Characteristics and Outcomes of Pregnancies in Women with Heart Failure

A Retrospective Cohort Study in the Sentinel System

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Disclosures

- The views expressed in this presentation represent those of the presenters and do not necessarily represent the official views of the U.S. FDA.

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Introduction

- Heart Failure (HF) is relatively rare among women of childbearing age

    - Prevalence (NHANES): 0.2% in 20 to 39 age group; 1.7% in 40 to 59 age group [1]

    - Prevalence (our study in Sentinel): 0.5% among women 15 to 54 years [2]

- Given the significant risk of maternal and fetal complications, pregnancy is rare among women with HF

    - 2.5 to 3.5 live birth deliveries per 1,000 women of childbearing age (i.e., 15-54) with HF per year [2]

- These patients are also difficult to manage because some standard HF treatments are contraindicated during pregnancy [3]

- Little is known about characteristics and outcomes of pregnancies in women with HF

NHANES: National Health and Nutrition Examination Survey
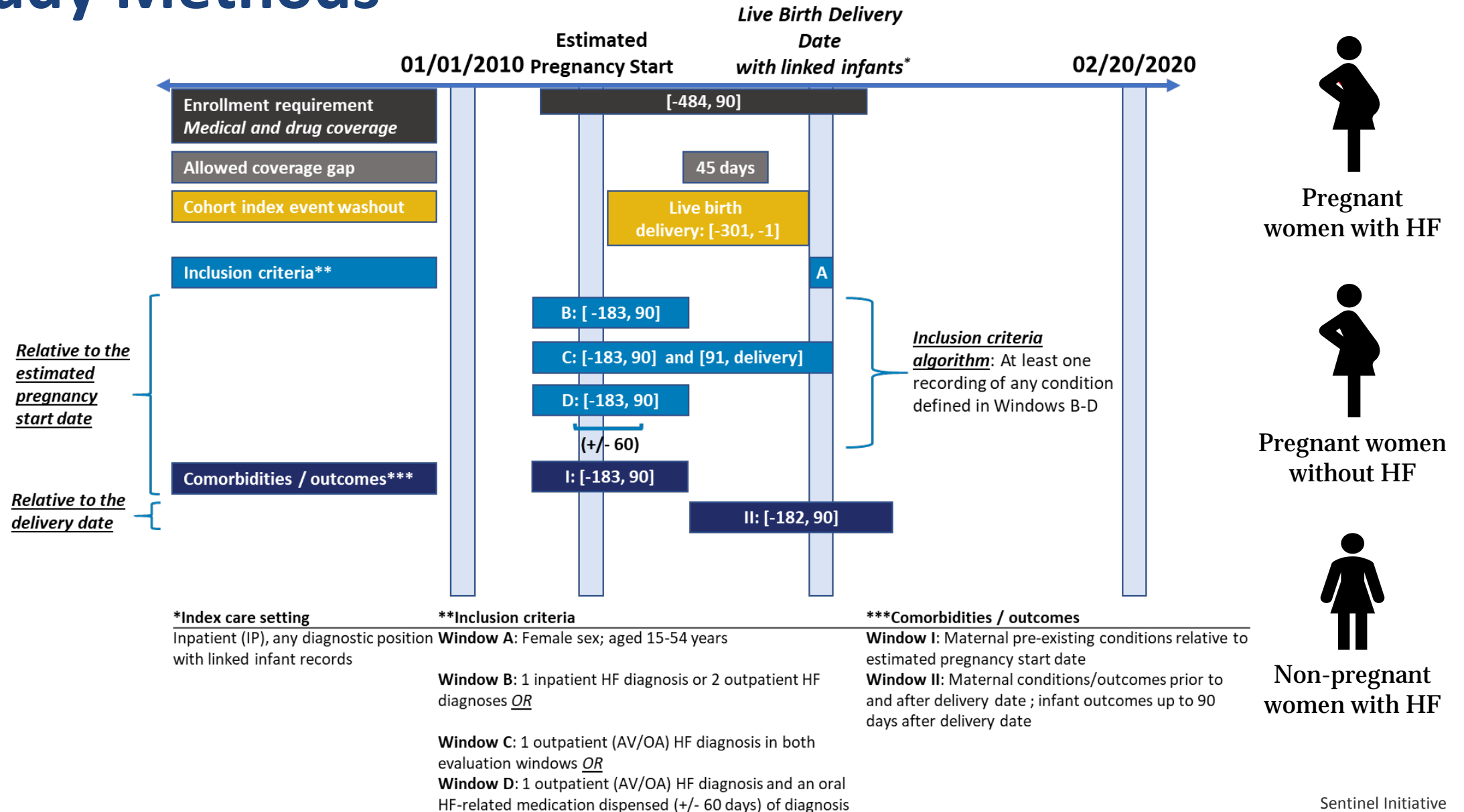1. Mogos et al. Circ Heart Fail. 2018;11(1):e004005.
2. Li et al. ICPE 2021 virtual meeting: Presentation ID: 1716456; Poster #: P-393
3. Regitz-Zagrosek et al. Eur Heart J. 2011;32(24):3147

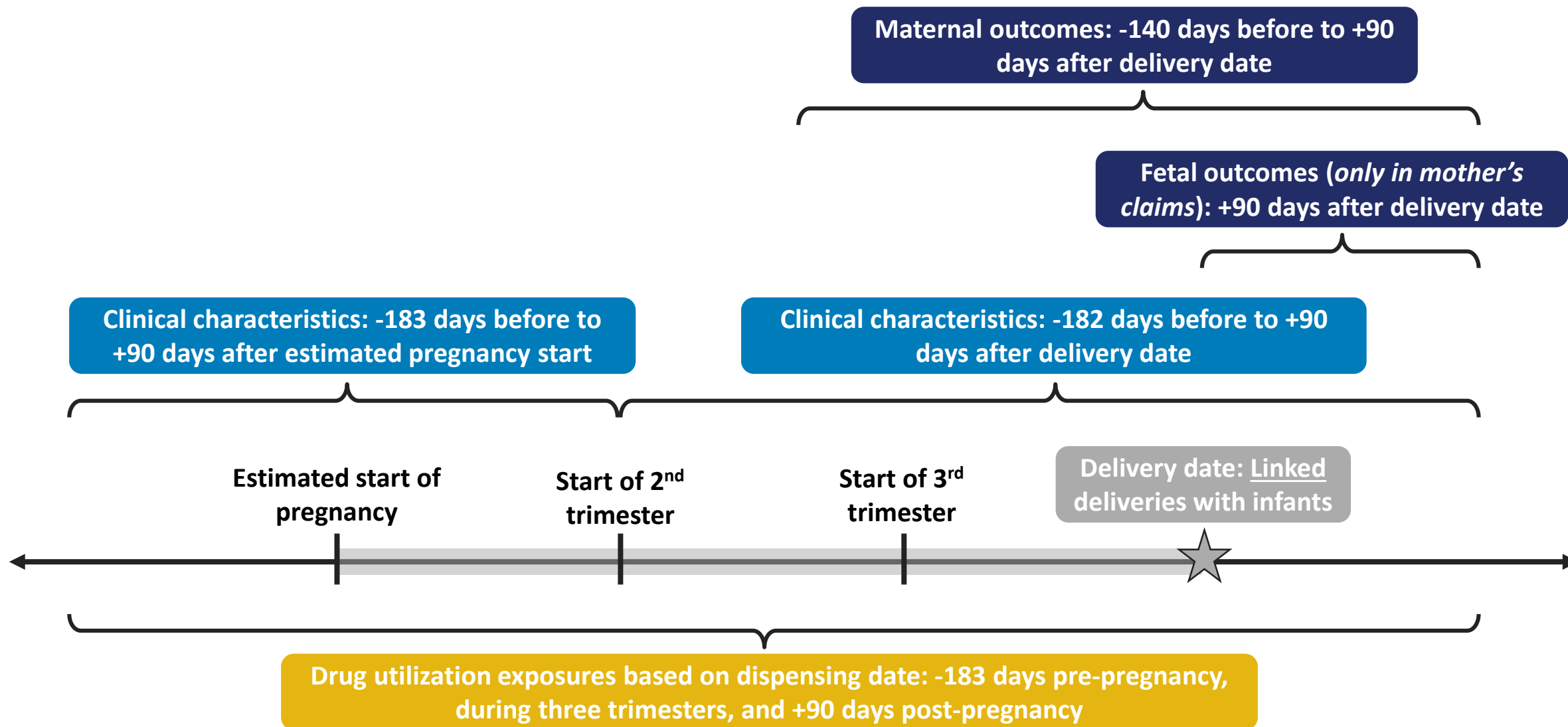# Study Objective and Population

- Describe characteristics, medication use, and outcomes of pregnancies in women with HF

- Pregnant women aged 15 to 54 years with a live birth delivery linked to an infant record were identified in four large claims-based data partners (i.e., three large national insurers and one state Medicaid system) in the FDA's Sentinel System from January 2010 to February 2020

Study Methods

Live Birth Delivery Date with linked infants*

Estimated 01/01/2010 Pregnancy Start

02/20/2020

Enrollment requirement *Medical and drug coverage* — [-484, 90]

Allowed coverage gap — 45 days

Cohort index event washout — Live birth delivery: [-301, -1]

Inclusion criteria*

A

B: [-183, 90]

C: [-183, 90] and [91, delivery]

D: [-183, 90]

(+/- 60)

Inclusion criteria algorithm: At least one recording of any condition defined in Windows B-D

Relative to the estimated pregnancy start date

Comorbidities / outcomes* — I: [-183, 90]

Relative to the delivery date — II: [-182, 90]

Pregnant women with HF

Pregnant women without HF

Non-pregnant women with HF

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*Index care setting
Inpatient (IP), any diagnostic position with linked infant records

**Inclusion criteria
Window A: Female sex; aged 15-54 years

Window B: 1 inpatient HF diagnosis or 2 outpatient HF diagnoses *OR*

Window C: 1 outpatient (AV/OA) HF diagnosis in both evaluation windows *OR*
Window D: 1 outpatient (AV/OA) HF diagnosis and an oral HF-related medication dispensed (+/- 60 days) of diagnosis

***Comorbidities / outcomes
Window I: Maternal pre-existing conditions relative to estimated pregnancy start date
Window II: Maternal conditions/outcomes prior to and after delivery date ; infant outcomes up to 90 days after delivery date

Study Methods

Maternal outcomes: -140 days before to +90 days after delivery date

Fetal outcomes (*only in mother's claims*): +90 days after delivery date

Clinical characteristics: -183 days before to +90 days after estimated pregnancy start

Clinical characteristics: -182 days before to +90 days after delivery date

Estimated start of pregnancy

Start of 2nd trimester

Start of 3rd trimester

Delivery date: <u>Linked</u> deliveries with infants

Drug utilization exposures based on dispensing date: -183 days pre-pregnancy, during three trimesters, and +90 days post-pregnancy

This analysis was designed on Sentinel Query Request Package (QRP) version 10.1.0

Maternal Characteristics and Maternal/Infant Outcomes

- **Comorbidities:**

  - **Maternal pre-existing conditions:** alcohol abuse, cardiac arrhythmia, cardiac valvular disease, cardiomyopathy, chronic kidney disease, congenital heart disease, pre-existing diabetes, drug abuse, preexisting hypertension, ischemic heart disease, overweight or obesity, pulmonary hypertension, rheumatic heart disease, thyroid disease, and tobacco use

  - **Conditions during pregnancy**: gestational diabetes and gestational hypertension

- **HF-related medication use:** ACE inhibitors, aldosterone antagonists, ARBs, ARNIs, beta blockers, digoxin, diuretics, hydralazine and nitrates, and ivabradine

- **Heath service utilization:** mean # of ambulatory encounters, mean # of emergency room encounters, mean # of inpatient hospital encounters, mean # of unique drug classes dispensed, and mean # of unique dispensings

- **Maternal and infant outcomes:** postpartum hemorrhage, preeclampsia, peripartum cardiomyopathy, preterm delivery, cesarean section, small for gestational age, congenital cardiac malformation, and any major malformation.

ACE: angiotensin-converting-enzyme; ARB: Angiotensin II receptor blocker; ARNI: angiotensin receptor neprilysin inhibitor
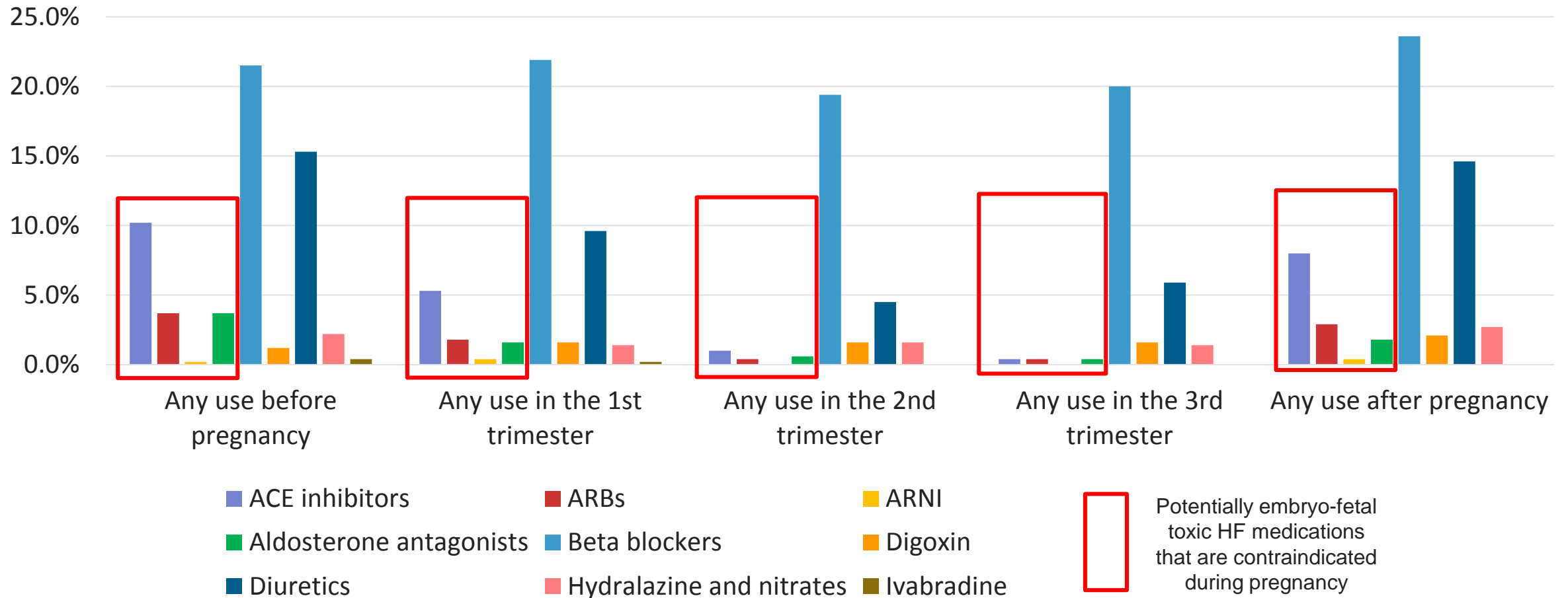
Select demographic and clinical characteristics of pregnant women with HF, non-pregnant women with HF, and pregnant women without HF in the Sentinel System

Characteristics	Pregnant women with HF	Age matched non-pregnant women with HF	Pregnant women without HF
# of pregnancies	489	489	1,245,931
Mean Age	32.4	32.4	31.6
Comorbidities			
Cardiac arrhythmia	22.8%	29.4%	1.0%
Cardiac valvular disease	24.0%	27.4%	0.6%
Cardiomyopathy	21.8%	32.5%	0.0%
Chronic kidney disease	3.1%	11.7%	0.2%
Congenital heart disease	13.1%	10.2%	0.3%
Diabetes (preexisting)	12.3%	21.3%	1.5%
Hypertension (preexisting)	42.5%	57.7%	3.1%
Ischemic heart disease	9.2%	14.5%	0.1%
Overweight or obesity	24.4%	30.3%	5.0%
Rheumatic heart disease	7.4%	8.2%	0.1%
Thyroid disease	20.7%	19.6%	8.4%
Health service utilization			
# of ambulatory encounters	16.4	20.4	8.4
# of unique dispensings	15.1	25.7	6.0

- Comorbidities and health service utilization assessed in the 183 days pre-pregnancy or first trimester

- Women with HF (regardless of pregnancy status) had more comorbidities and used more health services compared with women without HF

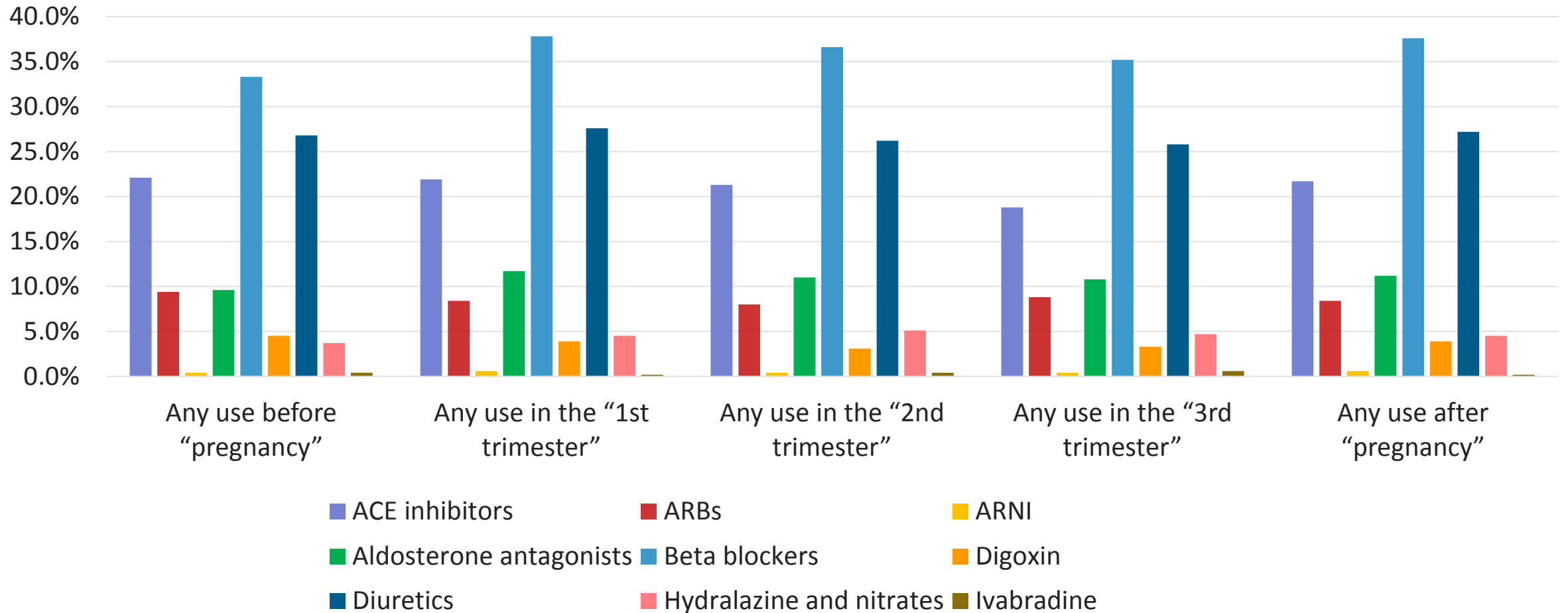- Women with HF who became pregnant were relatively healthier than matched non-pregnant women with HF

Different patterns of HF-related medication use before, during, and after pregnancy among pregnant women with HF

Pregnant women with HF

Legend:
- ACE inhibitors
- ARBs
- ARNI
- Aldosterone antagonists
- Beta blockers
- Digoxin
- Diuretics
- Hydralazine and nitrates
- Ivabradine
- Potentially embryo-fetal toxic HF medications that are contraindicated during pregnancy

X-axis categories: Any use before pregnancy, Any use in the 1st trimester, Any use in the 2nd trimester, Any use in the 3rd trimester, Any use after pregnancy

No change in the use of HF-related medications during the corresponding matched time window among non-pregnant women with HF

Non-pregnant women with HF

ACE inhibitors | ARBs | ARNI
Aldosterone antagonists | Beta blockers | Digoxin
Diuretics | Hydralazine and nitrates | Ivabradine

HF-related medications were infrequently used among pregnant women without HF

Pregnant women without HF
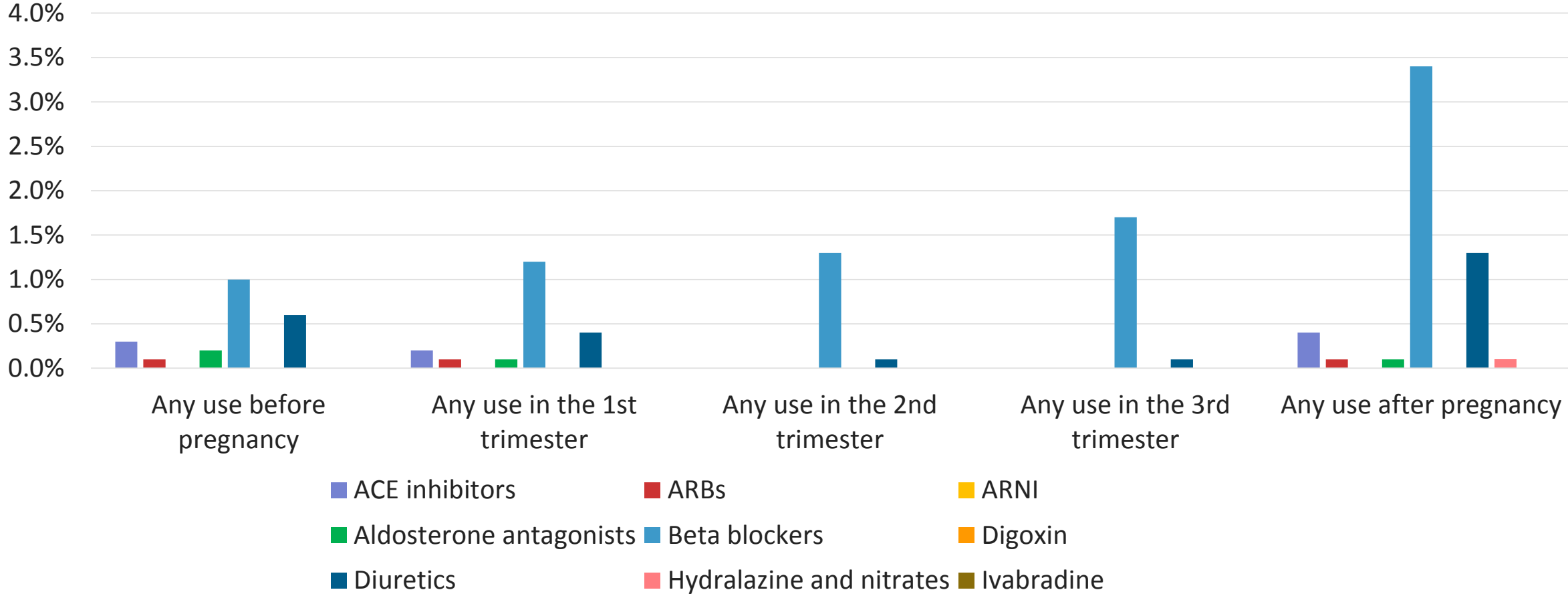
Pregnancies among women with HF had more adverse maternal and infant outcomes

	Pregnancies among women with HF (N = 489 pregnancies)		Pregnancies among women without HF (N = 1,076,117 pregnancies)	
	N	%	N	%
Maternal outcomes[1]				
Preeclampsia	73	15.0%	66,966	6.2%
Peripartum cardiomyopathy	43	8.8%	1,041	0.1%
Postpartum hemorrhage	22	4.5%	33,236	3.1%
Preterm delivery	62	12.7%	56,504	5.3%
Multiple gestation	< 5	N/A	934	0.1%
Cesarean section	175	35.9%	272,625	25.3%
Infant outcomes[2,3]				
Small for gestational age (SGA)	8	1.6%	18,998	1.8%
Congenital cardiac malformation	7	1.4%	726	0.1%
Ventricular septal defect	0	0.0%	7	< 0.1%
Right ventricular outflow tract obstruction	0	0.0%	< 5	< 0.1%
Other cardiac malformation	7	1.4%	721	0.1%
Any major malformation	8	1.6%	2,878	0.3%

1. Maternal outcomes including preeclampsia were assessed in [-140, 30], peripartum cardiomyopathy [-140, 90], preterm delivery [-30, 30], multiple gestation and cesarean section on date of delivery.
2. Infant outcomes including SGA were assessed in [0, 30], and congenital cardiac malformation and any major malformation [0, 90] relative to delivery date.
3. Infant outcomes were only ascertained from mother's claims

Study Limitations

- Only captured pregnancies ending in live birth deliveries

- "Naïve" comparison between pregnancies in women with and without HF

- Misclassification of cases, medication use, and outcomes

  - Infant outcomes were only ascertained from mother's claims

Conclusion

- Among women with HF, exposure to potentially embryo-toxic HF medications during pregnancy was rare

- Pregnancies in women with HF seemed to have higher frequencies of adverse maternal outcomes and major fetal malformations, especially major cardiac malformations, when compared to pregnancies in women without HF

Thank you for your attention !

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