

# New Developments in Atrial Fibrillation

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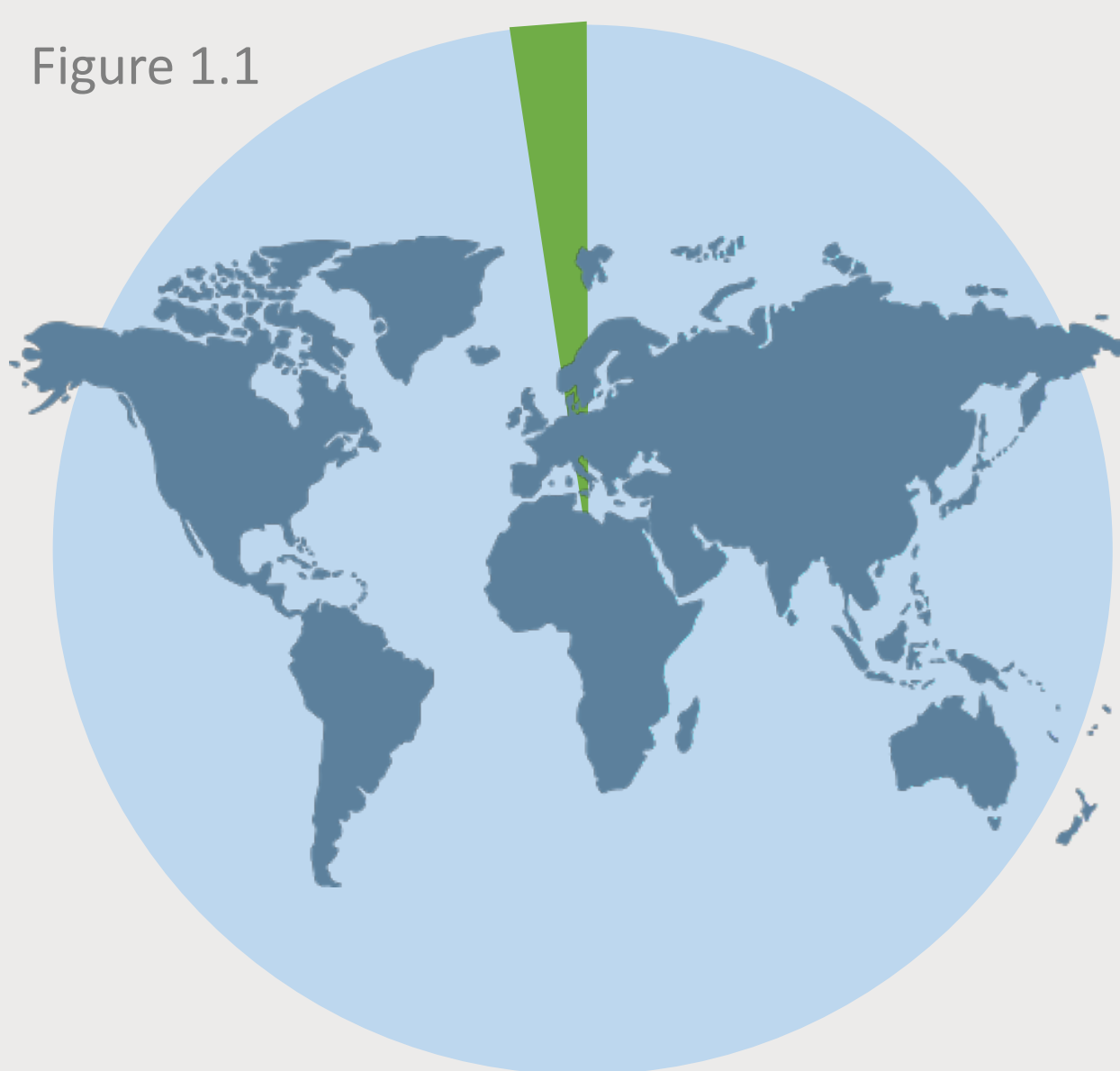
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## INTRODUCTION

As we've entered the twenty-first century, a "silent epidemic" continues to perpetuate across the globe. Atrial Fibrillation (AF) has assumed increasing importance as the global demographic tide results in a rapidly growing population of elderly individuals. With a global prevalence of over 0.5 percent (Figure 1.1)<sup>3</sup>, an understanding of the epidemiology and treatment of AF is crucial to reducing the impact of this disease on a changing patient population. Since the turn of the decade in 2010, the biological mechanisms and symptoms of AF have been established in the larger medical community. As such, focus within the field of AF has turned towards treatment. With constantly evolving technology and increased growth in biomedical engineering and cardiac electrophysiology, new and innovative treatment solutions have shown noninferiority to previously standard treatments. Many patients never notice AF as it often occurs with no signs or symptoms, hence "silent epidemic." While these symptoms are troublesome for patients, the real threat lies in the increased risk of stroke that accompanies the condition. Within the past decade, there have been two major developments in AF treatment and stroke prevention: the novel oral anticoagulant (NOAC) and the left atrial appendage closure (LAAC) device.

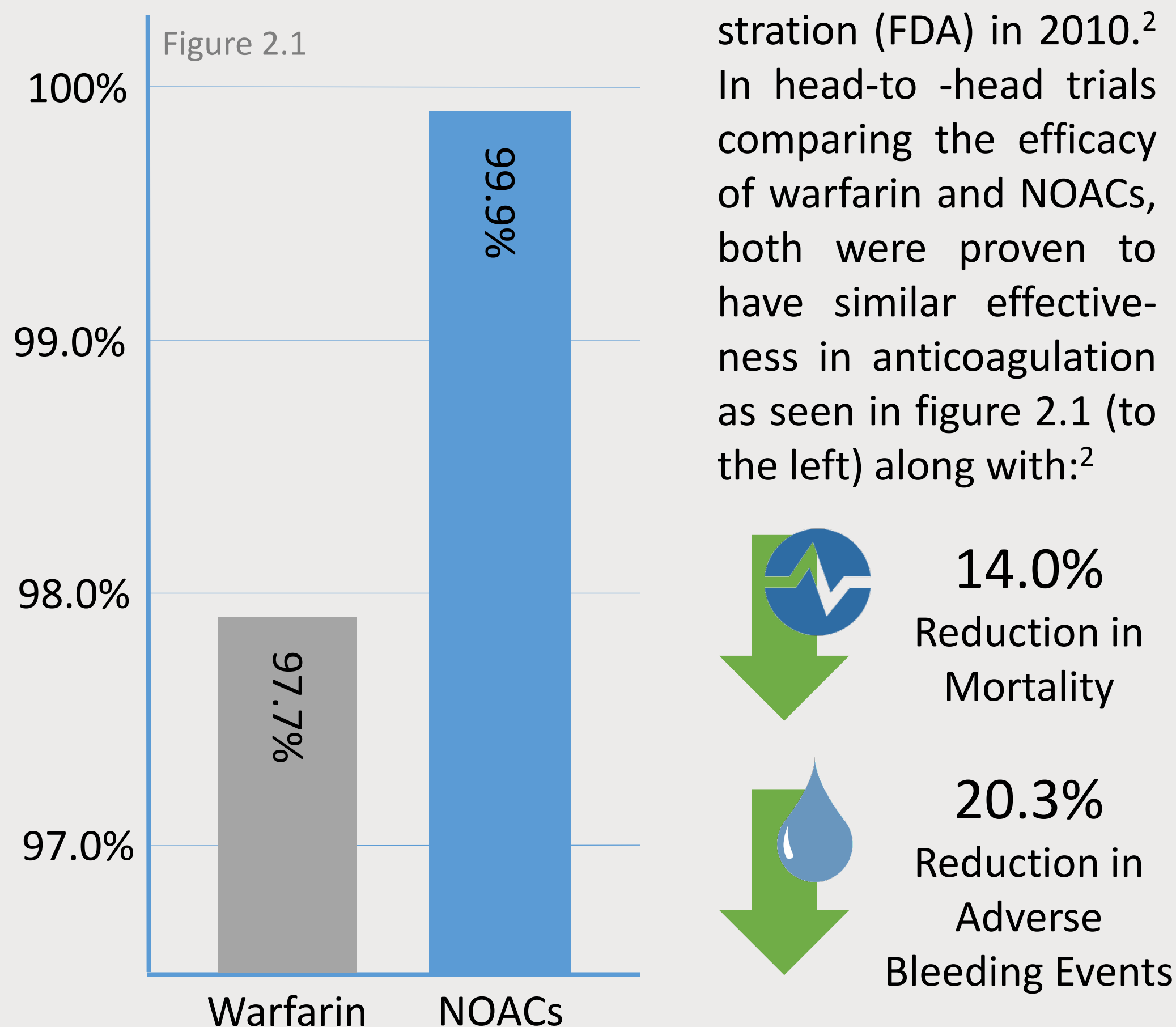


0.50%  
Of the World Population has  
Atrial Fibrillation

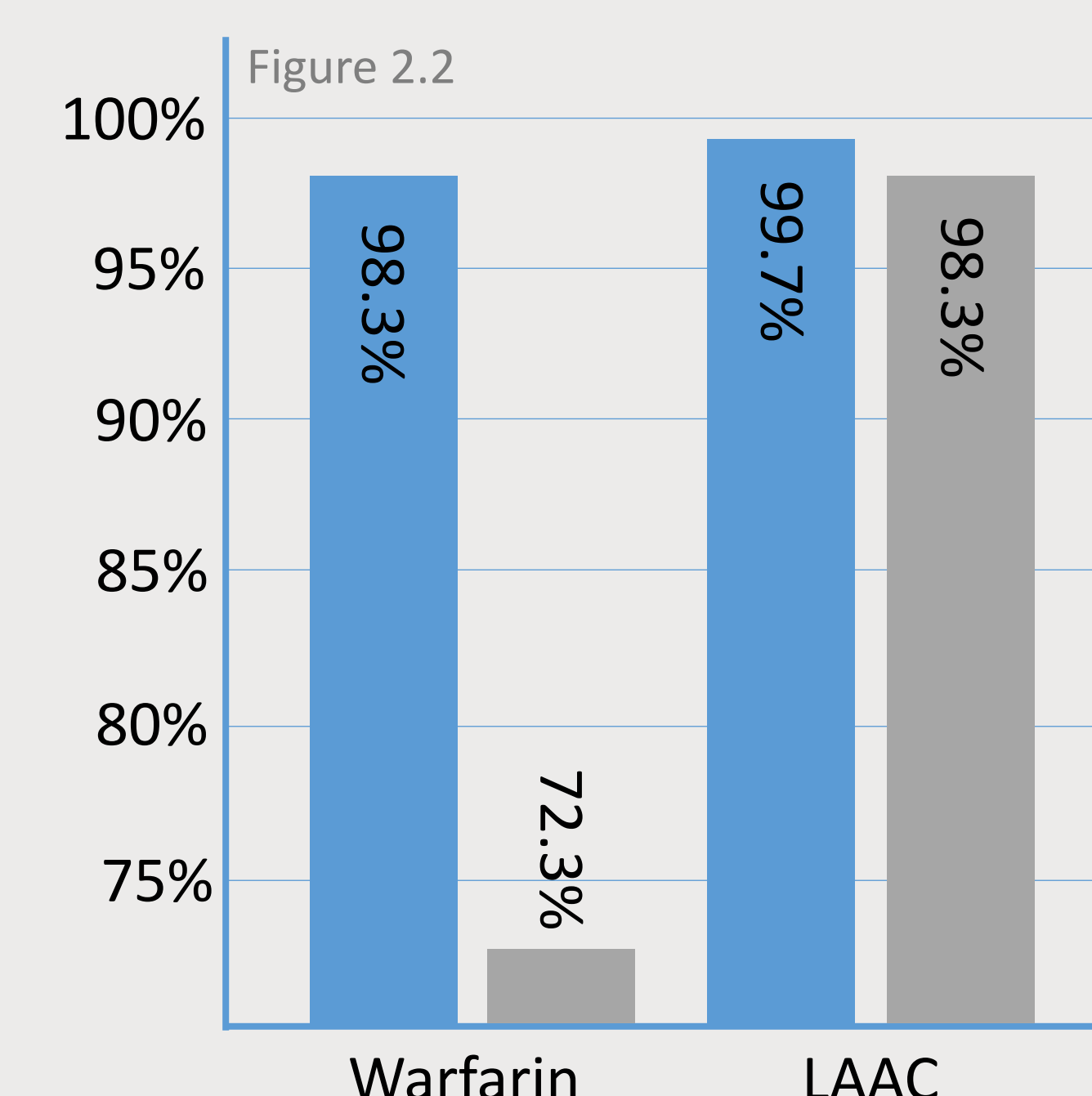
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## RESULTS

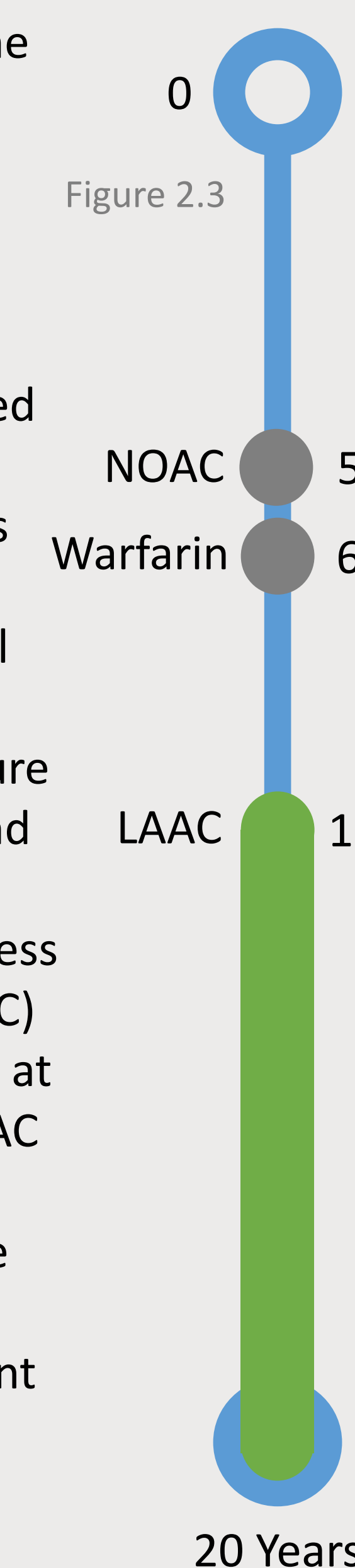
Vitamin K antagonists, such as warfarin, were the only type of oral anticoagulant approved for stroke prevention until 2008. The development of a non-Vitamin K anticoagulant began in 2008 and the first NOAC was approved by the U.S. Food and Drug Administration (FDA) in 2010.<sup>2</sup> In head-to-head trials comparing the efficacy of warfarin and NOACs, both were proven to have similar effectiveness in anticoagulation as seen in figure 2.1 (to the left) along with:<sup>2</sup>



In March 2015, the FDA approved the use of the first LAAC device for stroke prevention in AF patients, named the *Watchman*, based on the results of two major studies: PREVAIL and PROTECT-AF.<sup>3</sup> Of all implantations performed between 2015 and 2017, 95.6% of procedures were successful.<sup>4</sup> A 5-year follow-up study to the PREVAIL and PROTECT-AF trial showed that LAAC achieved noninferiority in comparison to warfarin (blue) and hemorrhagic/fatal stroke, and post-procedural bleeding rates favored LAAC (grey) as seen in Figure 2.2 (below).<sup>6</sup>



In a study assessing the cost-effectiveness of LAAC, warfarin, and NOACs, analysis was conducted over a lifetime (20 years) horizon with a modeled population of 10,000 patients aged 70 years (9.60% annual stroke rate and 3.74% annual bleeding rate).<sup>5</sup> The analysis, shown in figure 2.3 (to the right), found that LAAC achieved a higher cost-effectiveness over dabigatran (NOAC) at year 5 and warfarin at year 6. At year 10, LAAC has the highest cost-effectiveness of all the treatments and remained the dominant treatment over the lifetime analysis.<sup>5</sup>



## METHODS

Initially, popular sources, including Mayo Clinic, John Hopkins Medicine, and the Harvard Medical, and PubMed were searched to determine current understanding of AF and latest trends in the field. Articles published by these sources were initially searched for stated content, then screened to determine relevance to the subject. Once new developments in AF were determined, key points and terms were identified based on articles. The key terms were then used to search PubMed for articles related to left atrial appendage (LAAC) closure or management, novel oral anticoagulants (NOAC), warfarin or Vitamin K oral anticoagulants, stroke prevention in AF, and combined AF procedures. The articles were screened by publishing date and title, and then by abstract. Date was checked to ensure recency of articles and data. Lastly, bibliographies of articles deemed appropriate were manually searched. This process resulted in 11 articles cited in this literature review, all of which, aside from one, have been published within the past six years. Access to scholarly journals and the PubMed database was provided by the University of North Carolina University Libraries.

## DISCUSSION

NOACs and LAAC both proved to be noninferior to warfarin for stroke prevention in patients with AF, with both showing a statistically significant reduction in stroke and embolic events (efficacy) and mortality and adverse bleeding events (patient risk) when compared to warfarin. Though warfarin was effective as an anticoagulant, the drug has a very narrow therapeutic window. Additionally, warfarin has several drug-food interactions related to Vitamin K which reduce the effectiveness of the drug and put the patient at risk if the patient is not aware of their diet.<sup>2</sup> With the significant majority of AF patients over the age of 65, reducing the number of situations in which the patient can put themselves at risk is especially important as older populations tend to require low maintenance treatment to maintain drug efficacy. The *Watchman* implant has made a previously unsafe and largely unsuccessful procedure into a preferred treatment option for AF patients. As opposed to surgically removing the left atrial appendage (LAA), the *Watchman* device is a mesh cage which is placed in the LAA and is expanded, preventing the formation of blood clots in the LAA (Figure 3.1).<sup>3</sup> LAAC devices provide a benefit over both NOACs and warfarin as it doesn't require the need to take daily medication or go for routine examinations, providing low maintenance treatment for potential life-long usage. Though research is limited, combined CA-LAAC procedures have shown positive results and making the implant a standardized addition to traditional AF treatment would be a proactive step in improving patient wellbeing.<sup>1</sup> Though it may seem that warfarin has already become obsolete for AF treatment and stroke

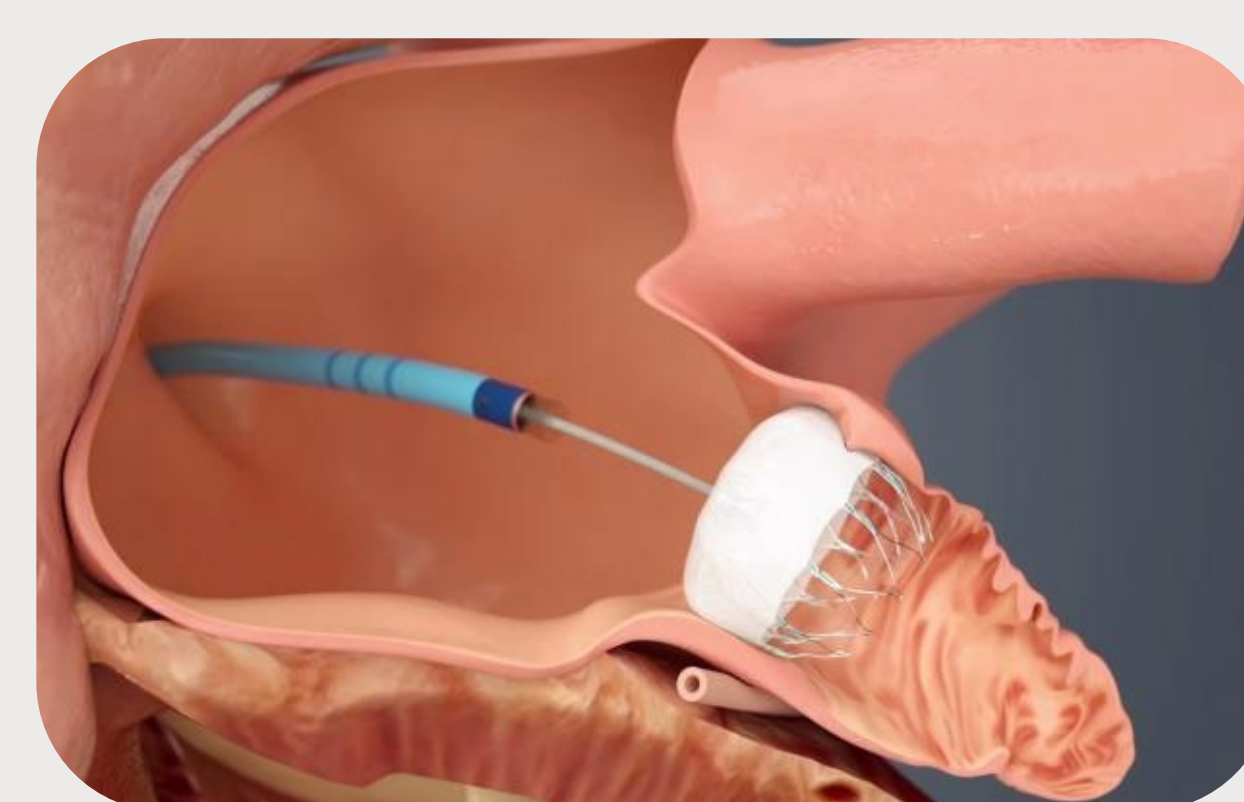


Figure 3.1 The *Watchman* LAAC device being implanted into the right atrial appendage in the heart via catheter

prevention, as of the year this review was conducted, that is currently not the case. In the cost-effectiveness analysis, LAAC was shown to have the highest cost-effectiveness over time. Yet, LAAC has a steep up-front cost that a large population in the United States and worldwide can not afford, nonetheless reasonably access.<sup>5</sup> Additionally, all NOACs cost more than warfarin per prescription, resulting in many individuals with AF preferring the immediate lower cost of warfarin in exchange for the potential risks.

**IN CONCLUSION:** Though both NOACs and LAAC devices have proven noninferiority to existing options, both treatments require additional time to mature, not only as treatments, but as products in which patients who need the benefits can receive them, no matter their geographic or socioeconomic status.

## ACKNOWLEDGEMENTS

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