Introduction

Recently, the US Preventive Services Task Force stated that the current evidence base for atrial fibrillation (AF) screening is insufficient to balance the benefits or harms of screening [1]. Both in terms of screening type, frequency, and methods. The European Hearth Rhythm Association (EHRA) suggested focusing AF screening on target populations at higher risk [2]. The STROKESTOP randomized controlled trial (RCT) of systematic screening inviting all 75–76 year-old residents in two Swedish regions to either screening for AF or control reported a small net benefit of screening [3]. Similarly, the LOOP Study using more sophisticated continuous screening methods by implantable loop recorders did also find more AF detected, anticoagulation (AC) treatment initiated and a (non-significant) reduction in strokes (HR 0.80; 95% I 0.61–1.05) [4]. Additional ongoing RCTs will add to the future evidence base of AF screening.

However, an important finding in STROKESTOP was that non-participants had significantly worse outcomes. In a group of potentially non-participants feasibility of opportunistic screening in a domiciliary setting with municipality preventive home visits to citizens ≥75 years was investigated. Handheld ECG device was used by trained municipality caregivers followed by cardiologist assessment. Eighty-five percent consented to being screened, and seven of 477 screened were found with AF. Opportunistic screening in preventive home visits had a high participation rate and was feasible. Randomized trials are needed before making any firm conclusions.

Feasibility of screening for atrial fibrillation in a domiciliary setting: opportunistic one-time screening at preventive home visits in municipalities

Peter Bo Poulsen\textsuperscript{a}, Ulla Hemmingsen\textsuperscript{b}, Tine Anette Melgaard\textsuperscript{c}, Heidi Buch Elleby\textsuperscript{d}, Dorte Wedell-Wedellsborg\textsuperscript{e}, Lars Dybro\textsuperscript{f}, Ida Marie Lund\textsuperscript{g}, Ulrik Dixen\textsuperscript{h} and Lars Frost\textsuperscript{h,i}.

\textsuperscript{a}Pfizer Denmark, H&V, Ballerup, Denmark; \textsuperscript{b}Training and Rehabilitation, The Municipality of Vordingborg, Vordingborg, Denmark; \textsuperscript{c}Healthcare Center Mølledamvej, Center for Health, Culture and Leisure, The Municipality of Rebild, Støvring, Denmark; \textsuperscript{d}Welfare and Health, The Municipality of Horsens, Horsens, Denmark; \textsuperscript{e}WW Projects, København K, Denmark; \textsuperscript{f}Pfizer Denmark, Medical Affairs, Ballerup, Denmark; \textsuperscript{g}Department of Cardiology, Copenhagen University Hospital, Amager Hvidovre Hospital, Hvidovre, Denmark; \textsuperscript{h}Department of Cardiology, University Research Clinic for Innovative Patient Pathways, Regional Hospital of Silkeborg, Silkeborg, Denmark; \textsuperscript{i}Institute of Clinical Medicine, Aarhus University Hospital, Denmark

ABSTRACT

Current evidence base for atrial fibrillation (AF) screening is insufficient. An important finding in the STROKESTOP study was that non-participants had significantly worse outcomes. In a group of potentially non-participants feasibility of opportunistic screening in a domiciliary setting with municipality preventive home visits to citizens ≥75 years was investigated. Handheld ECG device was used by trained municipality caregivers followed by cardiologist assessment. Eighty-five percent consented to being screened, and seven of 477 screened were found with AF. Opportunistic screening in preventive home visits had a high participation rate and was feasible. Randomized trials are needed before making any firm conclusions.

Materials and methods

The study was designed as an observational study of opportunistic AF screening during preventive home visits in three Danish municipalities – Horsens, Vordingborg and Rebild. GPs were pre-informed about the study.

Citizens fulfilling inclusion criteria (1. ≥75 years of age, 2. no known AF diagnosis or AC treatment, 3. no home care or living in nursing home, 4. understanding Danish) and having provided informed consent were consecutively included from February 2019 to March 2020.

CONTACT Peter Bo Poulsen peterbo.poulsen@pfizer.com Lautrupvang 8, Ballerup, DK-2750, Denmark.
Based on prevalence of AF among ≥75 years of age (9.6% [7]), citizens ≥75 years of age in the three municipalities and a precision of 5% the minimum number to be screened was estimated to 393 [8].

The outcomes measures were participation rate and proportion of newly detected patients with AF. This was also investigated for two age-strata (75–84 and ≥85). Furthermore, significant non-AF arrhythmia was assessed.

The municipality caregiver who visited the citizen collected study data and performed the one-all ECG screening (two repeated measurements) using a handheld CE-marked Zenicor ECG Medical System. This device has been scientifically validated in 30+ published studies, is simple to use, and does not reveal the screening result on the device. The municipality staff received in-depth device training prior.

The ECG recordings were transferred via mobile network to a central and encrypted internet-based server, where a cardiologist assessed all recordings. Information on assessment result—signs of (1) AF, (2) no AF or (3) significant non-AF arrhythmia—was sent to the municipalities. In case of AF the citizen was informed by phone within 24 h and by letter. The municipalities encouraged the citizen to contact their own GP for clinical examination. Figure 1 shows the information flow.

Data on age, gender, cohabitation status and self-reported comorbidities were entered by the municipality staff in an electronic case report form with log-in on a secure internet-based domain with encrypted data transfer and continuous log system.

The full data set and the two age-strata were analyzed using descriptive statistics, i.e. mean, standard deviation and 95% confidence intervals (CI), frequencies and percentages using SAS statistical program version 9.3 (Cary, NC, USA). The study was approved by the Danish Data Agency. No approval was needed from the Danish National Committee on Health Research Ethics.

Results

In total 1434 citizens in the three municipalities were visited. Among these 477 were screened following informed consent. Non-screening was due to existing AF diagnosis or receiving AC treatment (28%) or due to personal reasons, e.g. spouse recently died, terminal cancer or mental disorder (12%). Of those visited and eligible 15% did not consent to participate.

Average age of the screened was 81 years with slightly more females (Table 1). 53% reporting at least one comorbidity with hypertension and diabetes mellitus being the most frequent.

In total seven of the 477 screened were found with AF following cardiologist review of the ECG recordings, which corresponds to a detection rate of 1.5% (95%CI 0.6–3.0) (Table 1). To detect one AF case 68 citizens has to be screened. Most detected AF cases were found in the 75–84 age-subset, predominantly men and living alone (57%).

Furthermore, a total of 31 citizens (6.5%) were found with signs of other significant non-AF arrhythmia such as AV-block (1), bradycardias (5), and supra and ventricular ectopic beats (21), as judged by cardiologists to be of potentially clinical importance.

Discussion

The present study investigated the feasibility of opportunistic screening of AF in three Danish municipalities utilizing an existing domiciliary setting like preventive home visits. A benefit of the domiciliary setting was that only 15% of those visited did not consent to participate. In systematic screening studies based on invitation the non-participation rate has shown to be up to 50% [3]. The AF detection rate found (1.5%) was around the same level as found in a previous GP-lead opportunistic screening study [6]. The result was also very much in line with other screening studies, although none of these were from the domiciliary setting [9].

The study had some limitations.

First, one-time opportunistic screening is a simple setup that only detect AF at time of screening. More intense and sophisticated methods with consecutive measurements, e.g. [4], may have detected silent or paroxysmal AF cases.
Second, EHRA guidelines proposed focus of screening on patients with multiple AF risk factors [2]. This requires careful selection of a proper domiciliary setting. It was, however, the case with Danish preventive home visits, where all citizens were 75+ years and with multi-morbidity closely correlated with age.

Third, not all citizens accepted a preventive home visit by the municipality and 15% of those visited did not consent to being screened. This lowered the study representativeness.

Fourth, 28% of citizens were not screened due self-reported AF or use of AC treatment. Record examination could have validated this but was out of scope.

In conclusion, the study found that opportunistic screening in a domiciliary setting like municipality preventive home visits to citizens with potential multiple risk factors for AF was feasible, had a high participation rate and detected new AF cases. This might be one way to approach high risk patients, who do not accept systematic screening. The findings do, however, need to be tested in a full RCT of opportunistic screening versus no screening prior to make firm conclusions on its implementation.

Acknowledgement

Andreas Habicht, Signifikans Aps., provided as a paid contractor to Pfizer Denmark Aps. database management and assisted in the statistical analysis. Mette Mortensen, Pfizer, assisted with the project management and contact to the municipality during the study.

Author Contributors

PBP, LF, UD, UH, LD and DWW conceived the study and contributed to the design of the study. UH, TAM, HBE, IML and DWW participated in the data collection and clinical data assessment in the study. PBP performed the analyses and wrote the first draft of the manuscript. All authors contributed to revising and finalizing the manuscript. PBP (corresponding author) guarantees all aspect of the reliability and freedom from bias of the data presented and discussion of their interpretation.

Ethics approval

The study was approved by the Danish Data Agency. The National Committee on Health Research Ethics was also informed about the study, however, as the study does not investigate biomedical samples it is not covered by the law on pharmaceutical studies or the law on biochemical studies and did not need approval by the Danish ethics committee.

Disclosure statement

UD and LF were paid by Pfizer Denmark Aps. for their work as a member of the study steering committee. LF has been an advisory board member for BMS/Pfizer and MSD and is supported by a grant from the Health Research Foundation of Central Denmark Region. UH was a member of the study steering committee but was not paid by Pfizer Denmark Aps. for her participation and work on the study in accordance with the agreement made between Pfizer and the Municipality of Vordingborg. IML was paid by Pfizer Denmark Aps. for her specialist assessment of ECG’s and correspondence with the municipalities. TAM and HBE were both working on the study in Rebild and Horsens Municipalities, but were fully paid by each of the two municipalities and did not in accordance with the agreements between Pfizer and the two municipalities receive any payments from Pfizer. DWW was a paid contractor to Pfizer Denmark Aps. for her work as the CRO project leader role of the study and work as a member of the study steering committee. PBP and LD are full-time employees of Pfizer Denmark Aps. and were both members of the study steering committee. The authors report no other competing interests in this work.

Data availability statement

Data are not available as these are stored on an external database external to sponsor.

Funding

This study was sponsored by the Alliance of BMS Denmark and Pfizer Denmark Aps. Each of the municipalities and their employees involved in the AFFORD-2 study are acknowledged for their work and participation. The municipalities and their employees did not receive any payment for their participation in the study.

Table 1. Screened citizens—characteristics and AF cases (N = 477).

| Subject characteristics | Mean (SD; min–max) | 95%CI |
|-------------------------|-------------------|--------|
| Average age             | 80.9 (4.7; 75–95 years of age) | 80.5–81.3 |
| 75–84 years of age/≥85 years of age | 373 (78)/104 (22) |        |
| Females                 | 268 (56)          |        |
| Living alone            | 237 (50)          |        |
| Self-reported comorbidities |                |        |
| Congestive heart failure| 11 (2)            |        |
| Hypertension            | 217 (46)          |        |
| Diabetes Mellitus       | 54 (11)           |        |
| Prior stroke or TIA or thromboembolism | 28 (6) |        |
| Vascular disease        | 45 (9)            |        |
| AF cases (detection rate) |                  |        |
| All ages (N = 477)      | 7 (1.5%)          | 0.6–3.0 |
| 75–84 years of age (n = 373) | 5 (1.3%)     | 0.44–3.1 |
| ≥85 years of age (n = 104) | 2 (1.9%)      | 0.2–6.8 |

N: Number of subjects; n: Number of subjects belonging to specific subgroup; SD: Standard Deviation; CI: Confidence interval.
References

[1] Mandrola J, Foy A. Screening for atrial fibrillation-new devices, same challenges. JAMA Intern Med. 2022;182(3):251–253.

[2] Mairesse GH, Moran P, Van Gelder IC, ESC Scientific Document Group, et al. Screening for atrial fibrillation: a European Heart Rhythm Association (EHRA) consensus document endorsed by the Heart Rhythm Society (HRS), Asia Pacific Heart Rhythm Society (APHRS), and Sociedad Latinoamericana de Estimulaci ón Cardio y Electrofisiolog ía (SOLAECE). Europace. 2017;19(10):1589–1623.

[3] Svennberg E, Friberg L, Frykman V, et al. Clinical outcomes in systematic screening for atrial fibrillation (STROKESTOP): a multicentre, parallel group, unmasked, randomised controlled trial. Lancet. 2021;398(10310):1498–1506.

[4] Svendsen JH, Diederichsen SZ, Højberg S, et al. Implantable loop recorder detection of atrial fibrillation to prevent stroke (The LOOP Study): a randomised controlled trial. Lancet. 2021;398(10310):1507–1516.

[5] Hindricks G, Potpara T, Dagres N, ESC Scientific Document Group, et al. 2020 ESC guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. Eur Heart J. 2021;42(5):373–498.

[6] Hald J, Poulsen PB, Qvist I, et al. Opportunistic screening for atrial fibrillation in a real-life setting in general practice in Denmark - the Atrial Fibrillation Found On Routine Detection (AFFORD) non-interventional study. PLoS One. 2017;12(11):e0188086.

[7] Larsen KL, Ovesen C, Frost L, et al. Trends in preadmission oral anticoagulant use and clinical outcome in atrial fibrillation patients admitted with acute stroke in Denmark. Eur Heart J Qual Care Clin Outcomes. 2020;6(2):112–120.

[8] Naing L, Winn T, Rusli BN. Practical issues in Calculating the Sample Size for Prevalence Studies. Arch Orofac Sci. 2006;1:9–14.

[9] Lowres N, Olivier J, Chao T-F, et al. Estimated stroke risk, yield, and number needed to screen for atrial fibrillation detected through single time screening: a multicountry patient-level meta-analysis of 141,220 screened individuals. PLoS Med. 2019;16(9):e1002903.