



# *Integrated Management Program Advancing Community Treatment of Atrial Fibrillation (IMPACT-AF) study*

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# Background

- In the 1980s, medical knowledge was estimated to have been doubling every 8 years; by 2020, it is expected to double every 73 days.<sup>1</sup>
  - Medical students graduating in 2020 will have experienced at least four doublings of medical knowledge over the course of their training<sup>1</sup>
- As of 11 October 2018, 5251 journals were indexed on Medline<sup>2</sup>, and 813,598 articles had been cataloged in fiscal year 2017 (Oct-Sep)<sup>3</sup>
  - There were 10 new clinical trials completed each day in 1975, 55 in 1995, and 95 in 2015<sup>4</sup>
- It is impossible for busy clinicians to assimilate this exponential growth in knowledge, let alone assess it critically and optimally apply it
  - Complicating matters, much of what is published today will quickly be out of date

1. Densen P. *Trans Am Climatol Clin Assoc.* 2011;122:48-58; 2. <https://www.ncbi.nlm.nih.gov/nlmcatalog?term=currentlyindexed>;  
3. [https://www.nlm.nih.gov/bsd/stats/cit\\_added.html](https://www.nlm.nih.gov/bsd/stats/cit_added.html); 4. Catillon M. [www.nber.org/aging/valmed/WhitePaper-Catillon10.2017.pdf](http://www.nber.org/aging/valmed/WhitePaper-Catillon10.2017.pdf).



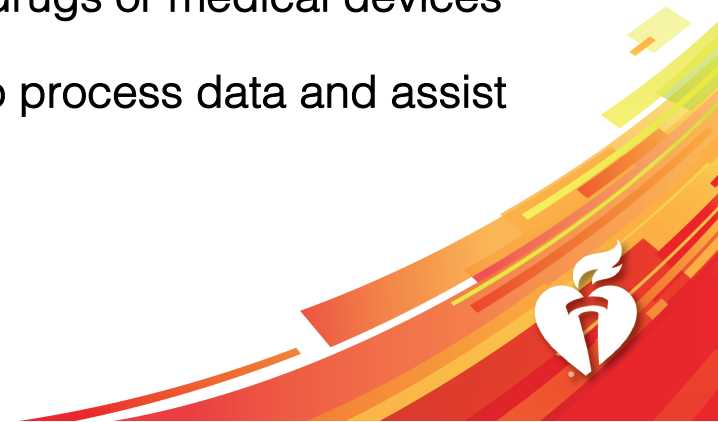
# Background

- Many medical conditions are on the increase, especially those that are age-related, such as AF whose prevalence is projected to grow 2-3 fold by 2050<sup>1-3</sup>
- Specialists are challenged to keep current with specific conditions; generalists, such as primary care physicians, must treat a broad number of disorders
  - A typical primary care doctor must now stay abreast of about 10,000 diseases and syndromes, 3,000 medications, and 1,100 laboratory tests<sup>4</sup>
- Effective point of care decision support in this era of information overload and an ever-changing therapeutic environment has become critical
  - Failure to follow and respond to clinical data and/or keep current with rapidly evolving guidelines can contribute to variation in care and adverse patient outcomes
- There is a need for consistency in patient care and communication
  - *“I find the doctors aren’t on the same page, and they tell you something different.”*  
- Nova Scotia patient living with AF



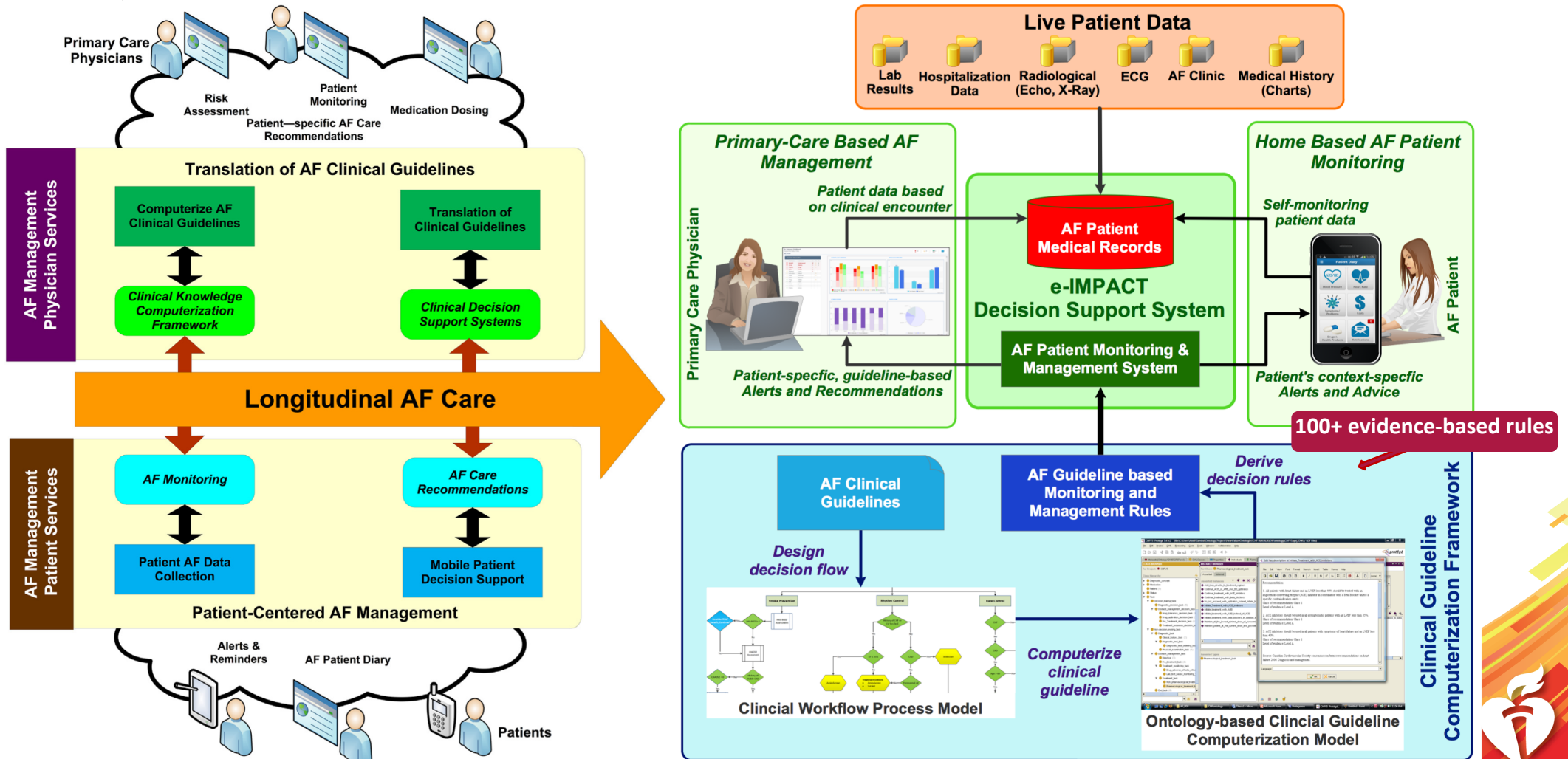
# Rationale

- Clinical Decision Support Systems (CDSS) are intelligent systems that digitize and operationalize evidence-based guidelines, clinical pathways and algorithms to provide personalized, timely and evidence-informed functions<sup>1,2</sup>
  - Specifically, they monitor patient-specific clinical data, proactively identify potential adverse events, and assist physicians by providing diagnostic and therapeutic recommendations<sup>1</sup>
- Such tools are being widely developed and increasingly implemented, yet few have had their clinical efficacy objectively assessed in randomized trials
- Given their potential to influence patient health and health care costs, any decision support tools should be held to the same level of stringent evaluation as drugs or medical devices
- IMPACT-AF assessed the clinical efficacy of a CDSS designed to process data and assist AF management in primary care





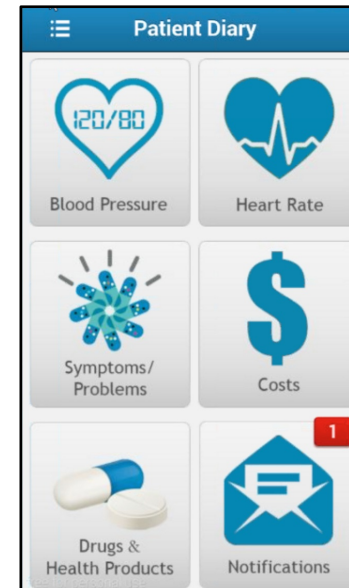
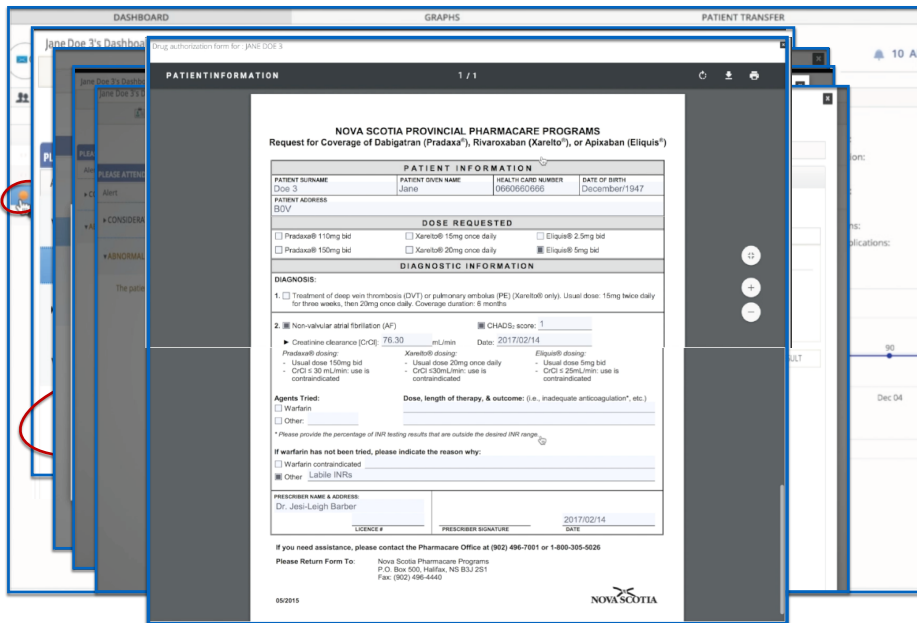
# IMPACT-AF CDSS Functional Overview



COX J, et al. *Am Heart J* 2016;201:149-157, van Woertse W, et al. A mobile and intelligent patient diary for chronic disease self-management. in Sarkar IN, Georgiou A, Mazzoncini de Azevedo Marques P (Eds). *MEDINFO 2015: eHealth-enabled Health. Proceedings of the 15<sup>th</sup> World Congress on Health and Biomedical Informatics* © 2015 IMIA and IOS Press. doi:10.3233/978-1-61499-564-7-118.



# IMPACT-AF CDSS Functional Overview



Physician monitoring system that provides:

- Stroke prevention – auto calculation of risk scores
- Rate/rhythm control guidance
- OAC/NOACs – initiation/dosing/switching
- Perioperative anticoagulation management
- Graphical displays of health trends for A Fib population

Patient self-monitoring system\* that provides:

- Personalized alerts and recommendations
- A Fib management resources
- FAST guidelines (National Stroke Association)
- Enhanced communication regarding care

\*Optional for patients

# IMPACT-AF Trial Design

- Investigator-initiated, prospective, pragmatic, randomized, unblinded, cluster trial
  - Unblinded as there was no benchmark CDSS for comparison and a sham tool with no utility to providers would not have been used
  - Conducted in the Province of Nova Scotia, Canada
    - Single-payer, publicly-funded, universally available health-care system
    - Oldest Canadian population, ethnically homogeneous (6% visible minority), 57% vs. 43% urban-rural split
    - One quaternary care academic hospital providing the majority of provincial continuing medical education
  - Units of randomization were individual primary care providers/group practices
    - Allocated 1:1 to intervention (CDSS use) vs. control (usual care) arms, with randomization additionally stratified by urban vs. rural practice setting
  - Units of analysis were the patients managed by the providers as randomized



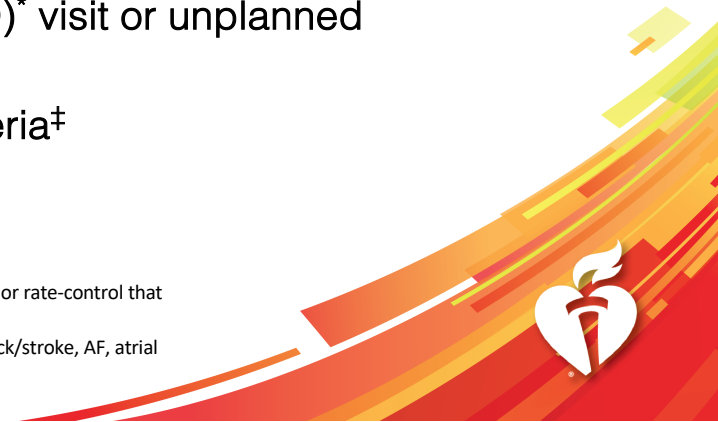
# IMPACT-AF Eligibility Criteria and Outcomes

- Study inclusion criteria
  - Physicians
    - Full time practice and managing adults
    - Access to high speed internet
  - Patients
    - Resident of Nova Scotia 18 years of age or older
    - Have electrocardiographically confirmed AF or documentation of past diagnosis and management
    - Able to provide informed consent
- Study outcomes
  - Primary efficacy: Composite of AF-related emergency department (ED)\* visit or unplanned cardiovascular (CV) hospitalization<sup>†</sup>
  - Primary safety: Major bleeding over 12 months per modified ISTH criteria<sup>‡</sup>

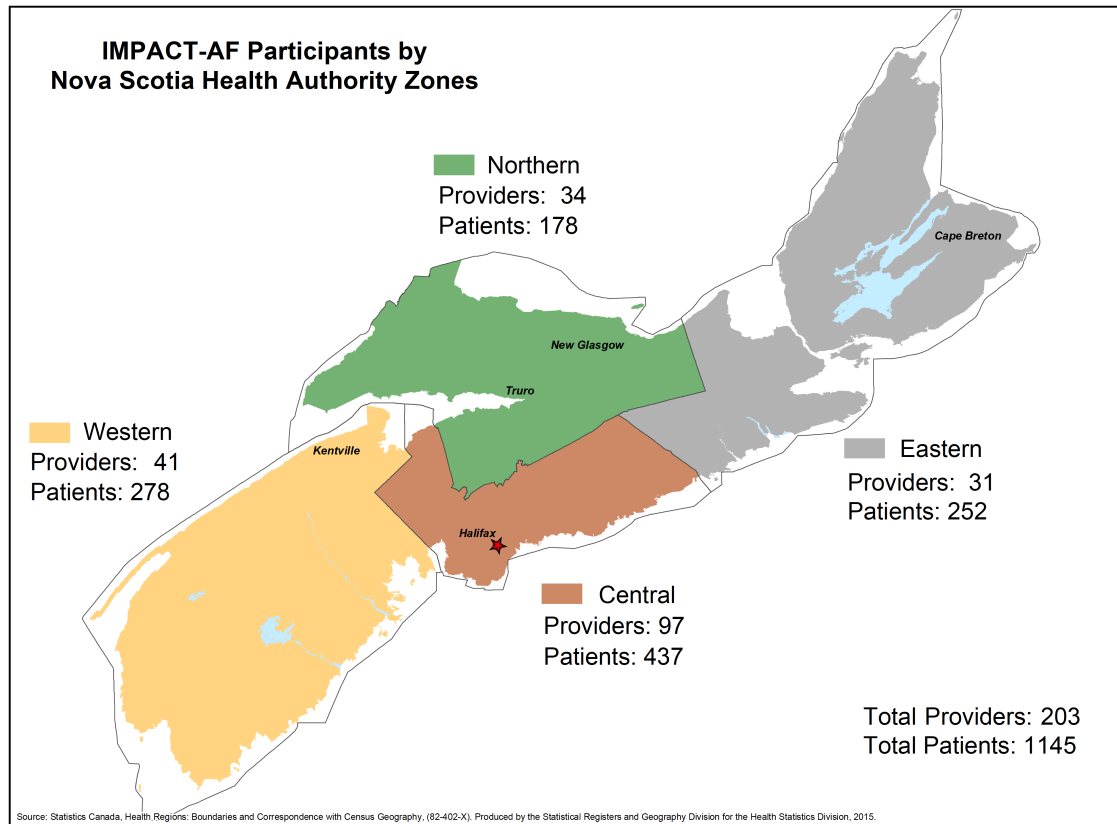
\*Any presentation with palpitations, rapid heart rate, presyncope/syncope, dyspnea, transient chest discomfort, or hemodynamic instability resolving with AF cardioversion or rate-control that does not result in hospitalization

<sup>†</sup> Any unplanned admission with >1 overnight stay in hospital due to one of the following reasons: acute coronary syndrome, presyncope or syncope, transient ischemic attack/stroke, AF, atrial flutter, pulmonary embolism or deep vein thrombosis or systemic embolism, worsening congestive heart failure including pulmonary edema or dyspnea of cardiac origin

<sup>‡</sup> Modified to include emergent need of use of parenteral oral anticoagulant reversal agents other than vitamin K



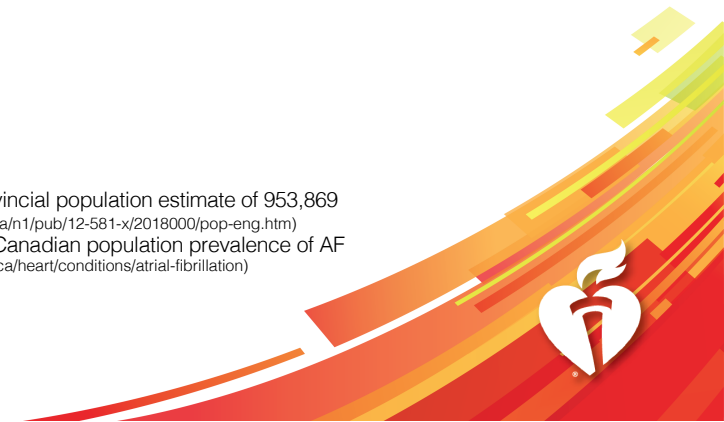
# IMPACT-AF Trial Recruitment



Health Care Zones	Primary Care Providers	
	Total Study Eligible	Total Recruited
Northern	130	34 (26%)
Eastern	145	31 (21%)
Central	378	97 (26%)
Western	174	41 (24%)
Province overall	827	203 (25%)

1145 patients recruited = 12% of all Nova Scotians with AF\*

\*Based on a 2017 provincial population estimate of 953,869 (<https://www150.statcan.gc.ca/n1/pub/12-581-x/2018000/pop-eng.htm>) and an estimated 1% Canadian population prevalence of AF (<https://www.heartandstroke.ca/heart/conditions/atrial-fibrillation>)





# IMPACT-AF Baseline Patient Characteristics

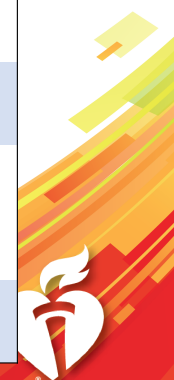
Characteristics	Usual Care	CDSS
Number of Practices Recruited	61	56
Number of Patients Recruited	548	597
Patient age - years		
Mean (SD)	72.1 (9.8)	72.5 (10.1)
Median (Quartiles 1, 3)	73 (66, 79)	73 (66, 80)
Male sex - n [%]	354 [64.6]	343 [57.5]
Rural care location – n [%]	303 [55.3]	322 [53.9]
Stroke Risk - mean [SD]		
CHADS <sub>2</sub>	2.5 [1.6]	2.6 [1.7]
CHA <sub>2</sub> DS <sub>2</sub> -VASc	3.6 [1.8]	3.7 [1.8]
Medical conditions – n [%]		
Congestive heart failure	138 [25.4]	153 [25.9]
Hypertension	419 (77.2)	472 [80.0]
Diabetes	160 [29.5]	167 [28.3]
Prior stroke, transient ischemic attack or systemic embolism	92 [16.9]	117 [19.8]
Vascular disease	195 [35.9]	203 [34.4]
Antithrombotic treatment for those ≥ 65 years or CHA <sub>2</sub> DS <sub>2</sub> ≥ 1 – n [%]	512 [93.4]	559 [93.5]
Aspirin only	39 [7.6]	53 [9.5]
Other antiplatelet only	1 [0.2]	4 [0.7]
Warfarin only	187 [36.5]	196 [35.1]
Non-vitamin K antagonist only	142 [27.7]	188 [33.6]
Any dual/triple antithrombotic therapy	39 [7.6]	53 [9.5]
No treatment for stroke	104 [20.3]	65 [11.6]

# IMPACT-AF Efficacy Outcomes At 12 Months

Outcome (Usual Care is reference)	Usual Care (N=548)		CDSS (N=597)		Hazard Ratio (95% CI)	p-value
	No. of Patients	No. of Events	No. of Patients	No. of Events		
<b>Primary</b>						
AF related ED visits or Unplanned CV hospitalization	71	133	77	112	1.02 (0.73, 1.41)	0.93
<b>Secondary</b>						
AF related ED visits	49	98	51	75	0.98 (0.65, 1.49)	0.92
Unplanned CV hospitalization*	27	35	33	39	1.06 (0.63, 1.77)	0.84
Stroke	3	3	6	6	1.89 (0.44, 8.17)	0.39
Ischemic*	2	2	5	5	0.92 (0.13, 6.50)	0.93
Other*	1	1	1	1	0.92 (0.06, 14.65)	0.95
All-cause mortality†	21	-	28	-	1.19 (0.69, 2.05)	0.54

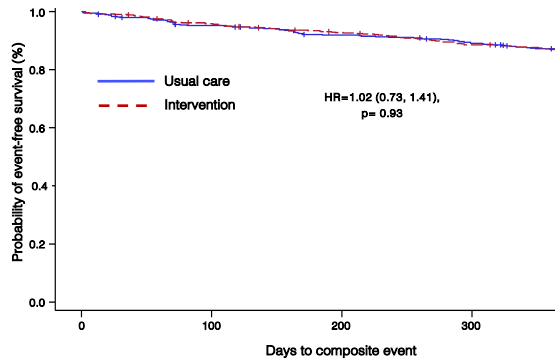
\* Model did not converge

† Logistic regression analysis results = odds ratio rather than hazard ratio

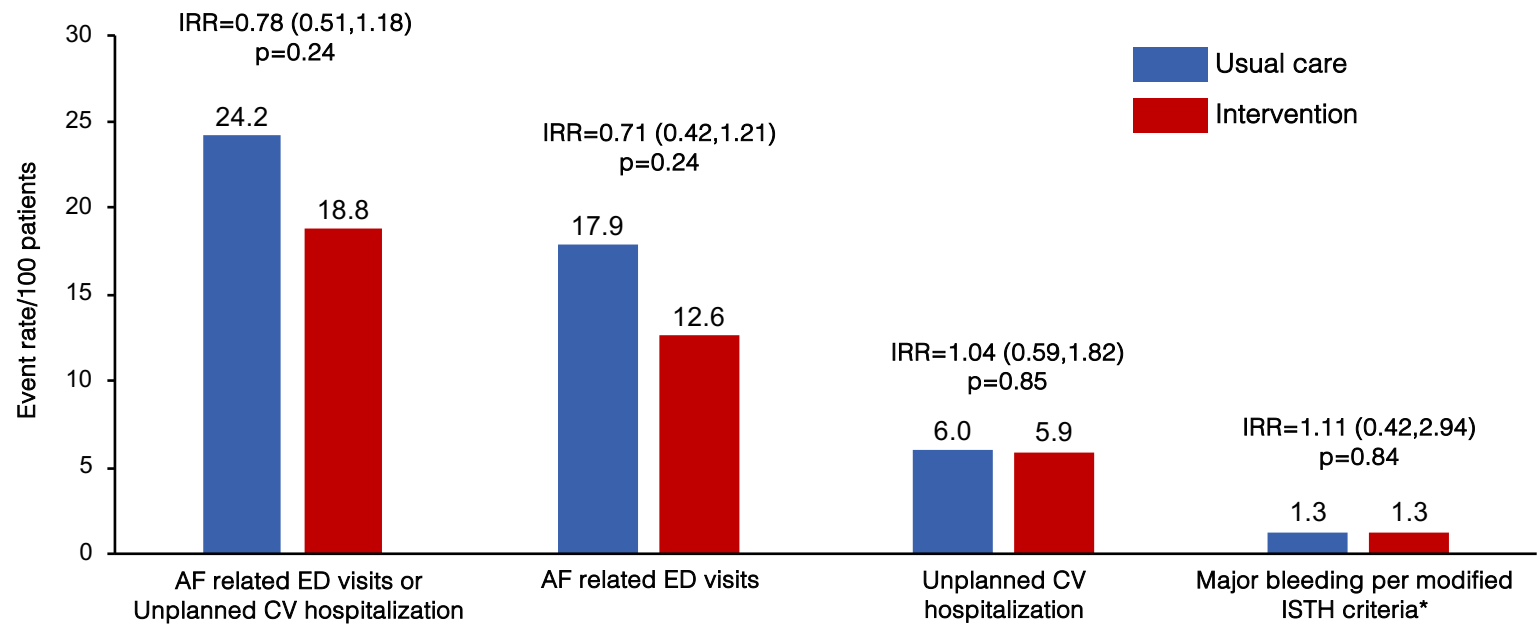


# IMPACT-AF Primary Efficacy Event Rates

Time to first AF-related ED visit or unplanned CV hospitalization



Total number of AF-related ED visit or unplanned CV hospitalization events over 12-months



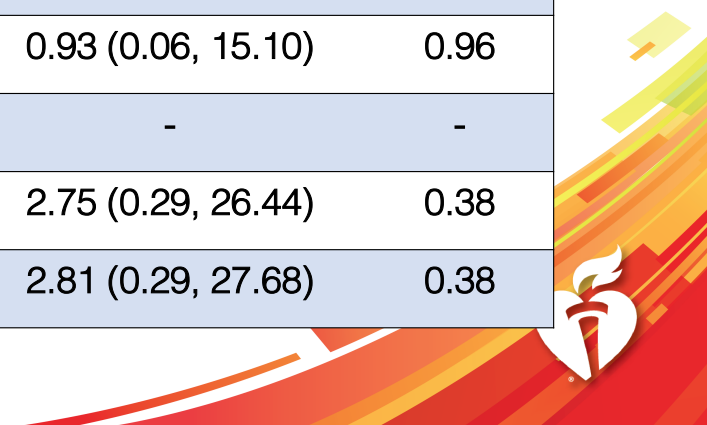
HR=hazard ratio; IRR=incident rate ratio

# IMPACT-AF Safety Outcomes At 12-Months

Outcome (Usual Care is reference)	Usual Care (N=548)		CDSS (N=597)		Hazard Ratio (95% CI)	P-value
	No. of Patients	No. of Events	No. of Patients	No. of Events		
<b>Primary</b>						
Major bleeding per modified ISTH criteria*	7	7	7	8	0.91 (0.32, 2.60)	0.87
<b>Secondary</b>						
Hemoglobin decrease $\geq 2$ g/dl†	4	4	2	2	0.46 (0.08, 2.49)	0.36
Transfusion $\geq 2$ units	1	1	1	1	0.93 (0.06, 15.10)	0.96
Fatal bleeding‡	0	0	2	2	-	-
Intracranial hemorrhage‡	1	1	3	3	2.75 (0.29, 26.44)	0.38
Reversal Agent received	1	1	3	3	2.81 (0.29, 27.68)	0.38

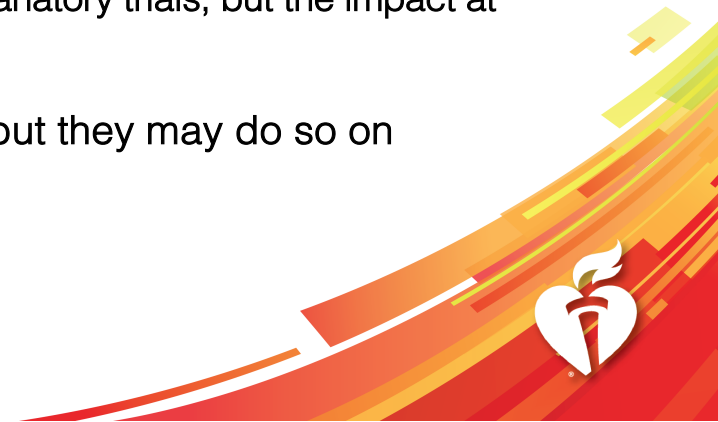
\*Modified to include emergent need of use of parenteral oral anticoagulant reversal agents other than vitamin K

† Model did not converge



# IMPACT-AF Discussion Points

- Plausible reasons why significant benefit was not seen with the CDSS
  - Real-world challenges to any health care technology assessment that even a pragmatic trial design cannot control for
    - The CDSS *suggested* approaches to care, but physicians and patients *could choose* to proceed otherwise
    - Steep user learning curve to effective technology use more difficult than under ideal conditions
  - User interface may have not been sufficiently attractive or user-friendly
    - Graphic designers were not employed, the CDSS was not fully integrated into electronic medical records
  - Study duration was too short to see a potential impact on clinical outcomes
    - Effect estimates for pragmatic trials are usually smaller than is seen in explanatory trials; but the impact at the population level can be very large, particularly on resource utilization
  - Often, CDSS interventions will not show effects on clinical outcomes; but they may do so on processes of care





# IMPACT-AF Conclusions

- IMPACT-AF was unable to show a significant effect on time to AF-related ED visit or unplanned CV hospitalizations for primary care physicians using a computer decision support system vs usual care
- Nonetheless, incident rate ratios suggest the potential for marked reductions in events with such tools, but more and better user training and longer duration of use will be required to confirm this
- An important lesson of the study should be that any health care app or device, let alone a computer decision support system, must be rigorously assessed and ideally via a randomized controlled trial

