TEMPUS

Instructions for Use

Tempus ECG-AF

Test: Tempus ECG-AF

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INDICATIONS FOR USE

Tempus ECG-AF is intended for use to analyze recordings of 12-lead ECG devices and detect signs associated with a patient experiencing atrial fibrillation and/or atrial flutter (collectively referred to as AF) within the next 12 months. It is for use on resting 12-lead ECG recordings collected at a healthcare facility from patients:

- 65 years of age or older,
- without pre-existing or concurrent documentation of atrial fibrillation and/or atrial flutter,
- who do not have a pacemaker or implantable cardioverter defibrillator, and
- who did not have cardiac surgery within the preceding 30 days.

Performance of repeated testing of the same patient over time has not been evaluated and results SHOULD NOT be used for patient monitoring.

Tempus ECG-AF only analyzes ECG data. Results should be interpreted in conjunction with other diagnostic information, including the patient's original ECG recordings and other tests, as well as the patient's symptoms and clinical history. Tempus ECG-AF is not for use in patients with a history of AF, unless the AF occurred after a cardiac surgery procedure and resolved within 30 days of the procedure. It is not for use to assess risk of occurrence of AF related to cardiac surgery.

Results do not describe a person's overall risk of experiencing AF or serve as the sole basis for diagnosis of AF, and should not be used as the basis for treatment of AF.

Results are not intended to rule-out AF or the need for follow-up.

INTERPRETATION OF RESULTS

RESULT: INCREASED RISK

Interpretation

This result indicates the patient is at increased risk of experiencing new onset AF within the 12 months following the analyzed ECG tracing.

This result does not represent an AF diagnosis.

Next Steps

In combination with other clinical information, consider the need for follow-up to detect AF.

Do not initiate any AF treatments, including use of anticoagulant medication, based on this result.

RESULT: NO INCREASED RISK

Interpretation

This result indicates the patient is not at increased risk of experiencing new onset AF within the 12 months following the analyzed ECG tracing.

This result does not rule out current or future AF.

Next Steps

Continue to evaluate for AF in accordance with current medical practice standards.

RESULT: UNCLASSIFIABLE

Interpretation

The provided ECG tracing could not be analyzed based on characteristics of the tracing and/or associated patient data.

Next Steps

Continue to evaluate for AF in accordance with current medical practice standards.

GENERAL WARNINGS AND PRECAUTIONS

Tempus ECG-AF has not been evaluated in and **SHOULD NOT** be used for:

- **Patients younger than 65 years of age**
- **Patients with pre-existing or concurrent documentation of atrial fibrillation and/or atrial flutter**
- **Patients with a pacemaker or implantable cardioverter defibrillator**
- **Patients who have had cardiac surgery within the preceding 30 days**

Tempus ECG-AF should not be used for patient monitoring (e.g., to track changes in patient status in response to medication or other therapy).

Results do not represent a diagnosis of AF.

Results should not be used as the basis for invasive monitoring, such as with an implantable loop recorder.

Results should not be used to direct any therapy against AF itself, including anticoagulation therapy.

Tempus ECG-AF should not be used for repeated testing of the same patient within a 12 month period.

FOLLOW-UP

Increased Risk Result

Clinicians should consider the following for patients receiving an "increased risk" result:

- More frequent follow-up
- Close attention to AF symptoms such as palpitations, shortness of breath, lightheadedness
- Additional electrocardiogram testing or non-invasive cardiac monitoring that is deemed clinically indicated

An 'increased risk' result should not be used as the basis for invasive monitoring, such as with an implantable loop recorder.

No Increased Risk or Unclassifiable Result

Clinicians should continue to follow these patients for signs and symptoms of atrial fibrillation per the standard of care, including:

- Clinically indicated electrocardiogram testing
- If there is a suspicion of AF based on symptoms, risk factors, or clinical signs, additional monitoring for AF should continue to be ordered

RESULTS DESCRIPTION

AF Risk Results

- Results of the device are reported as "increased risk" or "no increased risk" to indicate the risk of a patient experiencing new onset AF within the 12 months following the analyzed ECG tracing.
- Results should be considered in accordance with the established performance of the test for predicting new onset AF in the 12 months following an ECG, as described in the *Model Training and Performance Testing* section.
- Any decisions related to patient care should be based on the independent judgment of the treating clinical provider and should take into account all information related to the patient, including the patient's original ECG recordings, symptoms, clinical history, and any other relevant tests.

An "increased risk" result should be evaluated in conjunction with other available clinical information for that patient to help inform whether to conduct further diagnostic follow-up. Typical diagnostic follow-up testing could include non-invasive ECG monitoring to detect previously undiagnosed AF that is deemed clinically indicated. Implantable recorders or any cardiac monitors that require a surgical procedure, such as an implantable loop recorder, should not be considered.

Results do not establish a diagnosis of AF at the time of the test and do not mean that AF will definitely present within the next 12 months or at any future time. "Increased risk" results should not be used as a criterion for treatment with any medications, including anticoagulants.

A "no increased risk" result does not rule out current AF or mean that a patient will not develop AF within the next 12 months or at any future time. Patients should continue to be evaluated in accordance with current medical practice standards using all available clinical information, including consideration of known risk factors for AF.

Unclassifiable Test Result

An "unclassifiable" result indicates that input data do not meet input data specifications; see *Specifications* section. Patients should continue to be evaluated in accordance with current medical practice standards using all available clinical information, including consideration of known risk factors for AF.

A result of "unclassifiable" will be generated if the input data, including the ECG tracing, fails any input data checks. The device will return an "unclassifiable" result if:

- the trace value from any lead does not change within a specified tolerance for a period of 1 second or longer
- the trace value from any lead exceeds a specified voltage threshold
- the tracing has an incompatible ECG sampling frequency
- the tracing has incompatible ECG lead resolution values
- the patient's age at the time the ECG was taken cannot be determined, or the patient was less than 65 years old at the time the ECG was taken
- the tracing is from an ECG instrument from an incompatible ECG manufacturer

For details on input data requirements, see *Specifications* section.

SPECIFICATIONS

Input Data

The device requires data and metadata from a 10 second 12-lead resting electrocardiogram recording, including:

- **Lead trace data** from the input ECG including Lead I, Lead II, Lead V1, Lead V2, Lead V3, Lead V4, Lead V5, Lead V6, as base64 encoded strings of signed 16-bit integer arrays
- **Sample rate** in Hz as a string that equals "500"
- **Sample count** as a string that equals "5000"
- **Lead amplitude per bit** as a string representing microvolts per bit, greater than 0μV and less than or equal to 5μV
- **Patient sex** as a string of "male", "female", or "unknown"
- **Patient age** in unit values of years, months, weeks, days, or hours, or date of birth and recording acquisition date, with a value greater than or equal to 65 years
- **Manufacturer** of the input ECG as either "GE Healthcare" or "Philips"

The device is only compatible with ECG recordings collected using 'wet' Ag/AgCl electrodes with conductive gel/paste, and using FDA authorized resting 12-lead resting ECGs from GE Medical Systems (e.g., CSYS, MAC2K, MAC35, MAC55 and MAC5K, etc.) and Philips Medical Systems (e.g., PageWriter TC and PageWriter Touch).

Output Data

See *Interpretation of Results* section.

MODEL TRAINING AND PERFORMANCE TESTING

The Tempus ECG-AF algorithm was developed using an extensive dataset of patients and ECGs (the training dataset), and then tested (in a performance study) to establish performance in a set of patients representative of the population in which it is intended to be used.

The training dataset comprised more than half a million patients and over one and a half million ECGs collected from more than 10 distinct hospitals and clinics. This dataset was used to train a machine-learning model via supervised learning. The model was trained to identify patients in whom AF was diagnosed within 12 months after an analyzed ECG, based on ECG data, age, and sex. Demographic characteristics of the training dataset are described in Table 1.

The performance of Tempus ECG-AF in identifying patients who will be diagnosed with new onset AF in the 12 months following an ECG was evaluated in a retrospective study. This study used a real-world dataset of patients from 3 geographically distinct sites with a range of clinically-used ECG machines. Seven models of 12-lead ECG machines were included in the study as providing ECG inputs to the Tempus ECG-AF software. These were: CSYS, MAC2K, MAC35, MAC55 and MAC5K (GE Medical Systems) and PageWriter TC and PageWriter Touch (Philips Medical Systems). No data present in the training dataset were used in the performance study. In the performance study, Tempus ECG-AF was applied to patients meeting inclusion/exclusion criteria who received a 12-lead ECG, comprehensively capturing the intended use population. All patients in the performance study had a clinically acquired ECG, were age 65 or greater at the time of the ECG, did not have a history of AF, did not have a pacemaker or ICD, and did not have cardiac surgery within 30 days prior to the ECG. Demographic characteristics of the performance study are described in Table 1. The AF status of each patient in the 1 year following the ECG was determined by evaluation of their clinical records. Results of "increased risk" or "no increased risk" were generated by Tempus ECG-AF and compared to the AF status to establish device performance.

Table 1. Demographic and Clinical Characteristics of the Training Datasets and Performance Study Populations

PARAMETER	PERFORMANCE STUDY	TRAINING DATASET
N	**4,017**	**1,597,424**
Age		
Mean (SD)	**75.33 (7.16)**	**59.55 (16.64)**
Median	**74.18**	**60.83**
Min/Max	**65.00 / 89.98**	**18.00 / 90.00**
Age groups n (%)		
< 65	**0 (0)**	**949,277 (59)**
[65, 70)	**1,166 (29)**	**181,254 (11)**
[70, 75)	**1,004 (20)**	**160,647 (10)**
[75, 80)	**7,91 (19)**	**131,944 (8)**
≥ 80	**1,056 (26)**	**174,302 (11)**
Sex n (%)		
Female	**2,254 (56)**	**823,040 (52)**
Male	**1,761 (44)**	**774,144 (48)**
Unknown	**2 (<1)**	**240 (<1)**
Race n (%)		
White	**3,281 (82)**	**1,538,164 (96)**
Black	**433 (11)**	**42,294 (3)**
Asian	**120 (3)**	**10,207 (1)**
Other	**141 (4)**	**2,863 (<1)**
Unknown	**42 (1)**	**3,896 (<1)**
Ethnicity n (%)		
Hispanic	**382 (10)**	**39,213 (2)**
Not Hispanic	**3,615 (90)**	**1,432,954 (90)**
Unknown	**20 (<1)**	**125,257 (8)**
CHA_2DS_2VASc* score n (%)		
< 2	**128 (3)**	
≥ 2	**3,889 (97)**	**N/A**
< 4	**1,698 (42)**	
≥ 4	**2,319 (58)**	
Clinical Characteristics n (%)**		
Heart failure	**441 (11)**	
Hypertension	**3,232 (80)**	
Diabetes	**1,341 (33)**	**N/A**
Stroke/TIA/TE	**622 (15)**	
Vascular disease	**1,290 (32)**	
Conduction delay on ECG***	**539 (13)**	
BMI		
[0, 18.5)	**83 (2)**	**21,775 (1)**
[18.5, 24.9)	**899 (22)**	**264,761 (17)**
[25, 29.9)	**1,405 (35)**	**383,579 (24)**
≥ 30	**1,611 (40)**	**592,606 (37)**
Unknown	**19 (<1)**	**334,703 (21)**

**The CHA_2DS_2VASc scoring system is used to estimate stroke risk in patients with AF, CHA_2DS_2VASc scores were not captured in the training dataset*

***Patients may have more than one clinical characteristic and therefore percentages do not sum to 100; clinical characteristics were not captured in the training dataset*

****Conduction delay is considered QRS > 120 msec*

The established performance of Tempus ECG-AF is based on the performance characteristics demonstrated in the performance study, as shown in Tables 2, 3, and 4.

Table 2. Device Performance (Performance Study Dataset)

1-year AF incidence	**6.0%**
Sensitivity *(95% CI)*	**31%** *(25%, 37%)*
Specificity *(95% CI)*	**92%** *(91%, 92%)*
Positive predictive value *(95% CI)*	**19%** *(15%, 23%)*
Negative predictive value *(95% CI)*	**95%** *(95%, 96%)*

Table 3. Confusion matrix (Performance Study Dataset)

		ACTUAL (FROM EHR)		
		AF Positive	**AF Negative**	**Total**
PREDICTED (DEVICE RESULT)	**"Increased risk" (positive)**	**74**	**317**	**391**
	"No increased risk" (negative)	**166**	**3460**	**3626**
	Total	**240**	**3777**	**4017**

Tempus ECG-AF demonstrated a sensitivity of 31% for classifying patients that developed clinically recognized AF in the next 1 year and a specificity of 92% for classifying patients that did not develop clinically recognized AF in the next 1 year. The positive predictive value (PPV) was 19%, meaning that 19 out of every 100 patients classified as "increased risk" developed clinically recognized AF within the next 1 year. The negative predictive value (NPV) was 95%, meaning that 95 out of every 100 patients classified as "no increased risk" did not develop clinically recognized AF within the next 1 year. The 1-year incidence of clinically recognized AF in the performance study was 6.0%.

PPV and NPV can be used to calculate the number needed to screen (NNS), the number of people that need to be tested to identify one patient that will go on to develop clinically recognized AF within the next 1 year. The NNS for Tempus ECG-AF was 7.1, meaning that approximately 7 patients need to be tested with Tempus ECG-AF to identify one patient that will go on to develop clinically recognized AF within the next 1 year.

Table 4. Likelihood Ratios (Performance Study Dataset)

Positive likelihood ratio	**3.67**
Negative likelihood ratio	**0.76**

The Tempus ECG-AF positive likelihood ratio (PLR) was 3.67 and the negative likelihood ratio (NLR) was 0.76. This means that a patient who develops AF within 1 year is 3.67 times more likely to have a device result of "increased risk," compared to a patient who does not develop AF. Conversely, a patient who develops AF within 1 year is 0.76 times as likely (i.e. is 24% less likely) to have a device result showing "no increased risk" compared to a patient who does not go on to develop AF.

The pre and post-test probabilities of AF occurring within the next 1 year, for patients receiving an "increased risk" result, are shown in Table 5, based on the positive likelihood ratio.

Table 5. Pre and Post-Test Probabilities for "Increased Risk" Results*

PRE-TEST PROBABILITY	POST-TEST PROBABILITY
1%	**3.57%**
3%	**10.19%**
6%	**18.98%**
10%	**28.97%**
20%	**47.85%**

**Based on a Positive Likelihood Ratio of 3.67*

TECHNICAL SUPPORT

For technical support or inquiries, please contact the Tempus Cardiology Support team at **support@tempus.com** or by calling **800.739.4137**.