ASSESSING THE EFFECT OF SPACEFLIGHT ON THE PROPENSITY FOR ASTRONAUTS TO DEVELOP DISC HERNIATION
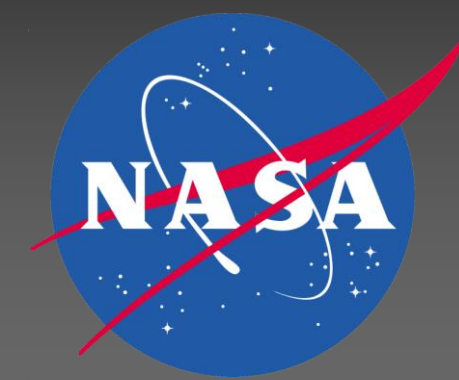
A. Feiveson,[1] C. Méndez,[2] J. Somers[3]

[1]NASA Johnson Space Center, [2]MEI Technologies, [3]Wyle Science, Technology and Engineering Group

Corresponding Author: Alan Feiveson, Ph.D.
NASA Johnson Space Center
alan.h.feiveson@nasa.gov, 281-483-6603

Background

A previous study [1] reported that the instantaneous risk of developing a Herniated Nucleus Pulposus (HNP) was higher in astronauts who had flown at least one mission, as compared with those in the corps who had not yet flown. However, the study only analyzed time to HNP after the first mission (if any) and did not account for the possible effects of multiple missions. While many HNPs occurred well into astronauts' careers or in some cases years after retirement, the higher incidence of HNPs relatively soon after completion of space missions appears to indicate that spaceflight may lead to an increased risk of HNP. In addition, when an HNP occurs after spaceflight, is it related to previous spaceflight exposure? The purpose of this study was to investigate whether multiple missions, age, vehicle landing dynamics, and flight duration affect the risk of developing an HNP using a competing risks model. The outcome of the study will inform the Human System Risk Board assessment of back pain, inform the risk of injury due to dynamic loads, and update the previous dataset, which contained events up to December 31, 2006.

Methods

The study was done using data queried by an epidemiologist from the electronic medical record and provided by the Lifetime Surveillance of Astronaut Health. The data included all 330 United States Astronauts beginning at selection and continuing throughout their life from 1959 through February 2014. HNP diagnoses were confirmed by Magnetic Resonance Imaging, Computerized Tomography, Myelography, operative findings, or through clinical corroboration by a neurologist or neurosurgeon. In this analysis, cases of HNP diagnosed at or before the time an astronaut was selected into the astronaut corps were ignored.

Survival Model. We modeled the distribution of T_{min}, the time from selection into the astronaut corps until first diagnosis of HNP. Explanatory variables fall into two categories:

Flight-related explanatory variables. number and timing of missions, mission duration(s), type of landing vehicle(s), experience as pilot of a high-performance jet aircraft. For purposes of this study, "long-duration" missions were those flown on Skylab, MIR, or ISS. Others were considered "short-duration" missions. Landing vehicles were classified into "STS" (Space Shuttle) or "capsule" (all others).

Demographic explanatory variables. age, gender, weight, height, and BMI.

An important component of the model allows for the possibility that only some astronauts are susceptible to developing a HNP during their active careers or after retirement. For astronauts in the "susceptible" (**S**) category, if a HNP had not been incurred by the time of their last physical exam, T_{min} was treated as *censored* at that time, meaning that these astronauts would have eventually developed a HNP had they been observed longer. On the other hand, non-susceptible astronauts (**N**) are those that would never develop a HNP no matter how long they were observed. In practice, susceptibility is treated probabilistically; i.e. we cannot tell on an individual basis whether or not a particular astronaut who did not develop a HNP during the study period is in the **S** or **N** category, but we were able to estimate the proportion of susceptible astronauts as a function of how many missions they flew (0 – 7).

Analysis goals. The main analysis goal was to separate effects of spaceflight from those of just being in the astronaut corps on the distribution of T_{min}. Secondary goals were to investigate the degree to which number of missions, age, gender, etc. also had an effect on T_{min}.

Survival Model Details. Multiple stochastic processes take place for each astronaut; T_0 = time from selection to HNP (influenced by astronaut training and lifestyle) and T_i = time from selection to HNP after the i-th spaceflight mission ($i = 1, 2,.., n$).

$$T_{min} = \min_{i=0,1,...,n} T_i$$

Hazard Functions. The distributions of T_0 and T_i as well as $P(\mathbf{N})$, the probability that an astronaut is in the **N** category are modeled through their *hazard functions*. A hazard function $h(t)$ is a measure of instantaneous risk of HNP at time t given that one has not occurred previously. For example, in Figure 1, the probability of a first HNP occurring in the small time window shown is approximately the value of the hazard function times the width of the window. Here, t is defined as elapsed time from the date of selection.

In this application, hazard functions are modeled as proportional to Weibull density functions:

Weibull Density Function

$$w(t; p, \theta) = \frac{p}{\theta}\left(\frac{t}{\theta}\right)^{p-1} e^{-\left(\frac{t}{\theta}\right)^p}$$

Hazard Function Components.

Astronaut training and lifestyle:

$$h_0(t) \equiv A_0 w(t; p_0, \theta_0); \quad (t > 0)$$

After each spaceflight mission:

$$h_i(t) \equiv A w(t - t_i; p, \theta) \quad (t > t_i)$$

where A_0, p_0, θ_0, A, p, and θ are parameters that in general depend on the explanatory variables. The effect of the explanatory variables an the hazard function parameters is estimated by the method of maximum likelihood. Figure 2 illustrates how the component hazard functions reflect differences in the explanatory variables. Survival Function for $T_{min} = \min_{i=0,1,...,n} T_i$

$$P(T_{min} > t) = P(T_0 > t, T_1 > t,..,T_n > t)$$
$$= \prod_{i=0}^{n} e^{-H_i(t)}$$
$$= e^{-\Sigma H_i(t)}$$

where $H_i(t) = \int_0^t h_i(u)du$ $H_i(t) = \int_0^t h_i(u)du$

Probability of non-susceptibility. The proportion of astronauts that would never develop HNP's no matter how long they were observed is given by

$$P(\mathbf{N}) = e^{-\Sigma H_i(\infty)} = e^{-A_0 - nA}$$

where n is the number of space missions. Reflecting the increased cumulative risk as more flights are undertaken, Figure 3 shows how the $P(\mathbf{N})$ would decrease if everyone had equally spaced missions 3 years apart. This calculation was made with model parameters estimated from the study data.

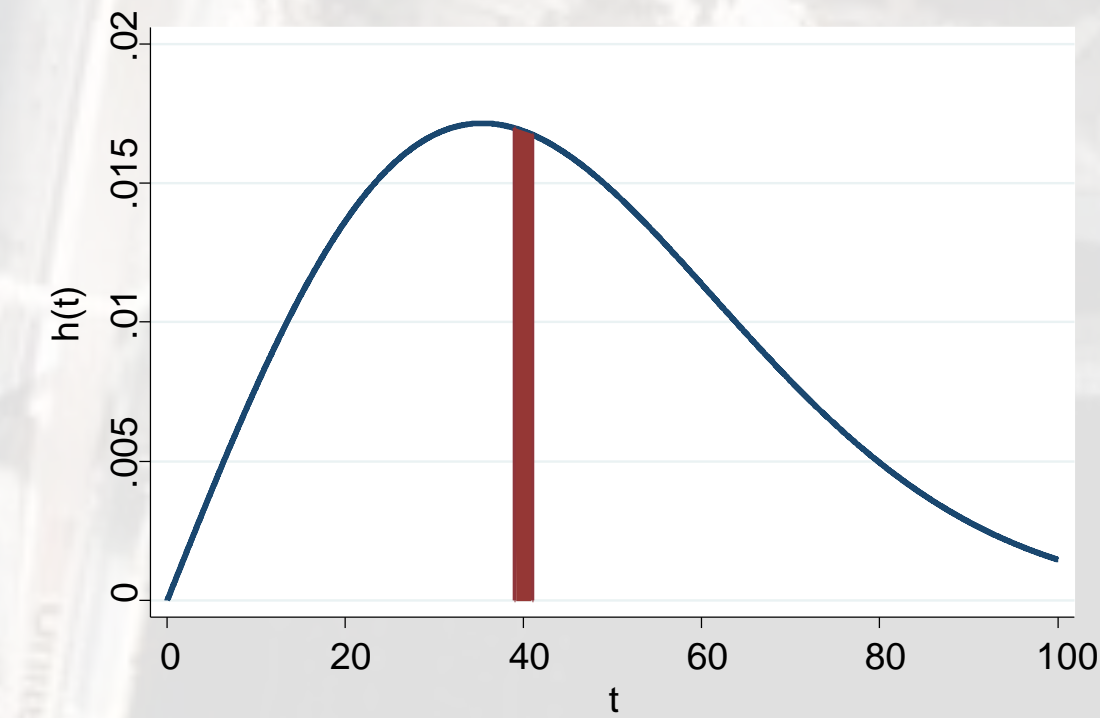*Probability that an HNP at time t was caused by Spaceflight.*

$$P(S|t) = \frac{f_S(t)}{f_S(t) + f_0(t)}$$

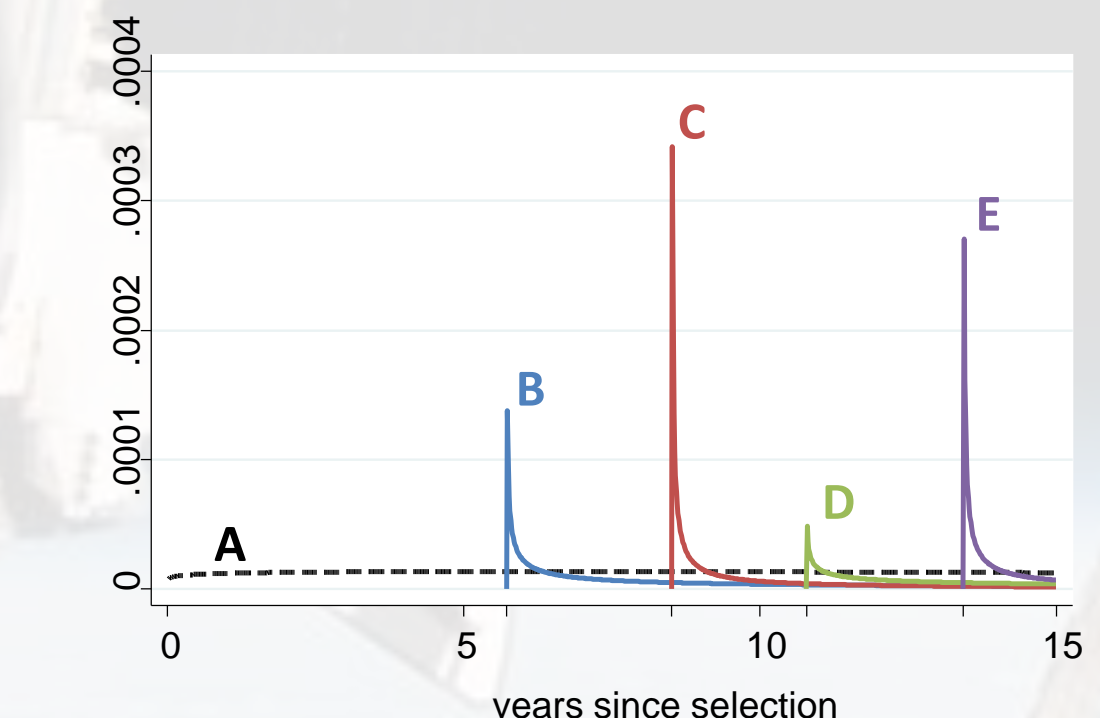(Density functions $f_S(t)$ and $f_0(t)$ are obtained from hazard functions).

Figure 4 illustrates how this probability changes with respect to the number and spacing of missions, as well mission duration and landing vehicle type.

Table 1. Crewmember Demographics

| Group	Number of Crewmembers
All Astronauts	330
Sex	
Male	282
Female	48
Number of Capsule Landings	
0	258
1	52
2	13
3	3
4	4
Number of Long Duration Missions	
0	273
1	51
2	6
Number of Missions	
0	31
1	70
2	86
3	60
4	57
5	19
6	5
7	2

Figure 1. Hazard Function

Figure 2. Hazard Function Component Model. Hypothetical crewmember with:
(A) hazard function associated with being an astronaut without spaceflight experience
(B) a short-duration flight with a Shuttle landing,
(C) a long-duration flight with a Shuttle landing ,
(D) a short-duration flight with a capsule landing, and
(E) a long-duration flight with a capsule landing
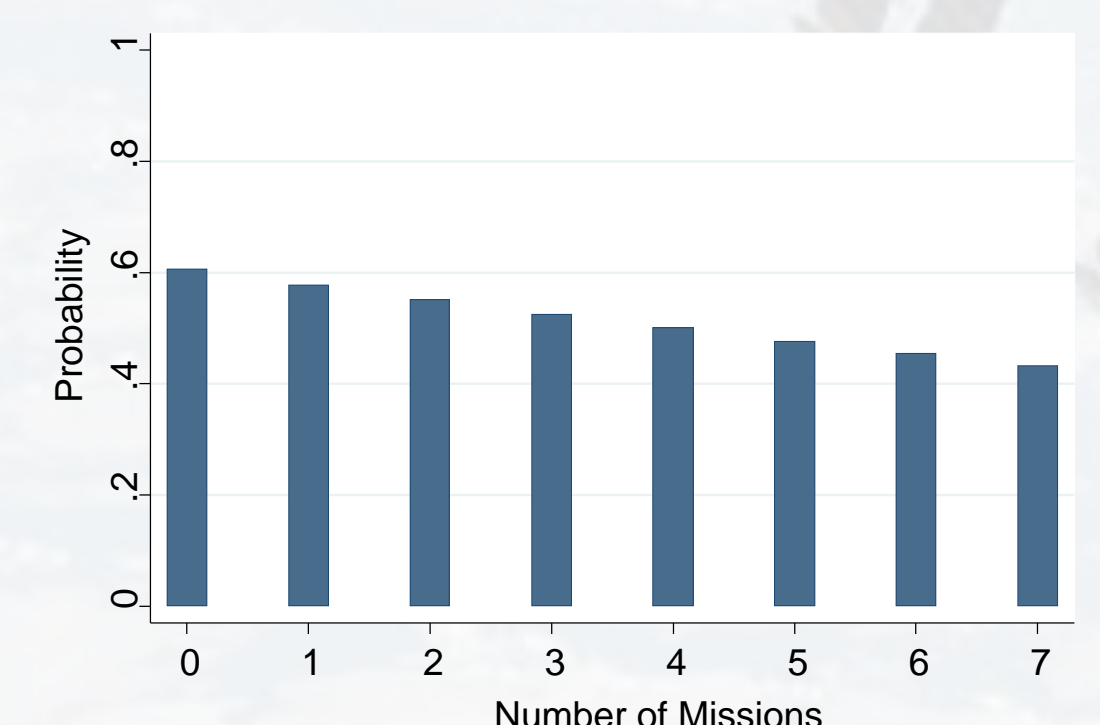
Figure 3. Probability of never incurring an HNP after each subsequent mission flown, each separated by 3 years.
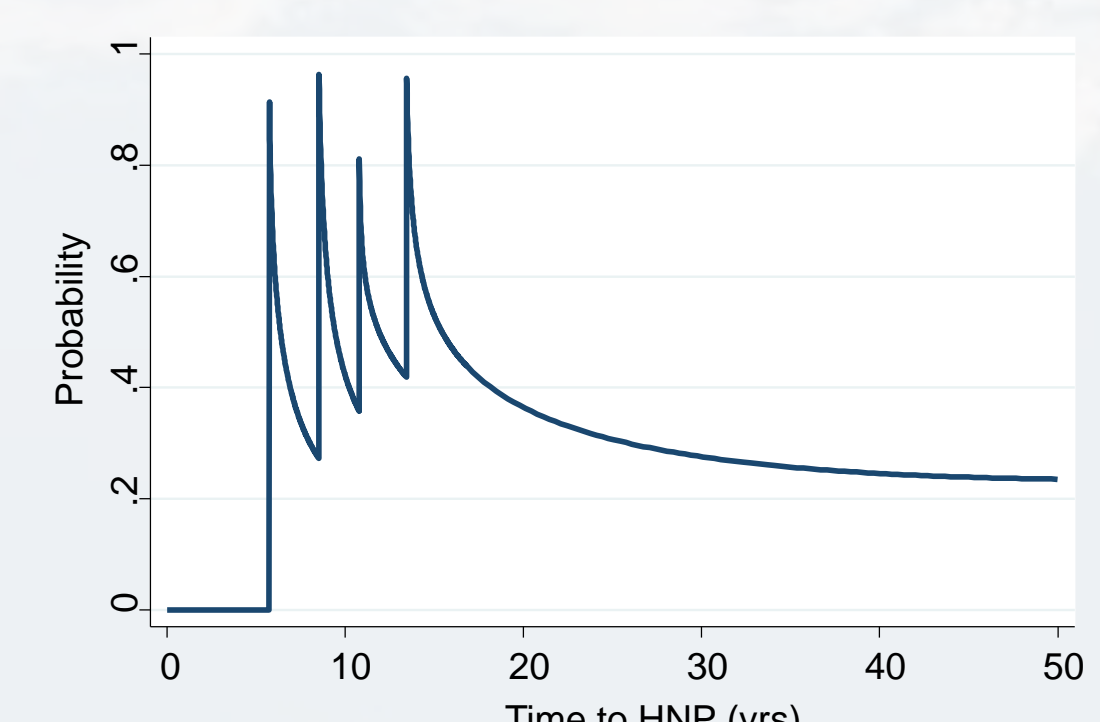

Figure 4. Probability that an HNP may be attributable to spaceflight. Using the same hypothetical astronaut in Figure 2, each of the peaks represents a mission, with the probability increasing immediately post-flight each mission.

Results

Survival Model. Figure 5 shows the probability of a HNP occurring as a function of years after astronaut selection a) without any distributional assumptions (solid line), and b) with our survival model (red dots). The overall trends agree well. Deviations of the dots from the solid line reflect how our model accounts for variation in HNP risk due to differing numbers and spacing of missions for the 330 astronauts.

Figure 6 shows how the probability of an HNP within one year of a mission landing was estimated to increase with the number of missions. However because of the lower numbers of astronauts with many missions, the accuracy of this estimated probability becomes worse (increased error bounds) as the number of missions increases.
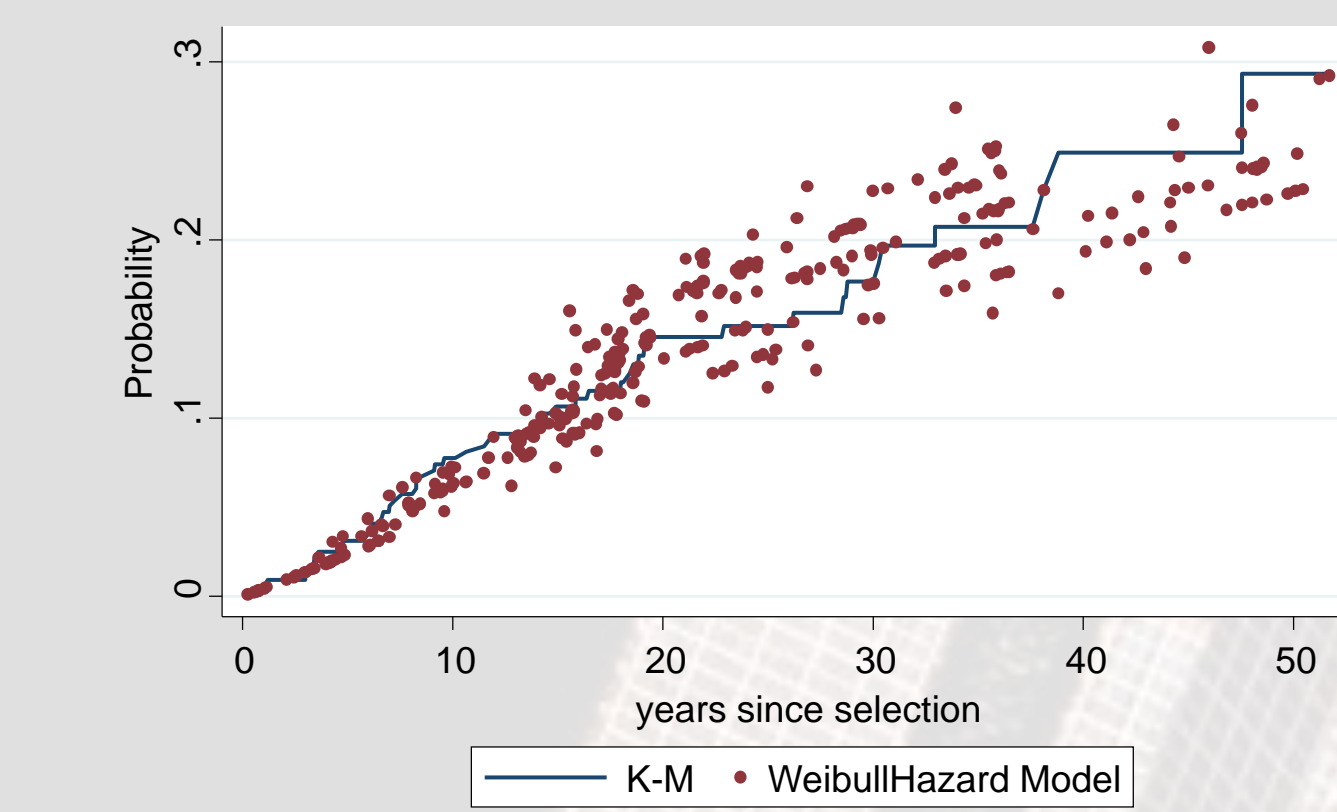

**Figure 5.** Model Fit comparison of mixture cumulative density functions
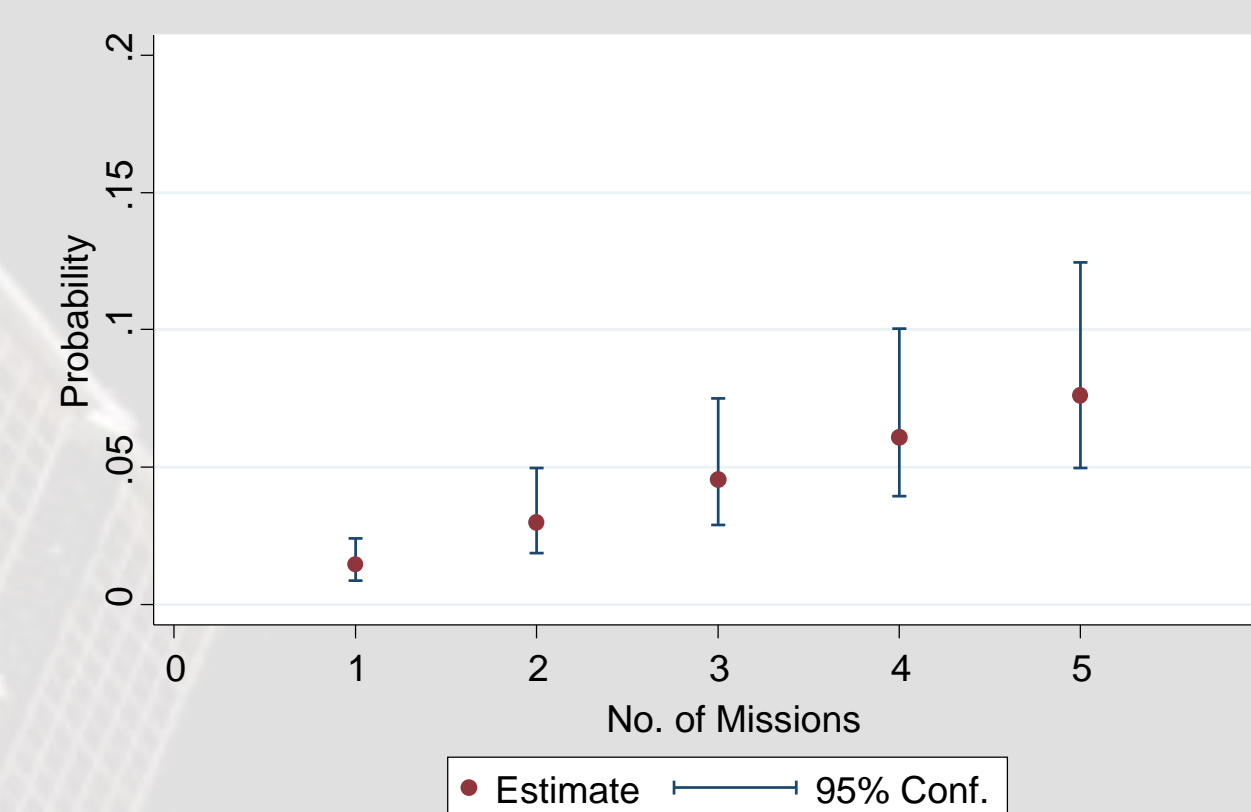
Figure 6. Probability of an HNP given 1 year of landing given missions spaced 3 years apart and the first mission occurring 5 years after selection.

One of the most important questions addressed by this study was to separate the effects of spaceflight from those of the general astronaut training and lifestyle:

Overall effect of spaceflight and mission characteristics. To test for an overall effect of spaceflight on propensity to develop a HNP, the survival model was fit with and without the spaceflight component(s). The difference in the log likelihoods was 8.25, which corresponds to p= 0.0009 ($\chi^2 = 2 \times 8.25 = 16.50$; 3 d.f.) as shown in Figure 7.
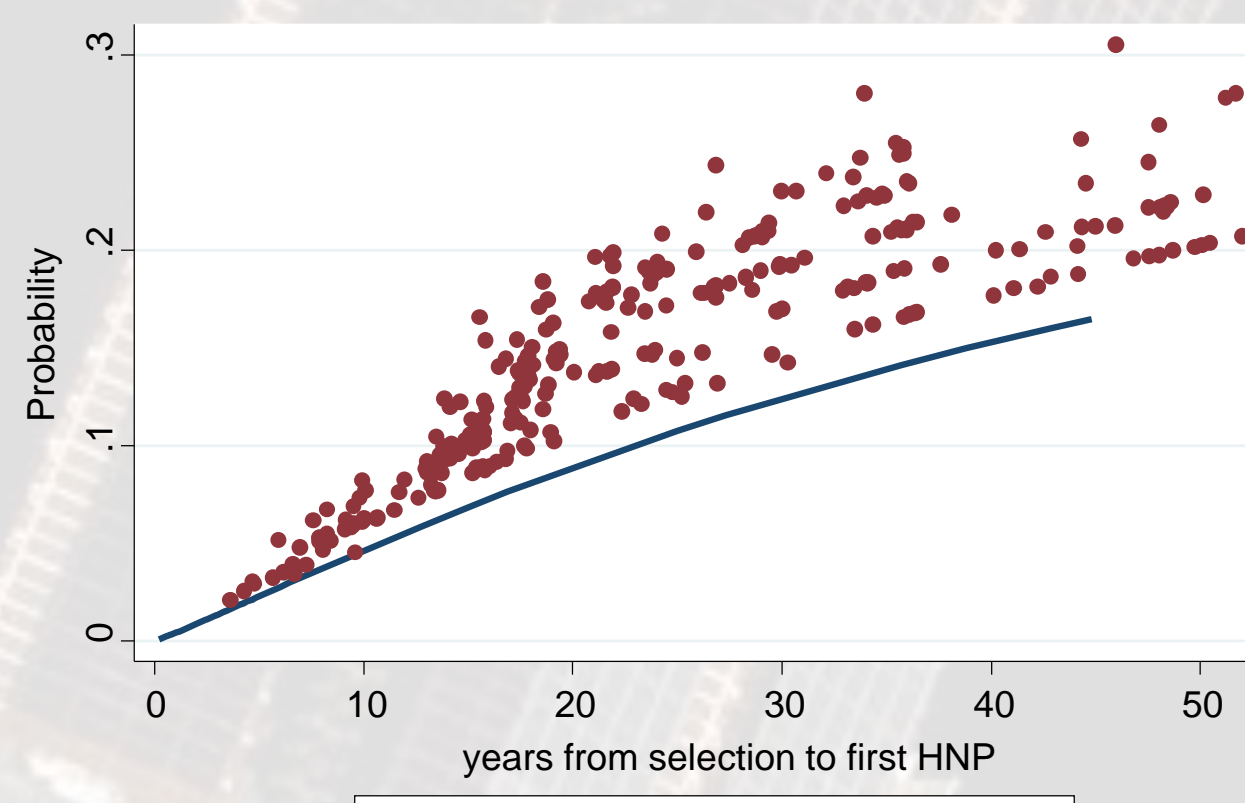
Figure 7. Cumulative Probability of Time to First HNP
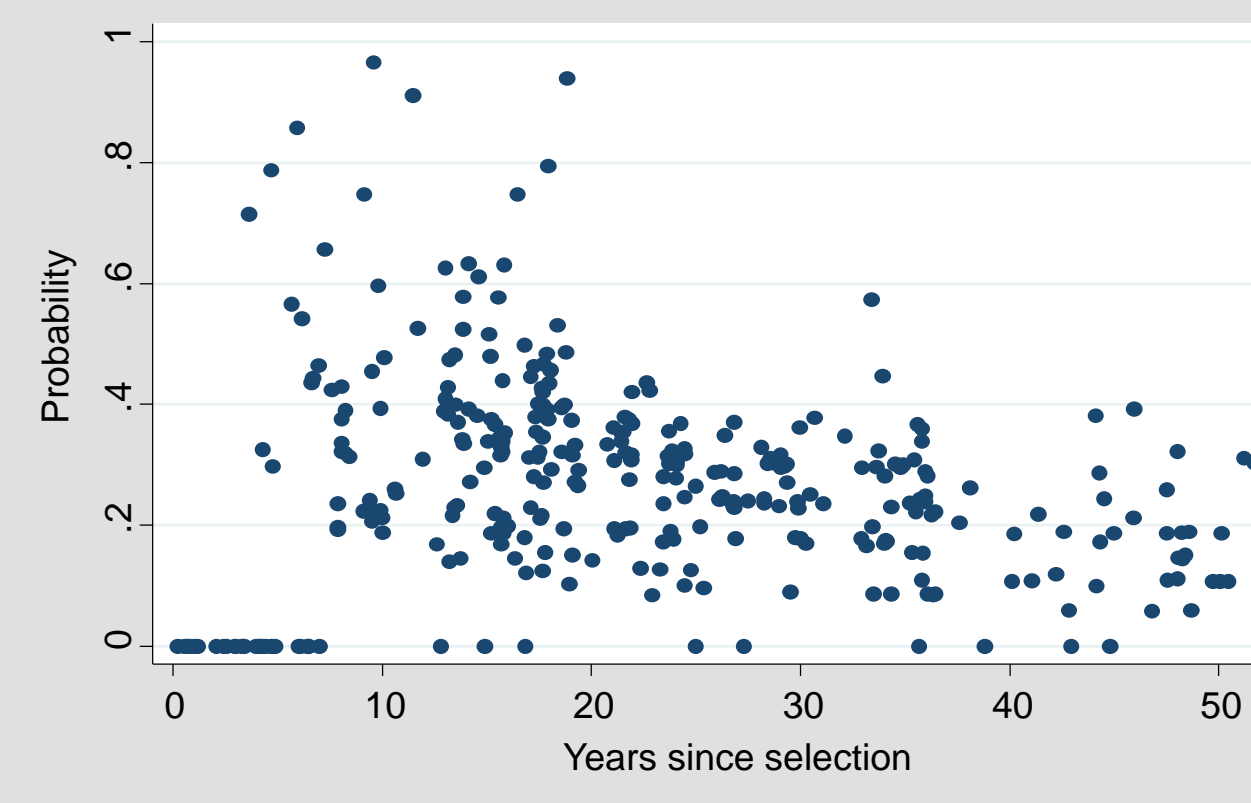
Figure 8. Conditional Probability HNP is due to spaceflight

Conditional probability of HNP due to spaceflight. After fitting the survival model, we were able to estimate the conditional probability that an HNP occurring at a given time could be attributed to spaceflight (Figure 8). To create this figure we used the actual observation times and mission characteristics for each of 330 astronauts to calculate what this probability would be if HNPs had actually occurred at each one of those times. In reality only 51 HNPs were observed (not shown here). Higher values correspond to HNPs occurring soon after mission landings.

There were 745 astronaut-missions flown by all astronauts. Of these, only 58 (7.8%) were "long duration" and 98 (13.2%) were capsule landings. No evidence of an effect of either flight duration or landing vehicle on HNP propensity after spaceflight was seen (Table 4).

Effect of demographic explanatory variables. There was no strong evidence that gender, height, weight, BMI, or a history of high-performance jet aircraft piloting had an effect on HNP risk (Table 5). However astronauts that were older at the time of selection appeared to have higher risk (p = 0.038). In addition, pre-Shuttle astronauts had generally lower risk of HNP (p = 0.012).

Table 2. HNP Occurrence by Demographic

Group	Number of Crewmembers	First HNP Event/Location	Proportion of Crewmembers
All Astronauts	330	51 Total	15%
		19 Cervical	6%
		3 Thoracic	1%
		29 Lumbar	9%
Male	282	45 Total	16%
		15 Cervical	5%
		3 Thoracic	1%
		27 Lumbar	10%
Female	48	6 Total	13%
		4 Cervical	8%
		0 Thoracic	0%
		2 Lumbar	4%
No Missions	31	3 Total	10%
		0 Cervical	0%
		0 Thoracic	0%
		3 Lumbar	10%
1 Mission	70	9 Total	13%
		3 Cervical	4%
		1 Thoracic	1%
		5 Lumbar	7%
2 Missions	86	14 Total	16%
		5 Cervical	6%
		1 Thoracic	1%
		8 Lumbar	9%
3 or More Missions	143	25 Total	17%
		11 Cervical	8%
		1 Thoracic	1%
		13 Lumbar	9%

Table 3. Numbers of reported HNPs, by characteristics of last previous mission before HNP or end of study period for each individual

		HNP	no HNP	Total	% HNP
Long-duration missions	no*	46	244	290	15.9
	yes	5	35	40	12.5
Capsule landings	no*	40	233	273	14.7
	yes	11	46	57	19.3

* Includes no missions before HNP or end of study period

Table 4. Effect of Mission-related Factors on HNP RISK (Survival Model)

Factor	risk direction	p-value
Overall spaceflight	worse	0.0009
Long-duration missions	none	0.328
Capsule landings	none	0.642

Table 5. Effect of Demographic Factors on HNP Risk

Factor	risk direction	p-value
Female	better	0.677
Higher BMI	worse	0.195
Greater age at selection	worse	0.038
Greater height	none	0.954
Greater weight	worse	0.357
HPJA* pilot	none	0.901
pre-STS	better	0.012

* High-performance jet aircraft

Discussion

Analysis of the data revealed clear evidence that spaceflight is associated with increased risk of HNP, thus supporting the conjecture suggested by a higher incidence of HNPs shortly after missions. In arriving at this finding we fit a survival model that took into account differences in type, number and timing of missions as well as the periods of observation for each astronaut. In addition we allowed for the possibility that a certain proportion of astronauts are not susceptible to HNP and would not develop one no matter how long they were observed. The model-based conditional probabilities that each of the 44 HNPs that occurred after at least one mission were attributable to spaceflight, ranged from 0.97 (shortly after a mission) to about 0.2 or lower (at least 30 years after selection). The average value of these probabilities was 0.44.

Other than a detrimental effect of initial age (i.e. at selection), we did not find evidence that HNP risk was affected by demographic factors such as gender, height, weight, or whether an astronaut had experience piloting a high-performance jet aircraft. It did appear that astronauts from the pre-Shuttle era, were at lower risk of eventually developing an HNP (p = 0.012). Finally, we did not find evidence that either mission duration or type of landing vehicle had an effect.

Limitations

Because this was an observational study it is difficult to separate out the effects of the many spaceflight and demographic factors on HNP risk or to claim causality. In particular, we had no control over when long-duration or capsule-landing missions occurred, thus creating substantial confounding of these factors with HNP reporting and diagnosis practices as well as changing criteria for astronaut selection since the pre-Shuttle era. Also, HNP time of incidence was recorded at the time of diagnosis, not at the time of occurrence.

Because the data span the entire Astronaut Corps, effects from improved spaceflight deconditioning countermeasures may obscure the risk of developing an HNP, particularly related to mission length. A majority of the long-duration missions occurred in the past 25 years, when countermeasures have been implemented. In addition, the relatively low numbers of long-duration flights and female astronauts adversely affects the power of tests for these effects.

Finally, the current study only examines data from U.S. crewmembers. Supplementing the data with HNP reports from other Space Agencies could allow more insight into these effects.

Future Work

To better assess the effects of spaceflight on HNP risk, additional crewmember data would be ideal. In addition to the U.S. Astronauts included in this study, additional information may be available from the international partners, which could increase the dataset substantially. Additional countermeasures for crewmembers immediately after landing may also be advised to prevent HNP occurrence at the times of highest risk. Finally, continued surveillance of crewmembers after spaceflight could allow a better understanding of this trend.

These results may also be beneficial to current studies of the intervertebral disc and additional analysis of these data in concert with the data from the current studies may improve our understanding of the mechanism of HNP after spaceflight.

Acknowledgements

References

Johnston, S. L., Campbell, M. R., Scheuring, R., and Feiveson,A. H (2010) . Risk of Herniated Nucleus Pulposus among U.S. Astronauts. *Aviat Space Environ Med* 81, 566-74