HEALTHPALS

Top Performing Atrial Fibrillation Drugs in the US:

An Analysis of the ACC PINNACLE Registry® using the HealthPals CLINT™ Precision Population Health AI Platform

SUMMARY

The opportunity to prevent major cardiovascular events (CVEs) is enormous - 80% of heart attacks and strokes are preventable with appropriate detection and treatment of high risk individuals[1]. However, there is a systemic failure to detect and adhere to guideline-driven treatments that is leading to significant gaps in care for high risk patients. By combining real world patient data and an evidence-based AI engine, we can now illuminate these gaps in care and work with health systems to close them. The first part of this solution is to gain visibility into the magnitude and nature of guideline adherence gaps (care gaps). New evidence is published regularly, and medical societies incorporate this evidence at a deliberate frequency into their treatment guidelines. However, the adoption of guideline-driven medical therapy (GDMT) is painstakingly - and one can argue dangerously - slow, often taking more than 10 years to reach even 50% market adoption.

This whitepaper focuses on the current state of stroke prevention strategies for Atrial Fibrillation (AF), detailing: the general care gaps in anticoagulant utilization, which anticoagulant drugs are most frequently being used to close gaps, and how practices vary geographically in their adherence patterns. A novel, guideline-encoded engine, CLINT™ (Health-Pals, Inc.), is now producing a diverse array of analyses on guideline adherence in the US. HealthPals is an Innovation Collaborator of the American College of Cardiology (ACC) and is using the ACC's NCDR patient registry data to produce the most comprehensive and up-to-date trends in the US clinical treatment landscape.

Key Takeaways

- From July 2017 to June 2018, 22% of new onset AF patients did not receive the proper anticoagulation treatment according to the applicable AF guidelines for that year; for the same AF patients over that period of time, a care gap percent of 15% was observed for statin therapy and 6% for anti-hypertensive therapy. The overall care gap percentage in PINNACLE® for blood glucose lowering medications was 10%.

- In the PINNACLE® data set, Apixaban (Eliquis®) became the second most prescribed anticoagulant in 2016, outpacing Rivaroxaban (Xarelto®), and then surpassing Warfarin (Coumadin®) as the #1 prescribed anticoagulant for Atrial Fibrillation (AF) patients in 2018.

- The two states with the largest percentage of anticoagulant care gaps are all in the Midwest (IL, OH), and the two best performing states are in the Northeast (NY, NH). A possible explanation for this regional variability may be the representation in PINNACLE® of more rural clinics than in the Northeast.
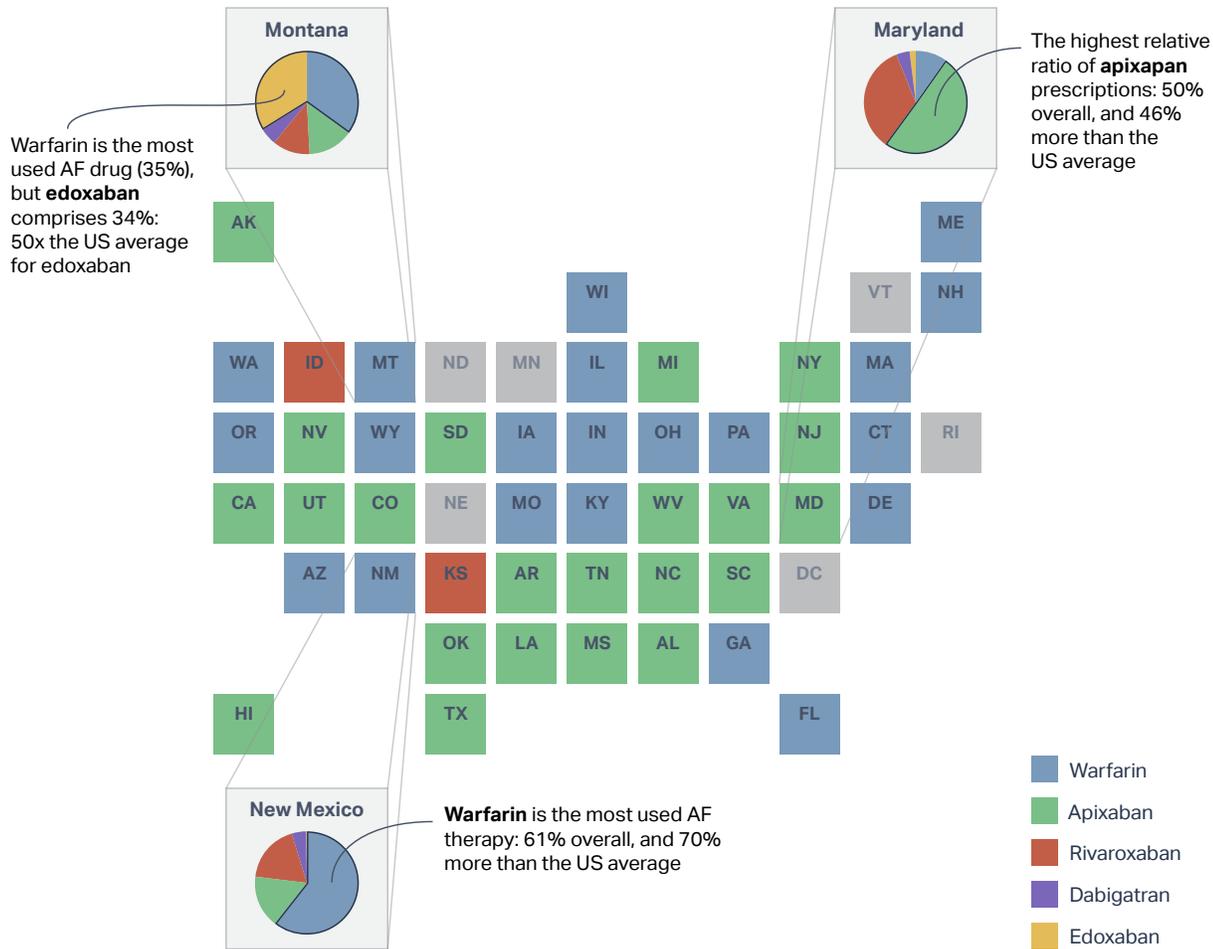
Montana

Warfarin is the most used AF drug (35%), but **edoxaban** comprises 34%: 50x the US average for edoxaban

Maryland

The highest relative ratio of **apixapan** prescriptions: 50% overall, and 46% more than the US average

New Mexico

Warfarin is the most used AF therapy: 61% overall, and 70% more than the US average

- Warfarin
- Apixaban
- Rivaroxaban
- Dabigatran
- Edoxaban

Figure 1: Overview of AF Therapy Strategies by State in 2018

A state-by-state geographic representation of anticoagulant usage in AF patients, broken into the utilization percentage of individual drugs. The overall state color matches that of the largest market share medication. Notably, there is a near-even mix of DOAC-dominant versus coumadin-dominant states currently, with high variability in the breakdown of different DOAC usage percentages within each state.

ADHERENCE OF CARDIOMETABOLIC DRUGS – A BRIEF OVERVIEW

Maintaining adherence to guideline-driven medical practice is increasingly challenging. With nearly 1 million new medical publications annually (Figure 2) and with clinical guidelines being updated regularly with 'new' best practices, medical interventions that were common only 10 years ago are being phased out or significantly modified. Updates to medical guidance are intended to improve clinical outcomes, but as a side effect, physicians are unable to stay up-to-date on the changes.

According to the RAND Corporation, around 50% of all medical decisions across specialties are not evidence-based due to the combination of large volumes of new medical evidence and increased patient load on physicians. When factoring this in with physicians not having enough time to consider the chronic conditions of each patient[2], it isn't surprising to see that an enormous burden of care gaps has accumulated within chronic disease management worldwide.
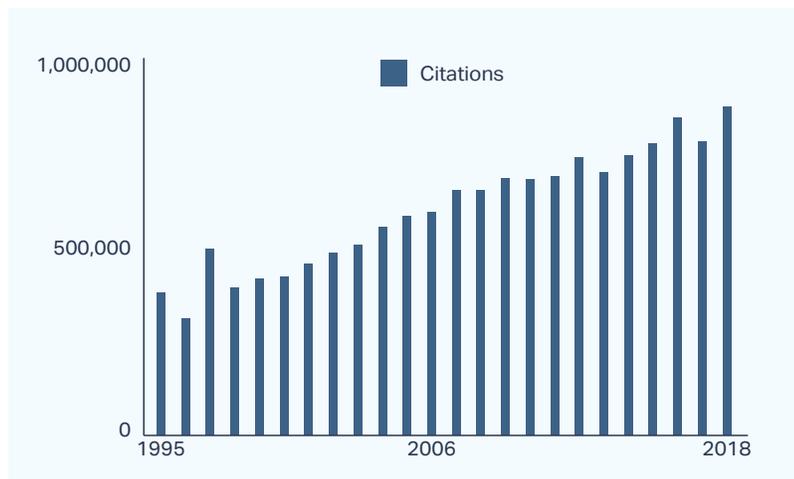

Figure 2: Increasing number of PubMed Articles published annually approaches 1 million (reprinted from https://www.nlm.nih.gov/bsd/stats/cit_added.html).
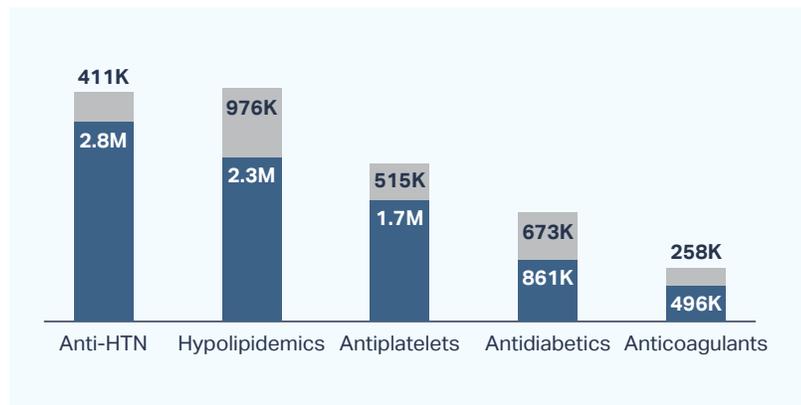
Persistent care gaps adversely affect patient outcomes. For instance, in atrial fibrillation, clinical trial data demonstrates a significant increase in cumulative stroke risk when patients with a CHADS2VASC risk score ≥ 2 (risk score of 2 = 2.2%; risk score of 9 = 15.2% annual stroke risk) do not take an anticoagulant medication such as a Direct-Acting Oral Anticoagulant (DOAC) or warfarin[3].

Figure 3: Care gaps Across CVD and Comorbidities, from 2013 to 2018

Analysis of 6.5 million patients in the PINNACLE Registry shows a large proportion of care gaps (gray portions of bars) exist across multiple related conditions. These gaps are likely an underestimation of the true chronic disease management gaps for each disease state, as they do not reflect whether there is adequate control of a condition, only whether or not a medication has been started for it. For instance, a patient already on a guideline-indicated anti-HTN medication may still not be well controlled on that medication or dose. More detailed analyses of care gaps within each medical condition are available on CLINT™, which also accounts for the efficacy of treatments longitudinally, producing guideline-driven indications for additional medications or dose adjustments.

The decision to use a specific DOAC or warfarin may vary due to a variety of factors: patient/physician preference, formulary variation, insurance, medical, or socioeconomic factors, but the end result is that patient outcomes are suffering by not aligning with guideline-driven care. Figure 3 demonstrates the current care gap landscape across the major cardiovascular comorbidities, illustrating that these care gaps span most clinical domains and that the need to impact practice habits is not isolated to one condition, but usually involves many of them.

It is well established that improving adherence rates to guideline-driven medical therapy (GDMT) produces significant reductions in mortality rates[4]. In order to improve adherence rates directly and across a large population, several hurdles must be overcome. Obtaining granular clinical patient data is the first and most critical step. A large, longitudinal, EMR-derived dataset that is specifically enriched for cardiovascular risk allows for a more comprehensive understanding of the gaps in care for those disease states. Once that data is made accessible, even in a de-identified form, the following key functionalities must be built, validated, and leveraged to yield actionable results at scale:

1 Apply codified guideline algorithms to every patient's clinical features to produce a checklist of applicable interventions across an entire clinic or health system population

2 Register whether each patient has already been administered their personalized intervention checklist, and if not, classify those omissions as care gaps

3 Examine the longitudinal history of patients who have already been administered indicated treatments, and determine whether those treatments have adequately controlled the disease state. For instance, whether a patient's blood pressure or diabetes is well controlled, and if not, whether additional dosage or new medications should be added.

In summary, creating a nuanced evidence-based AI engine that can produce a guideline-checklist for each patient with high fidelity to the intent of the guidelines has been a limiting factor to population management for guideline adherence. The HealthPals' CLINT™ platform is this engine, and through its collaboration with the ACC, HealthPals is improving visibility into where and why these gaps exist, as well as providing an actionable roadmap to preventing cardiovascular events across the US.

Most population health solutions target insurance claims-based analytics but are not usable at the point of care. They do not transform granular, EMR-extracted patient data into actionable medical interventions and as a result, they may fail to influence medical decision-making. To solve the problem at the scale required, a next-level population health tool was developed to encapsulate up-to-date medical guidelines, process large amounts of data, and understand patients longitudinally and from the bottom up. These insights are then used to create a path to aid and execute strategic changes at various levels, from the individual clinic level to public policy.

ANTICOAGULATION IN ATRIAL FIBRILLATION

AF is a common occurrence in the US which leads to over 750,000 hospitalizations and contributes to about 130,000 deaths each year[5]. The economic burden of AF is also significant: the US spends around $6 billion annually treating it[5], and the number of patients suffering from this arrhythmia is expected to double from 6.1 million patients today[5], to 12.1 million by 2030[6].

Patients with AF are susceptible to forming clots within the atria, which in turn can lead to strokes. To address this problem, many are put on anticoagulants to prevent blood clots. There are a variety of anticoagulants available, but the most common include Warfarin, Apixaban, and Rivaroxaban. The risk of stroke decreases to near normal risk levels if patients are put on anticoagulation. The emergence of 2009 clinical trial data of DOACs as an equivalent, if not superior, drug to warfarin for anticoagulation in the setting of AF eventually led to the inclusion of DOAC agents in the 2014 ACC/AHA AF guidelines as a Class I recommendation. But more importantly, anticoagulation itself is a practice that has variable adherence within the population. Due to the stroke risk arising from neglecting to anticoagulate AF patients appropriately, the first whitepaper topic of the ACC and HealthPals is focused upon the adoption rates of AF anticoagulation in the PINNACLE® Registry.

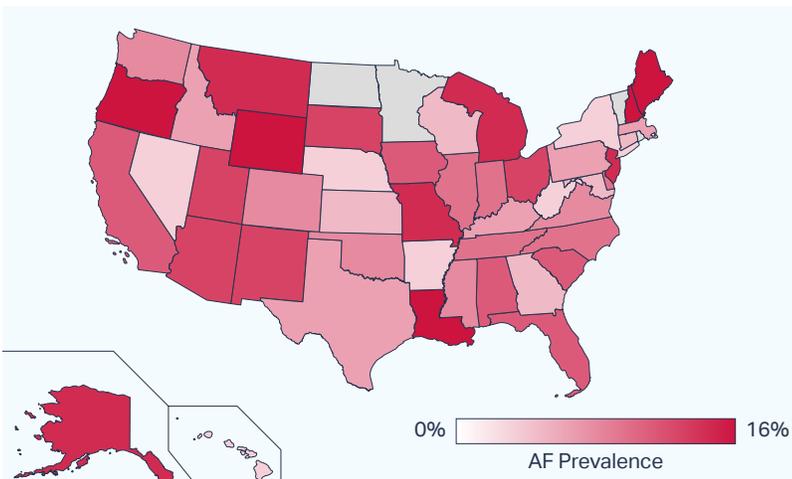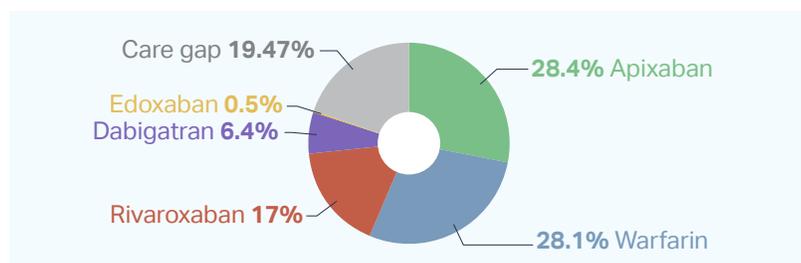*The number of patients suffering from this arrhythmia is expected to double, reaching 12.1 million by 2030*

0%   16%

AF Prevalence

Figure 4: AF Prevalence by State of Atrial Fibrillation patients in the PINNACLE® Registry as a percentage of the total.

AF DRUG TRENDS AND GAPS IN CARE

The prevalence of AF is expectedly higher in people ≥ 65 years of age or older (9%), while about 2% of people who are below the age of 65 have AF[5]. Figure 4 shows the prevalence of AF by state in the PINNACLE Registry. A more detailed geographic breakdown of AF prevalence at the county and zip code levels is available through the ACC and CLINT™, along with AF anticoagulation care gaps, and the longitudinal change in AF prevalence over the past 8 years in those same geographic distributions. Key questions that arise from Figure 4 include the patient cohort differences within each anticoagulant or care gap segment, which may speak to why these treatments were chosen. In addition, the outcomes of cohorts administered different treatment strategies is being tracked and evaluated to determine the optimal treatment strategies for specific patient feature sets. Granular breakdowns of cohorts of treated and untreated individuals within each geographic region is also possible through this analysis, along with patient signatures that predict the likelihood of developing AF and of suffering a persistent care gap in anticoagulation.

Figure 5: Anticoagulation Treatment Strategies

Proportional usage of anticoagulation agents for stroke prevention in AF in patients with a CHADS2VASC ≥ 2. Notably, there is ~ 20% care gap overall in this population, representing a significant green field opportunity for medical intervention. Also, Apixaban is the market leader, over Warfarin, and is significantly more prevalent in usage (28%) than the 2nd leading DOAC, Rivaroxaban (17%).
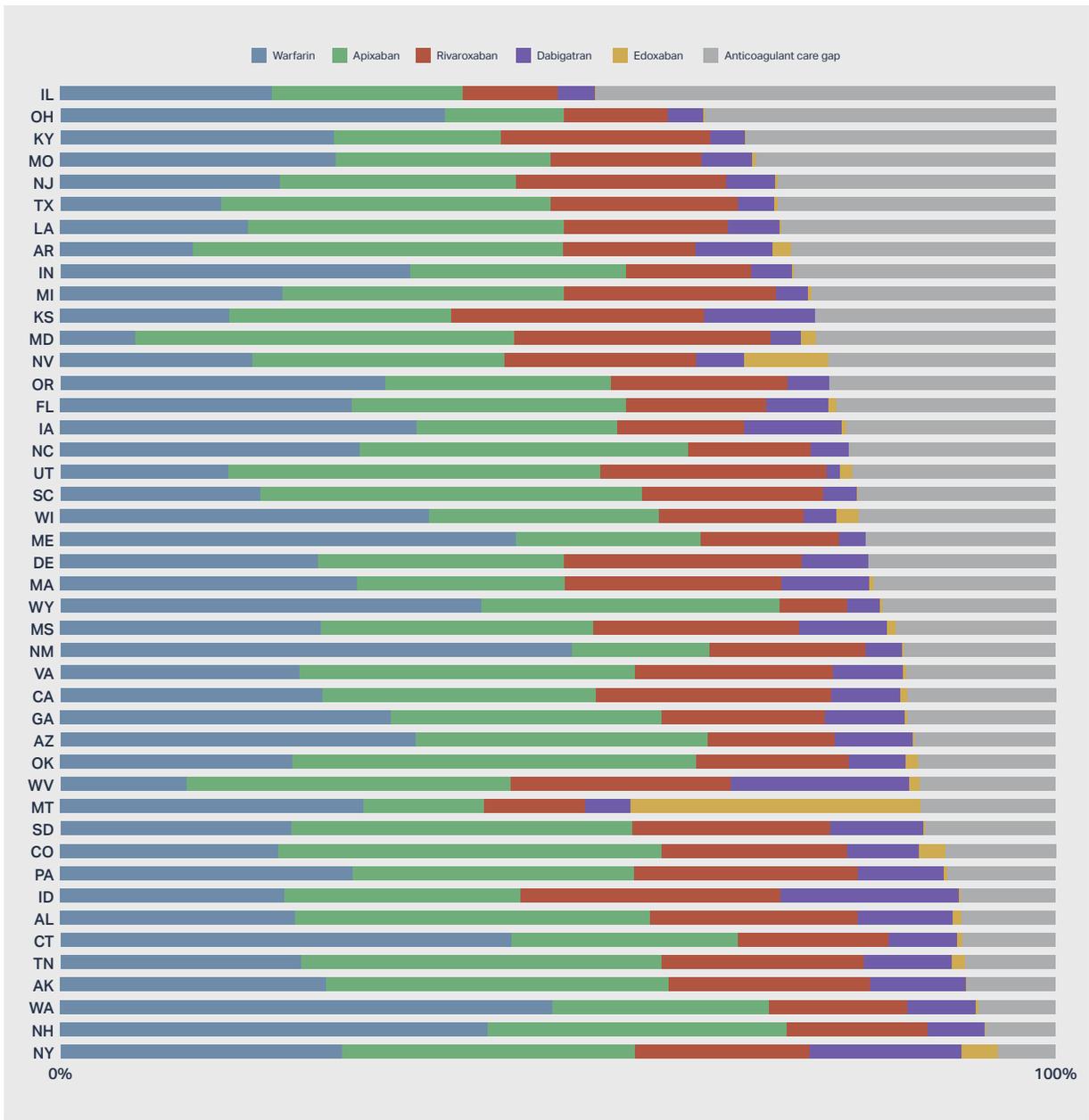
In February 2019, an updated guideline for anticoagulation in AF was issued by the ACC/AHA. The most significant change from the previous guideline was the recommendation of prescribing DOACs over Warfarin in patients with AF. Although the overview of this whitepaper does not include PINNACLE Registry data from after the guideline update, it is critical to understand the baseline practice variability leading to anticoagulant care gaps as well as the general treatment strategies of AF. To better understand the differences, the US population was analyzed at several different levels, displaying any treatment, or lack thereof, at the state, county, or clinic level. Figure 5 shows the PINNACLE® Registry breakdown of proportional anticoagulant treatments. In 2018, Apixaban overtook Warfarin as the most prescribed anticoagulant for AF, with Rivaroxaban trailing at third, and Dabigatran and Edoxaban in the 4th and 5th positions, respectively. This chart also demonstrates a 19% overall care gap for anticoagulation. Further details on drug dosing, the velocity of change in drug prescription habits, and the regional variation at the zip code level is available with more detailed analysis through CLINT™.

Figure 6: AF Therapy Strategies by State in 2018

The current anticoagulation usage and breakdown for every state. Overall care gaps are visualized in the grey portions of each row, with the states with the most care gaps listed at the top and decreasing as you move down the chart. Also notable is the individual state breakdowns with regard to specific anticoagulation agents.

Figure 6 shows the breakdown of AF treatments and anticoagulant care gaps by state, ordered by number of gaps. While a state by state breakdown is helpful in understanding the current and highest priority issues, examining past changes helps us anticipate what to expect in the future. As mentioned before, the AF anticoagulation landscape has changed drastically during the past few years. Looking at these changes is particularly useful for tracking drug market performance after an event such as a change in medical guidelines. For example, the AHA/ACC released guidelines in 2014 that indicated the use of DOACs, and as Figure 7 shows, there is a steep growth in the relative use of Apixaban immediately following the publication of those guidelines. Additionally, the clinic features and patient features that may explain differences rates of adherence to anticoagulation guidelines and practice variability are being developed through CLINT™.
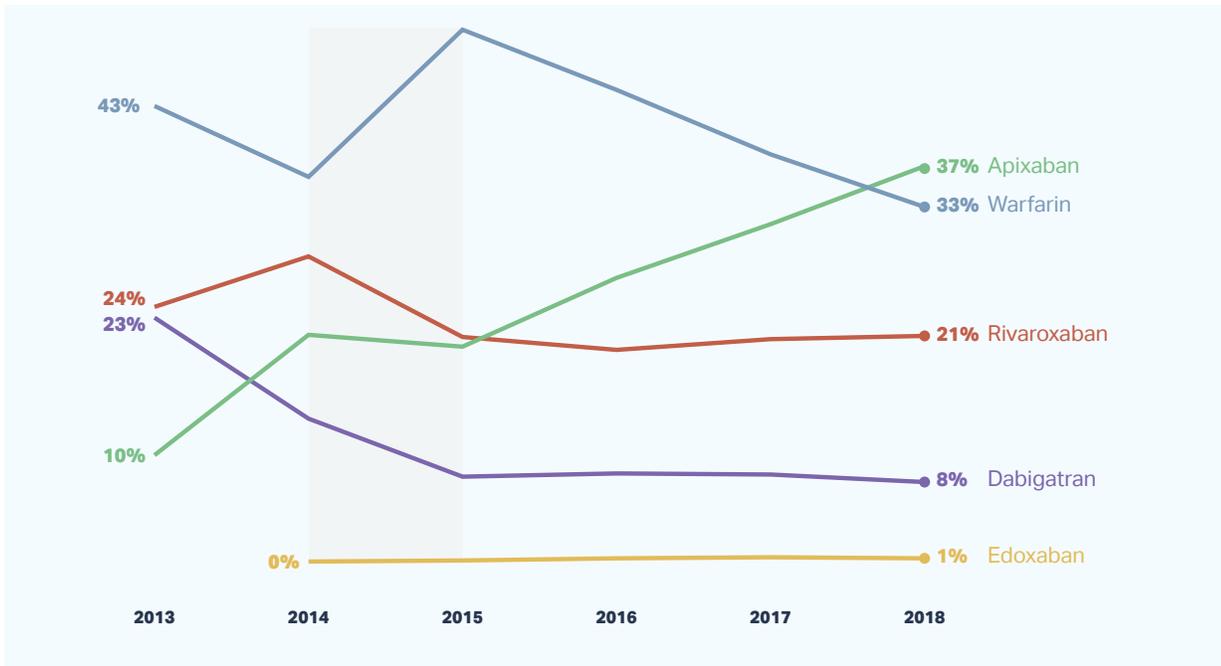

Figure 7: Market Performance of Anticoagulants from 2013-2018
Longitudinal prescription prevalence of individual anticoagulation agents. The 2014 ACC/AHA AF guidelines played a role in the increase in Apixaban usage and decrease in Warfarin usage. The relative flat impact of the guidelines on the usage of Dabigatran, Rivaroxaban, and Edoxaban can likely be explained by other related market events and factors.

The use of Warfarin has been decreasing in the past few years and was overtaken by the use of Apixaban in 2018. Overall Apixaban usage is expected to continue to rise, but due to the 2019 ACC/AHA guideline update, the usage of all DOACs is anticipated to rise, and so the impact on market shares of each DOAC remain to be seen.

WHAT'S NEXT?

Anational perspective on the adoption of drugs within the marketplace is essential to understanding the magnitude and locations of opportunities to improve outcomes. The ACC has formed a collaboration with a technology company, HealthPals, that possesses a powerful engine (CLINT™) to map registry patient data into guideline-driven insights. This whitepaper was dedicated to revealing the most frequently used anticoagulants in eligible AF patients, as well as documenting the highest performing regions of the US in adherence to medical guidelines surrounding AF. The ultimate goals of this collaboration are to inform health systems to the specific areas (and potentially, specific patients) in need of guideline adherence, and to develop applications of this technology and data model that are suitable for life science companies, payers, and large single payer health systems.

It is evident that a rapid change in medicine and healthcare has produced large numbers of gaps, due to slow adoption times of new therapies, and poor adherence to indicated treatments. These gaps need to be resolved using a data driven approach in order to affect a population level change and to broadly reduce the rates of cardiovascular events nationwide. To learn more about how these guideline changes introduce market opportunities for new diagnostics, drugs, or therapies, and how upcoming guideline changes will impact market performance trends of existing drugs, contact HealthPals.

In addition to improving health systems, these insights are of highest value to life science company leadership. Research, development, and marketing of new drugs can be guided by studying market performance and clinical outcomes of existing drugs, and understanding how existing drugs can be repurposed to reach new markets. Uncovering insights like these will speed up the research and development pipeline and help target specific markets, while potentially saving hundreds of millions of dollars in clinical trial costs.

This whitepaper was meant to answer important questions regarding the magnitude and patterns of adequate AF anticoagulation. In addition, the ability to identify care gaps amongst the highest risk individuals may create layers of positive impact on the preventive programs at health systems. Future whitepapers will examine more deeply the mechanisms and reasons behind the high rates of care gaps.

For more information about HealthPals and CLINT™, find us on healthpalsinc.com or hello@healthpalsinc.com

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