Utilization of laboratory results data to enhance pregnancy cohort identification in a distributed data network

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BACKGROUND

- **Pregnancy laboratory result values could improve the identification of pregnancies**
- Defining the beginning of pregnancy is important for proper classification of exposure to therapy throughout the duration of pregnancy and pregnancy laboratory results have the potential to refine the estimated start of pregnancy
  - Several algorithms exist to estimate the beginning of pregnancy in databases
  - Most of these methods seek to define the beginning of pregnancy in live births often estimating gestation with a fixed duration of 270-280 days
  - Other methods estimate the beginning of pregnancy based on the first prenatal visit or other early administrative pregnancy markers
  - Gestational age has been estimated from birth weight using growth charts
- We sought to utilize pregnancy lab results to close the gap in knowledge of determining the best method for identifying pregnancies and estimation of gestational age in administrative data

OBJECTIVES

- **To determine the utility of available pregnancy laboratory result values to enhance cohort identification of pregnant women**, including women who may not have delivered a live born infant
- In women with a live born delivery we compared the estimated gestational length with lab result values to a 270 day gestational age metric to determine whether pregnancy labs were more effective in identifying gestational age
- Assessed whether positive pregnancy laboratory result values in live birth deliveries occurred within the initial 90 days of the 270 day gestational age metric

METHODS

Study design

- Retrospective cohort study

Data source

- Three representative data partner sites from Mini-Sentinel were selected from the 12 that contribute Mini-Sentinel Distributed Database laboratory result values.
  - Small integrated delivery system (site 1)
  - Larger integrated delivery system (site 2)
  - Large national insurer (site 3)

Study population

- Females between the ages of 14 and 50 with medical and drug coverage with enrollment between January 1, 2008 and December 31, 2013
- Included only the first qualifying pregnancy for each woman in the analysis
- Index date: first indication of pregnancy based on earliest date of a positive pregnancy laboratory result value, prenatal care visit or procedure, and/or prenatal pregnancy diagnosis code or procedure code

Outcomes

1. Live born delivery (term, preterm using categories available from diagnosis codes)
2. Pregnancy loss (ectopic and other extra-uterine, fetal death, stillborn, miscarriage, and therapeutic/elective abortion)
3. Disenrollment, death, end of study timeframe
4. No end of pregnancy indicator found in the dataset

Covariate definitions

- Age at index date
- Year of cohort entry
- Medical utilization categorized as separate indicator variables and as a count of outpatient encounters during the 183 days prior to the index date.
  - Emergency department visit
  - Hospitalization
  - Non-acute institutional stay

Statistical analysis

- For a pregnancy that included a pregnancy lab result value, we described the mean, median, and range of the number of pregnancy lab results per woman
- Determined if the presence of the first pregnancy lab result value would have changed the timing of when a pregnancy was first identified in electronic data among women with live born deliveries whose pregnancies were indicated by both diagnosis or procedure codes and lab result
- Calculated the proportion of women who would have had a pregnancy identified earlier using the pregnancy lab result and estimated the “lead time” gained
- Determined the proportion of women who would have had a pregnancy identified earlier using codes and summarized the “lead time” gained by using the coded information vs. the positive lab result
- Compared gestational age calculations from method that uses the delivery date minus 270 days to approach using lab result plus codes and codes alone
- Among women with a pregnancy lab result, we further characterized the first trimester as the initial 90 days as defined by the 270 day gestational age and determined the number of women with only a pregnancy lab result, only a code, or both pregnancy lab result and codes in the first trimester

RESULTS

- 268,219 patients contributed a pregnancy to the analysis
- Variability in availability of result values and pregnancy outcomes across data partners
- Only 5.1% had a positive pregnancy result value without any pregnancy-related code
- Availability of at least one pregnancy result value varied across sites from 22.3% at the large health insurer site to 67.9% at the smaller integrated delivery system site
- For women whose first indicator of pregnancy was the lab result value, the vast majority (98.1%) fell within the 270 day gestational age metric

Figure 1: Cohort Identification

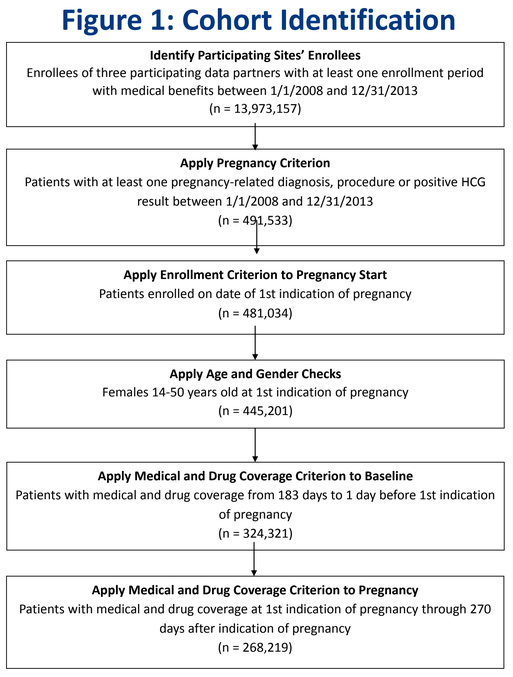

Table 1: Characteristics of the Pregnancy Cohort Overall and by Site

Characteristic	Total, N (%)	Data Partner Site, N (%)		
		Site 1	Site 2	Site 3
Number of women	268,219	24,649	187,471	56,099
Age in years, mean (SD)	30.5 (7.1)	29.7 (6.7)	30.7 (7.3)	30.3 (6.5)
Pregnancy outcome [b]				
Single live birth: Term	157,076 (58.6)	15,060 (61.1)	107,675 (57.4)	34,341 (61.2)
Single live birth: Preterm	10,261 (3.8)	974 (4.0)	6,796 (3.6)	2,491 (4.4)
Multiple births	4,027 (1.5)	386 (1.6)	2,614 (1.4)	1,027 (1.8)
Abortion	21,357 (8.0)	1,127 (4.6)	19,991 (10.7)	239 (0.4)
Miscarriage	29,899 (11.1)	2,637 (10.7)	20,696 (11.0)	6,566 (11.7)
Fetal death	2,006 (0.7)	214 (0.9)	1,440 (0.8)	352 (0.6)
Extra-uterine	3,146 (1.2)	240 (1.0)	2,127 (1.1)	779 (1.4)
Abnormal conception outcome [c]	2,083 (0.8)	195 (0.8)	1,252 (0.7)	636 (1.1)
Outcome not found	38,364 (14.3)	3,816 (15.5)	24,880 (13.3)	9,668 (17.2)
Reason outcome not found				
Death	7 (0.0)	0 (0.0)	4 (0.0)	3 (0.0)
End of study (estimated due date beyond 12/31/2013)	14,287 (5.3)	1,603 (6.5)	10,015 (5.3)	2,669 (4.8)
Unknown	24,070 (9.0)	2,213 (9.0)	14,861 (7.9)	6,996 (12.5)
Pregnancy Identification by Pregnancy Indicator				
Prenatal diagnosis or procedure only	125,240 (46.7)	7,515 (30.5)	76,554 (40.8)	41,171 (73.4)
Pregnancy outcome only	23,741 (8.9)	1,922 (7.8)	18,092 (9.7)	3,727 (6.6)
Qualitative or Quantitative HCG lab result value [e]				
No HCG lab result	127,613 (47.6)	7,919 (32.1)	76,108 (40.6)	43,586 (77.7)
Only negative HCG lab result	21,368 (8.0)	1,518 (6.2)	18,538 (9.9)	1,312 (2.3)
1+ Positive HCG lab result; women with lab result and no pregnancy diagnosis	13,665 (5.1)	679 (2.8)	12,582 (6.7)	404 (0.7)
1+ Positive HCG lab result; women with diagnosis and lab result	105,573 (39.4)	14,533 (59.0)	80,243 (42.8)	10,797 (19.2)
Qualitative HCG lab				
No Qualitative HCG lab result	175,406 (65.4)	15,535 (63.0)	105,342 (56.2)	54,529 (97.2)
Only negative Qualitative HCG lab result	22,882 (8.5)	2,884 (11.7)	19,312 (10.3)	686 (1.2)
1+ Positive Qualitative HCG lab; women with lab result and no pregnancy diagnosis	10,213 (3.8)	420 (1.7)	9,692 (5.2)	101 (0.2)
1+ Positive Qualitative HCG lab; women with pregnancy diagnosis and lab result	59,718 (22.3)	5,810 (23.6)	53,125 (28.3)	783 (1.4)
Quantitative HCG lab [d]				
No Quantitative HCG lab result	190,236 (70.9)	11,091 (45.0)	134,599 (71.8)	44,546 (79.4)
Only negative Quantitative HCG lab result	9,443 (3.5)	412 (1.7)	8,153 (4.3)	878 (1.6)
1+ Positive Quantitative HCG lab; women with lab results and no pregnancy diagnosis	4,604 (1.7)	361 (1.5)	3,921 (2.1)	322 (0.6)
1+ Positive Quantitative HCG lab result; women with pregnancy diagnosis and lab result	63,936 (23.8)	12,785 (51.9)	40,798 (21.8)	10,353 (18.5)
Medical Utilization [f]				
Ambulatory visits, mean (SD)	6.4 (7.1)	6.6 (7.5)	6.6 (7.2)	5.7 (6.5)
Emergency department visit, % yes	31,408 (11.7)	2,534 (10.3)	22,541 (12.0)	6,333 (11.3)
Hospitalization, % yes	10,398 (3.9)	668 (2.7)	8,373 (4.5)	1,357 (2.4)
Institutional stay, % yes	1,399 (0.5)	2 (0.0)	57 (0.0)	1,340 (2.4)
HCG injections	6,037 (2.3)	570 (2.3)	5,288 (2.8)	179 (0.3)
Tumor that may influence HCG	1,769 (0.7)	77 (0.3)	1,413 (0.8)	279 (0.5)

[a] Women included in the cohort have enrollment in the health plan for at least 183 days prior to the cohort entry date and 270 days after the cohort entry date. Cohort entry date is the date of first indicator of pregnancy (i.e., diagnosis code, procedure code, or laboratory test result)
[b] Within 270 days after the cohort entry date
[c] ICD9 codes 630, 631 (i.e. Hydatidiform mole or other abnormal products of conception)
[e] Quantitative lab considered positive if >25 mIU/mL
[f] Within 183 days prior to earliest pregnancy indication

Table 2: Characteristics of the Pregnancy Cohort by Pregnancy Outcome

Characteristic	Total N = 268,219 (100%)	Single Live Birth		Multiple births N = 4,027 (1.5%)	Pregnancy Loss					Outcome not found N = 38,364 (14.3%)
		Term N = 157,076 (58.6%)	Preterm N = 10,261 (3.8%)		Abortion N = 21,357 (8.0%)	Miscarriage N = 29,899 (11.1%)	Fetal death N = 2,006 (0.7%)	Extra-uterine N = 3,146 (1.2%)	Abnormal conception [b] N = 2,083 (0.8%)	
Age in years, mean (SD)	30.5 (7.1)	30.5 (6.7)	29.8 (6.2)	31.9 (5.7)	27.3 (7.8)	31.6 (6.8)	31.4 (6.4)	34.0 (7.8)	31.6 (7.1)	31.1 (8.0)
Qualitative (QL) or Quantitative (QN) HCG lab result [c]										
No HCG lab result	127,613 (47.6)	83,690 (53.3)	5,282 (51.5)	1,966 (48.8)	5,803 (27.2)	9,737 (32.6)	829 (41.3)	1,098 (34.9)	628 (30.1)	18,580 (48.4)
Only negative HCG lab result	21,368 (8.0)	12,741 (8.1)	358 (3.5)	107 (2.7)	743 (3.5)	1,742 (5.8)	74 (3.7)	857 (27.2)	75 (3.6)	4,671 (12.2)
≥ 1 Positive HCG lab; women with lab result and no pregnancy dx	13,665 (5.1)	28 (0.0)	107 (1.0)	0 (0.0)	6,953 (32.6)	3,014 (10.1)	16 (0.8)	274 (8.7)	192 (9.2)	3,081 (8.0)
N of labs, mean (SD)	1.3 (0.8)	1.2 (0.4)	1.1 (0.4)	0	1.1 (0.3)	1.5 (0.9)	1.6 (1.1)	1.9 (1.4)	1.6 (1.0)	1.5 (1.3)
≥ 1 Positive HCG lab; women with PG diagnosis and lab result	105,573 (39.4)	60,617 (38.6)	4,514 (44.0)	1,954 (48.5)	7,858 (36.8)	15,406 (51.5)	1,087 (54.2)	917 (29.1)	1,188 (57.0)	12,032 (31.4)
N of labs, mean (SD)	1.8 (1.3)	1.5 (0.9)	1.7 (1.1)	2.0 (1.2)	1.5 (1.1)	2.4 (1.5)	2.1 (1.8)	4.5 (3.0)	3.0 (2.0)	2.2 (1.9)
QL HCG lab result										
No QL HCG lab	175,406 (65.4)	107,961 (68.7)	7,056 (68.8)	3,073 (76.3)	7,664 (35.9)	19,066 (63.8)	1,265 (63.1)	1,944 (61.8)	1,393 (66.9)	25,984 (67.7)
Only negative QL HCG lab	22,882 (8.5)	13,873 (8.8)	577 (5.6)	289 (7.2)	987 (4.6)	2,129 (7.1)	135 (6.7)	765 (24.3)	168 (8.1)	3,959 (10.3)
≥ 1 Positive QL HCG lab; women with lab result only	10,213 (3.8)	11 (0.0)	26 (0.3)	0 (0.0)	6,554 (30.7)	1,283 (4.3)	12 (0.6)	113 (3.6)	51 (2.4)	2,163 (5.6)
N of labs, mean (SD)	1.0 (0.2)	1.0 (0.0)	1.0 (0.2)	. (.)	1.0 (0.1)	1.0 (0.2)	1.1 (0.3)	1.1 (0.4)	1.0 (0.2)	1.0 (0.2)
≥ 1 Positive QL HCG lab; women with diagnosis and lab result	59,718 (22.3)	35,231 (22.4)	2,602 (25.4)	665 (16.5)	6,152 (28.8)	7,421 (24.8)	594 (29.6)	324 (10.3)	471 (22.6)	6,258 (16.3)
N of labs, mean (SD)	1.0 (0.2)	1.0 (0.2)	1.1 (0.2)	1.0 (0.3)	1.1 (0.2)	1.1 (0.2)	1.1 (0.3)	1.1 (0.4)	1.1 (0.3)	1.1 (0.2)
QN HCG lab result [c]										
No QN HCG lab	190,236 (70.9)	119,644 (76.2)	7,341 (71.5)	2,467 (61.3)	17,313 (81.1)	13,623 (45.6)	1,253 (62.5)	1,680 (53.4)	738 (35.4)	26,177 (68.2)
Only negative QN HCG lab	9,443 (3.5)	3,775 (2.4)	153 (1.5)	57 (1.4)	452 (2.1)	1,533 (5.1)	23 (1.1)	306 (9.7)	61 (2.9)	3,083 (8.0)
≥ 1 Positive QN HCG; women with lab result and no PG dx	4,604 (1.7)	19 (0.0)	88 (0.9)	0 (0.0)	590 (2.8)	2,307 (7.7)	6 (0.3)	263 (8.4)	179 (8.6)	1,152 (3.0)
N of labs, mean (SD)	1.5 (1.2)	1.2 (0.4)	1.0 (0.2)	. (.)	1.3 (0.8)	1.3 (0.8)	2.2 (1.6)	1.5 (1.2)	1.4 (0.9)	2.1 (1.7)
≥ 1 Positive QN HCG; women with PG dx and lab results	63,936 (23.8)	33,638 (21.4)	2,679 (26.1)	1,503 (37.3)	3,002 (14.1)	12,436 (41.6)	724 (36.1)	897 (28.5)	1,105 (53.0)	7,952 (20.7)
N of labs, mean (SD)	2.0 (1.4)	1.7 (1.0)	1.9 (1.1)	2.2 (1.1)	1.9 (1.4)	2.4 (1.4)	2.3 (1.9)	4.2 (2.9)	2.8 (1.9)	2.4 (2.1)
HCG injections	6,037 (2.3)	2,178 (1.4)	183 (1.8)	505 (12.5)	82 (0.4)	1,256 (4.2)	81 (4.0)	130 (4.1)	102 (4.9)	1,520 (4.0)
Tumor that may influence HCG	1,769 (0.7)	951 (0.6)	44 (0.4)	19 (0.5)	50 (0.2)	98 (0.3)	5 (0.2)	304 (9.7)	20 (1.0)	278 (0.7)

[a] Within 270 days after the cohort entry date
[b] ICD9 codes 630, 631 (i.e. Hydatidiform mole or other abnormal products of conception)
[c] Quantitative lab considered positive if >25 mIU/mL

Table 3: Number and Percent of Pregnancies Identified by HCG Lab Results Only, Stratified by End of Pregnancy Indicator, Overall and by Site

End of Pregnancy Indicator	Number with Prenatal Positive Lab Result Only divided by Total Number with that End of Pregnancy Indicator (%)			
	Total, N (%)	Data Partner Site, N (%)		
		Site 1	Site 2	Site 3
Term single live births	28/157,076 (0.0)	6/15,060 (0.0)	18/107,675 (0.0)	4/34,341 (0.0)
Preterm single live births	107/10,261 (1.0)	7/974 (0.7)	97/6,796 (1.4)	3/2,491 (0.1)
Abortions	6,953/21,357 (32.6)	73/1,127 (6.5)	6,877/19,991 (34.4)	3/239 (1.3)
Miscarriages	3,014/29,899 (10.1)	226/2,637 (8.6)	2,649/20,696 (12.8)	139/6,566 (2.1)
Fetal deaths	16/2,006 (0.8)	0/214 (0.0)	16/1,440 (1.1)	0/352 (0.0)
Extra-uterine pregnancies	274/3,146 (8.7)	27/240 (11.3)	215/2,127 (10.1)	32/779 (4.1)
Abnormal product of conception	192/2,083 (9.2)	32/195 (16.4)	147/1,252 (11.7)	13/636 (2.0)
Multiple births	0/4,027 (0.0)	0/386 (0.0)	0/2,614 (0.0)	0/1,027 (0.0)
End of pregnancy indicator not found	3,081/38,364 (8.0)	308/3,816 (8.1)	2.563/24,880 (10.3)	210/9,668 (2.2)
Total	13,665	679	12,582	404

Table 4. First Pregnancy Indicator among Pregnancies with Prenatal Positive Lab Result and Prenatal Code and Single Live Birth Outcome Code, Overall and by Site

Pregnancy Indicator	Total, N = 65,131 (%)	Data Partner Site		
		Site 1 N =10,395 (%)	Site 2 N = 46,824 (%)	Site 3 N = 7,912 (%)
Positive lab result occurs before diagnosis/procedure code	39,559 (60.7)	3,433 (33.0)	34,596 (73.9)	1,530 (19.3)
Positive lab result occurs on the same day as the diagnosis/procedure code	12,742 (19.6)	1,548 (14.9)	9,413 (20.1)	1,781 (22.5)
Positive lab result occurs after diagnosis/procedure code	12,830 (19.7)	5,414 (52.1)	2,815 (6.0)	4,601 (58.2)

- Among women with both a positive lab and a code who delivered a single live birth, 60.7% (39,559/65,131) had their pregnancy identified earlier using the lab result value, the result value preceded the coded diagnosis by a mean (SD) of 15.7 (12.2) days

CONCLUSION

- The majority of pregnancies were identified with a prenatal diagnosis or procedure code with or without a positive lab result (39.4% and 46.7%, respectively). Five percent of the cohort had no pregnancy-related code in the dataset and were identified by positive lab result value.
- Among the pregnancies ending in elective abortion or miscarriage as identified by codes, one third of the abortions and 10% of the miscarriages had no earlier evidence of pregnancy in the administrative data except a positive laboratory result value.
- There is the potential for using pregnancy lab data to refine conception estimates.