Hypertension Cliff

Branch Baseline

Hypertension is the medical term for high blood pressure. Diagnosis is by sphygmomanometry. Blood pressure readings include 2 numbers, systolic and diastolic. One or both may be used to diagnose hypertension (Merck Manual, 2010). The Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High blood pressure classified blood pressure, as normal (less than 120/80), pre-hypertension (120-139/80-89), stage 1 hypertension (140-159/90-99, and stage 2 (160 or higher/100 or higher). (Merck Manual, 2010); (Chobanian, 2003)

By etiology, blood pressure is primary or essential when it does not have a known cause. Secondary hypertension has an identified cause, usually due to a renal disorder. No changes or symptoms occur in early uncomplicated hypertension. Complicated hypertension involves target organs and changes are graded in 4 groups, grade 1 to 4, constriction of arterioles, constriction and sclerosis of arterioles, hemorrhages and exudates plus vascular changes, and papilledema. (Merck Manual, 2010)

Incidence Data Included in the Model

The model imports the following incidence information from the IMM database: incidence data category, space adaption status, incidence data, incidence and occurrence distribution data and incidence data characteristics. Data category defines the type of data available for incidence calculations (i.e. raw data vs. fixed data). Space adaptation identifies medical events that onset occurs in the first 5 days of flight and does not reoccur. Incidence values vary by data category and define the number of medical events per person-year or medical events per person-at-risk for each medical condition. Incidence values can be modified by crew characteristics such as gender. Modifying characteristics are noted below and incidence values are listed individually for each characteristic. Distributions are assigned to medical events incidence values and occurrences in the model. For each crew member in a given trial, the incidence and number of occurrences of each medical condition are randomly selected from these probability distributions. Detailed descriptions of the distributions are included in the IMM Technical Description Document.

Incidence	
Data Category:	Fixed
Space Adaptation:	No
Incidence Type:	Rate

Distribution Data	
Incidence:	Fixed
Occurrence:	Poisson

Data Characteristics	
Fixed Rate:	0.00646

Incidence Comments

De novo Hypertension has never occurred in space flight. Lacking phenomenological data, incidence was estimated using terrestrial population data.

The Aerobics Center Longitudinal Study (ACLS) investigated prospectively the relationship between physical activity, cardio respiratory fitness (CRF), and the development of hypertension in initially normotensive individuals. A total of 2,346 men reported hypertension during a mean 18 years of follow-up. Event rates per 10,000 man-years adjusted for age and examination year were 86.2, 76.6, and 66.7 across physical activity groups of sedentary, walker/jogger/runner (WJR), and sport/fitness, respectively, and 89.8, 78.4, and 64.6 for low, middle, and high CRF, respectively (trend P < 0.0001) (Chase, 2009). The high CRF group is more similar to the astronaut population. Hypertension incidence is 0.00646 person-years (64.6/10,000)

Information Regarding Prevention

Selection criteria

Causes for rejection include in general, any medical condition that, in the judgment of the Multilateral Space Medicine Board (MSMB) may compromise mission operations, performance of duties, or crew health or safety.

In the cardiovascular area, disqualifying conditions include hypertension, i.e. systolic blood pressure greater than 140mmHg, or diastolic greater than 90mmHg. Hypertension pharmacologically controlled to less than 140mmHg systolic and 90mmHg diastolic requires Special Consideration by the MSMB (International Space Station Program, 2009).

Incidence Level of Evidence (LOE)

The IMM level of evidence appropriate assessment of the quality of the IMM input data. Since IMM incorporates input data from a wide variety of sources including astronaut population, terrestrial or analog populations, and external models, an innovative approach to assess the quality of input data was required. Information obtained from the astronaut population and/or space flight is the more relevant so it is assigned the highest level of evidence and less relevant data sources are assigned a lower level of evidence.

Citation	LOE Value	LOE Category
Chase, 2009	4	Incidence

Alternative Incidence Data

Hypertension is an extremely common diagnosis, currently affecting about 76.4 million Americans over the age of 20, or about one in three adults. Circa 20% of this population is unaware they have hypertension, and 52.2% do not have it controlled (Roger, 2012).

Analog populations

Hypertension, benign essential, was found among submariners. There were 3 cases in the cardiovascular disease group, causing 33 sick days. Malignant hypertension was not reported (Tansey, 1979). No information on EVAC caused by condition. Our estimated incidence, during the period 1963-67, is 0.000338 person-years. (3/ 3, 240 000 man-days = 9.25e-7 x 365 = 3.379e-4)

Between 1959 and 1999 5.5% of active and inactive NASA astronauts (21 of 291) have been diagnosed with hypertension during annual examination. 13.9% (121 of 870) of comparison participants had corresponding hypertension diagnoses over a similar time period. The comparison participants had more than double the hypertension prevalence rate of the astronauts, but still had a lower rate than the general population. Cross-sectional data of LSAH participants by age group show that most of them have average systolic pressure around or below 120 mmHg. Up to age 49, male comparisons show the same trend of systolic pressure measurements, although with slightly higher values, with that of the male astronauts. Male comparison participants aged 50 and older showed a higher increase of their systolic pressure as compared to male astronauts aged 50 and older. The diastolic pressure measurements for the male comparisons do not show a corresponding upward trend. The small sample size of female participants does not allow for age group comparisons beyond the 40-44 age group (LSAH, 2012).

The Millennium Cohort baseline questionnaire (2001–2003) was completed by 77 047 US active-duty and Reserve/National Guard members. Follow-up was completed by 55 021 responders approximately 3 years later (2004–2006). Multivariable logistic regression was used to estimate the 3-year risk of newly reported hypertension, adjusting for general and mental health, demographics, and occupational and behavioral characteristics. After applying exclusion criteria, our analyses included 36 061 service members, many of whom had deployed on military operations. Subanalyses of deployers included 8829 participants. Newly reported hypertension was identified in 6.9% of the cohort between baseline and follow-up. Among deployers, those reporting multiple combat exposures were 1.33 times more likely to report hypertension compared with noncombat deployers (95% CI: 1.07 to 1.65). Although military deployers, in general, had a lower incidence of hypertension than non deployers, deployment with multiple stressful combat exposures appeared to be a unique risk factor for newly reported hypertension. Exact systolic/diastolic values are not included. The 3 year cumulative incidence reported for deployed no combat, 5.4% (Odds ratio 0.77; 95% CI 0.67 to 0.89) By birth year 1960-69 (age 34-44 at time of initial follow up, 2004) 6.9%; birth year 1960 and earlier (age 44+) 10.8% birth year 1960-69 (age 34-44 at time of initial follow up) 6.9 (Granado, 2009). We estimated the annualized rates at 0.023 (2.3/100) and 0.036 (3.6/100) respectively. The annual incidence for deployed non combat is estimated at 0.018 (1.8/100).

Treatment and Outcomes

Based on the best evidence available best and worst case percentage ranges are assigned. The medical condition is divided into three clinical phases in all three clinical phases a functional impairment is assigned. The clinical phase I and II's functional impairments remain for the duration for that respective clinical phase. The function impairment in clinical phase III represents final impairment for this medical condition and remains for the rest of the mission. Other mission end states include evacuation and loss of crew life.

The IMM checks medical resource availability once the number of medical events and scenarios has been established. If there is not sufficient essential resources called out in the CliFF, then the medical condition will go down an untreated best or worst case scenario pathway.

The table below summarizes the treated and untreated best and worst case scenarios.

	Clinical Phase I Diagnosis & Initial Treatment[1]		**Clinical Phase II On-going Treatment / Convalescence[2]**		**Clinical Phase III Recovered / Mission End State[3]**		
	FI* (%)	**Duration (hrs)**	**FI* (%)**	**Duration (hrs) (Min - ML - Max)**	**FI* (%)**	**EVAC** (%)**	**LOCL** (%)**
ISS-based Treatment (best case scenario %: 86 - 91)	100	0.25	0 - 10	720 - 720 - 720	0 - 2	0	0
ISS-based Treatment (worst case scenario %: 9 - 14)	100	0.5	2 - 23	720 - 720 - 720	0 - 10	0 - 1	0
Untreated Best Case	N/A	N/A	2 - 23	720 - 720 - 720	0 - 10	0	0
Untreated Worst Case	N/A	N/A	11 - 40	720 - 720 - 720	2 - 40	0 - 100	0

[1]Clinical Phase I: Clinical phase I covers only the initial assessment of the affected crew member to define his or her medical condition, and completion of appropriate initial treatment to stabilize the crew member. While the affected crew member is being assessed, he or she is not able to perform any assigned tasks, thus Functional Impairment during this phase is considered 100%. In the untreated case, there is no diagnosis performed or treatment given, therefore Functional Impairment and Duration will always be "not applicable".

[2]Clinical Phase II: On-going Treatment and Convalescence- During clinical phase II, the affected crew member is receiving any appropriate follow-on treatment for his or her medical condition to allow the crew member to recover as much as he or she is able to recover in the ISS environment. Clinical phase II also encompasses relapses or reoccurrences of the same original medical condition in clinical phase I necessitating additional treatment or recovery time due to unsuccessful primary treatment response. The duration in Clinical Phase II is expressed in minimum, most likely (ML) and maximum hours. This was updated for future capabilities in IMM but is currently not being used by the model.

[3]Clinical Phase III: Recovered/Mission End State- Clinical phase III is reached once the affected crew member has recovered from the medical condition as much as he or she is able to recover in the ISS environment. This may or may not be recovery from the given medical condition to the full extent possible. If this "recovered" state results in an evacuation or loss of the crew member, this will be noted in the mission end state results.

*Functional Impairment (FI) is a measure of the affected crew member's health and performance ability.

**Two mission end state results are addressed in the CliFF: 1) Evacuation (EVAC) - crew and patient are evacuated from the spacecraft due to the medical condition, and 2) Loss of crew (LOCL) - death of affected crew member due to medical condition. EVAC is considered as an end state result if any of the following criteria are met: 1) potential LOCL, 2) potential significant permanent impairment, or 3) potential intractable pain. Probability distributions are assigned for each range of values within the Table of Treatments and Outcomes.

Refer to the Integrated Medical Model Technical Document for more information on how risk is reported by the IMM, Crew Health Index (CHI) and Quality Adjusted Mission Time calculations.

Definition and Probability of Best and Worst Case Scenario: (includes definitions of best and worst case scenarios and identifies the probability of those scenarios.)

Scenario Comments

Best case scenario is defined as Hypertension Stage 1, i.e. Systolic 140-159 and/or Diastolic 90-99 mmHg

Worst case scenario is defined as Hypertension Stage 2, i.e. Systolic 160 or higher and/or Diastolic 100 mmHg or higher.

Hypertension classification is displayed in the CliFF Appendix

Best case versus worst case percentages

The percentage of worst case is based on a 2004 hypertension study among active duty service members not taking medicine for hypertension (Smoley, 2008). Stage 2 hypertension was reported for the 25-39 and 40-65 year old cohorts at 1.2 and 2.6% while 12.0 and 16.6% had stage 1 hypertension. We estimated the worst case percentage range at 9 to 14% (1.2/1.2+12=9% and 2.6/ 2.6+16.6 = 13.54) Thus the best case percentage is 86-91%.

Best Case Comments

Hypertension functional impairments (FI) calculation follows the IMM mild non-space adaptation template. Hypertensive Cardiovascular Disease ratings are based on Table 4-11, p.67 (American Medical Association, 2008). For further information refer to the CliFF Appendix.

By definition, FI during Clinical Phase I is 100%. Duration is estimated at 15 minutes, to follow the procedure indicated in the ISS Medical checklist for physical exam. During Clinical Phase II, FI is estimated at 0 to 10%. Duration is estimated in 720 hours, 30 days, to allow for uncertainty because there is no cure for hypertension and it will require permanent use of anti hypertensive drugs after diagnosis. During Clinical Phase III, FI is estimated at 0-2% due to ongoing need for medication treatment and potential side effects from medication; EVAC and LOCL are not expected in the best case scenario.

Worst Case Comments

Hypertension functional impairments (FI) calculation follows the IMM mild non-space adaptation template. Hypertensive Cardiovascular Disease ratings are based on Table 4-11, p.67 (American Medical Association, 2008). For further information refer to the CliFF Appendix.

By definition, functional impairment (FI) is 100% during **Clinical Phase I.** Duration is estimated to be 30 minutes, to follow the procedure indicated in the ISS Medical checklist for physical exam, urinalysis, and scheduling a PMC conference. During **Clinical Phase II**, FI is estimated at 2 to 23%. Duration is estimated arbitrarily at 720 hours, 30 days, similar to the best case scenario. During **Clinical Phase III**, symptoms may or may not resolve. FI is estimated at 0 to 10%. If malignant hypertension is present it may require hospitalization to be controlled. The incidence has been estimated at 1% (Bechgaard, 1976); (KINCAID-SMITH, 1958). Thus EVAC is estimated at 0 to 1%. LOCL is not expected

Untreated Best Case Comments

Hypertension functional impairments (FI) calculation follows the IMM mild non-space adaptation template. Hypertensive Cardiovascular Disease ratings are based on Table 4-11, p.67 (American Medical Association, 2008). For further information refer to the CliFF Appendix.

During Clinical Phase II, FI is estimated in 2 to 23%. Duration is estimated at 720 hours, 30 days, similar to the treated best case scenario. During **Clinical Phase III**, recovery may or may not occur without treatment; FI is estimated at 0 to 10%. EVAC is not worth considering because of the minimal risk associated with stage 1 hypertension and it is estimated at 0% similar to the treated best case. LOCL is not expected.

Untreated Worst Case Comments

Hypertension functional impairments (FI) calculation follows the IMM mild non-space adaptation template. Hypertensive Cardiovascular Disease ratings are based on Table 4-11, p.67 (American Medical Association, 2008). For further information refer to the CliFF Appendix.

During **Clinical Phase II**, FI is estimated at 11 to 40%. Duration is estimated at 720 hours, 30 days, similar to the treated scenario; although if EVAC is necessary it may happen earlier. During **Clinical Phase III**, hypertension would not resolve and FI is estimated at 2 to 40% without treatment. Based on the need for definitive care and to account for uncertainty, EVAC would have to be seriously considered for untreated cases of Stage 2 hypertension and it is estimated at 0-100% for this scenario (Poulter, 1992); (Lloyd-Jones, 2005). LOCL is not expected.

Treatment and Options Level of Evidence (LOE)

The IMM level of evidence appropriate assessment of the quality of the IMM input data. Since IMM incorporates input data from a wide variety of sources including astronaut population, terrestrial or analog populations, and external models, an innovative approach to assess the quality of input data was required. Information obtained from the astronaut population and/or space flight is the more relevant so it is assigned the highest level of evidence and less relevant data sources are assigned a lower level of evidence.

Citation	LOE Value	LOE Category
Smoley, 2008	2	BCWC
American Medical Association, 2008	3	FI
Bechgaard, 1976	4	EVAC
KINCAID-SMITH, 1958	4	EVAC
Poulter, 1992	4	EVAC
Lloyd-Jones, 2005	4	EVAC

Additional Comments

We searched PubMed using the terms Hypertension AND Incidence, Hypertension AND Epidemiology, Hypertension AND Medevac. Results were refined by relevance and date

The Resource Table (RT)

Resource	Units Required Best Case	Units Required Worst Case	Units Available At Start Of Mission	Consumable	Essential	Rationale
Blood Pressure Cuff (regular, large)	1	1	2	No	Yes	Measure blood pressure
Blood Pressure Monitor	1	1	1	No	Yes	Measure blood pressure
Cotton balls	0	1	40	Yes	No	To obtain urine sample
ECG Monitor (Device, USB Charge Cable, Lead Set Cable, Cue Card)	0	1	1	No	Yes	Measure and monitor ECG
Lopressor (Metoprolol) 50 mg	60	60	60	Yes	Yes	Anti hypertensive
Nitroglycerin tablet 0.4mg	0	10	25	Yes	Yes	Anti hypertensive
Otoscope (Head, Handle, and USB cable)	1	1	1	No	Yes	Light source for eye exam
Pack of 12 ECG electrodes	0	1	5	Yes	Yes	Measure and monitor ECG
Stethoscope	1	1	2	No	Yes	To measure blood pressure
Urine chemstrips	0	1	10	Yes	Yes	Urinalysis
Urine Color Chart	0	1	1	No	No	To evaluate urine test

Resource Comments

There is no procedure for hypertension in the ISS Medical Checklist (Mission Operations Directorate (MOD), 2011). All resources included in the table are available on board.

Terrestrial standards (Chobanian, 2003) recommend use of diuretics as first line treatment, Diamox is available on board but it has not been included due to metabolic acidosis risk. (Lexicomp, 2011)

Required Resources Level of Evidence (LOE)

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Citation	LOE Value	LOE Category
Chobanian, 2003	3	Resources

Level Of Evidence

Input Data	LOE Average
Incidence	4
Functional Impairment	3
Best Case / Worst Case	2
EVAC / LOCL	4
Resources	3
QUALITY OF EVIDENCE	**3.2**

Description	Range
Excellent	1-2
Good	2.1-3
Fair	3.1-4
Poor	4.1-5

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