Socioeconomic disparities in use of rhythm control therapies in patients with incident atrial fibrillation: A Finnish nationwide cohort study

Konsta Teppo, Jussi Jaakkola, Fausto Biancari, Olli Halminen, Miika Linna, Jari Haukka, Jukka Putaala, Pirjo Mustonen, Janne Kinnunen, Alex Luojus, Saga Itäinen-Strömberg, Juha Hartikainen, Aapo L. Aro, K.E. Juhanu Airaksinen, Mika Lehto

University of Turku, Turku, Finland
Heart Unit, Satakunta Central Hospital, Pori, Finland
Heart Center, Turku University Hospital, Turku, Finland
Heart and Lung Center, Helsinki University Hospital and University of Helsinki, Helsinki, Finland
Clinica Montevergine, GVM Care & Research, Mercogliano, Italy
Department of Industrial Engineering and Management, Aalto University, Espoo Finland
Aalto University, Espoo, Finland
Neurology, Helsinki University Hospital, and University of Helsinki, Helsinki, Finland
University of Helsinki, Helsinki, Finland
University of Eastern Finland, Kuopio, Finland
Heart Center, Kuopio University Hospital, Kuopio, Finland
Lohja Hospital, Department of Internal Medicine, Lohja, Finland

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ABSTRACT

Background: In patients with atrial fibrillation (AF), socioeconomic disparities have been reported in the use of oral anticoagulant therapy and outcomes, but whether income also affects the utilization of antiarrhythmic therapies (AATs) for rhythm control is unknown. We assessed the hypothesis that AF patients with higher income are more likely to receive AATs.

Methods: The nationwide retrospective registry based FinACAF cohort study covers all patients with AF from all levels of care in Finland. Patients were divided in AF diagnosis year and age-group specific income quintiles according to their highest annual income during 2004–2018. The primary outcome was the use of any AAT, including cardioversion, catheter ablation, and fulfilled antiarrhythmic drug (AAD) prescription.

Results: We identified 188,175 patients (mean age 72.6 ± 13.0 years; 49.6% female) with incident AF during 2010–2018. Patients in higher income quintiles had consistently higher use of all AAT modalities. When compared to patients in the lowest income quintile, the adjusted incidence rate ratios (95% CI) in the highest quintile were 1.53 (1.48–1.59) for any AAT, 1.71 (1.61–1.81) for AADs, 1.43 (1.37–1.49) for cardioversion, and 2.00 (1.76–2.27) for catheter ablation. No temporal change during study period was observed in the magnitude of income disparities in AAT use, except for a decrease in income-related differences in the use of AADs.

Conclusion: Profound income-related disparities exist in AAT use among patients with AF in Finland, especially in the use catheter ablation.

1. Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia with a prevalence as high as 4.1%, and it is associated with substantial mortality and morbidity, including ischemic stroke, dementia, and heart failure [1–4]. AF symptoms range from none to disabling, often impairing daily life with exercise intolerance and arrhythmia-related psychological distress, thereby reducing quality of life [5]. While rate control is a reasonable treatment strategy in many patients with AF, certain aspects clearly support electing a rhythm control strategy, i.e., pursuing to
restore and maintain sinus rhythm using antiarrhythmic therapies (AATs), including catheter ablation and cardioversion procedures and antiarrhythmic drugs (AADs) [3]. Rhythm control strategy has been shown to relieve symptoms and improve quality of life in symptomatic AF patients, and symptoms are the primary indication for AATs in current guidelines [3]. A recent study also suggested that early pursuit of rhythm control strategy could reduce the risk of adverse cardiovascular outcomes [6]. Furthermore, in selected patients with AF and heart failure, catheter ablation has been shown to decrease hospitalizations and mortality as well as improve functional capacity and left ventricular ejection fraction [7,8].

Previous literature has indicated that socioeconomic inequality in health is pervasive and rising, with differences in health care financing mechanisms affecting the magnitude of health disparities [9–12]. Finland, as other Nordic countries, has a universal and tax-funded health care system, full coverage of public health insurance and high reimbursement rates of medical treatment [13,14]. Notwithstanding, socioeconomic health disparities exist in Finland in terms of somatic and psychiatric morbidity, self-rated health, and mortality [15].

In patients with AF, lower income and socioeconomic status have been associated with lower overall use of oral anticoagulant therapy and lower use of newer generation direct oral anticoagulants as well as with worse outcomes [16–19]. However, evidence on the association of income level with the utilization of AATs is limited. Therefore, the present nationwide cohort study, covering all patients with AF in Finland, aimed to investigate the impact of patients’ income on the use of AATs in patients with incident AF during 2010–2018.

### 2. Methods

#### 2.1. Study Population

The FinACAF Study (Finnish AntiCoagulation in Atrial Fibrillation) (ClinicalTrials Identifier: NCT04645537; ENCePP Identifier: EUPAS29845) is a retrospective nationwide registry-based cohort study including all patients with an AF diagnosis in Finland during 2004–2018 [4]. Patients were identified from three national health care registers (hospitalizations and outpatient specialist visits: HILMO; primary health care: AvoHILMO; and National Reimbursement Register upheld by Social Insurance Institute: KELA). The inclusion criterion for the cohort was an International Classification of Diseases, Tenth Revision (ICD-10) diagnosis code I48 (including atrial fibrillation and atrial flutter, together referred as AF) recorded between 2004 and 2018 and cohort entry occurred at the date of the first recorded AF diagnosis. The exclusion criteria were age <18 years at AF diagnosis and permanent migration abroad before December 31st, 2018. The present substudy was conducted within a cohort of patients with incident AF, established in previous studies of the FinACAF cohort [20–22]. However, patients entering the cohort before the introduction of AF specific ablation codes in 2010 were excluded. Follow-up continued until death or 31st December 2018, whichever occurred first. The patient selection process is summarized in Supplementary Fig. 1.

#### 2.2. Income

We received each patient’s highest annual taxable income (in 1000-euro accuracy) during the FinACAF study’s observation period 2004–2018 from the national Tax Register. To avoid patients’ identifiability due to high incomes, the annual income was capped to a maximum of 100 000 euros. Since income level is associated with age and the mean income level of patients may vary according to the cohort entry year, the patients were divided into age group and AF diagnosis year specific income quintiles, i.e., each 10-year age group during each cohort entry year was divided into income quintiles using age group and entry year specific cut-points [23]. Since different definitions of income levels may significantly affect the results, sensitivity analysis was
The study conforms to the Declaration of Helsinki as able data. Informed consent was waived due to the retrospective registry mismized, and the research group received individualized, but unidentifi

### Comorbidities

| Comorbidities                  | Income quintiles 1 (lowest) | Income quintiles 2 | Income quintiles 3 | Income quintiles 4 | Income quintiles 5 (highest) |
|-------------------------------|-----------------------------|--------------------|-------------------|-------------------|-----------------------------|
| Abnormal liver function       | 274 (0.7)                   | 208 (0.6)          | 182 (0.5)         | 171 (0.5)         | 163 (0.4)                   |
| Abnormal renal function       | 2 034 (5.2)                 | 1 571 (4.4)        | 1 663 (4.4)       | 1 546 (4.1)       | 1 449 (3.9)                 |
| Alcohol abuse                 | 3 184 (8.1)                 | 1 676 (4.7)        | 1 264 (3.4)       | 1 130 (3.0)       | 921 (2.5)                   |
| Cancer                        | 7 743 (19.7)                | 7 181 (20.0)       | 7 989 (21.3)      | 7 984 (21.1)      | 8 738 (23.3)                |
| Coronary heart disease        | 9 994 (25.4)                | 8 308 (23.1)       | 8 674 (23.1)      | 8 473 (22.4)      | 7 867 (20.9)                |
| Dementia                      | 2 710 (6.9)                 | 1 930 (5.4)        | 1 920 (5.1)       | 1 816 (4.8)       | 1 582 (4.2)                 |
| Diabetes                      | 10 535 (26.8)               | 8 791 (24.4)       | 8 681 (23.1)      | 8 021 (21.2)      | 7 149 (19.0)                |
| Dyslipidemia                  | 19 694 (50.1)               | 18 538 (51.6)      | 19 265 (51.3)     | 19 306 (51.1)     | 18 869 (50.2)               |
| Hypertension                  | 30 663 (77.9)               | 27 735 (77.1)      | 28 783 (76.7)     | 28 275 (75.1)     | 27 450 (73.1)               |
| Prior bleeding                | 5 037 (12.8)                | 4 014 (11.2)       | 4 190 (11.2)      | 4 204 (11.1)      | 4 045 (10.8)                |
| Prior ischemic stroke         | 5 265 (13.4)                | 4 119 (11.5)       | 4 241 (11.3)      | 4 001 (10.6)      | 3 712 (9.9)                 |
| Prior myocardial infarction   | 4 112 (10.5)                | 3 306 (9.2)        | 3 368 (9.0)       | 3 313 (8.8)       | 2 825 (7.5)                 |
| Psychiatric disorder          | 8 910 (22.6)                | 5 942 (16.5)       | 5 088 (15.6)      | 4 418 (11.7)      | 3 679 (9.8)                 |
| CHA\textsuperscript{2}-VASC score | 3.8 (1.9)                 | 3.6 (1.9)          | 3.5 (1.9)         | 3.3 (1.9)         | 3.1 (1.8)                   |
| Modified HAS-BLED score (max 8) | 2.7 (1.0)                 | 2.6 (1.0)          | 2.6 (1.0)         | 2.5 (1.0)         | 2.5 (1.0)                   |

Values denote n (%). Abbreviations: CHA\textsuperscript{2}-VASC, congestive heart failure, hypertension, age ≥ 75 years, diabetes, history of stroke or TIA, vascular disease, age 65–74 years, sex category (female); modified HAS-BLED score, hypertension, abnormal renal or liver function, prior stroke, bleeding history, age ≥ 65 years, alcohol abuse, concomitant antiplatelet/NSAIDs (no labile INR, max score 8).

2.3. Use of AATs

As an indicator of a pursuit of rhythm control strategy, the primary outcome was the use of any AAT, including recorded cardiovascular (Nordic Classification of Surgical Procedure (NCSP) codes: TPF20, WVA50, WX904), catheter ablation (NCSP codes: TPF44, TPF45, TPF46), and fulfilled AAD prescription (ATC code C01B antiarrhythmics class I and III, plus ATC code C07AA07 sotalol). The outcome was considered to occur on the date of first fulfilled AAD prescription or procedure date after cohort entry, whichever occurred first. The secondary outcomes were cardioversion and catheter ablation procedures and fulfilled AAD prescription individually.

2.4. Study Ethics

The study protocol was approved by the Ethics Committee of the Medical Faculty of Helsinki University, Helsinki, Finland (nr. 15/2017) and granted research permission from the Helsinki University Hospital (HUS/46/2018). Respective permissions were obtained from the Finnish register holders (KELA 138/522/2018; THL 2101/5.05.00/2018; Population Register Centre VRK/1291/2019–3 and Tax Register VH/874/07.01.03(2019)). The patients’ identification numbers were anonymized, and the research group received individualized, but unidentifiable data. Informed consent was waived due to the retrospective registry nature of the study. The study conforms to the Declaration of Helsinki as revised in 2002.

2.5. Statistical analysis

Statistical analyses were performed with the IBM SPSS Statistics software (version 27.0, SPSS, Inc., Chicago, Illinois) and R (version 4.0.5, https://www.R-project.org). The chi-square test was used to analyze differences between proportions, and the one-way analysis of variance to compare continuous variables. Poisson regression was used to estimate incidence as well as unadjusted and adjusted incidence rate ratios (IRRs) for each AAT category and income quintile. Use of AATs may be hindered by mortality occurring during the study period, and therefore, competing risk analyses using the Fine-Gray regression model with all-cause death as a competing event were performed to estimate the unadjusted and adjusted redistribution hazard ratios for incidence of AATs in income quintiles. In the Fine-Gray and Poisson regression models, adjustments were made for age (categorical variable in 10-year groups), gender, calendar year of AF diagnosis, education level, dementia, cancer, alcohol use disorder, psychiatric disorders, prior stroke, abnormal liver function, abnormal kidney function, diabetes, hypertension, coronary artery disease and heart failure. The definitions of the comorbidities are displayed in Supplementary Table 1.

Additionally, to assess temporal changes in the use of AATs according to income level, we determined the proportion of patients receiving AATs within one-year follow-up from cohort entry. Patients entering the cohort in 2018 were excluded from this analysis, since they had less than one year of follow-up. To statistically quantify whether the possible income-related disparities in the likelihood of receiving AATs within one year follow-up changed over study period, an interaction term between income quintile and cohort entry year as a continuous variable was fitted to the model. Further, to statistically quantify whether the possible income-related disparities in the likelihood of receiving AATs within one year follow-up changed over study period, an interaction term between income quintile and cohort entry year as a continuous variable was fitted to the model. Additionally, competing risk analyses using the Fine-Gray regression model may be hindered by mortality occurring during the study period, and therefore, competing risk analyses using the Fine-Gray regression model with all-cause death as a competing event were performed to estimate the unadjusted and adjusted cumulative incidence hazard ratios for incidence of AATs in income quintiles. In the Fine-Gray and Poisson regression models, adjustments were made for age (categorical variable in 10-year groups), gender, calendar year of AF diagnosis, education level, dementia, cancer, alcohol use disorder, psychiatric disorders, prior stroke, abnormal liver function, abnormal kidney function, diabetes, hypertension, coronary artery disease and heart failure. The definitions of the comorbidities are displayed in Supplementary Table 1.

3. Results

Overall, 188,175 patients (49.6% female) with incident AF in Finland during 2010–2018 were identified, and the mean age at diagnosis was 76.6 years (SD 11.6) in females and 69.3 years (SD 13.3) in males. Patients with higher income were more often male, had higher education and lower prevalence of cardiovascular comorbidities, psychiatric disorders, and alcohol abuse than patients with lower income levels (Table 1).
IRRs estimated by Poisson regression and adjusted for age, sex, calendar year of AF diagnosis, education level, dementia, cancer, alcohol use disorder, psychiatric change significantly during follow-up (income quintile 3). The differences in any AAT use between income quintiles did not depend on disparities in the use of any AAT were observed across the observation period and in all age groups (Supplementary Figures 2 and 3). Likelihood of repeat ablation procedures was similarly higher in patients with higher income when compared to patients in the lowest income quintile (Tables 2 and 3). The overall use of cardioversion between income quintiles were observed across the observation period, although the differences between the 2nd and 3rd quintiles were small and partly inconsistent (Supplementary Figure 2). The magnitude of income disparities in use of cardioversion did not change significantly over time (income quintile × cohort entry year \( p = 0.17 \), Supplementary Figure 2 and Supplementary Table 3).

3.2. Antiarrhythmic drugs

A total of 15 066 (8.0%) patients received AADs during the study period. The unadjusted and adjusted incidence of AAD use were higher in patients with higher income, when compared to patients in the lowest income quintile (Tables 2 and 3). Overall, use of AADs decreased over time and differences between income quintiles were observed across the study period, although some inconsistency appeared between the 2nd, 3rd, and 4th quintiles (Supplementary Figure 2). Of note, the income-related disparities in AAD use decreased significantly over the study period (income quintile × cohort entry year \( p < 0.001 \), Supplementary Table 3). When analyzing specific AADs, patients in higher income quintiles were more likely to receive flecainide, dronedarone, amiodarone and sotalol than patients in the lowest income quintile (Supplementary Table 4).

3.3. Cardioversions

Overall, 49 491 cardioversion procedures were performed in 30 413 (16.2%) patients. The unadjusted and adjusted rates of cardioversion were consistently higher in patients with higher income when compared to patients in the lowest income quintile (Tables 2 and 3). A similar trend was observed in the proportion of patients undergoing more than one cardioversion (Supplementary Table 4). Disparities in the performance of cardioversion between income quintiles were observed across the observation period, although the differences between the 2nd and 3rd quintiles were small and partly inconsistent (Supplementary Figure 2). The magnitude of income disparities in use of cardioversion did not change significantly over time (income quintile × cohort entry year \( p = 0.39 \), Supplementary Table 3).

3.4. Catheter ablations

A total of 5 021 catheter ablation procedures were performed on 4 120 (2.2%) patients during 2010–2018. The adjusted catheter ablation incidence increased steadily towards higher income quintiles (Tables 2 and 3). Likelihood of repeat ablation procedures was similarly higher in higher income quintiles (Supplementary Table 4). The overall use of catheter ablation increased steadily during 2010–2018 and income-related disparities in the use of ablation procedures were seen across

### Table 2

| Outcome          | Income quintile | Interventions | Proportion of patients with interventions | Patient years (in 1000 years) | Incidence (per 1000 patient years) | Unadjusted IRR | Adjusted IRR |
|------------------|----------------|--------------|------------------------------------------|-------------------------------|-------------------------------------|----------------|--------------|
| Any AAT          | 1st            | 5 767        | 14.7%                                    | 101.8                         | 56.7 (55.2–58.1)                    | (Reference)    | (Reference)  |
|                  | 2nd            | 7 236        | 20.1%                                    | 94.6                          | 76.5 (74.7–78.3)                    | 1.35           | 1.18         |
|                  | 3rd            | 7 924        | 21.1%                                    | 100.0                         | 79.2 (77.5–81.0)                    | 1.40           | 1.25         |
|                  | 4th            | 8 781        | 23.2%                                    | 100.0                         | 87.8 (86.0–89.7)                    | 1.55           | 1.36         |
|                  | 5th            | 9 800        | 26.1%                                    | 98.0                          | 100.0 (98.1–102.0)                  | 1.77           | 1.53         |
| AADs             | 1st            | 2 007        | 5.1%                                     | 115.1                         | 24.7 (24.4–25.1)                    | (1.71–1.82)    | (1.48–1.59)  |
|                  | 2nd            | 2 703        | 7.5%                                     | 111.5                         | 22.3 (21.6–23.0)                    | (1.39–1.47)    | (1.15–1.29)  |
|                  | 3rd            | 3 080        | 8.2%                                     | 117.9                         | 26.1 (25.2–27.1)                    | 1.50           | 1.36         |
|                  | 4th            | 3 391        | 9.0%                                     | 120.5                         | 28.1 (27.2–29.1)                    | 1.62           | 1.47         |
| Cardioversion    | 1st            | 4 474        | 11.4%                                    | 106.4                         | 42.0 (40.8–43.3)                    | 1.31           | (1.53–1.71)  |
|                  | 2nd            | 5 565        | 15.5%                                    | 101.0                         | 55.1 (53.7–56.6)                    | (1.76–1.96)    | (1.39–1.56)  |
|                  | 3rd            | 6 043        | 16.1%                                    | 107.1                         | 56.4 (55.0–57.9)                    | 1.34           | 1.19         |
|                  | 4th            | 6 822        | 18.1%                                    | 107.7                         | 63.4 (61.9–64.9)                    | 1.51           | 1.31         |
| Catheter ablation| 1st            | 384          | 1.0%                                     | 121.3                         | 3.2 (2.9–3.5)                       | (1.61–1.73)    | (1.37–1.49)  |
|                  | 2nd            | 671          | 1.9%                                     | 119.6                         | 5.6 (5.2–6.1)                       | 1.77           | (1.38–1.53)  |
|                  | 3rd            | 834          | 2.2%                                     | 127.0                         | 6.6 (6.1–7.0)                       | (1.56–2.01)    | (1.22–1.57)  |
|                  | 4th            | 997          | 2.6%                                     | 130.8                         | 7.6 (7.2–8.1)                       | 2.01           | 1.60         |
|                  | 5th            | 1 234        | 3.3%                                     | 132.3                         | 9.3 (8.8–9.9)                       | (1.84–2.34)    | (1.41–1.80)  |

Abbreviations: AAD, antiarrhythmic drug; AAT, antiarrhythmic therapy; IRR, incidence rate ratio. 95% confidence intervals in parenthesis. Unadjusted and adjusted IRRs estimated by Poisson regression and adjusted for age, sex, calendar year of AF diagnosis, education level, dementia, cancer, alcohol use disorder, psychiatric disorders, prior stroke, abnormal liver function, abnormal kidney function, diabetes, hypertension, coronary heart disease and heart failure.
The observed differences in the utilization of AATs between income quintiles are likely multifactorial. Patients with lower socioeconomic status may have a higher threshold in seeking care unless substantial symptoms are present. Although practically all cardioversion and ablation procedures in Finland are performed in the public healthcare, more frequent use of the private sector in patients with higher income may increase prescriptions of AADs, as well as indirectly the use of cardioversion and ablation procedures through higher rate of hospital referrals. Additionally, both patient preference and advocacy for more intensive or invasive AATs may differ between income classes. Furthermore, varying levels of health literacy, differences in trust between patients and clinicians, and possible systemic biases within the health care system and society may contribute to the observed differences in treatment. Finally, the higher prevalence of cardiovascular comorbidities, dementia, and alcohol abuse disorder in lower income quintiles undoubtedly affect the clinical decision making of AATs. Nevertheless, even after adjusting for several patient characteristics, a clear disparity emerged in AAT use between income quintiles, suggesting possible inequity in the provided care.

However, our findings must be interpreted bearing in mind the several limitations of this study, especially the challenges inherent to retrospective cohort studies based on administrative data. Hence, our results represent associations and not necessarily causality between income and AAT use. Furthermore, since we lacked data on AF symptom burden, AF subclassifications and the actual reasons for withholding AATs, assumptions of lower AAT use signalling lower quality of care should be drawn with caution, especially considering the historical development in AF treatments, and that studies suggesting outcome benefits of rhythm control strategy have been published mainly in the end or after our study period [3,6,8]. Additionally, importantly, we lacked information on whether the patient had atrial flutter or atrial fibrillation. Although our analyses were adjusted for several patient characteristics, residual confounding cannot be excluded. Despite these limitations, the results of this large nationwide cohort study highlight important treatment differences based on income level, notwithstanding the Finnish welfare state model with universal and tax-funded health care. The findings emphasize the need for further efforts to ensure equitable access to all AF treatments. Future studies are needed to investigate the factors underlying the observed income disparities in the utilization of AATs, and in particular, whether they reflect clinically well-founded reticence or unfounded inequity in the provided care.

In conclusion, profound income-related disparities exist in the use of AATs in patients with AF in Finland, especially in the use of catheter ablation procedures. These findings are of special importance in a country that aims to ensure equity in healthcare irrespective of socioeconomic background.
Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Konsta Teppo: none. Jussi Jaakkola: none. Fausto Biancari: none Olli Halminen: none. Jukka Putaala: Dr. Putaala reports personal fees from Boehringer-Ingelheim, personal fees and other from Bayer, grants and personal fees from BMS-Pfizer, personal fees from Portola, other from Amgen, personal fees from Herantis Pharma, personal fees from Terve Media, other from Vital Signum, personal fees from Abbott, outside the submitted work. Pirjo Mustonen: Consultant: Roche, BMS-Pfizer-alliance, Novartis Finland, Boehringer Ingelheim, MSD Finland. Jari Haukka: Consultant: Research Jansen R&D; Speaker: Bayer Finland. Miika Linna: Speaker: BMS-Pfizer-alliance, Bayer, Boehringer-Ingelheim. Juha Hartikainen: Research grants: The Finnish Foundation for Cardiovascular Research, EU Horizon 2020, EU FP7. Advisory Board Member: BMS-Pfizer-alliance, Novo Nordisk, Amgen. Speaker: Cardiome, Bayer. K.E. Juhani Airaksinen: Research grants: The Finnish Foundation for Cardiovascular Research; Speaker: Bayer, Pfizer and Boehringer-Ingelheim. Member in the advisory boards: Bayer, and AstraZeneca. Mika Lehto: Consultant: BMS-Pfizer-alliance, Bayer, Boehringer-Ingelheim, and MSD; Speaker: BMS-Pfizer-alliance, Bayer, Boehringer Ingelheim, MSD, Terve Media and Orion Pharma. Research grants: Aarne Koskelo Foundation, The Finnish Foundation for Cardiovascular Research, and Helsinki and Uusimaa Hospital District research fund, Boehringer-Ingelheim. Aapo Aro: Research grants: Finnish Foundation for Cardiovascular Research; Speaker: Abbott, Johnson & Johnson, Sanofi, Bayer, Boehringer-Ingelheim.

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Concept and design: Teppo, Jaakkola, Putaala, Mustonen, Haukka, Airaksinen, Lehto.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Teppo.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Teppo, Jaakkola.

Obtained funding: Lehto.

Administrative, technical, or material support: Jaakkola, Halminen, Haukka.

Supervision: Jaakkola, Putaala, Mustonen, Haukka, Airaksinen, Lehto.

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Role of the Funder/Sponsor

The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Data Availability Statement

Because of the sensitive nature of the data collected for this study, requests to access the dataset from qualified researchers trained in human subject confidentiality protocols may be sent to the Finnish national register holders (KELA, Finnish Institute for Health and Welfare, Population Register Center and Tax Register).

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijjcha.2022.101070.

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