Bayesian Analysis for Risk Assessment of Selected Medical Events in Support of the Integrated Medical Model Effort

Kelly M. Gilkey, Michael P. McRae, Elise A. Griffin, Aditya S. Kalluri, and Jerry G. Myers
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Summary

The Exploration Medical Capability project is creating a catalog of risk assessments using the Integrated Medical Model (IMM). The IMM is a software-based system intended to assist mission planners in preparing for spaceflight missions by helping them to make informed decisions about medical preparations and supplies for combating and treating various medical events. IMM uses Probabilistic Risk Assessment, which deals with low-probability, high-consequence events of complex physiological processes, although high-probability, low-consequence events are also of interest. The objective is to use statistical analyses to inform the IMM decision tool with estimated probabilities of medical events occurring during an exploration mission. Because data regarding astronaut health are limited, Bayesian statistical analysis is used. Bayesian inference combines prior knowledge, such as data from the general U.S. population, the U.S. Submarine Force, or the analog astronaut population located at the NASA Johnson Space Center, with observed data for the medical condition of interest. The posterior results reflect the best evidence for specific medical events occurring in flight. Bayes' theorem provides a formal mechanism for combining available observed data with data from similar studies to support the quantification process. This is especially relevant when dealing with physiological data from the astronaut corps, where data are relatively sparse (zero in some cases). Bayes' theorem depends on the consideration of all uncertainties (both known and unknown) that are fundamental to the assessment of risk. All Bayesian updates were performed using the open-source numerical update code called the Bayesian inference Using Gibbs Sampling (WinBUGS). WinBUGS is a computer software program that uses Markov-chain Monte Carlo methods to perform Bayesian analysis of complex statistical models.

The IMM team performed Bayesian updates on the following medical events: angina, appendicitis, atrial fibrillation, atrial flutter, dental abscess, dental caries, dental periodontal disease, gallstone disease, herpes zoster, renal stones, seizure, and stroke.

1.0   Introduction

The Integrated Medical Model (IMM) is a software-based system that will quantify health risks, identify medical needs, develop potential mitigation procedures, and assist in the preparation of spaceflight missions. Because data regarding astronaut health are limited, the IMM team used Bayesian statistical analysis. Bayesian inference combines prior knowledge, such as data from a similar study, with observed data for the event of interest. The outcome is a posterior result that reflects the best evidence for specific medical events occurring in flight. The IMM team performed Bayesian updates on the following medical events: angina, appendicitis, atrial fibrillation, atrial flutter, dental abscess, dental caries, dental periodontal disease, gallstone disease, herpes zoster, renal stones, seizure, and stroke.

1.1   Bayesian Analysis

Because classical statistical techniques are not suitable for assessing the risk of low-probability, high-consequence events, an alternative risk-modeling framework, Probabilistic Risk Assessment (PRA), was developed that works within a scenario-based concept of risk that best informs decision making (Ref. 1). PRA integrates a collection of models and quantifies integral risk metrics and their uncertainties (e.g., the probability of the loss of crew and the associated uncertainty). This modeling framework is supported by the application of Bayes' theorem of probability. The theorem provides a formal mechanism for combining all available information, such as engineering and qualification test data, field experience, expert judgment, and data from similar systems to support the quantification process. This is especially relevant when dealing with astronaut medical event data, which are relatively sparse (zero in some cases). Bayes' theorem depends on an honest treatment of the uncertainties that are fundamental to risk assessment and is based on a subjective interpretation of probability (Ref. 1).

Within PRA aleatory models, most of the parameters are uncertain. This layer of imprecision is defined as epistemic uncertainty, which represents how accurate the developer's state of knowledge is about the model, regardless of the model type. If an aleatory model is used (e.g., binomial) or a deterministic model is used (e.g., a fault tree), and if any parameter of these models is uncertain, then the model has epistemic uncertainty. Bayesian quantification methods are utilized to determine the nature of the epistemic uncertainty. In the Bayesian approach, probability quantifies the degree of belief and is used to describe the plausibility of an event. Frequentist inference generally relies on a mathematically consistent way to incorporate nonempirical data, which allows for the propagation of uncertainties throughout the logic model

(Ref. 1). Often this approach is not available for astronaut medical event data. A solution is to incorporate Bayesian analysis, allowing for an alternative interpretation of probability. Information about the parameter, beyond what is in the data, is included in the estimate, and Monte Carlo sampling is used to propagate uncertainties through the logic analysis.

Some of the typical uncertainties associated with PRA assumptions include disagreement or lack of accuracy when the probabilities of physical processes are estimated, limited knowledge of the parameters in phenomenological equations, unknown parameter values, inaccurate parameter values, and the inherent variability of stochastic processes. The Bayesian approach provides a formal mechanism for combining all available information, such as engineering and qualification test data, field experience, expert judgment, and data from similar systems. The types of information available for parameter values might include prior data—general engineering knowledge and historical information from similar events—and observed data for the event of interest in the system under study.

1.2   Methods

For the medical events investigated in this study, the astronaut population and the occurrences are very low. Consequently, Bayesian methods were deemed to be necessary to produce better estimates of the probable incidence rates. The Bayesian process allows researchers to make inferences to determine the probability that a hypothesis is true, conditional on all available evidence. In these Bayesian updates, preflight and in-flight astronaut data (obtained from the Lifetime Surveillance of Astronaut Health (LSAH), see Appendix A) became the experimental data, and prior data were found through a variety of sources, including the general U.S. population, the U.S. Submarine Force, and the analog astronaut population at the NASA Johnson Space Center. The analog population is a group of people with similar physiological characteristics such as age, height, weight, health conditions, and lifestyles—including activity levels and health habits—as members of the astronaut corps. Preflight and in-flight calculations varied slightly for different medical events, based on when specific medical events started being tracked by LSAH and what data were available at the time of the specific request (Ref. 2). The renal stone data request was the first request made to LSAH, and in-flight astronaut data for this medical event includes shuttle transport system missions (STS–1 to STS–114), International Space Station missions (Expeditions 1 to 8 and 10 to 13), and Mir missions (seven astronauts total). The subsequent requests (in chronological order of request) were stroke, appendicitis, dental problems (abscess, caries, and periodontal disease), herpes zoster, atrial fibrillation, and atrial flutter (requests made in June 2010), and angina, seizure, and gallstone disease (requests made in December 2010).

All prior data used to define the incidence rate were assumed to be lognormal. The Poisson distribution was chosen to be the governing probability distribution (i.e., likelihood) for incidence values because it includes time (person-years) as an element in the probability equation. Time is an essential variable because it allows the probabilities to increase as the time of a space mission increases. Because Poisson distributions were used, an average rate for the incidences of these medical events had to be assumed. Consequently, the Bayesian update approach was used to calculate the distribution (mean and uncertainty) of the incidence rate associated with the Poisson distribution, and this approach is described for each of the medical events addressed in the report.

When Bayesian analyses are performed, certain data must be present for the calculations. For the prior data, the mean incidence rate and the error factor (EF) were required to adequately parameterize the assumed lognormal distribution. The EF represents the variance in the model, which is defined as the square root of the ratio of the 95th and 5th percentiles. This definition for the EF can be leveraged to relate percentiles of the standard normal distribution to define the percentiles of the lognormal distribution as illustrated by Bedford and Cooke (Ref. 3). In this case,

$$\ln(EF) = \Phi(0.95) \times \sigma = 1.645 \times \sigma$$

where σ is the standard deviation, Φ is the cumulative distribution function, 0.95 is the standard deviation at the 95th percentile of the distribution, and 1.645 is a constant representing the value of Φ at 0.95. For additional discussion on how the EF can be calculated from the confidence interval (CI) (see Appendix B).

The numerical update code called Bayesian inference Using Gibbs Sampling (WinBUGS) was used to perform all Bayesian updates. WinBUGS is a computer software program that performs Bayesian analysis of complex statistical models using Markov-chain Monte Carlo methods. It grew from a statistical research project at the Medical Research Council Biostatistics Unit, but it is now being developed jointly with the Imperial College School of Medicine at St. Mary's, London. This open-source software is available on the Web.

In most cases, the Bayesian process followed a standardized approach that combined the prior data with observed astronaut incidence data. Depending on the medical event, two or more Bayesian updates had to be performed with WinBUGS to adequately capture all the available data relating to the condition being examined. Appendix C provides the procedures that were used to construct and implement multiple Bayesian analyses of each medical event. An outline of the general procedure for completing a Bayesian update follows (Ref. 1):

(1) Begin with a probabilistic model for the process of interest and encode the aleatory uncertainty. For these analyses, this involves identifying the conditions that most affect the event, the type of data (incidence rates), and how the conditions and data are represented.

(2) Specify a prior distribution for the parameter(s) in this update, quantifying epistemic uncertainty (quantifying the degree of belief about the possible parameter values). For the IMM Bayesian analysis, this involved reviewing data identified in the Clinical Findings Form and reviewing the literature to capture appropriate (multistep) prior data.

(3) Obtain the observed data for the population of interest. Here data from the LSAH were heavily leveraged to support the reserved data requirements. In the case of no known incidents, only the total observation times in the appropriate segregated time span (in-flight and pre-flight) were required.

(4) Obtain the posterior (i.e., updated) distribution for the parameter(s) of interest. Here one or more WinBUGS scripts were created to perform the Markov-chain integration of the Bayesian analysis.

(5) Check the validity of the output. Output validity has several meanings, including convergence of the Markov chain, indicating that an appropriate representation of the data has been numerically determined, as well as the adequacy of the integrated calculations to represent the true understanding of the incidence rate and the associated uncertainty.

For this analysis, 75 000 Monte Carlo samplings were used for all medical events because this was a relatively safe indication that the Markov chain had reached its steady state. As rule of thumb for convergence, the WinBUGS manual suggests running until the Monte Carlo error is <5 percent of the sample mean or until the Brooks-Gelman-Rubin statistic is <1.2. These conditions were achieved with 75 000 samples in all cases. Analysis validity was confirmed through review with IMM team subject matter experts with regard to both the process and the analysis findings.

2.0 Medical Events

The following medical events were analyzed: angina, appendicitis, atrial fibrillation, atrial flutter, dental abscess, dental caries, dental periodontal disease, gallstone disease, herpes zoster, renal stones, seizure, and stroke.

2.1 Angina Pectoris

Angina pectoris is chest pain that occurs when part of the heart muscle does not get enough oxygenated blood. It is not a disease, but is typically a symptom of coronary heart disease—the most common type of heart disease in adults and occurs when plaque builds up on the inner walls of the coronary arteries, which can lead to a heart attack (Ref. 4). There are several different types of angina: stable, unstable, variant (Prinzmetal's angina), and microvascular. The most common type of angina is stable angina, which has a regular pattern and occurs when the heart is working harder than usual

(Ref. 4). Stable angina is not a heart attack, but it can suggest that a heart attack is more likely in the future. There are many different risk factors for angina pectoris, including high cholesterol, high blood pressure, smoking, diabetes or insulin resistance, being overweight or obese, inactivity, unhealthy diet, metabolic syndrome, familial history, and age—angina risk increases for males over the age of 45 and females over the age of 55 (Ref. 4).

Because of the potential severe medical problems associated with angina pectoris, understanding the probability of angina pectoris occurring in flight was deemed to be necessary. Incidence rates from the general population (Ref. 5), the analog astronaut population, and the active astronaut corps (Ref. 6, personal communication) were used to find this probability. A Bayesian update was used to combine these data to yield a probability distribution for the average incidence of angina pectoris during exploration missions.

2.1.1 Data and Methods

The data describing the average rate of angina incidence in the general population came from an article in the British Heart Journal (Ref. 5). The article follows 110 patients (70 males and 40 females) who were 70 years of age or less with no history of coronary heart disease when they presented for the first time with typical angina. All data were supplied as incidences per 1000 person-years and were reported for males and females between the ages of 41 and 50. Table 1 reports the average rates of angina for males and females, the corresponding 95-percent CIs, and the EFs (which were calculated as described in Appendix B, Section B.1). Total CI data (for males and females) between the ages of 41 and 50 were not presented in this article and were, therefore, not calculated in this analysis.

Incidences of angina in the analog astronaut population per person-years were obtained from LSAH (see Table 2 and Ref. 6, personal communication) because of the high number of risk factors for angina pectoris.

Incidences of angina in the astronaut corps and the number of person-years for preflight and in-flight astronauts were obtained from LSAH (see Table 3 and Ref. 6, personal communication). There were no cases of angina during any point in the study.

TABLE 1.—INCIDENCE OF ANGINA PECTORIS IN ADULTS IN THE UNITED KINGDOM

Statistic	Males	Females
Angina incidence in adults 41 to 50 years of age per 1000 person-years	0.63	0.47
95-percent confidence interval (CI) for angina incidence in adults per 1000 person-years	0.24 to 1.02	0.12 to 0.82
Angina incidence in adults 41 to 50 years of age per person-year	6.3×10^{-4}	4.7×10^{-4}
Error factor (EF) for angina incidence in adults 41 to 50 years of age	1.77	2.08

TABLE 2.—INCIDENCE OF ANGINA PECTORIS IN
THE ANALOG ASTRONAUT POPULATION
[From Lifetime Surveillance of Astronaut Health (LSAH).]

Statistic	Males	Females
Total person-years	2213.0	2808.6
Angina cases	6	0
Angina incidence rate, events per person-year	2.71×10^{-4}	0

TABLE 3.—INCIDENCE OF ANGINA PECTORIS IN
PREFLIGHT AND IN-FLIGHT MISSION-READY,
ACTIVE ASTRONAUTS
[From Lifetime Surveillance of Astronaut Health (LSAH).]

Statistic	Males	Females
Preflight astronauts		
Total person-years	1970.4	264.8
Angina cases	0	0
Angina incidence rate, events per person-year	0	0
In-flight astronauts		
Total person-years	32.0	6.5
Angina cases	0	0
Angina incidence rate, events per person-year	0	0

2.1.2 Bayesian Updates To Improve Estimates of Angina Incidence Rates, and Analysis Results

The following steps were taken with WinBUGS to improve the estimate of the angina incidence rate in the astronaut corps and to find an approximation suitable for the IMM effort. Three steps and Bayesian updates were performed. The first step used the general population data (Ref. 5) as priors to update the analog astronaut population data (Ref. 6, personal communication). This step was performed two times, once each for males and females. The posterior results from this step describe the angina incidence rates for the analog astronaut population. In the second step, the data from these posterior results, namely the mean and the 5th and 95th percentiles, were used as the priors to update the preflight astronaut data for males and females. In the third step, the data from the preflight posterior results were used as the priors to update the in-flight astronaut data for males and females. Ultimately, four probability distributions were found to describe the incidence rate for angina in preflight and in-flight male and female astronauts. Appendix C provides the code used in WinBUGS, and an outline of the input data for each step follows.

Step 1: The general United Kingdom population incidence rates per person-year for females and males, and the associated EFs from Table 1, were used for the priors in WinBUGS. The updated analog astronaut population data from LSAH included the number of person-years and the number of angina cases for males and females (Table 2). The posterior results from this Bayesian update were Poisson probability distributions for males and females in the analog astronaut population. Table 4 shows the means, 5th and 95th percentiles, and standard deviations.

TABLE 4.—RESULTS OF BAYESIAN ANALYSIS
FOR ANGINA PECTORIS IN THE ANALOG
ASTRONAUT POPULATION

Angina incidence rate, λ_{analog}, events per person-year		
Statistic	Males	Females
Mean	4.15×10^{-4}	3.72×10^{-4}
Standard deviation	9.99×10^{-5}	1.55×10^{-4}
5 percent	2.69×10^{-4}	1.77×10^{-4}
95 percent	5.93×10^{-4}	6.63×10^{-4}

TABLE 5.—RESULTS OF BAYESIAN ANALYSIS FOR
ANGINA PECTORIS IN PREFLIGHT MISSION-READY,
ACTIVE MALE AND FEMALE ASTRONAUTS

Angina incidence rate, $\lambda_{astronaut}$, events per person-year		
Statistic	Males	Females
Mean	3.96×10^{-4}	3.65×10^{-4}
Standard deviation	9.38×10^{-5}	1.53×10^{-4}
5 percent	2.62×10^{-4}	1.74×10^{-4}
95 percent	5.56×10^{-4}	6.53×10^{-4}

TABLE 6.—RESULTS OF BAYESIAN ANALYSIS
FOR ANGINA PECTORIS IN IN-FLIGHT
MALE AND FEMALE ASTRONAUTS

Angina incidence rate, $\lambda_{astronaut}$, events per person-year		
Statistic	Males	Females
Mean	3.95×10^{-4}	3.64×10^{-4}
Standard deviation	9.21×10^{-5}	1.53×10^{-4}
5 percent	2.64×10^{-4}	1.74×10^{-4}
95 percent	5.61×10^{-4}	6.53×10^{-4}

Step 2: The posterior results from Step 1—the means and the 5th and 95th percentiles from Table 4—along with the LSAH preflight data in Table 3 were used in WinBUGS to update the preflight astronaut data. The posterior results from this Bayesian update were Poisson probability distributions for angina incidence in preflight male and female astronauts. Table 5 shows the means, 5th and 95th percentiles, and standard deviations.

Step 3: The posterior results from Step 2—the means and the 5th and 95th percentiles from Table 5, along with the LSAH in-flight data in Table 3 were used in WinBUGS to update the in-flight astronaut data. The posterior results from this Bayesian update were Poisson probability distributions for angina incidence in in-flight male and female astronauts. Table 6 shows the means, 5th and 95th percentiles, and standard deviations.

2.1.3 Discussion

This analysis should be considered rather limited because it assumes an average incidence rate of angina pectoris, with no specific data for important factors such as overall health, diet, activity levels, metabolic syndrome, and familial history. The general population data from Gandhi et al. (Ref. 5) include a large proportion of smokers and ex-smokers (34 and

43 percent, respectively) and a large proportion of individuals classified as overweight and obese (50 and 27 percent, respectively). An individual was classified as overweight if he or she had a body mass index of 25 to 29 kg/m^2, and an individual was classified as obese if he or she had a body mass index greater than or equal to 30 kg/m^2. In addition, there may be minor differences between the diets and lifestyles of the United Kingdom population used in Gandhi et al. and the U.S. astronaut population. However, both populations are from well-developed, industrial countries in similar temperate regions. Accordingly, the present analysis assumes that their diets are similar to a high degree. The use of the analog astronaut population data may help to counteract some of the inaccuracies from these differences. The analog astronaut population may more closely reflect the actual risk factors that might influence an astronaut's propensity to develop angina pectoris. In spite of the limitations, the assumptions, and the data available, this analysis is probably a reasonable approximation of the incidence of angina pectoris during exploration missions. The current results can serve as a baseline for future studies that include more data and risk parameters.

2.2 Appendicitis

Because appendicitis may greatly affect the performance, health, and morale of crewmembers, evaluating the probability that an astronaut may encounter appendicitis during an exploration mission was deemed to be necessary. Appendicitis, the inflammation of the appendix, could be life-threatening for a crewmember lacking immediate medical care. The probability of an astronaut encountering appendicitis was estimated using data from the general U.S. population (Refs. 7 and 8) as well as from astronaut data from LSAH (Ref. 9, personal communication). A Bayesian update was used to combine the incidence rates from these sources to estimate the probability distribution for the rate of appendicitis during exploration missions.

2.2.1 Data and Methods

General population data regarding the incidence rate of appendicitis was extracted using a longitudinal, nationally representative, population-based study that was conducted on the incidence of appendicitis in the general U.S. population by the National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Survey (3-year average, 2003 to 2005) (Ref. 8). Because this source does not differentiate gender and ethnicity data by age, incidence rates differentiating between males and females and between whites and blacks were not been included in this calculation. Only the data for the hospital discharges (all-listed diagnoses) were included, because these data are presumably more reliable than data from ambulatory care visits. The incidence is 98/100 000 in females and 118/100 000 in males, for a ratio

TABLE 7.—INCIDENCE OF APPENDICITIS IN U.S. ADULTS 45 TO 64 YEARS OF AGE

Appendicitis incidence in adults 45 to 64 years of age per 100 000 persons per year[a]	93
Appendicitis incidence rate in adults 45 to 64 years of age, events per person-year	9.30×10^{-4}

[a]All-listed diagnoses for hospital discharges.

TABLE 8.—INCIDENCE OF APPENDICITIS IN PREFLIGHT AND IN-FLIGHT MISSION-READY, ACTIVE ASTRONAUTS
[From Lifetime Surveillance of Astronaut Health (LSAH).]

Statistic	Males	Females	Total
Preflight astronauts			
Total person-years	1400	244	1644
Appendicitis cases	2	0	2
Appendicitis incidence rate, events per person-year	1.43×10^{-3}	0	1.22×10^{-3}
In-flight astronauts			
Total person-years	31.9	6.4	38.3
Appendicitis cases	0	0	0
Appendicitis incidence rate, events per person-year	0	0	0

of 1:1.20. Table 7 shows the incidence rate of appendicitis in U.S. adults 45 to 64 years of age (Ref. 8). The rate for adults 45 to 64 years of age was used because it more accurately reflects the age of active astronauts and because the incidence rate is lower than that for people 15 to 24 years of age (which have the highest incidence rate, Ref. 8). Data from Addiss et al. (Ref. 7), which included data for males and females that was differentiated by age groups, was used to estimate the EF as 1.2.

Incidences of appendicitis in the analog astronaut population were obtained from the LSAH (Ref. 9, personal communication) and are summarized in Table 8. There were no occurrences of appendicitis in in-flight astronauts, and there were no occurrences in female astronauts. The highest incidence rate was in preflight male astronauts. Because there were no age-differentiated data for males and females available for the general population, the data for male and female astronauts were combined.

2.2.2 Bayesian Updates To Improve Estimates of Appendicitis Incidence Rates, and Analysis Results

The following steps were taken with WinBUGS to improve the estimate of the incidence rate of appendicitis in the astronaut corps and provide a first-order approximation suitable for the IMM effort. General population data (Ref. 8) were used to determine an informed lognormal conjugate for the incidence rate of appendicitis in the general U.S. population ($\lambda_{general}$). This was used as a prior to update LSAH preflight data in Step 1 of the Bayesian implementation,

yielding an updated appendicitis incidence rate. In Step 2, the posterior result of Step 1 was used as the prior and was updated with LSAH in-flight data in WinBUGS. The result was an estimation of the appendicitis incidence rate in astronauts during an exploration mission. Appendix C provides the code used in WinBUGS as well as the sampling procedure.

Step 1: First, WinBUGS was informed with the mean incidence rate of the general population from Table 7 and the EF (1.2).

Step 2: The input parameters of Step 1 were used to perform a Bayesian update with 75 000 Monte Carlo samples on the number of events and time (person-years) from the LSAH preflight data (Table 8).

Step 3: The posterior result of Step 2—the mean incidence rate—was dissected and used as the prior for the second update. The 5th and 95th percentiles from the lognormal Poisson distribution in Step 2 were used to calculate the EF. Table 9 shows the results for preflight astronauts.

Step 4: The input parameters of Step 1 were used to perform a second Bayesian update with 75 000 Monte Carlo samples on the number of in-flight events and person-years from the LSAH in-flight data (Table 8). Appendix C provides details.

This process returned an estimate of the rate of appendicitis in in-flight astronauts with respect to the general population (Table 10). This rate can be used as the input rate to a Poisson distribution to estimate the probability of appendicitis occurring in flight.

TABLE 9.—RESULTS OF BAYESIAN ANALYSIS FOR APPENDICITIS IN TOTAL PREFLIGHT MISSION-READY, ACTIVE ASTRONAUTS

Appendicitis incidence rate, $\lambda_{astronaut}$, events per person-year	
Mean	9.35×10^{-4}
Standard deviation	1.04×10^{-4}
5 percent	7.75×10^{-4}
Median	9.29×10^{-4}
95 percent	1.11×10^{-3}

TABLE 10.—RESULTS OF BAYESIAN ANALYSIS FOR APPENDICITIS IN TOTAL IN-FLIGHT ASTRONAUTS

Appendicitis incidence rate, $\lambda_{astronaut}$, events per person-year	
Mean	9.34×10^{-4}
Standard deviation	1.03×10^{-4}
5 percent	7.76×10^{-4}
Median	9.28×10^{-4}
95 percent	1.11×10^{-3}

This approximation is limited in that it assumes an average incidence rate of appendicitis irrespective of environmental conditions and the cause of appendicitis. There also were limitations in the data for the general population in that the incidence rate data for males and females and for blacks and whites were not age-differentiated. Everhart reports that the rate in whites was twice that of blacks and that the rate for males was 20 percent greater than for females (Ref. 8, these statements, however, do not take into account the ages being reported). According to another source for general population data, the highest incidence rates of appendicitis are found in 15 to 24 year olds, with 74 percent of all appendicitis cases found in 5 to 34 year olds (Ref. 10). In the mission-ready astronaut corps, the mean age for females is 43.8 years and the mean age for males is 45.3 years. Another assumption was made to use only hospital discharge data, not ambulatory care data, because patients being discharged from the hospital presumably carry a more definitive diagnosis of appendicitis because of the availability of better imaging technology and the increased likelihood that exploratory surgery was conducted (Ref. 8). However, these Bayesian updates yield a reasonable representation of the appendicitis incidence rate given the occurrence data available and the assumptions made during construction of the estimate.

Future estimates may be more accurate if data for males, females, and different ethnicities are available for various age ranges. More accurate estimates also could be made with further analysis of appendicitis occurrence in post-flight astronauts as well as greater understanding of the physiological pathways that lead to the obstruction, inflammation, and infection of the appendix. The current data will serve as the baseline for future estimates that utilize additional physiological parameters.

2.3   **Atrial Fibrillation**

One of the most common forms of heart arrhythmias is atrial fibrillation (AF). It is characterized by rapid, haphazard atrial contractions. Although AF is known to increase the likelihood of stroke and can be an underlying factor for death, it generally is not immediately threatening. AF is accompanied by debilitating symptoms, such as dizziness, shortness of breath, heart palpitations, and fatigue. Although these symptoms may not pose great difficulties for the general population, an AF episode could be detrimental to an astronaut crew on a space mission. Because of this high risk, determining the probability of AF was deemed to be necessary to help keep astronauts safe. Incidence rates from the astronaut corps (Ref. 11, personal communication) and the general population (Ref. 12) were used to determine this probability. A Bayesian update was used to combine these data to yield a probability distribution for AF incidence.

2.3.1 Data and Methods

The average rate of AF incidence in the general population used in this probability estimate came from an article in the journal Circulation (Ref. 12). These data were gathered from a cohort of patients at the Mayo Clinic in Olmsted County, Minnesota, from 1980 to 2000. An AF event was included if it was the first event for a particular patient and was verified by an electrocardiogram. These data were separated by age and year. In an attempt to closely approximate the current astronaut population, the most recent data from 1995 to 2000 for males and females under 55 were used. Data included the 95-percent CI for males, females, and the total from 1995 to 2000. However, these data were not specific to age, but were for all ages from 1995 to 2000. It was assumed that the 95-percent CI for all ages could be used as the 95-percent CI for those under 55. Appendix B, Section B.2, provides the steps for calculating the EF. All data were supplied as incidences per 1000 person-years. Table 11 gives the average AF incidence per person-year for men, women, and total, along with the EFs.

Incidences of AF in the astronaut corps and the number of person-years for preflight and in-flight astronauts were obtained from LSAH (see Table 12). There were no cases of AF in females during any point in the study.

2.3.2 Bayesian Updates To Improve Estimates of Atrial Fibrillation Incidence Rates, and Analysis Results

The following steps were taken with WinBUGS to improve the estimate of the AF incidence rate in the astronaut corps to find an approximation suitable for the IMM effort. Two steps and Bayesian updates were performed. The first step used the general population data (Ref. 12) as priors to update the LSAH preflight data (Ref. 11, personal communication). This step was performed three times, once each for males, females, and the total. The posterior results from this step describe the AF incidence rate for preflight astronauts. In the second step, the data from these posterior results, namely the means and the 5th and 95th percentiles, were then used as the priors to update the in-flight astronaut data for males, females, and the total. Ultimately, six probability distributions were found describing the AF incidence rate for preflight and in-flight male, female, and total astronauts. Appendix C shows the code used in WinBUGS, and an outline of the input data for each step follows.

Step 1: For females, males, and the total, the AF incidence per person-year in the general U.S. population (Table 11) and the EF were used for the priors in WinBUGS to update the number of AF cases for male and female astronauts from LSAH data (Table 12). Table 13 gives the posterior data from this step.

Step 2: The posterior results from Step 1—the means and the 5th and the 95th percentiles (Table 13) were used as the priors in WinBUGS to update the in-flight astronaut data from LSAH (Table 12). Table 14 shows the posterior results of this Bayesian update: a Poisson probability distribution for the means, 5th and 95th percentiles, and standard deviations of the AF incidence rate of in-flight astronauts.

TABLE 11.—INCIDENCE OF ATRIAL FIBRILLATION (AF) IN U.S. ADULTS

Statistic	Males	Females	Total
AF incidence in adults under 55 years of age per 1000 person-years	0.64	0.21	0.425
95-percent confidence interval (CI) for AF incidence in adults per 1000 person-years	0.32 to 0.96	0.01 to 0.41	0.24 to 0.60
AF incidence rate in adults under 55 years of age, events per person-year	6.40×10^{-4}	2.10×10^{-4}	4.25×10^{-4}
Error factor (EF) for AF incidence in adults under 55 years of age	1.56	2.97	1.45

TABLE 12.—INCIDENCE OF ATRIAL FIBRILLATION (AF) IN PREFLIGHT
AND IN-FLIGHT MISSION-READY, ACTIVE ASTRONAUTS
[From Lifetime Surveillance of Astronaut Health (LSAH).]

Statistic	Males	Females	Total
Preflight astronauts			
Total person-years	6502.7	336.8	6839.5
AF cases	4	0	4
AF incidence rate, events per person-year	6.15×10^{-4}	0	5.85×10^{-4}
In-flight astronauts			
Total person-years	31.8	6.5	38.3
AF cases	0	0	0
AF incidence rate, events per person-year	0	0	0

TABLE 13.—RESULTS OF BAYESIAN ANALYSIS
FOR ATRIAL FIBRILLATION (AF) IN PREFLIGHT
MISSION-READY, ACTIVE MALE, FEMALE,
AND TOTAL ASTRONAUTS

AF incidence rate, $\lambda_{astronaut}$, events per person-year			
Statistic	Males	Females	Total
Mean	6.29×10^{-4}	2.02×10^{-4}	4.43×10^{-4}
Standard deviation	1.51×10^{-4}	1.46×10^{-4}	9.39×10^{-5}
5 percent	4.12×10^{-4}	5.60×10^{-5}	3.06×10^{-4}
95 percent	9.02×10^{-4}	4.76×10^{-4}	6.11×10^{-4}

TABLE 14.—RESULTS OF BAYESIAN ANALYSIS FOR
ATRIAL FIBRILLATION (AF) IN IN-FLIGHT MALE,
FEMALE, AND TOTAL ASTRONAUTS

AF incidence rate, $\lambda_{astronaut}$, events per person-year			
Statistic	Males	Females	Total
Mean	6.28×10^{-4}	2.02×10^{-4}	4.42×10^{-4}
Standard deviation	1.52×10^{-4}	9.99×10^{-6}	9.36×10^{-5}
5 percent	4.12×10^{-4}	1.86×10^{-4}	3.06×10^{-4}
95 percent	9.05×10^{-4}	2.19×10^{-4}	6.09×10^{-4}

2.3.3   Discussion

These results are limited because they assume an average AF incidence rate and do not include specific data for ethnicity, previous cardiac diseases, or health. Also, assumptions were made when non-age-specific 95-percent CI were used for age-specific data. Understanding these limitations is necessary in applying these results. In spite of this limitation, the assumptions, and the data available, Table 13 and Table 14 present a reasonable approximation of AF incidence. These results can serve as a baseline for future studies that include further investigations into the causes of AF and more data and risk parameters for AF.

2.4   Atrial Flutter

Although atrial flutter (AFL) is less prevalent than AF, both are characterized by rapid atrial contractions. In contrast to AF, the quick AFL contractions are conducted in a regular pattern relative to ventricular contractions. Like AF, AFL is not immediately life threatening, though it can raise the chance of stroke. In addition, both atrial arrhythmias have similar debilitating symptoms, and both conditions could threaten the success of an astronaut if they were to occur in space. So that the proper amount of medications can be on hand for future in-flight AFL cases, the probability of AFL must be determined. A Bayesian update was used to combine experimental data from AFL incidence rates from the astronaut corps (Ref. 11, personal communication) and prior AFL incidence data from the general population (Ref. 13) to find this probability.

2.4.1   Data and Methods

The general population data describing the rate of AFL used in this probabilistic calculation came from Granada et al. (Ref. 13). This study examined the rate of AFL from the Marshfield Epidemiologic Study Area in Wisconsin from 1991 to 1995. AFL cases were confirmed with electrocardiograms, using the International Classification of Disease code ICD 427.32 to define AFL. To approximate the age of the astronaut corps, the data recorded for men, women, and the total under the age of 50 were used. Included with these data were the 95-percent CI for men, women, and the total. These 95-percent CI were not specific to age, however, so they were too wide to be applied directly to the data for adults less than 50 years of age. Ratios between the number of AFL cases and 95-percent CI width of all ages versus the incidence rates and 95-percent CI width for those under 50 were used to find a new 95-percent CI width for adults under 50 years of age. Appendix B, Section B.3, gives the steps for this calculation as well as for the calculation of the 95-percent CI into the EF. These data gave the number of incidences and the number of person-years for males, females, and the total. Table 15 gives the calculated incidence rates and the corresponding EFs.

AFL incidence data for the astronaut corps were supplied by LSAH (Ref. 11, personal communication). The number of AFL cases and person-years were included for in-flight and preflight male, female, and total astronauts, as shown in Table 16.

2.4.2   Bayesian Updates To Improve Estimates of Atrial Flutter Incidence, and Analysis Results

The following steps were taken with WinBUGS to improve the estimate of the AFL incidence rate in the astronaut corps and provide an approximation suitable for the IMM effort. This process took two steps. The first step was to update in WinBUGS the AFL incidence rate data for preflight astronauts performed three times, once each for males, females, and the total. The posterior results from the first step, including the means and the 5th and 95th percentiles, were used as the priors for another Bayesian update to the in-flight astronaut data. This was performed three times (once each for males, females, and the total) and yielded the Poisson probability distribution curves for the likelihood of an AFL occurrence in space. After these two steps, six Bayesian updates were performed with WinBUGS: for preflight and in-flight male, female, and total astronauts. Appendix C provides the WinBUGS code that was used, and an outline of each step, including the data used, follows.

Step 1: The general population incidence rates and EFs for males, females, and the total (Table 15) were used as the priors for a Bayesian update with WinBUGS on the number of cases and person-years for preflight astronauts from LSAH (Table 16). Table 17 shows the posterior results from this step.

TABLE 15.—INCIDENCE OF ATRIAL FLUTTER (AFL)
IN U.S. ADULTS FROM 1991 TO 1995

Statistic	Males	Females	Total
AFL cases in adults under 50 years of age	6	2	8
Number of person-years in the study	84 915	82 250	167 165
95-percent confidence interval (CI) for AFL in adults per 100 000 person-years	±0.24	±0.14	±0.13
AFL incidence rate for adults under 50 years of age per person-year	$7.07×10^{-5}$	$2.43×10^{-5}$	$4.79×10^{-5}$
Recalculated 95-percent CI for AFL incidence in adults per 100 000 person-years	±0.013	±0.004	±0.006
Error factor (EF) for AFL incidence in adults under 55 years of age	1.17	1.18	1.11

TABLE 16.—INCIDENCE OF ATRIAL FLUTTER (AFL) IN
PREFLIGHT AND IN-FLIGHT MISSION-READY,
ACTIVE ASTRONAUTS
[From Lifetime Surveillance of Astronaut Health (LSAH).]

Statistic	Males	Females	Total
Preflight astronauts			
Total person-years	6502.7	336.8	6839.4
AFL cases	0	0	0
AFL incidence rate, events per person-year	0	0	0
In-flight astronauts			
Total person-years	31.8	6.5	38.3
AFL cases	0	0	0
AFL incidence rate , events per person-year	0	0	0

TABLE 17.—RESULTS OF BAYESIAN ANALYSIS FOR
ATRIAL FLUTTER (AFL) IN PREFLIGHT MISSION-READY,
ACTIVE MALE, FEMALE, AND TOTAL ASTRONAUTS

AFL incidence rate, $\lambda_{astronaut}$, events per person-year			
Statistic	Males	Females	Total
Mean	$7.05×10^{-5}$	$2.43×10^{-5}$	$4.77×10^{-5}$
Standard deviation	$6.71×10^{-6}$	$2.45×10^{-6}$	$3.04×10^{-6}$
5 percent	$6.00×10^{-5}$	$2.05×10^{-5}$	$4.29×10^{-5}$
95 percent	$8.21×10^{-5}$	$2.85×10^{-5}$	$5.29×10^{-5}$

TABLE 18.—RESULTS OF BAYESIAN ANALYSIS FOR
ATRIAL FLUTTER (AFL) IN IN-FLIGHT MALE,
FEMALE, AND TOTAL ASTRONAUTS

AFL incidence rate, $\lambda_{astronaut}$, events per person-year			
Statistic	Males	Females	Total
Mean	$7.05×10^{-5}$	$2.43×10^{-5}$	$4.77×10^{-5}$
Standard deviation	$6.74×10^{-6}$	$2.42×10^{-6}$	$3.04×10^{-6}$
5 percent	$6.00×10^{-5}$	$2.05×10^{-5}$	$4.29×10^{-5}$
95 percent	$8.21×10^{-5}$	$2.84×10^{-5}$	$5.29×10^{-5}$

Step 2: This step used WinBUGS to combine the posterior results from Step 1—the means and the 5th and 95th percentiles (Table 17)—with the in-flight astronaut data from Table 16. The result of this Bayesian update was the Poisson probability distribution for the AFL incidence rate in in-flight male, female, and total astronauts. Table 18 shows the means, the 5th and 95th percentiles, and the standard deviations.

2.4.3 Discussion

Like the AF analysis, this analysis is also limited because it assumes an average incidence rate of AFL. There are no specific data for important risk factors such as ethnicity or previous cardiac diseases and health. Also assumptions were made when non-age-specific 95-percent CI were used for age-specific data. These limitations should be kept in mind when this analysis is used. Despite the limitations, however, this analysis is a reasonable approximation of AFL incidence and can serve as a baseline until further investigations into the risk parameters and causes of AFL are made.

2.5 Dental Abscess

Because a dental abscess may greatly affect crewmember performance, health, and morale, evaluating the probability that an astronaut may encounter a dental abscess during an exploration mission was deemed to be necessary. An abscess results from the infection of pulp material in the tooth caused by complications such as decayed, cracked, or broken teeth (Ref. 14). U.S. Submarine Force (Ref. 15) and astronaut data from LSAH (Ref. 16, personal communication) were used to estimate the probability of an astronaut encountering dental abscess. The submarine crew data analysis defined periapical abscesses as 2010 ICD–9–CM code 522 (pulp and periapical), and the astronaut data from LSAH defined dental abscess as "abscess diagnosis," with no reference to ICD–9 coding. A Bayesian update was used to combine information from these sources to estimate the average incidence rate of abscess.

2.5.1 Data and Methods

Submarine force data were used because of the physiological similarity of the U.S. Submarine Force to astronauts. Deutsch (Ref. 15) conducted studies from 1997 to 2000 on the incidence of various dental emergencies in U.S. Submarine Force personnel. The medical history of submarine missions was useful for this statistical analysis because of their similarities to exploration-class missions. For example, both occur in confined, remotely located environments where professional medical care is not immediately available. Also, a medical event of low probability and high consequence could cause a mission to cease (Refs. 17 and 18). Although there are similarities between a submarine mission and a space exploration mission, it is important to note that smoking was

TABLE 19.—INCIDENCE OF DENTAL ABSCESS IN
240 PATROLS OF THE U.S. SUBMARINE FORCE

Total person-years..	5946.9
Total visits due to abscess	21
Abscess incidence rate, events per person-year................	3.53×10^{-3}
95-percent confidence interval (CI)	0.69 to 3.80
Error factor (EF)	1.48

TABLE 20.—INCIDENCE OF DENTAL ABSCESS IN
PREFLIGHT AND IN-FLIGHT MISSION-READY,
ACTIVE MALE ASTRONAUTS
[From Lifetime Surveillance of Astronaut Health (LSAH).]

Preflight astronauts	
Total person-years..	475.2
Number of crewmembers..	77
Abscess cases	19
Abscess incidence rate, events per person-year	4.0×10^{-2}
In-flight astronauts	
Total person-years..	31.9
Abscess cases..	0
Abscess incidence rate, events per person-year	0

TABLE 21.—RESULTS OF BAYESIAN ANALYSIS
FOR DENTAL ABSCESS IN PREFLIGHT MISSION-
READY, ACTIVE MALE ASTRONAUTS

Abscess incidence rate, $\lambda_{astronaut}$, events per person-year	
Mean	8.26×10^{-3}
Standard deviation	1.80×10^{-3}
5 percent	5.64×10^{-3}
Median	8.09×10^{-3}
95 percent	1.15×10^{-2}

TABLE 22.—RESULTS OF BAYESIAN ANALYSIS
FOR DENTAL ABSCESS IN IN-FLIGHT
MALE ASTRONAUTS

Abscess incidence rate, $\lambda_{astronaut}$, events per person-year	
Mean	8.16×10^{-3}
Standard deviation	1.80×10^{-3}
5 percent	5.58×10^{-3}
Median	7.98×10^{-3}
95 percent	1.14×10^{-2}

significantly associated with the occurrence of a periodontal-related emergency and also with the occurrence of any dental emergency. There is probably a greater percentage of smokers among the U.S. Submarine Force than among astronauts. In addition, the submarine study is limited in that it applies only to adult men and that the overwhelming majority (88.5 percent) of the sailors followed in this study were Caucasian. In addition, submarine crew members are generally more senior than the average sailor (70.5 percent were 25 years old or older). Table 19 shows the submarine crew data. The EF was determined from the 95-percent CI as outlined in Appendix B, Section B.4.

Table 20 shows the LSAH dental abscess data for the astronaut corps from LSAH (Ref. 16, personal communication). For this analysis, data for the mission-ready, active female astronaut population was not used because the U.S. Submarine Force data used in the Bayesian update was for males only.

2.5.2 Bayesian Updates To Improve Estimates of Dental Abscess Incidence Rates, and Analysis Results

The following steps were taken with WinBUGS to improve the estimate of the incidence rate of dental abscess in the astronaut corps and provide a first-order approximation suitable for the IMM effort. One Bayesian update was performed using data for the U.S. Submarine Force and for mission-ready, active male astronauts. The submarine crew data were used to form an informed lognormal conjugate prior for the incidence rate of dental abscess in the U.S. Submarine Force and data on preflight incidences in male astronauts, yielding an updated incidence rate of abscess. In Step 3, the posterior result of Step 1 was used as the prior and was updated in WinBUGS with LSAH in-flight data. The result was an estimate of the incidence rate of abscess in astronauts during an exploration mission. Appendix C provides the code used in WinBUGS as well as the sampling procedure.

Step 1: WinBUGS was informed with the mean abscess incidence rate for the U.S. Submarine Force and the EF from Table 19.

Step 2: A Bayesian update was performed with 75 000 Monte Carlo samplings on the number of events and person-years for preflight male astronauts from LSAH data (Table 20).

Step 3: The mean incidence rate for preflight astronauts from Step 1 (Table 21) was used as the prior for the second update, and the EF was calculated as 1.43 from the 95th and 5th percentiles from Step 1.

Step 4: A second Bayesian update was performed with 75 000 Monte Carlo samples on the input parameters of Step 3: the number of events and person-years for in-flight male astronauts (Table 20). Appendix C provides details.

This process returned an estimate of the incidence rate of dental abscess in the astronaut corps ($\lambda_{astronaut}$) with respect to the U.S. Submarine Force. This can be used as the input rate to a Poisson distribution to estimate the probability of abscess occurring during flight. Table 22 illustrates the results of the implementation.

2.5.3 Discussion

The number of events per person-years for the submarine population (Table 19) is 3.53×10^{-3} versus 8.16×10^{-3} for male astronauts (Table 22). In both submarine and astronaut data, there may be cases of underreporting. Astronaut health is typically tracked through annual physicals, where questions related to dental health may or may not be asked. There may be demographic differences between the submarine and astronaut data, including rates of smoking, age differences, and racial differences. The age difference may be important to note because recommended preventative dental practices

tend to evolve over time. Current recommended dental practices include daily flossing, brushing teeth twice a day for at least 2 minutes, seeing a dentist twice a year, and drinking fluoridated water (the number of communities in the United States with fluoridated water grows each year) (Refs. 19 to 22). The differences between population demographics and access to fluoridated water may lead to discrepancies in incidence rates. Also, because women do not serve as submarine crewmembers, female astronaut data were not used in this Bayesian calculation. Future analyses should include data for women.

2.6 Dental Caries

Because dental caries may greatly affect crewmember performance, health, and morale, evaluating the probability that an astronaut may encounter dental caries during an exploration mission was deemed to be necessary. Caries are caused by certain bacteria in the oral flora that release acid as a byproduct of carbohydrate metabolism. The acid dissolves the calcium phosphate of the enamel and dentin (Refs. 20 and 21). U.S. Submarine Force data (Ref. 15) and astronaut data from LSAH (Ref. 16, personal communication) were used to estimate the probability of an astronaut encountering dental caries. The submarine crew data defined dental caries as 2010 ICD–9–CM code 521 (hard tissues and caries), and the astronaut data from LSAH defined dental caries as "primary caries, secondary caries, or order unknown," with no reference to ICD–9 coding. For this analysis, the sum of all three caries categories was used for astronauts. A Bayesian update was used to combine the information from these sources to estimate the average rate of caries.

2.6.1 Data and Methods

The medical history of submarine missions was useful because they are similar to exploration-class missions. For example, both occur in confined, remotely located environments where professional medical care is not immediately available. Also, a medical event of low probability and high consequence could cause a mission to cease (Refs. 17 and 18). It is important to note that smoking was significantly associated with the occurrence of a periodontal-related emergency and also with the occurrence of any dental emergency. It is likely that there is a greater percentage of smokers among sailors than among the astronaut corps. This study is limited in that it included only adult men and that the overwhelming majority (88.5 percent) of these men were Caucasian. In addition, submarine crew members are generally more senior than the average sailor (70.5 percent were 25 years old or older). Table 23 shows the submarine crew data. The EF was determined from the 95-percent CI as outlined in Appendix B, Section B.4.

TABLE 23.—INCIDENCE OF DENTAL CARIES IN 240 PATROLS OF THE U.S. SUBMARINE FORCE

Total person-years	5946.9
Total visits due to caries	29
Caries incidence rate, events per person-year	4.88×10^{-3}
95-percent confidence interval (CI)	0.3 to 1.53
Error factor (EF)	1.11

TABLE 24.—INCIDENCE OF DENTAL CARIES IN PREFLIGHT AND IN-FLIGHT MISSION-READY, ACTIVE MALE ASTRONAUTS
[From Lifetime Surveillance of Astronaut Health (LSAH).]

Preflight astronauts	
Total person-years	475.2
Number of crewmembers	77
Caries cases	168
Caries incidence rate, events per person-year	3.54×10^{-1}
In-flight astronauts	
Total person-years	31.9
Caries cases	0
Caries incidence rate, events per person-year	0

Table 24 shows the data from LSAH (Ref. 16, personal communication). For this analysis, data for the mission-ready, active female astronaut population was not used because the U.S. Submarine Force data only included males.

2.6.2 Bayesian Updates To Improve Estimates of Dental Caries Incidence Rates, and Analysis Results

The following steps were taken with WinBUGS to improve the estimate of the incidence rate of dental caries in the astronaut corps and provide a first-order approximation suitable for the IMM effort. One Bayesian update was done using data for the U.S. Submarine Force and for mission-ready, active male astronauts. The submarine crew data were used to form an informed lognormal conjugate prior for the incidence rate of dental caries in U.S. Submarine Force personnel as well as for preflight incidences in male astronauts, yielding a posterior result for the updated incidence rate of caries. In Step 3, the posterior result of Step 1 was used as the prior, and updated LSAH in-flight data were used in WinBUGS. The result was an estimate for the incidence rate of abscess in astronauts during an exploration mission (Table 24). Appendix C shows the code used in WinBUGS as well as the sampling procedure.

Step 1: WinBUGS was informed with the U.S. Submarine Force mean incidence rate and the EF from Table 23.

Step 2: A Bayesian update was performed with 75 000 Monte Carlo samplings on the number of events and person-years for preflight male astronauts from LSAH data (Table 24). Table 25 shows the results.

TABLE 25.—RESULTS OF BAYESIAN ANALYSIS
FOR DENTAL CARIES IN PREFLIGHT MISSION-
READY, ACTIVE MALE ASTRONAUTS

Caries incidence rate, $\lambda_{astronaut}$, events per person-year	
Mean	9.42×10^{-3}
Standard deviation	5.94×10^{-4}
5 percent	8.48×10^{-3}
Median	9.40×10^{-3}
95 percent	1.04×10^{-2}

TABLE 26.—RESULTS OF BAYESIAN ANALYSIS
FOR DENTAL CARIES IN IN-FLIGHT MISSION-
READY, ACTIVE MALE ASTRONAUTS

Caries incidence rate, $\lambda_{astronaut}$, events per person-year	
Mean	9.41×10^{-3}
Standard deviation	5.95×10^{-4}
5 percent	8.46×10^{-3}
Median	9.39×10^{-3}
95 percent	1.04×10^{-2}

Step 3: The mean incidence rate from Step 1 (Table 25) was used as the prior for the second update, and the EF was calculated as 1.11 from the 95th and 5th percentiles from Step 1.

Step 4: A second Bayesian update was performed with 75 000 Monte Carlo samples on the input parameters of Step 3: the number of in-flight events and person-years for in-flight male astronauts from LSAH data (Table 24). Appendix B, Section B.4, provides details.

This process returned an estimate of the incidence rate of dental caries in the astronaut corps ($\lambda_{astronaut}$) with respect to the U.S. Submarine Force. This incidence rate was used as input to a Poisson distribution to estimate the probability of caries occurring during flight. Table 26 shows the results.

2.6.3 Discussion

The number of dental caries events per person-year was 4.88×10^{-3} in the U.S. Submarine Force versus 9.41×10^{-3} for male astronauts. In both the submarine crew and astronaut data, there may be cases of underreporting. Astronaut health is typically tracked through annual physicals, where questions related to dental health may or may not be asked. There may be demographic differences between the submarine crew and astronaut data, including rates of smoking, age differences, and racial differences. The age difference may be important to note because recommended preventative dental practices tend to evolve over time, as described in Section 2.5.3 and in References 17 to 21. The differences between population demographics and access to fluoridated water may have produced discrepancies in incidence rates. Also, because women do not serve as submarine crewmembers, female

astronaut data were not used in this Bayesian calculation. Future analyses should include data for women.

2.7   Dental Periodontal Disease

Because periodontal disease may greatly affect crewmember performance, health, and morale, evaluating the probability that an astronaut may develop periodontal disease during an exploration mission was deemed to be necessary. Periodontal disease involves inflammation and infection that destroy the tissues that support the teeth, including the gums, the periodontal ligaments, and the tooth sockets (alveolar bone) (Ref. 22). Gingivitis is a form of periodontal disease due to the long-term effects of plaque deposits. U.S. Submarine Force data (Ref. 15) and astronaut data from LSAH (Ref. 16, personal communication) were used to estimate the probability of an astronaut encountering periodontal disease. The submarine crew data defined periodontal disease as 2010 ICD–9–CM code 523 (gingival and periodontal disease), and LSAH defined periodontal disease as "periodontal disease diagnosis," with no reference to ICD–9 coding. A Bayesian update was used to combine information from these sources to estimate the average rate of periodontal disease.

2.7.1   Data and Methods

The medical history of submarine missions was useful for this statistical analysis because these missions are similar to exploration-class missions: both occur in confined, remotely located environments where professional medical care is not immediately available. Also, a medical event of low probability and high consequence could cause a mission to fail (Refs. 17 and 18). Data from Deutsch (Ref. 15) regarding the incidence of periodontal disease and gingivitis in the U.S. Submarine Force were used because of these similarities (see Table 27). However, it is important to note that smoking was significantly associated with the occurrence of a periodontal-related emergency as it was with the occurrence of any dental emergency. The percentage of smokers among sailors is probably greater than among the astronaut corps. The U.S. Submarine Force study is limited in that it applies only to adult men, and the overwhelming majority (88.5 percent) of these men were Caucasian. In addition, submarine crew members are generally more senior than the average sailor (70.5 percent were 25 years old or older). Table 27 shows the results, where the EF was determined from the 95-percent CI as outlined in Appendix B, Section B.4.

The IMM team obtained data regarding the incidence of periodontal disease in the astronaut corps from LSAH (Ref. 16, personal communication) (see Table 28). Because the U.S. Submarine Force data used in this Bayesian update was for males only, data for the mission-ready, active female astronaut population were not used.

TABLE 27.—INCIDENCE OF GINGIVAL AND
PERIODONTAL DISEASE IN 240 PATROLS
OF THE U.S. SUBMARINE FORCE

Total person-years 5946.9	
Total visits due to periodontal disease 10	
Periodontal disease incidence rate, events per person-year................................... 1.68×10^{-3}	
95-percent confidence interval (CI) .... 0.33 to 4.19	
Error factor (EF) 6.24	

TABLE 28.—INCIDENCE OF PERIODONTAL DISEASE
IN PREFLIGHT AND IN-FLIGHT MISSION-READY,
ACTIVE MALE ASTRONAUTS
[From Lifetime Surveillance of Astronaut Health (LSAH).]

Preflight astronauts
Total person-years.. 475.2
Number of crewmembers 77
Periodontal disease cases 56
Periodontal disease incidence rate, events per person-year .... 1.18×10^{-1}
In-flight astronauts
Total person-years.. 31.9
Periodontal disease cases 0
Periodontal disease incidence rate, events per person-year 0

TABLE 29.—RESULTS OF BAYESIAN ANALYSIS FOR
PERIODONTAL DISEASE IN TOTAL PREFLIGHT
MISSION-READY, ACTIVE MALE ASTRONAUTS

Periodontal disease incidence rate, $\lambda_{astronaut}$, events per person-year	
Mean	1.10×10^{-1}
Standard deviation	1.52×10^{-2}
5 percent	8.62×10^{-2}
Median	1.09×10^{-1}
95 percent	1.36×10^{-1}

TABLE 30.—RESULTS OF BAYESIAN ANALYSIS
FOR PERIODONTAL DISEASE IN IN-FLIGHT
MALE ASTRONAUTS

Periodontal disease incidence rate, $\lambda_{astronaut}$, events per person-year	
Mean	1.03×10^{-1}
Standard deviation	1.41×10^{-2}
5 percent	8.16×10^{-2}
Median	1.02×10^{-1}
95 percent	1.28×10^{-1}

2.7.2 Bayesian Updates To Improve Estimates of Periodontal Disease Incidence Rates, and Analysis Results

The following steps were taken with WinBUGS to improve the estimate of the incidence rate of periodontal disease in the astronaut corps and provide a first-order approximation suitable for the IMM effort. One Bayesian update was performed using U.S. Submarine Force data and data for mission-ready, active male astronauts. The submarine crew data were used to form an informed lognormal conjugate prior for the incidence rate of periodontal disease in U.S. Submarine Force personnel and male astronauts, yielding a posterior result of the updated incidence rate of periodontal disease. In Step 3, the posterior result of Step 1 was used as the prior and was updated with LSAH in-flight data in WinBUGS. The result was an estimation of the incidence rate of periodontal disease in astronauts during an exploration mission. Appendix C provides the code used in WinBUGS as well as the sampling procedure.

Step 1: WinBUGS was informed with the U.S. Submarine Force mean incidence rate and the EF from Table 27.

Step 2: A Bayesian update was performed with 75 000 Monte Carlo samplings on the number of events and person-years for preflight male astronauts from LSAH data (Table 28).

Step 3: The mean incidence rate for preflight astronauts from Step 1 (Table 29) was used as the prior for the second update, and the 95th and 5th percentiles from Step 1 were used to calculate the EF.

Step 4: A second Bayesian update was performed with 75 000 Monte Carlo samples on the input parameters of Step 3: the number of events and person-years for in-flight male astronauts from LSAH data (Table 28). Appendix C provides details.

This process returned an estimate of the incidence rate of periodontal disease in the astronaut corps ($\lambda_{astronaut}$) with respect to the U.S. Submarine Force (Table 30). This rate can be used as the input rate to a Poisson distribution to estimate the probability of periodontal disease occurring during flight.

2.7.3 Discussion

The number of periodontal disease events per person-year in the submarine population is 2 orders of magnitude less than that of the male astronauts. In both the submarine and astronaut data, there may be cases of underreporting. Astronaut health is typically tracked through annual physicals, where questions related to dental health may or may not be asked. In addition, there may be demographic differences between the submarine crew and astronaut data, including rates of smoking, age, and race. The age difference may be important to note because recommended preventative dental practices tend to evolve over time, as described in Section 2.5.3 and References 19 to 22. These differences and differences in access to fluoridated water may lead to discrepancies in incidence rates. Also, because women do not serve as submarine crewmembers, female astronaut data were not used in this Bayesian calculation. Future analyses should include data for women.

2.8 Gallstone Disease

The presence of cholesterol stones or bile pigment-based stones in the gallbladder is a relatively common condition that can lead to a variety of serious complications. Risk factors for gallstone disease include age, obesity, diabetes mellitus, pregnancy, and alcohol use. In addition, during the reproductive years, the condition is about 4 times more likely in women than in men. This gender discrepancy diminishes with age. Although gallstones may be asymptomatic, the complications of symptomatic gallstone, or biliary disease may have a negative impact on crewmember health, morale, and performance. The current standard treatment for most complications of biliary disease is cholecystectomy, or surgical removal of the gallbladder (Ref. 23). Three of the severe complications of gallstone disease are acute cholecystitis, acute biliary pancreatitis, and acute cholangitis. Acute cholecystitis, or inflammation of the gallbladder, can lead to progressive pain, fever, and possible necrosis of the gallbladder. Treatment requires antibiotics and early surgical intervention (Ref. 23). Biliary pancreatitis occurs when a gallstone passes into and through the common bile duct, leading to abdominal pain and potential inflammation. Treatment for this condition includes endoscopic removal of the stone and cholecystectomy (Ref. 23). Cholangitis is the infection of an obstructed bile duct, causing pain and fever (Ref. 24). Owing to the debilitating symptoms of these conditions and the difficulties that surgical treatment requirements pose for space exploration missions, calculating the incidence rate of severe gallstone disease in astronauts was deemed to be necessary. A Bayesian update was used to combine the incidence rates of acute cholecystitis, biliary pancreatitis, and cholangitis from a general population study with data on the incidence of severe gallstone disease in the astronaut corps from LSAH to yield a probability distribution describing the incidence rate of severe gallstone disease in astronauts (Ref. 6, personal communication).

2.8.1 Data and Methods

So that a first-order estimate of the incidence rate of severe gallstone disease in the astronaut and general populations could be obtained, the assumption was first made that gallstone disease occurs at some characteristic constant rate ($\lambda_{gallstone}$) over the period of interest. This allowed the number of gallstone events to be represented as a Poisson process with characteristic rate $\lambda_{gallstone}$.

The probability distribution describing this rate in the general population was determined from a study published in the Canadian Medical Association Journal that used data from the Canadian Institute for Health Information, the Ontario Health Insurance Plan physicians claims database, and the Registered Persons Database to determine the annual incidence rates of acute cholecystitis, acute biliary pancreatitis, and acute cholangitis per 100 000 people from 1988 to 2000. The study determined incidence rates for the three events separately. In addition, incidence rates were stratified by males and females and by age (Ref. 6, personal communication).

Independence of occurrence was assumed for the different age groups and different diseases when these incidence rates were combined for the Bayesian analysis (as described in Appendix D) to make sure that the estimate of severe gallstone disease incidence in the total general population would be as similar as possible to that in the astronaut corps. Incidences provided in the study for ages 18 to 44 and 45 to 64 were combined to estimate the incidence of severe gallstone disease for a general population aged 18 to 64. It was assumed that the distributions describing the two groups were independent. The incidence rates for the three separate diseases determined in this fashion were summed to provide an estimate of the total severe gallstone disease incidence, again with the assumption that the distributions were independent. This procedure was repeated for men, women, and the total.

Appendix D provides the method used to combine incidence rates with the assumption of statistical independence of the age groups and conditions. Table 31 summarizes the incidence rates in the general population that were determined via this procedure. The study provided 95-percent CIs for each incidence rate that were combined in a fashion consistent with independent distributions and were used to determine estimates for the standard error of the general population incidence rates. These standard error estimates were used to construct 90-percent CIs for the incidence rates, which were used, in turn, to calculate the EFs. Table 31 provides the calculated incidence rates for men, women, and the total, along with the EFs. Appendix B, Section B.5, summarizes the technique used to determine the EF from the 95-percent CI provided in Reference 25.

Data concerning the incidence of severe gallstone disease in the astronaut corps were obtained from the LSAH (Ref. 6, personal communication), as summarized in Table 32. There were no occurrences of severe gallstone disease in in-flight astronauts, and there were no occurrences at any stage in female astronauts. The three preflight occurrences of gallstone

TABLE 31.—CALCULATED INCIDENCE OF GALLSTONE DISEASE IN ONTARIO FROM 1988 TO 2000

Statistic	Males	Females	Total
Gallstone cases in adults 18 to 64 years of age per 100 000 person-years (derived)	76.9	126.6	101.7
90-percent confidence interval (CI) for gallstone disease occurrences (derived)	76.1 to 77.6	125.6 to 127.5	101.2 to 102.3
Gallstone incidence in adults 18 to 64 years of age, events/person-year	7.69×10^{-4}	1.27×10^{-3}	1.02×10^{-3}
Error factor (EF) for gallstone incidence in adults 18 to 64 years of age	1.01	1.01	1.01

TABLE 32.—INCIDENCE OF GALLSTONE DISEASE IN
PREFLIGHT AND IN-FLIGHT MISSION-READY,
ACTIVE MALE AND FEMALE ASTRONAUTS
[From Lifetime Surveillance of Astronaut Health (LSAH).]

Statistic	Males	Females	Total
Preflight astronauts			
Total person-years	1970.4	264.8	2235.2
Gallstone cases	3	0	3
Gallstone incidence rate, $\lambda_{astronaut}$, events per person-year	1.52×10^{-3}	0	1.34×10^{-3}
In-flight astronauts			
Total person-years	32.0	6.5	38.5
Gallstone cases	0	0	0
Gallstone incidence rate, $\lambda_{astronaut}$, events per person-year	0	0	0

disease in men were all 3 to 6 years preflight. Table 32 shows the preflight and in-flight incidence rates.

2.8.2 Bayesian Updates To Improve Estimates of Gallstone Incidence Rates, and Analysis Results

The following steps were taken with WinBUGS to obtain a first-order estimate of the incident rate of gallstone disease in the astronaut corps. The analysis combined information from the Canadian general population with available information on gallstone incidence in astronauts. Informed lognormal priors for the incidence rate of gallstone disease in the general population was determined from information in Urbach et al. (Ref. 25), as described in Appendix D. Step 1 of the Bayesian analysis used this prior to update the LSAH preflight data on gallstone disease incidence in astronauts. This resulted in posterior results describing the incidence rate in preflight astronauts. The posterior results were used as priors for the second step, which updated the LSAH data for gallstone disease incidence in in-flight astronauts. The result was a first-order estimate of the incidence rate of severe gallstone disease in astronauts on a long-duration exploration-class mission. This procedure was performed three times, once each for male, female, and total astronauts. In each Bayesian update, 75 000 update steps were used. Appendix C provides the code used in WinBUGS, and an outline of the input data used in each step follows.

Step 1: For males, females, and the total, the general population incidence rates and EFs were used to inform the lognormal priors in WinBUGS. The LSAH preflight data that were updated included the number of gallstone disease cases and the recorded number of person-years for each population. Table 33 shows the gallstone incidence rates for preflight astronauts and provides the posterior results from this step: the incidence of gallstone disease in male, female, and total preflight astronauts.

Step 2: The posterior results from Step 1—the means and the 5th and the 95th percentiles (Table 33)—were used as priors in WinBUGS to update the LSAH data for in-flight astronauts

TABLE 33.—RESULTS OF BAYESIAN ANALYSIS
FOR GALLSTONE DISEASE IN PREFLIGHT
MISSION-READY, ACTIVE ASTRONAUTS

Gallstone incidence rate, $\lambda_{astronaut}$, events per person-year			
Statistic	Males	Females	Total
Mean	7.69×10^{-4}	1.27×10^{-3}	1.02×10^{-3}
Standard deviation	4.65×10^{-6}	7.64×10^{-6}	6.12×10^{-6}
5 percent	7.62×10^{-4}	1.25×10^{-3}	1.01×10^{-3}
95 percent	7.77×10^{-4}	1.28×10^{-3}	1.03×10^{-3}

TABLE 34.—RESULTS OF BAYESIAN ANALYSIS FOR
GALLSTONE DISEASE IN IN-FLIGHT ASTRONAUTS

Gallstone incidence rate, $\lambda_{astronaut}$, events per person-year			
Statistic	Males	Females	Total
Mean	7.69×10^{-4}	1.27×10^{-3}	1.02×10^{-3}
Standard deviation	4.65×10^{-6}	7.68×10^{-6}	6.18×10^{-6}
5 percent	7.62×10^{-4}	1.25×10^{-3}	1.01×10^{-3}
95 percent	7.77×10^{-4}	1.28×10^{-3}	1.03×10^{-3}

(Table 32). This Bayesian update resulted in probability distributions for the incidence of gallstone disease in male, female, and total astronauts during spaceflight (Table 34).

2.8.3 Discussion

Like the other analyses presented in this study, this analysis is limited because it assumes a constant incidence rate for gallstone disease without accounting for physiological and environmental risk factors. Future analyses should consider important risk factors, including age, obesity, and diet. In addition, assumptions of independence were made to compute a general gallstone disease incidence rate from the disease-specific rates obtained from the literature, but the incidence rates for different conditions and age groups might not be wholly independent. Furthermore, this analysis uses the combined incidence rates of three severe complications of gallstone disease as an estimate of the incidence rate for total gallstone disease, but these three conditions alone may not provide a sufficiently broad consideration of the complications of gallstone disease. This is evident in the fact that the incidence rate of gallstone disease in the in-flight male astronauts (1.52×10^{-3} events/person-year) is almost twice that of the general male population (7.69×10^{-4} events/person-year in Ref. 25)—a counterintuitive result. In addition, minor differences may exist between the diets and lifestyles of the Ontario population used and the U.S. astronaut population (Ref. 25). However, both populations are from well-developed, industrial countries in similar North American temperate regions. Accordingly, for the present analysis it was assumed that the diets are similar to a high degree. Incorporation of additional possible complications or related conditions might improve this estimate. Any use of these results must account for these limitations, but this analysis is "a reasonable estimate" of the incidence rate of gallstone-related diseases in astronauts.

The accuracy of this analysis could be improved if more data relating to the risk factors for and the physiology of gallstone formation and related complications were incorporated. The current results can serve as a baseline for future gallstone disease predictions.

2.9 Herpes Zoster

The first infection of the varicella-zoster virus results in chicken pox. Reactivation of this virus in the cranial nerve or the dorsal root ganglia results in a painful rash known as herpes zoster (HZ) (Ref. 26)—a skin disease more commonly known as shingles. The cause for reactivation is unknown, but higher incidence rates are found for the elderly, and reactivation is generally associated with a weakened immune system (Ref. 26). Because the virus lives in the nerve, HZ is extremely painful. The probability of HZ incidences must be calculated to ensure that enough medications are supplied for any and all shingles outbreaks during a space mission. The general population data used in this calculation must roughly match the age of active astronauts because HZ reactivation rates increase exponentially with age. The general population data used came from a 2005 article in the *Journal of General Internal Medicine* (Ref. 26). A Bayesian update was use to combine these data with HZ incidence data from the astronaut corps to yield a probability distribution describing the average HZ incidence rate in astronauts.

2.9.1 Data and Methods

For the general population data, Reference 26 pulled HZ incidence rates from the Medstat MarketScan database, which

2001. Incidences of HZ were defined by the 9th revision of the ICD. Data included the number of HZ cases per the number of person-years for males, females, and the total who were 40 to 49 years of age. These data were simplified to incidences per person-year for males, females, and the total. The 95-percent CI per 1000 person-years also is given for males, females, and the total for ages 40 to 49. These intervals were converted into the EFs for males, females, and the total. Appendix B, Section B.6, shows the steps for these conversions, and Table 35 shows the average HZ incidence per person-year for males, females, and the total, along with the corresponding EFs.

The LSAH supplied data that describe the incidence of HZ and the number of person-years for preflight and in-flight male, female, and total astronauts (Table 36 and Refs. 27 and 28, personal communications).

2.9.2 Bayesian Updates To Improve Estimates of Herpes Zoster Incidence Rates, and Analysis Results

The following steps were taken with WinBUGS to improve the estimate of the incidence rate of HZ in astronauts and provide an approximation suitable for the IMM effort. The first step was to perform a Bayesian update on the preflight astronaut data for HZ incidence with the general population data from Reference 26. An update was performed for males, females, and the total. The posterior results from this step describe the incidence rate of HZ in preflight astronauts. The means and the 5th and 95th percentiles from this first step then served as the priors for the second step and were used to perform a Bayesian update on the in-flight astronaut data. The update yielded the incidence rates of HZ in in-flight

TABLE 35.—INCIDENCE OF HERPES ZOSTER (HZ) IN U.S. ADULTS FROM 2000 TO 2001

Statistic	Males	Females	Total
HZ cases in adults 40 to 49 years of age	473	740	1213
Number of person-years in the study	190 653	228 677	419 330
95-percent confidence interval (CI) for HZ incidence in adults 40 to 49 years of age per 1000 person-years	2.3 to 2.8	3.0 to 3.5	2.7 to 3.0
HZ incidence rate in adults 40 to 49 years of age per person-year	2.5×10^{-3}	3.2×10^{-3}	2.9×10^{-3}
Error factor (EF) for HZ incidence in adults 40 to 49 years of age	1.09	1.07	1.04

TABLE 36.—INCIDENCE OF HERPES ZOSTER (HZ) IN PREFLIGHT AND
IN-FLIGHT MISSION-READY, ACTIVE ASTRONAUTS
[From Lifetime Surveillance of Astronaut Health (LSAH).]

Statistic	Males	Females	Total
Preflight astronauts			
Total person-years	1985.9	273.1	2259.0
HZ cases	8	0	8
HZ incidence rate, events per person-year	4.0×10^{-3}	0	3.5×10^{-3}
In-flight astronauts			
Total person-years	32.5	6.5	39.0
HZ cases	1	0	1
HZ incidence rate, events per person-year	3.08×10^{-3}	0	2.56×10^{-3}

TABLE 37.—RESULTS OF BAYESIAN ANALYSIS FOR
HERPES ZOSTER (HZ) IN PREFLIGHT MISSION-READY,
ACTIVE MALE, FEMALE, AND TOTAL ASTRONAUTS

HZ incidence rate, $\lambda_{astronaut}$, events per person-year			
Statistic	Males	Females	Total
Mean	2.50×10^{-3}	3.23×10^{-3}	2.90×10^{-3}
Standard deviation	1.31×10^{-4}	1.33×10^{-4}	6.91×10^{-5}
5 percent	2.29×10^{-3}	3.02×10^{-3}	2.78×10^{-3}
95 percent	2.72×10^{-3}	3.45×10^{-3}	3.01×10^{-3}

TABLE 38.—RESULTS OF BAYESIAN ANALYSIS
FOR HERPES ZOSTER IN IN-FLIGHT MALE,
FEMALE, AND TOTAL ASTRONAUTS

Herpes incidence rate, $\lambda_{astronaut}$, events per person-year			
Statistic	Males	Females	Total
Mean	2.51×10^{-3}	3.23×10^{-3}	2.90×10^{-3}
Standard deviation	1.31×10^{-4}	1.30×10^{-4}	7.04×10^{-5}
5 percent	2.30×10^{-3}	3.02×10^{-3}	2.79×10^{-3}
95 percent	2.73×10^{-3}	3.45×10^{-3}	3.02×10^{-3}

astronauts. Appendix C provides the WinBUGS code used, and an outline of the data for these steps follows.

Step 1: The general population HZ incidence per person-year for males, females, and the total and the corresponding EFs used as the priors in this step came from Reference 26. The LSAH data updated in this step included the number of preflight person-years and HZ incidences for males, females, and the total. Table 35 shows the incidence rates and the corresponding EFs for the general population, and Table 36 shows the incidences for preflight astronauts. Table 37 shows the posterior results: Poisson probability distributions for males, females, and the total.

Step 2: The means and the 5th and 95th percentiles from the posterior results of Step 1 (Table 37) were used as the priors for this step. Table 36 shows the LSAH data for in-flight astronauts, and Table 38 shows the posterior results from Step 2: the incidence of HZ in in-flight astronauts.

2.9.3 Discussion

Understanding the limitation of assuming an average rate for HZ incidence is necessary for the appropriate use of these data. HZ incidence rate increases exponentially with age (the rate for 50 to 59 year olds is double the rate for 40 to 49 year olds). Therefore, capturing the ages closest to the astronaut corps is imperative (Ref. 26). In spite of these limitations, this analysis is a reasonable approximation of HZ incidence. These data could also be used as a baseline for any future studies relating to HZ.

2.10   Renal Stones

Data from LSAH (Ref. 29, personal communication) and the National Institutes of Health (NIH) (Ref. 30) were used to estimate the probability of an astronaut developing a renal stone during or after space flight. A Bayesian update was used to combine information from these sources to estimate the average rate of renal stone formation. This analysis uses only data pertaining to renal stone occurrence, not data related to blood or urine chemistry.

2.10.1   Data and Methods

The LSAH temporal distribution of renal stone formation provided to the IMM team indicates that the assumptions that (1) the rates (λ) of renal stone incidences are constant over the period of interest and (2) the probability of occurrence follows a Poisson distribution are probably erroneous. However, the authors believe that these assumptions are currently the "best approximation" on the basis of nonattributable data from short-duration-mission (<20 days) participants. Only one data point is available for renal stone incidence during long-duration missions (~180 days) at this time.

Table 39 shows the general population incidence rate of renal stones from the NIH as of 2004 (Ref. 30). The incidence of renal stones differed for males and females, but for this analysis, the differences between males and females were not considered, and the average incidence rate of renal stones of 1.8×10^{-3} was used. An EF of 2.236 was found by taking the square root of the ratio 3 to 0.6.

The LSAH data for the astronaut population at Johnson were of interest because renal stone incidence is geographically dependent because of dietary habits, lifestyle, and other factors. The LSAH data were used to capture discrepancies due to geography. Table 40 shows the renal stone incidence data for this ground-based comparison population from Pietrzyk et al. (Ref. 31).

There have been no incidences of renal stones in in-flight astronauts (Table 41 and Ref. 31). In Table 41, the total number of person-years reported includes the timeframe for in-flight data.

TABLE 39.—INCIDENCE OF RENAL STONES IN
THE U.S. GENERAL POPULATION AS OF 2004

Statistic	Males	Females
Renal stone cases, events per 1000 person-years	1 to 3	0.6 to 1
Mean number of events per 1000 person-years............................1.8		
Renal stone incidence rate, events per person-year ....1.8×10^{-3}		

TABLE 40.—INCIDENCE OF RENAL STONES IN THE
ANALOG ASTRONAUT POPULATION
[From Lifetime Surveillance of Astronaut Health (LSAH).]

Number of participants	927
Renal stone cases	74
Number of person-years...	17 740.8
Renal stone incidence rate, events per person-year............	4.2×10^{-3}

TABLE 41.—INCIDENCE OF RENAL STONES
IN IN-FLIGHT ASTRONAUTS
[From Lifetime Surveillance of Astronaut Health (LSAH).]

Renal stone cases	0
Number of person-years...	25.1
Renal stone incidence rate, events per person-year........................	0

2.10.2 Bayesian Updates To Improve Estimates of Renal Stone Incidence Rates, and Analysis Results

The following steps were taken with WinBUGS to improve the estimate of the renal stone incidence rate for astronauts and provide a first-order approximation suitable for the IMM effort. One Bayesian update was performed without distinguishing between data for males and females. The data from the NIH (Ref. 30) were used to form an informed lognormal conjugate prior for the incidence rate of renal stones in the general U.S. population ($\lambda_{general}$). This prior was used to update the LSAH astronaut data in Step 1 of the Bayesian implementation, yielding a posterior result for the updated incidence rate of renal stones. In Step 2, the posterior result of Step 1 was used as the prior to update the LSAH in-flight astronaut data in WinBUGS. The result was an estimation of the incidence rate of renal stone formation in astronauts during an exploration mission. Appendix C provides the code used in WinBUGS as well as the sampling procedure.

Step 1: WinBUGS was informed with the mean incidence rate $\lambda_{general}$ from Table 39 and the EF (2.236).

Step 2: A Bayesian update was performed with 75 000 Monte Carlo samples on the input parameters of Step 1: the number of events and person-years for preflight astronauts from Table 40.

Step 3: The posterior result of Step 2—the mean incidence rate (Table 42) was dissected and used as the prior for the second update. The 5th and 95th percentiles from the lognormal Poisson distribution in Step 2 (Table 43) were used to calculate the EF.

Step 4: A second Bayesian update was performed with 75 000 Monte Carlo samples on the input parameters of Step 1: the number of events and person-years for in-flight astronauts (Table 41).

This process returned an estimate of the incidence rate of renal stone formation in in-flight astronauts with respect to the general population and the LSAH analog population (Table 43). This can be used as the input rate to a Poisson distribution to estimate the probability of a renal stone occurrence.

TABLE 42.—RESULTS OF BAYESIAN ANALYSIS
FOR RENAL STONES IN THE ANALOG
ASTRONAUT POPULATION

Renal stone incidence rate, λ_{analog}, events per person-year	
Mean	3.97×10^{-3}
Standard deviation	4.58×10^{-4}
5 percent	3.24×10^{-3}
95 percent	4.74×10^{-3}

TABLE 43.—RESULTS OF BAYESIAN ANALYSIS
FOR RENAL STONES IN IN-FLIGHT
ASTRONAUTS (ESTIMATE)

Renal stone incidence rate, $\lambda_{astronaut}$, events per person-year	
Mean	3.96×10^{-3}
Standard deviation	4.60×10^{-4}
5 percent	3.25×10^{-3}
95 percent	4.76×10^{-3}

2.10.3 Discussion

This analysis should be considered limited in that it assumes an average incidence rate of renal stones, irrespective of the renal stone type or environmental conditions. The results are a reasonable representation of the renal stone incidence rate given the data available and the assumptions made during construction of the estimate.

More accurate estimates could be made with further analysis of differences between males and females and the urinary and serum chemistry values that pertain to renal stone formation. The current data will serve as the baseline for future estimates that utilize biochemical renal stone forming and inhibiting parameters.

2.11 Seizure

Because a seizure may greatly affect crewmember performance, health, and morale, evaluating the probability that an astronaut may experience a seizure during an exploration mission was deemed to be necessary. A seizure is a major disruption of electrical signaling between neurons in the brain, and epilepsy is a disorder characterized by the recurrence of seizures. In normal brain function, neurons communicate with other neurons, glands, and muscles via electrochemical impulses. These neuronal impulses propagate along the axon, initiating the release of neurotransmitters that flow across the synaptic cleft to the dendrites of an adjacent cell. A balance between excitatory and inhibitory neurotransmitters controls the firing of electrical impulses. When excitatory neurotransmitters exceed the threshold, an action potential results. A seizure is an episode of continual and uncontrolled neuronal firing causing convulsions, muscle contractions, and unconsciousness. Seizures may be triggered by head trauma, physical

and emotional stress, fatigue, and external stimuli. However, most cases of seizure are idiopathic (Ref. 32). Data from the general population (Ref. 33) and astronaut data from the LSAH (Ref. 6, personal communication) were used to estimate the probability of an astronaut experiencing a seizure. A Bayesian update was used to combine the incidence rates of seizure from these sources to yield an appropriate incidence rate of seizure. The rate was assumed to be constant, and a Poisson probability distribution was assumed to govern the probability of seizure.

2.11.1 Data and Methods

General population data for the incidence rate of a first unprovoked (idiopathic) seizure were obtained from a Rochester, Minnesota, epidemiologic project (Ref. 33). A seizure was defined as an abnormal and excessive discharge of a set of neurons in the brain. In this study, incidence rates of epilepsy and of all unprovoked seizures were considered. An idiopathic seizure is one that occurs without an identified cause. Of all seizures, 61 to 66 percent are idiopathic and 23 to 35 percent are generalized tonic-clonic (Refs. 33 and 34). The incidence per 100 000 person-years of a first unprovoked seizure in adults 40 to 54 years of age was slightly higher in males (29) than in females (25). For this estimate, the incidence rate of seizures in males and females was averaged as shown in Table 44. Because there is not a significant variation in the incidence of seizure between males and females, the average incidence rate was considered appropriate. The incidence of seizure is related to age—incidence rates were high for infants younger than 1 year and highest for persons older than 75 years of age. CI information was not available for a first unprovoked seizure. Therefore, the EF was estimated from the 90th-percentile CI constructed from total population data for epilepsy. A person experiencing a single unprovoked seizure was not diagnosed with epilepsy and thus was not included in the CI data. The incidence rate of a first unprovoked seizure was 33 percent higher than the incidence rate of epilepsy, primarily because individuals who experienced only one unprovoked seizure were added. Data for this estimate were averaged from three age ranges: 40 to 44, 45 to 49, and 50 to 54, yielding an average age of 47 years. The EF was estimated to be 1.19 from a 90th-percentile CI constructed from male and female data from a population aged 40 to 54 years (see Appendix B, Section B.7).

Data for the incidence of seizure in the astronaut corps were obtained from the LSAH (Ref. 6, personal communication), and are summarized in Table 45. There were no occurrences of seizure in in-flight astronauts.

TABLE 44.—INCIDENCE OF TOTAL SEIZURES IN THE GENERAL POPULATION AGED 40 TO 54 YEARS IN ROCHESTER, MINNESOTA, FROM 1935 TO 1984

Average incidence per 100 000 person-years 27	
Seizure incidence rate, events per person-year .... 2.7×10^{-4}	

TABLE 45.—INCIDENCE OF SEIZURES IN PREFLIGHT AND IN-FLIGHT MISSION-READY, ACTIVE ASTRONAUTS
[From Lifetime Surveillance of Astronaut Health (LSAH).]

Statistic	Males	Females	Total
Preflight astronauts			
Total person-years	1970.4	264.8	2235.2
Seizure cases	0	0	0
Seizure incidence rate, events per person-year	0	0	0
In-flight astronauts			
Total person-years	32.0	6.6	38.6
Seizure cases	0	0	0
Seizure incidence rate, events per person-year	0	0	0

TABLE 46.—RESULTS OF BAYESIAN ANALYSIS FOR SEIZURES IN TOTAL PREFLIGHT MISSION-READY, ACTIVE ASTRONAUTS

Seizure incidence rate, $\lambda_{astronaut}$, events per person-year	
Mean	2.68×10^{-4}
Standard deviation	2.84×10^{-5}
5 percent	2.24×10^{-4}
Median	2.67×10^{-4}
95 percent	3.17×10^{-4}

2.11.2 Bayesian Updates To Improve Estimates of Seizure Incidence Rates, and Analysis Results

The following steps were taken with WinBUGS to improve the estimate of the incidence rate of seizure in the astronaut corps and provide a first-order approximation suitable for the IMM effort. The general population data (Ref. 33) were used to determine an informed lognormal conjugate prior for the incidence rate of seizure in the general U.S. population ($\lambda_{general}$). This prior was used to update LSAH preflight data in Step 1 of the Bayesian implementation, yielding a posterior result of the updated incidence rate of seizure. In Step 2, the posterior result of Step 1 was used as the prior and was updated with LSAH in-flight data in WinBUGS. The result was an estimation of the incidence rate of seizure in astronauts during an exploration mission. Appendix C contains the code used in WinBUGS as well as the sampling procedure.

Step 1: WinBUGS was informed with the mean incidence rate of the general population from Table 44 and the EF.

Step 2: A Bayesian update was performed with 75 000 Monte Carlo samples on the input parameters of Step 1: the number of events and person-years for preflight astronauts from LSAH (Table 45).

Step 3: The posterior result of Step 2—the mean incidence rate (Table 46) was dissected and used as the prior for the second update, and the 5th and 95th percentiles from the lognormal Poisson distribution in Step 2 were used to calculate the EF.

Step 4: A second Bayesian update was performed with 75 000 Monte Carlo samples on the input parameters of Step 1: the number of events and person-years for in-flight astronauts (Table 45). Appendix C provides details.

TABLE 47.—RESULTS OF BAYESIAN ANALYSIS
FOR SEIZURES IN TOTAL IN-FLIGHT
ASTRONAUTS

Seizure incidence rate, $\lambda_{astronaut}$, events per person-year	
Mean	2.70×10^{-4}
Standard deviation	2.88×10^{-5}
5 percent	2.25×10^{-4}
Median	2.68×10^{-4}
95 percent	3.19×10^{-4}

Table 47 shows the results: an estimate of the incidence rate of seizure in in-flight astronauts with respect to the general population. This rate can be used as the input rate to a Poisson distribution probability to estimate the probability of seizure occurring in flight.

2.11.3   Discussion

This analysis is limited in that it assumes an average incidence rate of seizure irrespective of the environmental conditions and the cause of seizure. In addition, the EF was calculated with epilepsy data, not unprovoked seizure data, because Reference 33 did not have CI data on the first unprovoked seizure. Also, data regarding repeated occurrences of seizures could influence the predicted rate of incidence because it is known that having a single seizure greatly increases the likelihood of subsequent seizures. The results should be used with an understanding of these limitations. However, these results probably give a reasonable representation of the incidence rate of seizures given the data available and the assumptions made when the estimate was constructed.

More accurate estimates could be made with further analysis of seizure occurrence in post-flight astronauts and greater understanding of the cause of seizures. The current analysis data will serve as the baseline for future estimates of the incidence of seizures in astronauts.

2.12   Stroke

Because a stroke may greatly affect crewmember performance and health, evaluating the probability that an astronaut may experience a stroke during an exploration mission was deemed to be necessary. The most common type of stroke is ischemic stroke (also referred to as a cerebral infarction) (Ref. 35), where blood flow to the brain is blocked by blood clots and/or by fatty deposits called plaque in the blood vessel linings. According to the Centers for Disease Control (CDC), about 85 percent of all strokes are ischemic (Ref. 35). This analysis only used data pertaining to stroke incidence for ages similar to those of mission-ready astronauts, not data related to blood pressure or other physiological conditions. A Bayesian update was used to combine the incidence rates of stroke from the LSAH (Ref. 36, personal communication) and the general U.S. population (Ref. 37) to estimate the average rate of stroke.

2.12.1   Data and Methods

As of 2010, the American Heart Association (Ref. 37) gave the incidence rate of ischemic stroke in U.S. residents 45 to 54 years of age as 1.1 to 2.7 per 1000 person-years for males and 0.7 to 2.2 per 1000 person–years for females.

Reference 37 considers the higher incidence rates for black men and women (2.7 and 2.2, respectively) to be unreliable, although a rationale for this view is not specified. The lower incidence rate data are for white men and women (1.1 and 0.7, respectively). This Bayesian calculation only includes the data for whites (see Table 48), although data for black men and women were used in calculating the EFs: males, 1.567; females, 1.773; and total, 1.254. Data from this publication indicate that the prevalence of stroke among Hispanics and Latinos is higher than among whites but smaller than among blacks (Ref. 37).

As of 2007 there were 101 astronauts that were mission ready (20 females and 81 males). The LSAH data were given for males and females, so data for white males, females, and the total were used for the general population calculation. For this analysis, gender, age, ethnicity, and type of stroke—ischemic—were simplified and assumed to be lognormal, as shown in Table 48.

Data received from LSAH (Ref. 36, personal communication) are given in Table 49. Of the two incidents of preflight stroke, one occurred 0 to 3 years prior to flight and one occurred 3 to 6 years prior to flight. The fact that there were no strokes recorded for female astronauts may negate the assumption of an average incidence rate for the entire period of interest.

TABLE 48.—INCIDENCE OF STROKE IN U.S. ADULTS
45 TO 54 YEARS OF AGE

Statistic	Males	Females	Total
Stroke incidence in white adults aged 45 to 54 years per 1000 person-years	1.1	0.7	0.9
Mean stroke incidence rate in adults aged 45 to 54 years, events per person-year	1.10×10^{-3}	7.00×10^{-4}	9.00×10^{-4}

TABLE 49.—INCIDENCE OF STROKE IN PREFLIGHT AND
IN-FLIGHT MISSION-READY, ACTIVE ASTRONAUTS
[From Lifetime Surveillance of Astronaut Health (LSAH).]

Statistic	Males	Females	Total
Preflight astronauts			
Total person-years	3478.6	336.8	3815.4
Stroke cases	2	0	2
Stroke incidence rate, events per person-year	5.75×10^{-4}	0	5.24×10^{-4}
In-flight astronauts			
Total person-years	31.8	6.5	38.3
Stroke cases	0	0	0
Stroke incidence rate, events per person-year	0	0	0

2.12.2 Bayesian Updates To Improve Estimates of Stroke Incidence Rates, and Analysis Results

The following steps were taken with WinBUGS to improve the estimate of the incidence of stroke in astronauts and provide a first-order approximation suitable for the IMM effort. Two steps and Bayesian updates were performed. The first step used the general population data (Ref. 37) as a prior to update the LSAH preflight data (Ref. 36, personal communication). This step was performed three times, once each for males, females, and the total. The posterior results from this step describe the stroke incidence rates for preflight astronauts. In the second step, the data from these posterior results, namely the means and the 5th and 95th percentiles, were used as the priors to update the in-flight astronaut data for females, males, and the total. Ultimately, six probability distributions were found describing the stroke incidence rate for preflight and in-flight male, female, and total astronauts. Appendix C provides the code used in WinBUGS, and an outline of the input data for each step follows.

Step 1: The stroke incidence per person-year for the general U.S. population for females, males, and the total and the EFs were used as the priors in WinBUGS to update the LSAH data (Table 49) for the number of stroke cases and person-years for males, females, and the total. Table 50 provides the posterior results from this step.

Step 2: A Bayesian update was performed with the posterior results from Step 1—the means and the 5th and 95th percentiles (Table 50) to update the LSAH in-flight astronaut data (Table 49). The result was a probability distribution for the stroke incidence rate in in-flight astronauts (Table 51).

TABLE 50.—RESULTS OF BAYESIAN ANALYSIS FOR
STROKE IN PREFLIGHT MISSION-READY, ACTIVE
MALE, FEMALE, AND TOTAL ASTRONAUTS

Stroke incidence rate, $\lambda_{astronaut}$, events per person-year			
Statistic	Males	Females	Total
Mean	9.81×10^{-4}	6.80×10^{-4}	8.78×10^{-4}
Standard deviation	2.42×10^{-4}	2.41×10^{-4}	1.17×10^{-4}
5 percent	6.37×10^{-4}	3.64×10^{-4}	6.99×10^{-4}
Median	9.54×10^{-4}	6.42×10^{-4}	8.70×10^{-4}
95 percent	1.4×10^{-3}	1.1×10^{-3}	1.1×10^{-3}

TABLE 51.—RESULTS OF BAYESIAN ANALYSIS FOR
STROKE IN IN-FLIGHT MALE, FEMALE,
AND TOTAL ASTRONAUTS

Stroke incidence rate, $\lambda_{astronaut}$, events per person-year			
Statistic	Males	Females	Total
Mean	9.80×10^{-4}	6.80×10^{-4}	8.77×10^{-4}
Standard deviation	2.38×10^{-4}	2.36×10^{-4}	1.22×10^{-4}
5 percent	6.41×10^{-4}	3.71×10^{-4}	6.93×10^{-4}
Median	9.52×10^{-4}	6.42×10^{-4}	8.69×10^{-4}
95 percent	1.4×10^{-3}	1.1×10^{-3}	1.1×10^{-3}

2.12.3 Discussion

This analysis is limited in that it assumes an average incidence rate of stroke, with little data regarding stroke type or environmental conditions. Also, because the data for blacks in the general population were considered to be unreliable, this analysis only considered data from white males and females from the general population. These results should be used with a full understanding of these limitations. However, they are reasonable representations of the incidence rate of stroke given the data available and the assumptions made when the estimate was constructed.

More accurate estimates could be made with further analysis of stroke incidence in post-flight astronauts and the physiological data that pertain to stroke occurrence. If more reliable data for the general U.S. population (specifically for different ethnicities) becomes available in the future, this analysis should be updated with that data. The current data will serve as the baseline for future estimates.

3.0   Discussion

Tables 52 and 53 summarize the results of the Bayesian analyses for all medical events in preflight and in-flight astronauts.

A review of the data for various medical events demonstrates limitations that are common to all events. The analysis of each medical condition assumes an average incidence rate despite environmental effects and contributing physiological factors. There are certainly discrepancies between the general U.S. population, the U.S. Submarine Force, the analog astronaut population at the NASA Johnson Space Center, and the astronaut corps. The data reported in the literature for the various medical events has inherent uncertainty and reliability problems depending on the manner in which the study or survey was conducted.

There are a host of factors that could improve the IMM team's ability to make more accurate estimates of the incidence rates, including incorporating biomedical parameters into the model and having access to more precise data (in the astronaut corps and in the general U.S. and submarine populations) related to age, ethnicity, gender, previous medical conditions, existing lifestyle choices, and so on. Having age-, ethnicity-, and gender-specific CI would greatly improve the calculation of the total incidence rates. However, given that these Bayesian analyses were performed to support the IMM by providing input source data, the intrinsic nature of this probabilistic model and its associated sensitivity analyses of output data will also guide the need for future updates. As components of IMM source input data, the incidence rate data described herein will be subject to periodic review to ensure that they are current and relevant as described in the IMM Configuration Management Plan (Ref. 38).

TABLE 52.—RESULTS OF BAYESIAN ANALYSIS FOR ALL MEDICAL EVENTS IN PREFLIGHT MISSION-READY, ACTIVE MALE, FEMALE, AND TOTAL ASTRONAUTS

Medical event incidence rate, $\lambda_{astronaut}$, events per year			
Statistic	Males	Females	Total
Angina pectoris			
Mean	3.96×10^{-4}	3.65×10^{-4}	N/A
Standard deviation	9.38×10^{-5}	1.53×10^{-4}	N/A
Appendicitis			
Mean	N/A	N/A	9.35×10^{-4}
Standard deviation	N/A	N/A	1.04×10^{-4}
Atrial fibrillation (AF)			
Mean	6.29×10^{-4}	2.02×10^{-4}	4.43×10^{-4}
Standard deviation	1.51×10^{-4}	1.46×10^{-4}	9.39×10^{-5}
Atrial flutter (AFL)			
Mean	7.05×10^{-5}	2.43×10^{-5}	4.77×10^{-5}
Standard deviation	6.71×10^{-6}	2.45×10^{-6}	3.04×10^{-6}
Dental abscess			
Mean	8.26×10^{-3}	N/A	N/A
Standard deviation	1.80×10^{-3}	N/A	N/A
Dental caries			
Mean	9.42×10^{-3}	N/A	N/A
Standard deviation	5.94×10^{-4}	N/A	N/A
Dental periodontal disease			
Mean	1.10×10^{-1}	N/A	N/A
Standard deviation	1.52×10^{-2}	N/A	N/A
Gallstone disease			
Mean	7.69×10^{-4}	1.27×10^{-3}	1.02×10^{-3}
Standard deviation	4.65×10^{-6}	7.64×10^{-6}	6.12×10^{-6}
Herpes zoster (HZ)			
Mean	2.50×10^{-3}	3.23×10^{-3}	2.90×10^{-3}
Standard deviation	1.31×10^{-4}	1.33×10^{-4}	6.91×10^{-5}
Renal stones			
Mean	N/A	N/A	3.97×10^{-3}
Standard deviation	N/A	N/A	4.58×10^{-4}
Seizure			
Mean	N/A	N/A	2.68×10^{-4}
Standard deviation	N/A	N/A	2.84×10^{-5}
Stroke			
Mean	9.81×10^{-4}	6.80×10^{-4}	8.78×10^{-4}
Standard deviation	2.42×10^{-4}	2.41×10^{-4}	1.17×10^{-4}

TABLE 53.—RESULTS OF BAYESIAN ANALYSIS FOR ALL MEDICAL EVENTS IN IN-FLIGHT MALE, FEMALE, AND TOTAL ASTRONAUTS

Medical event incidence rate, $\lambda_{astronaut}$, events per year			
Statistic	Males	Females	Total
Angina pectoris			
Mean	3.95×10^{-4}	3.64×10^{-4}	N/A
Standard deviation	9.21×10^{-5}	1.53×10^{-4}	N/A
Appendicitis			
Mean	N/A	N/A	9.34×10^{-4}
Standard deviation	N/A	N/A	1.03×10^{-4}
Atrial fibrillation (AF)			
Mean	6.28×10^{-4}	2.02×10^{-4}	4.42×10^{-4}
Standard deviation	1.52×10^{-4}	9.99×10^{-6}	9.36×10^{-5}
Atrial flutter (AFL)			
Mean	7.05×10^{-5}	2.43×10^{-5}	4.77×10^{-5}
Standard deviation	6.74×10^{-6}	2.42×10^{-6}	3.04×10^{-6}
Dental abscess			
Mean	8.16×10^{-3}	N/A	N/A
Standard deviation	1.80×10^{-3}	N/A	N/A
Dental caries			
Mean	9.41×10^{-3}	N/A	N/A
Standard deviation	5.95×10^{-4}	N/A	N/A
Dental periodontal disease			
Mean	1.03×10^{-1}	N/A	N/A
Standard deviation	1.41×10^{-2}	N/A	N/A
Gallstone disease			
Mean	7.69×10^{-4}	1.27×10^{-3}	1.02×10^{-3}
Standard deviation	4.65×10^{-6}	7.68×10^{-6}	6.18×10^{-6}
Herpes zoster (HZ)			
Mean	2.51×10^{-3}	3.23×10^{-3}	2.90×10^{-3}
Standard deviation	1.31×10^{-4}	1.30×10^{-4}	7.04×10^{-5}
Renal stones			
Mean	N/A	N/A	3.96×10^{-3}
Standard deviation	N/A	N/A	4.60×10^{-4}
Seizure			
Mean	N/A	N/A	2.70×10^{-4}
Standard deviation	N/A	N/A	2.88×10^{-5}
Stroke			
Mean	9.80×10^{-4}	6.80×10^{-4}	8.77×10^{-4}
Standard deviation	2.38×10^{-4}	2.36×10^{-4}	1.22×10^{-4}

Appendix A.—Data from Lifetime Surveillance of Astronaut Health (LSAH)

Table 54 shows the data that were supplied by LSAH.

TABLE 54.—LIFETIME SURVEILLANCE OF ASTRONAUT HEALTH (LSAH) DATA

Preflight astronauts			In-flight astronauts		
Statistic	Males	Females	Statistic	Males	Females
Angina pectoris					
Total person-days	719 196	96 669	Total person-days	11 680	2372.5
Total person-years	1970.4	264.8	Total person-years	32.0	6.5
Angina cases	0	0	Angina cases	0	0
Appendicitis					
Total person-days	510 875	89 019	Total person-days	11 643.5	2336
Total person-years	1399.7	243.9	Total person-years	31.9	6.4
Appendicitis cases	2	0	Appendicitis cases	0	0
Atrial fibrillation (AF)					
Total person-days	2 373 481	122 915	Total person-days	11 607	2372.5
Total person-years	6502.7	336.8	Total person-years	31.8	6.5
AF cases	4	0	AF cases	0	0
Atrial flutter (AFL)					
Total person-days	2 373 481	122 915	Total person-days	11 607	2372.5
Total person-years	6502.7	336.8	Total person-years	31.8	6.5
AFL cases	0	0	AFL cases	0	0
All dental problems studied					
Total person-days	173 450.6	43 855.2	Total person-days	11 643.5	2336
Total person-years	475.2	120.2	Total person-years	31.9	6.4
Caries cases	168	24	Caries cases	0	0
Abscess cases	19	1	Abscess cases	0	0
Periodontal disease cases	56	9	Periodontal disease cases	0	0
Gallstone disease					
Total person-days	719 196	96 669	Total person-days	11 680	2372.5
Total person-years	1970.4	264.8	Total person-years	32.0	6.5
Gallstone cases	3	0	Gallstone cases	0	0
Herpes zoster (HZ)					
Total person-days	724 861	99 684	Total person-days	11 862.5	2372.5
Total person-years	1985.9	273.1	Total person-years	32.5	6.5
HZ cases	8	0	HZ cases	1	0
Renal stones[a]					
Total person-days	N/A	N/A	Total person-days		9161.5
Total person-years	N/A	N/A	Total person-years		25.1
Renal stone cases	N/A	N/A	Renal stone cases		0
Seizure					
Total person-days	719 196	96 669	Total person-days	11 680	2372.5
Total person-years	1970.4	264.8	Total person-years	32.0	6.5
Seizure cases	0	0	Seizure cases	0	0
Stroke					
Total person-days	1 269 681	12 2915	Total person-days	11 607	2372.5
Total person-years	3478.6	336.8	Total person-years	31.8	6.5
Stroke cases	2	0	Stroke cases	0	0

[a]Totals only—no breakdown by males and females.

Appendix B.—Calculating Error Factor From 95-Percent Confidence Intervals

For general population data to be applicable to these Bayesian updates, the error factor (EF) for each data set had to be found. Although no data in this study gave the EF, some data gave the standard deviation, leading to an easy conversion to the EF. However, many times the standard deviation was not given, so the EF had to be calculated using the 95-percent confidence interval (CI). The general steps involved converting the 95-percent CI into a 90-percent CI. From the 90-percent CI, the 95th and 5th percentiles were found and then used in a simple equation to calculate the EF. The specific calculation steps for each medical event varied. These steps are shown in Sections B.1 to B.7.

B.1 Angina Pectoris

The following steps were used to obtain the EF for the angina data:

(1) The 95-percent CI width was used to find the standard deviation σ from Equation (B1) from Lapin's book (Ref. 39):

$$\sigma = \frac{\sqrt{n}\left(\text{width}_{95\%}\right)}{z_{\alpha/2}} \tag{B1}$$

where $z_{\alpha/2}$ is 1.96 for the 95-percent CI, n is the number of participants, and width$_{95\%}$ is 1.2 for males and 0.55 for females.

(2) Next, Equation (B1) and σ were used to find the 90-percent CI width:

$$z_{\alpha/2} \times \frac{\sigma}{\sqrt{n}} = \text{width}_{90\%} \tag{B2}$$

where $z_{\alpha/2} = 1.64$ for the 90-percent CI. The 90-percent CI width was calculated as 1.00 for males and 0.46 for females.

(3) Then, the 95th percentile was found by adding the 90-percent CI width to the mean, and the 5th percentile was found by subtracting the 90-percent CI width from the mean.

The 95th percentile was calculated as 5.80 for males and 1.56 for females. The 5th percentile was calculated as 3.80 for males and 0.64 for females.

(4) Finally Equation (B3) was used to find *EF*:

$$EF = \sqrt{\frac{95\text{th}}{5\text{th}}} \tag{B3}$$

EF was calculated as 1.24 for males and 1.56 for females.

B.2 Atrial Fibrillation

The following steps were used to obtain the EF for atrial fibrillation (AF) data:

(1) The 95-percent CI width was used to find σ from Equation (B1), where $z_{\alpha/2}$ is 1.96 and width$_{95\%}$ is 0.32 for males, 0.2 for females, and 0.18 for the total. Next Equation (B1) and σ were used to find the 90-percent CI width—resulting in Equation (B2), where $z_{\alpha/2} = 1.64$ for the 90-percent CI.
(2) Then, the 95th percentile was found by adding the 90-percent CI width to the mean, and the 5th percentile was found by subtracting the 90-percent CI width from the mean.
(3) Finally, Equation (B3) was used to find EF.

B.3 Atrial Flutter

With the atrial flutter (AFL) data, additional steps had to be taken prior to converting the 95-percent CI into the 90-percent CI. The CIs were too wide to be applied directly to the rates of AFL for adults under 50 years of age because doing so would have created negative values for the 5th and 2.5th percentile. A proportion was set up to counter this problem. The proportion was between the number of cases for adults under 50 years of age and the number of cases for all ages. It was set equal to the proportion of the unknown 95-percent CI width x for adults under 50 years of age and the known 95-percent CI width for all ages. An example of the calculation for the 95-percent CI for men under 50 years of age follows:

$$\frac{\text{AFL cases in men under 50 years}}{\text{AFL cases in all men}}$$
$$= \frac{95\% \text{ CI width for men under 50 years}}{95\% \text{ CI width for all men}}$$

$$\frac{6 \text{ AFL cases}}{112 \text{ AFL cases}} = \frac{x}{0.24} \tag{B4}$$

$$x = \pm 0.011$$

This assumption of proportional 95-percent CI was applied to the women and total adults under 50 years of age as well. The three calculated 95-percent CIs for adults under 50 years of age follow:

Men: ±0.013-percent cases per 100 000 person-years
Women: ±0.004-percent cases per 100 000 person-years
Total: ±0.006-percent cases per 100 000 person-years

Because the journal article used (Ref. 13) did not include the number of participants for each age group and gender, Equation (B1), which was used to find the 90-percent CI for the AF data, could not be used directly to find the 90-percent CI for the AFL data. However, because σ and n remain constant for the 90- and 95-percent CIs, they can be canceled out, leaving Equation (B5):

$$90\% \text{ CI} = \frac{1.64}{1.96}\left(95\% \text{ CI}\right) \tag{B5}$$

The 95th and 5th percentiles and the EF for AF were found with following the steps. More specifically, Steps 3 and 4 for determining the EF from the AF section were used.

B.4 Dental Events (Abscess, Caries, and Periodontal Disease)

The following steps were used to obtain the EF for the dental data:

(1) The 95-percent CI width was used to find σ from Equation (B1), where $z_{\alpha/2}$ is 1.96 for the 95-percent CI and width$_{95\%}$ is 1.6 for abscess, 0.615 for caries, and 1.93 for periodontal disease.

(2) Next, Equation (B1) and σ were used to find the 90-percent CI width—resulting in Equation (B2), where $z_{\alpha/2}$ = 1.64 for the 90-percent CI.

The 90-percent CI width was calculated as 1.3 for abscess, 0.51 for caries, and 1.61 for periodontal disease.

(3) Then, the 95th percentile was found by adding the 90-percent CI width to the mean, and the 5th percentile was found by subtracting the 90-percent CI width from the mean.

The 95th percentile was calculated as 4.80 for abscess, 5.41 for caries, and 3.31 for periodontal disease. The 5th percentile was calculated as 2.20 for abscess, 4.39 for caries, and 0.09 for periodontal disease.

(4) Finally, Equation (B3) was used to find *EF*.

EF was calculated as 1.48 for abscess, 1.11 for caries, and 6.24 for periodontal disease.

B.5 Gallstone Disease

The following steps were used to obtain the EF for the gallstone data:

(1) The 95-percent CI was used to determine the standard error *SE* from a modified form of Lapin's equation (Ref. 39):

$$SE = \frac{\text{width}_{95\%}}{z_{\alpha/2}} \tag{B6}$$

where $SE = \sigma/\sqrt{n}$ and $z_{\alpha/2}$ =1.96 for the 95-percent CI.

(2) The standard error was used to compute the 95th and 5th percentiles according to the following definition:

95th percentile = mean + $z_{\alpha/2}$ (*SE*)
5th percentile = mean + $z_{\alpha/2}$ (*SE*)

where $z_{\alpha/2}$ = 1.64 for the 90-percent CI.

(3) Then, the EF was computed with Equation (B3).

B.6 Herpes Zoster

The following steps were used to obtain the EF for the herpes data:

(1) The 95-percent CI was converted to the 90-percent CI using Equation (B7) from Lapin (Ref. 39, p. 311):

$$z_{\alpha/2} \times \frac{\sigma}{\sqrt{n}} = \text{width} \tag{B7}$$

where $z_{\alpha/2}$ is 1.96 for the 95-percent CI and 1.64 for the 90-percent CI.

(2) Next, the 5th and 95th percentiles were found from the 90-percent CI. The 95th percentile was found by adding the 90-percent CI width to the mean, and the 5th percentile was found by subtracting the 90-percent CI from the mean.

(3) Finally, the EF was found from Equation (B3).

Because Reference 26 did not include the number of participants or the standard deviation for each age group and gender, Equation (B7) could not be used directly. Entering the variables for the 95- and 90-percent CIs into the formula resulted in Equation (B8):

$$95\% \; CI: \text{width}_{95\%} = 1.96\left(\frac{\sigma}{n}\right)90\% \; CI: \text{width}_{90\%CI}$$
$$= 1.64\frac{\sigma}{n} \tag{B8}$$

Because σ and n were constant for both CIs, they could be canceled out and substitution could be performed to yield Equation (B9):

$$90\% \; CI = \frac{1.64}{1.96}\left(95\% \; CI\right) \tag{B9}$$

B.7   Seizure

The following steps were used with the data from Hauser, Annegers, and Kurland (Ref. 33 and Table 55) to obtain the EF for the seizure data.

TABLE 55.—SEIZURE INCIDENCE OVER 10-YEAR PERIODS
PER 100 000 PERSON-YEARS IN THE GENERAL POPULATION
OF ROCHESTER, MINNESOTA, AGED 40 TO 54 YEARS

Age	Years that data were collected				
	1935 to 1944	1945 to 1954	1955 to 1964	1965 to 1974	1975 to 1984
40 to 44	12	32	42	19	26
45 to 49	7	35	29	20	23
50 to 54	26	31	49	18	32

The mean seizure incidence (total) per 100 000 people was 26.73, and the standard deviation was 10.95.

A 90-percent CI was constructed as follows:

$$0.90 = P\left(-z \le Z \le z\right) \tag{B10}$$

$$z = \frac{\bar{x} - \mu}{\left(\dfrac{\sigma}{\sqrt{n}}\right)} \tag{B11}$$

$$z = \Phi^{-1}\left(1 - \frac{\alpha}{2}\right) = \Phi^{-1}\left(0.95\right) = 1.645 \tag{B12}$$

where P is probability, z is the normal deviate of the stated percentile, μ is the true mean, and Φ is the cumulative density function. For significance level $\alpha = 0.10$, sample mean $\bar{x} = 26.73$, standard deviation $\sigma = 10.95$, and number of samples $n = 15$,

$$0.90 = P\left(22.08 \le \mu \le 31.38\right) \tag{B13}$$

Thus, the EF was found by

$$EF = \sqrt{\frac{95\%}{5\%}} = \sqrt{\frac{31.38}{22.08}} = 1.19 \tag{B14}$$

Appendix C.—Bayesian Inference Using Gibbs Sampling (WinBUGS) Procedure and Code

C.1   WinBUGS Procedure

To estimate of the probability of a certain medical event, open WinBUGS and create a new document. Type the WinBUGS script for the medical event of interest (see Section C.2). Next, open the Specification Tool under the Model tab. Highlight "model" in the code and click "check model" in the Specification Tool. WinBUGS will respond with "model is syntactically correct" in the status bar. If the model is not syntactically correct, follow the prompts given by WinBUGS in the status bar to modify the code. After the model is checked, load the data by highlighting "list" in the code and click "load data." WinBUGS will respond "data loaded." Click "compile," and WinBUGS will respond "model compiled." Click "gen inits," and WinBUGS will respond "initial values generated, model initialized." Now open the Sample Monitor Tool under the Inference tab. Type "lambda" into the drop-down box labeled "node," click "set," and then select. Type "1001" into the box labeled "beg" and highlight "5," "median," and "95" under "percentiles." Now open the Update Tool under the Model tab. In the "updates" box, type "75000" and click "update." When the model has completed its iterations, the results of the update may be viewed by returning to the Sample Monitor Tool, selecting "lambda" under node, and clicking the "stats" button. The lognormal Poisson distribution that was constructed may be viewed by clicking the "density" button on the Sample Monitor Tool.

C.2   WinBUGS Code

C.2.1   Angina

Males
```
model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2}
list(mean= 0.00063, EF= 1.77, events= 6, time= 22137.0)
```

```
model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2}
list(mean= 0.000415, EF=1.48, events= 0, time= 1970.4)
```

```
model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2}
list(mean= 0.000396, EF=1.46, events= 0, time= 32.0)
```

Females
```
model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2}
list(mean= 0.00047, EF= 2.08, events= 0, time= 2808.6)
```

```
model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2}
list(mean= 0.000372, EF=1.94, events= 0, time= 264.8)
```

```
model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2}
list(mean= 0.000365, EF=1.94, events= 0, time= 6.5)
```

C.2.2   Appendicitis

Total
```
model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2}
list(mean= 0.000930, EF= 1.2, events= 2, time= 1644)
```

```
model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2}
list(mean= 0.000935, EF=1.198, events= 0, time= 38.3)
```

C.2.3   Atrial Fibrillation

Males
model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2}
list(events=4, time=6502.7, mean=0.000640, EF=1.56)

model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2
EF <- pow(div, 1/2)
div <- super/sub}
list(events=0, time=31.8, mean=0.000629, super=0.000902,
sub=0.000412)

Females
model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2}
list(events=0, time=336.8, mean=0.000210, EF=2.97)

model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2
EF <- pow(div, 1/2)
div <- super/sub}
list(events=0, time=6.5, mean=0.000202, super=0.000476,
sub=0.000560)

Total
model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2}
list(events=4, time=6839.4, mean=0.000425, EF=1.45)

model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2
EF <- pow(div, 1/2)
div <- super/sub}
list(events=0, time=38.3, mean=0.000443, super=0.000611,
sub=0.000306)

C.2.4   Atrial Flutter

Males
model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2}
list(events=0, time=6502.7, mean=0.0000707, EF=1.17)

model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2
EF <- pow(div, 1/2)
div <- super/sub}
list(events=0, time=31.8, mean=0.0000705, super=0.0000821,
sub=0.0000600)

Females
model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2}
list(events=0, time=336.8, mean=0.0000243, EF=1.18)

model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2
EF <- pow(div, 1/2)
div <- super/sub}
list(events=0, time=6.5, mean=0.0000243, super=0.0000285,
sub=0.0000205)

Total

```
model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2}
list(events=0, time=6839.4, mean=0.0000479, EF=1.11)

model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2
EF <- pow(div, 1/2)
div <- super/sub}
list(events=0, time=38.3, mean=0.0000477, super=0.0000529,
sub=0.0000429)
```

C.2.5   Dental Abscess

```
model { events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2}
list(events=19, time=475.2, mean=0.00353, EF=1.48)

model { events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2}
list(events=0, time=31.9, mean=0.00826, EF=1.43)
```

C.2.6   Dental Caries

```
model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2}
list(events=168, time=475.2, mean=0.00488, EF=1.11)

model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2}
list(events=0, time=31.9, mean=0.00942, EF=1.11)
```

C.2.7   Dental Periodontal Disease

```
model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2}
list(events=56, time=475.2, mean=0.00168, EF=6.24)
model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2}
list(events=0, time=31.9, mean=0.110, EF=1.26)
```

C.2.8   Gallstone Disease

Males

```
model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2}
list(events=3, time=1970.4, mean=0.000769, EF=1.01)

model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2}
list(events=0, time=32.0, mean=0.0007691, EF=1.01)
```

Females

```
model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2}
list(events=0, time=264.8, mean=0.001266, EF=1.01)

model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2}
list(events=0, time=6.5, mean=0.001266, EF=1.01)
```

Total

```
model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2
time <- menpreflight + womenpreflight}
list(events=3, menpreflight=1970.4, womenpreflight = 264.8,
mean=0.001017, EF=1.01)
```

```
model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2
time <- meninflight + womeninflight}
list(events=0, meninflight=32.0, womeninflight = 6.5,
mean=0.001017, EF=1.01)
```

C.2.9   Herpes Zoster

Males
```
model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2}
list(events=8, time=1985.9, mean=0.0025, EF=1.09)
```

```
model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2
EF <- pow(div, 1/2)
div <- super/sub}
list(events=1, time=32.5, mean=0.00250, super=0.00272,
sub=0.00229)
```

Females
```
model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2}
list(events=0, time=273.1, mean=0.0032, EF=1.07)
```

```
model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2
EF <- pow(div, 1/2)
div <- super/sub}
list(events=0, time=6.5, mean=0.00323, super=0.00345,
sub=0.00302)
```

Total

```
model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2}
list(events=8, time=2259.0, mean=0.0029, EF=1.04)
```

```
model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2
EF <- pow(div, 1/2)
div <- super/sub}
list(events=1, time=39.0, mean=0.00290, super=0.00301,
sub=0.00278)
```

C.2.10   Renal Stones

```
model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2}
list(events=74, time=17740.8, mean=0.0018, EF=2.236)
```

```
model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
EF <- pow(x,1/2)
x <- p95/p5
mu <- log(mean) - pow(sigma, 2)/2}
list(mean= 0.00397, p95= 0.00474, p5= 0.00324, events= 0,
time= 25.1)
```

C.2.11 Seizure

Total

model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2}
list(mean= 0.00027, EF= 1.19, events= 0, time= 2235.2)

model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2}
list(mean= 0.00027, EF=1.19, events= 0, time= 38.6)

C.2.12 Stroke

Males

model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2}
list(events=2, time=3478.6, mean=0.00110, EF=1.567)

model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2}
list(events=0, time=31.8, mean=0.000981, EF=1.482)

Females

model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2}
list(events=0, time=336.8, mean=0.000700, EF=1.773)

model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2}
list(events=0, time=6.5, mean=0.000680, EF=1.739)

Total

model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2}
list(events=2, time=3815.3, mean=0.000900, EF=1.254)

model {events ~ dpois(mean.poisson)
mean.poisson <- lambda*time
lambda ~ dlnorm(mu, tau)
tau <- 1/pow(sigma, 2)
sigma <- log(EF)/1.645
mu <- log(mean) - pow(sigma, 2)/2}
list(events=0, time=38.3, mean=0.000878, EF=1.254)

Appendix D.—Statistical Combination of Independent Distributions

Although the objective of the current study is to obtain estimates of incidence rate for various medical events in astronauts, these rates are not always available for the events under investigation. Instead, rates may be available for more specific complications or diseases, which must then be combined in a statistically correct fashion to provide an estimate of the total incidence of the disease category under study. In the current study, the analysis of gallstone disease serves as a primary example. Urbach et al. (Ref. 25) provided incidence data stratified by age and gender for three different gallstone-related conditions: namely, acute cholecystitis, acute biliary pancreatitis, and acute cholangitis. For an estimate of total gallstone disease incidence in the general population to be obtained, these incidence rates—and their associated uncertainties—needed to be combined in a statistically accurate fashion. The method in which this was accomplished is presented in this appendix.

Combination of individual disease incidence rates depends on an assumption of independence. This assumption allows the uncertainties of the incidences to be combined in a fashion dictated by the rules of probability. As noted in the following discussion, the variance of the scaled sum of two independent distributions is simply the sum of their variances, multiplied by the square of the scaling factor:

Let X and Y be two independent random variables, and let $Z = a(X + Y)$:

$$\sigma_z^2 = a^2 \left(\sigma_x^2 + \sigma_y^2 \right) \tag{D1}$$

Accordingly, the following relationship holds for the standard deviation of the combined distribution:

$$\sigma_z = a\sqrt{\sigma_x^2 + \sigma_y^2} \tag{D2}$$

This relation was applied to the data available for the various gallstone conditions in order to determine the combined incidence of general gallstone disease. The raw data presented in Reference 25 provided separate incidence rates for three different gallstone conditions and for three discrete age groups: 18 to 44, 45 to 64, and ≥65. Because the present study required an estimate of total gallstone disease incidence in the astronaut-like age range, 18 to 64, six separate distributions had to be combined in this manner for males and females in the three ranges.

Assumptions were made in the interpretation of the incidence rates presented in Reference 25 to leverage Equation (D2) in combining the uncertainties of independent distributions. (1) The incidence of a given condition in a particular age group was assumed to be independent of the incidence of the same condition in other age groups. (2) The incidence of a particular condition was assumed to be independent of the incidence of the other two conditions. (3) The incidence in males was assumed to be independent of the incidence in females.

Reference 25 provided the annual incidence per 100 000 persons for each category, as well as a 95-percent CI for this value. The standard error of each incidence rate was determined as follows:

$$95\% \; CI - (\text{mean} - 1.96 \cdot SE, \; \text{mean} + 1.96 \cdot SE)$$

$$\therefore SE = \frac{95\% \; CI \; \text{upper limit} - 95\% \; CI \; \text{lower limit}}{3.92} \tag{D3}$$

The standard error of the mean SE is the standard deviation of the sample mean of a population distribution. Therefore, the standard error can be used in the same fashion as the standard deviation σ is used in Equation (D2) to properly account for uncertainty when independent incidence rates are combined.

It was assumed that age groups were independent from each other, so an incidence rate λ for ages 18 to 64 was found for each specific condition by averaging the λ provided for ages 18 to 44 and 45 to 64. The standard error for the new combined distribution was determined from Equations (D2) and (D3):

$$\lambda_{18 \text{ to } 64} = \frac{1}{2} \left(\lambda_{18 \text{ to } 44} + \lambda_{45 \text{ to } 64} \right) \tag{D4}$$

$$\therefore SE_{18 \text{ to } 64} = \frac{1}{2} \sqrt{SE_{18 \text{ to } 44}^2 + SE_{45 \text{ to } 64}^2}$$

This process was used for all three gallbladder conditions for data for both males and females to determine an incidence rate for each condition. These three conditions were then combined in a simple additive fashion, again with the assumption of the independence of incidence and applying the formula for determining combined standard error:

$$\lambda_{\text{total}} = \left(\lambda_1 + \lambda_2 + \lambda_3 \right) \tag{D5}$$

$$\therefore SE_{\text{total}} = \sqrt{SE_1^2 + SE_2^2 + SE_3^2}$$

This process was applied to incidence data for both males and females, yielding values of the total gallstone disease incidence. The total incidence rate was determined by averaging the incidence rates for males and females, again combining the standard errors with the same procedure used to average the age-specific incidence rates.

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14. ABSTRACT
The Exploration Medical Capability project is creating a catalog of risk assessments using the Integrated Medical Model (IMM). The IMM is a software-based system intended to assist mission planners in preparing for spaceflight missions by helping them to make informed decisions about medical preparations and supplies needed for combating and treating various medical events using Probabilistic Risk Assessment. The objective is to use statistical analyses to inform the IMM decision tool with estimated probabilities of medical events occurring during an exploration mission. Because data regarding astronaut health are limited, Bayesian statistical analysis is used. Bayesian inference combines prior knowledge, such as data from the general U.S. population, the U.S. Submarine Force, or the analog astronaut population located at the NASA Johnson Space Center, with observed data for the medical condition of interest. The posterior results reflect the best evidence for specific medical events occurring in flight. Bayes' theorem provides a formal mechanism for combining available observed data with data from similar studies to support the quantification process. The IMM team performed Bayesian updates on the following medical events: angina, appendicitis, atrial fibrillation, atrial flutter, dental abscess, dental caries, dental periodontal disease, gallstone disease, herpes zoster, renal stones, seizure, and stroke.

15. SUBJECT TERMS
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