAVI
Czech Republic		55097	(DRG) Transapical implantation of a biological heart valve	TAVI
Czech Republic		55225	Transcatheter implantation of a biological heart valve by surgery	TAVI
Czech Republic		91757	(DRG) Transaortic transcatheter aortic valve implantation	TAVI
Denmark	SKS	KFMD00	Reduction of mechanical aortic valve prosthesis	sAVR
Denmark	SKS	KFMD10	Insertion of biological aortic valve prosthesis	sAVR
Denmark	SKS	KFMD20	Insertion of aortic valve homograft	sAVR
Denmark	SKS	KFMD30	Reconstruction of aortic root with homograft and coronary reimplantation	sAVR

Denmark	SKS	KFMD33	Reconstruction of aortic root with xenograft and coronary reimplantation	sAVR
Denmark	SKS	KFMD40	Reconstruction of aortic root with pulmonary autograft and coronary reimplantation	sAVR
Denmark	SKS	KFMD96	Second insertion of aortic valve prosthesis	sAVR
Denmark	SKS	KFMD14	Percutaneous insertion of biological aortic valve prosthesis	TAVI
Denmark	SKS	KFMD11	Transapical insertion of biological aortic valve prosthesis	TAVI
Denmark	SKS	KFMD12	Transaortal TAVI (TAVI aortic valve implantation)	TAVI
Denmark	SKS	KFMD12A	Transaortal TAVI (TAVI aortic valve implantation) through ministerial anatomy	TAVI
Denmark	SKS	KFMD12B	Transaortal TAVI (TAVI aortic valve implantation) through mini-trachotomy	TAVI
England	OPCS Primary Code	K26.1	Allograft replacement of aortic valve	sAVR and TAVI
England	OPCS Primary Code	K26.2	Xenograft replacement of aortic valve	sAVR and TAVI
England	OPCS Primary Code	K26.3	Prosthetic replacement of aortic valve	sAVR and TAVI
England	OPCS Primary Code	K26.4	Replacement of aortic valve NEC	sAVR and TAVI
England	OPCS Secondary Code	Y49.4	Transapical approach to heart	TAVI
England	OPCS Secondary Code	Y53	Approach to organ under image control	TAVI

England	OPCS Secondary Code	Y68	Other approach to organ under image control	TAVI
England	OPCS Secondary Code	Y78	Arteriotomy approach to organ under image control	TAVI
England	OPCS Secondary Code	Y79	Approach to organ through artery	TAVI
Finland	THL	FMD	Replacement of aortic valve	sAVR
Finland	THL	FMD00	Replacement of aortic valve using mechanical prosthesis	sAVR
Finland	THL	FMD10	Replacement of aortic valve using biological prosthesis	sAVR
Finland	THL	FMD20	Replacement of aortic valve using homograft	sAVR
Finland	THL	FMD22	Percutaneous transluminal replacement of aortic valve using biological prosthesis	TAVI
Finland	THL	FMD24	Percutaneous transapical replacement of aortic valve using biological prosthesis	TAVI
Finland	THL	FME10	TAVI, subclavian route	TAVI
Finland	THL	FME20	TAVI, transfemoral route	TAVI
Finland	THL	FME30	TAVI, transapical route	TAVI
Finland	THL	FME40	TAVI, transient	TAVI
Finland	THL	FME60	TAVI, Valve-in-Valve	TAVI
Finland	THL	FME70	Catheter intervention for aortic valve prosthesis, other route	TAVI
France	CCAM	DBMA001	Reconstruction of the aortic pathway by annulus enlargement with valve replacement, by thoracotomy with extracorporeal circulation	sAVR
France	CCAM	DBMA006	Reconstruction of the aortic annulus with replacement of the valve by non-stented	sAVR

			bioprosthesis, by thoracotomy with extracorporeal circulation	
France	CCAM	DBMA009	Reconstruction of the aortic annulus with replacement of the valve by mechanical prosthesis or stented bioprosthesis, by thoracotomy with extracorporeal circulation	sAVR
France	CCAM	DBMA010	Reconstruction of the aortic annulus with replacement of the valve by homografting, by thoracotomy with extracorporeal circulation	sAVR
France	CCAM	DGKA011	Replacement of the ascending thoracic aorta with replacement of the aortic valve, without reimplantation of the coronary arteries, by thoracotomy with extracorporeal circulation	sAVR
France	CCAM	DGKA015	Replacement of the ascending thoracic aorta with replacement of the aortic valve, with reimplantation of the coronary arteries, by thoracotomy with extracorporeal circulation	sAVR
France	CCAM	DGKA018	Replacement of the ascending thoracic aorta and the horizontal aorta with replacement of the aortic valve, without reimplantation of the coronary arteries, by thoracotomy with extracorporeal circulation	sAVR
France	CCAM	DGKA014	Replacement of the ascending thoracic aorta and the horizontal aorta with replacement of the aortic valve, with reimplantation of the coronary arteries, by thoracotomy with extracorporeal circulation	sAVR
France	CCAM	DBLA002	Placement of a valve conduit between a ventricle and the aorta, by thoracotomy with extracorporeal circulation	sAVR
France	CCAM	DBKA001	Replacement of the aortic valve by homografting, by thoracotomy with extracorporeal circulation	sAVR
France	CCAM	DBKA003	Replacement of the aortic valve by non-stented bioprosthesis, thoracotomy with extracorporeal circulation	sAVR

France	CCAM	DBKA006	Replacement of the aortic valve by mechanical prosthesis or stented bioprosthesis, by thoracotomy with extracorporeal circulation	sAVR
France	CCAM	DBKA011	Replacement of the aortic valve by prosthesis in a non-anatomical position, by thoracotomy with extracorporeal circulation	sAVR
France	CCAM	DBKA009	Replacement of the aortic valve and the left atrioventricular valve by mechanical prosthesis or by stented bioprosthesis, by thoracotomy with extracorporeal circulation	sAVR
France	CCAM	DBLF001	Placement of an aortic bioprosthesis, via the transcutaneous arterial route	TAVI
France	CCAM	DBLA004	Placement of an aortic bioprosthesis, by approaching the apex of the heart by thoracotomy without CEC	TAVI
Germany	OPS	5-351.0	Aortic valve replacement	sAVR
Germany	OPS	5-352.0	Redo aortic valve replacement	sAVR
Germany	OPS	5-35a.00	Endovascular aortic implantation	TAVI
Germany	OPS	5-35a.01	Transapical aortic impl. w/o closure	TAVI
Germany	OPS	5-35a.02	Transapical aortic impl. with closure	TAVI
Germany	OPS	5-35a.03	Endovascular, with primary balloon expandable implant	TAVI
Germany	OPS	5-35a.04	Endovascular, with primary self-expanding implant	TAVI
Norway	NCSP	FMD00	Replacement of aortic valve using mechanical prosthesis	sAVR
Norway	NCSP	FMD10	Replacement of aortic valve using biological prosthesis	sAVR
Norway	NCSP	FMD20	Replacement of aortic valve using homograft	sAVR
Norway	NCSP	FMD30	Replacement of aortic root using homograft and reimplantation of coronary arteries	sAVR
Norway	NCSP	FMD33	Replacement of aortic valve using xenograft and reimplantation of coronary arteries	sAVR

Norway	NCSP	FMD40	Aortopulmonary root replacement using autograft of aortic root with reimplantation of coronary arteries and homograft to pulmonary ostium (Ross operation)	sAVR
Norway	NCSP	FMD96	Other prosthetic replacement of aortic valve	sAVR
Norway	NCSP	FMK12A	Percutaneous transluminal implantation of biological aortic valve prosthesis	TAVI
Norway	NCSP	FMK14A	Percutaneous transapical implantation of biological aortic valve prosthesis	TAVI
Poland	NFZ	5.54.01.0000043	Mechanical valve implantation or use of a technical product with a value comparable to the price of a mechanical valve ≥ 18 years	sAVR
Poland	NFZ	5.54.01.0000044	Biological valve implantation or use of a technical product with a value comparable to the price of a biological valve ≥ 18 years	sAVR
Poland	NFZ	5.54.01.0000045	Treatment on the heart and aorta with use of implantable technical or biological product with a total value comparable to the price of two mechanical valves ≥ 18 years	sAVR
Poland	NFZ	5.54.01.0000046	Implantation of two biological valves or use of a technical product with a value comparable to the price of two biological valves ≥ 18 years	sAVR
Poland	NFZ	5.54.01.0000071	Mechanical valve implantation or use of a technical product with a value comparable to the price of a mechanical valve < 18 years	sAVR
Poland	NFZ	5.54.01.0000072	Biological valve implantation or use of a technical product with a value comparable to the price of a biological valve < 18 years	sAVR
Poland	NFZ	5.54.01.0000073	Treatment on the heart and aorta with use of implantable technical or biological product with a total value comparable to the price of two mechanical valves < 18 years	sAVR

Poland	NFZ	5.54.01.0000074	Implantation of two biological valves or use of a technical product with a value comparable to the price of two biological valves < 18 years	sAVR
Poland	NFZ	5.54.01.0000057	Transfemoral TAVI	TAVI
Poland	NFZ	5.54.01.0000058	Transapical TAVI	TAVI
Spain	ICD-10	02RF4JZ	Aortic valve replacement, with synthetic substitute, percutaneous endoscopic approach [sutureless sAVR]	sAVR
Spain	ICD-10	02RF4KZ	Aortic valve replacement, with non-autologous tissue substitute, percutaneous endoscopic approach [sutureless sAVR]	sAVR
Spain	ICD-10	02RF47Z	Aortic valve replacement, with autologous tissue substitute, percutaneous endoscopic approach [sutureless sAVR]	sAVR
Spain	ICD-10	02RF48Z	Aortic valve replacement, with zooplastic tissue, percutaneous endoscopic approach [sutureless sAVR]	sAVR
Spain	ICD-10	02RF0JZ	Aortic valve replacement, with synthetic substitute, open approach	sAVR
Spain	ICD-10	02RF0KZ	Aortic valve replacement, with non-autologous tissue substitute, open approach	sAVR
Spain	ICD-10	02RF07Z	Aortic valve replacement, with autologous tissue replacement, open approach	sAVR
Spain	ICD-10	02RF08Z	Aortic valve replacement, with zooplastic tissue, open approach	sAVR
Spain	ICD-10	02RF3JH	Aortic valve replacement, with synthetic substitute, percutaneous, transapical approach	TAVI
Spain	ICD-10	02RF3KH	Aortic valve replacement, with non-autologous tissue substitute, percutaneous, transapical approach	TAVI
Spain	ICD-10	02RF37H	Aortic valve replacement, with autologous tissue replacement, percutaneous, transapical approach	TAVI

Spain	ICD-10	02RF38H	Aortic valve replacement, with zooplastic tissue, percutaneous, transapical approach	TAVI
Spain	ICD-10	02RF3KZ	Aortic valve replacement, with non-autologous tissue substitute, percutaneous approach	TAVI
Spain	ICD-10	02RF37Z	Aortic valve replacement, with autologous tissue substitute, percutaneous approach	TAVI
Spain	ICD-10	02RF38Z	Aortic valve replacement, with zooplastic tissue, percutaneous approach	TAVI
Spain	ICD-10	02RF3JZ	Aortic valve replacement, with synthetic tissue, percutaneous approach	TAVI
Sweden	NOMESCO	FMD00	Replacement of aortic valve using mechanical prosthesis	sAVR
Sweden	NOMESCO	FMD10	Replacement of aortic valve using biological prosthesis	sAVR
Sweden	NOMESCO	FMD20	Replacement of aortic valve using homograft	sAVR
Sweden	NOMESCO	FMD30	Replacement of aortic root using homograft and reimplantation of coronary arteries	sAVR
Sweden	NOMESCO	FMD33	Replacement of aortic valve using xenograft and reimplantation of coronary arteries	sAVR
Sweden	NOMESCO	FMD40	Aortopulmonary root replacement using autograft of aortic root with reimplantation of coronary arteries and homograft to pulmonary ostium (Ross operation)	sAVR
Sweden	NOMESCO	FMD96	Other prosthetic replacement of aortic valve	sAVR
Sweden	NOMESCO	FMD12	Percutaneous transluminal replacement of aortic valve using biological prosthesis	TAVI
Sweden	NOMESCO	FMD13	Percutaneous transapical replacement of aortic valve using biological prosthesis	TAVI
Switzerland	CHOP	35F111	Aortic valve replacement by allograft (homograft), via total sternotomy	sAVR
Switzerland	CHOP	352220	Aortic valve replacement by autotransplantation [Ross surgery]	sAVR

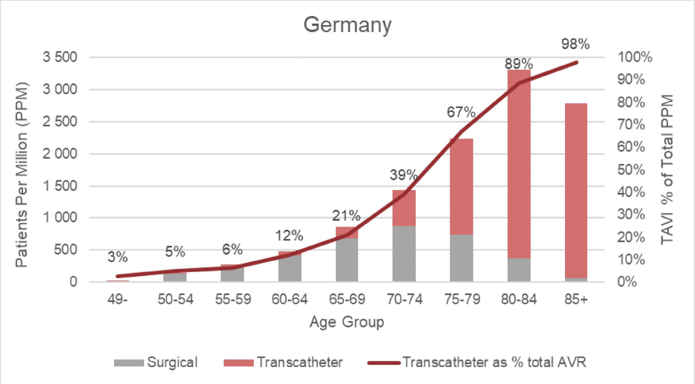
Switzerland	CHOP	35F122	Aortic valve replacement by xenograft (bioprosthesis), via minimally invasive thoracotomy (partial upper sternotomy, lateral thoracotomy)	sAVR
Switzerland	CHOP	35F121	Aortic valve replacement by xenograft (bioprosthesis), via total sternotomy	sAVR
Switzerland	CHOP	35F131	Aortic valve replacement by xenograft, stentless, via total sternotomy	sAVR
Switzerland	CHOP	352110	Aortic valve replacement with graft, bioprosthesis	sAVR
Switzerland	CHOP	352112	Aortic valve replacement with graft, bioprosthesis stentless, open surgery	sAVR
Switzerland	CHOP	352100	Aortic valve replacement with graft, not specified	sAVR
Switzerland	CHOP	352199	Aortic valve replacement with graft, other	sAVR
Switzerland	CHOP	352111	Aortic valve replacement with graft, self-expanding bioprosthesis, sutureless, open surgery	sAVR
Switzerland	CHOP	352120	Implantation of a valved vascular prosthesis, biological aortic valve	sAVR
Switzerland	CHOP	352221	Open replacement of a mechanical aortic valve prosthesis	sAVR
Switzerland	CHOP	352230	Implantation of a valved vascular prosthesis, mechanical aortic valve	sAVR
Switzerland	CHOP	352299	Other aortic valve replacement, other	sAVR
Switzerland	CHOP	35F109	Aortic valve replacement by prosthetic heart valve or valved vascular prosthesis, other	sAVR
Switzerland	CHOP	35F112	Aortic valve replacement by allograft (homograft), via minimally invasive thoracotomy (partial upper sternotomy, lateral thoracotomy)	sAVR
Switzerland	CHOP	35F132	Xenograft aortic valve replacement, stentless, via minimally invasive thoracotomy (partial upper sternotomy, lateral thoracotomy)	sAVR
Switzerland	CHOP	35F141	Aortic valve replacement with self-expanding xenograft, sutureless, via total sternotomy	sAVR

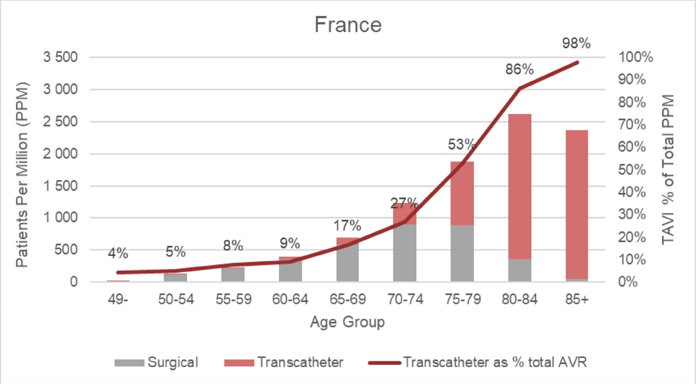
Switzerland	CHOP	35F142	Aortic valve replacement by self-expanding xenograft, suture-free, via minimally invasive thoracotomy (partial upper sternotomy, lateral thoracotomy)	sAVR
Switzerland	CHOP	35F151	Aortic valve replacement by mechanical prosthesis, via total sternotomy	sAVR
Switzerland	CHOP	35F152	Aortic valve replacement by mechanical prosthesis, via minimally invasive thoracotomy (partial upper sternotomy, lateral thoracotomy)	sAVR
Switzerland	CHOP	35F161	Aortic valve replacement by valved vascular prosthesis, biological, via complete sternotomy	sAVR
Switzerland	CHOP	35F162	Aortic valve replacement by valved vascular prosthesis, biological, via minimally invasive thoracotomy (partial upper sternotomy, lateral thoracotomy)	sAVR
Switzerland	CHOP	35F171	Aortic valve replacement by valved vascular prosthesis, mechanical, via total sternotomy	sAVR
Switzerland	CHOP	35F172	Aortic valve replacement by valved vascular prosthesis, mechanical, via minimally invasive thoracotomy (partial upper sternotomy, lateral thoracotomy)	sAVR
Switzerland	CHOP	35F181	Aortic valve replacement by decellularized allograft (homograft), via total sternotomy	sAVR
Switzerland	CHOP	35F123	Aortic valve replacement by xenograft (bioprosthesis), endovascular approach	TAVI
Switzerland	CHOP	35F126	Aortic valve replacement by xenograft (bioprosthesis), endovascular approach, transcaval approach	TAVI
Switzerland	CHOP	35F124	Aortic valve replacement by xenograft (bioprosthesis), transapical	TAVI
Switzerland	CHOP	35F125	Aortic valve replacement by xenograft (bioprosthesis), transapical, with use of a percutaneous apical access and closure system	TAVI

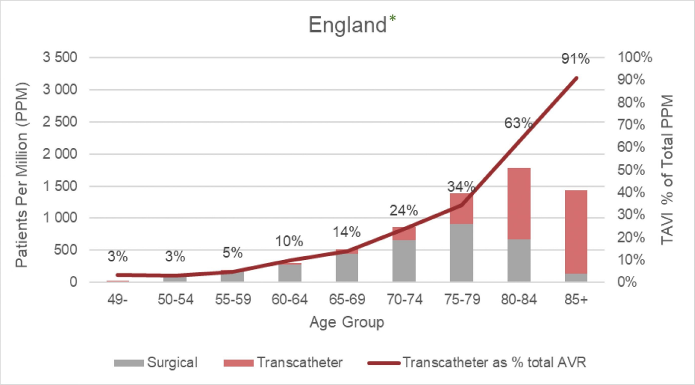
Switzerland	CHOP	352210	Minimally invasive implantation of an aortic valve, not specified	TAVI
Switzerland	CHOP	352219	Minimally invasive implantation of an aortic valve, other	TAVI
Switzerland	CHOP	352213	Minimally invasive implantation of an aortic valve, transaortic approach	TAVI
Switzerland	CHOP	352211	Minimally invasive implantation of an aortic valve, transapical	TAVI
Switzerland	CHOP	352212	Minimally invasive implantation of an aortic valve, transapical, with use of a percutaneous apical access and closure system	TAVI
Switzerland	CHOP	359611	Aortic valve replacement, endovascular, transluminal	TAVI
Switzerland	CHOP	35F133	Xenograft aortic valve replacement, stentless, endovascular approach	TAVI
Switzerland	CHOP	35F134	Xenograft stentless transapical aortic valve replacement	TAVI
Switzerland	CHOP	35F135	Xenograft aortic valve replacement, stentless, transapical, using percutaneous apical access and closure system	TAVI
Switzerland	CHOP	35F143	Aortic valve replacement with self-expanding xenograft, sutureless, endovascular approach	TAVI
Switzerland	CHOP	35F144	Aortic valve replacement with self-expanding xenograft, sutureless, transapical	TAVI
Switzerland	CHOP	35F145	Aortic valve replacement by self-expanding xenograft, sutureless, transapical, using percutaneous apical access and closure system	TAVI

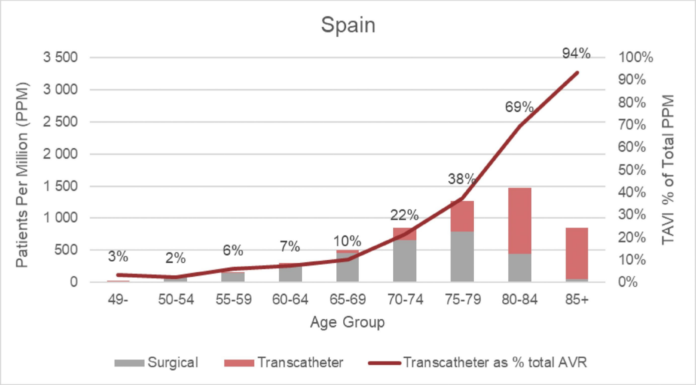
Legend: sAVR, surgical aortic valve replacement; TAVI, transcatheter aortic valve implantation

Patients per million by age and therapy, 2020

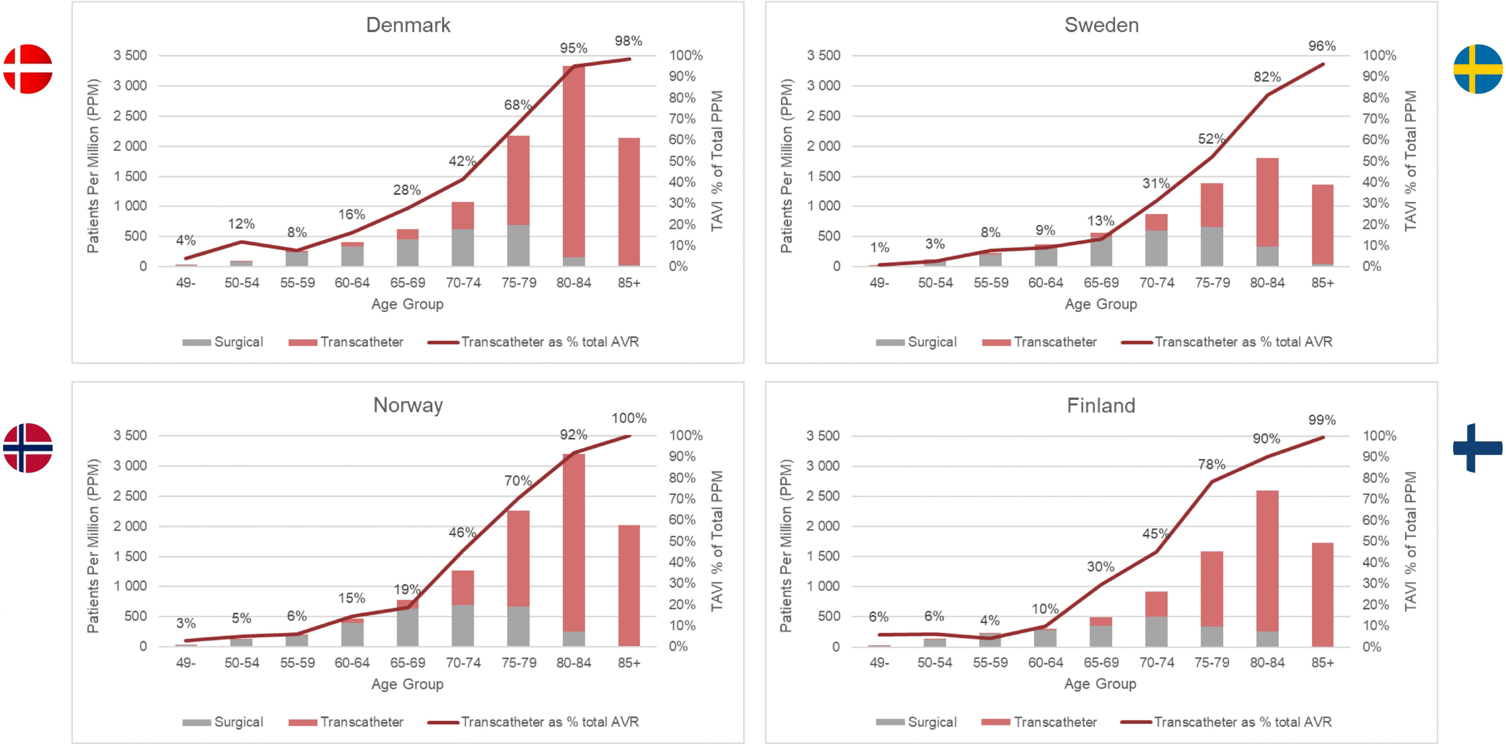




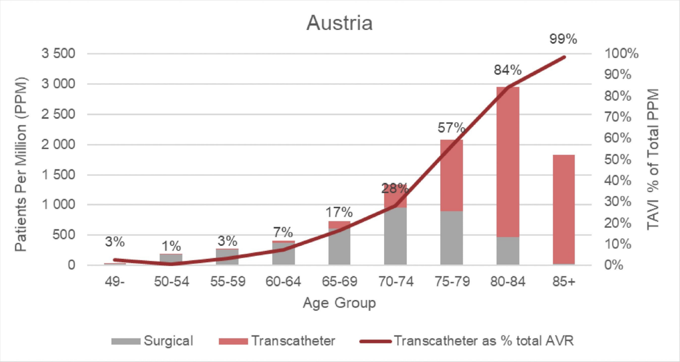


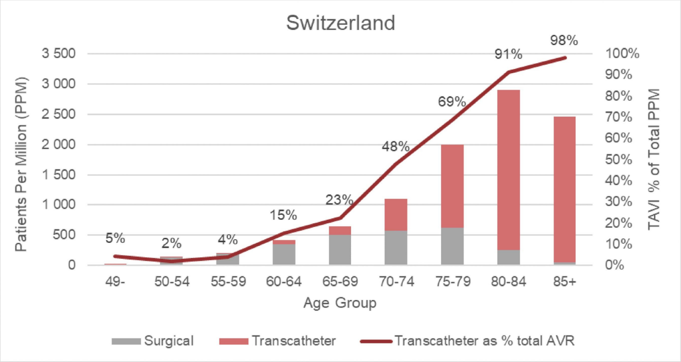


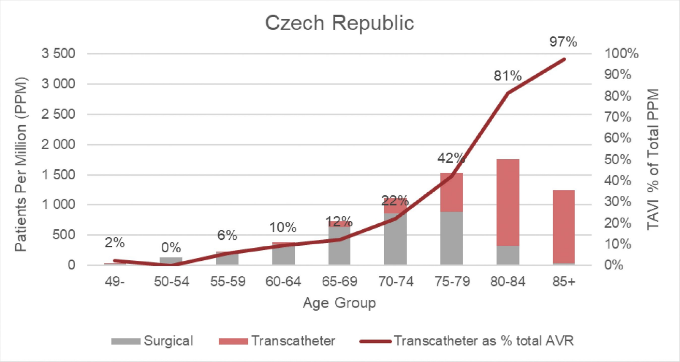
Patients per million by age and therapy, 2020

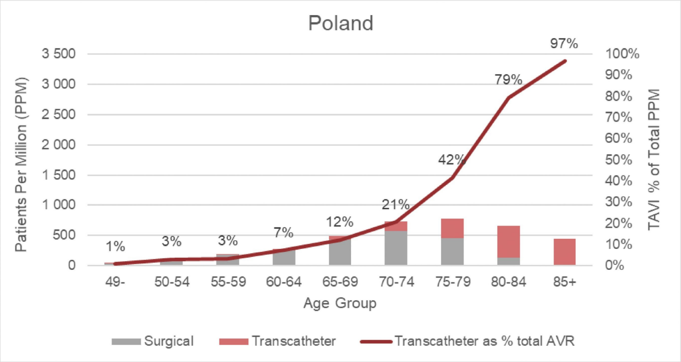


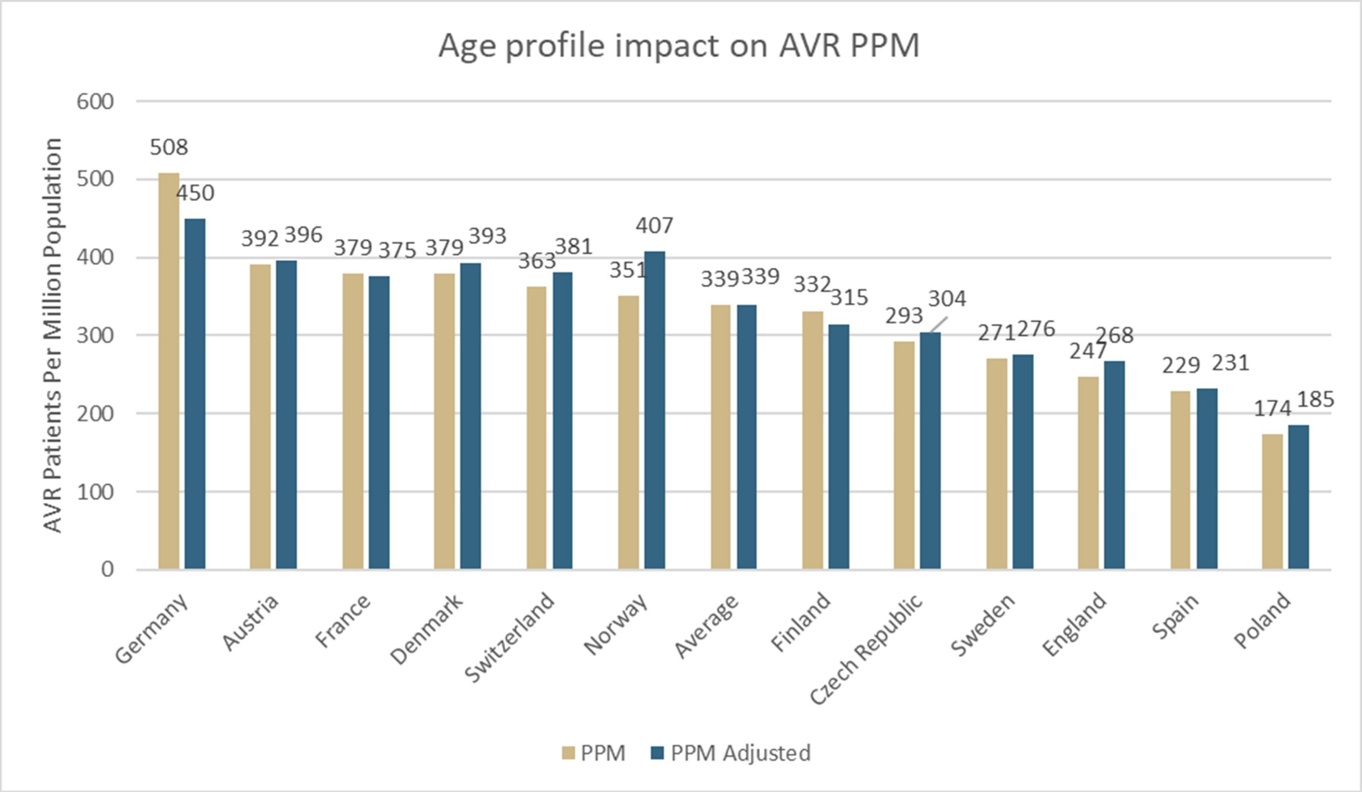
Patients per million by age and therapy, 2020

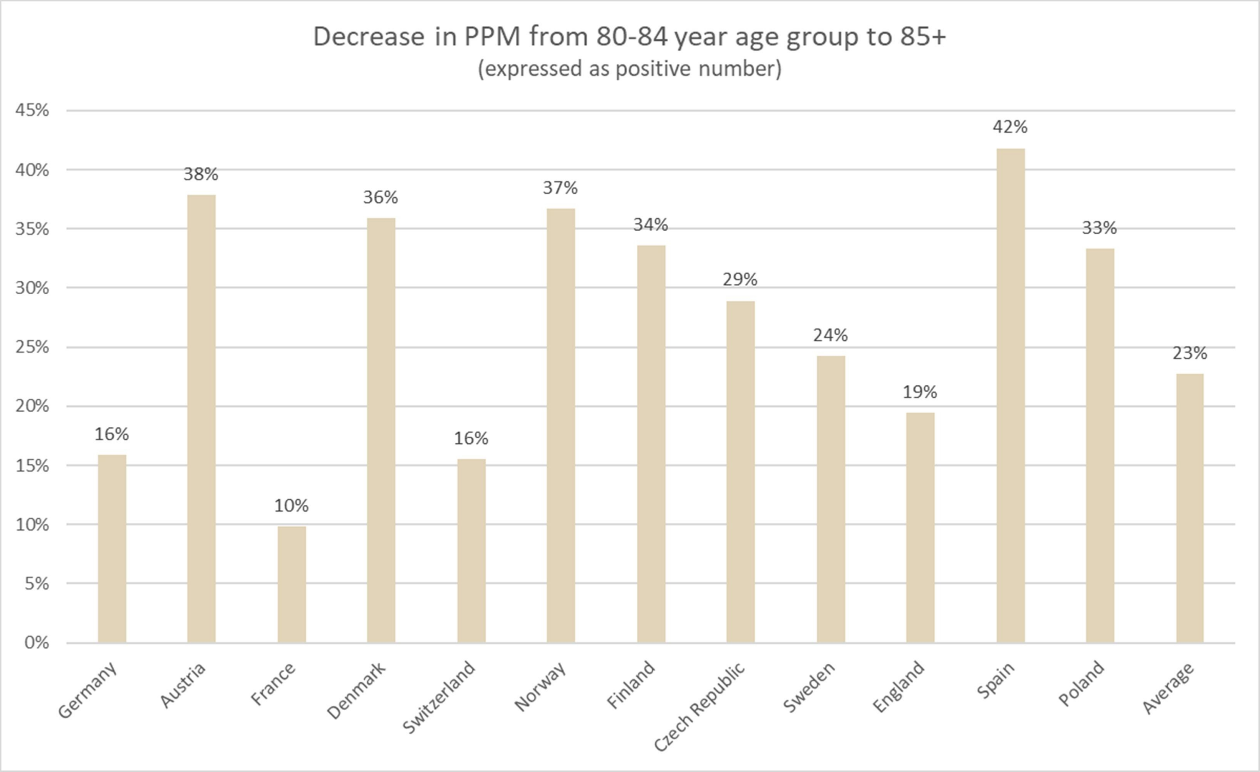









Age profile impact on AVR PPM
AVR Patients Per Million Population
600
500
400
300
200
100
0
508
450
392
396
379
375
379
393
363
381
351
407
339
339
332
315
293
304
271
276
247
268
229
231
174
185
Germany
Austria
France
Denmark
Switzerland
Norway
Average
Finland
Czech Republic
Sweden
England
Spain
Poland
PPM
PPM Adjusted



Decrease in PPM from 80-84 year age group to 85+
(expressed as positive number)
45%
40%
35%
30%
25%
20%
15%
10%
5%
0%
16%
38%
10%
36%
16%
37%
34%
29%
24%
19%
42%
33%
23%
Germany
Austria
France
Denmark
Switzerland
Norway
Finland
Czech Republic
Sweden
England
Spain
Poland
Average

Summary

Aortic stenosis (AS) is predicted to become more common as the population ages, which will increase the number of people who are diagnosed with AS in future. The goal of the present study titled "**Patterns of Aortic Valve Replacement in Europe: Adoption by Age**" was to carefully examine the temporal changes in the use of aortic valve replacement (AVR), including surgical AVR (sAVR) and transcatheter aortic valve implantation (TAVI), in a few selected European countries categorized by age.

To gather data, we used 12 national statistical systems from throughout Europe covering the period between 2015 to 2020. We retrieved data on the number of surgeries conducted and determined specific codes for sAVR and TAVI procedures. The information included the gender and the age of the patients, which were divided into five-year intervals from 50 to 85 years. Besides, patients under 50 years and those aged 85 years and above were grouped together.

According to our study, the rate of AVR procedures per million people (PPM) in various nations in 2020 was found to vary significantly. The rate in Germany was 508 PPM, whereas the rate in Poland was 174 PPM. The frequency of AVR PPM also rose with age and peaked in people between the ages of 80 and 84. An average yearly growth rate of 3.9% was seen between 2015 and 2019 in the number of AVR procedures. In contrast to lower age groups, this increase was most noticeable among people 80 years and older. An increase from 30% in 2015 to 35% in 2019 was seen in the percentage of AVR operations that were performed on older age groups. In summary, for patients 85 years and older, TAVI was the chosen course of treatment for 96% of men and 98% of women. Also, as age advances, TAVI procedures constitute a larger proportion of all AVR procedures. Therefore, our study findings highlight the value of considering age when identifying and treating people with aortic valve disease.

We appreciate you taking the time to read through our resubmission, and we look forward to your positive decision. We are pleased to submit an original article to contribute to the pages of the Cardiology journal.