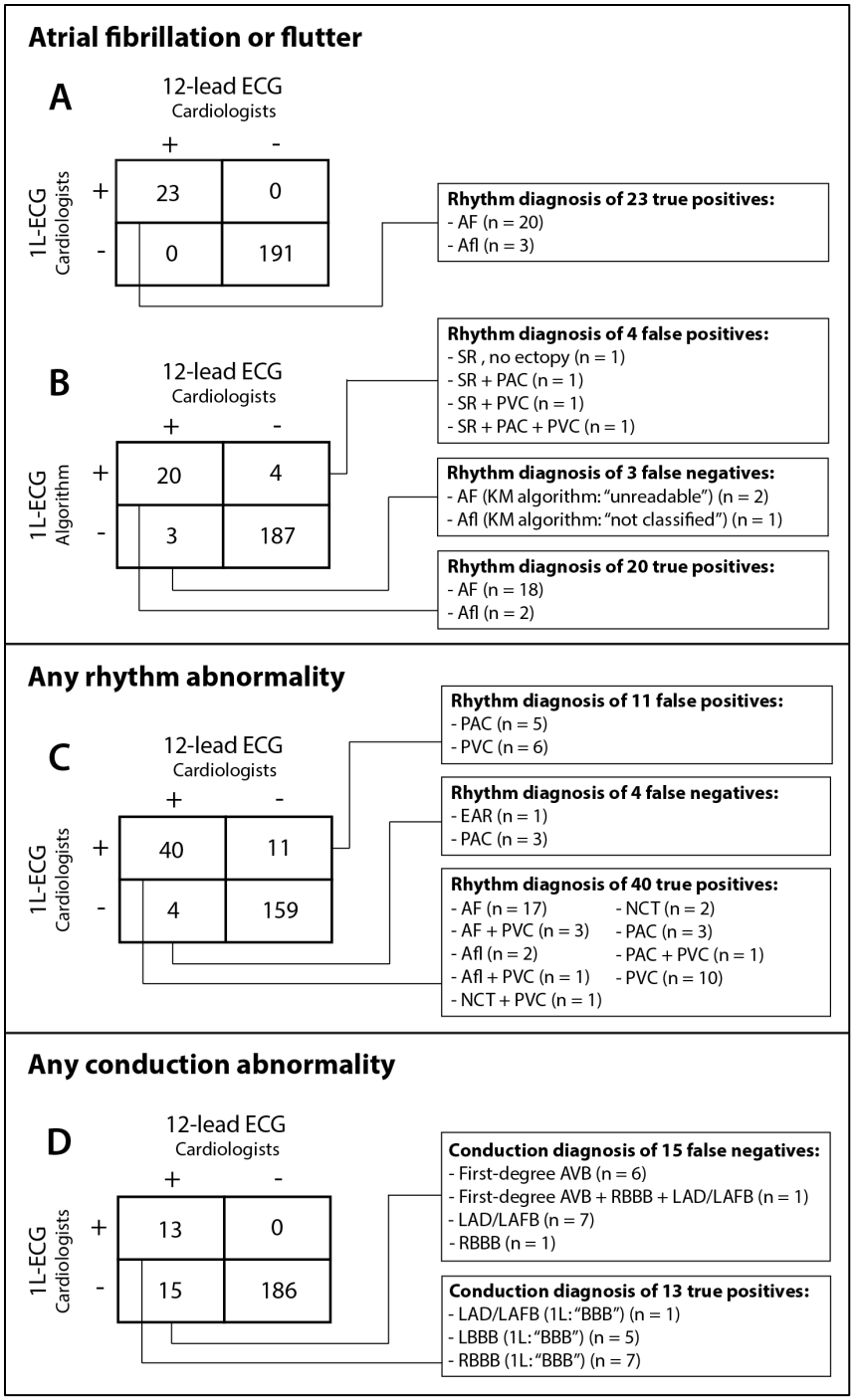
Supplemental material for

Himmelreich JC, Karregat EP, Lucassen WA, et al. Diagnostic accuracy of a smartphone-operated, single-lead electrocardiography device for detection of rhythm and conduction abnormalities in primary care. *Ann Fam Med.* 2019;17(5):403-411.

Supplemental figures

Supplemental Figure 1. 2x2 contingency tables of the primary and secondary analyses (n = 214)

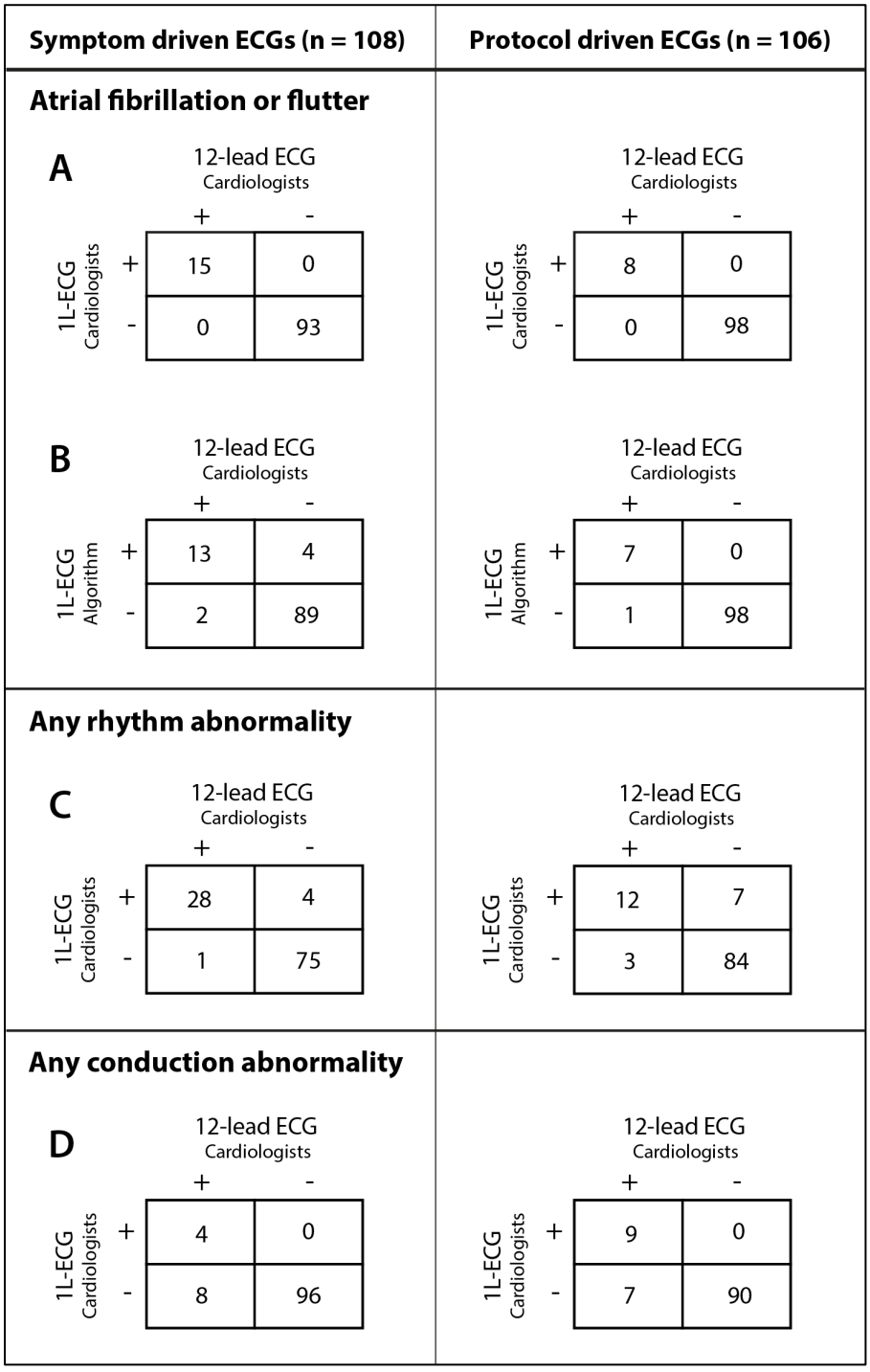


A: primary analysis on AF/Afl, the 1L-ECG as assessed by cardiologists versus 12-lead ECG; B: primary analysis on AF/Afl, the 1L-ECG as assessed by the smartphone algorithm versus 12-lead ECG; C: secondary analysis on any rhythm abnormality, the 1L-ECG as assessed by cardiologists versus 12-lead

ECG; D: secondary analysis on any conduction abnormality, the 1L-ECG as assessed by cardiologists versus 12-lead ECG.

1L, single-lead; AF, atrial fibrillation ; Afl, atrial flutter; AVB, atrioventricular block; BBB, bundle branch block; EAR, ectopic atrial rhythm; ECG, electrocardiogram; LAD/LAFB, left axis deviation and/or left anterior fascicular block; LBBB, left bundle branch block; NCT, narrow complex tachycardia; PAC, premature atrial complex; PVC, premature ventricular complex; RBBB, right bundle branch block; SR, sinus rhythm.

Supplemental Figure 2. Diagnostic accuracy of the KardiaMobile single-lead ECG: 2x2 contingency tables of the stratified analysis according to indication for ECG



A: primary analysis on AF/Afl, the 1L-ECG as assessed by cardiologists versus 12-lead ECG; B: primary analysis on AF/Afl, the 1L-ECG as assessed by the smartphone algorithm versus 12-lead ECG; C: secondary analysis on any rhythm abnormality, the 1L-ECG as assessed by cardiologists versus 12-lead ECG; D: secondary analysis on any conduction abnormality, the 1L-ECG as assessed by cardiologists versus 12-lead ECG.

1L, single-lead; ACA, any conduction abnormality; AF, atrial fibrillation ; Afl, atrial flutter; ARA, any rhythm abnormality; ECG, electrocardiogram; KM, KardiaMobile.

Supplemental Tables

Supplemental Table 1. Diagnostic accuracy measures of the interpretation of the single-lead ECG by cardiologists or the smartphone algorithm using 12-lead ECG as reference standard: stratified analysis according to indication for ECG

Outcome Assessor	Sensitivity (95%CI)	Specificity (95%CI)	LR+ (95%CI)	LR- (95%CI)	PPV (95%CI)	NPV (95%CI)
Symptom driven ECGs (n = 108)						
Atrial fibrillation or flutter						
Cardiologists	100% (78.2-100)	100% (96.1-100)	∞*	0**	100%#	100%#
Smartphone algorithm	86.7% (59.4-98.3)	95.7% (89.4-98.8)	20.2 (7.6-53.6)	0.14 (0.04-0.51)	76.5% (55.0-89.6)	97.8% (92.5-99.4)
Any rhythm abnormality						
Cardiologists	96.6% (82.2-99.9)	94.9% (87.5-98.6)	19.1 (7.3-49.7)	0.04 (0.01-0.25)	87.5% (72.9-94.8)	98.7% (91.6-99.8)
Any conduction abnormality						
Cardiologists	33.3% (9.9-65.1)	100% (96.2-100)	∞*	0.67 (0.45-0.99)	100%#	92.3% (88.9-94.7)
Protocol driven ECGs (n = 106)						
Atrial fibrillation or flutter						
Cardiologists	100% (63.1-100)	100% (96.3-100)	∞*	0**	100%#	100%#

Smartphone algorithm	87.5% (47.4-99.7)	100% (96.3-100)	∞*	0.12 (0.02-0.78)	100%[#]	99.0% (94.0-99.8)
Any rhythm abnormality						
Cardiologists	80.0% (51.9-95.7)	92.3% (84.8-96.9)	10.4 (4.9-22.1)	0.22 (0.08-0.60)	63.2% (44.6-78.5)	96.6% (91.0-98.7)
Any conduction abnormality						
Cardiologists	56.3% (29.9-80.3)	100% (96.0-100)	∞*	0.44 (0.25-0.76)	100%[#]	92.8% (88.1-95.7)

LR+, positive likelihood ratio; LR-, negative likelihood ratio; N/A, not applicable; NPV, negative predictive value; PPV, positive predicting value; 95%CI, 95% confidence interval. *, LR+ is infinite and 95%CI is not applicable when specificity = 100%(14, 15); **, LR- is 0 and 95%CI is not applicable when sensitivity = 100%(14, 15); #, 95%CI is not applicable when PPV or NPV = 100%(14, 16).

Supplemental Table 2. Diagnostic accuracy of the AF detection smartphone algorithm versus 12-lead ECG: sensitivity analysis including only patients with non-truncated 1L-ECG recordings (n = 208)

Assessor	Sensitivity (95%CI)	Specificity (95%CI)	LR+ (95%CI)	LR- (95%CI)	PPV (95% CI)	NPV (95%CI)
Smartphone algorithm	87.0% (66.4-97.2)	97.8% (94.6-99.4)	40.2 (15.1-107.4)	0.13 (0.05-0.38)	83.3% (65.2-93.0)	98.4% (95.5-99.4)

LR+, positive likelihood ratio; LR-, negative likelihood ratio; N/A, not applicable; NPV, negative predictive value; PPV, positive predicting value; 95%CI, 95% confidence interval.

Supplemental Table 3. Characteristics of previous studies that reported sensitivity and specificity of the KM 1L-ECG for rhythm and/or conduction abnormalities

Study	Population	Outcome	n	Reference standard	Assessment of reference by:		
					ALG	C/EP	PCP
Brasier 2018(1)	In-house patients with presumed AF and matched controls in SR	AF	408	Visual assessment of the 1L-ECG	x	x	
Chan 2016(2)	Patients with hypertension, DM or age ≥65 years	AF	1,013	Visual assessment of the 1L-ECG	x	x	
Chan 2017(3)	Patients ≥65 years with hypertension or DM attending an outpatient clinic	AF	2,052	Visual assessment of the 1L-ECG	x	x	
Desteghe 2017(4)	Hospitalized patients at cardiology or geriatric wards	AF	378	6- or 12-lead ECG immediately prior to 1L-ECG	x	x	
Haberman 2015(5)	Healthy young adults, elite athletes and cardiology clinic patients	AF/Afl, AVB, BBB	381	12-lead ECG immediately after 1L-ECG	x	x	
Koshy 2018(6)	Patients before and after elective cardioversion	AF/Afl	51	12-lead ECG immediately prior to 1L-ECG	x	x	x
Lau 2013(7)	Known AF and non-AF patients	AF	204	12-lead ECG max 6 hours before 1L-ECG	x	x	
Lowres 2014(8)	All people aged ≥65 years entering a pharmacy	AF	996	Visual assessment of the 1L-ECG	x	x	
Lowres	Patients with postoperative AF	AF	42	Visual assessment of the 1L-ECG	x	x	

2016(9)	following cardiac surgery						
Orchard 2016(10)	People aged ≥65 years attending flu vaccination	AF	915	Visual assessment of the 1L-ECG	x	x	
Tarakji 2015(11)	Patients with AF undergoing ablation who had iPhones	AF/Afl	55	Simultaneous TTM		x	
William 2018(12)	AF patients who were admitted for antiarrhythmic drug initiation	AF	52	12-lead ECG immediately prior to 1L-ECG	x	x	
Williams 2015(13)	Outpatients known to be in AF or SR	AF	95	Simultaneous 12-lead ECG		x	

AF, atrial fibrillation; Afl, atrial flutter; ALG, smartphone algorithm; AVB, atrioventricular block; BBB, bundle branch block; C/EP, cardiologist and/or electrophysiologist; DM, diabetes mellitus; ECG, electrocardiogram; PCP, primary care physician; SR, sinus rhythm; TTM, transtelephonic monitor; 1L, single-lead.

Supplemental Table 4. Outcomes of previous studies that reported sensitivity and specificity of the KM 1L-ECG for rhythm and/or conduction abnormalities

Study	Mode of Assessment	Reference standard	Outcome					
			AF		AVB		BBB	
			Sensitivity	Specificity	Sensitivity	Specificity	Sensitivity	Specificity
Brasier 2018(1)	Visual	-	-	-	-	-	-	-
	Algorithm	1L-ECG	99.6%	97.8%	-	-	-	-
Chan 2016(2)	Visual	-	-	-	-	-	-	-
	Algorithm	1L-ECG	71.4%	99.4%	-	-	-	-
Chan 2017(3)	Visual	-	-	-	-	-	-	-
	Algorithm	1L-ECG	66.7%	99.5%	-	-	-	-
Desteghe 2017(4)	Visual	12L-ECG	96.2%*	95.6%*	-	-	-	-
	Algorithm	12L-ECG	65.9%	97.6%	-	-	-	-
Haberman 2015(5)	Visual	12L-ECG	94.4%	99.4%	77.3%	96.4%	72.4%	94.9%
	Algorithm	-	-	-	-	-	-	-
Koshy 2018(6)	Visual	12L-ECG	87% (C/EP)*	96% (C/EP)*	-	-	-	-
			81% (PCP)*	90% (PCP)*				

	Algorithm	12L-ECG	100%[#]	95%[#]	-	-	-	-
Lau 2013(7)	Visual	12L-ECG	98%*	92%*	-	-	-	-
	Algorithm	12L-ECG	98%	97%	-	-	-	-
Lowres 2014(8)	Visual	-	-	-	-	-	-	-
	Algorithm	1L-ECG	98.5%	91.4%	-	-	-	-
Lowres 2016(9)	Visual	-	-	-	-	-	-	-
	Algorithm	1L-ECG	94.6%	92.9%	-	-	-	-
Orchard 2016(10)	Visual	-	-	-	-	-	-	-
	Algorithm	1L-ECG	95%	99%	-	-	-	-
Tarakji 2015(11)	Visual	TTM	97%	100%	-	-	-	-
	Algorithm	-	-	-	-	-	-	-
William 2018(12)	Visual	12L-ECG	100%	89%	-	-	-	-
	Algorithm	12L-ECG	96.6%	94%	-	-	-	-
Williams 2015(13)	Visual	12L-ECG	91.4%*	81.1%*	-	-	-	-
	Algorithm	-	-	-	-	-	-	-

AF, atrial fibrillation; Afl, atrial flutter; AVB, atrioventricular block; BBB, bundle branch block; C/EP, cardiologist and/or electrophysiologist; ECG, electrocardiogram; PCP, primary care physician; SR, sinus rhythm; TTM, transtelephonic monitor; 1L, single-lead; 12L, 12-lead. * Study reported

separate sensitivity and specificity for multiple individual assessors. Values in this table represent the mean sensitivity and specificity for all assessors reported within the original study; [#] unclassified recordings excluded from analysis by the original study.

Supplemental Methods

Definitions of items scored in all recordings

The cardiologists scored each recording for rhythm (sinus rhythm, atrial fibrillation, atrial flutter, narrow complex (non-sinus) tachycardia, broad complex (non-sinus) tachycardia, ectopic atrial rhythm), presence of ectopic beats (premature atrial or ventricular complexes) and conduction disorders (atrioventricular block defined as PR interval >200ms, bundle branch block defined as QRS duration >120ms, and left axis deviation and/or left anterior fascicular block) according to a scoring template especially designed for this study.

Patients with multiple symptoms and/or comorbidities

In case of multiple symptoms in a symptom driven ECG we used the first reported symptom in the medical record as the index symptom for that patient. When a patient was due to receive a protocol driven ECG, but also reported to have had cardiac symptoms prior to the appointment for ECG, we still counted this ECG as protocol driven since the timing of the ECG was not influenced by the symptoms.

In case of multiple comorbidities in protocol driven ECGs we assessed for which chronic care program the ECG was primarily intended. Since Dutch primary care physicians label all patients who are in the cardiovascular risk management (CVRM) program as 'CVRM patient', we counted the protocol driven ECGs of patients with the CVRM label as such. In case of multiple comorbidities but no CVRM label, we assessed what the stated primary reason was for making the ECG appointment as assessed by documentation of the current and/or previous consultations.

References in appendix

1. Brasier N, Raichle CJ, Dorr M, Becke A, Nohturfft V, Weber S, et al. Detection of atrial fibrillation with a smartphone camera: first prospective, international, two-centre, clinical validation study (DETECT AF PRO). Europace. 2018.

2. Chan PH, Wong CK, Poh YC, Pun L, Leung WW, Wong YF, et al. Diagnostic Performance of a Smartphone-Based Photoplethysmographic Application for Atrial Fibrillation Screening in a Primary Care Setting. J Am Heart Assoc. 2016;5(7).

3. Chan PH, Wong CK, Pun L, Wong YF, Wong MM, Chu DW, et al. Head-to-Head Comparison of the AliveCor Heart Monitor and Microlife WatchBP Office AFIB for Atrial Fibrillation Screening in a Primary Care Setting. Circulation. 2017;135(1):110-2.

4. Desteghe L, Raymaekers Z, Lutin M, Vijgen J, Dilling-Boer D, Koopman P, et al. Performance of handheld electrocardiogram devices to detect atrial fibrillation in a cardiology and geriatric ward setting. Europace. 2017;19(1):29-39.

5. Haberman ZC, Jahn RT, Bose R, Tun H, Shinbane JS, Doshi RN, et al. Wireless Smartphone ECG Enables Large-Scale Screening in Diverse Populations. J Cardiovasc Electrophysiol. 2015;26(5):520-6.

6. Koshy AN, Sajeev JK, Negishi K, Wong MC, Pham CB, Cooray SP, et al. Accuracy of blinded clinician interpretation of single-lead smartphone electrocardiograms and a proposed clinical workflow. Am Heart J. 2018.

7. Lau JK, Lowres N, Neubeck L, Brieger DB, Sy RW, Galloway CD, et al. iPhone ECG application for community screening to detect silent atrial fibrillation: a novel technology to prevent stroke. Int J Cardiol. 2013;165(1):193-4.

8. Lowres N, Neubeck L, Salkeld G, Krass I, McLachlan AJ, Redfern J, et al. Feasibility and cost-effectiveness of stroke prevention through community screening for atrial fibrillation using iPhone ECG in pharmacies. The SEARCH-AF study. Thromb Haemost. 2014;111(6):1167-76.

9. Lowres N, Mulcahy G, Gallagher R, Ben Freedman S, Marshman D, Kirkness A, et al. Self-monitoring for atrial fibrillation recurrence in the discharge period post-cardiac surgery using an iPhone electrocardiogram. Eur J Cardiothorac Surg. 2016;50(1):44-51.

10. Orchard J, Lowres N, Freedman SB, Ladak L, Lee W, Zwar N, et al. Screening for atrial fibrillation during influenza vaccinations by primary care nurses using a smartphone electrocardiograph (iECG): A feasibility study. Eur J Prev Cardiol. 2016;23(2 suppl):13-20.

11. Tarakji KG, Wazni OM, Callahan T, Kanj M, Hakim AH, Wolski K, et al. Using a novel wireless system for monitoring patients after the atrial fibrillation ablation procedure: The iTransmit study. Heart Rhythm. 2015;12(3):554-9.

12. William AD, Kanbour M, Callahan T, Bhargava M, Varma N, Rickard J, et al. Assessing the accuracy of an automated atrial fibrillation detection algorithm using smartphone technology: The iREAD Study. Heart Rhythm. 2018.

13. Williams J, Pearce K, Benett I. The effectiveness of a mobile ECG device in identifying AF: sensitivity, specificity and predictive value. Br J Cardiol 2015;22:70-2.

14. MedCalc Statistical Software version 18.10.2: MedCalc Software, Ostend, Belgium; 2018 [Available from: https://www.medcalc.org/calc/diagnostic_test.php, last accessed 05 Nov 2018.

15. Gardner IA, Greiner M. Receiver-operating characteristic curves and likelihood ratios: improvements over traditional methods for the evaluation and application of veterinary clinical pathology tests. Vet Clin Pathol. 2006;35(1):8-17.

16. Mercaldo ND, Lau KF, Zhou XH. Confidence intervals for predictive values with an emphasis to case-control studies. Stat Med. 2007;26(10):2170-83.

Abbreviations in appendix:

1L = single-lead;

12L = twelve-lead;

ACA = any conduction abnormality, includes AVB; BBB; LAD/LAFB; LBBB; RBBB;

AF = atrial fibrillation;

Afl = atrial flutter;

ALG = AF detection algorithm;

ARA = any rhythm abnormality**,** includes AF; Afl; BCT; EAR; NCT; PAC; PVC;

AVB = atrioventricular block

BBB = bundle branch block;

BCT = broad complex (non-sinus) tachycardia

C/EP = cardiologist or electrophysiologist;

DM = diabetes mellitus;

EAR = ectopic atrial rhythm;

ECG = electrocardiogram;

ELR = external loop recorder;

KM = KardiaMobile;

LAD/LAFB = left axis deviation and/or left anterior fascicular block;

LBBB = left bundle branch block;

N/A = not applicable;

NCT = narrow complex (non-sinus) tachycardia;

PAC = premature atrial complex;

PCP = primary care physician;

PVC = premature ventricular complex;

RBBB = right bundle branch block;

SR = sinus rhythm;

TTM = transtelephonic monitor;