Treacher Collins syndrome. A compound heterozygote consisting of 2 missense alleles in the TCOF1 gene was identified as a compelling pathogenic allele, necessitating further functional investigation. The study helped validate the use of the intuitive iobio tools in such analyses, strengthening the case for greater involvement of medical professionals in data analysis. DISCUSSION/SIGNIFICANCE OF IMPACT: The performed analyses demonstrated that the whole genome sequencing data for the family being studied was of a very high quality, although 1 gene demonstrated a local region of almost zero coverage. This ensured that study conclusions can be presented with confidence. A variant associated with Treacher Collins syndrome 1 in ClinVar was uncovered in the TCOF1 gene, however, given it's benign rating, this variant was not considered further. The most interesting candidate was a compound heterozygote, consisting of 2 missense mutations, also in the TCOF1 gene. These mutations occurred with allele frequencies of 22% and 8% in the general population, and additional molecular and functional studies are currently being pursued.

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HOME Cell 2.0. Extending i2b2 to support community health outcome monitoring and evaluation via web-accessible software

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OBJECTIVES/SPECIFIC AIMS: The primary objective of this effort is to develop and distribute an easy to use i2b2 component that is capable of evaluating diverse complex relationships for a wide variety of exposures and outcomes over time. In this manner we are able to leverage the unique design of the i2b2 database to support health services research, comparative effectiveness, and quality improvement using a single tool. Furthermore, our novel database redesign has the potential to provide user-friendly access to individual and group CHC data for CER. METHODS/STUDY POPULATION: For this project we used software experts, clinical informatics specialists, and the existing i2b2 open-source software to convert our legacy HOME Cell into a web-client version. The tool will be used to study health outcomes within a network of Boston based Community Health Centers and the largest safety-net hospital in New England, Boston Medical Center. RESULTS/ANTICIPATED RESULTS: The new web-client HOME Cell will allow i2b2 users to model virtually any exposure (including therapeutic interventions such as medications or tests) in i2b2 against any outcome accounting for complex temporal relationships and other factors. In addition we plan to use our new Community Health Center views to enhance our community engagement activities by allowing direct access to their data for our partners. DISCUSSION/SIGNIFICANCE OF IMPACT: Our project addresses multiple national priorities related to data sharing, clinical research informatics, and comparative effectiveness. The web-client version of the HOME Cell substantially improves our community's access to HOME Cell functionality and is a novel, sharable resource for use within the CTSA/NCATS community. Our approach provides a new way to perform large-scale collaborative research without the need to actually move patient-level data and has demonstrated that CER, health services research, and quality measurement can share a common framework. In addition, and as demonstrated in our earlier pilot work, the HOME Cell also has the potential to support large-scale multivariate analyses in a distributed manner that does not require sharing of patient-level data. We believe our approach has great promise for supporting the reuse of clinical data for rapid, transparent, health outcome assessments on a national scale. Our efforts support multiple strategic goals including: (1) support for building national clinical and translational research capacity by enhancing a broadly adopted informatics tool (i2b2); (2) enhanced consortium-wide collaborations by offering a tool that can be easily shared within the CTSA network to support multi-institutional collaboration; and (3) improving the health of our communities by offering a tool that has the potential to provide new insights into health care processes and outcomes that could drive innovation and improvement activities.

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Will the Veteran Affairs (VA) electronic medical records (EMR) database reveal a signal that angiotensin II inhibiting medications ameliorate depression?

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OBJECTIVES/SPECIFIC AIMS: Angiotensin type 1 receptor blockers (ARBs) and angiotensin-converting enzyme inhibitors (ACEIs) are frequently prescribed for hypertension and associated cardiovascular and renal complications. In animal models, these drugs also reduce anxiety and depression. OBJECTIVE—to determine if Veteran Affairs (VA) clinical pharmacy data indicate a protective effect of ARBs and/or ACEIs for major depression. METHODS/STUDY POPULATION: Pharmacy records from nationwide VA electronic medical records (EMR) were extracted for patients prescribed ARBs, ACEIs, α-blockers, β-blockers, calcium channel blockers, or diuretics (n = 4,081,359). Patients were excluded if: they had not received medications for 6 months with >70% coverage; were diagnosed with substance/alcohol abuse, dementia, psychosis, schizophrenia, or prescribed insulin. The study population was categorized as "ARB/ACEI" (A/A) or "Never ARB/ACEI" (NA/A). Using the Greedy Matching Algorithm, subjects were matched on a 1:1 ratio for sex and race over a 5 year age range resulting in 2 equal groups of n = 1,350,236 each. Subjects were older (M = 71.6, SD = 12) and mostly men (97%). RESULTS/ANTICIPATED RESULTS: In the A/A Versus NA/A, respectively, the incidence of anti-depressant use was greater during (9.9% vs. 8.9%) but was lower after (11.8% vs. 12.2%) the study period. PHQ-2 scores (Mean ± SD) were statistically lower, albeit similar, during (0.79 ± 1.56 vs. 0.85 ± 1.63) and after (1.00 ± 1.73 vs. 1.07 ± 1.79) the study period. DISCUSSION/SIGNIFICANCE OF IMPACT: These preliminary data suggest that inhibiting angiotensin II action does not provide a protective effect on major depression when compared with other classes of antihypertensive drugs. This study illustrates how "Big Data" may inform the design, or obviate the need, for large-scale randomized-controlled trials.

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Passive intracranial EEG-based localization of the central sulcus during sleep

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OBJECTIVES/SPECIFIC AIMS: To investigate the performance of a metric for passive localization of central sulcus. METHODS/STUDY POPULATION: We studied 7 patients with intractable epilepsy undergoing intra-cranial EEG (icEEG) monitoring at Yale, in whom central sulcus (CS) localization was obtained by standard methods. Our method takes advantage of inherent properties of the primary motor cortex (MC), which exhibits enhanced icEEG band-power and coherence across the CS. For each contact x we calculated the z-score of a composite power and synchrony value $\log_{10}(px)\,x;cx$, where px is sum of the root mean square of the icEEG in the high gamma band (80–115 Hz) for contact x over the 6–10 minutes of NREM sleep studied, and cx is the mean magnitude squared coherence in the same band using a 500-ms Hamming window between contact x and all other contacts. z-score values lower than threshold (th) were set to 0. Finally, we calculated a metric $m = z/d$, where d is the mean Euclidian distance of each contact from contacts with z scores greater than 0. The last step was implemented to emphasize local network activity. RESULTS/ANTICIPATED RESULTS: We report the results of a pilot study to test the performance of a new operator independent method for passive identification of CS with intractable epilepsy undergoing icEEG monitoring at Yale, in whom CS localization was obtained by standard methods. The sensori-motor (SM) cortex exhibited higher EEG-gamma power compared with non-SM cortex ($p < 0.0002$). There was no significant difference between the motor/premotor and sensory cortex ($p < 0.47$). CS was successfully localized in all patients with thresholds between 0.4 and 0.6. In 2 patients, knowledge of anatomy was needed to distinguish the MC from adjacent epileptic foci. The primary hand and leg motor areas exhibited the highest metric values consistently followed by the tongue motor area. Higher threshold values were very specific (94%) for the anterior bank of the CS but not sensitive. Intermediate threshold values achieved a reasonable trade-off (0.4: 89% specific and 70% sensitive). DISCUSSION/SIGNIFICANCE OF IMPACT: We present and successfully implement a rapid procedure for task-free and stimulation free localization of the central sulcus during sleep based on intrinsic electrophysiological properties of the primary motor strip which exhibits increased power and enhanced local connectivity. We successfully localized the central sulcus in all patients. When implementing appropriate thresholds, our proposed metric M is very specific for the anterior lip of the central sulcus which may make it ideal to identify this important anatomical landmark. Our method is sensitive for epileptogenic regions as well, therefore basic knowledge about central sulcus anatomy may be needed in cases where there is an epileptogenic lesion in the vicinity of the central suclus. Our method makes a few a priori assumptions: The regions around the central sulcus are adequately sampled and the occipital or parieto-occipital regions are not included in the analysis. In order for the method to function properly, nonsensori-MC should be sampled adequately as well. In the future, normative data could be generated for the composite product of connectivity × power which may replace within-patient z-scoring. Our method is rapid and can be implemented on short segments of

https://doi.org/10.1017/cts.2017.67 Published online by Cambridge University Press

ECoG data. The proposed method may be potentially used for identification of seeds in the motor cortex for subsequent network analysis and further studies may delineate its potential use in the operating room.

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Functional analysis of the cutaneous microbiome in psoriatic disease

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OBJECTIVES/SPECIFIC AIMS: Psoriasis is one of the most common inflammatory diseases of the skin, affecting about 2%–3% of the US population. Despite its high prevalence, its pathogenesis remains poorly understood. The ability of the microbiome to modify host immunity and metabolism suggests that it may contribute to the development of psoriasis and its cardiometabolic comorbidities. This study aims to characterize the psoriatic skin microbiome and understand the functional role that these bacteria may play. METHODS/STUDY POPULATION: 16s rRNA sequencing of site-matched skin swabs from 8 psoriasis patients and 8 healthy controls was used to identify bacteria and determine their relative abundance and microbial community diversity in the sample. PICRUSt was used to infer the functional roles of the bacteria from 16s rRNA amplicon data. RESULTS/ANTICIPATED RESULTS: Lesional psoriasis skin had lower α diversity ($p = 0.04$), less Actinobacteria ($p = 0.0001$), but higher Firmicutes ($p = 0.009$) compared with controls. At the genus level, lesional skin had more Alloiococcus ($p = 0.01$) and Aerococcus ($p = 0.01$) and demonstrated a trend towards lower Propionibacterium ($p = 0.08$) and higher Gallicola ($p = 0.09$) compared to controls. Interestingly, Alloiococcus ($p = 0.003$) and Gallicola ($p = 0.04$) were also higher in nonlesional skin compared with controls. Furthermore, lesional and nonlesional skin shared an increased abundance of *Acinetobacter* sp., *Staphylococcus pettenkoferi*, and *Streptococcus* sp., relative to controls. Lesional and nonlesional psoriasis skin did not differ significantly in microbiome composition. Predictive functional analysis revealed that both the healthy and psoriatic skin microbiome were enriched with bacteria capable of amino acid and carbohydrate metabolism suggest these functions might have a general role in host-microbe interaction. DISCUSSION/SIGNIFICANCE OF IMPACT: These data reveal intriguing differences in the cutaneous microbiome of psoriatic individuals and healthy controls and suggest that bacterial metabolism may play an important role in host-microbe interaction.

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Prescription opioid dependence in Western New York: Using data analytics to find an answer to the opioid epidemic

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OBJECTIVES/SPECIFIC AIMS: Dependence and abuse of prescription opioid pain medication has substantially increased over the last decade. The consistent rise in opioid dependence contributes to the rising prescription drug overdose deaths over the last decade. The study of the distribution and determinants of opioid dependence among patients who are treated with chronic pain medications prescribed by their healthcare providers would aid in answering some key questions about potential abuse and overdose on opioids. The descriptive epidemiology of opioid dependence would help in identifying the vulnerable age group, race, ethnicity, and type of opioid pain medications that more commonly result in dependence. METHODS/STUDY POPULATION: We implemented an Observational Medical Outcomes Partnership/Observational Health Data Sciences and Informatics (OMOP/OHDSI) database, to hold structured EHR data from our Allscripts patient records. We also created a high-throughput phenotyping, natural language processing system that can parse 7,000,000 clinical notes in 1.5 hours. This runs as a web service and provides a modular component based NLP system. After the full semantic parse, we match the content against any number of ontologies. For each match we tag it as either a positive, negative, or uncertain assertion. We then perform automated compositional expressions. The codes are stored in a Berkley database (BDB) NOSQL database and the compositional expressions are stored in Neo4J (a graph database) and Graph DB (a triple store). This flexibility allows rapid retrieval of complex questions in real time. The High-Throughput Phenotyping (HTP) Natural Language Processing (NLP) Subsystem (HTP-NLP) is software that produces, given biomedical text, semantic annotations of the text. The semantic annotations identify conceptual entities—their attributes, the relations they have with other entities and the events they participate in, as expressed in the input text. The conceptual entities, relations, attributes, and events identified are specified by various knowledge representations (KRs) as documented in Coding Sources. Examples of coding sources are medical terminologies [eg, SNOMED CT, RxNorm, LOINC and open biomedical ontologies (OBO) foundry ontologies, eg, gene ontology (GO), functional model of anatomy, OBI, and others]. The annotation results may be displayed or output in formats suitable for further processing. Entity identified is assigned a truth value from 0 to 1. Values from the text are assigned to entities from ontologies such as SNOMED CT. The retrospective analysis of EHR data from local clinic patients was performed using queries on the problem list, demographic data, and medication list of all the patients in the database. The OMOP/OHDSI database was collected from Allscripts EHRs from 2010 to 2015. This common data model helps in the systematic analysis of disparate observational databases of clinic records from the primary care and family medicine clinics in Western New York region. The database contained 212,343 patient records that were parsed and deidentified. Specific research IDs were assigned to each of the patient records and stored in a secure firewall device for data analytics. The entire 212,343 records were queried for opioid dependence from the ICD-9 and 10 diagnostic codes and SNOMED CT codes mapped to both the clinical notes and the problem list for each patient based on the mapped ICD and SNOMED CT codes. In total, 1356 patients were identified as to having opioid dependence. The records were stratified into 7 age groups from age 18 to 28 and ending with age 79–89 years. RESULTS/ANTICIPATED RESULTS: Of the 212,343 patients in the database 1356 patients revealed opioid dependence on the problem list, ICD9-10 codes and prescription opioid pain medication with or without Buprenorphine and Naloxone (Suboxone) in the medication list. The prevalence of opioid dependence in the clinic population was 0.64% (95% CI: 0.61%–0.67%) over a 5-year period. The 7,000,000 patient records generated 750,000,000 SNOMED CT codes (on average 107 codes per record). The highest numbers of opioid dependence were seen in the 29 to 38 years' age group. That comprised 39.38% (95% CI: 36.78%–41.98%) of the total opioid dependent population but accounted for only 2.03% of whole clinic population in this age group (95% CI: 1.86% to 2.2%). The subjects were then stratified by race and ethnicity. There were 1005 patients with opioid dependence, in the non-Hispanic population (total number 108,402). Among the White non-Hispanic or Latino population with opioid dependence, 41.33% (95% CI: 38.27%–44.39%) were 29–38 years old. The next common age group among the White Non-Hispanic opioid dependent subjects was 19–28 years, comprising of 22.48% (95% CI: 19.88%–25.08%) of the total number of White non-Hispanic or Latino opioid dependent population. Among the total clinic population Hispanics comprise 51.24%, but they comprise only 2.58% (95% CI: 1.74%–3.42%) of the total opioid dependent population. The non-Hispanic population comprise 51.05% of total clinic population while the percent of people who are opioid dependent is 83.26% (95% CI: 83.04%–83.48%) of the total 1356 opioid dependent population. DISCUSSION/SIGNIFICANCE OF IMPACT: The trends of opioid dependence among the clinic population in the study indicate that the prevalence is more in a certain section of the population. The predominance is among the non-Hispanic White population in the 19–38 years of age. The prevalence in younger age implies that the complications related to opioid dependence would be there for a longer duration of time. The prevalence of dependence in this clinic population would be rising if this trend continues. Interventions at curbing prescription opioid dependence is necessary for the vulnerable population. The findings suggest that a broad based approach is necessary to address this problem. The distribution of opioid dependence in this patient population indicate the need for special attention to these specific age group and race ethnicities. The young age of many of the addicted patients demonstrate the risks of legitimate opioid prescriptions in leading this age group towards addiction and implies the need for routine screening for substance abuse. The evidence of complications of opioid overdose among long-term opioid users and risk of abuse with other agents including illicit agents makes the need for an approach that uses real-time interventions in addition to effect long-term improvement in addiction rates. A potentially cost-effective approach to implement monitoring programs and clinical decision support tools would be to develop inter operable linkage from the EHRs to the state Department of Healths' prescription monitoring programs.

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Pioneering the pathway with big data to eliminate hepatitis C viral infection (EHCV)

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OBJECTIVES/SPECIFIC AIMS: Hepatitis C viral (HCV) infections are rising significantly both in young adults and as newly diagnosed cases in "baby boomers." New HCV therapeutics cure over 95% of cases, and a call has been

https://doi.org/10.1017/cts.2017.67 Published online by Cambridge University Press