Assessment of **RE**mote **HEA**rt **R**hythm **S**ampling using the AliveCor heart monitor to scr**E**en for **A**trial **F**ibrillation: **The REHEARSE-AF Study**

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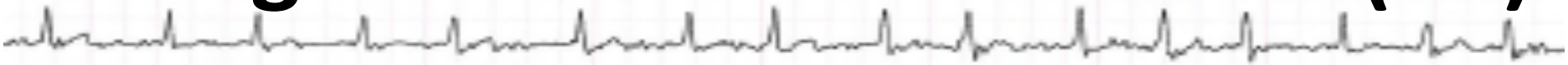
Disclosures

- *The study was funded predominantly by the Welsh Government (Health Technology and Telehealth Fund) and in part by a project grant from AliveCor.*
- *The study data were analysed and reported independently without involvement of the company.*
- *No authors have received personal remuneration from AliveCor Inc.*

Background: Atrial Fibrillation (AF)



- Increasingly common in ageing populations
- Predisposes to formation of cardiac thrombus
- Often Asymptomatic
- Implicated in significant % ischaemic strokes
- Effective anticoagulation can reduce AF-associated stroke risk by over 60%
- More effective identification and treatment could reduce stroke risk

WHITE PAPER

Screening for Atrial Fibrillation

A Report of the AF-SCREEN International Collaboration

- Screen-detected AF is not a benign condition
- With additional stroke factors, carries sufficient risk of stroke to justify consideration of anticoagulation.
- Handheld ECG devices have the advantage of providing verifiable ECG trace guidelines require for AF diagnosis…
- Preferred as screening tools.
- RCTs required

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Hypotheses

Primary Hypothesis

- Twice weekly single lead ECG monitoring with the AliveCor Kardia Mobile system will lead to earlier detection of AF versus routine care over a period of 1 year

Additional Hypotheses

- Diagnosis of AF with regular single lead ECG monitoring will be achieved at an acceptable cost
- Twice weekly ECG monitoring with the AliveCor Kardia device will be acceptable to participants

Study Entry Criteria

Inclusion Criteria

- Individuals over 65y with a CHADS-VASc score ≥2
- Access to the internet via Wifi.

Exclusion criteria

- Confirmed diagnosis of (P)AF,
- Receiving Oral Anticoagulant Therapy,
- Known contraindication to anticoagulation
- Permanent cardiac pacing implant.
- Unable to operate the AliveCor Kardia system after instruction

AliveCor Kardia Mobile

Protocol (1)

- Brief History and Examination
- AliveCor system instruction and ECG recording
- Patients Randomized to regular ECG monitoring (iECG) using AliveCor Kardia (iPod) or routine care (RC)

iECG

- Asked to record and submit single lead ECG device twice weekly for 52 weeks (Monday and Wednesday) or if symptomatic
- ECGs uploaded automatically to secure server via WiFi
- Automated ECG analysis + Expert Cardiac Physiolologist over read
- Cardiologist over read of abnormal ECGs (+ 10% normal ECG)
- Prompt medical review if AF (other significant arrhythmia)

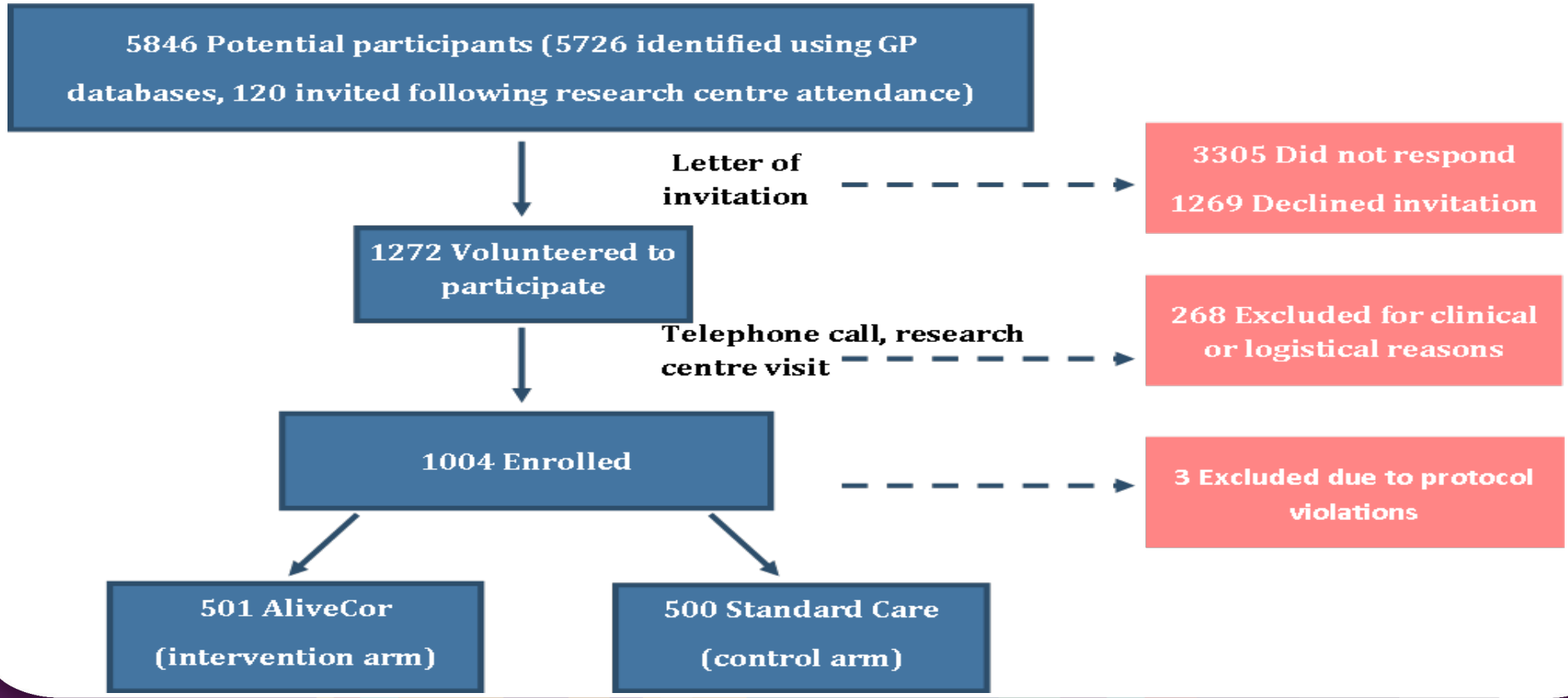
RC

- Usual routine clinical care with local medical practitioner(s)

Protocol (2)

- Notification of Adverse Events by patients/care teams (at time of event where possible)
- Telephone Review of all patients at 12, 32, 52 weeks
- Correspondence with primary care at 52 weeks
- Review of all participants' NHS records for death/CV admissions
- Follow up review of source clinical records for all adverse events, including ECG review of reported arrhythmias
- Participant experience survey conducted at 52 weeks
- Health economic evaluation (cost-per AF diagnosis)

Recruitment



Baseline Patient Data

	iECG (N=500)	RC (N=501)	P
Sex M/F	48%/52%	45%/55%	0.30
Mean age (SD)	72.6 y (5.4)	72.6 y (5.4)	0.98
• *Age 65-74 y*	*328*	*330*	*0.93*
• *Age >= 75 y**	*172*	*171*	*0.93*
Heart Failure	5 (1%)	9 (2%)	0.28
Hypertension	268 (54%)	272 (55%)	0.75
Diabetes Mellitus	129 (26%)	140 (28%)	0.43
Stroke or TIA	35 (7%)	28 (6%)	0.37
Vascular Disease	71 (14%)	79 (16%)	0.50
CHADS-VASc (SD)	3.0 (1.0)	3.0 (1.0)	0.57

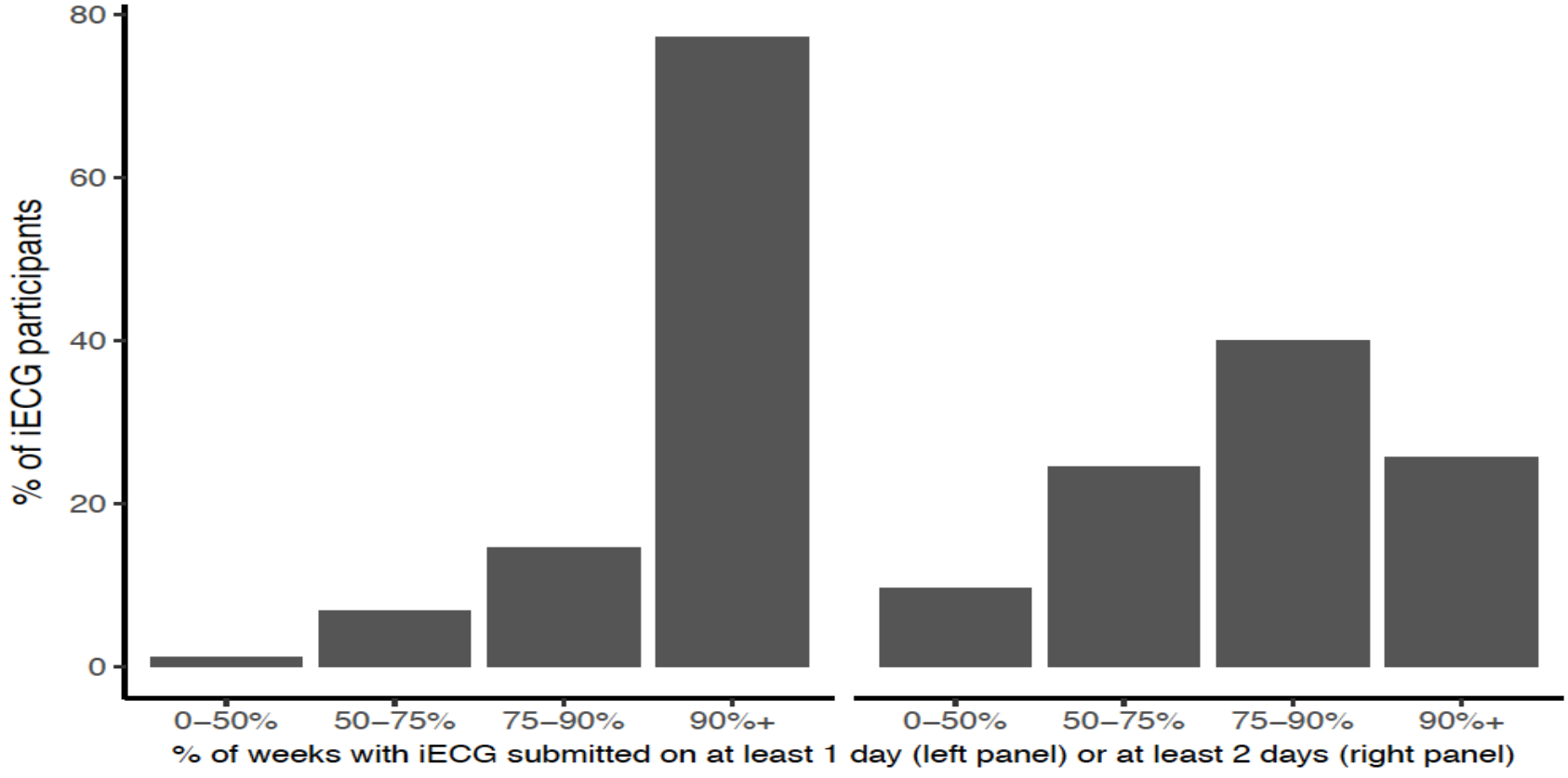
Baseline medication use was also similar in the two study groups

ECG Analysis*

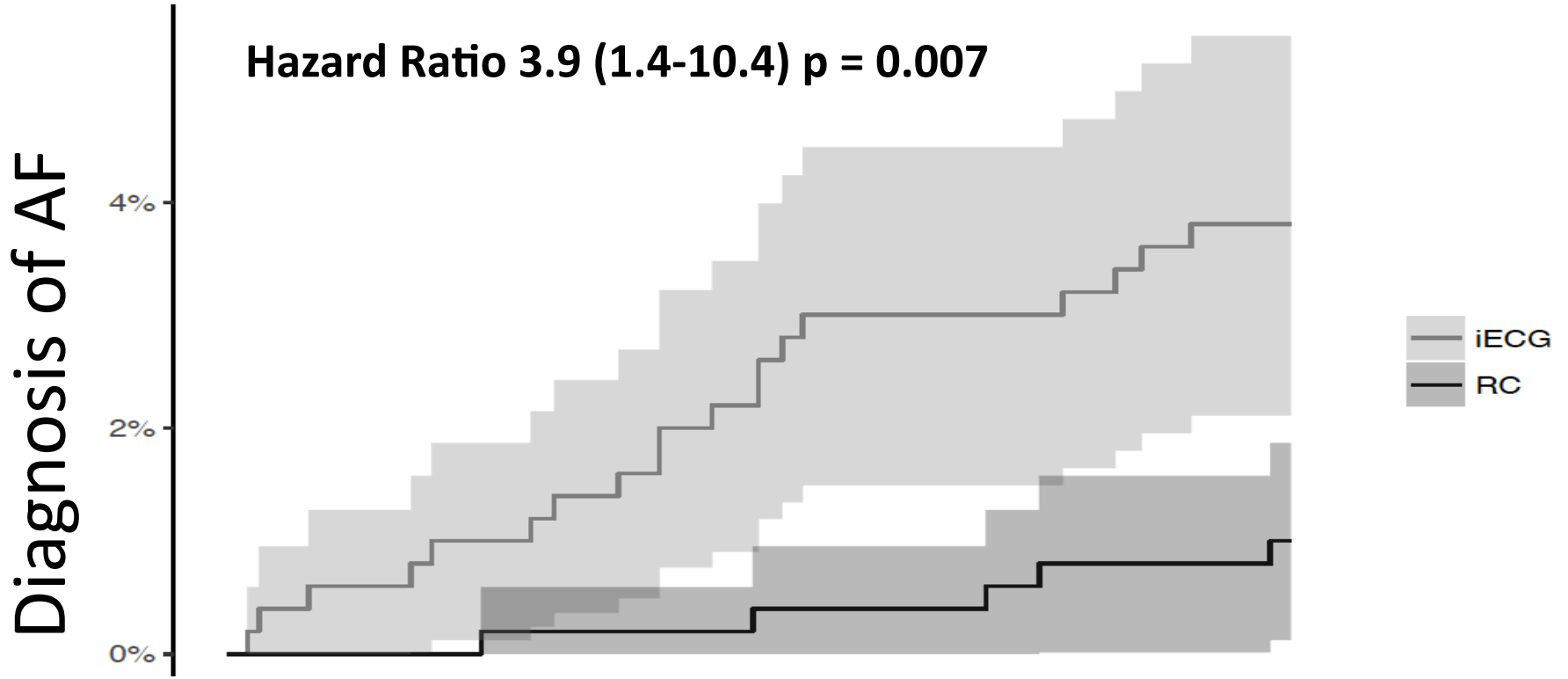
- 60 440 iECGS recorded and transmitted for 500 iECG participants
- 76% of iECGs reported “normal” by the automated algorithm AliveCor version 2.2.0 [build 21] (no over read-confirmed AF)
- 21% of iECGs reported “undetermined” by automated algorithm
  - Only 6 of these “undetermined” ECGs finally confirmed AF
- 1% of iECGs reported as “AF” by the automated algorithm
  - only 5% of these finally confirmed to be AF
- 2.2% of submitted iECGs were considered uninterpretable

**Full detailed diagnostic performance analysis to be presented/published elsewhere*

Compliance with ECG Monitoring Protocol



Diagnosis of AF



Cost per AF diagnosis according to iECG pathway £8,255 (€9,070)

Predictors of AF

	Hazard Ratio (95% CI)	p-value
Gender M/F	1.9 (0.9, 4.5)	0.11
Age >= 75	2.3 (1.0, 5.1)	0.04
Hypertension	0.91 (0.6, 1.4)	0.68
Diabetes Mellitus	1.1 (0.7, 1.6)	0.79
Stroke or TIA	1.2 (0.6, 2.5)	0.64
Arterial Disease	1.5 (1.0, 2.4)	0.05
CHADS-VASc Score ≥4	2.3 (1.0, 5.1)	0.04

CHADS-VASc ≥4 - only significant independent predictor of AF (MVA: Adjusted hazard ratio=4.0, 95% CI 1.1 to 15.2, p = 0.04)

Serious Adverse Events

Adverse event	iECG (N)	RC (N)	p-value
Death	3	5	0.51
Stroke/TIA/SE	6	10	0.34
Clinically Significant Bleeds	2	1	0.56
DVT/PE	3	1	0.31
Other cardiovascular	8	13	0.27
Respiratory	7	3	0.20
Other Neurological	3	2	0.65
Musculoskeletal/Fall	14	14	0.99
Gastroenterological	10	10	0.99
Renal / Urological	2	5	0.26
Other	7	6	0.78

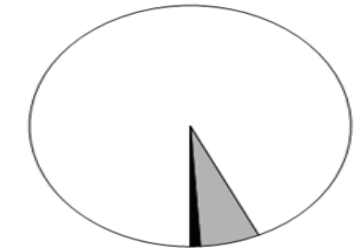
Participant General Experience Survey

	iECG (mean)	RC (mean)	P
Awareness of Arrhythmia Risk	6.8	6.1	0.001
Anxiety re Arrhythmia Risk	2.2	2.5	0.003
Likely to intend to visit Physician re Heart Rhythm Concerns	7.1	7.5	0.04
Preference to Switch to Other Study Arm	1.9	6.2	<0.0001

- *Participants*' experience (reported using a 1-10 visual analogue scale)

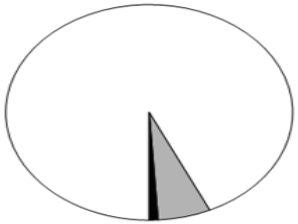
iECG Participant Experience Survey

Overall Satisfaction



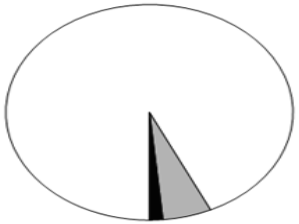
- Extremely or very satisfied
- Generally satisfied
- Slightly or not at all satisfied

Anxiety Regarding Heart Rhythm



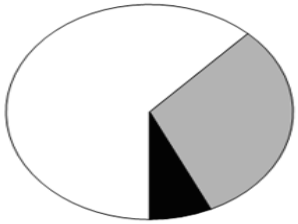
- Not at all anxious or slightly anxious
- Moderately anxious
- Very or extremely anxious

Restriction of Lifestyle



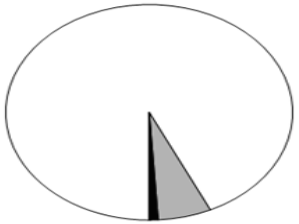
- Not at all restricted
- Slightly restricted
- Moderately or severly restricted

Confidence in Use of Device



- Extremely or very confident
- Generally confident
- Slighty or not at all confident

Acceptance of Information Sharing



- Extremely or very comfortable
- Generally comfortable
- Slightly or not at all comfortable

Conclusions

- Regular twice-weekly iECG screening in people over 65y (CHADS-VASc score ≥2) results in an almost four-fold increase in the diagnosis of AF over the course of a year at a cost of ≈€9000 per AF diagnosis
- Such an approach appears highly acceptable to this patient population
- Whilst these data suggest that this strategy has the potential to reduce the risk of stroke and systemic embolism, the full clinical impact and cost-effectiveness requires further evaluation in a larger, prospective outcome trial.

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Kathie Wareham, Matthew Hanney, Dr G. Davies, Dr C. Johns, Dr D. Owen, Swansea JCRF research team
Francis White, Art Akamoto (AliveCor inc)

Circulation

ORIGINAL RESEARCH ARTICLE

Assessment of Remote Heart Rhythm Sampling Using the AliveCor Heart Monitor to Screen for Atrial Fibrillation: The REHEARSE-AF Study

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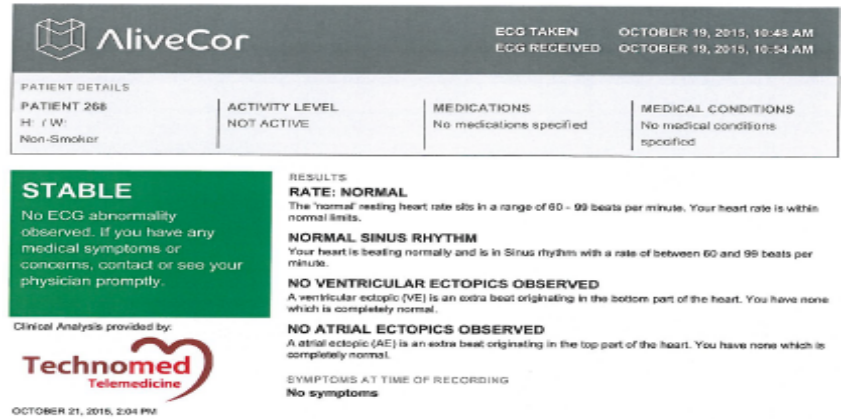
ECG Analysis



AliveCor

ECG TAKEN OCTOBER 19, 2015, 10:48 AM
ECG RECEIVED OCTOBER 19, 2015, 10:54 AM

PATIENT DETAILS

PATIENT 268	ACTIVITY LEVEL	MEDICATIONS	MEDICAL CONDITIONS
H: / W:	NOT ACTIVE	No medications specified	No medical conditions specified
Non-Smoker			

STABLE

No ECG abnormality observed. If you have any medical symptoms or concerns, contact or see your physician promptly.

Clinical Analysis provided by:

Technomed Telemedicine

OCTOBER 21, 2015, 2:04 PM

RESULTS

RATE: NORMAL
The 'normal' resting heart rate sits in a range of 60 - 99 beats per minute. Your heart rate is within normal limits.

NORMAL SINUS RHYTHM
Your heart is beating normally and is in Sinus rhythm with a rate of between 60 and 99 beats per minute.

NO VENTRICULAR ECTOPICS OBSERVED
A ventricular ectopic (VE) is an extra beat originating in the bottom part of the heart. You have none which is completely normal.

NO ATRIAL ECTOPICS OBSERVED
A atrial ectopic (AE) is an extra beat originating in the top part of the heart. You have none which is completely normal.

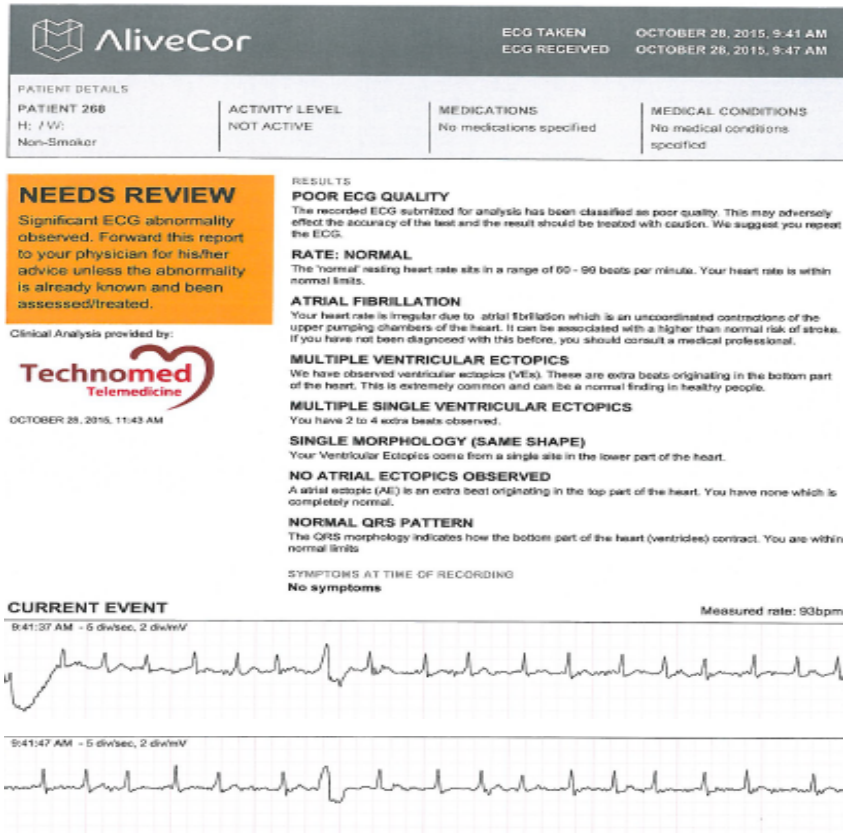
SYMPTOMS AT TIME OF RECORDING
No symptoms

CURRENT EVENT

Measured rate: 64bpm

10:48:38 AM - 5 div/sec, 2 div/mV

10:48:46 AM - 5 div/sec, 2 div/mV



AliveCor

ECG TAKEN OCTOBER 28, 2015, 9:41 AM
ECG RECEIVED OCTOBER 28, 2015, 9:47 AM

PATIENT DETAILS

PATIENT 268	ACTIVITY LEVEL	MEDICATIONS	MEDICAL CONDITIONS
H: / W:	NOT ACTIVE	No medications specified	No medical conditions specified
Non-Smoker			

NEEDS REVIEW

Significant ECG abnormality observed. Forward this report to your physician for his/her advice unless the abnormality is already known and been assessed/treated.

Clinical Analysis provided by:

Technomed Telemedicine

OCTOBER 28, 2015, 11:43 AM

RESULTS

POOR ECG QUALITY
The recorded ECG submitted for analysis has been classified as poor quality. This may adversely effect the accuracy of the test and the result should be treated with caution. We suggest you repeat the ECG.

RATE: NORMAL
The 'normal' resting heart rate sits in a range of 60 - 99 beats per minute. Your heart rate is within normal limits.

ATRIAL FIBRILLATION
Your heart rate is irregular due to atrial fibrillation which is an uncoordinated contractions of the upper pumping chambers of the heart. It can be associated with a higher than normal risk of stroke. If you have not been diagnosed with this before, you should consult a medical professional.

MULTIPLE VENTRICULAR ECTOPICS
We have observed ventricular ectopics (VEs). These are extra beats originating in the bottom part of the heart. This is extremely common and can be a normal finding in healthy people.

MULTIPLE SINGLE VENTRICULAR ECTOPICS
You have 2 to 4 extra beats observed.

SINGLE MORPHOLOGY (SAME SHAPE)
Your Ventricular Ectopics come from a single site in the lower part of the heart.

NO ATRIAL ECTOPICS OBSERVED
A atrial ectopic (AE) is an extra beat originating in the top part of the heart. You have none which is completely normal.

NORMAL QRS PATTERN
The QRS morphology indicates how the bottom part of the heart (ventricles) contract. You are within normal limits

SYMPTOMS AT TIME OF RECORDING
No symptoms

CURRENT EVENT

Measured rate: 93bpm

9:41:37 AM - 5 div/sec, 2 div/mV

9:41:47 AM - 5 div/sec, 2 div/mV

Health Economic Evaluation

- Costs estimated from the perspective of the UK NHS and personal social services (NICE 2011[1])
- Utilised relevant clinical information logged as part of the research investigation, together with appropriate published unit costs([2-4])
- Costs were determined according to how the care would be delivered as per iECG protocol in routine practice

1. NICE:2011. Retrieved from https://www.nice.org.uk/Media/Default/About/what-we-do/Into-practice/Costing_Manual_update_050811.pdf. Accessed July 2017
2. Curtis L and Burns A. Retrieved from http://www.pssru.ac.uk/project-pages/unit-costs/2015/. Accessed July 2017
3. Curtis L and Burns A. Retrieved from http://www.pssru.ac.uk/project-pages/unit-costs/2016/index.php. Accessed July 2017
4. Department of Health. NHS Reference Costs 2015/2016 (Microsoft Excel spreadsheet). 2016. Retrieved from https://www.gov.uk/government/publications/nhs-reference-costs-collection-guidance-for-2015-to-2016. Accessed July 2017

AF Screening Methods

- Pulse Palpation*
- Modified BP monitors*
- Photoplethysmography*
- Conventional ECG recording
- Handheld Single Lead ECG Monitors

** Require ECG validation*