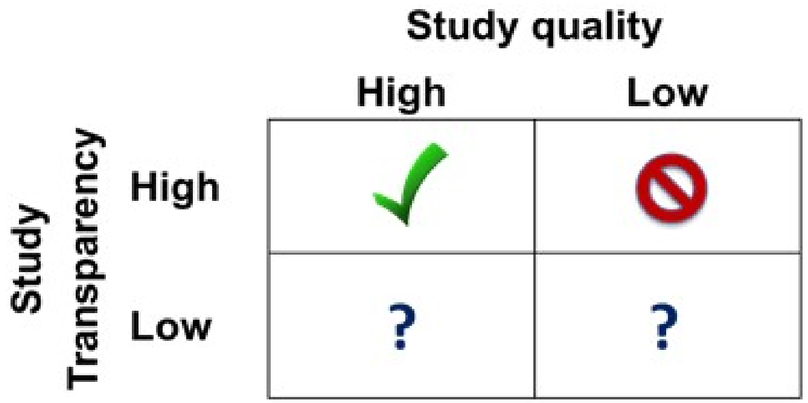
Evaluating a structured reporting template to increase transparency and reduce review time for healthcare database studies

Importance of transparency for RWE from databases

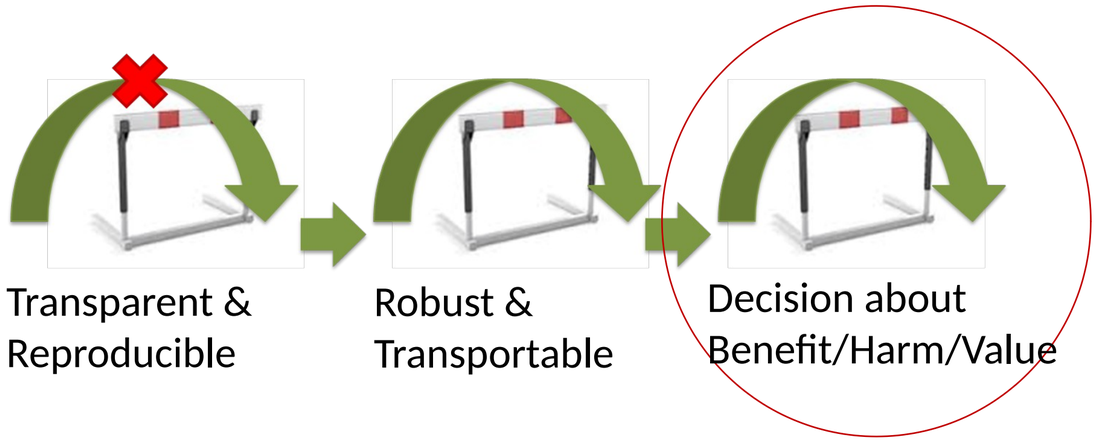
Quality and rigor of database studies are variable…

- Broad dismissal of database studies as inferior, less valid



Lack of transparency is an important barrier to use of
‘real world’ evidence from databases for decision making

- Without transparency, unable to assess validity/relevance



Steps to increase transparency about how RWE is generated

The International Society for Pharmacoeconomics and Outcomes Research (**ISPOR**)/ International Society for Pharmacoepidemiology (**ISPE**)
Joint Task Force on Real World Evidence for Healthcare Decision-Making

transparency in **process** for database studies (e.g. “what did you plan to do?”)

WILEY

ORIGINAL REPORT

Good practices for real-world data studies of treatment and/or comparative effectiveness: Recommendations from the joint ISPOR-ISPE Special Task Force on real-world evidence in health care decision making

Marc L. Berger[1] | Harold Sox[2] | Richard J. Willke[3] | Diana L. Brixner[4] | Hans-Georg Eichler[5] | Wim Goettsch[6] | David Madigan[7] | Amr Makady[6] | Sebastian Schneeweiss[8] | Rosanna Tarricone[9] | Shirley V. Wang[8] | John Watkins[10] | C. Daniel Mullins[11]

transparency in study **execution** (e.g. “what did you actually do?)

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Reporting to Improve Reproducibility and Facilitate Validity Assessment for Healthcare Database Studies V1.0

Shirley V. Wang[1,2] | Sebastian Schneeweiss[1,2] | Marc L. Berger[3] | Jeffrey Brown[4] | Frank de Vries[5] | Ian Douglas[6] | Joshua J. Gagne[1,2] | Rosa Gini[7] | Olaf Klungel[8] | C. Daniel Mullins[9] | Michael D. Nguyen[10] | Jeremy A. Rassen[11] | Liam Smeeth[6] | Miriam Sturkenboom[12] |
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Specific reporting to improve transparency and reproducibility and facilitate validity assessment

DATA SOURCE

- Data provider
- Data extraction date (DED)*
- Data sampling
- Source data range (SDR)*
- Type of data
- Data linkage, other supplemental data
- Data cleaning
- Data model conversion

DESIGN

- Design diagram

INCLUSION/EXCLUSION CRITERIA

- Study entry date (SED)*
- Person or episode level study entry
- Sequencing of exclusions
- Enrollment window (EW)*
- Enrollment gap
- Inclusion/Exclusion definition window
- Codes
- Frequency and temporality of codes
- Diagnosis position (if relevant/available)
- Care setting
- Washout for exposure
- Washout for outcome

CONTROL SAMPLING

- Sampling strategy
- Matching factors
- Matching ratio

EXPOSURE DEFINITION

- Type of exposure
- Exposure risk window (WRW)
- Induction period
- Stockpiling
- Bridging exposure episodes
- Exposure extension
- Switching/add on z
- Codes, frequency and temporality of codes, diagnosis position, care setting
- Exposure Assessment Window (EAW)*

FOLLOW UP TIME

- Follow-up window (FW)*
- Censoring criteria

OUTCOME DEFINITION

- Event date (ED)*
- Validation
- Codes, frequency, and temporality of codes, diagnosis position, care setting

COVARIATE DEFINITIONS

- Covariate assessment window (CW)*
- Comorbidity/risk score
- Healthcare utilization metrics
- Codes, frequency, and temporality of codes, diagnosis position, care setting

STATISTICAL SOFTWARE

- Statistical software program used

* key temporal anchors

Specific reporting to improve transparency and reproducibility and facilitate validity assessment

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Annals of Internal Medicine RESEARCH AND REPORTING METHODS

Graphical Depiction of Longitudinal Study Designs in Health Care Databases

Sebastian Schneeweiss, MD, ScD; Jeremy A. Rassen, ScD; Jeffrey S. Brown, PhD; Kenneth J. Rothman, DrPH; Laura Happe, PharmD, MPH; Peter Arlett, MD; Gerald Dal Pan, MD, MHS; Wim Goettsch, PhD; William Murk, PhD; and Shirley V. Wang, PhD

Published online March 12, 2019

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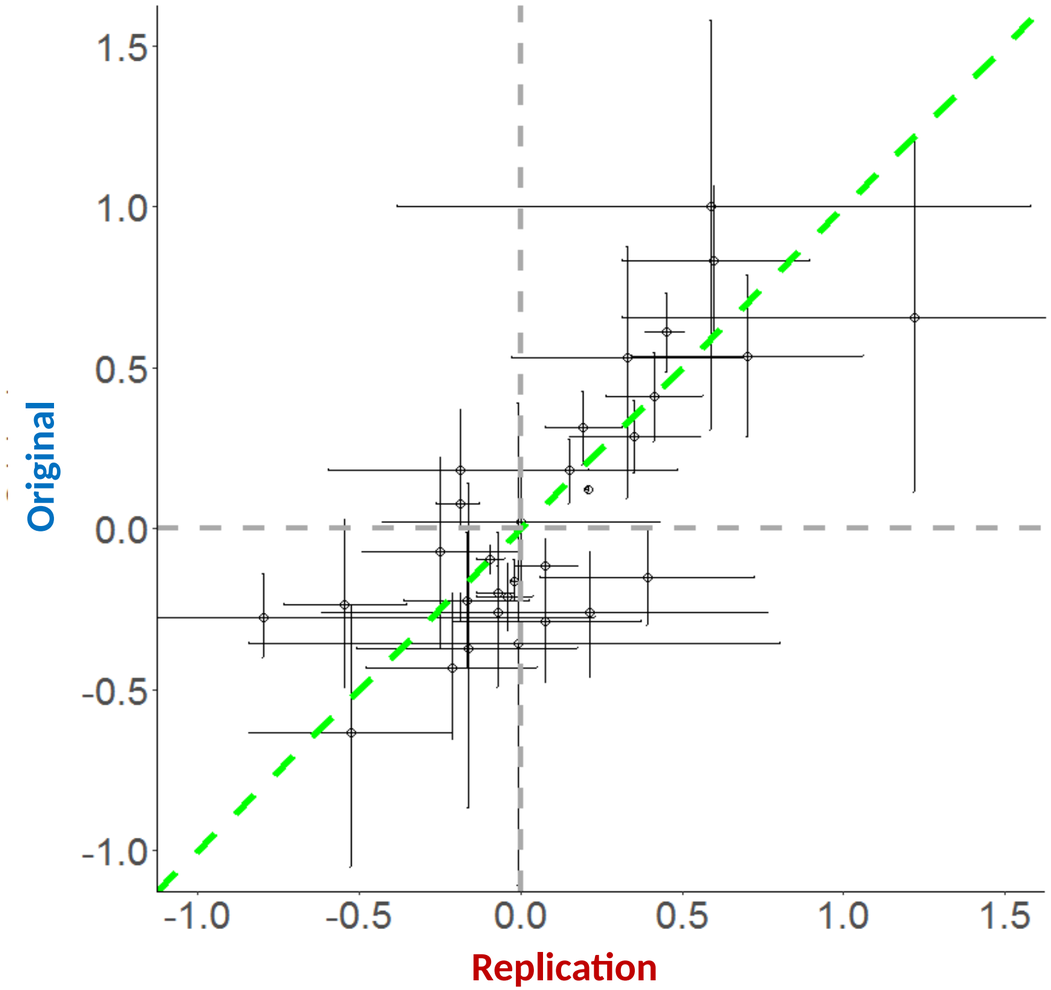
Interim results from large scale replication of peer-reviewed database studies

Calibration of effect estimates[1] for publication versus direct replication



Take home points:

Glass half full	Glass half empty
• **74%** of effect estimates on same side of null	• **26%** of effect estimates on opposite side of null
• **88%** of CI had any overlap[2]	• **12%** of CI had no overlap[2]
• If CI overlapped, **40%** of CI range was shared[3]	• If CI overlapped, **60%** of CI range was not shared[3]

Correlation coefficient: 0.62 (moderate)

Point estimate on same side of null and p-value on same side of 0.05: 54%

[1] Log hazard, odds, risk ratio
[2] Binomial test p-value for observed vs expected <0.001
[3] Proportion overlapping =
[4] Unweighted estimate. Inverse variance weighted correlation coefficient = 0.42

Go to structured template

Example from JAMA Internal Medicine

Abstract:

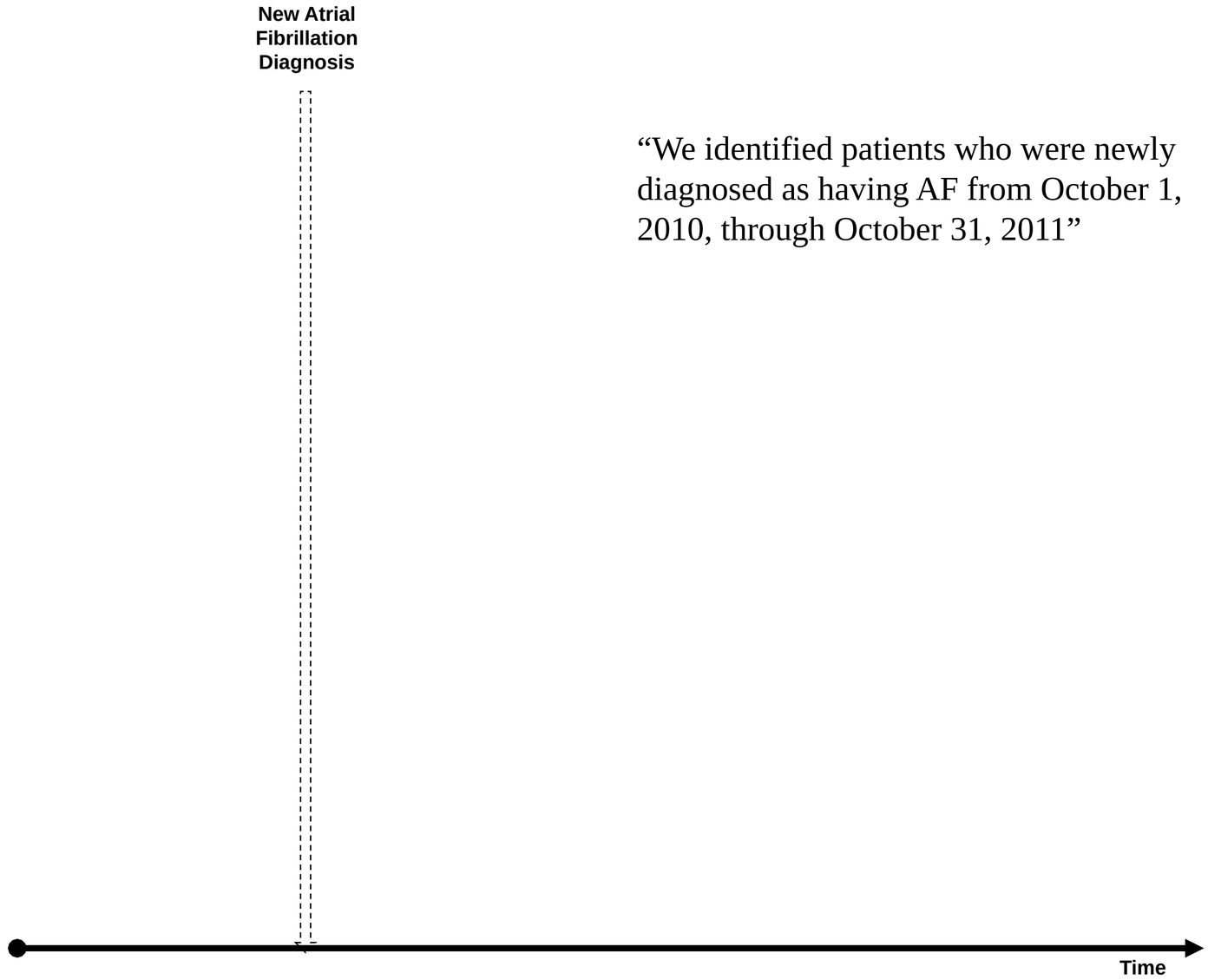
We identified participants as those newly diagnosed as having atrial fibrillation (AF) from October 1, 2010, through October 31, 2011, and who **initiated dabigatran or warfarin** treatment within 60 days of initial diagnosis.

Methods:

We identified patients who were **newly diagnosed as having AF** from October 1, 2010, through October 31, 2011, by using the CMS Chronic Condition Warehouse indicator that traced the first diagnosis date back to January 1, 1999. The diagnosis of AF was defined as having 1 inpatient or 2 outpatient claims with primary or secondary International Classification of Diseases, Ninth Revision (ICD-9), code 427.31. We also required that individuals in our study sample had **filled an outpatient prescription for either dabigatran or warfarin within 2 months** of the first diagnosis (N = 9562). Those who **filled prescriptions for dabigatran and warfarin during the first 2 months after diagnosis** were excluded (N = 158). We followed up each individual from the first prescription of dabigatran or warfarin until discontinuation of use for more than 60 days, switch of anticoagulants, death, or December 31, 2011. Our final overall study sample included 1,302 dabigatran users and 8,102 warfarin users.

lo attrition table or design diagram was provided.

mple from JAMA Internal Medicine



“We identified patients who were newly diagnosed as having AF from October 1, 2010, through October 31, 2011”

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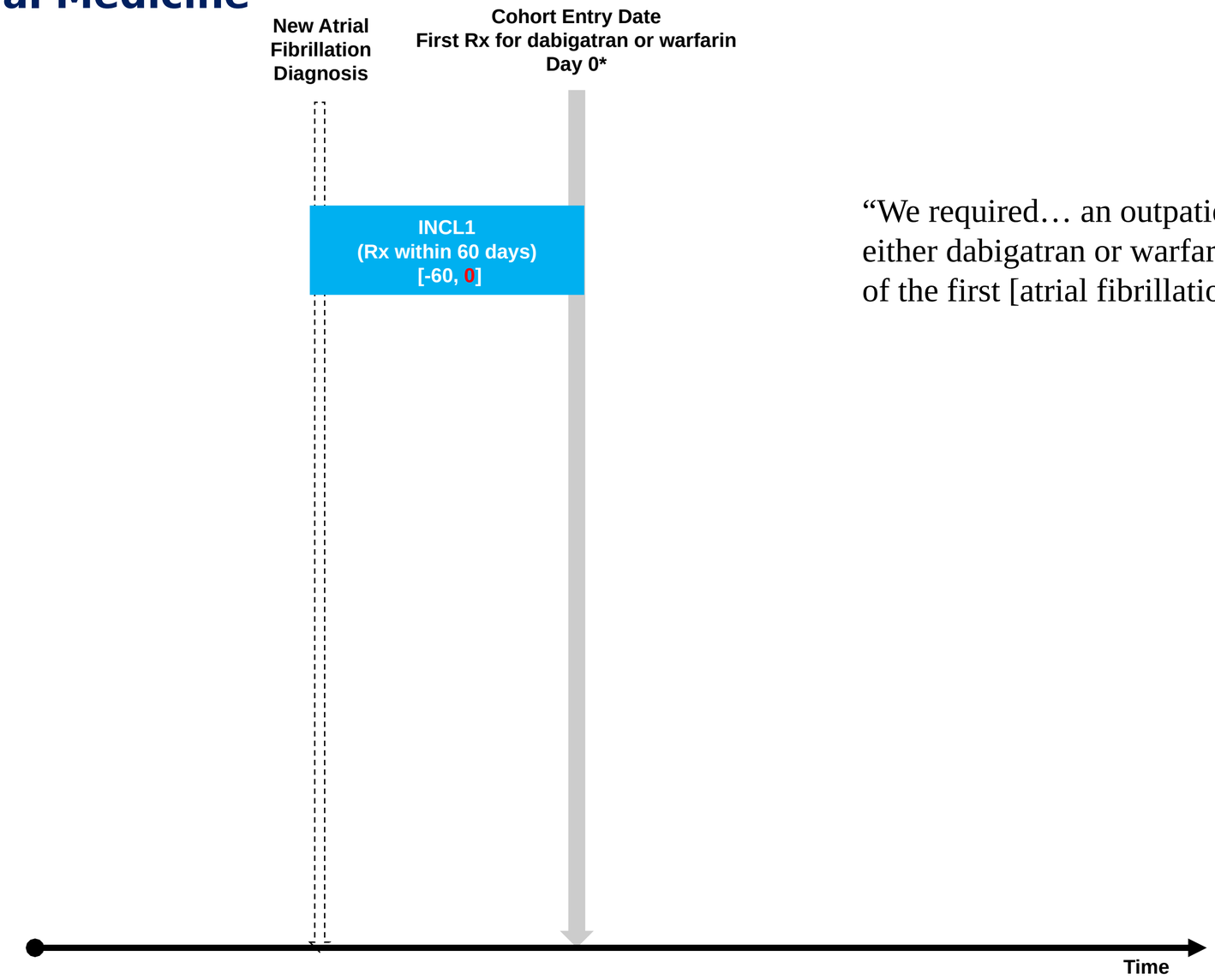

"We required… an outpatient prescription for either dabigatran or warfarin within 2 months of the first [atrial fibrillation] diagnosis."

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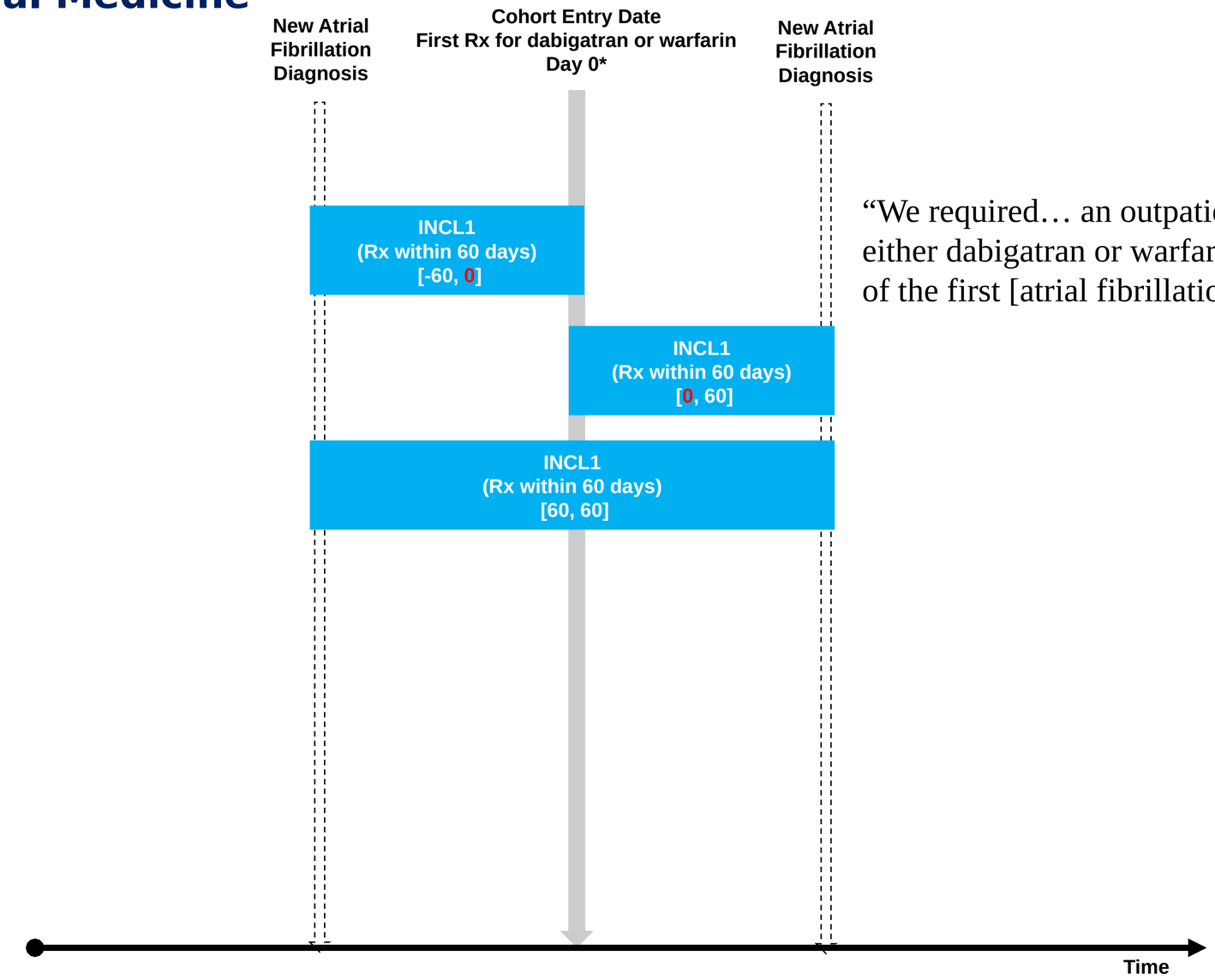

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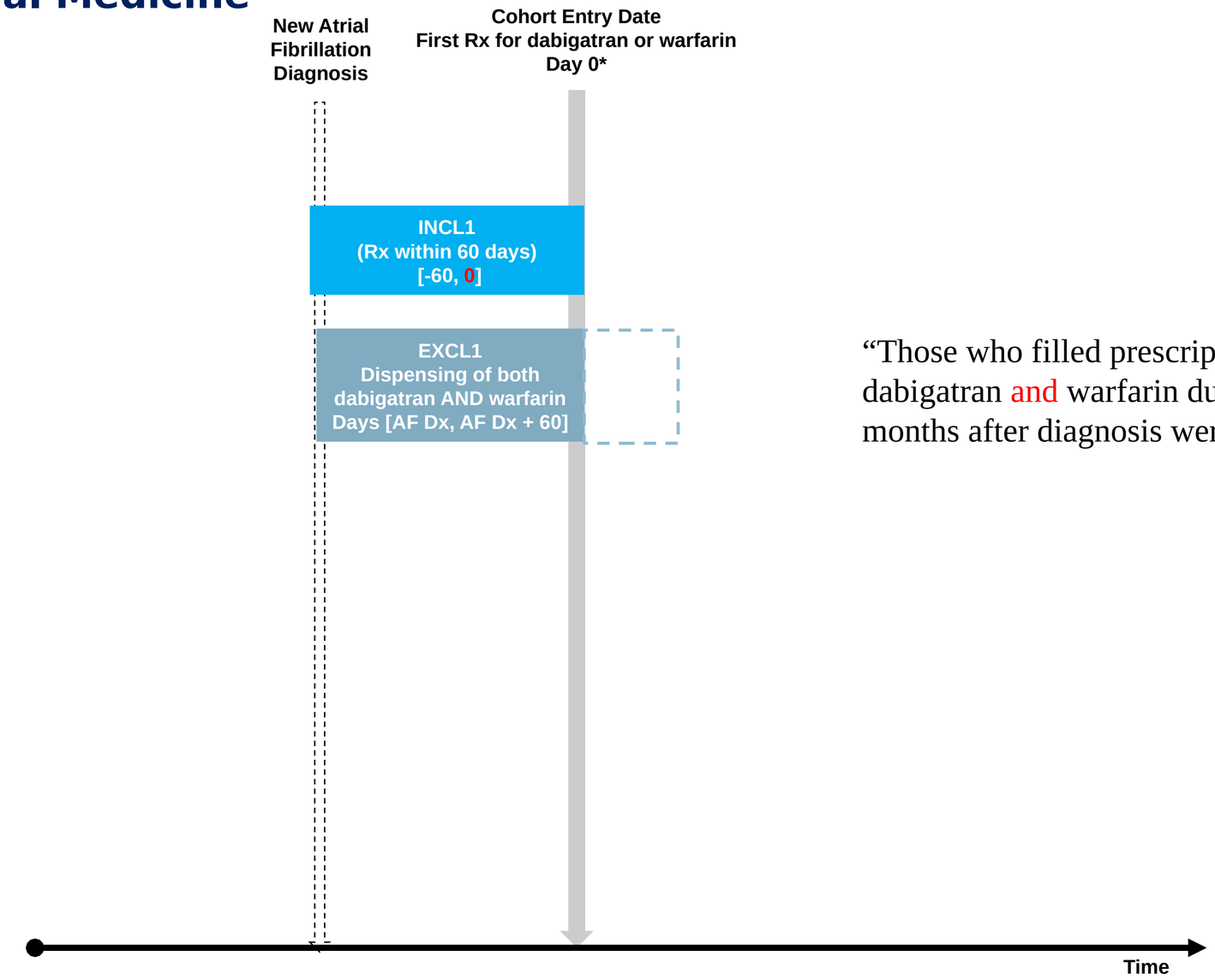

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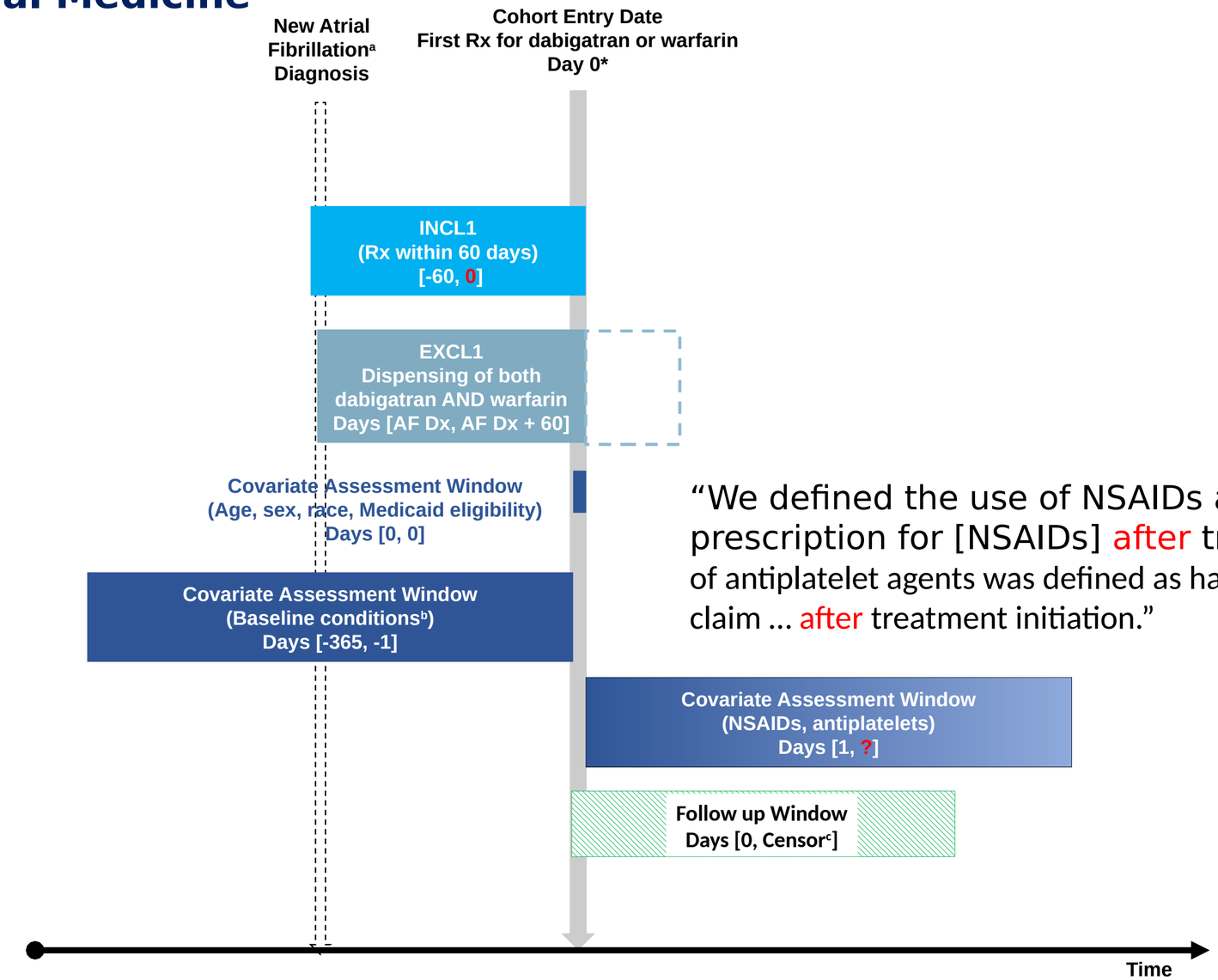

"We defined the use of NSAIDs as having at least one prescription for [NSAIDs] after treatment initiation. Use of antiplatelet agents was defined as having at least one pharmacy claim … after treatment initiation."

a. Atrial Fibrillation (AF) was defined as having 1 inpatient or 2 outpatient claims with primary or secondary diagnosis position of ICD-9 code 427.31.
b. Baseline conditions included: Metastatic cancer, CHADS2 score, Chronic kidney disease, Hypertension, Previous stroke or TIA, Acute MI, Diabetes, Congestive heart failure, Acquired hypothyroidism, History of bleeding, History of hospitalization, # of CMS priority comorbidities categorical, Use of NSAIDs, and Use of antiplatelets.
c. Earliest of: discontinuation of initial drug, switching of study drugs, death, end of study period (12/31/11), disenrollment.

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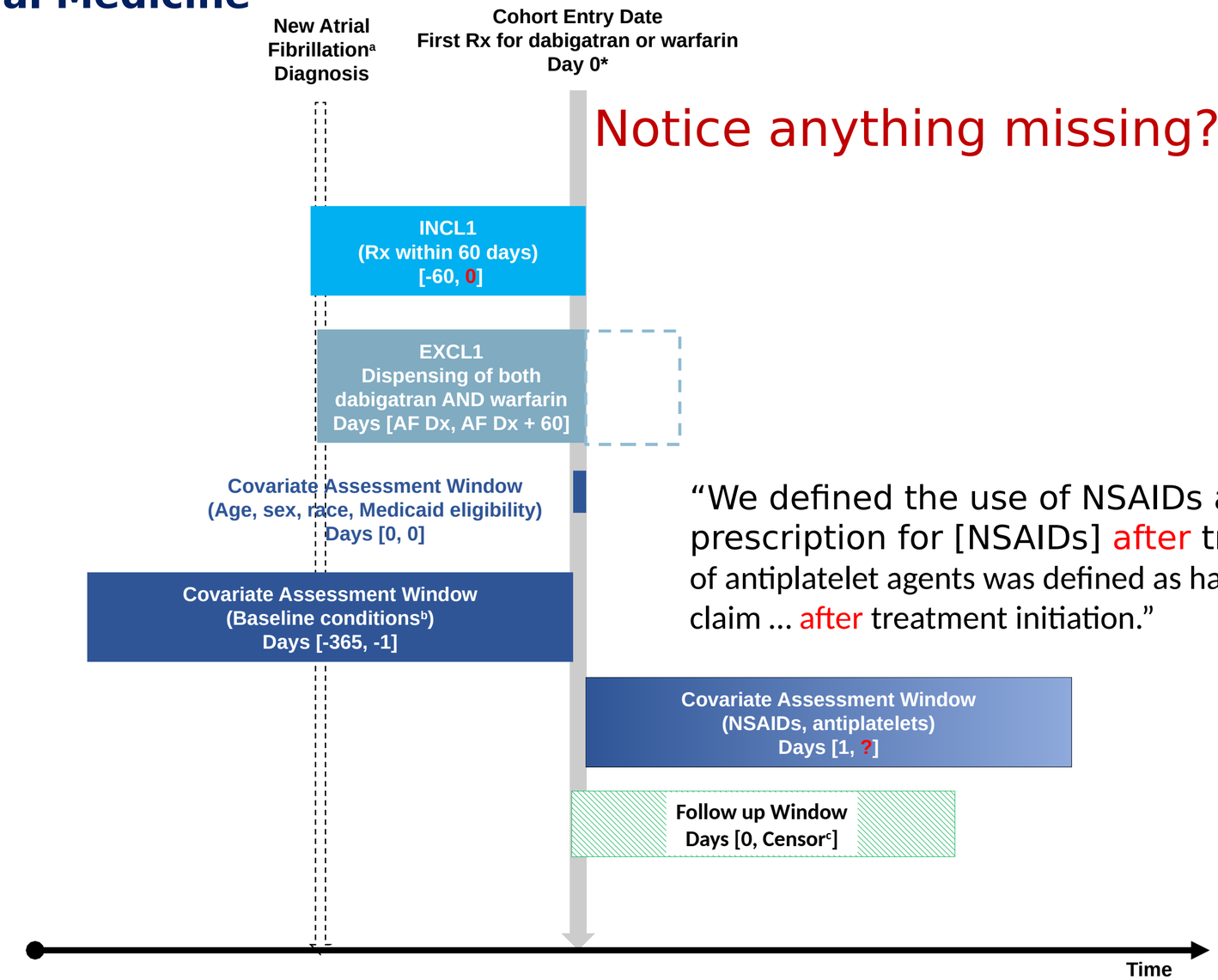

Notice anything missing?

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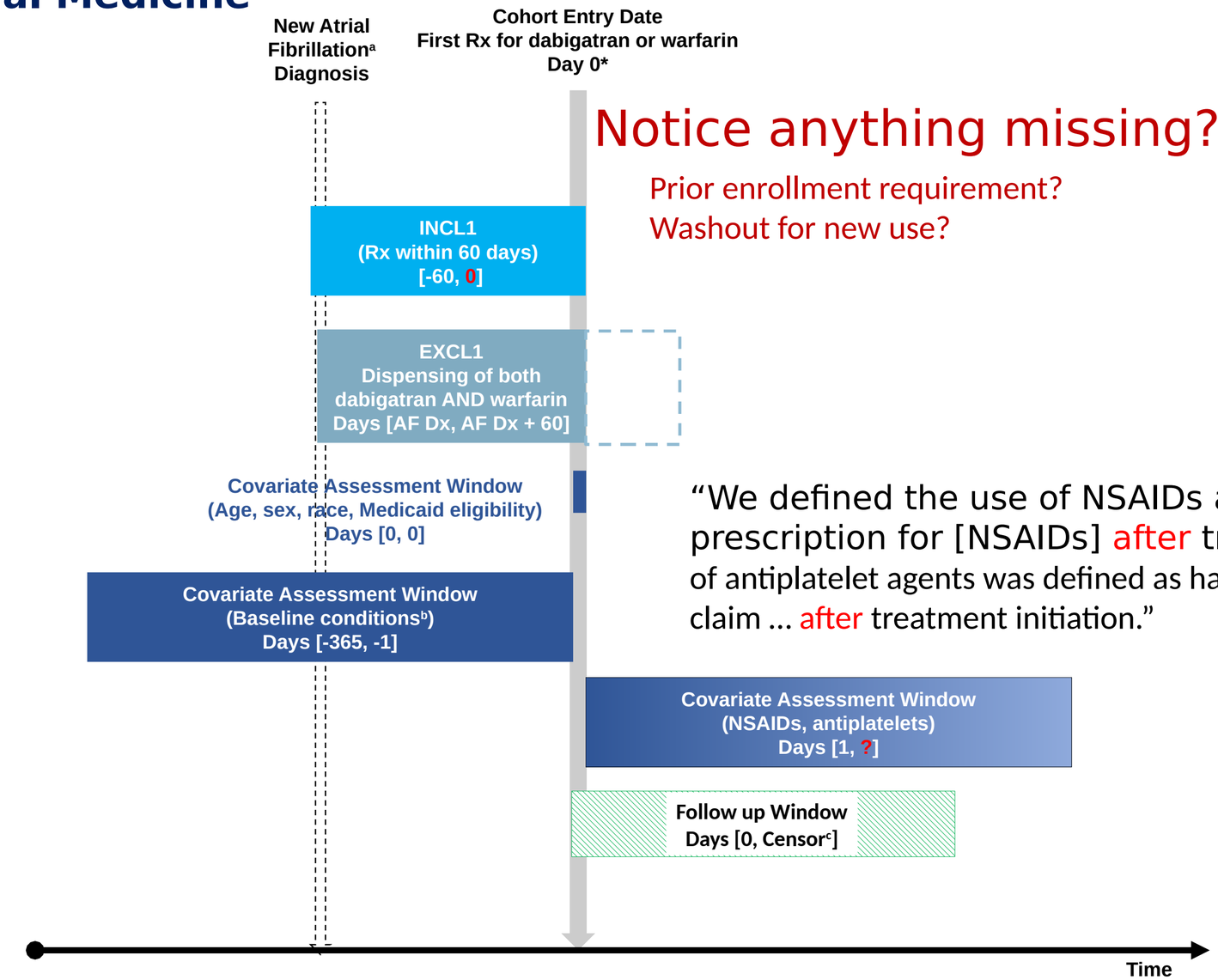

Notice anything missing?

Prior enrollment requirement?
Washout for new use?

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mple from JAMA Internal Medicine

SUMMARY SPECIFICATION FOR ANALYTIC STUDY POPULATION

Example Drug A versus Drug B on risk of Outcome Y

A. Meta-data about data source and software

Study Period:	10/1/2009 - 12/31/2011
Eligible Cohort Entry Period:	10/1/2010 - 10/31/2011
Data Source:	Medicare
Data Extraction Date/Version:	
Data sampling/extraction criteria:	5% random sample of enrollees in data source between January 1, 2010 - Decemeber 31, 2011
Type of data:	Administrative claims
Data linkage:	None
Data conversion:	None
Software to create study population:	

B. Index Date (day 0) defining criterion	**Description**	**Number of entries**	**Type of entry**	**Washout window**	**Incident w.r.t.**	**Index date (day 0)**
Exposure	Dabigatran	Single	Prevalent			Date of incident dispensation
Comparator	Warfarin	Single	Prevalent			Date of incident dispensation

C. Inclusion Criteria	**Description**	**Order of application**	**Assessment window**	**Care Settings[1]**	**Primary Dx**	**Applied to:**
Enrollment/coverage	Medical and drug coverage			n/a	n/a	Exposure, comparator
Max. enrollment gap allowed	N/A					Exposure, comparator
Atrial Fibrillation (AF)	1 inpatient OR 2 outpatient diagnoses	Before selection of index date	[-60, 0]	IP, OP	No	Exposure, comparator

D. Exclusion Criteria	**Description**	**Order of application**	**Assessment window**	**Care Settings[1]**	**Primary Dx**	**Applied to:**
Atrial Fibrillation (AF)	Atrial Fibrillation (AF)	Before selection of index date	[Jan 1 1999, -60]	Any	No	Exposure, comparator
Days supply on index date (Dabigatran/Warfarin)	Days supply > 0 for Dabigatran OR Warfarin	Before selection of index date	[0, 0]	n/a	n/a	Exposure, comparator
Dabigatran AND Warfarin User	Both dispensed within 60 days of new AF diagnosis	After selection of index date	[AF Dx, AF Dx +60]	n/a	n/a	Exposure, comparator

Discussion Questions

Impressions

1) What did you think about the template and user guide, overall?

2) How does this differ or converge with you or your organization's typical process, with respect to technical/statistical analysis protocols and public reporting of methods for a study?

Challenges

3) How would you describe the clarity and usability of the template?

4) Would you anticipate any benefits of developing study protocols or reporting on study implementation using such a template?

5) What are the main challenges you would foresee in using this template as a researcher or a reviewer?

Suggestions

6) Based on the challenges described earlier, how could this template be improved to better fit your use cases?

Adoption

7) How likely would it be for you to use or recommend using the template to others in the future?

8) What strategies would you suggest to widely educate and encourage adoption of use of a structured protocol and reporting template?