ESTIMATING THE RATE OF OCCURRENCE OF RENAL STONES IN ASTRONAUTS

J. Myers[1], D. Goodenow[1], S Gokoglu[1], and M. Kassemi[2]

[1]National Aeronautics and Space Administration Glenn Research Center
[2]National Center for Space Exploration Research (NCSER).

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Renal Stone Likelihood during Space flight

Misery

Agony

- **Evidence of altered urine volume and chemistry**
  - – Lower output
  - – Elevated Calcium (diet and bone demineralization)
  - – Alterations in oxalate uptake
  - – Countermeasures
    - Citrate treatments
    - Bisphosphonates
    - Individualized diet and intense exercise (ARED)

One way to estimate incidence

- **Based on Bayesian analysis including**
  - Summary of Urological Diseases in America 2004
  - JSC Control Population Data
  - Inflight/Post Flight Data (up to ~2012)

Astronaut - inflight 3.65 (+/- 0.46) events per 1000 person years

- Purely related to incidence/diagnosis of a stone
- Does not account for changes in urine chemistry or counter measeures

Gilkey et al 2012 – NASA/TP -2012-217120

Can we do better?

- **Consider**
  - Kassemi et al* population balance equation (PBE) model has been shown to differentiate stone forming potential based on urine chemistry and crystallization kinetics in idealized representations of space flight and ground urine chemistry

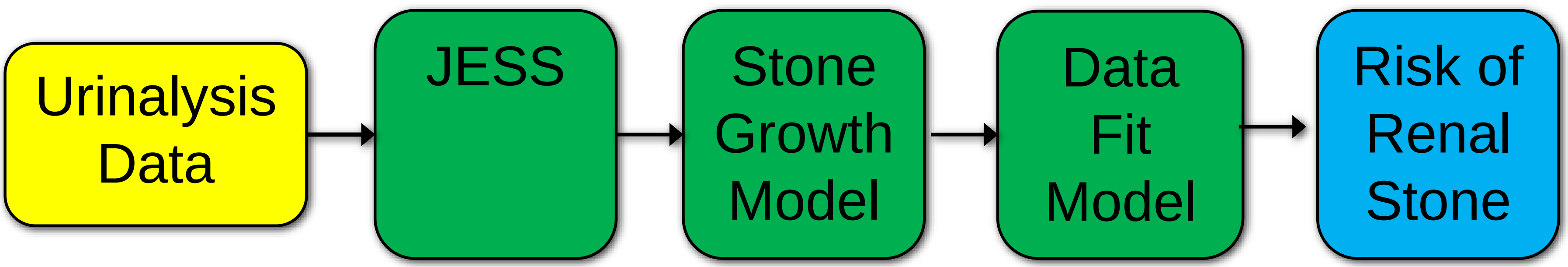
- **Surmise**
  - The ability to quantitatively differentiate stone forming potential from a given set of urine chemistries can be used to better estimate the likelihood of stone formation in astronauts

- **Approach**
  - Develop a probabilistic simulation model utilizing the PBE model to distinguish the stone forming potential across the expected range of urine chemistry combinations for astronauts.

*Kassemi et al. HRP-IWS 2016

Probabilistic model for Renal Stone Incidence Likelihood

- **Renal Stone occurrence model**
  - Complex Simulation model of renal stone growth
  - Couples deterministic model output and randomly sampled input parameters to quantify the risk of stone formation and treatment using MATLAB



Key Components

Urinalysis Data

- **Taken from astronaut pre-flight data, and Cleveland Clinic stone former data**

JESS

- **A commercial code that calculates the chemical speciation**
- **Outputs the RSS (SI) which is a measure of supersaturation**

Stone Growth Model-Kassemi et al population balance model

- **Takes in speciated urine chemistry**
- **Produces a population density of steady state crystal growth sizes distributed from 20 nm to 2 mm**

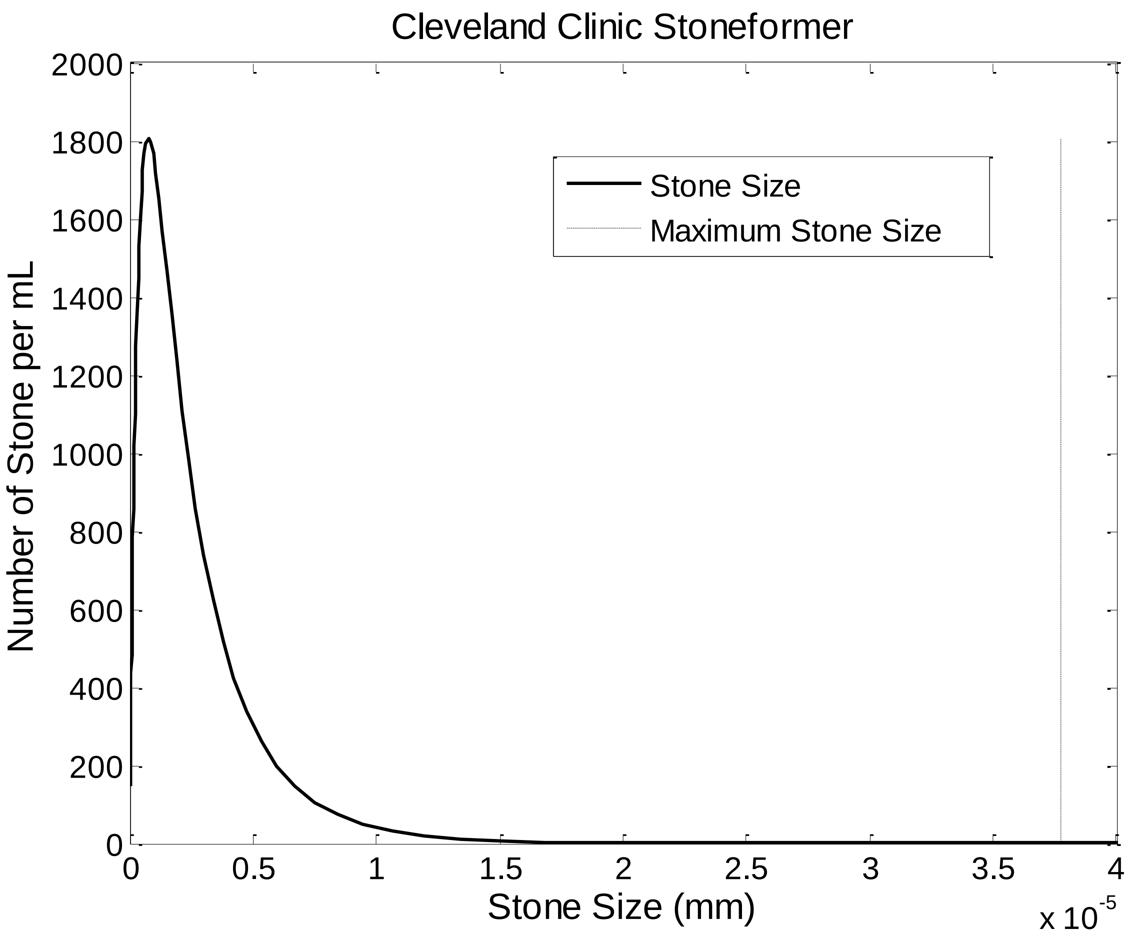
Data Fit Model

- **Takes in the crystal sizes for various data types and correlates to known incidence rates for those data types such as stone formers and non-stone formers**

Risk Model Output

- **Outputs the risk of renal stones**

Data Fit Model Input: Kidney Stone Size



- **Max Stone Size is defined as 1 stone/mL of urine**

Datasets taken from

- **Piertzyk et al Renal Stone Formation Among Astronauts, Aviation, Space, and Environmental Medicine • Vol. 78, No. 4, Section II • April 2007, Pre and Post-flight**
- **Cleveland Clinic Stone former dataset**

Simulation Analysis – Incidence data

Distributions	Minimum per 100,000 person years	Maximum per 100,000 person years	Sources
Pre-Flight-Non-Stone former	85	117	**Minimum and Maximum**-Lieske et al, “***Renal Stone epidemiology in Rochester, Minnesota: An update***”, Kidney international (2006) 69, 760-764. Age and Sex adjusted to reflect astronaut core
Stone former	121	1093	**Minimum** - Lieske et al, “***Renal Stone epidemiology in Rochester, Minnesota: An update***”, Kidney international (2006) 69, 760-764. Age and Sex adjusted to represent Astronaut Core **Maximum**-1093.12 “***Urologic Diseases in America - 2012 Chap 9***” - Upper Urinary Tract Total (all demographics). Age adjusted - Demographic adjusted
Inflight	85	396	**Minimum**- Same as Non-Stone former Minimum **Maximum**-Gilkey et al. “***Bayesian Analysis for Risk Assessment of Selected Medical Events in Support of the Integrated Medical Model Effort***”, NASA/TP - 2012-217120
Postflight	396	1676	**Maximum**-Gilkey et al. “***Bayesian Analysis for Risk Assessment of Selected Medical Events in Support of the Integrated Medical Model Effort***”, NASA/TP - 2012-217120 **Maximum**- Derived from 2015 LSAH data request ID#: 10669; 6 CaOx events in 358 person years, ***interval 1 year post-flight***

- All Distributions except the Post Flight max are multiplied by the a uniform distribution to remove the kidney stones of other varieties. 70.7 to 78.1% of kidney stones are calcium oxalate stones per Lieske et al 2006.
    - ***Only Non-Stone former, Stone former, and Post Flight values are currently used by the model***

Simulation analysis – Data Fit Model Flow Chart

Takes in Data- Max Stone size and Incidence rates

Samples the number of incidences over 100,000 years for each data point of max stone size with the corresponding incidence distribution

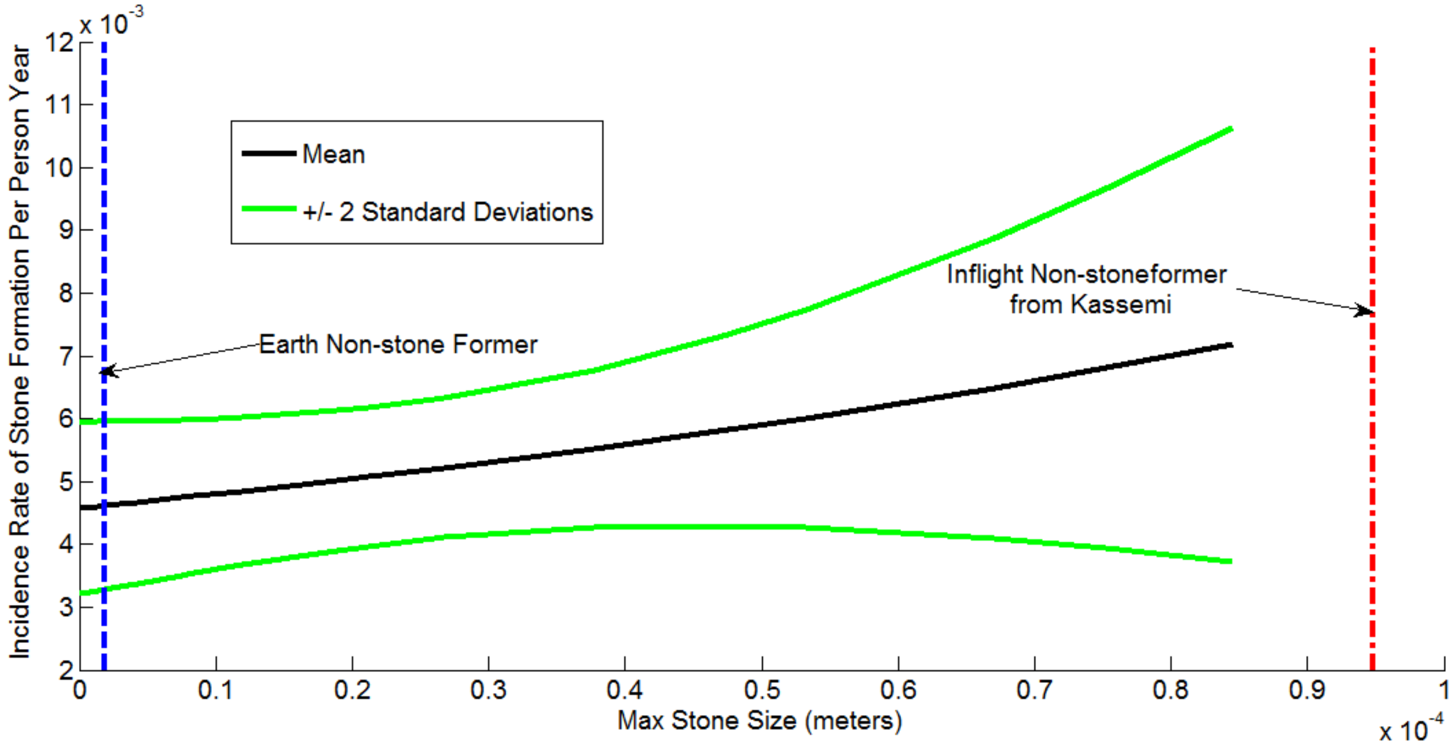
Repeats 10,000 times

Matches each set of incidences to a Poison distribution with the form

$$e^{b_1+b_2*maxStoneSize}$$

Averages the total distributions and calculates the standard deviation

Simulation analysis – output response surface



Datasets Used for Mean Curve

- **8 Preflight Non-Stone formers**
- **9 Post Flight Stone formers**
- **9 Cleveland Clinic Stone formers**

Conclusions and future work

Conclusion

- **Prototype Completed**
  - Designed to expands prior Bayesian estimates
  - Includes multiple factors related to renal chemistry and crystal formation
  - Relies on population and astronaut data to make rate estimates
  - Further data is needed before the model validation

Future Work

- **Expand the training dataset to incorporate the entire application range**
  - LSAH/LSDA correlated data request
  - Length of time from astronaut urinalysis measurement to stone formation
  - More astronauts pre, post flight, and post stone formation
  - More terrestrial stone former and non-stone former sample sets
- **Address remaining programming and CM requirements**
  - Final review and documentation to NASA standards
- **Validation**
  - Select data removed prior to model training
  - Used as referent data for performance assessment and validation

Thank you!

Questions?