

Anxiety Cliff

Branch Baseline

Anxiety and depression are the two most common mental health problems seen in the general medical setting. The four most common anxiety disorders (excluding simple phobias that seldom present clinically) are generalized anxiety disorder, panic disorder, social anxiety disorder, and posttraumatic stress disorder. In space anxiety may manifest as symptoms considered within the range of a normal response to circumstances, or may meet the criteria for a disorder. The differential diagnosis for anxiety on orbit includes other mental disorders, withdrawal from certain medications, exposure to toxins, endocrine dysfunction or other medical illnesses. (Kroenke, 2007)

In the US space program there have been a total of 37 events reported in flight all in the range of normal response to mild symptoms that were short lived. (Walton, 2010).

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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

Female Data Characteristics

Fixed Rate:	0.0071
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Male Data Characteristics

Fixed Rate:	0.0019
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Incidence Comments

Prevalence studies in psychiatric epidemiology outnumber incidence investigations. The Stirling County Study is a longitudinal investigation based on repeated cross-sectional surveys and cohort follow up investigations carried out between 1952 and 1970. For a diagnosis of anxiety, the diagnostic algorithm requires a positive evidence of typical symptoms of autonomic hyperactivity and motor tension in conjunction with apprehension, especially apprehension about having a nervous breakdown; it causes impairment in one's ordinary role, and persists over a minimum duration of one month. The incidence rates for anxiety, for the age 40-49 cohort are 1.9 for male, and 7.1 for female. Both per 1,000 per year (Murphy, 1988) Rates per person year are 0.0019 for male and 0.0071 for female.

Information Regarding Prevention

Selection criteria

Disqualifying conditions include: Any behavior or mental condition that in the opinion of the MSMB makes or is likely to make the individual a hazard to flight safety, crew coordination, or mission execution. The following disorders, or history thereof, are permanently disqualifying for ISS duties: psychotic, bipolar, dissociative, impulse control, somatoform, factitious hallucinogen persisting perceptual disorder, paraphilia, abuse or neglect of a child or adult. Disorders that interfere with social or occupational functioning or that require ongoing treatment: Narcolepsy, and Personality Disorder. Delirium, Dementia, Amnesia. Adjustment Disorder, if the episode exceeded 6 months, hospitalization was required, three or more episodes have occurred, and use of psychiatric medications (other than symptomatic use of anxiolytics or hypnotics for a period of less than 30 days). Gender Identity Disorder. Substance Abuse or Dependence. (Note: Nicotine-related Disorders are not necessarily disqualifying.) History of a Substance Abuse or Dependence. (Note: Consideration for waiver requires completion of an approved treatment program, total abstinence for at least 90 days after the program, and active participation in an after-care program) Characterological behaviors that show evidence of immaturity, instability, impulsiveness, lack of judgment, or an impaired capacity to adapt to stressful situations. (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
Murphy, 1988	4	Incidence

Alternative Incidence Data

Analog Populations

We have one anecdotal report of anxiety (Burrough, 1998) Based on subject matter expert opinion (Beven, 2011), this event may be considered as having anxiety features. There were total 37 events in flight. 32 in STS, 1 in ISS, 3 in Skylab, and 1 in MIR events listed as annoyance, fatigue, irritation, tension and frustration. Their etiology was noise, EVA, lack of sleep and interpersonal conflict. Majority of events were mild and short lived. We do not know if any medication was provided for these events. (Walton, 2010) In flight events have been separated for convenience even though we understand they may co-exist and may have occurred concurrently. The other conditions are addressed in the Depression and Behavioral Emergency Clinical Findings Forms. We will reserve using this incident rate for long duration exploration class missions.

A study to determine work related and personal factors associated with occupational stress in submariners surveyed a random stratified sample of UK Naval service personnel. In total, 116 questionnaires from a total of 219 were returned (a 53% response rate). Of the 116 questionnaires returned, 105 were fully completed; therefore, this was the sample used in the remainder of the analyses. A total of 51% of the respondents were married and the average age was 34 years (range: 19-50 years, SD 7.9 years). In total, 40% of submariners in the 2007 sample were found to be suffering from stress. The findings showed that stress rates in submariners were stable across time, similar to the general Royal Navy. This is in direct contrast to a report issued by the Health and Safety Executive, which states that stress is an increasing problem in the UK. While the stress rate in submariners at 40% is considerably higher than that of the general British population, it does not appear to be increasing. The main personal and demographic factors associated with stress in submariners were low organizational commitment, over-commitment to role, emotional lability and age. The main occupational factors associated with higher stress levels were physical working conditions aboard submarines, lack of peer support and lack of leader support. For submariners, and possibly for other groups working in isolated and extreme environments, the constraints of a restricted environment introduce additional factors that can be associated with stress. (Brasher, 2010)

An analysis of 10 years of data collected on US Navy Polaris submarine patrols over the ten year period 1963-1973 reported a total of 1685 medical events treated. Illness rates are indicated as new/cases/1000 man-days. There were a total of 58 psychiatric diseases during the 1963-73 period with an illness rate of 0.002 and 0.038; for the 1963-67 and 1968-73 periods respectively. There were total 25 anxiety reaction events and one stress reaction; causing 35 and 1 sick days respectively. Time range was 1.8 to 3 days (Table A6). There were 3 EVACs and one

death, but no information on which conditions caused these events. Illness rate and rate of days lost were significantly higher than those observed in the surface population ($P < 0.05$) (Tansey, 1979). Rates per person year are 0.00073 and 0.01387 (0.002 and 0.038 *365 / 1000). The average of these two incidence rates is 0.0073 per person-years. Anxiety events accounted for 43.1% (25/58) of total psychiatric events, or a rate of 0.0031463. Three EVACs occurred but there is no information by condition.

A study to determine first hospitalization incidence rates for neurotic disorders in a military healthy population and to determine the duration, severity and post hospital outcomes was conducted. Data were extracted from automated medical record for all active duty navy personnel admitted between 1980 and 1988. Patients with neuroses are examined by physicians and not admitted in civilian life. In the military, neurotic symptoms may noticeably affect the ability to carry out normal activities, particularly in confined and crowded shipboard environments, and are more likely to result in hospitalization for evaluation and treatment. Anxiety groups and other-neurotic disorders not otherwise specified (NOS) had the best prognosis. The number of first hospitalization during the period 1980-1988 was 5932 and the incidence of new cases was 132.7 per 100,000 person years. The largest number of cases was in the NOS group, followed by neurotic depression, (n 1229) 27/100,000, and the **anxiety** group, (n 981) 22/100,000. For 17% of the patients, the examining physician categorized the condition as existing before entering the service. The depressive group and hysteria has the highest proportion of women. All male racial subgroups had higher rates for younger personnel, with a slight subsequent increase in the older than 45 year age group. Among all racial subgroups of women the 17-19 year age range had the highest incidence. There were no female patients older than 45 years. (Gunderson, 2001) Rates per person-year are overall 0.001327, depression 0.00027, and **anxiety** 0.00022

Epidemiology of psychiatric illnesses experienced by US soldiers in combat was obtained by retrospective review of casualty rosters and electronic medical records. Population consisted of 4122 soldiers, 3797 men and 325 women. Age range 18-52, average 27. There were 308 psychiatric casualties, overall 59.8 per 1000 soldier combat-years which represented 23% of all disease and non-battle injury (DNBI). 88% were treated and returned to duty. 11% were medically evacuated and 1% died. All incidence rates are per 1000 at risk combat-years. Overall incidence rate for anxiety was 9.7. By gender, incidence rate was 14.8 for females and 9.3 for males. There were 50 **anxiety** events of which 1 MEDEVAC (2%) and 0 died. (Goodman, 2011) Anxiety rates per person year are 0.0097 overall, 0.0148 female, and 0.0093 male.

By age, 35 years old and older had the lowest adjusted rate ratio while the 18-23 cohort had the highest; 1 and 1.8; 95% Confidence Interval (CI) 1.21-2.69. By gender, adjusted rate ratio for males was higher than females; 1 and 1.9; 95% CI 1.39-2.63. Trends are similar to civilian population trends. (Goodman, 2011)

Non-Analog Populations

A study to determine trends in mental health-related visits to US emergency departments was conducted. From 1992 to 2001, there were 53 million mental health-related visits, representing an increase from 4.9 percent to 6.3 percent of all emergency department visits and an increase from 17.1 to 23.6 visits per 1,000 U.S. population across the decade. The most prevalent diagnoses were substance-related disorders (22 percent of visits), mood disorders (17 percent), and **anxiety** disorders (16 percent). Anxiety disorders (ICD or DSM-IV codes 300.00 to 300.61 except 300.4 dysthymia) include generalized anxiety disorder, panic disorder, obsessive-compulsive disorder, posttraumatic stress disorder, acute stress disorder, agoraphobia, and anxiety not otherwise specified (NOS). An estimated 17 million visits were for a mental health-related primary complaint (that is, as conveyed to the clinician by the patient), but many more involved a psychiatric diagnosis (that is, the assessment of the patient's condition by the clinician). Among the estimated 53 million mental health-related visits overall, the most common diagnoses were substance-related disorders (30 percent), mood disorders (23 percent), and anxiety disorders (21 percent). Psychoses constituted 10 percent and suicide attempts 7 percent of all documented mental health-related visits. These five major subgroups accounted for 79 percent of all mental health-related visits. The mean age of patients who made mental health-related visits was 39.5 years. Incidence rates of mental health-related emergency department visits are per 1,000 U.S. population, period 2000-2001, overall 22.3; 95% CI 20.5-24.1; age cohort 15-69, 25.0, 95% CI 22.4-27.7 Incidence increased with age. (Larkin, 2005). Overall rates per person-years for the 15-69 age group were 0.025, 95% CI 0.0224-0.0277. We estimated 16% of these rates for anxiety disorders at 0.004 (25/1000 *1

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 %: 91 - 100)	100	0.25	0 - 10	0 - 36 - 72	0	0	0
ISS-based Treatment (worst case scenario %: 0 - 9)	100	0.5	5 - 20	120 - 2100 - 4320	0 - 10	0 - 5	0
Untreated Best Case	0	0	5 - 20	0 - 36 - 72	0 - 10	0	0
Untreated Worst Case	0	0	10 - 30	120 - 264 - 408	5 - 30	0 - 100	0

¹Clinical 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".

²Clinical 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.

³Clinical 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 anxiety that resolves spontaneously or requires minimal pharmacological therapy or psychological counseling.

Worst case scenario is defined as severe anxiety that requires prolonged pharmacologic therapy and/or psychological counseling.

Percentages of worst versus best case scenario were estimated using terrestrial data. Epidemiology studies in Canada have broken out the prevalence rate of anxiety disorders by severity and suggest that 9.2% of the population will suffer from mild anxiety disorders, 2.2% will suffer from chronic, and 1.2% will suffer from serious conditions with significant disability. (Provincial Strategy Advisory Committee for Anxiety Disorders, 2002) All 3 severity percentages were added (16.6) and 1.2% of severe disorders resulted in 9.5% of worst case scenario. To allow for uncertainty the worst case is estimated at 0-9%, thus the best case scenario is 91-100%.

Best Case Comments

The functional impairments (FI) calculation for Anxiety follows the IMM mild non-space adaptation template. Description of symptoms is based on Anxiety Table p. 370. Ratings are based on Impairment Score of Brief Psychiatric Rating Scale (BPRS) Table 14-9, p. 357. (American Medical Association, 2008)

By definition in Clinical Phase I, FI is 100%. Duration of physical exam as described in ISS checklist for the best case scenario is estimated as 15 minutes. During Clinical Phase II, FI is estimated in 0 to 10%. Duration is estimated as 0 to 72 hours. In Clinical Phase III, full recovery is expected and FI is 0%. By definition EVAC and LOCL are not expected for the best case scenario.

Worst Case Comments

The functional impairments (FI) calculation for Anxiety follows the IMM mild non-space adaptation template. Description of symptoms is based on Anxiety Table p. 370. Ratings are based on Impairment Score of Brief Psychiatric Rating Scale (BPRS) Table 14-9, p. 357. (American Medical Association, 2008)

By definition in Clinical Phase I, FI is 100%. Duration of physical exam and medication as described in ISS checklist is estimated as 30 minutes. During Clinical Phase II, FI is estimated in 5 to 20%. Duration is estimated in 120 hours to 4320 (5 days to 6 months)(Bandelow, 2012). In Clinical Phase III, full recovery may or may not occur and FI is estimated at 0-10%. EVAC has occurred in analog populations. (Goodman, 2011)) To allow for uncertainty EVAC is estimated at 0-5%. By definition, LOCL is not expected for this condition.

Untreated Best Case Comments

The functional impairments (FI) calculation for Anxiety follows the IMM mild non-space adaptation template. Description of symptoms is based on Anxiety Table p. 370. Ratings are based on Impairment Score of Brief Psychiatric Rating Scale (BPRS) Table 14-9, p. 357. (American Medical Association, 2008)

During Clinical Phase II, FI is estimated at 5 to 20%. Duration is 0 to 72 hours, similar to the treated best case scenario. In Clinical Phase III, recovery may or may not occur without treatment. FI is estimated at 0-10%. EVAC and LOCL are not expected for this condition.

Untreated Worst Case Comments

The functional impairments (FI) calculation for Anxiety follows the IMM mild non-space adaptation template. Description of symptoms is based on Anxiety Table p. 370. Ratings are based on Impairment Score of Brief Psychiatric Rating Scale (BPRS) Table 14-9, p. 357. (American Medical Association, 2008)

During Clinical Phase II, FI is estimated at 10 to 30%. Duration is estimated in 120 to 408 hours (5-17 days), similar to the treated worst case scenario. In Clinical Phase III, recovery is unlikely and FI is estimated at 5-30%. With no pharmacological treatment available, behavioral treatment can be provided. To allow for uncertainty EVAC is estimated at 0 to 100%. LOCL is not expected for this scenario.

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
American Medical Association, 2008	3	FI
Goodman, 2011	2	EVAC
Provincial Strategy Advisory Committee for Anxiety Disorders, 2002	4	BCWC

The Resource Table (RT)

Resource	Units Required Best Case	Units Required Worst Case	Units Available At Start Of Mission	Consumable	Essential	Rationale
Ativan (Lorazepam) 1 mg tablet	6	30	30	Yes	Yes	Anti anxiety
ECG Monitor (Device, USB Charge Cable, Lead Set Cable, Cue Card)	0	1	1	No	Yes	Measure and monitor ECG
Pack of 12 ECG electrodes	0	1	5	Yes	Yes	To monitor heart rate and rhythm
Psychotherapy	1	1	1	No	Yes	Cognitive behavioral therapy
Zoloft (Sertraline) 50 mg	0	180	60	Yes	Yes	Anti depressant and for severe anxiety

Resource Comments

The ISS medical checklist does not address Anxiety, except as part of behavioral emergency.

The resources included are available on board and have been included following Clinical Practice guidelines (Bandelow, 2012) (Canadian Psychiatric Association, 2006) (Mission Operations Directorate (MOD), 2011).

Required Resources Level of Evidence (LOE)

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Citation	LOE Value	LOE Category
Canadian Psychiatric Association Committee for Management of Anxiety Disorders, 2006	3	Resources
NASA Mission Operations Directorate (MOD), 2011	2	Resources
Bandelow, 2012	3	Resources

Level Of Evidence

Input Data	LOE Average	Description	Range
Incidence	4	Excellent	1-2
Functional Impairment	3	Good	2.1-3
Best Case / Worst Case	4	Fair	3.1-4
EVAC / LOCL	2	Poor	4.1-5
Resources	2.66666666666667		
QUALITY OF EVIDENCE	3.13333333333333		

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