

An Informatics Roadmap to Facilitate DRESS Epidemiology and Pharmacogenomics Studies

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Background

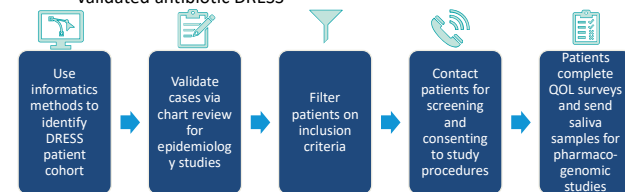
- Drug reaction with eosinophilia and systemic symptoms (DRESS) affects 1-10 in 10,000 drug exposures¹⁻³.
- Though rare, DRESS is a severe drug reaction with great diversity in presentation, which presents challenges for case identification
- Further challenges include⁴:
 - Diagnostic codes lack specificity
 - Not available as coded entries in the adverse and allergic reaction modules in the electronic health record (EHR)
 - Lack of mandatory reporting to the FDA by clinicians
 - Inconsistency and limited data from voluntary reporting
- Goal: To **develop a roadmap** for leveraging large-scale **EHR data and informatics technology** to improve **DRESS case identification** and advance understanding of DRESS using **epidemiology and pharmacogenomic studies** with the following aims:
 - Aim 1: Informatics - Develop and disseminate informatics methods to identify and validate a DRESS patient cohort using longitudinal EHR data
 - Aim 2: Epidemiology - Identify risk factors for, and sequelae of, antibiotic-associated DRESS
 - Aim 3: Pharmacogenomics – Discover HLA and genetic associations form DRESS patients

Methods

- Study setting: a multisite and multidisciplinary collaborative study between Mass General Brigham (MGB; formerly Partners HealthCare System) in Boston, MA, and Vanderbilt University Medical Center in Nashville, TN
- Data sources
 - EHRs of 11 million patients spanning five decades (1980-2022) at MGB
- Identify potential DRESS cases using informatics methods
 - Natural language processing [NLP] and machine learning [ML] leveraged to identify cases using EHR and claims data
 - Focus on three record areas:
 - Coded and free text data of the allergy list
 - Coded and free text data on the problem list
 - Potentially relevant ICD9/ICD10 codes
- Case validations
 - Chart review via data collected data in REDCap
 - Validate DRESS cases based on certainty of diagnosis as Definite or Probable
 - Each case scored independently by two expert reviewers in dermatology and/or allergy/immunology
 - Confirmed cases must have ALDEN and RegiSCAR scores ≥ 4
- Epidemiology and Pharmacogenomics Studies
 - To determine overall DRESS prevalence and clinical presentation
 - Nested case-control studies within the full MGB population to examine

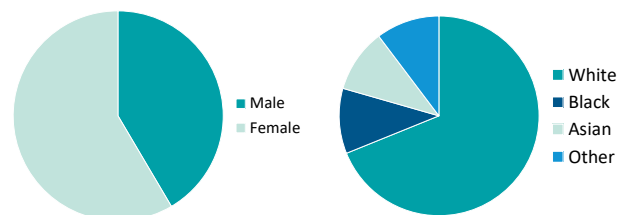
risk factors for, and sequelae of, DRESS

- Inclusion criteria:
 - Patient currently alive and 18+ at the time of DRESS
 - Patient must have experienced DRESS due to an antibiotic
 - DRESS case must have been validated as Definite or Probable after chart review
- Patients **screened for eligibility**, and **consent** to validated **questionnaires and interviews** on their **symptoms and quality of life (QOL)** since their DRESS episode
 - Collected **demographic information** to further epidemiological analysis
- Eligible patients also consent to return **saliva samples** for genetic testing
 - Identify candidate HLA and genetic associations from patients with validated antibiotic DRESS

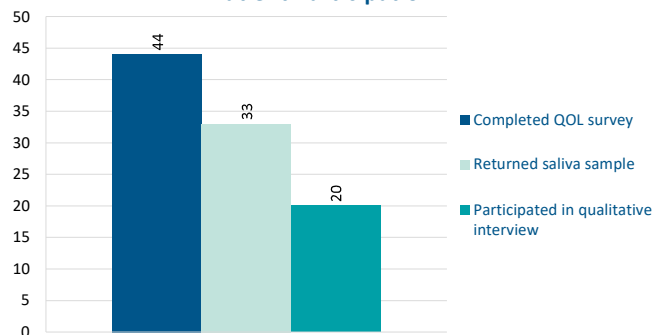


Results

- The project is ongoing. These are the results to date as of October 7, 2022
- 366 patients validated with definite or probable DRESS
 - Majority female (n=214, 58.5%)
 - Mean age = 52.4
 - Standard Deviation of age = 19.0
- Contacted 214 eligible patients with antibiotic DRESS
 - 92 (43.0%) interested in participating in the studies



Patient Participation



Conclusions

- Sets example and precedent for:
 - Collaborative studies led by a multidisciplinary research team
 - Diverse clinical and research knowledge
 - Developing an informatics roadmap that can utilize large-scale EHR data for phenotyping that will facilitate subsequent epidemiology and pharmacogenomics studies
- Utilizing our informatics methods, we identified 266 more DRESS cases than predicted (100), allowing us to do more robust DRESS studies

References

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