Impact of mandatory preoperative dental screening on post-procedural risk of infective endocarditis in patients undergoing transcatheter aortic valve implantation: a nationwide retrospective observational study

Lytfi Krasniqi,[a,f,] Lars Peter Schødt Riber,[a,f] Henrik Nissen,[b] Christian Juhl Terkelsen,[c] Niels Holmark Andersen,[d] Phillip Freeman,[d] Jonas A. Povlsen,[c] Oke Gerke,[e,f] Marie-Annick Clavel,[b] and Jordi Sanchez Dahl[b,f]*

[a]Department of Cardiac, Thoracic and Vascular Surgery, Odense University Hospital, Denmark
[b]Department of Cardiology, Odense University Hospital, Denmark
[c]Department of Cardiology, Aarhus University Hospital, Denmark
[d]Department of Cardiology, Aalborg University Hospital, Denmark
[e]Department of Nuclear Medicine, Odense University Hospital, Denmark
[f]Department of Clinical Research, University of Southern Denmark, Denmark

Summary

Background Guidelines recommend preoperative dental screening (PDS) prior to cardiac valve surgery, to reduce the incidence of prosthetic valve infective endocarditis (IE). However, limited data support these recommendations, particular in patients undergoing transcatheter aortic valve implantation (TAVI). We aimed to investigate the effect of mandatory PDS on risk of IE in patients undergoing TAVI.

Methods In this observational study, a total of 1133 patients undergoing TAVI in Western-Denmark from 2020 to 2022 were included. Patients were categorized based on two implemented PDS practices: mandatory PDS (MPDS group), and no referral for PDS (NPDS group). Outcome data were retrieved from Danish registries and confirmed using medical records. The primary outcome was incidence of IE. Secondary outcomes were all-cause mortality and composite outcome of all-cause mortality and IE.

Findings Of 568 patients in the MPDS group 126 (22.2%) underwent subsequent oral dental surgery, compared to 8 (1.4%) among 565 patients in the NPDS group. During a median follow-up of 1.9 years (interquartile range 1.4–2.5 years), 31 (2.7%) developed IE. The yearly incidence IE rate was 1.4% (0.8–2.3) and 1.5% (0.8–2.4) in MPDS and NPDS, respectively, p = 0.86. All-cause mortality rates were similar between groups (estimated 2-year overall mortality of 6.7% (4.8–9.2) vs. 4.7% (3.2–6.9), MPDS and NPDS, respectively, p = 0.15). Consistent findings were found in 712 propensity score-matched patients.

Interpretation Mandatory PDS did not demonstrate reduced risk of IE or all-cause mortality compared to targeted PDS in patients undergoing TAVI.

Funding The funder had no role in the study design, data management, or writing.

Keywords: TAVI; Preoperative dental screening; Infectious endocarditis

Introduction

Infective endocarditis (IE) is associated with high mortality and morbidity.[1] Patients with a prosthetic left-sided valve are considered at high-risk for developing IE with a yearly incidence rate of 1% in tertiary centers,[2] affecting about one out of 20 patients over 10 years.[3] Accordingly, recent American Heart Association (AHA)[4] and European Society of Cardiology (ESC) guidelines strongly recommend that potential sources of dental sepsis should be eliminated at least two weeks

Translation: For the Danish translation of the abstract see Supplementary Materials section.

Research in context

Evidence before this study
Before prosthetic valve implantation, it is recommended to eliminate potential sources of dental sepsis, unless the procedure is urgent. We searched databases like PubMed for peer-reviewed studies in English and the Danish Dental Journal for peer-reviewed studies and commentaries up to August 13, 2023. We manually checked the reference lists of relevant journals for additional insights. Our primary search terms included "Valvular Heart Disease Guidelines", "Preoperative dental screening", "Preoperative dental examination", "Oral health assessment before surgery", "Pre-surgical dental evaluation", "Dental risk assessment before surgery", and related terms. We considered studies published between 1923 and 2023. No studies specifically addressing this topic were identified from our search.

Added value of this study
Previous research has considered oral health and risks of infectious endocarditis, but the specific link between mandatory preoperative dental screenings and post-TAVI infectious endocarditis incidence remains unexplored. Our study fills this gap, evaluating the association of dental sepsis source eradication with preventing infectious endocarditis post-TAVI.

Challenging the widely-held belief, our findings suggest that mandatory dental screenings and subsequent interventions do not necessarily reduce post-surgical infection risks in Denmark. This study accentuates the complexities of post-TAVI endocarditis risks, urging a reevaluation of dental screening universality, especially in areas with high dental health profiles. We've suggested the potential merit of individualized assessments, particularly for those with poor dental health, guiding healthcare professionals to adapt preoperative strategies based on the broader context.

Implications of all the available evidence
Our unique exploration into the association between preoperative dental screenings and infectious endocarditis post-TAVI has revealed that merely eradicating potential dental sepsis sources was not associated with lower risk of infectious endocarditis or all-cause mortality in patients undergoing TAVI. This insight redefines preventive measures and calls for more nuanced clinical approaches.

before implantation of a prosthetic valve, unless the procedure is urgent.[5] These recommendations are not based on randomized trials, but mainly based on registries describing the incidence of IE in patients undergoing surgical aortic valve replacement (SAVR). Currently, transcatheter aortic valve implantation (TAVI) has widely been adopted as an alternative to SAVR, in some centers even surpassing its use among low-risk patients. Though the approximate yearly risk of IE in TAVI of 0.8%[6] is similar to that of SAVR,[7] current guidelines solely recommend preoperative dental screening (PDS) in patients undergoing SAVR and do not give any specific recommendations for patients undergoing TAVI.[8,9] Consequently, a recent survey has demonstrated large regional differences in PDS practices prior to TAVI.[10]

In line with this, the three tertiary centers performing TAVI in Western Denmark, have implemented two different dental screening practices during the last years. One consisting of mandatory PDS (MPDS) with additional elimination of sources of dental sepsis, and another with no referral for PDS (NPDS).

Thus, the aim of this registry-based, observational cohort study was to investigate the impact of different PDS practices on the risk of IE in patients undergoing TAVI in Western Denmark.

Methods
This retrospective study was approved by the data processing activities (Journal nr.: 21/21488), Odense, Denmark of the Region of Southern Denmark. The study followed the Strengthening the Reporting of Observational Studies in Epidemiology reporting (STROBE) guidelines.[11]

Participants and data source
Western Denmark, includes three of the four national tertiary centers performing TAVI, Aarhus University hospital, Aalborg University hospital, and Odense University hospital. While Aalborg and Odense have performed MPDS since the first TAVI procedure in 2007, Aarhus University Hospital has not performed PDS during the last 4 years.

We included all patients with severe aortic stenosis undergoing solitary transfemoral TAVI from January 2020 to April 2022, excluding those undergoing concomitant percutaneous intervention (PCI) or with a history of cardiac surgery. Patients were categorized in two groups according to the PDS procedure followed by the institution—Aarhus University Hospital (NPDS) and Aalborg/Odense University Hospital (MPDS). The study population was identified using the Western Danish Heart Registry (WDHR), which maintains comprehensive data concerning preexisting conditions, as well as perioperative and postoperative details, on all patients undergoing cardiac procedures at the relevant centers.[12] All patients were followed until death or the end of the follow-up period in March 2023, whichever came first.

Hypertension and dyslipidemia were defined as treatment with a hypertensive or lipid-lowering agent, respectively. PDS as well as oral surgical procedures

were considered, if they occurred within six months prior to TAVI and up to a week following the procedure. Low-risk patients were defined according to guidelines with EuroSCORE2 <4%.[9]

All follow-up data, including any re-interventions, were retrieved from the validated and highly reliable National Danish Patient Registry.[13] All cases of registered endocarditis cases were further confirmed by review of medical records.

Outcomes and missing data

We performed an analysis of the entire cohort, and a propensity score-matched (PSM) group. The primary outcome was IE. Secondary outcomes were all-cause mortality, the composite outcome of all-cause mortality and IE, and IE in the subset of patients who underwent oral surgical procedure. The International Classification of Diseases (ICD) 10 and procedure codes are reported in the Supplement (Supplemental Table S1). Missing data were reported in the tables with [].

Statistics

Continuous data were presented as mean (standard deviation (SD)) if normal distributed and as median (IQR) if non-normal distributed. Categorical data were presented as proportions. Inter-group comparisons were done with Student's t tests or Wilcoxon rank sum test, Chi-squared test or Fisher's exact test, as appropriate.

Time-to-death was calculated as the time from the date of TAVI to the date of death from all-causes. Time-to-event analysis comprised non-parametric Kaplan–Meier plots, as well as log-rank tests and semi-parametrical Cox Proportional Hazards regression. The assessment of proportional hazard assumptions was performed through Schoenfeld residuals and Kaplan–Meier predicted plots reported, if not satisfied. A multivariate model was created adjusting dental screening practice for predefined, clinically relevant variables (age, sex, history of endocarditis, cardiac implantable electronic device, and oral surgery prior TAVI). Complete case analyses were performed.

We intended to calculate numbers needed to prevent an IE case irrespective of the significance level between groups.

PSM was performed to balance the baseline characteristics between the three counties (Odense & Aalborg vs. Aarhus). The score was generated with 6 categories, and a caliper of 0.2 was used as recommended.[14] Matching method is described in detail in the supplement (Supplemental Table S2).

Point estimates are supplemented by respective 95% confidence intervals (CI), when appropriate. A p-value of less than 0.05 is considered statistically significant. Statistical analysis is performed with STATA/IC 17 (StataCorp., College Station, Texas 77845, USA).

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

We identified 1325 patients with a history of TAVI in Western Denmark from January 2020 to April 2022. After excluding patients with a history of cardiac surgery (n = 145) or undergoing concomitant PCI (n = 47), the final cohort of patients undergoing solitary TAVI was 1133 patients (MPDS group n = 565, Aarhus University Hospital and NPDS group n = 219, Aalborg University Hospital, n = 349 Odense University Hospital). No patients were lost during follow-up. There were missing data for the following variables: body mass index (2.6%), body surface area (2.2%), Left ventricular ejection fraction (4.7%), smoking habits (10.2%), and creatinine clearance (2.7%). Compared to those in the NPDS group, patients in the MPDS group were older, and presented with higher comorbidity burden resulting in a higher EuroSCORE II (2.90 (IQR 1.83–4.58) vs. 1.94 (IQR 1.37–3.26), p < 0.01) (Table 1).

A total of 92% of patients in the MPDS, underwent dental screening (median 28 (IQR 12–55) days prior to TAVI) compared to 3% in the NPDS (median 72 (IQR 31–105) days).

These differences resulted in a significantly higher rate of patients undergoing all oral surgical procedures, including dental extraction (22% (n = 126) vs. 1.4% (n = 8), MPDS vs. NPDS group, p < 0.01).

Of these, dental extractions specifically were performed in (15.1% (n = 86) vs. 1.2% (n = 7), respectively, p < 0.01). Four out of all the dental extractions subsequently developed IE, three of which were linked to oral foci.

Outcome

During a total follow-up time of 2201 person-years, with a median follow-up of 1.9 years (interquartile range 1.4–2.5 years), we identified 36 cases registered as IE, and upon journal review, 5 of these cases were found not to be IE. A total of 31 (2.7%) cases were diagnosed with IE, and 61 (5.4%) patients died (cause of death is presented in Supplemental Table S3a). The yearly IE incidence was 1.4% (95% CI 0.9–2.0) with no differences depending on PDS practice (1.4% (95% CI 0.8–2.3) vs. 1.5% (95% CI 0.8–2.4), MPDS and NPDS, respectively, p = 0.86) (Fig. 1, Supplemental Table S3b). All-cause mortality rates were similar in patients undergoing mandatory and no PDS (estimated 2-year overall mortality of 6.7% vs. 4.7%, respectively, p = 0.15) (Fig. 2).

Concordantly, no significant difference was observed in the combined outcome of all-cause mortality and IE, with estimated 2-year rates of MPDS vs. NPDS of 9.4%

	Entire cohort			Propensity score-matched cohort		
	Mandatory preoperative dental screening N = 568	No preoperative dental screening N = 565	p-value	Mandatory preoperative dental screening N = 356	No preoperative dental screening N = 356	Stand. diff.
Male sex	296 (52.1%)	322 (57%)	0.10	188 (52.8%)	195 (54.8%)	0.04
Age (years)	82.0 (5.6)	80.3 (6.4)	<0.001	81.0 (5.6)	81.8 (5.9)	−0.14
Body mass index, (kg/m^2)	27.4 (5.1) [5]	27.6 (4.9) [24]	0.60	27.8 (5.5) [1]	26.9 (4.6)	0.18
Body surface area (m^2)	1.88 (0.2) [4]	1.90 (0.2) [21]	0.04	1.89 (0.2)	1.87 (0.2)	0.07
EuroSCORE2	2.90 (1.83–4.58)	1.94 (1.37–3.26)	<0.001	2.40 (1.65–3.77)	2.29 (1.64–3.82)	0.04
0–4	388 (68.3%)	469 (83.0%)	<0.001	278 (78.1%)	275 (77.2%)	0.04
4–8	133 (23.4%)	77 (13.6%)		59 (16.6%)	64 (18.0%)	
≥8	47 (8.3%)	19 (3.4%)		19 (5.3%)	17 (4.8%)	
Left ventricular ejection fraction (%)	52.9 (12.0) [32]	53.2 (10.5) [21]	0.49	53.4 (11.6) [25]	52.7 (10.8) [4]	0.06
NYHA classification, I/II/III/IV	31/184/313/40	15/361/181/8	<0.001	13/175/158/10	15/161/173/7	0.10
Previous endocarditis	116 (20.4%)	88 (15.6%)	0.034	64 (18.0%)	66 (18.5%)	0.01
Hypertension	415 (73.1%)	391 (69.2%)	0.15	264 (74.2%)	250 (70.2%)	0.09
Atrial fibrillation	100 (17.6%)	169 (29.9%)	<0.001	86 (24.2%)	73 (20.5%)	0.09
Diabetes Mellitus	47 (8.3%)	36 (6.4%)	0.22	29 (8.1%)	24 (6.7%)	0.05
Dyslipidemia	332 (58.5%)	323 (57.2%)	0.66	204 (57.3%)	196 (55.1%)	0.05
Previous myocardial infarction	40 (7.0%)	34 (6.0%)	0.49	24 (6.7%)	27 (7.6%)	0.03
Previous percutaneous intervention	103 (18.1%)	102 (18.1%)	0.97	61 (17.1%)	62 (17.4%)	0.01
Peripheral vascular disease	61 (10.7%)	13 (2.3%)	<0.001	15 (4.2%)	13 (3.7%)	0.03
Smoking status, previous/active	282/39 [18]	230/49 [97]	0.16	169/28 [12]	143/33 [57]	0.10
Creatinine clearance (ml/min)	58.9 (24.0) [5]	66.5 (27.1) [26]	<0.001	61.8 (25.7)	60.4 (23.9)	0.06
Chronic obstructive pulmonary disease	106 (18.7%)	88 (15.6%)	0.17	62 (17.4%)	56 (15.7%)	0.05
Cardiac implantable electronic device	37 (6.5%)	37 (6.6%)	0.98	22 (6.2%)	20 (5.6%)	0.02

Abbreviations: NYHA, New-York Heart Association. Continuous data presented as mean (SD) [number with missing] and categorical data as n (percentage).

Table 1: **Baseline characteristics.**

and 7.4%, respectively (p = 0.10) (Fig. 3). A total of 47 (4.1%) patients had a newly implanted cardiac implantable electronic devices, 2 of them (4.3%) were later diagnosed with IE (HR of endocarditis 1.51, 95% CI 0.36–6.36, p = 0.57; adjusted HR 1.51, 95% CI 0.34–6.77, p = 0.59). Among the 134 (10.1%) patients undergoing oral surgery prior to TAVI, 5 (3.7%) were hospitalized due to IE with no difference between the 52 (38.8%) patients undergoing oral surgical procedure <14 days (n = 3, 5.8%) and ≥14 days prior to TAVI (n = 2, 2.4%, p = 0.38).

Association model

In a univariate model, baseline characteristics associated with development of IE was only male sex, but not PDS practice (Supplemental Table S4). We tested different multivariate models, all including PDS practice, none of them demonstrating a significant association with risk of IE. After adjusting for age, sex, previous IE, cardiac implantable electronic device and PDS practice, sex was the sole factor associated with IE (Table 2). Male sex was associated with an increased risk of IE.

Microbiology

The distribution of microorganism of IE are presented in Supplemental Figure S1 (*Streptococcus mitis* (n = 8), *Streptococcus bovis* (n = 2), *Streptococcus dysgalactiae* (n = 1), *Streptococcus salivarius* (n = 2), *Staphylococcus epidermidis* (n = 2), *Staphylococcus lugdunensis* (n = 2), *Staphylococcus aureus* (n = 6), *Enterococcus faecium* (n = 6), *Citrobacter koseri* (n = 1) and unknown aetiologi (n = 1)) with no difference between groups (Supplemental Figure S1, Supplemental Table S5).

Propensity score-matched population

A total of 356 patients with MPDS were matched 1:1 with PSM patients with NPDS. Table 1 shows baseline characteristics for matched patients, with no clinically significant difference between groups.

The matched cohort demonstrating similar results, with no significant difference between the groups across all measured outcomes (Figs. 1–3). The incidence of IE was 3.1% not different depending on PDS practice (n = 11 vs. n = 11, mandatory and no dental screening, respectively, p = 0.99). After mandatory PDS, 85 patients
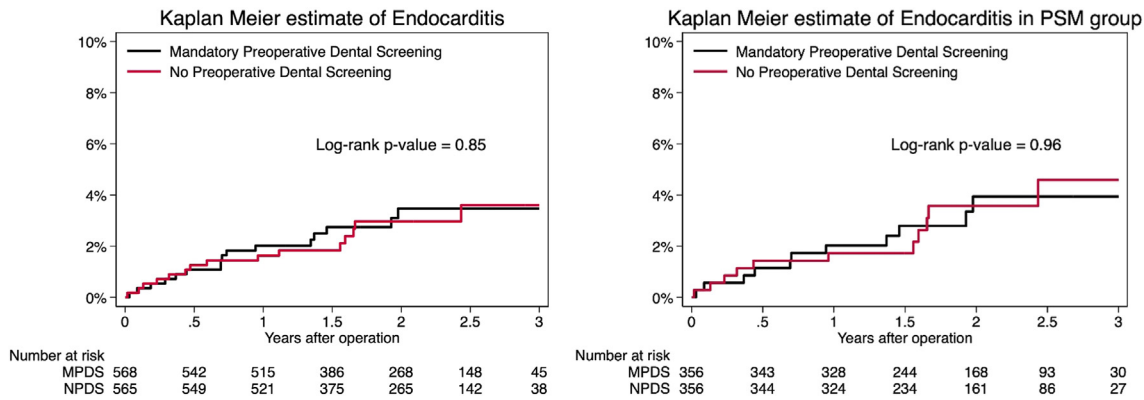
Fig. 1: Kaplan–Meier plot demonstrating the incidence of infective endocarditis in the entire cohort (left panel) and the matched cohort (right panel).
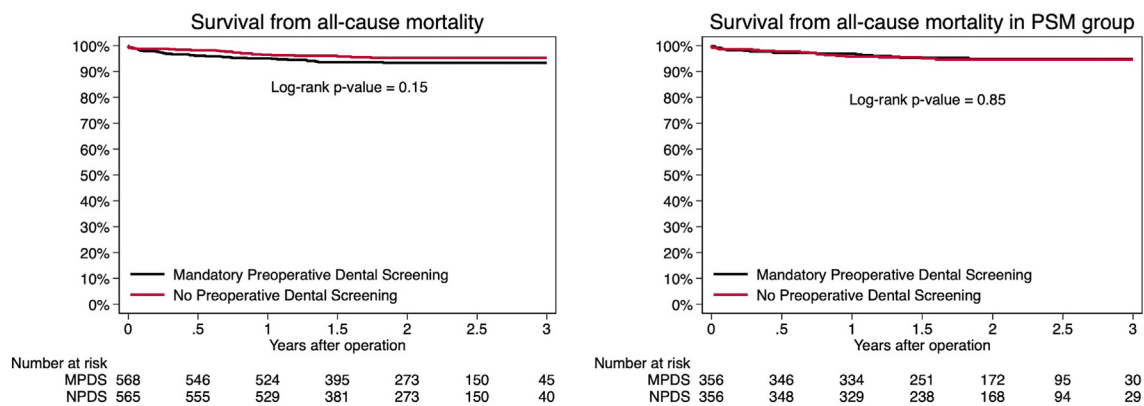

Fig. 2: Kaplan–Meier plot demonstrating the incidence of all-cause mortality in the entire cohort (left panel) and the matched cohort (right panel).
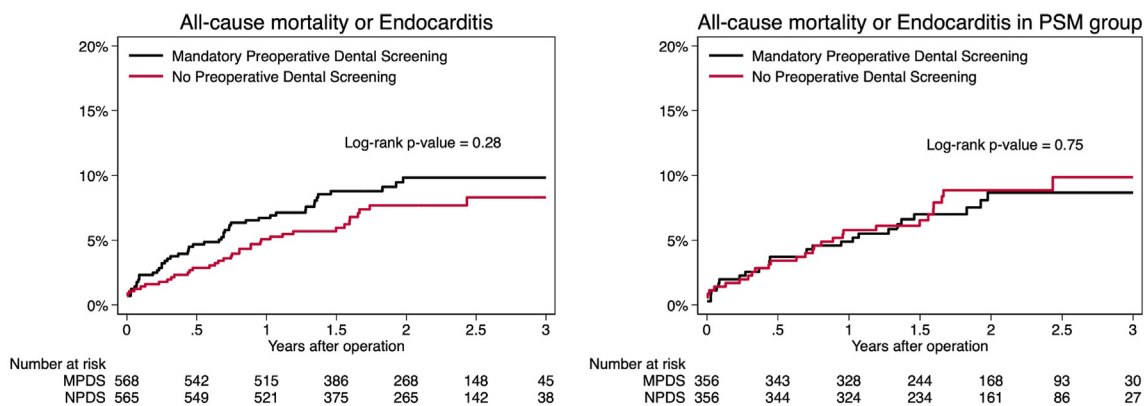

Fig. 3: Kaplan–Meier plot demonstrating the incidence of the combination of endocarditis or all-cause mortality in the entire cohort (left panel) and the matched cohort (right panel).

	Univariate analyses		Multivariate analysis	
	Hazard ratio (95% CI)	p-value	Hazard ratio (95% CI)	p-value
No preoperative dental screening	0.94 (0.46–1.89)	0.85	0.95 (0.44–2.05)	0.89
Male sex	3.0 (1.3–6.9)	0.012	2.98 (1.27–6.96)	0.011
Age	0.99 (0.94–1.05)	0.83	1.00 (0.94–1.06)	0.96
Body mass index	0.96 (0.89–1.04)[a]	0.28		
Body mass surface	1.55 (0.29–8.21)	0.61		
EuroSCORE2	0.99 (0.89–1.1)	0.83		
EuroSCORE 4–8	0.84 (0.32–2.20)	0.73		
EuroSCORE ≥8	0.58 (0.08–4.30)	0.60		
Left ventricular ejection fraction	0.99 (0.96–1.03)	0.75		
NYHA functional class	1.77 (0.86–3.64)	0.12		
Previous endocarditis	0.98 (0.4–2.4)	0.97	0.99 (0.41–2.45)	0.99
Hypertension	2.74 (0.96–7.8)	0.06		
Atrial fibrillation	1.5 (0.7–3.3)	0.27		
Diabetes Mellitus	0.4 (0.05–2.93)	0.37		
Dyslipidemia	0.7 (0.34–1.41)	0.31		
Previous myocardial infarction	1.02 (0.24–4.26)	0.98		
Previous percutaneous intervention	0.88 (0.34–2.3)	0.80		
Peripheral vascular disease	1.11 (0.26–4.64)	0.89		
Smoking status	1.2 (0.58–2.49)	0.63		
Creatinine clearance	1 (0.99–1.02)[a]	0.61		
COPD	0.53 (0.16–1.74)	0.30		
Cardiac implantable electronic device	0.45 (0.06–3.31)	0.43	0.41 (0.06–3.02)	0.38
Oral surgery prior TAVI	1.39 (0.53–3.61)	0.51	1.22 (0.43–3.46)	0.70
Tooth extraction prior TAVI	1.61 (0.56–4.60)	0.38		
MPDS: dicloxacillin and Gentamicin[b]	1.10 (0.49–2.45)	0.82		
MPDS: Gentamicin and cefuroxime[b]	1.02 (0.40–2.63)	0.97		

[a]Proportional hazards assumption for Cox regression was not met. [b]Antibiotic treatment is compared to cefuroxime alone, as used in the NPDS group.

Table 2: Association between covariates and risk of infective endocarditis at follow-up.

had oral surgical procedure prior to TAVI, and 5 (5.9%) were hospitalized due to IE. Among 356 patients with no PDS, 4 (1.1%) having prior dental surgery, 11 (3.1%) where hospitalized with endocarditis (p = 0.22).

Discussion

In this large nationwide registry study comparing two different PDS practices we demonstrate that MPDS, with subsequent elimination of potential sources of dental sepsis, was not associated with reduced risk of IE after TAVI. To our knowledge, this is the first study examining different PDS practices in patients undergoing TAVI.

The link between IE and dental status was first suggested 100 years ago by Lewis and Grant,[15] a theory that was further strengthened a decade later after Okell and Elliot demonstrated that 75% of individuals developed transient bacteremia following a dental extraction.[16] Consequently, the AHA and ESC has issued guidelines that recommend careful PDS to eliminate potential sources of dental sepsis prior to cardiac valve surgery, as these measures may reduce the incidence of

late prosthetic valve endocarditis caused by Streptococci.[4,5]

Two decades ago, in an observational study including 253 patients undergoing open heart valve surgery, Hakeberg et al. demonstrated a non-significant higher rate of sepsis/endocarditis despite similar survival in patients undergoing dental treatment prior to surgery compared to those who had oral health examined postoperatively.[17] The study was limited by a rather small sample size, and by design, but have since been corroborated by subsequent studies[18–20] and a recent meta-analysis.[21] In the latter PDS vs. no PDS prior to SAVR was associated with a similar all-cause mortality and risk of IE.[21] It is thus interesting that we, regardless of utilizing a larger sample size, were not able to demonstrate a reduction of postoperative IE risk in patients undergoing MPDS. Accordingly, we corroborate previous findings, but also extend them, as our patients, rather than open heart valve surgery, underwent TAVI. Furthermore, due to our larger sample size, we employed adjustment for potential confounders with consistent findings. Our findings thus stand in contrast to current guidelines as they suggest that mandatory

PDS with subsequent management of potential dental sepsis does not reduce the subsequent IE risk in patients undergoing TAVI. In our study, dental screening occurred approximately 1 month prior to TAVI, leading to oral surgery two weeks before surgery. Although some of our patients underwent elimination of potential dental sepsis foci later than the recommended 2 weeks, we were not able to demonstrate this specific threshold as clinically relevant, as no increased risk of IE was seen in those undergoing dental surgery less than 2 weeks prior to TAVI. These findings are in line with a small recent study describing the risk of IE following the revised Northern Ireland guidelines for oral surgery intervention during the COVID-19 pandemic, with no patients developing IE despite being referred for dental screening less than 2 weeks prior to surgery.[22] Our findings may at first sight contrast those from a recent large study intended to assess the risks of IE in nearly 8 million U.S. subjects with employer-provided Commercial/Medicare-Supplemental coverage. However, despite the study group demonstrated a significant temporal association between invasive dental procedures and subsequent IE in high-IE risk individuals, with the highest IE rate the first 30 days after dental procedure, this was limited to patients not treated with antibiotic prophylaxis.[23] The low risk of IE in high-IE risk patients undergoing dental procedures under relevant antibiotic prophylaxis indicates that dental surgery can be performed safely after cardiac surgery, and may explain the lack of association between MPDS with elimination of potential dental sepsis foci in our study.

In line with the historical findings by Lewis and Grant, but also from a recent Irish study[24] suggesting that 40% of IE may be caused by streptococcal species,[15] our study found that one third of IE cases were caused by streptococcal species potentially originating from dental foci.

It is thus interesting that more recent studies suggest that activities like tooth brushing, flossing and mastication are more likely causes of streptococcal-related IE rather than dental surgery, particularly in those with poor oral hygiene,[25,26] as these also may explain our negative results. Finally, while our results indicate that MPDS was not significantly associated with post-procedural risk of IE for patients undergoing TAVI in Denmark, it is important to highlight that Denmark has traditionally prioritized oral health, thereby influencing the two groups. According to the National Board of Health's Central Odontological Register and the public records of Danish Health Authority, there has been a significant improvement in dental status since 1972, although the rate of improvement has slowed down in recent years. Importantly, the incidence of tooth extraction in our study was lower than what has been reported in other studies, which may reflect healthier dental status in the Danish population.[24] This could potentially mean that the relevance and importance of MPDS may be more pronounced in areas where dental status is less optimal. Hence, it remains a possibility that selected patients with poor dental status may benefit from PDS, and further studies addressing this important topic should be encouraged.

Limitations
The study has several important limitations that must be considered. Some of these limitations include those inherent to retrospective studies such as missing data and a selection bias. We believe the latter may be a minor limitation given that the choice of PDS reflects differences in institutional dental screening practice rather than individual choices made by the clinician. Furthermore, all three tertiary centers in this study serve similar populations and perform TAVI with similar indications. The categorization into MPDS and NPDS groups was based on different hospital practices, introducing a confounding variable as we cannot discern between the effects of dental screening procedure and hospitals. Consequently, differences may not be solely attributable to the effects of MPDS. In addition to different dental screening strategies, our institutions also utilized different antibiotic protocols, implementing a potential bias. However, recent retrospective cohort analysis, by Rao and colleagues were not able to demonstrate that different antibiotic protocols lead to a different rate of IE.[27]

The Kaplan–Meier estimate may overstate the incidence of IE due to unaccounted competing risks like death; therefore, we also analyzed the compound outcome of IE and death to provide a more comprehensive assessment.

Finally, the number of IE events were few, and models should thus be interpreted with great caution. Although the low IE rate could imply that our study is underpowered to detect the impact of dental screening procedures on IE rate, numbers needed to treat would be high (namely, n = 524). Due to the retrospective nature of our study, the generally good dental health in Denmark, and the absence of E. Faecalis, which is a leading contributor to enterococcal IE, our findings should mainly be considered to be hypothesis generating, and randomized control trials are warranted. However, given the low event IE rate and the invasive nature of this preventive measure, we believe future studies should not only to focus on IE rate but also to include potential deleterious consequences of MPDS.

Conclusion
Mandatory PDS with subsequent elimination of sources of dental sepsis prior to surgery was not associated with lower risk of IE or all-cause mortality compared to targeted PDS in patients undergoing TAVI.

Literature Search: JSD and LK were responsible for the literature search.

Study Design: The study was designed by JSD, LK, HN, and LPR.

Data Collection: Data collection was carried out by LK and JSD.

Data Analysis, Tables, and Figures: LK and JSD managed the data analysis, creation of tables, and figures.

Data Interpretation: Data interpretation was undertaken by JSD, LK, LPR, HN, CJT, NHA, PF, JAP, OG, and MAC.

Writing–Original Draft: The original draft was written by JSD and LK.

Writing–Review & Editing: The review and editing of the manuscript were done by JSD, LK, LPR, HN, CJT, NHA, PF, JAP, OG, and MAC.

Revision: LK, JSD, OG, HN, CJT, and PF.

Data sharing statement

Data from this study, encompassing both individual participant information and a comprehensive data dictionary that defines each field, will be accessible to interested parties. Specifically, we'll be sharing deidentified participant data paired with the mentioned data dictionary. Study protocol and statistical analysis plan will be provided. Prospective researchers can anticipate data availability concurrent with the publication of our findings. To gain access, reach out to Lytfi.Krasniqi@rsyd.dk. Data will be shared with researchers whose proposed use has received approval. Access will be granted primarily for the replication of the results presented in our study. A signed data access agreement, compliant with regional legislation and data authority requirements, must be obtained prior to data release.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work the author(s) occasionally utilized ChatGPT for grammar assistance. After using this tool/service, the author(s) reviewed and edited the content as needed and take(s) full responsibility for the content of the publication.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanepe.2023.100789.

References

1 Que YA, Moreillon P. Infective endocarditis. *Nat Rev Cardiol*. 2011;8(6):322–336.
2 Piper C, Korfer R, Horstkotte D. Prosthetic valve endocarditis. *Heart*. 2001;85(5):590–593.
3 Ostergaard L, Valeur N, Ihlemann N, et al. Incidence and factors associated with infective endocarditis in patients undergoing left-sided heart valve replacement. *Eur Heart J*. 2018;39(28):2668–2675.
4 Baddour LM, Wilson WR, Bayer AS, et al. Infective endocarditis in adults: diagnosis, antimicrobial therapy, and management of complications: a scientific statement for healthcare professionals from the American Heart Association. *Circulation*. 2015;132(15):1435–1486.
5 Delgado V, Ajmone Marsan N, de Waha S, et al. 2023 ESC guidelines for the management of endocarditis. *Eur Heart J*. 2023;44(39):3948–4042.
6 Mentias A, Girotra S, Desai MY, et al. Incidence, predictors, and outcomes of endocarditis after transcatheter aortic valve replacement in the United States. *JACC Cardiovasc Interv*. 2020;13(17):1973–1982.
7 Butt JH, Ihlemann N, De Backer O, et al. Long-term risk of infective endocarditis after transcatheter aortic valve replacement. *J Am Coll Cardiol*. 2019;73(13):1646–1655.
8 Otto CM, Nishimura RA, Bonow RO, et al. 2020 ACC/AHA guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Joint Committee on clinical practice guidelines. *Circulation*. 2021;143(5):e72–e227.
9 Vahanian A, Beyersdorf F, Praz F, et al. 2021 ESC/EACTS guidelines for the management of valvular heart disease. *Eur Heart J*. 2021;43(7):561–632.
10 Buckley AJ, Hensey M, O'Connor S, Maree A. Dental screening prior to transcatheter versus surgical aortic valve replacement: international survey of current practices. *Catheter Cardiovasc Interv*. 2023;102(1):176–177.
11 von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet*. 2007;370(9596):1453–1457.
12 Schmidt M, Maeng M, Jakobsen CJ, et al. Existing data sources for clinical epidemiology: the Western Denmark Heart Registry. *Clin Epidemiol*. 2010;2:137–144.
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 Kuss O, Blettner M, Börgermann J. Propensity score: an alternative method of analyzing treatment effects. *Dtsch Arztebl Int*. 2016;113(35–36):597–603.
15 Lewis T, Grant RT. Observations relating to subacute infective endocarditis. *Heart*. 1923;10:21–77.
16 Okell CC, Elliott SD. Bacteriæmia and oral sepsis with special reference to the Ætiology of Subacute Endocarditis. *Lancet*. 1935;226(5851):869–926.
17 Hakeberg M, Dernevik L, Gatzinsky P, Eklof C, Kennergren C, Jontell M. The significance of oral health and dental treatment for the postoperative outcome of heart valve surgery. *Scand Cardiovasc J*. 1999;33(1):5–8.
18 Wu GH, Manzon S, Badovinac R, Woo SB. Oral health, dental treatment, and cardiac valve surgery outcomes. *Spec Care Dent*. 2008;28(2):65–72.
19 Deppe H, Auer-Bahrs J, Kolk A, Hall D, Wagenpfeil S. Need for dental treatment following cardiac valve surgery: a clinical study. *J Craniomaxillofac Surg*. 2007;35(6–7):293–301.
20 Kolk A, Pautke C, Hall D, Wagenpfeil S, Wolff KD, Deppe H. [The influence of surgical and restorative dental treatment prior to cardiac valve surgery on the long-term demand of dental treatment: a prospective clinical study]. *Wien Med Wochenschr*. 2009;159(23–24):608–619.
21 Lockhart PB, DeLong HR, Lipman RD, et al. Effect of dental treatment before cardiac valve surgery: systematic review and meta-analysis. *J Am Dent Assoc*. 2019;150(9):739–747.e9.
22 Ramadan M, Stewart V, Elsherif N, Milligan R, Beresford A, Marley J. Infective endocarditis and oral surgery input before cardiac surgery: time to prick the paradigm of pre-cardiac surgery assessments? *Br Dent J*. 2023;234(9):678–681.
23 Thornhill MH, Gibson TB, Yoon F, et al. Antibiotic prophylaxis against infective endocarditis before invasive dental procedures. *J Am Coll Cardiol*. 2022;80(11):1029–1041.
24 Buckley AJ, Tanner R, Armstrong B, et al. Transcatheter aortic valve implantation-related infective endocarditis: experience from an Irish tertiary referral centre. *Ir J Med Sci*. 2023;192(2):605–611.
25 Roberts GJ. Dentists are innocent! "Everyday" bacteremia is the real culprit: a review and assessment of the evidence that dental surgical procedures are a principal cause of bacterial endocarditis in children. *Pediatr Cardiol*. 1999;20(5):317–325.
26 Lockhart PB, Brennan MT, Thornhill M, et al. Poor oral hygiene as a risk factor for infective endocarditis-related bacteremia. *J Am Dent Assoc*. 2009;140(10):1238–1244.
27 Rao NR, Treister N, Axtell A, et al. Preoperative dental screening prior to cardiac valve surgery and 90-day postoperative mortality. *J Card Surg*. 2020;35(11):2995–3003.