World-wide Randomized Antibiotic EnveloPe CIED Infection PrevenTion Trial
WRAP-IT

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Cleveland Clinic, Cleveland Ohio

Lead Management: Case-based approach

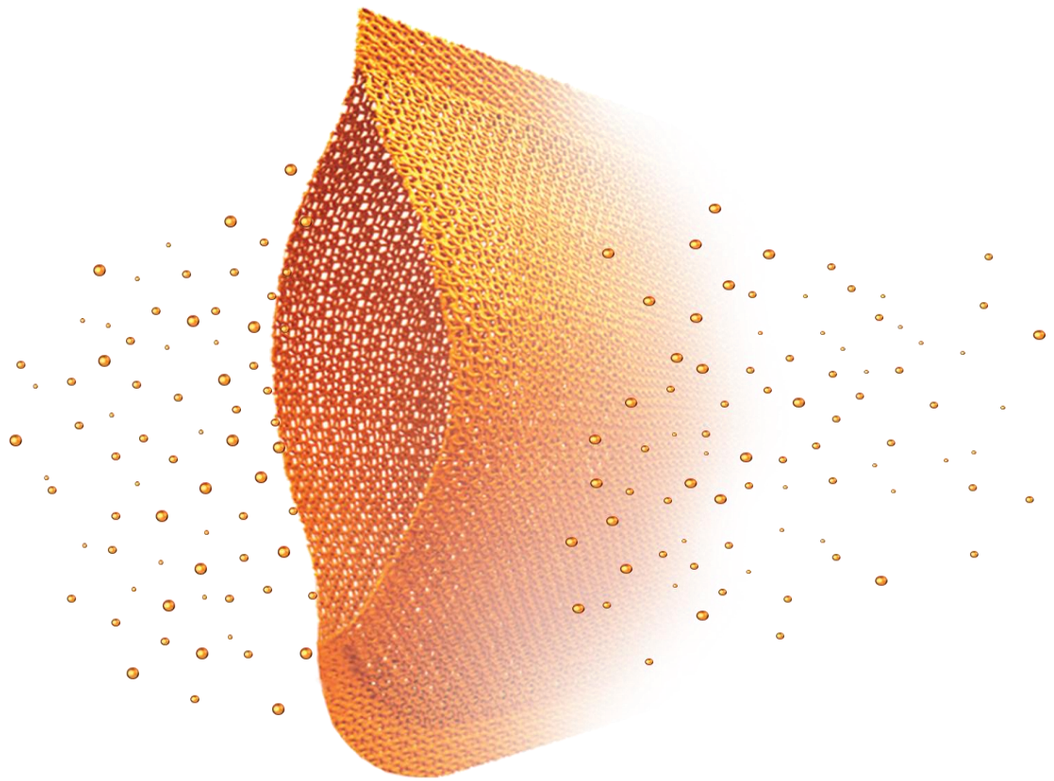
Heart Rhythm 2017 Satellite Symposium

Wednesday May 10, 2017 Chicago IL

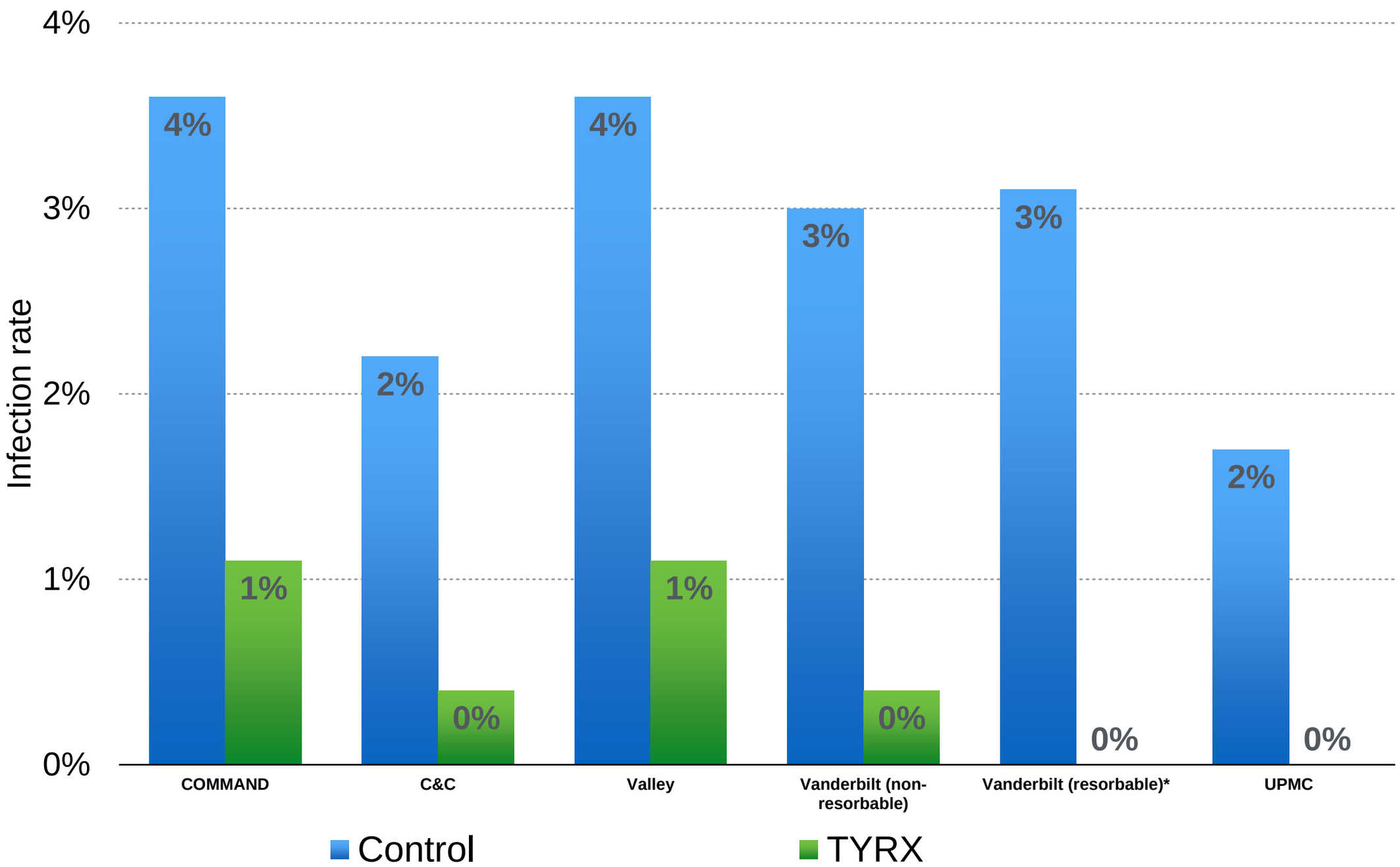
Cleveland Clinic

TYRX™ Absorbable Antibacterial Envelope (Medtronic TYRX)

- Fully absorbable mesh
- Holds pacemaker or ICD in place
- Multifilament knitted mesh with bioresorbable polymer
- 2 Antibiotics:
  - Rifampin
  - Minocycline
- FDA cleared 5/2013



TYRX™ first generation non-resorbable non-randomized studies



Bloom et. al. *Pace.* 2011
Citadel and Centurion Cardiostim 2015
Mittal S. et al. *Heart Rhythm* 2014
Kolek MJ et. al. *Pace.* 2013
Kolek MJ et. al. *J Cardio Electrophysiolo.* 2015
Shariff N et. al. *J Cardio Electrophysiolo.* 2015

Worldwide Randomized Antibiotic EnveloPe Infection PrevenTion Trial (WRAP-IT)

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Background Cardiac implantable electronic device (CIED) infection is a major complication that is associated with significant morbidity and mortality. The aim of this study is to determine whether Medtronic TYRX absorbable envelope reduces the risk of CIED infection through 12 months of follow-up post procedure.

Methods WRAP-IT is a randomized, prospective, multi center, international, single-blinded study. Up to 7,764 subjects who are undergoing CIED generator replacement, upgrade, or revision, or a de novo CRT-D implant, will be enrolled and randomized (1:1) to receive the TYRX envelope or not. The primary endpoint is major CIED infection throughout 12 months of follow up after the procedure. Data will be analyzed with an intention to treat approach. WRAP-IT will also assess the performance of Medtronic's lead monitoring algorithms in subjects whose CIED includes a transvenous right ventricular defibrillation system.

Conclusions WRAP-IT is a large randomized clinical trial that will assess the efficacy of TYRX absorbable envelope in reducing CIED infection, define its cost effectiveness, and will also provide a unique opportunity to better understand the pathophysiology and risk factors for CIED infection. (Am Heart J 2016;180:12-21.)

WRAP-IT: study design

- Target population:
  - CIED replacement or upgrades
  - Biv-ICD primary de-novo implants

- Multi center, world wide, single blinded, randomized study

- Randomized 1:1 envelope vs no envelope

- Stratified by device type

WRAP-IT: Endpoints

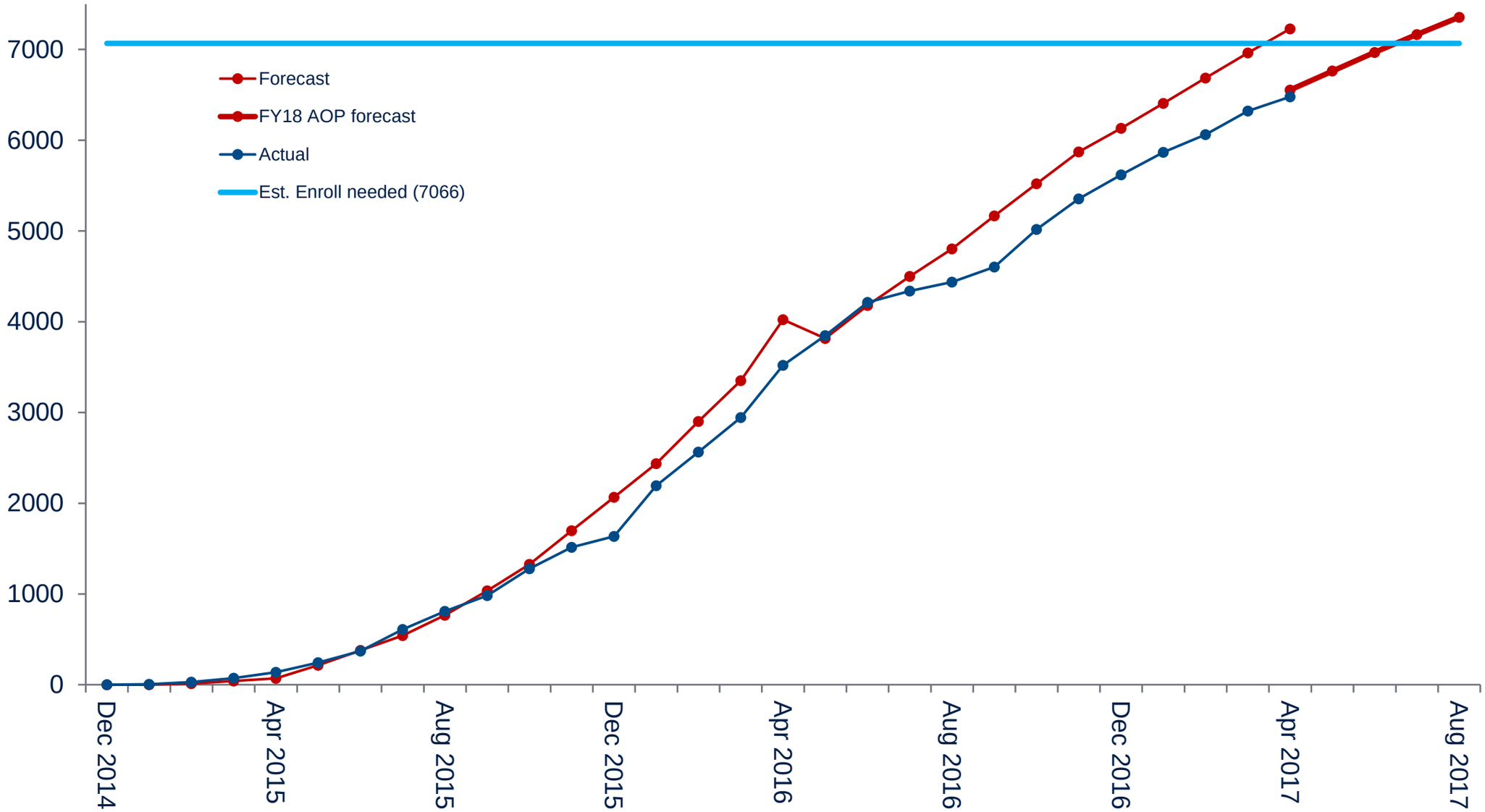
- **Primary:**
  - **CIED infection resulting in one or more of the following;**
    - CIED removal
    - CIED pocket revision
    - CIED infection treated with antibiotic therapy if the subject is not a candidate for system removal
    - Death due to CIED infection

- **Follow up 12 months**

Global Snapshot

Geography	Initiations (complete)	Enrollments (20-Apr-17)
US	121	4566
EMEA	50	1528
SEA	5	98
Canada	4	246
Hong Kong	2	36
Latin America	1	5
Worldwide	**183**	**6479**

World Wide Enrollment*



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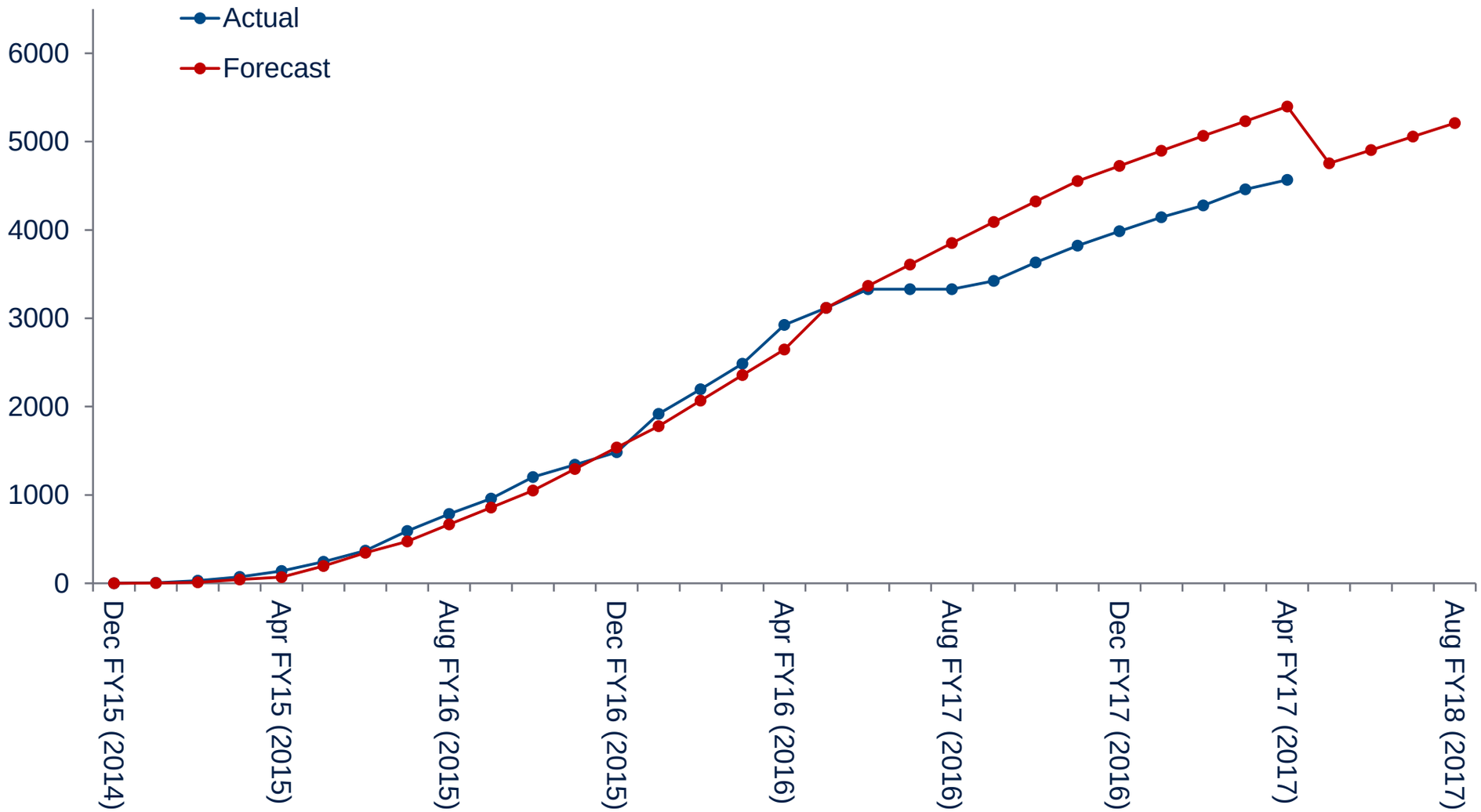
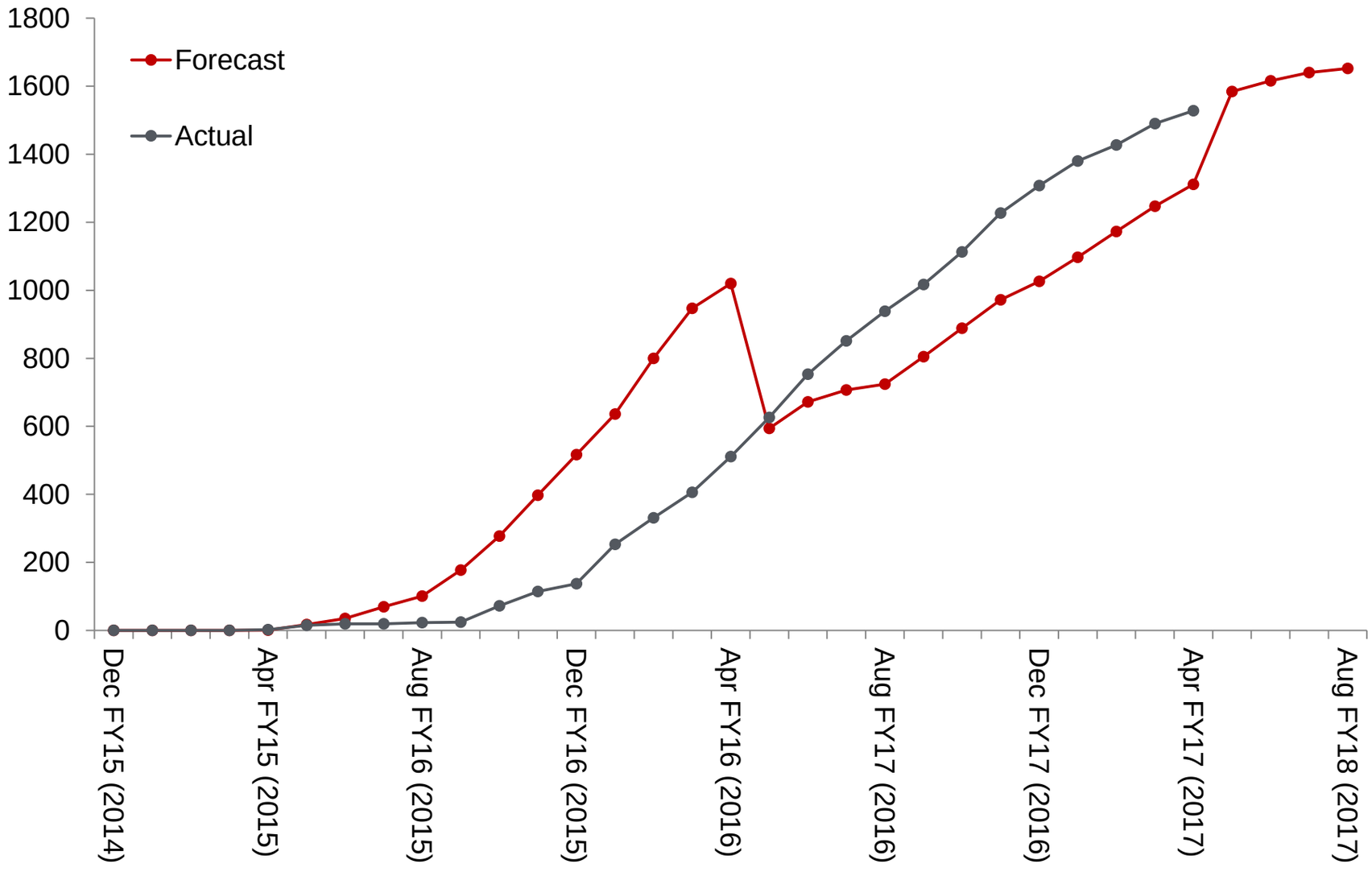
*Data up to April 20th 2017

US Enrollment*

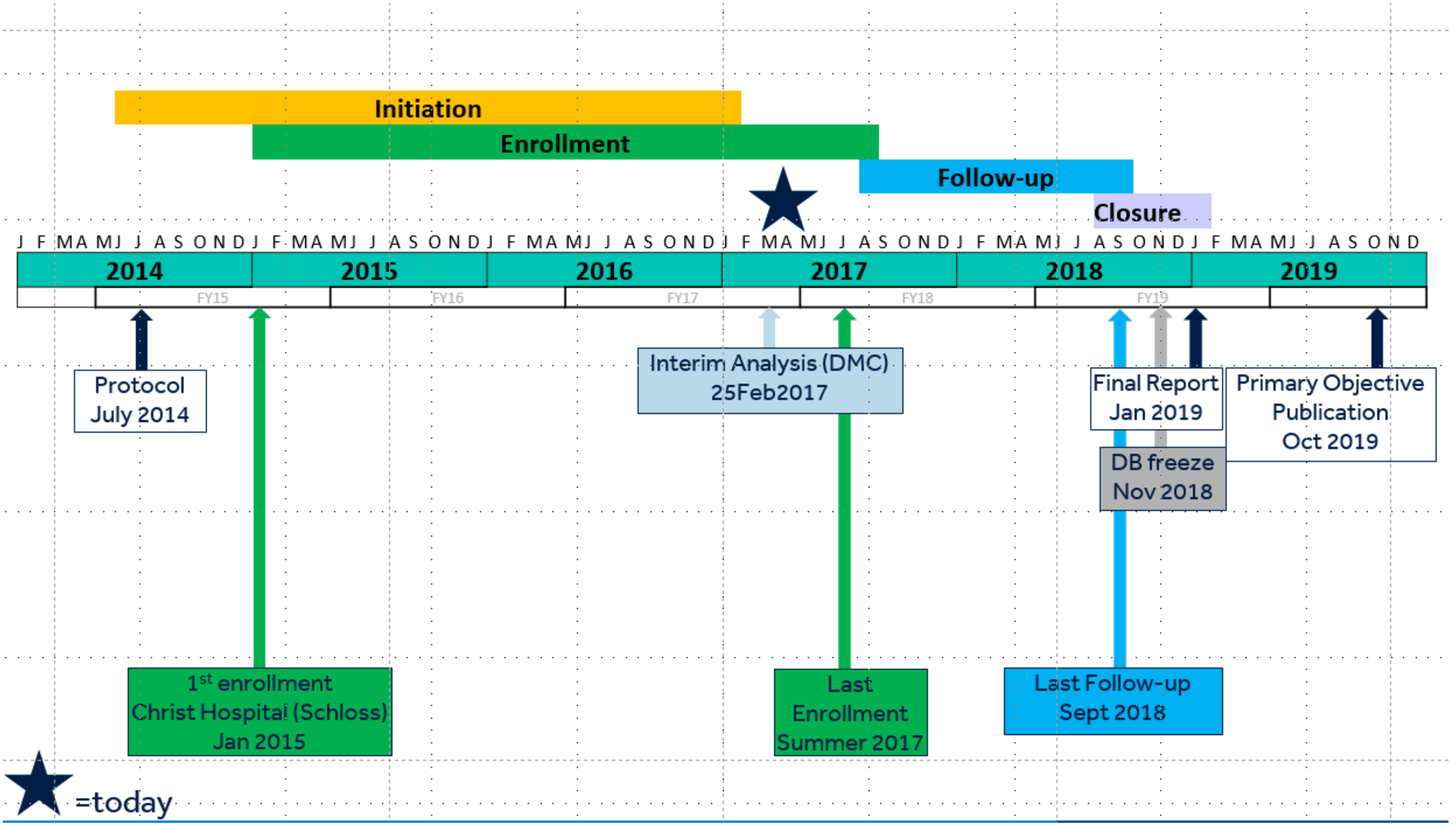


*Data up to April 20th 2017

EMEA Enrollment*



*Data up to April 20th 2017


Initiation
Enrollment
Follow-up
Closure
J F MA MJ J A S O N D J F MA MJ J A S O N D J F MA MJ J A S O N D J F MA MJ J A S O N D J F MA MJ J A S O N D J F MA MJ J A S O N D
2014
2015
2016
2017
2018
2019
FY15
FY16
FY17
FY18
FY19
Protocol
July 2014
1st enrollment
Christ Hospital (Schloss)
Jan 2015
Interim Analysis (DMC)
25Feb2017
Last
Enrollment
Summer 2017
Final Report
Jan 2019
DB freeze
Nov 2018
Last Follow-up
Sept 2018
Primary Objective
Publication
Oct 2019
=today

Thank You

@khaldountarakji