



GT Masters in Computer Science

- Georgia Tech has the largest Computer
 Science graduate program in the US
- In 2014, GT started the Online Master's in Computer Science (OMSCS)
 - OMSCS degree costs \$7K vs ~\$40K on-campus













CS6440: Intro to Health Informatics

- Broad introduction to EHRs, the US healthcare system, healthcare quality, healthcare data and vocabularies
 - Started by Dr. Mark Braunstein in 2012
 - Taught in OMSCS and on-campus
 - Strong focus on FHIR and Interoperability
- Student majors 85% Comp Sci and remainder including biomedical engineering, HCI, bioinformatics, industrial engineering



OHDSI in CS6440

- I took over the class in 2018
 - Decided to add an OHDSI block for Fall 2019 semester
- NB: GT has a more 'hardcore' health data analytics course taught by Dr. Jimeng Sun



Big Data for Healthcare

CSE6250 Prerequisites

- 1. Good machine learning and data mining concepts such as classification and clustering;
- 2. Proficient programming and system skills in Scala, Python and Java;
- 3. Proficient knowledge and experience in dealing with data and understand the ETL process(recommended skills include SQL, NoSQL such as MongoDB).



CS6440 Fall 2019

- People
 - 386 students
 - 14 TAs
 - Me
- Course Educational Infrastructure
 - Canvas (assignments, submissions)
 - Udacity (lectures)
 - Youtube (lectures)
 - Piazza (forum)
 - Slack



Goals of the OHDSI Block

- Learn the kinds of questions people ask using observational data (the OHDSI trinity)
- Get hands-on experience using the OHDSI
 framework to answer a question of your own
- Get excited about the possibilities of how health data can be used in FHIR application development (second part of the course)



Non-Goals of the OHDSI Block

- Become an expert in medicine / epi / stats / clinical research
- OHDSI best practices, conventions, ETL design, etc



Components of the Analytics Block

- Data Standards lectures and activities
- OHDSI Labs (slides, videos, exercises)
 - Intro
 - Lab I: Concept Set Design
 - Lab II: Cohort Design and Characterization
 - Lab III: Incidence Rates and Estimation Study
- Individual Health Analytics Project
 - Proposal, Design, Execution, Report



Examples from Lab

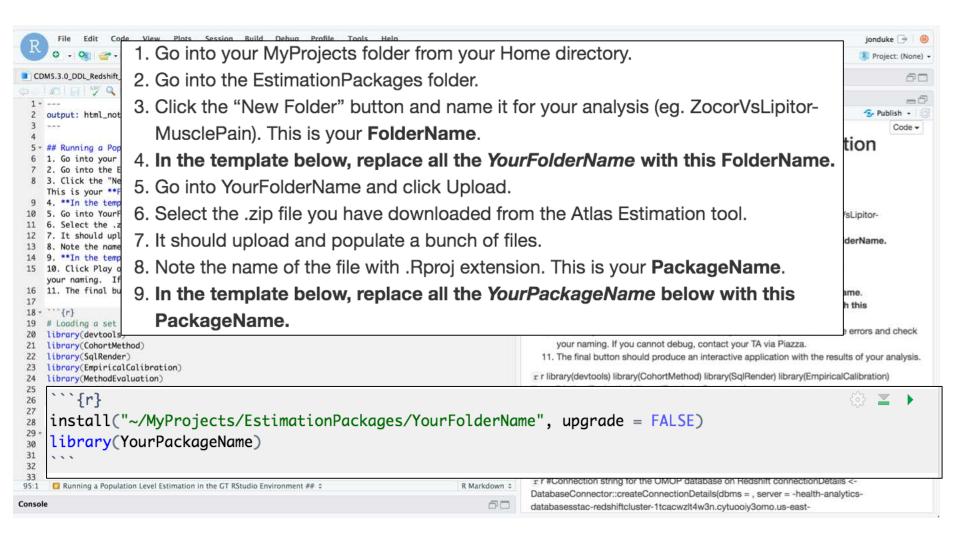
Here's the classic paper

Exercise 2.1

- Log into the GT Instance of Atlas
 - Go to the Incidence Rates function
 - Target Cohorts
 - [Lab II] Hyperlipidemia Used Statin (Target)
 - [Lab II] Hyperlipidemia Never Used Statin (Target)
 - Outcome Cohort
 - [Lab II] Dementia Patients
 - [vourUserName] Muscle Pain Patients
 - Set *Time at Risk* to Starts with Start Date plus 0 days and Ends with Start Date plus 9999 days
 - Save your analysis in the format [vourID] Statins Muscle Pain and Dementia
 - Click the Generation tab then the Generate button and select CMSDeSynPUF100k
 - When the job is finished running (~1-2 minutes), you will see the results below
 - Use the dropdowns for target and outcome cohorts to record the Rate per 1k vrs for Dementia and Muscle Pain for both target cohorts
 - Document a screenshot and URL of your analysis results

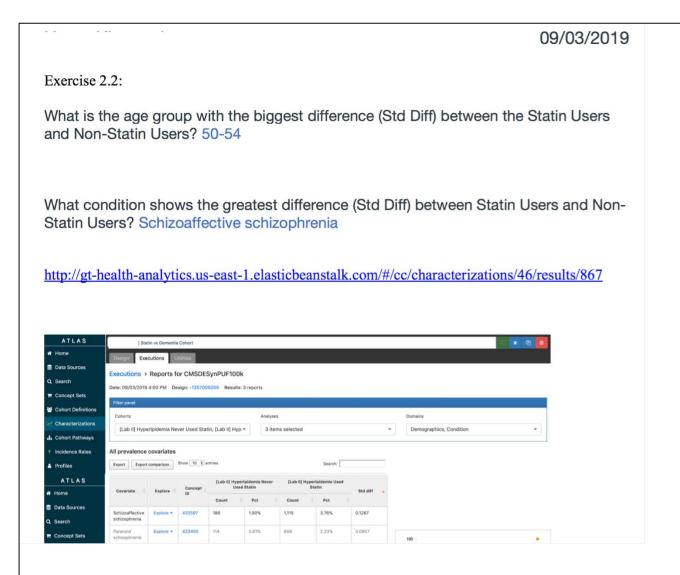


PLE Markdown Template for our Analytics Environment





Example Submission





Example Submission

Power

Data source

Synpuf

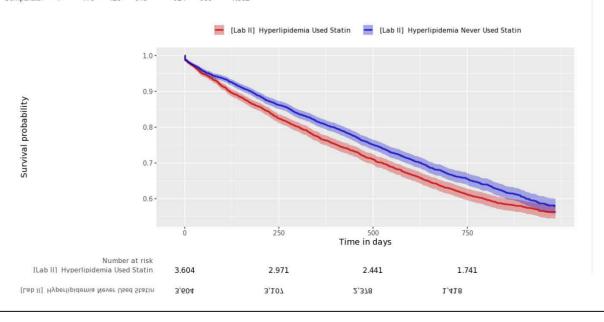
Analysis

☑ [faltoe3] Basic Analysis

Target subjects	Comparator subjects	Target years	Comparator years	Target events	Comparator events	Target IR (per 1,000 PY)	Comparator IR (per 1,000 PY)	MDRR
3,604	3,604	6,356	6,062	1,469	1,257	231.10	207.34	1.11

Table 1b. Time (days) at risk distribution expressed as minimum (min), 25th percentile (P25), median, 75th percentile (P75), and maximum (max) in the target ([Lab II] Hyperlipidemia Used Statin) and comparator ([Lab II] Hyperlipidemia Never Used Statin) cohort after propensity score adjustment.

Conort	IVIIII	FIU	F25	Wedian	F/3	F90	IVIAX	
Target	1	120	391	733	977	1,005	1,088	
Comparator	1	175	423	648	924	955	1.082	





Individual Health Analytics Project

- Propose a T vs C for outcome O question appropriate for SynPUF dataset
- Create concept sets and cohorts
- Perform Atlas Characterization and Incidence
- Generate Estimation Study and run in R
- Write a Report



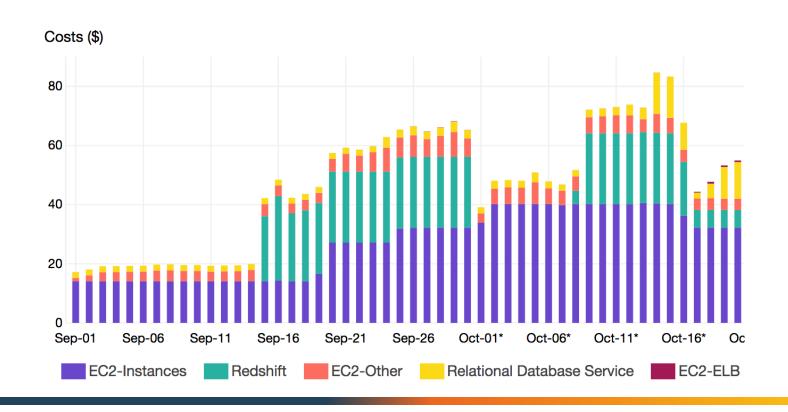
Our OHDSI Stack: OHDSI on AWS

- OMOP CDM
 - SynPUF 100k/2.3M
 - Redshift dc2.large x 2 nodes (later 4 nodes)
- Atlas
 - Elastic Beanstalk
 - t3.medium x 2-4 nodes (later t3.2xlarge x 2 nodes)
 - OHDSI Schema DB
 - RDS Aurora Postgres db.t3.medium (later r5.4xlarge)
- Rstudio
 - R5.4xlarge
 - 500GB (later 750GB)



Costs

- Initial costs ~\$20/day
- Project peaks \$50-75/day





Authentication

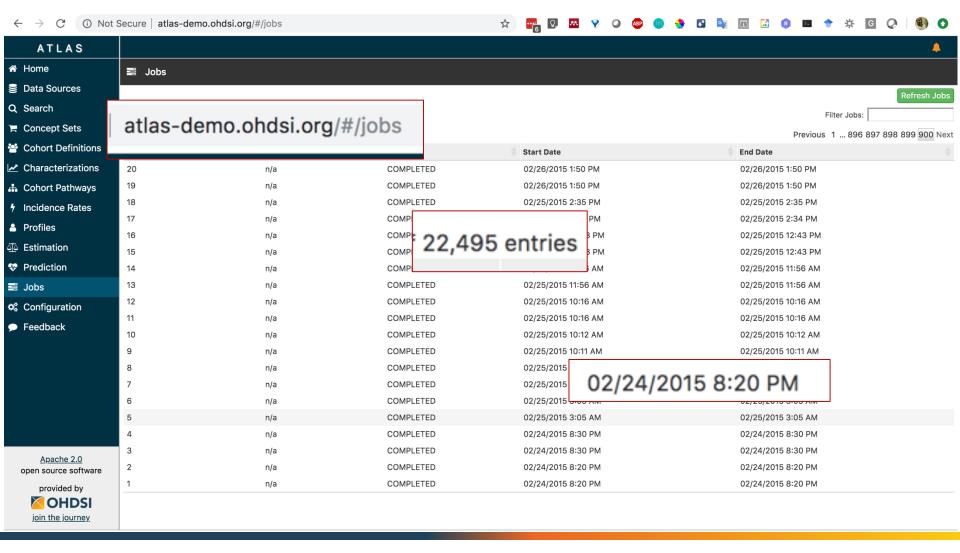
- We used Atlas security (Shiro)
- Each student was assigned a username / pw
- Does not hide other students' work, so all is visible to all
- But does let us track who did what when
- OHDSIonAWS sets up automatically same credentials for Atlas and RStudio



So how did it go?

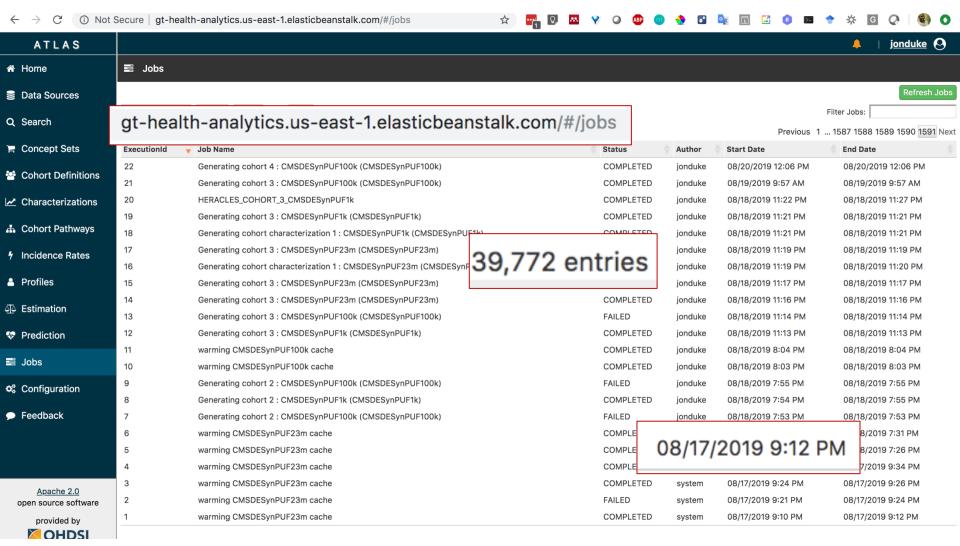


For Reference Atlas Jobs on ohdsi.org





Atlas Jobs on GT OHDSI



As of 10/14/2019



Output

- In 7 weeks, the class generated
 - 2239 concept sets
 - 2343 cohorts
 - 825 characterizations
 - 905 incidence rates
 - 846 estimation studies
 - 386 study reports



Example Project Reports

An analysis of pulmonary embolism patients and the effect of heparin on their chance to develop thrombocytopenia.

Which NSAID (nonsteroidal anti-inflammatory drugs), Ibuprofen or naproxen, is more likely to lead to a heart attack?

Which has a higher risk of hypoglycemia: Glyburide or Glipizide?

Are women with PCOS more prone to diabetes than women that do not have PCOS?



What went well

- Students reported enjoying the chance to analyze data
 - Many students explored questions of personal interest
- Many students expressed interest in getting more engaged in OHDSI
- It was gratifying to see them help each other in solving problems and working through challenges



Challenges

- We experienced a lot of challenges during the OHDSI block
- Although multi-factorial, I have categorized thematically
 - Vocabulary and concept set creation
 - Cohort definition
 - Running estimation studies
 - General infrastructure



Framing Potential Solutions

- For each challenge, I describe potential ideas
 - Note these do not distinguish things taking 5
 minutes and things taking 5 months
- Solutions tagged as
 - Things I could have taught better (T)
 - Potential software feature enhancements (S)
 - OHDSI Infrastructure (I)

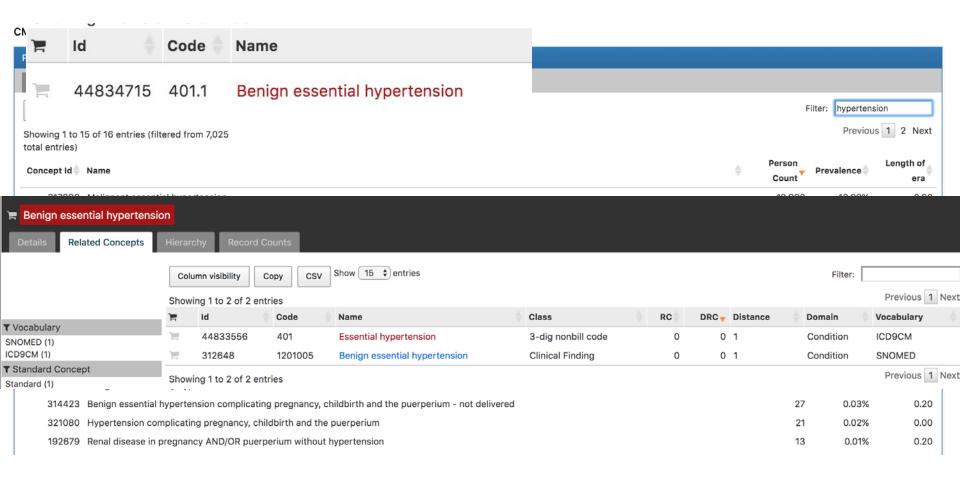


Vocabulary and Concept Sets

- Finding standard concepts
 - Students were initially guided to find common ICD9/10 codes and use the OMOP vocabulary to find SNOMED codes
 - This was often not successful in the SynPUF dataset

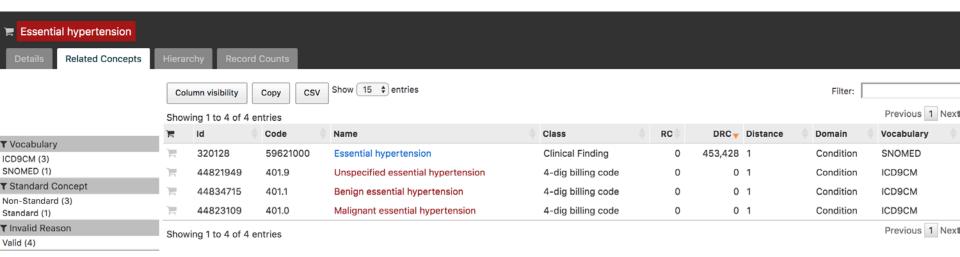


Example: Hypertension





Had to search a level up to find



But implications of DRC not sufficiently clear to students

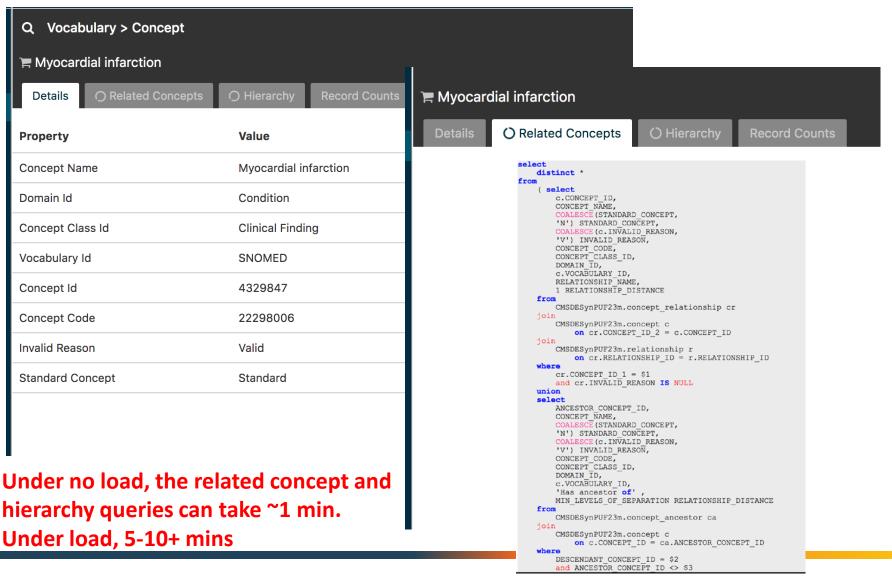


DRC vs RC

- Sometimes students failed to select descendants and thus had 0 patients in cohort
- But use of descendants in concept sets carries its own problems in running Estimation studies (see section on Estimation Studies)



The Most Expensive Query





The Most Expensive Query

 These are not rare queries, as they are run automatically every time any concept is clicked

С	olumn visibility	Сору	CSV Show 15 \$ entries			
Sho	wing 1 to 15 o	of 188 entries				Pr
Ħ	ld 🌼	Code	Name	Class	RC 🏺	
\equiv	4329847	22298006	Myocardial infarction	Clinical Finding	0	7:
$\overline{}_{\overline{i},\overline{i}}$	312327	57054005	Acute myocardial infarction	Clinical Finding	231,111	71
$\overline{y}_{\overline{i},\overline{i}}$	319038	66189004	Postmyocardial infarction syndrome	Clinical Finding	127,987	1
$\overline{\Xi}$	438170	73795002	Acute myocardial infarction of inferior wall	Clinical Finding	57,426	
$\overline{}_{\overline{-}}$	434376	54329005	Acute myocardial infarction of anterior wall	Clinical Finding	57,623	
$\overline{y}_{\overline{i},\overline{i}}$	438438	70211005	Acute myocardial infarction of anterolateral wall	Clinical Finding	39,955	:
$\overline{\Xi}$	435561	194861007	Certain current complications following acute myocardial infarction	Clinical Finding	20,054	:
$\overline{\Xi}$	438447	65547006	Acute myocardial infarction of inferolateral wall	Clinical Finding	23,245	:
1	441579	76593002	Acute myocardial infarction of inferoposterior wall	Clinical Finding	19,596	
$\overline{\mathbb{H}}$	436706	58612006	Acute myocardial infarction of lateral wall	Clinical Finding	19,398	
\equiv	438172	194863005	Atrial septal defect as current complication following acute myocardial infarction	Clinical Finding	18,044	
$\overline{y_{\overline{z}}}$	439693	194802003	True posterior myocardial infarction	Clinical Finding	16,606	
$\overline{\mathbb{H}}$	40398840	194815007	Aborted myocardial infarction	Clinical Finding	0	
$\overline{}_{\overline{i}}$	4126801	304914007	Acute Q wave myocardial infarction	Clinical Finding	0	
$\widetilde{g}_{\overline{i},\overline{i},\overline{i}}$	40398829	194805001	Acute Q wave myocardial infarction	Clinical Finding	0	



Concept Set Creation

- Ended up recommending that most people utilize Atlas Data Sources (ie ACHILLES) to find the concepts actually present in the dataset instead of using vocabulary-based lookup
 - Some exceptions for broad outcomes with many descendants (eg Cancer)
- Use of RxNorm ingredients vs Clinical Drugs was also not well-grokked by many student so did similar thing for drug era concepts



Potential Solutions

- More didactic time dedicated to DRC vs RC, RxNorm components (T)
- Change Atlas trigger for WebAPI call for related concepts and hierarchy to clicking on tabs (S)
- Reviewing DB query optimization strategies for vocabulary based queries (I)



Cohort Generation

- Cohorts had two flavors of problems
 - Cohorts that intrinsically fail to produce patients
 - Cohort that produce patients but are not well aligned with conducting an estimation study



Failing to produce patients

- Problems with concept sets as above
- Required continuous observation period excessively long for SynPUF (2 yrs total data)
- Despite extensive discussion on claims databases and SynPUF, still a lot of pediatric,
 OB, etc cohorts trying to be generated



Failing to produce patients

- Problems with concept sets as above
- Required continuous observation period excessively long for SynPUF (2 yrs total data)

Events having any of the following criteria:

a drug era of	[jyoo309] Ritalin 🔻						
with continuous observation of at least 730 ▼ days before and 0 ▼ days after event index date							
Limit initial eve	nts to: earliest event 🕈 per person.						



Failing to produce patients

- Problems with concept sets as above
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- Despite extensive discussion on claims databases and SynPUF, still a lot of pediatric,
 OB, etc cohorts trying to be generated



Zero Patient Blues

Cervicalgia - Hard time finding patients

I've been stuck on finding patients with neck pain in Atlas. Medical term is cervicalgia with ICD code M54.2.

Trying to generate data for cohorts but getting 0 results.

Hello TAs/Professor

My clinical question is

In patients with type-2 diabetes, does glipizide (sulfonylurea) increase the risk for cardiac event compared to patients who take metformin hydrochloride?

Zero patients in Cohort Thread

Are you getting Zero patients in your cohort on Atlas?

If so, start with the guidance of @731, @599, @638. If still Zero patients, you can post your cohorts here for feedback.

analyticsproject

Actions `

Actions



Cohorts that Fail in Estimation Studies

- With tips on concept finding and temporal settings, most students were able to generate populated cohorts and successfully run characterization and incidence rates in Atlas
- But many students who were able to produce T, C, and O cohorts and reasonable incidence rates were still unable to successfully run Estimation Studies



Estimation Study Errors

- Many studies failed in the compute covariate balance phase
- After investigation (thanks Jamie Weaver!), these errors were typically due to:
 - Insufficient prior observation period, often requiring 365 days of pre-index to compute
 - T and C cohorts too divergent (comparator cohort not an 'active comparator', just too different)
 - T / C cohort too small for any matched patients to emerge from PS-score matching process
 - Covariate exclusion concept sets included descendants, whereas CohortMethod prefers parent concepts only accompanied by "include descendants" in study design



Estimation Study Errors

- Some studies achieved patient matching but ended up with zero outcomes
 - This was often due to outcome cohort observation period requirements being too long for SynPUF
 - Or just small numbers of patients with the chosen outcome so matching ended up at zero
- MethodEvaluation will error if zero outcomes so cannot use Shiny app to view output on cohorts, covariate balance, etc



Estimation Study Errors

 Some studies failed in the Export phase with the mysterious camelCaseToSnakeCase error

 This is due to T and C cohorts being so similar that all patients are assigned a propensity of 0.5 for every covariate



Active Discussion on these Topics

неsolved

Unresolved





Elizabeth Margaret Shivers 1 month ago

I solved some of my errors by removing descendants from the concept sets. Worth a try.



Actions `

RStudio

With the intr cropped up



Paulina Flores 18 days ago Fixed! I added the covariate exclusion set to the wrong place, after fixing it the study did run successfully.

Before submitting your

- Make sure you have plenty of patients. If
 - Stop and follow
 - Rebuild your co
 - If still 0 patients



Tim Hall 18 days ago I finally got it working. There were 2 bugs on my part. Here's how I fixed it, in case this is helpful to anyone else:

2) The other problem was described by Dr. Duke in @987 as "You have enough patients but the backgrounds for your patients are too divergent for the mode to compute." To address this, I changed my clinical question (and therefore my cohorts in Atlas) like this:



Samantha He 22 days ago Fixed, ended up changing my concept sets to only include one without descendents and changed a gender requirement to get more records included.



Active Comparators Can Be Hard to Come By

- Picking a good active comparator takes some clinical informatics knowledge, so setting 400 CS students loose on their own questions with just one Dr. Duke was, in retrospect, unwise
- That said, it is hard to find a clinically accurate active comparator for many questions that real people ask, eg
 - Do women who get mammograms have a lower risk of breast cancer than women who don't?
 - Do women with PCOS have a higher risk for diabetes than women without PCOS?
 - Does long-term antibiotic use increase risk for myocardial infarction?



Does Zantac cause alopecia?

Compared to what?

People who don't take Zantac.

Not a good comparator.

Men who don't take Zantac.

Not a good comparator.

Men with GERD who don't take Zantac.

Not a good comparator.

Men with GERD who were given Prilosec?

Great study!

Umm, that wasn't my question...



Waxing Philosophically for a Moment

- CohortMethod is designed to perform a particular task— to compare a cohort X with active comparator cohort Y for viable outcome O in a database with sufficient patients to answer this
- It is a valid question of whether
 - I need to teach my students how to better design their questions to match CohortMethod expectations
 - OHDSI needs additional packages and/or guidance in our tools to allow people to answer basic (non studygrade) questions without running aground on errors



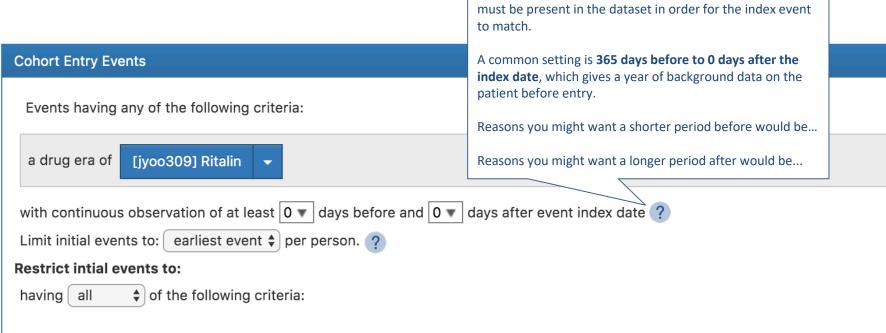
Waxing Philosophically for a Moment

- Likely a hybrid approach of expanded didactics, more guidance around errors, and additions to Atlas would bridge the gap
 - Atlas is extremely powerful and can produce almost everything you need for a good first look at a question (characterization, incidence)
 - Temporality is a killer, though, particularly for smaller databases, so maybe including decision support around cohort design that could help users understand implication of time restrictions with their data



Example Support in Atlas

Continuous observation period sets the duration the patient





Some Ideas

- More teaching on Active Comparators (T)
- Fixes to Atlas / PLE to clean up complications around descendants, exclusion set location (S)
- Cohort templates on OHDSI.org for how to answer certain kinds of common questions (T/S)
- Estimation templates on OHDSI.org with "liberal" study parameters (T/S)
- Kaplan-Meier curve in Atlas (S)
- More informative errors in study package (S)





RStudio

- Robust, stable, handled student load well
- With so many studies, did have problems with tmp folder filling up and crashing things
- But overall super stable

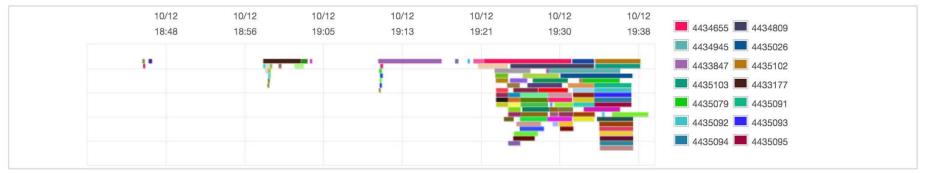


SynPUF OMOP CDM on Redshift

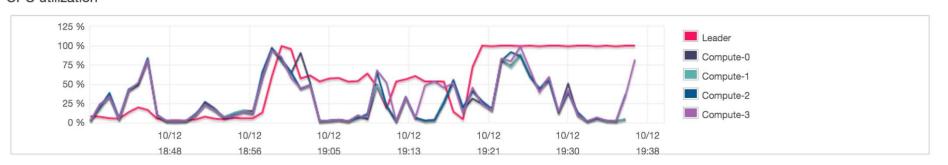
- Most queries (previous vocabulary exceptions noted) ran very fast under low user load
- But increased load really slowed things down

Queries

Hover over the queries graph or click on a query ID in the legend to inspect queries. Click and drag on any graph to zoom in.

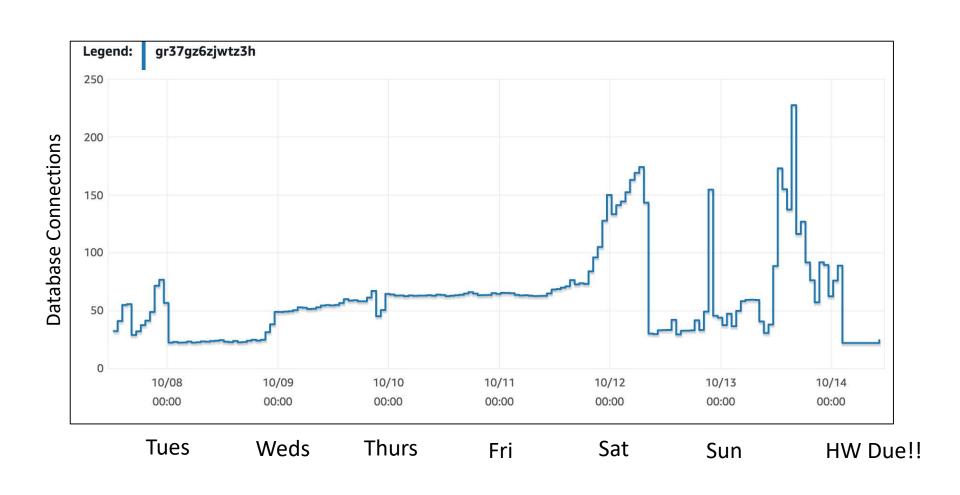


CPU utilization





What was the DB load?





Atlas / WebAPI

- The OHDSI ecosystem is of course many systems running together
- But as the 'tip of the spear', Atlas bore the brunt of the stability issues and ire from students
- Despite 2-4 nodes on Elastic Beanstalk, it required frequent rebooting to address issues of very slow or failing jobs under load



Atlas Job Performance

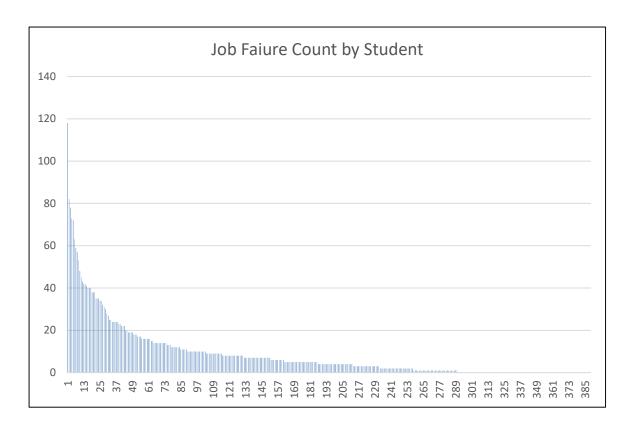
Type of Job	Proportion of Total		
Cohort Generation	81.07%		
Incidence Rate	12.04%		
Characterization	5.30%		
Other (eg cache)	1.59%		

Type of Job	COMPLETED	FAILED	STARTING	STOPPED	STOPPING
Cohort	93.62%	1.84%	4.02%	0.49%	0.02%
IR	86.31%	3.50%	4.62%	5.49%	0.00%
Characterization	78.51%	18.48%	0.00%	3.01%	0.00%
Other (eg cache)	84.30%	11.13%	3.96%	0.00%	0.00%
Overall	91.79%	3.07%	3.88%	1.22%	0.02%



Atlas Job Performance

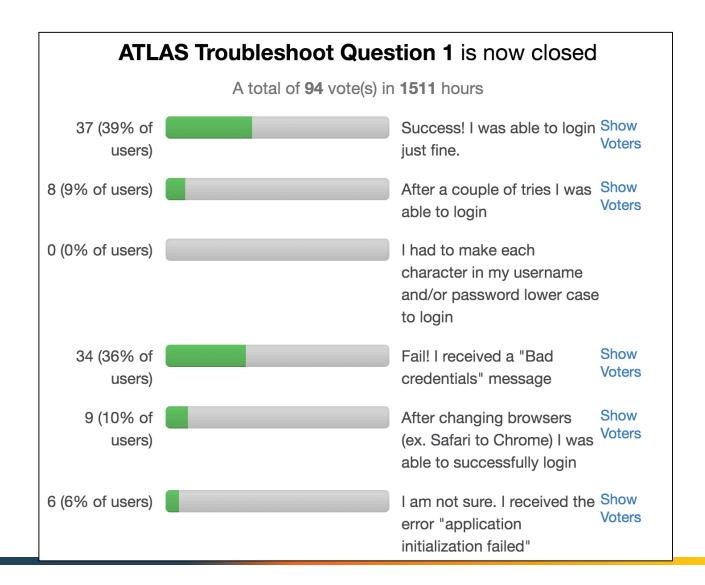
 74% of students experienced at least one failed job (range 1 to 118 failures per student)





Atlas Authentication

Some students had trouble logging into Atlas initially





Atlas Authentication

 Subsequently issues possibly related to sticky sessions or server reboots led many students to experience frequent logouts by the system



Evandro Coradini 2 days ago

Logged out constantly. Initiated incidents counts for the 23M db, but the process to generate the report is running in infinite loop (again).



Ben Stickrod 2 days ago

Same here, constantly logged out. Analyses hang up. Its become completely unusable. Either instance.

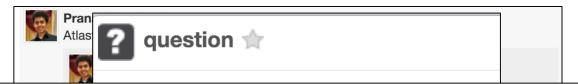


Tia Pope 1 day ago Rebooted, Can you retry?



Atlas / WebAPI

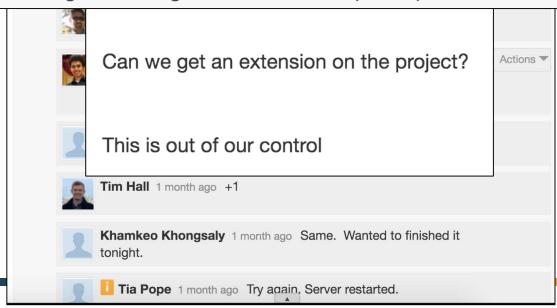
Atlas (and I) took some heat from the students





John Otken 22 days ago

Is it too late to change my cohorts to "Students using Atlas" and "Students needing Psychotherapy"? I don't even need Atlas to know the second cohort is 100%! (I'm getting constant log outs and generate never completes.)





But the OHDSI community is always there to lend a hand...



jduke99 7:15 PM

Atlas down. aware. on call with aws



James Wiggins! 🙏 1 On a Sunday night!



Nikit 7:16 PM

Thanks for being on this Dr. Duke. I'm sure it's just as frustrating for you as it is for us.



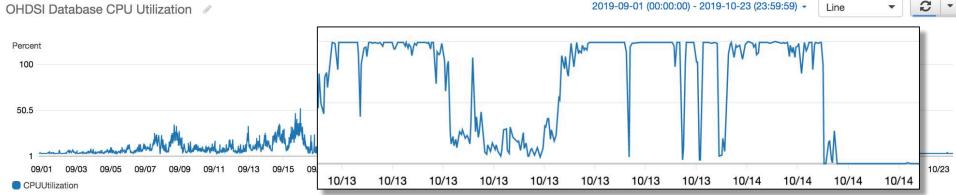






Possible Explanations

- My sense is that the Atlas issues were not due primarily to OMOP CDM database issues
- The number of users and number of jobs may have exacerbated existing small memory leaks
- But some cumulative effect was seen on the OHDSI PG database over the 6 weeks, which is likely a key factor beyond the application





Potential Solutions

- Don't run classes with 400 online students having midnight deadlines (T)
- As OHDSI looks towards Atlas 3.0, good opportunity to leverage the ever-growing technical expertise for enhancements to (I)
 - job/pipeline management
 - memory management
 - load testing
 - Other great things I have no idea about



So...



or



Actions `



Received several notes from students re OHDSI. Here's my favorite.

private question 🌟

ODSI In Hindsight

My experience with OHDSI in hindsight has been very good overall. It added a welcome dimension to this course.

OHDSI exposed us to technologies, we, otherwise, may not have seen - to expand our field of view and our toolkits, when approaching problems to solve, by taking us to the intersection of big data, pharmacology, pathology and non-infectious epidemiology all at once.

It is important that we are skilled in coherently blending disparate measures onto a page and narrating a story from beginning to end. This will add value to your career. So, the writing and research assignments have also been valuable.

I believe the technical, performance and availability issues with OHDSI, in hindsight, were not material to the outcome, when considering the generous level of "forbearance", extended to us by the instructors.

However, what is material is that one really needs to have some technical knowledge, even foreknowledge, of how input data "percolates" through the process pipeline in the estimation workflow. This knowledge will allow one to design a study to actually get an outcome. This is not desirable considering it forces the user to alter his study to accommodate the software, much like (Epic and SAP) force the user to change business processes. Although, in industry, they likely use more comprehensive observation datasets that make this a moot point. We were limited to a single Payor dataset skewed to a particular segment of the population and considering its CMS, to the local population. But that's OK for this course.

Thank you.



Next semester...

- We'll be teaching the OHDSI block again
 - Live class (come give a lecture at Georgia Tech!)
- Will expand the didactics to address some of the rough patches from this semester
- Maintain cloud-based Atlas but set up nodes for smaller units of the class (eg A-D, E-G, etc)
- Nuke the whole stack after the Labs in order to start fresh with Atlas, WebAPI, OHDSI DB
- Remove Atlas security



Conclusion

- Should OHDSI be easy to use for all?
 - No, OHDSI is a scientific platform for scientists to do research

BUT

- It was challenging for even a couple of scientists
 (me and Jamie) to debug many of the issues found
- As we look to deploy OHDSI environments at major scientific organizations (eg FDA, CDC, AMCs, pharma, etc), experiencing errors related to design or scale of users will set back adoption



Massive Thanks

- James Wiggins (AWS)
- Jamie Weaver (Janssen R&D)
- ...and all the awesome people who have built the many tools that I now have the luxury to gripe about. I'm on the shoulders of giants.



Questions?

