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ECONOMIC EVALUATION OF USING ADENOVIRUS TYPE 4 AND TYPE 7 VACCINES IN UNITED STATES MILITARY BASIC TRAINEES

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by

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DEDICATION

This dissertation is dedicated to my mom and dad, Charlie and Kathi Hodges,
for being my heroes, loving and supporting me, and making this dream possible

And my loving husband, Jonathan Vazquez,
for always believing in me when I do not believe in myself, loving me the way I am, and making me laugh when nobody else can.

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I would like to thank all of our brave soldiers, sailors, airmen, Marines, and Coast Guardsmen for your dedication, service and sacrifice and for defending our freedoms and way of life!

ECONOMIC EVALUATION OF USING ADENOVIRUS TYPE 4 AND TYPE 7 VACCINES IN UNITED STATES MILITARY BASIC TRAINEES

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Adenoviruses, particularly types 4 and 7, are associated with febrile respiratory illness (FRI) outbreaks in US military basic trainees. Vaccines against these two serotypes controlled FRI in basic trainees until production ceased in the mid-1990s. After contracting a new manufacturer, adenovirus vaccination of military basic trainees resumed in 2011. The purpose of this dissertation was to assess the cost – effectiveness of using the new adenovirus type 4 and type 7 vaccines for the prevention of FRI in US military basic trainees from the perspective of each military branch.

Two decision tree models comparing adenovirus vaccination to no adenovirus vaccination were used for this dissertation. The first model is similar to previous models used to assess the cost – effectiveness of the adenovirus vaccine in the military, where the outcome is number of FRI hospitalizations prevented. The second model created for this dissertation used information gathered from published literature and conversations with experts on the adenovirus vaccine. The outcome for the second model was number of training days lost (TDL) averted.

Results from part I indicated that adenovirus vaccination of basic trainees was cost – effective as measured by FRI hospitalizations prevented in all US military service branches but the Coast Guard. The model showed that reintroducing the adenovirus vaccine to basic trainees saved the Army $5.8 million, the Navy, $1 million, the Marine Corps, $238,000, and the Air Force, $5.2 million, annually. In addition, adenovirus vaccination prevented 1,221, 543, 317, 677 cases of FRI hospitalization annually in the Army, Navy, Marine Corps, and Air Force respectively.

In part II of this study, adenovirus vaccination of basic trainees was the dominant strategy as measured by TDL averted in all US military service branches but the Marine Corps and the Coast Guard. Results indicate that it would cost approximately $37.63 and $563.78 per TDL averted for the Marine Corps and Coast Guard respectively.

Both models used for this dissertation provide evidence supporting the cost – effectiveness of using the adenovirus vaccine in US basic trainees in all services but the Coast Guard.

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LIST OF ABBREVIATIONS

AdV: Adenovirus

AdV2: Adenovirus Serotype 2

AdV3: Adenovirus Serotype 3

AdV4: Adenovirus Serotype 4

AdV4p: Adenovirus Serotype 4 Prototype Strain

AdV4p1: Adenovirus Serotype Vaccine Strain

AdV5: Adenovirus Serotype 5

AdV6: Adenovirus Serotype 6

AdV7: Adenovirus Serotype 7

AdV11: Adenovirus Serotype 11

AdV14: Adenovirus Serotype 14

AdV21: Adenovirus Serotype 21

AFB: Air Force Base

APHC: Army Public Health Command

ARD: Acute Respiratory Disease

ARDS: Acute Respiratory Disease Summary

ARI: Acute Respiratory Illness

ASA: Adjusted Standardized Amount

CBA: Cost – Benefit – Analysis

CCA: Cost Consequence Analysis

CDC: Centers for Disease Control and Prevention

CEA: Cost – Effectiveness – Analysis

LIST OF ABBREVIATIONS (CONTINUED)

CIR: Cumulative Incidence

CMA: Cost – Minimization – Analysis

COI: Cost – of – Illness

CPI: Consumer Price Index

CPT: *Current Procedural Terminology*

CUA: Cost – Utility – Analysis

DHA: Defense Health Agency

DHA: Defense Health Agency

DMEM: Dulbecco's Modified Eagle's Medium

DoD: Department of Defense

DPSC: US Department of Defense Personnel Support Center

DRG: Diagnosis Related Group

EMEM: Eagle's Minimal Essential Medium

FBS: Fetal Bovine Serum

FDA: US Food and Drug Administration

FRI: Febrile Respiratory Illness

FY: Fiscal Year

GBS: Guillain – Barre Syndrome

HRQOL: Health Related Quality of Life

ICD – 9 – CM: *International Classification of Diseases, Ninth Edition, Clinical Modification*

LIST OF ABBREVIATIONS (CONTINUED)

ICER: Incremental Cost – Effectiveness Ratio

IDR: Incidence Density Rate

INB: Incremental Net Benefit

MHS: Military Health System

MTF: Military Treatment Facilities

NHRC: Naval Health Research Center

OUSD: Office of the Under Secretary of Defense

PCR: Polymerase Chain Reaction

PE: Pharmacoeconomics

PSA: Probabilistic Sensitivity Analysis

QALY: Quality Adjusted Life Year

SPGA: Sucrose, Phosphate, Gluconate, Albumin

SV – 40: Simian Virus

$TCID_{50}$: Tissue Culture Infectious Dose

TDL: Training Days Lost

UBO: Uniform Business Office

VAERS: Vaccine Adverse Event Reporting System

VE: Vaccine Effectiveness

VIS: Vaccine Information Statement

WRAIR: Walter Reed Army Institute of Research

CHAPTER 1: BACKGROUND

1.1. INTRODUCTION

Adenoviruses (AdVs), particularly serotypes 4 and 7, are associated with febrile respiratory illness outbreaks in United States military basic trainees. [1–6] Febrile respiratory illness (FRI) is a common cause of hospitalization and morbidity in military recruits, costing the US government millions of dollars in direct medical costs every year. [7] Adenovirus vaccines controlled FRI in military recruits until 1996, when the sole manufacturer, Wyeth, ceased production. In October 2011, after a twelve – year break and contracting with a new manufacturer, adenovirus vaccine administration to military basic trainees resumed. [8] Previous economic models agree that vaccination of military recruits against adenovirus is beneficial from the perspective of reducing military medical costs. [7, 9 - 10] However, these cost analyses have been modeled under the assumptions that adenovirus epidemiology in military recruits has not changed, does not differ between military service branches, and that the manufacturer's cost for the new vaccine would be comparable to that seen before production ceased in 1996. Therefore, this dissertation proposes a cost – effectiveness analysis, assessing vaccination costs, FRI cases prevented, and duty days lost, using the adenovirus types 4 and 7 vaccines versus no vaccination in US military basic trainees.

1.2. ADENOVIRUS OVERVIEW

Human adenoviruses are a group of ubiquitous pathogens causing mild human infections, including respiratory, gastrointestinal, renal, urinary tract, ocular surface infections,

opportunistic infections in immunocompromised patients, [1, 11 - 12] and possibly obesity. [13] Adenovirus infections occur worldwide, and between two and five percent of all respiratory infections are due to adenovirus. [12] Children less than four years of age, military basic trainees, adults in closed and crowded settings, and immunocompromised patients such as cancer and transplant patients are most susceptible to adenoviruses. In healthy hosts, approximately half of adenoviral infections are sub – clinical, yet the infections induce type - specific immunity. While the majority of adenovirus – associated disease is self – limiting, dissemination or pneumonia can be fatal in both immunocompromised and immunocompetent patients. [1]

Adenoviruses are responsible for sporadic cases and epidemics of febrile respiratory infections (FRIs), pharyngoconjunctival fever, keratoconjunctivitis or gastroenteritis. [1, 11 – 12, 14] However, this document focuses on epidemics of febrile respiratory infections. Patients with FRI have symptoms seen with upper respiratory tract infections or "common colds," including fever, runny nose, sore throat, and/or persistent cough. FRIs occur throughout the year, but a higher frequency of cases is seen in winter and spring. Adenovirus transmission occurs through direct contact with an infected individual, inhalation of small droplet aerosols, the fecal – oral route, or contact with contaminated environmental surfaces. [1, 11 – 12, 14] AdVs spread easily between humans and can survive for up to two weeks on environmental surfaces such as pillows and sinks. [15] The incubation period for respiratory infections ranges from two to fourteen days depending on the viral serotype and mechanism of transmission. Infections are most contagious in the first few days of illness; however, asymptomatic carriage of the adenovirus continues

for weeks or months.[16] Treatment of FRI consists of primarily treating symptoms. Considering adenovirus is self – limiting in people with healthy immune systems, no approved antiviral therapy exists.[16 - 18] Therefore, vector control and immunization are currently used as preventive measures.

1.3. ADENOVIRUS CLASSIFICATION

Adenoviruses are non – enveloped, double - stranded DNA viruses belonging to the *Adenoviridae* family. The lack of an envelope allows adenoviruses to evade destruction by chemical and physical agents and adverse pH conditions, allowing for prolonged survival outside the body and challenging infection – control measures.[1, 14, 19] Since AdVs were first isolated in the adenoids of a US military basic trainee in 1953, 53 serotypes (AdV1 – AdV53) associated with a variety of clinical syndromes have been identified. Based on physical, chemical, and biological properties, serotypes are grouped into species (A – G). Species B is divided into subspecies B1 and B2 based on DNA sequences. [20] Some AdV species are directly linked to different clinical syndromes, but more than half of the known serotypes are not associated with a specific clinical disease process.[1, 19] AdV species most often associated with respiratory infections include those within subspecies B1 (AdV3, AdV7, AdV11, and AdV21), subspecies B2 (AdV14), species C (AdV1, AdV2, AdV5, and AdV6), and species E (AdV4). Table 1.1 shows the serotypes associated with adenoviral respiratory clinical syndromes.

TABLE 1.1. ADENOVIRUS SEROTYPES AND ASSOCIATED DISEASE STATES

DISEASE	CLASSICAL FEATURES	PRINCIPAL SEROTYPES[a]
Acute febrile pharyngitis	Nasal congestion, pharyngitis, fever, sore throat	1, 2, **3**, 5, 6, **7**
Pharynconjunctival fever	Pharyngitis, conjunctivitis, fever	**3, 7**
Febrile respiratory illness (FRI) of recruits	Fever, nasal congestion, muscle pain, sore throat	**3, 4**, **7, 14, 21**
Pneumonia	Fever, respiratory distress, cough	1, 2, **3, 4, 7, 14, 21**

[a]All serotypes listed have been identified in each disease; serotypes in **bold** are those most often found in military basic trainees

Adapted from: Kunz AN, Ottolini M. The role of adenovirus in respiratory tract infections. *Curr Infect Dis Rep*. 2010; 12:81 -7.

1.4. LABORATORY DIAGNOSIS OF ADENOVIRUS

Cases of adenovirus are routinely diagnosed through clinical presentation and symptoms. [1, 11, 17, 19] However, it is difficult to distinguish between viral and bacterial respiratory infections without the use of laboratory techniques. Laboratory techniques used to diagnose adenovirus include viral cell culture, immunofluorescence, and polymerase chain reaction (PCR).[14, 21 - 22] Viral cell culture involves infecting living cells with a patient's specimen and observing for cellular changes due to the viral infection, known as cytopathic effects. [23] Viral isolation through cell culture was considered the "gold standard" for diagnosing adenovirus for decades. However, only 50 to 70 percent of samples yield positive results, the process takes five to seven days to see a result, and results are subjective because laboratory technicians observe and make a decision on the presence or absence of a virus. [19] Currently, researchers are shifting to molecular diagnostic techniques like PCR for viral isolation because results only take one to two

days, making PCR the ideal test during outbreaks and epidemics. The PCR technique amplifies the viral genetic sequence from a patient's specimen into many identical copies. In addition to more timely results, the sensitivity and specificity of PCR is higher. [22, 24 – 25] Viral isolation through immunofluorescent stains uses immunofluorescence and enzyme – linked immunosorbent assays. These techniques are based on the immunological reaction between an antibody and an antigen, are less expensive than PCR, and give results in two to three days. The sensitivity and specificity of these tests are low, so negative tests need to be confirmed with a cell culture, which adds four to five days. [14, 19, 22] Viral cell culture, antigen detection, and PCR are all effective diagnostic techniques that have different uses in different environments.

With the development of restriction enzyme analysis and multiplex PCR, identification of different genome types within serotypes is possible. [1, 26] Li and Wadell created a classification system based on restriction enzyme analysis, using *Bam*HI as the defining enzyme.[27 - 28] The different genome types are symbolized with a character of the alphabet. The prototype AdV strain for a specific serotype is labeled "p" whereas subsequent genome types are labeled "a" through "k." These genome types are further classified by restriction pattern using additional enzymes and are given an Arabic number (ie.,. Ad4p, Ad4p1, etc.). Researchers use this molecular characterization system to correlate specific genome types with geographic distribution and pathogenic potential, which is vital when creating effective vaccines. [1, 27 – 28]

1.5. THE UNITED STATES ARMED FORCES BASIC TRAINING ENVIRONMENT

Basic combat training is the process by which civilians from the United States and its territories are transformed into US Armed Forces service members able to perform basic military skills to defend the United States. This transformation is a result of immersing basic trainees into an environment consisting of their chosen military service branch's values, conduct, and military skills. [3, 29 - 30,] Each military service branch has a specific term for their initial training, but for simplicity, this document refers to the experience as "basic training" and the participants as "basic trainees." According to 2011 Department of Defense (DoD) figures, basic trainees range from 17 to 35 years of age, with 73 percent under the age of 21.[32] The DoD allows each service branch to set their own age limit, and all branches except the Army have an age limit less than 35 years of age. [33] Seventeen percent of basic trainees are female, 17 percent are Hispanic, 81 percent are non – Hispanic, and two percent listed ethnicity as unknown. [32] Before beginning basic training, basic trainees must undergo a physical examination, be free of chronic diseases, and pass their initial physical fitness test, so they are considered healthy. [34] Upon arriving at basic training, basic trainees go through entrance processing, which includes medical screenings and routine immunizations. Routine immunizations administered to basic trainees include one or all of the following vaccines: adenovirus, influenza, meningococcus, inactivated polio, typhoid, yellow fever, measles, mumps, rubella, varicella, hepatitis A, hepatitis B, diphtheria, tetanus, and pertussis. [35] By the end of entrance processing, basic trainees are divided into smaller groups known as units,

companies, platoons, or flights, depending on military branch. In these groups, basic trainees eat, sleep, and attend classes together in an intense, crowded environment. Each military branch has their own training requirements, but all include classroom, field, and physical fitness components. [29]

The following section gives a brief description of each branch of the United States Armed Forces and points out differences between training environments.

1.5.1. ARMY

The Department of the Army is the largest and oldest component of the Armed Forces, with about 550,000 active duty members called soldiers.[32] The Army's mission is to fight and win our Nation's wars by providing prompt, sustained land dominance across the full range of military operations and spectrum of conflict in support of combatant commanders. [36] Approximately 60,500 basic trainees enter the Army annually and attend basic combat training for 10 weeks, including one week of indoctrination and nine weeks of training. [31, 37 - 38] Currently, four Army basic training installations exist. Army basic training installations include: Fort Benning, Georgia; Fort Jackson, South Carolina; Fort Leonard Wood, Missouri; and Fort Sill, Oklahoma.

1.5.2. NAVY

The Department of the Navy includes the US Navy and US Marine Corps. [39] However, the Marine Corps is treated as a separate branch of the Armed Forces in this document. The Navy consists of 320,000 active duty sailors who "defend our right to travel and trade freely on the world's oceans and protects national interests overseas." [40] In the 2012

fiscal year, 36,329 civilians entered the Navy's eight-week basic training program, which occurs at the Recruit Training Command in Great Lakes, Illinois. [37, 41]

1.5.3. AIR FORCE

The Air Force includes 325,000 members referred to as airmen. [32] The Air Force's mission is "to fly, fight and win in air, space and cyberspace." [42] Basic military training lasts for eight – and – a – half weeks, where approximately 30,000 individuals become airmen annually. [37] Lackland Air Force Base (AFB) in San Antonio, Texas, is the only Air Force basic training site. Air Force trainees live, eat, and train as a flight that includes 55 airmen. [29] Week five of basic training is "Warrior Week," which is a field training exercise and "aims to expose recruits to field conditions, teach survival skills, threat assessment, the law of armed conflict, security, self – aid and buddy –aid, explosive ordinance recognition, and use of M – 16 rifle, conduct nuclear, chemical, and biological warfare training, and infuse the warrior spirit." [43]

1.5.4. MARINE CORPS

As mentioned above, the US Marine Corps is a division of The Department of the Navy. [39] The Marine Corps is a deployable and combat – ready force consisting of around 200,000 Marines. [32] Marines are "forward deployed to respond swiftly and aggressively in times of crisis," which is where their motto "First to Fight" comes from. [44] Each year, 30,500 civilians enter the 12 - week training program to become Marines. Two Marine Corps Recruit Depots exist in San Diego, California and Parris Island, South Carolina. [37]The final hurdle of Marine basic training is "The Crucible," which is an endurance test

lasting more than 50 hours that requires physical stamina, problem solving, and teamwork. [44]

1.5.5. COAST GUARD

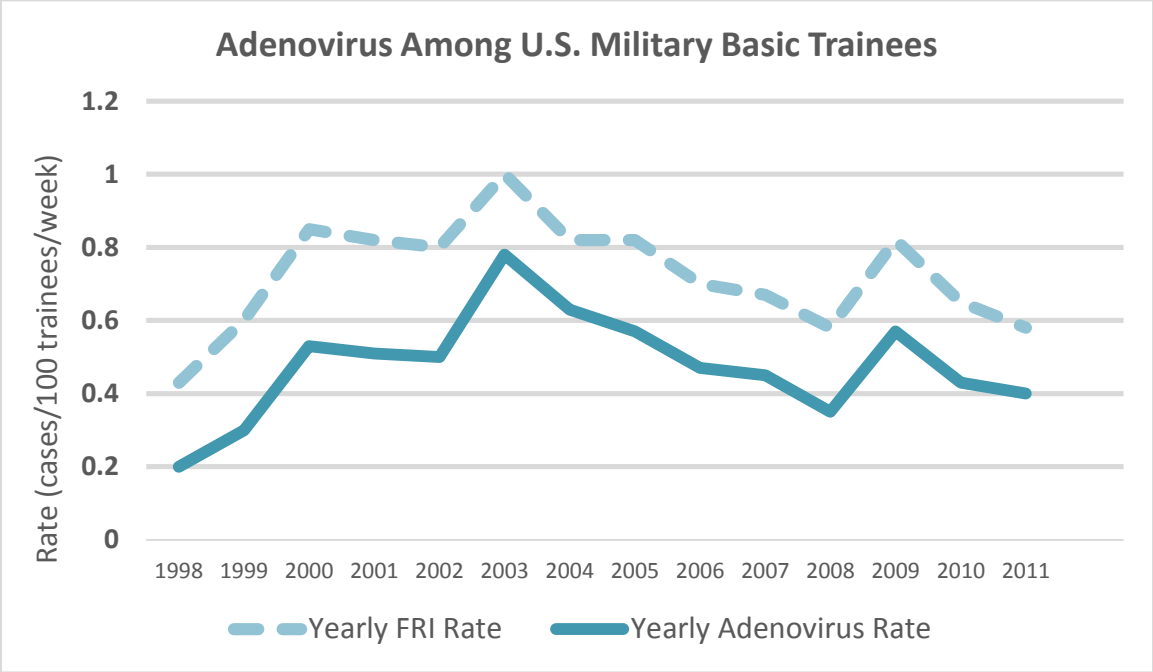
The US Coast Guard is unique because it is part of the Department of Homeland Security instead of the Department of Defense. During times of war and national emergencies, the US Coast Guard becomes a part of the Department of the Navy and functions as a specialized military service. [39] With only 38,000 active duty Coast Guardsmen, the Coast Guard is the smallest branch of the military. [30] The Coast Guard is "a military, multi – mission, maritime force offering a unique blend of military, law enforcement, humanitarian, regulatory, and diplomatic capabilities." [39] The Coast Guard has one basic training site in Cape May, New Jersey.

1.6. FEBRILE RESPIRATORY ILLNESS IN UNITED STATES MILITARY TRAINEES

The US military has used the names acute respiratory disease (ARD), acute respiratory illness (ARI), and febrile respiratory illness (FRI) to describe adenovirus – associated respiratory cases, but for simplicity, the term FRI is used throughout this document unless specifically noted. Adenovirus was first isolated from basic trainees in 1953 during an "influenza – like" epidemic at the Army base in Fort Leonard Wood, Missouri. This epidemic was unique because in contrast to "seasoned" soldiers, the incidence of FRI in basic trainees was abnormally high. It is assumed that the low rate found in "seasoned" soldiers was due to immunity gained early in their military career. [45 - 48] During the 1950s and 1960s, AdVs were responsible for more than 50 percent of FRIs

and 90 percent of pneumonia cases among healthy military basic trainees, [49] making adenovirus – associated febrile respiratory illness a major cause of morbidity, a burden to the military healthcare system, and a source of lost training time in military basic trainee populations. The Wyeth adenovirus vaccine introduced in 1971 reduced adenovirus – specific disease rates by 95 to 99 percent. [50] While adenovirus disease rates decreased, rates of other respiratory infections like influenza were much higher when the vaccine was not used. By 1996, AdV infections accounted for only four percent of total adenovirus morbidity in US military basic trainees. [51] The Wyeth adenovirus vaccine was manufactured and used by the DoD for 28 years. Wyeth discontinued production of their adenovirus vaccine in 1994, but vaccine stock was not completely exhausted until 1999.[52] Surveillance at eight basic training sites showed that about 73,000 AdV infections occurred between 1999 and 2004 (Figure 1.1.). [6] Adenovirus rates in US military basic trainees increased between 1998 and 2003 but started declining in 2004. [35] Even though FRI rarely causes death in healthy adults, adenovirus was responsible for five military deaths between 1967 and 1998 and eight military deaths between 1999 and 2010. [53]

FIGURE 1. 1. FEBRILE RESPIRATORY ILLNESS (FRI) AND ADENOVIRUS RATES, BY YEAR, US MILITARY BASIC TRAINEES, (1997 – 2012)



Adapted from: Hoke CH, Hawksworth A, Snyder CE. Initial assessment of impact of adenovirus type 4 and type 7 vaccine on febrile respiratory illness and virus transmission in military basic trainees, March 2012. *MSMR.* 2012; 19(3):2 – 5.

1.6.1. BASIC TRAINEE RISK FACTORS

Important factors making military basic trainees vulnerable to AdV and other infectious diseases include lack of pre – existing immunity, physical and mental stress, overcrowding, and poor hygiene habits. [46 – 48, 54] Due to lack of exposure during childhood to serotype - specific adenoviruses four and seven seen in basic training installations, susceptible civilians continuously arrive at basic training camps. Approximately 90 percent of incoming basic trainees are susceptible to at least one of these serotypes. [55] In addition, recent research shows that certain environmental conditions such as heat and cold plus over – exertion, sleep deprivation, and

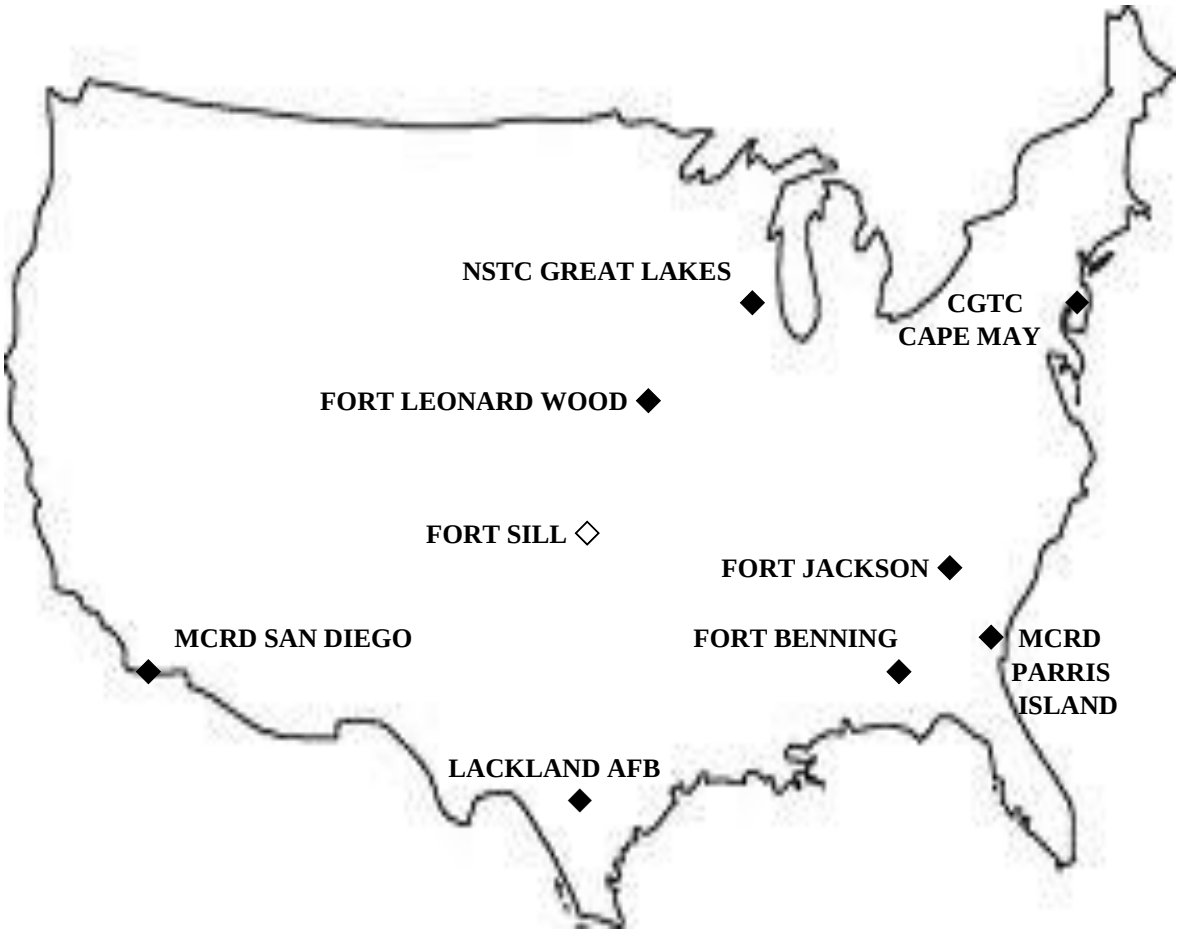
psychological stress can cause changes in your immune system resulting in a higher probability of contracting a respiratory illness. [56] Basic training exposes basic trainees to extreme environmental conditions and psychological stress to prepare them for combat situations where anything can happen. Due to the strict training schedule and trainee environment, basic trainees might relax their personal hygiene practices during basic training. Results of a survey administered during an adenovirus outbreak at Lackland AFB included comments from basic trainees about their personal hygiene practices. Basic trainee comments included "I've seen people wash their hands in toilet water because the latrine crew was going to have an inspection" and "trainees do not have enough time week 1 – 4 to wash." [48] These basic trainee comments characterize the relaxation of personal hygiene practices found in basic training, which, in turn, increases transmission of infectious respiratory infections. For decades, epidemiologists focused on the transmission of adenovirus through aerosol droplets and direct contact. Current epidemiology shows FRI in basic trainees is closely associated with overcrowding and transmission of adenovirus through environmental surfaces.[15, 48] Basic training is a unique experience and environment that facilitates disease transmission, and one sole factor is not responsible for the vulnerability of military basic trainees to adenovirus. The transmission of adenovirus in the basic training environment is a perfect example of the complex interaction between the host (susceptible basic trainee), agent (adenovirus), and environment (crowding). [35]

1.7. FRI SURVEILLANCE IN US MILITARY BASIC TRAINEES

1.7.1. THE NAVAL HEALTH RESEARCH CENTER FRI SURVEILLANCE

The Naval Health Research Center defines a case of febrile respiratory illness as a trainee **seeking medical care** that meets both of the following criteria: a fever of greater than or equal to 100.5^0F (38^0C) or equivalent and at least one sign or symptom of acute respiratory tract inflammation (e.g., sore throat, cough, runny nose, chest pain, shortness of breath, or headache). Also, any trainee having clinical or radiographic evidence of pneumonia is considered an FRI case. [52] In 1998, as the military was depleting their remaining Wyeth adenovirus vaccine supply, The Naval Health Research Center (NHRC) began documenting febrile respiratory infections at eight of the nine military basic training centers. These eight basic training centers include three Army, one Navy, one Air Force, two Marine Corps and one Coast Guard training installation (Figure 1.2) [57] The FRI surveillance program is voluntary, and currently, Fort Sill is the only basic training installation not participating. The definition for FRI mentioned above is used by NHRC for surveillance purposes. Personnel at each training installation collect data and specimens to determine rates of FRIs, identify types of pathogens in upper respiratory swabs obtained from sick personnel, and provide weekly reports to the military community. [52] The NHRC laboratory processes specimens for respiratory virus isolation from Army, Navy, and Air Force basic training posts. FRI rates are reported as numbers of cases per 100 trainees per week. Even though the military reintroduced the adenovirus vaccine in October of 2011, FRI surveillance continues, and the NHRC publishes reports weekly on its research project website. [57]

FIGURE 1.2. NHRC FEBRILE RESPIRATORY ILLNESS SURVEILLANCE SITES



◆ Febrile Respiratory Illness (FRI) Surveillance

◇ Army Acute Respiratory Surveillance site not included in FRI surveillance

1.7.2. ACUTE RESPIRATORY DISEASE (ARD) SURVEILLANCE PROGRAM

In 1966, the Army started its Acute Respiratory Disease Surveillance program that observed cases of ARD in individuals attending basic training. The Army's ARD surveillance definition has three criteria instead of just the two criteria used by NHRC mentioned above. In addition to fever and upper respiratory tract infection symptoms, a basic trainee must be given a limited duty profile or removed from duty for at least eight hours. A throat culture is ordered for all trainees meeting this ARD case definition. [58] ARD cases are found in outpatient settings like Troop Medical Clinics. In order to capture all ARD cases, it is important to search both inpatient and outpatient settings for a range of diagnoses. Table 1.2 shows *International Classification of Diseases, Ninth Edition Clinical Modification* codes often associated with respiratory illness. An ARD report is submitted weekly by each bases' Chief of Preventive Health to the ARD Surveillance System. The report contains the following data: company identification, number of men and women assigned, number of men and women ARD cases hospitalized, and week of training. Before submission, each report is reviewed for accuracy and potential ARD outbreaks. [35, 58] The Army Medical Surveillance Activity combines and analyzes weekly reports from each Army basic training installation. A weekly summary report is produced and distributed each Wednesday and is found on the US Army Public Health Command's website. [59]

TABLE 1.2. ICD – 9 – CM[a] DIAGNOSTIC CODES FOR RESPIRATORY ILLNESS

ACUTE UPPER RESPIRATORY DISEASE
460 Acute nasopharyngitis (common cold)
462 Acute pharyngitis
463 Acute tonsillitis
464 Acute laryngitis and tracheitis
464.0x Acute laryngitis
464.1x Acute tracheitis
464.2x Acute laryngotracheitis
464.3x Acute epiglottis
464.4 Croup
464.5x Supraglottitis, unspecified
465 Acute upper respiratory infections of multiple/unspecified sites
465.0 Acute laryngopharyngitis
465.8 Other multiple sites
465.9 Unspecified site
ACUTE BRONCHITIS AND BRONCHIOLITIS
466.0 Acute bronchitis
466.1 Acute bronchiolitis
466.19 Acute bronchiolitis due to other infectious organisms
PNEUMONIA
480.0 Pneumonia due to adenovirus
480.9 Viral pneumonia, unspecified
485.0 Bronchopneumonia, organism unspecified
486.0 Pneumonia, organism unspecified

[a] International Classification of Diseases, Ninth Edition, Clinical Modification

Source: Functional Proponent for Preventive Medicine Michael B. Cates. Army Acute Respiratory Disease (ARD) Surveillance Program. Memorandum for the Surgeon General of the Army. Falls Church, VA, 12 June 2006.

1.8. SPECIFIC SEROTYPES FOUND IN MILITARY BASIC TRAINEES

1.8.1 ADENOVIRUS SEROTYPE 4 (AdV4)

AdV4 is the prototype adenovirus strain and was first isolated in 1953 from FRI cases during an "influenza – like" epidemic at Fort Leonard Wood, Missouri. AdV4 is

responsible for sporadic infections in civilians but is the predominant serotype found in basic trainees. [60] In the United States from 2004 to 2006, AdV4 was responsible for 4.8 percent of respiratory AdV infections in civilians. However, during the same period, AdV4 was responsible for 92.8 percent of respiratory AdV infections in basic trainees. [1]

1.8.2. ADENOVIRUS SEROTYPE 7 (AdV7)

Ad7V is one of the most common adenovirus serotypes reported worldwide, and in combination with AdV4, is a predominant cause of FRI in military recruits. In terms of clinical presentation, AdV7 is indistinguishable from AdV4, but those infected with AdV7 often also experience gastrointestinal symptoms. AdV7 is not as efficient at spreading as other respiratory viruses, which is why it appears predominantly in closed or crowded communities. [26] Adenovirus 7 often occurs in conjunction with AdV3. In 1997, an outbreak of FRI, involving 541 cases at the Naval Recruit Training Command in Great Lakes, Illinois, was attributed to serotypes AdV7 and AdV3. Seventy percent of the cases were due to AdV7 and 24 percent to AdV3. [1, 61] Due to the appearance of AdV14 in 2007, which like AdV7 is a species B adenovirus, AdV7 has essentially disappeared as a cause of FRI in US military recruits. [1]

1.8.3. ADENOVIRUS SEROTYPE 3 (AdV3)

Globally, AdV3 is the most common serotype implicated in adenovirus infections. [1] However, in military recruits, it is only responsible for sporadic epidemics at basic training sites, and it often occurs in conjunction with AdV7. Between 2004 and 2006, AdV3 accounted for 2.6 percent of FRI cases among military basic trainees. [60] The

medical literature on AdV3 in military recruits is scarce, but AdV3 is known to cause severe respiratory illness, especially pneumonia.

1.8.4. ADENOVIRUS SEROTYPE 14 (AdV14)

In 1955, AdV14 was first discovered in Dutch military recruits. [62] However, a minimal number of cases of FRI due to AdV14 were reported between 1960 and 2006. In March and April of 2006, AdV14 isolates appeared in three of the eight United States basic training sites. However, this strain was an AdV14 variant associated with severe clinical illness. This AdV14 variant ultimately spread to all US basic training sites and caused outbreaks of variable severity. [63 - 65] In 2007, the AdV14 variant caused severe outbreaks at Lackland AFB and the Marine Corps Recruit Depot in Parris Island, SC and was responsible for an estimated 48 percent of 1147 trainee cases with FRI. [62, 66] Twenty – three of the FRI cases at Lackland Air Force base caused by the AdV14 variant resulted in hospitalization, where four recruits entered the intensive care unit and one died. [67]

1.8.5. ADENOVIRUS SEROTYPE 21 (AdV21)

In the 1960s, AdV21 was associated with FRI epidemics in Dutch basic trainees but only sporadic cases were noted over the next couple of decades. AdV21 is responsible for sporadic cases but not epidemics in American basic trainees. In the United States between the years of 2004 and 2006, AdV21 accounted for 2.4 percent of FRI cases in military basic trainees.[1] Over this same period, a statistically significant increase was seen in

AdV21 FRI cases in military basic trainees. [60] In addition, research shows that AdV21 is more prevalent than AdV4 and AdV7 among vaccinated trainees. [51] In 2007, a FRI outbreak due to AdV21 occurred at the US Coast Guard training site in New Jersey. Culture – positive throat swabs tested during this outbreak showed that AdV21 completely replaced the endemic serotype, 4p. [68] Although only a small percentage of trainees develop FRI because of AdV21, monitoring for AdV21 outbreaks in trainees is practical because of the increasing baseline prevalence and the reintroduction of the adenovirus vaccine.

1.8.6. ADENOVIRUS SPECIES C

Adenovirus species C includes serotypes AdV1, AdV2, AdV5, and AdV6. Species C adenoviruses are endemic in most countries and infect more than 80 percent of the population by the age of three. [11, 69] In the United States between 2004 and 2006, AdV1 and AdV2 accounted for 0.4 percent and 0.4 percent, respectively, of AdV respiratory isolates from military basic trainees. [1] Since the reintroduction of the adenovirus vaccine, the percentage of FRIs attributed to species C serotypes increased. Due to the fact that most children develop antibodies against adenovirus species C, only sporadic cases of FRI attributed to species C in basic military trainees are seen.

1.9. ADENOVIRUS PREVENTION

1.9.1 NON – VACCINE INFECTION CONTROL MEASURES

During the adenovirus vaccine's absence, the US military focused on non – vaccine infection control measures. These methods include personal measures, administrative procedures, and environmental controls.[70 - 72] Non – vaccine prevention measures differ not only between military services but between military service installations. Unlike a vaccination program, non – vaccine prevention methods involve guidelines and recommendations that are not always strictly enforced. Therefore, vaccination always seems to be the most practical control measure.

Personal measures to prevent adenovirus infections include hand hygiene, respiratory hygiene, cough etiquette, and mask wearing. [70 - 71] Epidemiologic evidence on the importance of personal measures as a means of preventing adenovirus in basic trainees is rare. One Navy program titled "Operation Stop Cough" implemented at the Naval Training Command included five daily, mandatory hand washes, installation of more liquid soap dispensers at sinks, and monthly education on hygiene importance for basic trainees. The program reduced total outpatient respiratory visits by 45 percent but had no influence on hospitalization rates for respiratory illness. [70, 73] Even though it was successful, continuing the program was difficult because of the time constraint placed on basic trainees. The importance of hand washing is emphasized to Army basic trainees, but certain barriers exist such as lack of training discipline, lack of time, and lack of facilities. Other personal measures recommended to prevent adenovirus infections

include covering one's mouth when coughing or sneezing and using masks to limit exposure to other trainees. [70] No evidence exists supporting the use of masks to prevent FRIs in the military, and currently, masks are not given to military basic trainees for FRI prevention. Personal measures to prevent adenovirus infections in basic trainees are less reliable than other control measures because they require individual compliance at a time when basic trainees have little to no control over their environment and schedule. [70, 72]

Administrative procedures to reduce respiratory infections include isolation of infectious trainees, bed spacing requirements and arrangement, and barrack/room hygiene. Isolating infectious trainees from susceptible trainees requires appropriate facilities and support, which requires more funding for the basic training installation. [70, 72] Some training sites include "respiratory disease barracks" or "fever flights," where infectious trainees live until they are healthy enough to return to training. [15] Crowding is a known risk factor in the transmission of respiratory illnesses, so to reduce crowding of basic trainees, the DoD has guidelines for per – person space requirements. Each basic trainee is to receive 72 square feet of floor space to minimize disease transmission unless an emergency waiver is issued. [48, 70] Using this DoD guideline that was adopted by the Marine Corps, the squad bays at the Marine Corps Recruit Depot in Parris Island should hold a maximum of 72 basic trainees. In contrast, the Marine Corps Recruit Training Order states that 88 basic trainees be held in two of their squad bays. A Marine Corps study reported that squad bays at the Marine Corps Recruit Depot in Parris Island were overcrowded 50 percent of the time between 2004 and 2007. [74] Overcrowding is also seen in Army basic training installations, especially during "summer surge." "Summer surge" is the time between

May and September when high school graduates enter basic training. During "summer surge," half of the Army basic training installations do not follow the DoD per – person guidelines. [71] One administrative recommendation that all basic training posts follow because it does not require any additional cost or resources is arranging bunks so individuals lay head – to – toe. This arrangement maximizes the amount of space between bunks and breathing room, while minimizing disease transmission. [70 – 72] Administrative procedures do not rely on personal compliance, but they do require policy implementation, which as seen above, is not always enforced.

Environmental controls to reduce respiratory infections include ventilation standards and air filters. [70] Since adenovirus is spread through aerosol droplets, indoor air quality issues facilitate transmission due to the increased concentration of adenovirus in the air. Indoor air quality is assessed by measuring carbon dioxide concentrations, where carbon dioxide concentration is a surrogate for air quality freshness. [72] The US Environmental Protection Agency and the American Society of Heating, Refrigerating, and Air – conditioning Engineers set the standard for a carbon dioxide concentration of 1000 parts per million (ppm) as an indicator for poor indoor air quality. [46 – 48, 75] Carbon dioxide levels above 1000 ppm are associated with adverse health effects such as eye irritation, headache, drowsiness, difficulty concentrating, fatigue, and upper respiratory symptoms. A 2000 AdV4 outbreak at Lackland Air Force Base showed that carbon dioxide levels exceeded 1000 ppm in all basic trainee classrooms with one classroom peaking at 5000 ppm. [48] In addition, during a 1997 outbreak at Fort Jackson, researchers found that when more than 40 basic trainees are in a sleeping "bay" the carbon dioxide threshold is exceeded. [48]

Even though the impact on adenovirus is minimal, traditional air filters remove pathogens from the air. However, dirty or missing air filters is a problem at basic training sites. During the peak of a 1998 AdV4 outbreak at Fort Jackson, an air filter study revealed a correlation between number of AdV4 – related hospitalizations and the proportion of air filters containing AdV4. [75] High – efficiency particulate air filters remove more respiratory illness agents out of the air than traditional filters, but research examining the impact of different types of filters on disease rates in basic training installations do not exist.

1.9.2. HISTORY OF ADENOVIRUS TYPE 4 AND 7 VACCINE

In the 1950s due to the significant impact adenovirus – associated FRI had on military basic trainees, researchers decided to develop an adenovirus vaccine. In 1956, researchers at the Walter Reed Army Institute of Research (WRAIR) developed an inactivated adenovirus vaccine protecting against serotypes AdV4 and AdV7, which were responsible for the majority of FRI cases in basic trainees. [32, 76 -77] However, in 1963, the vaccine license was revoked by the Food and Drug Administration (FDA) because of production and standardization problems. During this same time, researchers at the National Institutes of Health developed an inactivated polyvalent vaccine containing serotypes AdV3, AdV4, and AdV7. However, researchers subsequently found that serotypes AdV3 and AdV7 were oncogenic in hamsters, and tumor – bearing genomes from simian virus (SV – 40) had integrated with the adenovirus vaccine strains. [78] Due to these complications, use of the polyvalent vaccine ceased.

In addition to the inactivated polyvalent vaccine, a monovalent, live serotype AdV4 vaccine grown in human diploid embryonic cells was created in the early 1960s. This vaccine was distinctive because instead of the vaccine virus being attenuated, the vaccine was attenuated by the route of administration. The adenovirus vaccine was administered as an enteric – coated tablet that did not release the virus until it was in the lower intestinal tract. Using this route of administration allowed the virus to bypass the upper respiratory tract. Since adenovirus causes infections in the respiratory and gastrointestinal tract, the immunological response to the asymptomatic gastrointestinal infection protects against respiratory tract infections. [79] Between 1963 and 1966, clinical trials with this vaccine were performed on institutionalized adults and military basic trainees. A four – fold increase in type – specific neutralizing serum antibodies was observed in those receiving the vaccine. [80] The drawback of this vaccine was that it was highly type – specific. Since the vaccine protected against the specific serotype AdV4, basic trainees started developing FRI due to serotype AdV7. [76] This finding led to clinical trials of type AdV7 and AdV21 vaccines. Trials between 1964 and 1969 showed that simultaneous immunization with adenovirus serotype 4 and 7 enteric – coated tablets was both safe and effective. [77, 79, 81] The type 7 adenovirus tablet was added to the recruit immunization schedule in 1970. Due to the low rates of adenovirus serotypes 4 and 7 in the general population, the vaccine was only approved for use in military basic trainees. The adenovirus vaccine program had a significant impact on basic trainee morbidity, reducing total respiratory disease rates by 50 to 60 percent. [76] By 1984, both vaccines were routinely administered year round to basic trainees at all basic training camps. However,

in 1987, Lackland Air Force Base stopped administering the adenovirus vaccine to basic trainees because adenovirus was rarely identified at this base. [6]

Both of the vaccine tablets were given routinely as combined prophylactic oral doses until the manufacturer (Wyeth Laboratories) ended production in the mid – 1990s. In 1984, the Food and Drug Administration instructed Wyeth to update their adenovirus vaccine manufacturing facility. Since the US military was the only consumer of the vaccine, Wyeth asked the DoD for $ 5 million to assist in manufacturing repairs. This budget increase was denied by senior officials at the Pentagon. When the DoD and manufacturer failed to reach an agreement by 1995, production of the adenovirus vaccine ceased. Rationing their existing product, the military used the AdV4 vaccine until 1998 and the AdV7 vaccine until 1999. [52] Since early 1999, no adenovirus vaccine has been available. The incidence of FRI increased significantly to that of the pre – vaccine era in military basic trainees following the exhaustion of the adenovirus vaccine supply. Adenovirus outbreaks did not occur at Lackland AFB until 1999 when immunization ceased at other basic training camps. Recommendations from advisory bodies prompted the DoD to restore the adenovirus vaccine program, and in 2001, a contract was awarded to Barr Laboratories, Inc. [82] In October of 2004, then Assistant Secretary of Defense for Health Affairs, Dr. William Winkenwerder Jr., estimated that the initial vaccine production investment would be $50 million, and the annual cost of vaccine would be approximately $4 million. [83]

1.9.3. CURRENT ADENOVIRUS TYPE 4 AND TYPE 7 LIVE, ORAL VACCINE

Since the Wyeth vaccine was so successful in terms of efficacy and safety, the DoD wanted to acquire new vaccines "as similar as possible to the old vaccines." [84] Therefore, the new adenovirus type 4 and type 7 live vaccine tablets are manufactured from the same human adenovirus strains that Wyeth Laboratories developed, produced, and used. Wyeth transferred the adenovirus seeds and testing and production documents needed to produce the adenovirus vaccine to Barr Laboratories, Inc. In 2008, Teva Pharmaceuticals acquired Barr Laboratories, Inc., and the name of the subsidiary responsible for the new vaccine changed to Teva Women's Health, Inc. [85] With funding from the DoD, a new manufacturing and packaging facility with updated equipment and quality control procedures was built specifically for the production of the adenovirus vaccine. [86] Since Teva and Wyeth used similar starting materials and manufacturing processes, the old and new vaccines are nearly identical. Table 1.3 compares Wyeth and Teva's manufacturing processes for the adenovirus type 7 and type 7 vaccine.

Teva Women's Health, Inc. performed two clinical trials to show their adenovirus vaccine is safe, efficacious, and immunogenic. Since the military used the Wyeth vaccine for 20 years, the FDA only required a Phase I and Phase III clinical trial for vaccine approval. [87] The Phase I trial recruited participants attending the Combat Medic School at Fort Sam Houston in Texas to determine the immunogenicity and safety of the new adenovirus type 4 and type 7 vaccine tablets.

TABLE 1.3. COMPARISON OF TEVA AND WYETH ADENOVIRUS VACCINES MANUFACTURING PROCESSES[87]

COMPONENT	WYETH	TEVA	KEY DIFFERENCES	SIGNIFICANCE
Cells	Human Diploid Cells (WI – 38)	Human Diploid Cells (WI – 38)	None	None
Virus	ADV4[a] CL68578p12	ADV4 CL68578p15	None	None
	ADV7[b] 55142p13	ADV7 55142p16	None	None
Cell Growth Media	EMEM[c] Media + 10% FBS[e] and antibiotics	DMEM[d] Media + 10% FBS	Antibiotics removed	Minimal
Infection Media	Media + 2% FBS	Media + 2% FBS	None	None
MOI	Estimated 0.1 – 1.0 $TCID_{50}$/cell[f]	0.1 – 0.7 $TCID_{50}$/cell	None	None
Incubation	14 days	10 – 14 days	None	None
Harvesting	0.8/0.45 micron filters	0.8/0.45 micron filters	None	None
Stabilizer	10% SPGA[g]	10% SPGA	None	None

[a]ADV4 = adenovirus type 4; [b]ADV7 = adenovirus type 7; [c]EMEM = Eagle's Minimal Essential Medium; [d]DMEM = Dulbecco's Modified Eagle's Medium; [e]FBS = Fetal Bovine Serum; [f]$TCID_{50}$ = Tissue Culture Infectious Dose; [g]SPGA = Sucrose, Phosphate, Gluconate, Albumin

Thirty participants received the oral AdV4 and AdV7 vaccines manufactured by Teva Women's Health simultaneously, while 28 participants received an oral placebo. [49, 88] The immunogenicity outcome measure was the seroconversion rate, which is the percentage of study subjects who develop specific (adenovirus) antibodies in their sera as a result of vaccination. [89] The seroconversion rate at day 28 showed 73 percent of non – immune participants developed antibodies to AdV4 and 65 percent to AdV7. The most common adverse events were nasal congestion, cough, sore throat, headache, abdominal pain, arthralgia, nausea, and diarrhea. This Phase I trial showed that the new adenovirus vaccines are safe and able to induce an immune response in the study population. [49, 88]

A Phase III trial, including basic trainees from Fort Jackson and the Naval Training Center, evaluated efficacy and safety. [90] The primary endpoints for this trial were different for AdV4 and AdV7 because the AdV7 virus was not present in the basic trainee population during the study period. The primary efficacy endpoint for AdV4 was prevention of FRI through vaccination (vaccine efficacy), while the primary endpoint for AdV7 was serologic response to vaccination (immunogenicity). The AdV4 primary efficacy analysis included 49 people, where the placebo group had 48 people and the vaccine group had one person. [84, 87 – 88, 90] Since the only case of FRI occurred before the vaccine was protective, vaccine efficacy for AdV4 against FRI was 99.3 percent. Seroconversion rates for vaccine recipients were 94.5 percent for AdV4 and 93.8 percent for AdV7. During the six-month study period, 92 percent of basic trainees reported at least one adverse event (N = 17,654), while 1.2 percent reported serious adverse events (N = 57). The most common adverse events included headache, upper respiratory tract

infection, and arthralgia. Serious adverse events included psychiatric disorders and traumatic injuries. A significant difference was not found between the vaccine and placebo group in terms of adverse event numbers. [84, 87- 88, 90]

With data from both trials showing that the Teva adenovirus vaccines are safe, efficacious, and immunogenic, the FDA approved the Adenovirus Type 4 and Type 7, Live, oral enteric coated vaccine in March of 2011 for use only in US basic trainees between the ages of 17 and 50. In late October and early November of 2011, the US Armed Forces began administering the two – capsule adenovirus vaccine to basic trainees at all basic training installations. The current price per dose (AdV4 + AdV7) with the additional shipping cost is $126.12, which is approximately $30 million a year. Six months after the new adenovirus vaccine introduction, FRI rates had declined 75 percent. [8] To date the DoD has spent approximately $160 million* on the new Adenovirus vaccine program. Despite the positive preliminary results, the US Armed Forces continue to monitor FRI rates to evaluate the molecular epidemiology of adenovirus serotypes at basic training installations.

1.10. JUSTIFICATION FOR NEW COST STUDIES

1.10.1. VARIATION IN MOLECULAR EPIDEMIOLOGY OF ADENOVIRUS SEROTYPES AND GENOME TYPES

Scientific advancements, especially diagnostic techniques, occurring since the development of the Wyeth adenovirus vaccine allow researchers to understand adenovirus serotypes on a molecular level. Before 1997, FRI surveillance and diagnosis

* Value calculated by author using contract information

in basic trainees did not have laboratory support.[22] Scientific advancements used to understand adenovirus on a molecular level include restriction enzyme analysis, multiplex polymerase chain reaction techniques targeting fiber genes or hypervariable regions of the hexon genes, and sequencing of the fiber and hexon genes. With knowledge gained from these new techniques, researchers are able todetermine genetic variability within serotype strains circulating in the United States and at basic training installations. [1]

Epidemiological research shows that adenovirus serotypes have different geographical and temporal distributions and associated virulence. Single serotypes dominating in specific regions are replaced by other serotypes over a few years, which leads to small outbreaks and epidemics. [1, 91 – 93] Figure 1.3 shows the geographical and temporal distribution of adenovirus serotypes at basic training installations between the years 2002 and 2006. [63] In addition to serotype variance, data confirm that genetic variants within specific serotypes differ by geography and over time

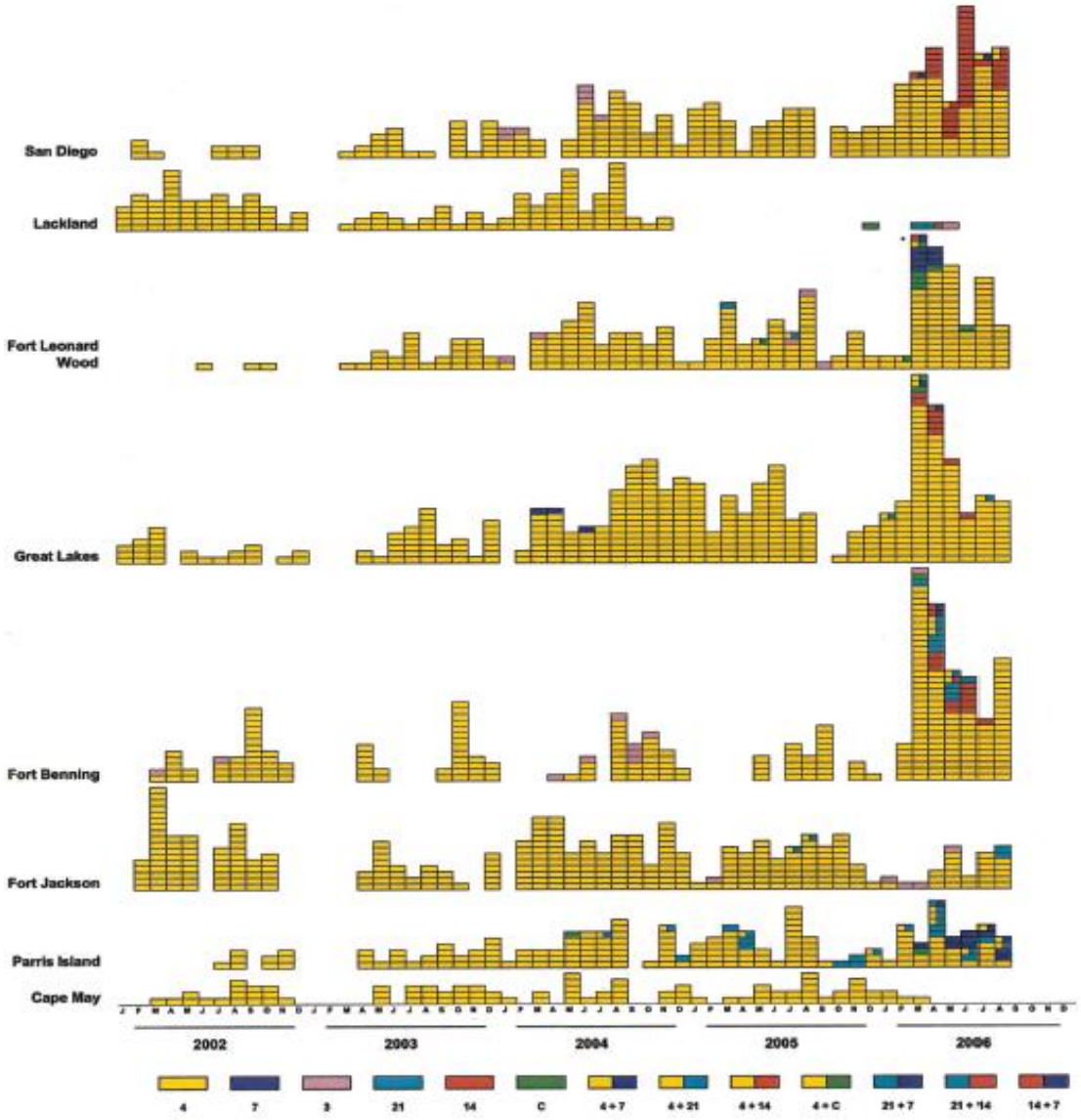


Figure 1.3. Serotype identification of 1867 adenovirus isolates from military recruits at 8 US basic training centers, 2002 – 2006. Each block represents 1 sample from a recruit with febrile respiratory illness. Split blocks represent co - infections with two serotypes. Changes in sampling volume are not representative of changes in disease rate but rather of changes in sampling effort. Ad – positive samples were chosen randomly for serotyping.

Source: Metzgar D, Osuna M, Kajon AE, Hawksworth AW, Irvine M, Russell KL. Abrupt emergence of diverse species B adenoviruses at US military recruit training centers. JID. 2007; 196:1469

The effectiveness of immunization can be hindered by the emergence of novel adenovirus serotypes and genome types. The effect of antigenic drift on the influenza vaccine was seen at Fort Jackson, South Carolina in 2011. Antigenic drift led to insufficient influenza vaccine efficacy, which led to 64 cases of influenza and one fatality in vaccinated basic trainees. [94] To determine if using the same virus strains used in the Wyeth vaccine in the Teva vaccine was appropriate, investigators completed comprehensive studies on strain variation in adenovirus serotypes AdV4 and AdV7. [91 – 92] In terms of AdV7, one study concluded there was essentially no variability among strains between the years of 1963 and 1997. All vaccine and wild – type strains recovered from military basic trainees between 1963 and 1997 had the AdV7a genome type. [92] Beginning in 1997, other AdV7 genome types commonly seen in US civilian populations were identified in the military basic trainee population. AdV7d2 appeared as the predominant strain, followed by AdV7b, AdV7p, and AdV7h. Evidence of differences in virulence between AdV7 genome types is inconclusive. However, some genome types such as AdV7b and AdV7h are regularly isolated from patients with serious clinical outcomes. [26] The evolution of AdV4 is more complex than AdV7 because of constant genetic drift that is emphasized by the replacement of former strains by new strains. The current strain circulating in military basic trainees is significantly different from the prototype (AdV4p) and vaccine strain (AdV4p1). The new variant strain looks like a recombinant between serotype AdV4 and an AdV – B1 serotype, probably AdV7. [91 - 92] Between 1997 and 2003, seven distinct genome types of AdV4 were found across the basic training installations, which

can be seen in Figure 1.4. All of the variant genome types were significantly different from the prototype (AdV4p) and vaccine strain (AdV4p1). [93] If

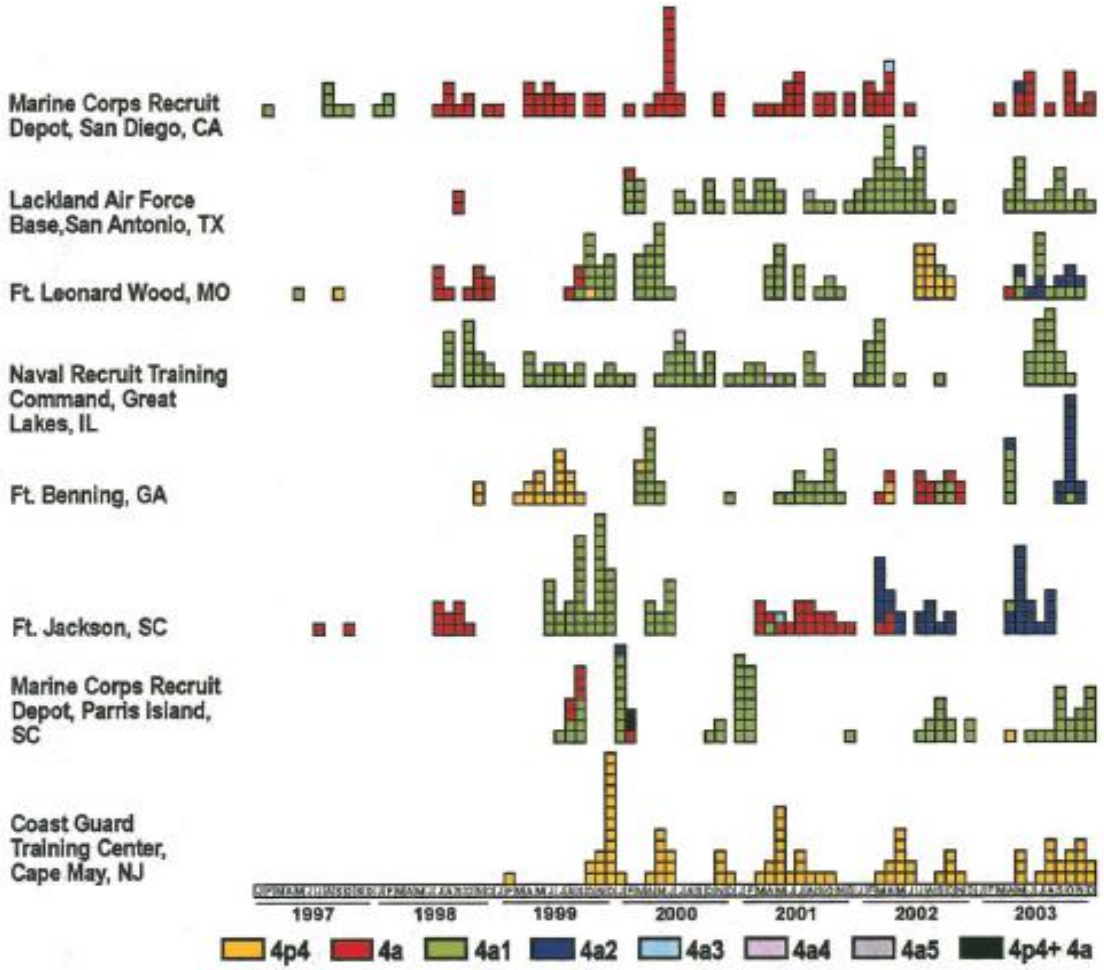


Figure 1.4. Geographic and temporal distribution of adenovirus 4 genome types in United States military basic training sites (1997 – 2003)

Source: Kajon AE, Moseley JM, Metzgar D, Huoung HS, Wadleigh A, Ryan MAK, Russell KL. Molecular epidemiology of adenovirus type 4 infections in US military recruits in the postvaccination era (1997 – 2003). *J Infect Dis.* 2007; 196:72.

AdV4 and AdV7 serotypes and genome types continue to drift, it is plausible the vaccine will not be as effective in the future.

1.10.2. US BASE REALIGNMENT AND CLOSURE

In addition to serotypes and genome types varying across current US basic training installations, the realignment and closure of many US basic training installations make the need for new adenovirus vaccine cost studies paramount. The original adenovirus epidemiologic and cost studies performed in the 1960s and 70s occurred at the basic training locations of the time that included: Fort Dix, New Jersey, Fort Lewis, Washington, Fort Campbell, Tennessee, Fort Ord, California, and Fort Polk, Louisiana. None of these Army bases are still used for basic training. Current basic training installations are in the Midwest and southeast United States, where the temperature and humidity have an influence on the spread of respiratory infections, so data collected will vary from previously collected data. As discussed above, the military service branches all have unique basic training programs and unique regulations, so it is difficult to generalize incidence data to all service branches. Two previous cost studies are discussed in Chapter 2 assessing cohorts of Army basic trainees. [7, 9] and one assessed a cohort Navy basic trainees [10] to determine cost – effectiveness of adenovirus vaccine. No cost studies exist that assess Marine Corps, Air Force, or Coast Guard basic trainees in terms of the cost – effectiveness of vaccines. This dissertation intends to add to the literature by creating specific models for each military service branch.

1.10.3. EVOLUTION OF VACCINE ECONOMIC MODELS

As diagnostic techniques advanced and military basic training installations changed, economic analyses of infectious diseases and vaccination evolved over the last decade. Economic models of vaccines that were based on decision analytic models are now incorporating transmission dynamics and herd immunity, so cost – effectiveness is not misrepresented. [95 – 98] These transmission dynamic models merge epidemiological models and pharmacoeconomic techniques to determine if the vaccine is a good value for the money invested. The modeler must understand the unique features of the disease and intervention to create a comprehensive model. However, by increasing the complexity of the model, the amount of uncertainty in your assumptions also increases. [97] For example, economic models account for uncertainty by varying parameters and performing sensitivity analyses. However, in addition to parameter uncertainty, transmission dynamic models often include structural uncertainty, model uncertainty, and methodological uncertainty. [97] The limitation with adenovirus is that its transmission in US basic trainees is still unclear. It is known that adenovirus is transmitted through aerosols and contact with fomites, but it is still unclear whether the environment, the basic trainees, or both are the original contaminant. A more in – depth explanation of models used for the economic evaluation of vaccines is given in Chapter 2, where the focus is specifically the economic evaluation of the adenovirus vaccine in US basic trainees.

CHAPTER 2

PHARMACOECONOMICS AND ECONOMIC STUDIES ON ADENOVIRUS VACCINE USED IN BASIC TRAINEES

2.1. INTRODUCTION

With increasing Department of Defense health care costs and a decreasing health care budget, economic evaluations of military vaccinations and other health care interventions are a priority. Vaccinations are considered one of the most cost – effective public health interventions in developed and developing countries. [96] However, policy makers want more pharmacoeconomic (PE) information on newer vaccines because of their high cost. [97] Costs associated with FRI morbidity and hospitalization in military basic trainees have always been a significant concern to the US military, but to date, only three cost studies investigating the adenovirus vaccine and its health outcomes have been published. The following chapter gives an introduction to pharmacoeconomic study techniques, takes an in – depth look at the three existing studies, and presents the objectives and hypotheses for this dissertation.

2.2. INTRODUCTION TO PHARMACOECONOMIC TECHNIQUES

Pharmacoeconomics is a "branch of health economics primarily concerned with identifying, measuring, and comparing the costs and outcomes of pharmaceutical products and services." [98] The two distinguishing characteristics of a PE evaluation include: (1) Are two or more alternatives being compared? (2) Are both costs and outcomes of alternatives examined? [99] A true pharmacoeconomic analysis must compare both costs and outcomes of at least two alternatives, while a partial PE analysis addresses

only one. A cost – of – illness (COI) evaluation is an example of a partial PE analysis because it only looks at overall costs. Four types of true PE analyses exist, including cost – minimization analysis (CMA), cost – effectiveness analysis (CEA), cost – utility analysis (CUA), and cost – benefit analysis (CBA). These true PE techniques all estimate costs in monetary units but are characterized by the different ways they measure health outcomes. [99 – 100] These PE techniques are discussed in the following sections.

2.2.1. Costs

In PE analyses, costs are grouped into categories, including direct medical costs, direct nonmedical costs, indirect costs, and intangible costs. The types of costs included in a PE analysis is dependent on the perspective of the evaluation. Direct medical costs are costs for any services or treatments used to detect, prevent, and treat disease and include hospitalizations, medications, and health professionals' time. Direct nonmedical costs are costs to patients and their families as a result of an illness or disease but are not purchased medical services. Examples of direct nonmedical costs are transportation to receive health care and home aides. [100 - 101] Indirect costs are costs of reduced productivity due to morbidity or mortality. Indirect costs include lost wages or income lost because of an early death. Indirect costs are determined by the human capital and willingness to pay approaches. The human capital approach values morbidity and mortality losses using standard labor wage rates to estimate an individual's earning capacity. The willingness – to – pay approach asks patients how much they are willing to spend to reduce the likelihood of illness. The human capital approach is controversial because it directly relates value of life to income, and the willingness – to – pay approach is subjective and

produces a variety of answers. Before choosing an approach to determine indirect costs, the researcher needs to determine which limitations are most important to them. Intangible costs are nonfinancial outcomes of a disease such as pain and suffering and are difficult to quantitatively measure. These cost categories are often mentioned in the literature, but they are not the only cost categories used in PE analyses. [100 – 101]

2.2.2. Cost – of – Illness Evaluation

The COI evaluation, also known as the burden of illness evaluation, identifies and estimates the overall cost of a particular disease in a target population. This type of evaluation measures direct and indirect costs associated with a specific disease. The COI technique does not compare two alternatives but does provide an estimate of the financial burden of illness. [101]

2.2.3. Cost – Minimization Analysis

Cost – minimization analysis is the simplest technique to perform because it assesses interventions that have identical outcomes. The aim of CMA is to determine the least costly way to deliver the same outcome. This type of analysis is often used when comparing generic and therapeutic equivalents or "me too" drugs. [100, 102] If evidence to support the equivalency of outcomes does not exist, a more comprehensive PE technique should be utilized.

2.2.4. Cost – Benefit Analysis

Cost – benefit analyses compare benefits due to an intervention with the costs of providing it, where both costs and benefits are measured in monetary units. The goal of a CBA is to establish which intervention has the highest net benefit, which is the difference between benefits and costs. Results of CBAs are presented as a benefit – to – cost ratio, a net benefit, or a net cost. The program or intervention with the highest net benefit or the greatest benefit – to – cost ratio are of value, meaning the benefits of an intervention outweigh the costs of providing it. [100, 102 – 103] Since all outcomes are assigned monetary values, CBA is useful for comparing interventions with different objectives. The human capital and willingness – to – pay approaches to determine indirect costs are often used in CBAs. However, using the human capital approach to determine the economic value of saving a life is problematic and leads to societal and ethical debates. Therefore, unless benefits of an intervention are already expressed in dollars, a CBA should not be performed. [101]

2.2.5. Cost – Effectiveness Analysis

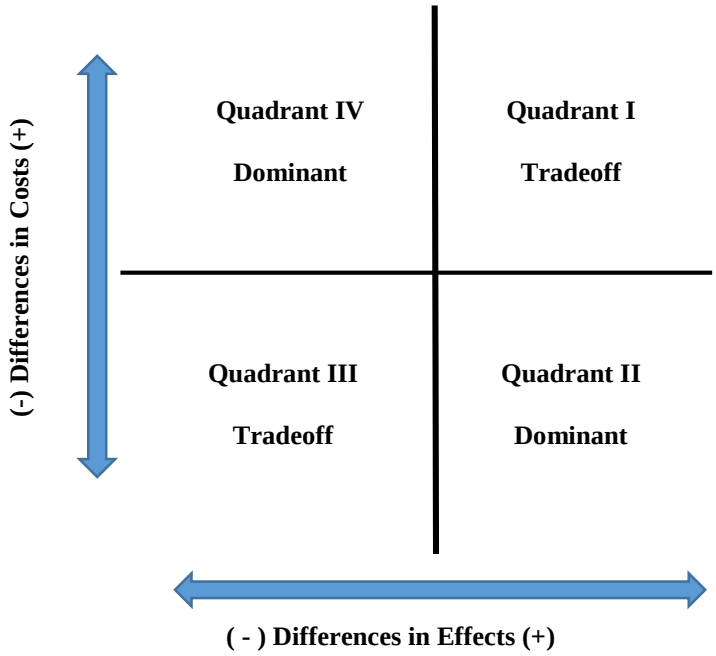
Cost – effectiveness analyses are the most common type of PE analyses found in the literature. Cost – effectiveness analyses measure costs in monetary values and outcomes in physical units, natural health units, or non – dollar units such as lives saved, cases cured, or changes in blood pressure. [101] CEAs assume there is a single treatment objective and selects the agent with the lowest cost. [102] Like CBAs, CEAs present their results as a ratio, either a cost – effectiveness ratio (CER) or an incremental cost – effectiveness ratio

(ICER). The CER signifies the dollar cost per specific clinical outcome gained, independent of intervention alternatives and condenses costs and outcomes into a single value. [101] Contrastingly, the ICER divides the difference in costs by the difference in units of effectiveness.

$$ICER = \frac{\Delta\, Costs}{\Delta\, Effectiveness}$$

The ICER denotes the additional cost required to get the additional effect when switching from one intervention (i.e., Drug A) to the other intervention (i.e., Drug B). If the result is a negative ICER, one treatment intervention, also known as the dominant treatment intervention, is more effective but less expensive. To help with interpretation and clarity, ICERs are presented on a cost – effectiveness grid or a cost – effectiveness plane. [98, 100] The cost – effectiveness plane is seen most often in the literature and is shown in Figure 2.1.

FIGURE 2.1. COST – EFFECTIVENESS PLANE [98]



An intervention is placed anywhere on the cost – effectiveness plane according to its incremental costs and effects. Costs are placed on the north – south axis, while the effects are placed on the east – west axis. Costs and effects can be negative, positive, or zero. The origin is the point where costs or effects are equal among treatment interventions. Each quadrant of the plane represents the differences in costs and effectiveness between the intervention and the "gold standard" alternative. [98, 100] If an intervention falls in quadrants II or IV, one intervention clearly dominates another treatment intervention. An intervention falling in quadrant IV is more expensive and less effective than its alternative. While an intervention falling in quadrant II is cheaper and more effective than

its alternative. If an intervention falls in quadrants I or III, it is up to the decision maker to determine if lower costs or greater effectiveness is more important. Quadrant I represents an intervention that is more expensive and more effective than its alternative. Conversely, quadrant III shows an intervention that costs less and is also less effective than its alternative. [98, 100]

Interpretation of the ICER is dependent on the decision maker's judgment. A newer measure known as the incremental net benefit ratio (INB) overcomes the subjectivity associated with the ICER. The INB technique takes into consideration the decision maker's maximum acceptable willingness to pay for an intervention, which is represented as lambda in the INB equation. The INB equation is calculated as follows: [100, 101]

$$INB = (\lambda * \Delta Effects) - \Delta Costs$$

If the resulting INB is positive, the intervention is considered cost – effective, while a negative INB is considered not cost – effective. A limitation of the INB measure is that a monetary value must be assigned to the health benefit in terms of how much a decision maker is willing to pay. However, it is still accepted because a sensitivity analyses is conducted using a range of λ values.[100]

2.2.6. Cost – Utility Analysis

Cost – utility analysis is similar to CEA, but CUA incorporates patient preferences and health related quality of life (HRQoL). Costs are measured in a monetary value and outcomes are measured in patient - weighted utilities instead of natural units. A utility measures the changes in a patient's satisfaction and well – being resulting from a move

between health states. [101 - 103] Utility value estimates range from zero to one, with zero indicating death and one indicating perfect health. Three methods commonly used to calculate utility for a specific health state include the rating scale, the standard gamble, and the time tradeoff method. In each of these methods, a specific health state is described to subjects who help determine where on a scale of zero to one the described health state falls. The resulting utility is then multiplied by the length of life associated with each intervention to get an outcome measure known as the quality adjusted life – year (QALY). Therefore, the QALY incorporates increases in survival time and changes in quality of life. Results of CUA are expressed as an ICER that translates into costs per QALY gained, where the intervention with the lowest cost per QALY is preferred. CUA is most appropriate when comparing interventions that extend life but have serious side effects, those that reduce morbidity instead of mortality, and when HRQoL is the most important outcome examined. CUA is not used as frequently as other PE techniques because of disagreements concerning utility measurement, difficulty comparing QALYs across populations, and difficulty quantifying patient preferences. [100]

2.3. DECISION ANALYSES

Decision analysis modeling is a powerful tool that "uses mathematical models to quantitatively compare multiple decisions while taking into account both costs and effects on quality of life." [104] The two main types of decision analyses include decision trees and Markov models. A decision tree "graphically presents treatment alternatives, outcomes, and probabilities, and algebraically reduces into a single value that can be used in comparisons." [105] Decision trees are the most basic form of decision analyses, so

concepts used in decision trees are used in more advanced analyses like Markov models. As implied by its name, the most critical component of a decision analysis is the clinical decision, usually focusing on the cost – effectiveness of screening and diagnostic tools or the choice between two alternative interventions. [104]

Decision analyses have several limitations that must be considered. Decision analyses are dependent on initial assumptions and the quality of data acquired from the literature. In addition, complex health states are oversimplified and the choice of which costs to use is subjective. [104] The QALY is often used in decision analyses, and researchers are concerned about incorporating personal, cultural, and psychological beliefs into a single value. [104, 106] Despite these limitations, decision analyses are a necessary tool for decision makers, especially with increasing health care costs.

2.3.1. DECISION TREES

After determining the clinical decision and intervention alternatives to evaluate, a decision tree is constructed. Each intervention has a branch extending from the initial node, which is a decision node indicating a choice between the alternatives. Chance and terminal nodes on subsequent branches of the decision tree symbolize the probability of experiencing a particular outcome and the outcome for each alternative, respectively. Each branch following a chance node includes cost and health outcomes of the corresponding alternative, and each chance node is assigned a probability. [100, 105] Once all of the components of the decision tree are gathered, the decision tree is analyzed. Costs for each branch from the chance node to the terminal node are summed, while the

probabilities for the same branches are multiplied. The sum total cost for the branch is then multiplied by the product of probabilities for the same branch to get a single weighted cost measure for that path. To calculate the average cost per alternative, sum the weighted cost measures for all paths corresponding with that alternative. An ICER or INB can now be calculated to help determine which alternative is most cost – effective. [100] Due to the difficulty in assigning dollar values to outcomes and costs varying between locations, it is best to determine the robustness of your model with sensitivity analyses. Sensitivity analyses allow researchers to vary probabilities, costs, and quality parameters, while keeping everything else constant. [104] Decision trees represent events that occur at a single point in time, so if evaluating chronic disease states where outcomes vary over time, a Markov model may be necessary. [99, 105, 107]

2.3.2. MARKOV MODELING

Diseases and conditions are often more complex than what is depicted in decision trees and occur over a period of time, so a Markov model is appropriate. A Markov model is a cyclic decision tree that is useful when the risk of an event is continuous, when timing of events is important, and when important events may happen more than once. [108] Markov models assume individuals are always in one of a finite number of health states, also known as Markov states. A general example of Markov states is "sick, well, or dead." Events are modeled as transitions from one health state to another, and the time spent in each state determines the overall expected outcome. [100, 108]

The first step in creating and running a Markov model is to establish the health states to be examined, including all significant states a patient experiences because of a disease or treatment. The second step is to determine possible transitions between states. Patients can transition from one health state to another and back again, but it is important to note that patients cannot be in more than one health state during a cycle. When an event only has short – term effects, a temporary health state is used.[100] Temporary health states only transition to other health states and not to themselves. In order to end a Markov process, the model must have at least one health state that a patient cannot leave in a later cycle. This state is known as the absorbing state, which is often the state when a patient dies. The third step in creating a Markov model is to choose the cycle length and number of cycles, which is dependent on the disease being modeled. Once a model is created, transition probabilities are estimated and costs and outcomes are calculated. In Markov models, outcomes are cumulative and are calculated for each cycle in the model instead of at the end like decision tree analyses. [99 – 100, 108 - 110]

Cohort and Monte Carlo simulations are two types of calculations used in Markov models. In a cohort simulation, a hypothetical group of patients, known as a cohort, begins the Markov process with a determined distribution of patients among the health states. In the following cycle, the cohort is divided according to the transition probabilities. The cohort is tracked through the model simultaneously and produces a Markov trace that shows the movement of the cohort through the health states and the cumulative utilities and costs calculated. The cumulative utility computed when the entire cohort reaches the absorbing state is the expected QALY of the cohort. In comparison to

Monte Carlo simulations, cohort simulations are faster to run, easy to correct, and more transparent. [99 – 100, 107, 111] A disadvantage of a cohort simulation is that it does not take into account variability or uncertainty at the patient level. The Monte Carlo technique tracks random individual patients as they transition through the model and records the resulting outcome. Patients are randomly sent through the model, and the path an individual takes is due to random variation. The total outcome measure is computed by summing the individual outcome measures. Monte Carlo simulations take into account uncertainty or variability at the patient level, take longer to run, and are not as transparent as cohort simulations. [99, 109 – 111]

2.3.3. SENSITIVITY ANALYSES

Markov models combine evidence from multiple sources, including published literature and scientific experts, into a single structure to be analyzed. Markov modeling always involves uncertainty. Four types of uncertainty that generally occur in Markov modeling are parameter uncertainty, analytical uncertainty, structure uncertainty, and generalizability. Parameter uncertainty encompasses the variation in model estimates such as data on probabilities, health outcomes, and costs. Analytical uncertainty refers to methods chosen such as costing measures, outcome measures, and inclusion of indirect costs. Structure uncertainty concerns how accurately the model simulates disease progression and health outcomes. Generalizability relates to how well results and findings from the population you studied extend to the general population. Sensitivity analyses are conducted to determine the robustness of a model in the presence of uncertainty. [109 – 110, 112]

Results from Markov models are dependent upon values assigned to probabilities and outcomes. Sensitivity analyses vary the probability and outcome values to measure the change in model output values. Sensitivity analyses are either deterministic or probabilistic. Deterministic analyses vary an uncertain parameter, or set of parameter values, one at a time while all other parameters are held at their baseline value. Since only one parameter is varied at a time, it is known as a one – way sensitivity analysis. The name of the sensitivity analysis changes with the number of parameters varied. [100] Limitations of deterministic sensitivity analyses include difficulty presenting results of multi – way analyses, arbitrarily choosing parameters to vary, highly subjective interpretation of results, and inadequately capturing interactions and correlations between parameters. These limitations are addressed when using a probabilistic sensitivity analysis. [112]

Probabilistic sensitivity analysis (PSA) uses simulation to produce a distribution of estimates to represent the variance of results. PSAs involve two distinct methods: first – order simulation and second – order simulation. In first order simulation, a single patient travels through the model a finite number of times to generate the distribution of estimates. In second – order simulation, parameters are assumed to have specific probability distributions. [109] A random sample of parameter values from the probability distribution is used to generate a distribution for the outcome. This process is repeated a finite number of times to get a distribution of parameter estimates. In addition to the probability that each alternative is effective, the output includes expected values for costs, effects, and benefits. [110]

2.4. ECONOMIC STUDIES ON ADENOVIRUS VACCINE USE IN MILITARY BASIC TRAINEES

In the 1950s and 1960s, adenovirus and vaccination in US military basic trainees was a priority for the DoD. After an effective vaccine was created for basic trainees in 1971, interest in this topic fell and did not increase again until adenovirus vaccination ceased in the late 1990s. [114] Economic evaluations on adenovirus and vaccination were only published when adenovirus vaccinations were a priority for the DoD. Therefore, only three economic evaluations on adenovirus and vaccination in military basic trainees have been published. [7, 9 - 10] Taking into consideration that the US military is the only consumer of the adenovirus vaccine worldwide, it is clear why literature on the topic is scarce. This section discusses the three published articles and differences between them.

2.4.1. Collis et al. (1973)

In a 1973 study, Collis et al. examined the costs and benefits of the Army's Adenovirus Surveillance Program that monitored FRI (Febrile Respiratory Illness) in basic trainees and the efficacy of the adenovirus type 4 and type 7 vaccine in reducing FRI due to these serotypes. Since this was an Army program, only Army male basic trainee costs were considered. At the time of this study, females were not administered the adenovirus vaccine because of unknown reproductive health concerns. The total cost of the Adenovirus Surveillance Program included vaccine development, purchases, and administration, which equaled $4.83 million. Direct costs of caring for a FRI patient amounted to $183.50 and included one pharmacy visit and a three - day stay at the

hospital. Indirect costs included the salary of the basic trainee during hospitalization plus costs of lost training time, which equaled $95.46. Thus, the total cost associated with the hospitalization of one trainee with FRI was $279. Using data collected the first two years the Army vaccinated basic trainees for both serotypes, it was estimated that the vaccine prevented 26,979 FRI hospitalizations. The money saved by using the vaccine and introducing the Army's Adenovirus Surveillance Program during 1970 and 1971 was $7.53 million. [7]

Collis et al.'s cost study aided Army policy makers in their decision to continue providing the adenovirus vaccine to basic trainees. In fact, this was the only cost study performed on the use of the adenovirus vaccine in basic trainees until 1998 when the DoD needed a new vaccine manufacturer. For decades, military preventive medicine physicians considered the risk of FRI to be the same in all military service branches. Therefore, the savings from this original study were extrapolated to the other service branches and assumed to be constant through the years.

2.4.2. Howell et al. (1998)

In 1998, Howell et al. conducted a cost – effectiveness analysis to evaluate the consequences of discontinuing the United States Army's year – round adenovirus vaccination program completely or vaccinating basic trainees during high risk months only. This study was performed from the perspective of the US Army. Outcomes associated with each policy change included expected vaccination costs, direct and indirect medical and military training cost savings, and the number of FRI

hospitalizations prevented. Reference case cost estimates are shown in Table 2.1. Outcomes were modeled for a projected cohort of 76, 171 male Army recruits entering training over a 1 – year period. When this study was performed, neither the DoD nor the Department of the Army had an official position on the use of adenovirus vaccines in women concerning reproductive health concerns, so only males were included in the model. Reference case cost and probability parameters were varied in sensitivity analyses to see how results were affected. [1]

TABLE 2.1. REFERENCE CASE COST ESTIMATES* IN HOWELL ET AL.'S STUDY

VARIABLE	REFERENCE CASE COST VALUE
Vaccine costs	
Tablet costs	$ 9.85
DPSC[a] Surcharge (55%)	$ 5.42
Administration	$ 0.05
Total	**$ 15.32**
Illness Related Costs	
Training costs (3 days @ $157/day)	$ 471
Outpatient medical costs	$ 51
Inpatient medical costs (3 days @ $537/day)	$ 1,612
Total	**$ 2,134**

*All costs calculated in 1995 U.S. dollars, using a 5% annual discount rate
[a] U.S. Department of Defense Personnel Support Center, Philadelphia, PA

Based on their analysis, discontinuing the vaccination program would cost $26.4 million in medical – related and training - related costs and would result in a projected 12,370 cases of FRI. A seasonal vaccination program would prevent 7,800 cases of FRI and save

$16.1 million over no vaccination. A year round vaccination program would save $15.5 million over no vaccination but would not prevent any more cases of FRI than the seasonal program. Therefore, the most cost – effective strategy would be the seasonal vaccination program. Expected costs under the three vaccination programs are shown in Table 2.2. The sensitivity analysis showed that if FRI incidence during the low – risk months were to increase, the year – round program would be the most cost – effective program.

TABLE 2.2. REFERENCE CASE EXPECTED COSTS UNDER THE THREE VACCINATION POLICIES IN HOWELL ET AL.'S STUDY

Vaccination Policy	Vaccine Costs	Medical Costs	Training Costs	Total Costs	Total Cost - Savings
No Vaccination		$20,558,940	$5,826,633	$26,385,573	
Year – round	$1,166,940	$ 7,595,895	$2,152,470	$10,933,585	$15,470,269
Seasonally	$ 583,477	$ 7,595,895	$2,152,470	$10,340,975	$16,053,739

Howell's article had several limitations that need to be discussed. The authors stated that this was a cost – effectiveness analysis, but after scrutinizing the article, it is clear that it more closely resembles a cost - benefit analysis (CBA). Conclusions for this analysis are misleading because no direct comparisons are made between a no vaccination policy, a year – round vaccination policy, and a seasonal vaccination policy. Another limitation of the analysis was that the authors assumed there was no risk of adenovirus infection between the months of April and August. This estimate was based on the seasonality of FRI seen in basic trainees during times of vaccination. However, during times of no vaccination, FRI rates were similar, regardless of season. [7]

2.4.3. Hyer et al. (2000)

Hyer et al. assessed the cost – effectiveness of reinstating the adenovirus vaccine program in Navy basic trainees. The authors compared three policy options, including no vaccination, seasonal vaccination, and year – round vaccination. The analysis was done from the perspective of the US Navy. Costs modeled in this decision tree analysis included outpatient costs, inpatient costs, training costs, and costs to resume production of the adenovirus vaccine. Number of FRI cases prevented and total costs associated with each policy option were compared to each other and the no vaccination policy option. [11] Outcomes were modeled for an actual cohort of 49,079 male and female Navy basic trainees who entered the Naval Recruit Training Center in 1997. Navy policy is to vaccinate all basic trainees because men and women are similarly exposed. Incidence of FRI, costs of illness, and vaccination program costs were varied in sensitivity analyses to determine how varying essential parameters affected the stability of the authors' conclusions.

Results of the analysis show that when compared to no vaccination, seasonal vaccination prevented 4,015 cases and saved $2.8 million per year, while year – round vaccination prevented 4,555 cases and saved $2.6 million per year. When comparing seasonal and year – round vaccination, a year – round vaccination policy cost an extra $263 per case of FRI prevented over seasonal vaccination. Cost – effectiveness ratios and ICERs are shown in Table 2.3. Either type of vaccination policy is cost – saving, but the seasonal vaccination policy is more cost – effective. [11]

TABLE 2.3. EXPECTED COSTS AND SAVINGS UNDER THE THREE VACCINATION POLICIES IN HYER ET AL.'S STUDY

Policy Options	Total Costs	Average C/E ratio* (cost/case prevented)	Incremental C/E ratio† (cost/case prevented)
No vaccination	$9,860,000		
Seasonal	$7,099,000	- $688	- $688
Year – round	$7,241,000	- $575	$263

* Average cost – effectiveness (C/E) ratio represents cost per case prevented with the seasonal or year – round options, compared to the no vaccination option. A negative ratio indicates a cost saving strategy

† Incremental cost – effectiveness (C/E) ratio represents cost per case prevented over the next most effective strategy. A negative ratio indicates a cost – saving strategy

Limitations of this analysis need to be considered when interpreting the results. Like the Army study previously discussed, this analysis used a vaccine – preventable FRI winter incidence rate that was 10 percent higher than the summer incidence rate. The summer incidence rate of FRI is about the same or even higher than the winter rate when the adenovirus vaccine is not in use.[7] At the time of this study, respiratory illness in basic trainees was usually classified as an "upper respiratory infection." However, upper respiratory infection was not specifically defined, so the FRI incidence rate may be higher than the actual rate. Despite these limitations, the sensitivity analysis showed the robustness of the model. [11]

2.5. ECONOMIC EVALUATIONS IN THE US MILITARY

When comparing economic evaluations of healthcare interventions found in published literature, it is important to be conscious of the environment in which the study was performed. Factors specific to the military add to the variation in military economic evaluations, including differences in policies between US military service branches,

differences between basic training sites, and differences in salaries and training costs across military service branches.

When performing and comparing economic evaluations focusing on the US military population, specific factors need to be considered. Each service branch of the US military has their own policies concerning preventive medicine and hospitalization. For example, Army basic trainees with FRI are usually hospitalized, while the Naval Recruit Training Command primary care clinic usually classifies respiratory illnesses in basic trainees as upper respiratory infections resulting in less hospitalizations. [11] As mentioned in Chapter 1, geography, poor air quality, and adenovirus serotype affect FRI rates, and surveillance shows the differences in FRI rates between basic training sites. In addition to differing policies, military service branches have varying salaries and training costs, so it is difficult to decide which service branches' costs should be used in an economic evaluation. However, in an effort to standardize costs in economic evaluations, especially in terms of military manpower, the DoD recently provided a list of cost estimates and methodologies for estimating and comparing full costs of active duty military, data sources and calculations for direct labor cost estimates, and a list of non – labor cost factors.[114] With the DoD providing more information about costs and calculations, military economic evaluations should be more standardized in the near future.

2.6. PROBLEM STATEMENT

As mentioned above, current literature on adenovirus and the Teva adenovirus vaccine is scarce, and previous economic research [9, 10] on the use of a hypothetical adenovirus

vaccine in basic trainees used manufacturer bids for vaccine costs and generalized their results to all service branches of the US military. However, since reinstating the adenovirus vaccination program, no cost analyses with the actual adenovirus vaccine price have been reported. In addition, no one has looked at the differences between service branches concerning costs. In part I of this study, a simple decision analytic model using parameters from each military service branch was used to determine the cost – effectiveness of the adenovirus vaccine in basic trainees. In part II of this study, another decision tree analysis using an outcome relevant to the military, basic trainees' training days lost (TDL), is created to calculate the incremental cost – effectiveness ratio.

2.7. STUDY OBJECTIVES

Lack of DoD health care funds makes it important that the funds they do have are used efficiently. Due to the high cost of the Teva adenovirus vaccine and the low mortality risk of FRI, this dissertation will evaluate the cost – effectiveness of using the adenovirus type 4 and type 7 vaccines versus no vaccination. Keep in mind that both decision tree analyses will be run separately for each service branch with service specific data.

This dissertation is divided into two parts. Part I uses the decision analysis model from Howell et al.'s and Hyer et al.'s study with current data, while the second part uses a decision tree developed using current, best available evidence on FRI and adenovirus vaccination.

Objectives of Part I include:

1. Estimate and compare annual direct medical costs, including only outpatient and inpatient costs associated with adenovirus vaccination and no vaccination

2. Estimate and compare annual lost training costs associated with adenovirus vaccination and no vaccination

3. Estimate and compare annual total costs associated with adenovirus vaccination and no vaccination

4. Determine whether using adenovirus vaccines in basic trainees is cost – effective in each service branch of the military based on incremental cost per FRI hospitalization case prevented

Objectives of Part II include:

5. Based on current, best available evidence on FRI and adenovirus vaccination, develop a decision analysis model to calculate training days lost (TDL), costs, and incremental cost – effectiveness

6. Estimate and compare total TDL associated with each adenovirus vaccination strategy

7. Estimate and compare average total cost associated with each adenovirus strategy.

STUDY OBJECTIVES (CONTINUED)

8. Evaluate the cost – effectiveness of adenovirus vaccines as measured by TDL averted by computing an ICER.

2.8. STUDY HYPOTHESES

Objective 1 involves using Howell et al.'s and Hyer et al.'s decision tree with current military service branch – specific information from the literature and experts on the adenovirus vaccine. Hypothesis 1 posits that direct medical costs, including inpatient and outpatient visits only, associated with adenovirus type 4 and type 7 vaccination are less than the direct medical costs associated with no vaccination.

H_1: Direct Medical Costs $_{\text{AdV Vaccination}}$ < Direct Medical Costs $_{\text{No Vaccination}}$

Objective 2 is to estimate and compare lost training costs associated with each vaccination strategy. Hypothesis 2 posits that lost training costs associated with adenovirus type 4 and type 7 vaccination are less than lost training costs associated with no vaccination

H_2: Lost Training Costs $_{\text{AdV Vaccination}}$ < Lost Training Costs $_{\text{No Vaccination}}$

STUDY HYPOTHESES (CONTINUED)

Objective 3 is to estimate and compare annual total costs associated with each vaccination strategy. Annual total costs include vaccine, direct medical, and training costs. Hypothesis 3 posits that total costs associated with adenovirus vaccination are less than total costs associated with no vaccination.

H_3: Total Costs $_{\text{AdV Vaccination}}$ < Total Costs $_{\text{No Vaccination}}$

Objective 4 is to evaluate the cost – effectiveness of adenovirus vaccines as measured by FRI hospitalizations prevented by computing an incremental cost – effectiveness ratio (ICER). A negative incremental cost – effectiveness ratio indicates a cost – saving strategy. Hypothesis 4 postulates that the ICER is less than zero.

H_4: ICER < 0

Objective 5 involves the development of a decision analysis model using military
- specific data collected from the literature and experts on the military's adenovirus vaccine. No hypothesis was developed for this objective.

Objective 6 is to estimate and compare total TDL associated with each adenovirus vaccination strategy Hypothesis 5 postulates that TDL associated with adenovirus vaccination is less than TDL associated with no vaccination.

H_5: TDL $_{\text{AdV Vaccination}}$ < TDL $_{\text{No Vaccination}}$

STUDY HYPOTHESES (CONTINUED)

Objective 7 is to calculate and compare average total cost associated with each adenovirus strategy. Hypothesis 6 posits that average total cost of adenovirus vaccination is less than average total cost of no vaccination.

$$H_6: \text{Avg. Total Cost}_{\text{AdV Vaccination}} < \text{Avg. Total Cost}_{\text{No Vaccination}}$$

Objective 8 is to evaluate the cost – effectiveness of adenovirus vaccines as measured by TDL averted by computing an ICER. Hypothesis 7 posits that the ICER is less than zero.

$$H_7: \text{ICER} < 0$$

Objectives 1 through 4 and objectives 6 through 8 and their corresponding hypotheses will be addressed for the Army, Navy, Air Force, Marine Corps, and Coast Guard. Therefore, each model will be run five times, once for each service branch, using service – specific data.

CHAPTER 3: METHODOLOGY

3.1. INTRODUCTION

This chapter presents the methodology proposed for two decision analysis models examining the cost – effectiveness of the adenovirus type 4 and type 7 vaccine in US military basic trainees. Specific topics to be discussed include: model characteristics, model inputs, costs, outcomes, and assumptions.

PART I

3.2. DECISION TREE MODEL CHARACTERISTICS

A computerized (TreeAge Software, Inc., Williamstown, MA) decision – analytic model was used to calculate the cost – effectiveness of alternative adenovirus type 4 and type 7 vaccination strategies in US military basic trainees. The model used was from Howell et al.'s and Hyer et al.'s articles discussed in Chapter 2. [10] The two alternative vaccination strategies included adenovirus vaccination and no vaccination. Outcomes associated with each vaccination strategy included number of febrile respiratory illness (FRI) hospitalization cases prevented, direct and indirect medical costs associated with FRI, lost military training costs, and vaccination costs. Outcomes were modeled for a hypothetical cohort of male and female basic trainees (age ≥17 years old) entering training over a one – year period. The number of basic trainees in each service branch's hypothetical cohort is shown in Table 3.1. These basic trainee population numbers were from fiscal year (FY) 2013 and were published quarterly on the DoD's website. [115] Reference case costs and probability parameters were based on Navy and Army

surveillance data for FRI, Department of Defense and Department of Homeland Security budget justification documents for fiscal year 2013, TRICARE reimbursement databases and guidelines, and experts on military vaccination, vaccine acquisition, and FRI surveillance. Clinical data and data on efficacy of adenovirus vaccination were gathered from a review of the literature.

It is important to note that since the Army has four basic training sites and the Marine Corps has two, their incidence data and cost estimates are weighted by the proportion of basic trainees attending each site during FY2013 and then combined into one measure for each branch. Incidence rates and inpatient and outpatient costs were obtained for each basic training site and a weighted total was calculated. This is the same method used in a previous Army study to combine rates from more than one basic training site. [11]

TABLE 3.1. HYPOTHETICAL POPULATION SIZES [116]

HYPOTHETICAL STUDY POPULATIONS [a]	
ARMY	**75,373**
NAVY	**36,565**
MARINE CORPS	**29,757**
AIR FORCE	**36,392**
COAST GUARD	**2,136**

[a] End strength accession numbers for FY 2013

3.3. PERSPECTIVE

This study was conducted from the perspective of each US military service branch. Military basic trainees were treated at Military Treatment Facilities (MTF), which included outpatient clinics and hospitals, and were covered by the Defense Health Agency's (DHA) TRICARE insurance program.

TRICARE is the health insurance program of the US Armed Forces that provides health benefits for military personnel, their dependents, and military retirees. Nine different plan options are available that include coverage for outpatient services, hospitalizations, immunizations and prescriptions. [116]

3.4. PROBABILITIES

The following probabilities were included in the model: (1) probability of FRI when adenovirus vaccination is not in use; (2) probability of FRI when adenovirus vaccination is in use; (3) probability of hospitalization for FRI; (4) and probability of outpatient treatment for FRI. Data for these probabilities were collected from published surveillance documents and published literature.

3.4.1. PRE – VACCINE INCIDENCE DATA

Research showed that the incidence of FRI varies by military service branch and military basic training site. Incidence rates for FRI from the pre – vaccine era for eight of nine basic training sites were obtained from FRI surveillance performed by the Naval Health Research Center (NHRC) and published in Russell et al.'s article discussed below. [6] The

one Army basic training site not included in the NHRC's surveillance was Fort Sill, so its pre-vaccine incidence data was calculated using the Army Public Health Command's (APHC) Acute Respiratory Disease Surveillance (ARDS) Summary, which was published weekly. [117] In addition to number of FRI cases, the ARDS included weekly unit size, so it was possible to calculate an incidence rate in trainee – weeks to correspond with incidence rates published in Russell et al.'s article.

3.4.1.1. Russell et al. Article

In 2006, Russell et al. published FRI surveillance results from eight military basic training sites during the five – year period from July 1999 to June 2004. Russell et al.'s study aimed to document FRI rates after adenovirus vaccine usage ceased and to define pathogen – specific FRI rates and site – specific trends in the basic trainee population. Surveillance data for the article came from the NHRC. As part of the NHRC's surveillance program, NHRC staff members conducted surveillance at all basic training sites. NHRC staff members gathered numerator data, which included individuals meeting the FRI case definition, and denominator data, which was the total basic trainee population at each site, and calculated weekly rates of FRI. Russell et al. used the resulting weekly FRI rates to calculate an average site – specific, five – year FRI rate that was reported as cases per 100 recruit - weeks. Since these rates were for the period after adenovirus vaccination ceased, these average site – specific, five – year FRI rates published by Russell et al. were used to calculate incidence probabilities for the no adenovirus vaccination alternative branch in this study's economic models.

Nearly 12 million recruit – weeks were followed over the five years, with 110,172 FRI cases occurring at the eight basic training sites. Over the five – year surveillance period, average site – specific FRI rates ranged from 0.34 cases per 100 recruit – weeks at the Marine Corps Recruit Depot in San Diego to 1.35 cases per 100 recruit – weeks at Lackland Air Force base. These rates are shown in Table 3.2. With the exception of Fort Leonard Wood and Fort Jackson, the FRI rates at the different basic training sites were significantly different from each other ($p < 0.0001$). This difference between basic training sites is one reason each service branch was analyzed separately in this dissertation.

TABLE 3.2. REFERENCE CASE FRI INCIDENCE PARAMETERS FOR THE PRE – VACCINE PERIOD

	INCIDENCE DENSITY	CUMULATIVE INCIDENCE [a]	REFERENCE
ARMY	0.89 cases/100 trainee - weeks	0.085	[6, 117]
NAVY	1.20 cases/100 trainee - weeks	0.092	[6]
MARINE CORPS	0.38 cases/100 trainee - weeks	0.045	[6]
AIR FORCE	1.35 cases/100 trainee - weeks	0.108	[6]
COAST GUARD	0.50 cases/100 trainee - weeks	0.039	[6]

[a] Cumulative incidence is the reference case probability value used in the analysis; Calculated using the formula $CIRt = 1 - e^{-ID\Delta t}$

The pre – vaccine era incidence data reported in Russell et al.'s article is an incidence density rate (IDR), where trainee – weeks, also known as person – time, is in the denominator. Person – time represents the total disease – free time experience for the population at risk, and the incidence density rate ranges from 0 to infinity. Therefore, it was not a probability and needed to be converted before it could be used in economic

models. An exponential function was used to convert the incidence density rate into a cumulative incidence risk (CIR), also known as just risk. [118]

The exponential function is shown below:

$$CIRt = 1 - e^{-IDR\Delta t}$$

The CIR was the probability that an individual develops a disease in a specified period of time and ranges from 0 to one. [118] Once the IDR was converted to a CIR, it could be used in economic models. Table 3.2 shows the resulting probabilities/cumulative incidence reached by using the exponential function.

3.4.2. INCIDENCE DATA AFTER REINTRODUCTION OF ADENOVIRUS VACCINE

Incidence data for after re – introduction of the adenovirus vaccine was collected from the weekly FRI surveillance reports published on the NHRC and APHC's respective websites. [117, 119] The APHC's Acute Respiratory Disease Surveillance summary included the number of FRI cases and number of trainees for each Army basic training site. To compute the Army's incidence rate for after re – introduction of the adenovirus vaccine, APHC surveillance summaries were collected for a year (April 21, 2012 – March 30, 2013) and a weighted average incidence rate was calculated. [118] This composite incidence rate was then converted into a CIR to be used in this study's economic models. FRI incidence rates for all other service branches were collected from the NHRC's weekly FRI surveillance updates. [119] Surveillance updates were collected weekly from August 4, 2012, until August 10, 2013, and an average incidence rate was calculated for each

service branch. These rates were converted into probabilities using the equation in the previous section.

TABLE 3. 3. REFERENCE CASE FRI INCIDENCE PARAMETERS FOR VACCINE PERIOD

	INCIDENCE DENSITY	CUMULATIVE INCIDENCE [a]	REFERENCE
ARMY	0.09 cases/100 trainee - weeks	0.009	[116]
NAVY	0.12 cases/100 trainee - weeks	0.010	[118]
MARINE CORPS	0.03 cases/100 trainee - weeks	0.004	[118]
AIR FORCE	0.17 cases/100 trainee - weeks	0.014	[118]
COAST GUARD	0.06 cases/100 trainee - weeks	0.005	[118]

[a] Cumulative incidence is the reference case probability value used in the analysis; Calculated using the formula $CIRt = 1 - e^{-ID\Delta t}$

The NHRC weekly surveillance update did not supply the reader with raw data, so to confirm that average incidence rates collected from the NHRC updates, pre - and post - vaccination program incidence probabilities were entered into the equation to compute vaccine effectiveness (VE). The Navy and Air Force have reported adenovirus vaccine effectiveness to be approximately 89.5 and 87 percent, [120, 121] respectively, and using Army incidence probabilities, adenovirus VE was calculated to also be 89 percent. Therefore, incidence probabilities for each service branch were entered into the vaccine effectiveness equation to determine if the calculated VE was between 87 and 89 percent. The vaccine effectiveness formula is: [122]

$$\frac{Risk\ in\ unvaccinated\ group - Risk\ in\ vaccinated\ group}{Risk\ in\ unvaccinated\ group} \text{ X } 100 = \text{VE (87\% - 89\%)}$$

The Navy and Air Force vaccine effectiveness values equaled values reported in previous articles. These percentages were interpreted as an 89 percent reduction in FRI occurrence in the vaccinated group. Since vaccine effectiveness values were not reported for the Marine Corps and Coast Guard, their average incidence rates could not be confirmed.

3.4.3. HOSPITALIZATION INCIDENCE

Following the discontinuation of the adenovirus vaccination program in the late 1990s, FRI outbreaks occurred at three basic training sites, Fort Jackson, Fort Benning, and Lackland AFB. In response to these outbreaks, the Army's Center for Health Promotion and Preventative Medicine and the Air Force's Institute for Environment, Safety, and Occupational Health Risk Analysis performed in – depth epidemiologic investigations. Each investigation consisted of several reports, including but not limited to, hospital cohort and FRI hospitalization surveillance, adenovirus carriage prevalence estimation, indoor air quality assessment, and personal practices among basic trainees. [46 – 48] Incidence of FRI hospitalization during the epidemiologic investigations was 2.4 per 100 trainee – weeks of training in the Army [46] and 2.6 per 100 trainee – weeks of training in the Air Force. [48] Since FRI hospitalization incidence rates were similar in the Army and Air Force and FRI hospitalization incidence rates were not available for the other service branches, an average FRI hospitalization incidence rate of 2.5 per 100 trainee – weeks of training was used for the other service branches. Risk of FRI hospitalization was calculated using the formula described earlier in this section and are shown in Table 3.4.

TABLE 3.4. REFERENCE CASE HOSPITALIZATION INCIDENCE PARAMETERS

	INCIDENCE DENSITY	CUMULATIVE INCIDENCE [a]	REFERENCE
ARMY	2.4 cases/100 trainee - weeks	0.213	[46]
NAVY	2.5 cases/100 trainee - weeks	0.181	[Estimate]*
MARINE CORPS	2.5 cases/100 trainee - weeks	0.259	[Estimate]*
AIR FORCE	2.6 cases/100 trainee - weeks	0.198	[48]
COAST GUARD	2.5 cases/100 trainee - weeks	0.181	[Estimate]*

[a] Cumulative incidence is the reference case probability value used in the analysis; Calculated using the formula $CIRt = 1 - e^{-ID\Delta t}$; * Estimates for the Navy, Marine Corps, and Coast Guard are an average of the Army and Air Force values.

3.5. COSTS

3.5.1. COSTS ASSOCIATED WITH FRI

3.5.1.1. TRAINING COSTS

Costs to the DoD associated with FRI included missed training costs, direct medical costs, including inpatient and outpatient costs, and vaccination costs. Training costs for this study included the cost of running the basic training site plus military personnel appropriation costs paid by the DoD. Cost of basic training per trainee in all military service branches but the Coast Guard was published in a 2004 report by the Office of the Under Secretary of Defense, Comptroller. Since Coast Guard basic training cost was unavailable, the average training cost of all other service branches was used as an estimate. [123] Costs included in this 2004 number included manpower costs, support equipment costs, facility costs, and all other costs associated with indoctrinating basic trainees into military culture, raising their standards of physical conditioning, and instructing them in basic military skills. [123] These 2004 costs were adjusted to 2013 US

dollars using the Consumer Price Index (CPI).[124] Once training costs were adjusted to 2013 US dollars, a daily training cost was calculated by dividing the basic training cost per trainee by the number of days spent in basic training, which varied by service branch. The second component of training costs for this analysis was the annual military appropriation costs paid by the DoD, also known as the annual composite rate. The DoD recommended using the annual composite rate when determining the cost of military personnel for budget and management studies and published this rate for each service branch on the Office of the Under Secretary of Defense (OUSD), Comptroller's website. [125] For this analysis, the annual composite rate for a basic trainee with a military pay grade of E-1 was used. A military pay grade of E – 1 was chosen because in 2012, 77.6 percent of civilians entering basic training had a high school education only, which indicated they entered basic training with a pay grade of E – 1. [126] Costs included in the DoD annual composite rate were average basic pay plus retired pay accrual, Medicare eligible health care accrual, basic allowance for housing, basic allowance for subsistence, incentive and special pay, permanent change of station expenses, and miscellaneous pay. [125] Military pay rates, including the DoD annual composite rate, for the Coast Guard were not published by the OUSD, Comptroller, so a DoD composite rate was estimated by averaging all other service branches' annual composite rates for an E – 1 pay rank. This method was used by the DoD in a recent economic publication. [127] The annual composite rate for each service branch was converted into a daily rate for use in this economic analysis. The resulting training cost for each service branch is shown in Figure 3.5 and used in calculations for outpatient and inpatient costs.

TABLE 3.5. REFERENCE CASE COST ESTIMATES PER TRAINEE PER DAY

SERVICE BRANCH		COST ($)†	REFERENCE
ARMY			
	Training cost per day per trainee	$240	[123]
	Daily average wage and DoD benefits	$137	[125]
	Total cost per trainee per day	***$377***	
NAVY			
	Training cost per day per trainee	$268	[123]
	Daily average wage and DoD benefits	$119	[125]
	Total cost per trainee per day	***$387***	
MARINE CORPS			
	Training cost per day per trainee	$171	[123]
	Daily average wage and DoD benefits	$115	[125]
	Total cost per trainee per day	***$286***	
AIR FORCE			
	Training cost per day per trainee	$112	[123]
	Daily average pay and DoD benefits	$110	[125]
	Total cost per trainee per day	***$222***	
COAST GUARD			
	Training cost per day per trainee	$254	[123]*
	Daily average wage and DoD benefits	$119	[125]*
	Total cost per trainee per day	***$373***	

*Estimates for the Coast Guard are averages of values from these references; DoD = Department of Defense;
†Costs rounded to the nearest dollar

3.5.1.2. OUTPATIENT COSTS

Outpatient costs were determined using Current Procedural Terminology (CPT) codes for outpatient office visits, including new and established patients. FRI did not have corresponding CPT codes, so the average FY 2013 DoD Uniform Business Office's (UBO) maximum allowable charge for outpatient office visits was used as a proxy for FRI outpatient costs. The Military Health System (MHS) Professional Services Coding Guidelines recommended using these CPT codes for upper respiratory infections. [129] Since the study population contains basic trainees, it was assumed that all basic trainees were new patients for one visit. CPT codes for new patient office visits were 99201, 99202, 99203, 99204, and 99205. [130] The CPT code used depends on the complexity of the patient's illness. The UBO maximum allowable charge for each new patient office visit CPT code (99201 – 99205) was collected and an average value was calculated to be included in the analysis. [128] Follow – up outpatient costs were determined using CPT codes for an established patient's office visits. The value used in the analysis for established patients was the average UBO maximum allowable charge for CPT codes 99211, 99212, 99213, 99214, and 99215. [128, 130] Outpatient costs for each service are shown in Tables 3.6 - 3.10.

According to Hyer et al., it was the opinion of preventive medicine physicians at the Navy's basic training site that 95 percent of basic trainees who were not hospitalized for FRI were treated with bed rest for 2.5 days. [10] Therefore, this model assumed that basic trainees with FRI who attended an outpatient clinic and were not hospitalized were

treated with bed rest in sick quarters for 2.5 days. The cost of one trainee in sick quarters was calculated with the following formula:

$$SQ_c = [\, cost\ of\ 1\ new\ outpatient\ vist + (2.5) * (Daily\ training\ cost)]$$

Furthermore, five percent of patients placed in sick quarters required one follow – up visit, where cost was calculated with the formula below:

$$SQF_c = [cost\ of\ 1\ new\ outpatient\ visit + (2.5) * (Daily\ training\ cost) + cost\ of\ 1\ established\ outpatient\ visit]$$

These equations were used to calculate the total cost, including training and direct medical costs, of a basic trainee spending 2.5 days in sick quarters.

TABLE 3.6. ARMY COST† ESTIMATES FOR FRI OUTPATIENT VISITS

CPT CODE	DESCRIPTION	REIMBURSEMENT	VALUE USED
99201	Office/Outpatient, New, minimal severity	$25	
99202	Office/Outpatient, New, minor severity	$47	
99203	Office/Outpatient, New, low/moderate severity	$72	**$83**
99204	Office/Outpatient, New, moderate/high severity; 45 minutes [a]	$123	
99205	Office/Outpatient, New, moderate/high severity; 60 minutes	$159	
99211	Office/Outpatient, Est., minimal severity	$9	
99212	Office/Outpatient, Est., minor severity	$24	
99213	Office/Outpatient, Est., low/moderate severity	$48	**$52**
99214	Office/Outpatient, Est., moderate/high severity; 25 minutes	$74	
99215	Office/Outpatient, Est., moderate/high severity; 40 minutes	$104	

CPT = Current Procedural Terminology; Est = Established patient; [a] Time included to distinguish between moderate/high severity categories; † = All costs rounded to the nearest dollar

TABLE 3.7. NAVY COST† ESTIMATES FOR FRI OUTPATIENT VISITS

CPT CODE	DESCRIPTION	REIMBURSEMENT	VALUE USED
99201	Office/Outpatient, New, minimal severity	$28	
99202	Office/Outpatient, New, minor severity	$53	
99203	Office/Outpatient, New, low/moderate severity	$83	**$97**
99204	Office/Outpatient, New, moderate/high severity; 45 minutes [a]	$141	
99205	Office/Outpatient, New, moderate/high severity; 60 minutes	$180	
99211	Office/Outpatient, Est., minimal severity	$10	
99212	Office/Outpatient, Est., minor severity	$27	
99213	Office/Outpatient, Est., low/moderate severity	$54	**$58**
99214	Office/Outpatient, Est., moderate/high severity; 25 minutes	$83	
99215	Office/Outpatient, Est., moderate/high severity; 40 minutes	$117	

FRI = Febrile Respiratory Illness; CPT = Current Procedural Terminology; Est.= Established patient; [a] Time included to distinguish between moderate/high severity categories; †= Costs rounded to the nearest dollar

TABLE 3.8. MARINE CORPS COST† ESTIMATES FOR FRI OUTPATIENT VISITS

CPT CODE	DESCRIPTION	REIMBURSEMENT	VALUE USED
99201	Office/Outpatient, New, minimal severity	$25	
99202	Office/Outpatient, New, minor severity	$48	
99203	Office/Outpatient, New, low/moderate severity	$74	**$87**
99204	Office/Outpatient, New, moderate/high severity; 45 minutes [a]	$126	
99205	Office/Outpatient, New, moderate/high severity; 60 minutes	$162	
99211	Office/Outpatient, Est., minimal severity	$9	
99212	Office/Outpatient, Est., minor severity	$24	
99213	Office/Outpatient, Est., low/moderate severity	$49	**$53**
99214	Office/Outpatient, Est., moderate/high severity; 25 minutes	$76	
99215	Office/Outpatient, Est., moderate/high severity; 40 minutes	$106	

FRI = Febrile Respiratory Illness; CPT = Current Procedural Terminology; Est = Established patient; [a] Time included to distinguish between moderate/high severity categories; †= Costs rounded to the nearest dollar

TABLE 3.9. AIR FORCE COST† ESTIMATES FOR FRI OUTPATIENT VISITS

CPT CODE	DESCRIPTION	REIMBURSEMENT	VALUE USED
99201	Office/Outpatient, New, minimal severity	$25	
99202	Office/Outpatient, New, minor severity	$47	
99203	Office/Outpatient, New, low/moderate severity	$72	**$85**
99204	Office/Outpatient, New, moderate/high severity; 45 minutes [a]	$123	
99205	Office/Outpatient, New, moderate/high severity; 60 minutes	$159	
99211	Office/Outpatient, Est., minimal severity	$9	
99212	Office/Outpatient, Est., minor severity	$24	
99213	Office/Outpatient, Est., low/moderate severity	$48	**$52**
99214	Office/Outpatient, Est., moderate/high severity; 25 minutes	$74	
99215	Office/Outpatient, Est., moderate/high severity; 40 minutes	$104	

FRI = Febrile Respiratory Illness; CPT = Current Procedural Terminology; Est = Established patient; [a] Time included to distinguish between moderate/high severity categories; † = Costs rounded to the nearest dollar

TABLE 3.10. COAST GUARD COST† ESTIMATES FOR FRI OUTPATIENT VISITS

CPT CODE	DESCRIPTION	REIMBURSEMENT	VALUE USED
99201	Office/Outpatient, New, minimal severity	$27	
99202	Office/Outpatient, New, minor severity	$58	
99203	Office/Outpatient, New, low/moderate severity	$79	**$95**
99204	Office/Outpatient, New, moderate/high severity; 45 minutes [a]	$135	
99205	Office/Outpatient, New, moderate/high severity; 60 minutes	$173	
99211	Office/Outpatient, Est., minimal severity	$9	
99212	Office/Outpatient, Est., minor severity	$26	
99213	Office/Outpatient, Est., low/moderate severity	$52	**$56**
99214	Office/Outpatient, Est., moderate/high severity; 25 minutes	$81	
99215	Office/Outpatient, Est., moderate/high severity; 40 minutes	$114	

FRI = Febrile Respiratory Illness; CPT = Current Procedural Terminology; Est = Established patient; [a] Time included to distinguish between moderate/high severity categories; † = Costs rounded to the nearest dollar

3.5.1.3. INPATIENT COSTS

Inpatient treatment costs were estimated using the TRICARE reimbursement amount for Diagnosis Related Groups (DRG) associated with respiratory diseases [131] and the DoD UBO's inpatient adjusted standardized amount (ASA) for admission to base – specific MTFs. [132] FRI was not associated with one specific DRG code, and the DoD did not support patient - level billing. Therefore, inpatient costs for this study were based on costs associated with TRICARE DRG code 203 for bronchitis and asthma without complications and comorbidities and TRICARE DRG code 206 for other respiratory system diagnoses without complications and comorbidities. DRG code 203 included patients with a primary diagnosis of acute bronchitis, acute bronchiolitis, and other specified disease of the upper respiratory tract, [133] while DRG code 206 included lower respiratory infections. [134] The relative weights for DRG codes 203 and 206 were 0.6022 and 0.7274, respectively, and were used to calculate the cost of a basic trainee's inpatient hospital stay. The cost of an inpatient hospital stay for FRI used in this study was an average of the reimbursement rates for the two DRG groups. Each base – specific MTF has its own applied ASA rate that was adjusted for indirect medical education costs. [132] All basic training sites were in an inpatient MTF catchment area except for the Navy and Coast Guard basic training sites. Since the Navy and Coast Guard were not associated with base – specific inpatient MTFs, their adjusted standardized amount was less than the other basic training sites because indirect medical education costs were not taken into account. The total inpatient cost used in the economic model for this study was the product of the MTF or facility's inpatient adjusted standardized amount and the DRGs

relative weight. [132] This calculated inpatient cost was the TRICARE reimbursement amount. This study assumed that the calculated TRICARE reimbursement amount was the actual cost allowed by the DoD for FRI inpatient hospitalization.

Previous research showed that hospitalization for FRI usually lasted four days and was followed by two outpatient visits. [10] Therefore, it was assumed that hospitalization lasted four days, so total inpatient cost was the sum of the cost of four missed training days, two outpatient visits, and the TRICARE reimbursement amount for FRI hospitalization that lasted four days. The TRICARE reimbursement amount for FRI hospitalization remained the same unless a patient's length of stay surpassed the maximum stay threshold, which was not the case in this analysis [132] Reference case inpatient hospitalization costs used in the decision tree are shown in Table 3.11. The following formula was used to calculate total inpatient cost:

$$INP_c = [Hospital\ DRG\ Cost + (4) * (Daily\ trainee\ cost) +$$

$$(2) * (Cost\ of\ established\ patient\ follow - up\ visit)]$$

Therefore, the total inpatient cost per basic trainee hospitalized for FRI included both training and direct medical costs.

TABLE 3.11. REFERENCE CASE INPATIENT HOSPITALIZATION REIMBURSEMENT FOR RESPIRATORY DISEASES USING TRICARE DIAGNOSIS – RELATED GROUPS (DRG)

SERVICE BRANCH	DRG	DESCRIPTION	REIMBURSEMENT	VALUE USED
ARMY				
	203	Bronchitis & asthma age > 17	$6,499	**$7,175**
	206	Other respiratory system diagnoses	$7,851	
NAVY				
	203	Bronchitis & asthma age > 17	$3,682	**$4,065**
	206	Other respiratory system diagnoses	$4,447	
MARINE CORPS				
	203	Bronchitis & asthma age > 17	$8,339	**$9,075**
	206	Other respiratory system diagnoses	$9,810	
AIR FORCE				
	203	Bronchitis & asthma age >17	$9,816	**$10,836**
	206	Other respiratory system diagnoses	$11,857	
COAST GUARD				
	203	Bronchitis & asthma age > 17	$3,822	**$4,219**
	206	Other respiratory system diagnoses	$4,617	

* All costs rounded to the nearest dollar

3.5.2. COSTS ASSOCIATED WITH ADENOVIRUS VACCINATION

The 2013 cost of the adenovirus vaccine per dose (1 AdV4 + 1 AdV7) was $125.45. An additional $0.67 was added to this base price for shipping. This information was received by personal communication with Dr. Clifford Snyder who was product manager for the adenovirus vaccine at the US Army's Medical Material Development Activity. Vaccines were administered to basic trainees during entrance processing, while basic trainees were completing other administrative tasks. The adenovirus vaccine was different from other vaccines because it was taken orally instead of being injected, thus basic trainees had minimal contact with a clinician. [9] Previous economic models included a small vaccine administration fee of $0.05 in 1997 US dollars, which was adjusted to 2013 dollars using a medical CPI inflation rate for this model. [124] After adjustment, the vaccine administration fee totals $0.10. The total vaccine cost per basic trainee was the sum of the vaccine price per dose, shipping cost, and administration fee and totals $126.22. Since this analysis focuses on individual service branch costs and outcomes, vaccination program costs such as start – up costs were not included in the model. The DoD was the only consumer of the adenovirus vaccine, so they were financially responsible for all doses Teva manufactures regardless of the number of basic trainees (Personal communication, Clifford Snyder). Those extra doses were not accounted for in this model.

3.6. OUTCOME MEASURE – PART I

For this decision tree analysis, expected costs savings, and an incremental cost – effectiveness ratio was calculated. The incremental cost – effectiveness ratio represented cost per case of FRI hospitalization prevented with adenovirus vaccination compared to no vaccination. Previous articles reported annual costs and outcomes, so annual values were reported for this analysis. To calculate annual number of hospitalizations for both vaccination strategies, the annual number of basic trainees was multiplied by the probability of developing FRI. The resulting product was then multiplied by the probability of being hospitalized for FRI. The following is an example for the Army, using the adenovirus strategy.

# of FRI hospitalizations = 75,373 * 0.009 = 678 (annual # of FRI cases)

= 678 * 0.213 = 144 annual FRI hospitalizations for Army

The difference of FRI hospitalizations between strategies was the annual number of FRI hospitalizations prevented. To get the average number of FRI hospitalizations prevented, which was needed for the ICER calculations, the number of FRI hospitalizations was divided by the annual number of basic trainees.

3.6.1. INVERTING EFFECTIVENESS CALCULATIONS

An assumption of cost – effectiveness analyses is that higher effectiveness values are always better. [135] However, in this dissertation, lower values of the

effectiveness measures, FRI hospitalizations and training days lost, represent a more effective treatment. Therefore, effectiveness measures should be minimized rather than maximized, which TreeAge handled by inverting the incremental effectiveness values. If not using TreeAge and effectiveness values need to be inverted, the following formula can be used to calculate the ICER.

$$ICER = \frac{(Total\ Cost\ B) - (Total\ Cost\ A)}{(Total\ Effectiveness\ A) - (Total\ Effectiveness\ B)}$$

3.7. SENSITIVITY ANALYSES – PART I

To determine the robustness of the model used in Part I, tornado diagrams were constructed to indicate variables that showed the most change when parameter values were varied. In addition, one – way sensitivity analyses were performed on each cost and probability parameter to determine their impact on cost – effectiveness.

3.8. ASSUMPTIONS FOR DECISION TREE – PART I

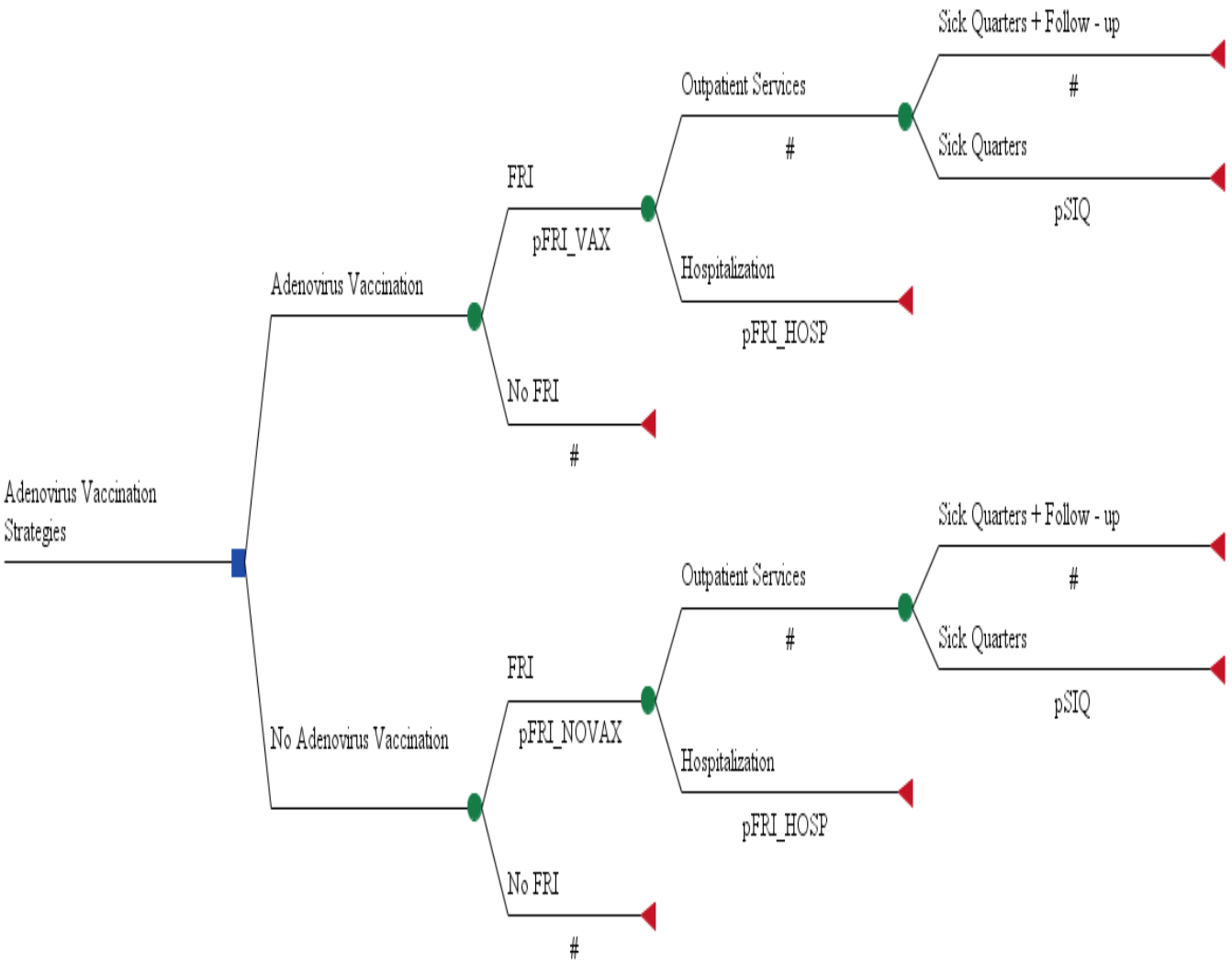
Assumptions made for this analysis are outlined below:

1. All basic trainees received the adenovirus vaccine within two days of arriving at the basic training camp (100% coverage)
2. Assumed costs accrued by vaccine adverse events were not substantial enough to be included in the analysis
3. All basic trainees were new patients for one visit

ASSUMPTIONS FOR DECISION TREE – PART I (CONTINUED)

4. Due to the lack of a CPT code associated with FRI, the average maximum allowable charge for outpatient office visits for new patients (CPT codes 99201 – 99205) and established patients (CPT codes 99211 – 99215) was assumed to estimate outpatient costs
5. Due to the lack of one specific FRI – associated DRG code, an average reimbursement rate for DRG code 203 and DRG code 206 was calculated
6. Assumed that TRICARE reimbursement amounts were the actual costs allowed by the DoD for FRI treatment
7. Patients who attended an outpatient clinic and were not hospitalized were treated in sick quarters for 2.5 days
8. Five percent of patients who attended an outpatient clinic and were not hospitalized were treated in sick quarters for 2.5 days and required one follow – up visit
9. In addition to two outpatient clinic visits, patients hospitalized for FRI missed four days of basic training

3.9. MODEL SCHEMATIC



PART II

3.10. ANALYTIC HORIZON

For this study, the analytic horizon was the length of basic training for each respective service branch. The Marine Corps has the longest basic training with 12 weeks, [44] followed by the Army with 10 weeks,[38] the Air Force with eight and a half weeks,[43] and the Navy and Coast Guard with eight weeks.[41] Duration of protection of the adenovirus vaccine was not known past eight weeks because that was the length of the phase III trial. [90] In addition, a basic trainee's risk of adenovirus decreased once he/she graduated from basic training. These factors supported the decision to have an analytic horizon equal to the length of basic training for this analysis.

3.11. MODEL INPUT

Several variables with the same value were used in all service branches in Part II. These values are shown in Table 3.12.

3.11.1. PROBABILITIES

The following probabilities were included in the second decision tree analysis: (1) probability of FRI before vaccination reintroduced; (2) probability of FRI after vaccination reintroduced; (3) probability of hospitalization for FRI; (4) probability of minor adverse events after vaccination; (5) probability of developing Guillain – Barre Syndrome (GBS) after adenovirus vaccination; and (6) probability of adenoviral pneumonia complications.

3.11.1.1. INCIDENCE OF FRI

Incidence data for FRI before and after the adenovirus vaccine was reintroduced to the basic trainee population collected by military surveillance activities used in the prior analysis were also used in this analysis and are found in Table 3.2.

3.11.1.2. PROBABILITY OF HOSPITALIZATION

Probability data for hospitalization due to FRI used in the prior analysis were also used in this analysis and are found in Table 3.4.

3.11.1.3. PROBABILITY OF DEVELOPING PNEUMONIA AS RESULT OF FRI

Current numbers on basic trainees with FRI that developed viral pneumonia were not in the literature. Therefore, data for the probability of developing pneumonia as a complication of FRI was obtained from dated studies. Well - controlled studies in the 1950s and 1960s found that five to ten percent of basic trainees with FRI developed severe signs and symptoms of pneumonia. [136 – 138] Another study published in 1971 on basic trainees who received the adenovirus vaccines found that 12 percent of basic trainees hospitalized for FRI developed pneumonia complications. [139]Using data from these studies, an average of eight percent was used as the percentage of basic trainees with FRI who developed pneumonia.

3.12. MORTALITY DUE TO ADENOVIRUS VACCINATION AND ADENOVIRUS INFECTION

Death from adenovirus - associated respiratory illness in military basic trainees was not common. From 1967 to 1998, while the adenovirus vaccine was still in use, five deaths due to adenovirus serotypes four and seven were reported in active duty military service members. [53] To determine the impact of adenovirus on military mortality when the adenovirus vaccine was not in use, the Mortality Surveillance Division of the Armed Forces Medical Examiner System collected records of active duty service members who died since 1998. [53] Eight out of approximately 14,000 non – combat related deaths were attributed to adenovirus, and seven of the eight deaths were basic trainees. Two cases were caused by adenovirus serotype 14, and two other cases were not associated with any serotype. Therefore, between 1999 and 2012, four deaths due to adenovirus serotypes four and seven occurred in active duty military service members. [53] Due to this small number, adenovirus mortality was not modeled in this analysis.

3.13. SAFETY OF THE ADENOVIRUS TYPE 4 AND TYPE 7 VACCINE

Thirty years of use by the DoD established the safety of Wyeth's adenovirus vaccine, where the most common adverse reaction associated with Wyeth's adenovirus vaccine was diarrhea. To evaluate the safety of the new Teva adenovirus vaccine, phase I and III clinical trials were performed. [49, 90] These trials showed that adverse events occurred at the same rate in the placebo and vaccine groups. Abdominal pain and diarrhea occurred more often in the vaccine group, but the difference in number of cases between the

placebo and vaccine groups did not reach statistical significance. Even though the difference between placebo and vaccine groups did not reach significance, The Vaccine Information Statement (VIS) for the adenovirus vaccine stated that systemic adverse reactions such as abdominal pain and diarrhea occurred approximately 10 percent of patients. [140] In addition to the phase I and III trials, a phase IV study examining the safety of Teva's adenovirus vaccine in the "real world" was scheduled to be completed at the beginning of 2013. Results of the phase IV study were not publically available, however, Teva reported adverse events observed in the phase IV study to the Center for Disease Control and Prevention's (CDC) Vaccine Adverse Event Reporting System (VAERS). All reports submitted by the manufacturer to VAERS concerning the adenovirus phase IV observational study were collected and reviewed by the author of this study. [141] The only adverse reaction occurring more often in the vaccine group was acute infective polyneuritis also known as Guillain – Barre Syndrome (GBS). A medical monitor reviewed VAERS reports to assess causal relationships between vaccines and adverse events and noted his/her conclusions on the VAERS report. The medical monitor who reviewed the reports on adenovirus and GBS determined that in those specific cases, GBS was possibly related to adenovirus vaccination. [142] Besides systemic adverse reactions and GBS, adverse event reports due to adenovirus vaccination were rare. Nonetheless, based on the two clinical trials and reports submitted to VAERS, systemic adverse events and GBS were included in the economic analysis. [49, 90, 142]

3.13.1. PROBABILITY OF SYSTEMIC ADVERSE REACTIONS

According to the CDC's VIS, systemic adverse reactions to the adenovirus vaccine included: upper respiratory infections, headache, nasal congestion, cough, arthralgia, sore throat, nausea, abdominal pain, diarrhea, and vomiting. [140] As mentioned in the previous section, these reactions occurred in approximately 10 percent of patients. Therefore, 0.10 is the probability used for the economic model.

3.13.2. PROBABILITY OF GUILLAIN BARRE – SYNDROME

Guillain – Barre syndrome (GBS) is a rare autoimmune disorder that damages nerve cells, causing muscle weakness and sometimes paralysis often associated with infectious illness and live vaccines. [143] Cases range from mild to severe disease and recovery depends on disease severity. Scientists believe that stimulation of the immune system plays a role in its development, but the cause is not fully understood. About two – thirds of people developing GBS symptoms do so several days or weeks after experiencing a respiratory illness. [143]

Since GBS was not identified in the phase I and phase III trials, risk of GBS was calculated using data from the phase IV observational study. The exposed (vaccinated) and unexposed (no vaccine) groups both had 55,989 participants. Three patients in the exposed group had GBS, while two patients in the unexposed group had GBS. [142] Risk in the exposed group was calculated by dividing three by the total number of participants in the exposed group. The calculated risk of the exposed group was 0.00005 and was the probability used in this economic analysis.

3.13.3. COSTS ASSOCIATED WITH PNEUMONIA COMPLICATIONS

Inpatient treatment costs for pneumonia complications of FRI were calculated the same way as inpatient costs for FRI, using MTF – specific adjusted standardized amounts and DRG discharge rates. Unlike FRI, adenoviral pneumonia was associated with a specific DRG code. Adenoviral pneumonia is classified under DRG code 194 for viral pneumonia with complications and comorbidities, with a DRG weight of 0.9779. As with other inpatient calculations, the final inpatient amount was calculated using the MTF specific ASA and the DRG code weight.

3.13.4. COSTS ASSOCIATED WITH GUILLAIN – BARRE SYNDROME (GBS)

GBS is a poorly understood disease that varies in severity and treatment.[143] A 2009 study on the epidemiology of GBS in the US military showed that after initial case presentation, follow – up encounters included physical therapy, occupational therapy, rehabilitation, and speech therapy.[144] Since treatment included encounters with various specialties and depended on the severity of disease, it was difficult to capture all costs related to GBS without performing a prospective observational study in basic trainees. In addition, including just one inpatient hospital visit for GBS will greatly underestimate the cost of GBS to the military. To avoid underestimating the cost of GBS, an average cost per patient with GBS as calculated in a 2008 article was used. [145]

In 2008, Frenzen published a study estimating the annual economic cost of GBS in the US in 2004 dollars that included direct costs of medical care and indirect costs due to lost productivity and premature death. [145] The mean cost per GBS patient was $318,966 in

2004 US dollars. To date, no deaths have been reported due to vaccine associated GBS in US military basic trainees. Direct costs of medical care for GBS were obtained from Frenzen's article, but because of differences in lost productivity and premature death rates between the general population and the US military, costs from lost productivity and premature death were excluded. Therefore, an average direct medical cost of GBS per patient was $196,317 in 2004 dollars. [145] This cost was adjusted to 2013 US dollars using the Consumer Price Index. [124] The 2013 average direct medical cost of GBS per patient used in this analysis was $243,342.66.

3.14. MODEL OUTCOMES

Since the outcome measure quality adjusted life year (QALY) is not operationally relevant to the DoD, the health – related outcome of training days lost (TDL) due to FRI was selected for the outcome of this cost – effectiveness analysis. Estimates for TDL for each branch of the decision tree were based on a review of the literature. Estimates for TDL included in this analysis are: (1) TDL due to systemic adverse reactions (2) TDL due to outpatient visits (3) TDL due to time spent in sick quarters (4) TDL due to time spent hospitalized for FRI (5) TDL due to time spent hospitalized for adenovirus pneumonia; (6) TDL due to reduced productivity.

3.14.1. TRAINING DAYS LOST TO SYSTEMIC ADVERSE REACTIONS

Systemic adverse events such as abdominal pain, diarrhea, headache and/or cough do not require a visit to a healthcare professional, but they do affect a basic trainee's productivity. Previous research on the effect vaccine adverse reactions have on work

productivity estimates that systemic adverse reactions decrease productivity by ten percent. [146] Systemic reactions can begin hours after vaccination and last up to two days, therefore, this study assumed systemic reactions lasted for 1.5 training days. [147] To calculate TDL due to systemic adverse reactions, number of days of decreased productivity was multiplied by the percentage of reduced effectiveness. Therefore, 0.15 training day was lost for each systemic adverse reaction.

3.14.2. TRAINING DAYS LOST TO GUILLAIN – BARRE SYNDROME

Once GBS symptoms develop, they can progress over the course of hours, days, or weeks. Most people reach the stage of greatest weakness within the first two weeks after symptoms appear. [143] Details in VAERS reports from the Phase IV study showed an average of 15 to 25 days between vaccination and disease onset. [142] This study assumed basic trainees developed GBS around the 21st day of training. Recovery from GBS is not quick, and the recovery period can range from a few weeks to a few years. [143] This analysis assumed that trainees did not return to basic training after a diagnosis of GBS. To calculate training days lost due to GBS, 21 training days were subtracted from the total number of basic training days for the respective service branch. For example, Army basic training lasts for 10 weeks, so subtract 21 days from 70 days to get 49 training days lost.

3.14.3. TRAINING DAYS LOST TO OUTPATIENT VISITS

Outpatient appointment times and basic trainee sick call, which is "a summons for those reporting sick to attend treatment," [148] both take time from training. One study performed

in Marine Corps basic trainees showed that on average, basic trainees spent around two hours at sick call. [149] A study performed by the Army looked at the benefits of a self – care program in soldiers and showed that on average, the length of time spent at a troop medical clinic visit was 1.4 hours. [150] An average of these two values (one hour, 40 minutes) was calculated, but since our outcome is in days, it was converted into 0.07 training day lost to be used in this analysis.

3.14.4. TRAINING DAYS LOST TO SICK QUARTERS

Previous Navy research stated that basic trainees receiving outpatient services who were not hospitalized spent an average of 2.5 days in sick quarters. [10] During an FRI outbreak at Fort Benning in 2000, basic trainees with FRI who were not hospitalized were placed in sick quarters for an average of 2.1 days. [47] Studies on training time lost to FRI in other service branches were not available. Therefore, an average of the two study values was calculated and used in this analysis. For this analysis, training days lost to sick quarters was 2.3 days.

3.14.5. TRAINING DAYS LOST TO FRI HOSPITALIZATION

Previous cost – effectiveness analyses used an average inpatient hospitalization stay of three to four days. [9 – 10] A 2002 study on an outbreak at the Naval Recruit Training Center showed that basic trainees lost an average of three training days because of fever and respiratory symptoms.[61] Another study of an FRI outbreak at an Army basic training site showed that basic trainees were hospitalized for an estimated 2.8 training days. [46] Based

on this literature, a three - day hospital stay, resulting in three lost training days, was used in this analysis.

3.14.6. TRAINING DAYS LOST TO ADENOVIRAL PNEUMONIA HOSPITALIZATION

Literature on the development of adenoviral pneumonia as a result of FRI in military basic trainees is limited. The one study found addressing adenoviral pneumonia was conducted at Lackland Air Force Base and showed that adenoviral pneumonia patients spent an average of four days in the hospital. [64] Since this was the only literature available, four days was chosen as the length of a hospital stay due to adenoviral pneumonia.

3.14.7. TRAINING DAYS LOST DUE TO LOST PRODUCTIVITY

Basic trainees with FRI participating in training are likely to be less efficient. Several economic studies have addressed the impact influenza – like illness has on a worker's productivity. Three levels of reduced efficiency were analyzed in these studies, including 70 percent, 50 percent, and 30 percent. [146] Even though these studies were not performed in military basic trainees, the calculation used to determine lost productivity could be used in the military population. To calculate training days lost, the number of days basic trainees wait before visiting a health care professional was needed. One epidemiologic investigation of an FRI outbreak at Fort Jackson revealed that on average, basic trainees waited 3.1 days before seeking medical treatment for an FRI. [46] Therefore, basic trainees were less efficient for 3.1 days before seeking medical attention. Since this was the only

value found concerning the length of time basic trainees wait before seeking health care, it was the value used to calculate training days lost. This pre – treatment duration was assumed to be the same for all basic trainees seeking treatment. To calculate lost training days using 50 percent as the percent of reduced effectiveness, the number of days of reduced productivity (3.1 days) was multiplied by 50 percent to get 1.6 training days lost due to decreased productivity. Information on reduced productivity after outpatient and/or inpatient treatment does not exist. Therefore, lost productivity was only considered for the time period before treatment.

All TDL variables are shown in table 3.12.

3.15. WILLINGNESS – TO – PAY THRESHOLD

Little research on the amount individuals are willing to pay to avoid febrile respiratory illness exists. Since the US military is currently the only consumer of the adenovirus vaccine, no information is available on the DoD's willingness – to – pay (WTP) for FRI prevention. The DoD uses a different WTP threshold for each new vaccine. A common willingness – to – pay value used in economic analyses is $50,000 per quality – adjusted life year (QALY). However, using this threshold to judge new treatment is criticized for being unrealistic, not generalizable, and not scientifically defined. [151] Using the WTP threshold of $50,000 for vaccines is impractical.

A WTP threshold for adenovirus – associated FRI hospitalization was not published in the literature. Therefore, for part I, the WTP threshold was based on results from a 2007 survey that used time trade off or willingness – to – pay questions to ask respondents to

value seasonal influenza illness, including hospitalization, and possible vaccine – related adverse events. Median WTP amounts to avoid an influenza – related hospitalization ranged from $500 to $2,750. [152] To determine the WTP threshold for part I of this study, an average of the two values was calculated, which resulted in a WTP threshold of $1,625. Therefore, the WTP threshold to avoid FRI hospitalization was $1,625 per case.

Since an adenovirus vaccine WTP threshold was not published, studies analyzing WTP for flu – like illness, acute illness, and the influenza vaccine were used in this analysis. A 2012 study used a survey – based approach to measure individuals WTP to avoid death, blindness, and specific illnesses, with one of those illnesses being flu – like illness. The study found that the mean individuals were WTP to prohibit an episode of flu – like illness was $403 per day, which was $409 per day in 2013 US dollars. [153] Another study measured individuals WTP to avoid one symptom day of acute illness. Results showed the median WTP to avoid one symptom day of acute illness in 2000 dollars ranged from $67 for an acute illness with mild symptoms to $114 for an acute illness with severe symptoms. These values were converted to 2013 US dollars, which equaled $91 and $154 for mild and severe symptoms respectively.[154] Lastly, a 2001 survey – based study in North Carolina found people's WTP to avoid one day of influenza was $15.49, which is $20 in 2013 US dollars. [155] The WTP values from these articles were averaged and resulted in a WTP of $184. However, for this analysis, the WTP was rounded to $200. .

TABLE 3.12. REFERENCE CASE INPUT VARIABLES FOR ALL SERVICE BRANCHES

VARIABLES	BASE	LOW	HIGH	SOURCE
PROBABILITIES				
[P] of sick quarters only	0.950	0.760	0.990	[10]
[P] developing adenoviral pneumonia	0.08000	0.072	0.152	[136 – 139]
[P] systemic adverse reactions	0.10000	0.080	0.120	[146]
[P] Guillain – Barre Syndrome (GBS)	0.00005	0.000005	0.0005	[141 – 142]
COSTS				
Adenovirus vaccine				
Tablet costs	$125.45			[Expert]†
Shipping costs	$0.67			[Expert]†
Administration	$0.10			[9 – 10]
AdV vaccine total	$126.22	$100.98	$151.46	
GBS per patient	$243,342.66	$194,674.13	$292,011.19	[145]
TRAINING DAYS LOST (TDL)				
Systemic adverse reactions	0.15	0.03	0.18	[146 – 147]
Outpatient visits	0.07	0.056	0.084	[149 – 150]
Sick quarters	2.30	1	3	[10, 47]
FRI Hospitalization	3	1	12	[9 – 10 , 46, 61]
Adenoviral pneumonia hospitalization	4	3	7	[64]
Lost productivity	1.6	0.93	2.17	[46, 146]
GBS TDL				
ARMY	49	39	59	[141 – 142]
NAVY	35	28	42	
MARINE CORPS	63	50	76	
AIR FORCE	39	31	47	
COAST GUARD	35	28	42	

[P] = Probability; AdV = Adenovirus; FRI = Febrile Respiratory Illness; GBS = Guillain – Barre Syndrome; † Personal communication with Clifford Snyder, Jr.

3.16. SENSITIVITY ANALYSES – PART II

To determine the robustness of the model used in Part II, a one – way sensitivity analysis was performed on each cost, effectiveness, and probability parameter. A tornado diagram was constructed to indicate variables that showed the most change. A probabilistic sensitivity analysis using Monte Carlo simulation was performed on all parameters simultaneously. Triangular, beta, and gamma distributions were used for TDL, probabilities, and cost estimates respectively. When range estimates were not available in the literature, estimates for costs and probabilities were varied by +/- 20 percent.

3.17. ASSUMPTIONS FOR DECISION TREE - PART II

Assumptions made for decision tree model two are outlined below:

1. All basic trainees received the adenovirus vaccine within two days of arriving at the basic training site
2. FRI was assumed to be contracted from the basic training environment and transferred from person – to – person, so the potential for herd immunity was not included in this analysis
3. Due to the lack of a CPT code associated with FRI, the average maximum allowable charge for outpatient office visits for new patients (CPT codes 99201 – 99205) and established patients (CPT codes 99211 – 99215) was assumed to estimate outpatient costs
4. Due to the lack of one specific FRI – associated DRG code, an average reimbursement rate for DRG code 203 and DRG code 206 was calculated

ASSUMPTIONS FOR DECISION TREE – PART II (CONTINUED)

5. TRICARE reimbursement amounts were the actual costs allowed by the DoD for FRI treatment
6. Patients who attended an outpatient clinic and were not hospitalized were treated in sick quarters for 2.3 days
7. Basic trainees developed GBS around day 21 of training
8. Basic trainees who developed GBS did not return to basic training
9. Lost productivity pre – treatment duration was the same for all basic trainees

3.17. INPUT TABLES

TABLE 3.13 ARMY MODEL INPUT VARIABLES

VARIABLES	BASE	LOW	HIGH	SOURCE	COMMENTS
PROBABILITIES					
[P] of FRI without vaccine	0.085	0.068	0.102	[6, 117]	
[P] of FRI with vaccine	0.009	0.008	0.010	[117]	
[P] of hospitalization due to FRI	0.213	0.135	0.440	[46]	
TRAINING/DoD COSTS†					
Training per day	$240	$192	$288	[123]	
DoD Costs per day	$137	$50	$151	[125]	
Total	$377	$242	$439		
OUTPATIENT COSTS					
Outpatient visit, New	$83	$73	$113	[128]	Average cost of CPT codes 99201 - 99205
Outpatient visit, Est.	$52	$44	$73	[128]	Average cost of CPT codes 99211 - 99215
INPATIENT COSTS					
FRI hospitalization (DRG 203/206)	$7,175	$5,740	$8,610	[131]	[(Adjusted standardized amount)*(DRG weight)]
Adenoviral pneumonia (DRG 194 with complications)	$10,554	$8,443	$12,665	[131]	

[P] = Probability; DoD = Department of Defense; CPT = Current Procedural Terminology; FRI = Febrile Respiratory Illness; DRG = Diagnosis Related Group;† = Costs rounded to the nearest dollar

TABLE 3.14 NAVY MODEL INPUT VARIABLES

VARIABLES	BASE	LOW	HIGH	SOURCE	COMMENTS
PROBABILITIES					
[P] of FRI without vaccine	0.092	0.074	0.110	[6]	
[P] of FRI with vaccine	0.010	0.008	0.012	[119]	
[P] of hospitalization due to FRI	0.181	0.145	0.217	[Estimate]	Estimate based on hospitalization data for other services
TRAINING/DOD COSTS†					
Training per day	$268	$214	$321	[123]	
DoD Costs per day	$119	$48	$138	[125]	
Total per day	$387	$262	$459		
OUTPATIENT COSTS					
Outpatient, New	$97	$83	$129	[128]	Average cost of CPT codes 99201 - 99205
Outpatient, Est.	$58	$49	$83	[128]	Average cost of CPT codes 99211 - 99215
INPATIENT COSTS					
FRI hospitalization (DRG 203/206)	$4,065	$3,252	$4,878	[131]	[(Adjusted standardized amount)*(DRG weight)]
Adenoviral pneumonia (DRG 194 with complications)	$3,964	$3,172	$4,757	[131]	

[P] = Probability; * Great Lakes, IL falls in a domestic catchment area, so an adjusted standardized amount for a military treatment facility is not available for this training center; DoD = Department of Defense; CPT = Current Procedural Terminology; FRI = Febrile Respiratory Illness; DRG = Diagnosis Related Group;† = Costs rounded to the nearest dollar

TABLE 3.15 MARINE CORPS MODEL INPUT VARIABLES

VARIABLES	BASE	LOW	HIGH	SOURCE	COMMENTS
PROBABILITIES					
[P] of FRI without vaccine	0.045	0.036	0.054	[6]	
[P] of FRI with vaccine	0.004	0.003	0.004	[119]	
[P] of hospitalization due to FRI	0.259	0.207	0.311	[Estimate]	Estimate based on hospitalization data for other service branches
TRAINING/DoD COSTS†					
Training per day	$171	$136	$205	[123]	
DoD Costs per day	$115	$50	$134	[125]	
Total Per Day	$286	$186	$339		
OUTPATIENT COSTS					
Outpatient Visit, New	$87	$74	$117	[128]	Average cost of CPT codes 99201 - 99205
Outpatient Visit, Est.	$53	$45	$77	[128]	Average cost of CPT codes 99211 - 92215
INPATIENT COSTS					
FRI hospitalization (DRG 203/206)	$9,075	$7,260	$10,890	[131]	[(Adjusted standardized amount)*(DRG weight)]
Adenoviral pneumonia (DRG 194 with complications)	$13,190	$10,558	$15,828	[131]	

[P] = Probability; DoD = Department of Defense; CPT = Current Procedural Terminology; FRI = Febrile Respiratory Illness; DRG = Diagnosis Related Group; † = All costs are rounded to the nearest dollar

TABLE 3.16 AIR FORCE MODEL INPUT VARIABLES

VARIABLES	BASE	LOW	HIGH	SOURCE	COMMENTS
PROBABILITIES					
[P] of FRI without vaccine	0.108	0.086	0.130	[6]	
[P] of FRI with vaccine	0.014	0.011	0.017	[119]	
[P] of hospitalization due to FRI	0.198	0.159	0.238	[48]	
TRAINING/DoD COSTS†					
Training per day	$112	$90	$135	[123]	
DoD Costs per day	$110	$47	$129	[125]	
Total Per Day	$222	$137	$264		
OUTPATIENT COSTS					
Outpatient, New	$85	$73	$113	[128]	Average cost of CPT codes 99201 - 99205
Outpatient, Est.	$52	$44	$73	[128]	Average cost of CPT codes 99211 - 99215
INPATIENT COSTS					
FRI hospitalization (DRG 203/206)	$10,836	$8,669	$13,003	[131]	[(Adjusted standardized amount)*(DRG weight)]
Adenoviral pneumonia (DRG 194 with complications)	$15,940	$12,752	$19,128	[131]	

[P] = Probability; DoD = Department of Defense; CPT = Current Procedural Terminology; FRI = Febrile Respiratory Illness; DRG = Diagnosis Related Group;†= All costs rounded to the nearest dollar

TABLE 3.17 COAST GUARD MODEL INPUT VARIABLES

VARIABLES	BASE	LOW	HIGH	SOURCE	COMMENTS
PROBABILITIES					
[P] of FRI without vaccine	0.039	0.031	0.047	[6]	
[P] of FRI with vaccine	0.005	0.004	0.006	[119]	
[P] of hospitalization for FRI	0.181	0.145	0.217	[Estimate]	Estimate based on hospitalization data for other services
TRAINING/DOD COSTS‡					
Training per day	$254*	$251	$301	[123]	
DoD Costs per day	$119	$49	$148	[125]	
Total Per Day	$373	$300	$449		
OUTPATIENT COSTS					
Outpatient, New	$95	$79	$128	[128]	Average cost of CPT codes 99201 - 99205
Outpatient, Est.	$56	$48	$83	[128]	Average cost of CPT codes 99211 - 99215
INPATIENT COSTS					
FRI hospitalization (DRG 203/206)	$4,219	$3,375	$5,063	[131]	[(Adjusted standardized amount)*(DRG weight)]
Adenoviral pneumonia (DRG 194 with complications)	$5,642	$4,575	$6,771	[131]	

[P] = Probability; *Training costs for the US Coast Guard are not available, so this is an estimate based on the average of other service branch training costs; † Cape May, New Jersey does not fall in a military treatment facility catchment area, so costs are based on adjusted standardized amount for domestic inpatient facility; ‡ = All costs are rounded to the nearest dollar; DoD = Department of Defense; CPT = Current Procedural Terminology; FRI = Febrile Respiratory Illness; DRG = Diagnosis related group

CHAPTER 4: RESULTS

Chapter 4 includes the results of each of the study objectives, cost – effectiveness analyses, and sensitivity analyses. Results are divided into two parts based on the model that was used.

4.1. OBJECTIVES FOR PART I

Part I used Howell et al.'s and Hyer et al.'s decision tree with current military service branch – specific information from the literature and experts on the adenovirus vaccine to accomplish objectives one through four.

4.1.1. OBJECTIVE 1 was to calculate and compare direct medical costs, including inpatient and outpatient costs only, for the adenovirus vaccination strategy and the no vaccination strategy. The hypothesis tested for this objective was that annual direct medical costs associated with adenovirus type 4 and type 7 vaccination were less than annual direct medical costs associated with no vaccination. This hypothesis was the same for all service branches of the US military.

H_1: Direct Medical Costs $_{\text{AdV Vaccination}}$ < Direct Medical Costs $_{\text{No Vaccination}}$

Direct medical costs associated with FRI treatment included outpatient office visits and hospitalizations. Vaccine costs were not included in direct medical costs.

4.1.1.1. ARMY

Direct medical costs for the Army were based on an annual basic trainee population of 75,373. The adenovirus vaccination program cost the Army approximately $1.1 million annually in direct medical costs, while no vaccination costs $10.4 million. This showed

that annual direct medical costs with the adenovirus vaccination program were less than direct medical costs associated with no adenovirus vaccination. Therefore, hypothesis 1 was not rejected for the Army.

4.1.1.2. NAVY

Direct medical costs for the Navy were based on an annual basic trainee population of 36,565. The adenovirus vaccination program cost the Navy approximately $330,838 in direct medical costs, while no adenovirus vaccination costs $2.83 million. This indicated that direct medical costs to the Navy associated with adenovirus program were less than those associated with no adenovirus vaccination, leading to hypothesis 1 not being rejected.

4.1.1.3. MARINE CORPS

Direct medical costs for the Marine Corps were based on an annual basic trainee population of 29,757. The adenovirus vaccination program cost the Marine Corps approximately $282,196 in direct medical costs, while no adenovirus vaccinations costs $3.27 million in direct medical costs. This showed that direct medical costs to the Marine Corps associated with the adenovirus program were less than those associated with no AdV vaccination, leading to hypothesis 1 not being rejected.

4.1.1.4. AIR FORCE

Direct medical costs for the Air Force were based on an annual basic trainee population of 36,392. The adenovirus vaccination program cost the Air Force approximately $1.1

million annually in direct medical costs, while no vaccination direct medical costs equaled $8.8 million. This showed that annual direct medical costs to the Air Force associated with the adenovirus program are less than those associated with no vaccination, leading to hypothesis 1 not being rejected.

4.1.1.5. COAST GUARD

Direct medical costs for the Coast Guard were based on an annual basic trainee population of 2,136. The adenovirus program cost the Coast Guard approximately $9,327 annually, while no vaccination direct medical costs equaled $72,274. This illustrated that annual direct medical costs to the Coast Guard associated with the adenovirus program were less than those associated with no vaccination, leading the researcher to not reject hypothesis 1.

4.1.1.6. SUMMARY HYPOTHESIS 1

Annual direct medical costs associated with adenovirus vaccination were less than those associated with no adenovirus vaccination in all service branches of the US military. Hypothesis 1 was not rejected for each service branch in the military.

4.1.2. OBJECTIVE 2 was to estimate and compare annual lost training costs associated with adenovirus vaccination and no vaccination. Hypothesis 2 posited that lost training costs associated with adenovirus type 4 and type 7 vaccination were less than lost training costs associated with no vaccination

$$\mathbf{H_2: Lost\ Training\ Costs_{\ AdV\ Vaccination} < Lost\ Training\ Costs_{\ No\ Vaccination}}$$

As mentioned above, training costs include actual training costs of the facility and costs to the DoD.

4.1.2.1. ARMY

The adenovirus vaccination strategy cost the Army approximately $720,447 annually in lost training costs, while the no adenovirus strategy cost the Army approximately $6.81 million in lost training costs. These numbers indicated that lost training costs for the adenovirus vaccination strategy were less than lost training costs for the no adenovirus vaccination strategy, leading the researcher to not reject hypothesis 2.

4.1.2.2. NAVY

The adenovirus vaccination strategy costs the Navy approximately $392,418 annually in lost training costs, while the no adenovirus strategy costs the Navy approximately $3.61 million in lost training costs. Therefore, annual lost training costs for the adenovirus vaccination strategy were less than annual lost training costs for the no vaccination strategy, leading the researcher to not reject hypothesis 2.

4.1.2.3. MARINE CORPS

The adenovirus vaccination strategy costs the Marine Corps approximately $98,098 annually in lost training costs, while the no adenovirus strategy costs the Marine Corps approximately $1.11 million in lost training costs. Therefore, annual lost training costs for the adenovirus vaccination strategy were less than annual lost training costs for the no vaccination strategy, leading the researcher to not reject hypothesis 2.

4.1.2.4. AIR FORCE

The adenovirus vaccination strategy costs the Air Force approximately $316,794 annually in lost training costs, while the no adenovirus strategy costs the Air Force approximately $2.4 million in lost training costs. Therefore, annual lost training costs for the adenovirus vaccination strategy were less than annual lost training costs for the no vaccination strategy, leading the researcher to not reject hypothesis 2.

4.1.2.5. COAST GUARD

The adenovirus vaccination strategy costs the Coast Guard approximately $11,563 annually in lost training costs, while the no adenovirus strategy costs the Coast Guard approximately $85,790 in lost training costs. Therefore, annual lost training costs for the adenovirus vaccination strategy were less than annual lost training costs for the no vaccination strategy, leading the researcher to not reject hypothesis 2.

4.1.2.6. SUMMARY HYPOTHESIS 2

Annual lost training costs associated with adenovirus vaccination were less than those associated with no adenovirus vaccination in all service branches of the US military. Hypothesis 2 was not rejected for each service branch in the military.

4.1.3. OBJECTIVE 3 was to estimate annual total costs associated with the adenovirus vaccination strategy and the no vaccination strategy. The hypothesis tested for objective 3 postulates that annual total costs associated with the adenovirus vaccination strategy are less than

annual total costs associated with the no adenovirus vaccination strategy. Annual total costs included vaccination, direct medical, and lost training costs.

H_3: Total Costs $_{AdV\ Vaccination}$ < Total Costs $_{No\ Vaccination}$

4.1.3.1. ARMY

The adenovirus vaccination strategy costs the Army approximately $11.3 million annually in total costs, while the no adenovirus strategy costs the Army $17.2 million in total costs. Therefore, total annual costs for the adenovirus vaccination strategy were less than total annual costs for the no vaccination strategy, leading the researcher to not reject hypothesis 3.

4.1.3.2. NAVY

The adenovirus vaccination strategy costs the Navy approximately $5.34 million in total annual costs, while the no adenovirus strategy costs the Navy $6.44 million in total annual costs. Therefore, total annual costs for the adenovirus vaccination strategy were less than total annual costs for the no vaccination strategy, leading the researcher to not reject hypothesis 3.

4.1.3.3. MARINE CORPS

The adenovirus vaccination strategy costs the Marine Corps approximately $4.14 million in total annual costs, while the no adenovirus strategy costs the Marine Corps $4.37 million in total annual costs. Therefore, total annual costs for the adenovirus vaccination

strategy were less than total annual costs for the no vaccination strategy, leading the researcher to not reject hypothesis 3.

4.1.3.4. AIR FORCE

The adenovirus vaccination strategy costs the Air Force approximately $6.04 million in total annual costs, while the no adenovirus strategy costs the Air Force $11.25 million in total annual costs. Therefore, total annual costs for the adenovirus vaccination strategy to the Air Force were less than total annual costs for the no vaccination strategy, leading the researcher to not reject hypothesis 3.

4.1.3.5. COAST GUARD

The adenovirus vaccination strategy costs the Coast Guard approximately $290,496 in total annual costs, while the no adenovirus strategy costs the Coast Guard $158,064 in total annual costs. In contrast to all other service branches, total annual costs for the adenovirus vaccination strategy to the Coast Guard were greater than total annual costs for the no vaccination strategy, leading to the rejection of hypothesis 3.

4.1.3.6. SUMMARY HYPOTHESIS 3

Annual total costs associated with adenovirus vaccination were less than those associated with no adenovirus vaccination in all service branches of the US military except for the Coast Guard. Hypothesis 3 was not rejected for the Army, Navy, Marine Corps, and Air Force, but rejected for the Coast Guard. All numbers for the first three hypotheses are shown in Table 4.1.

TABLE 4.1 REFERENCE CASE EXPECTED COSTS† UNDER ADENOVIRUS VACCINATION STRATEGIES FOR U.S. SERVICE BRANCHES

VACCINATION STRATEGY	VACCINE COSTS	MEDICAL COSTS	TRAINING COSTS	TOTAL COSTS	TOTAL COST SAVINGS
ARMY (n = 75,373)					
AdV Vaccination	$9,513,580	$1,071,923	$720,447	$11,305,950	$5,879,094
No Vaccination		$10,374,539	$6,810,505	$17,185,044	
NAVY (n = 36,565)					
AdV Vaccination	$4,615,234	$330,838	$392,418	$5,338,490	$1,096,950
No Vaccination		$2,827,052	$3,608,388	$6,435,440	
MARINE CORPS (n = 29,757)					
AdV Vaccination	$3,755,929	$282,196	$98,098	$4,136,223	$238,056
No Vaccination		$3,268,031	$1,106,248	$4,374,279	
AIR FORCE (n = 36,592)					
AdV Vaccination	$4,593,398	$1,130,879	$316,794	$6,041,071	$5,204,057
No Vaccination		$8,804,904	$2,440,224	$11,245,128	
COAST GUARD (n = 2,136)					
AdV Vaccination	$269,606	$9,327	$11,563	$290,496	- $132,432
No Vaccination		$72,274	$85,790	$158,064	

AdV: Adenovirus; †Costs are rounded to the nearest dollar

4.1.4. OBJECTIVE 4 was to evaluate the cost – effectiveness of adenovirus vaccines as measured by FRI hospitalizations prevented by computing an incremental cost – effectiveness ratio (ICER). A negative incremental cost – effectiveness ratio indicates a cost – saving strategy. Hypothesis 4 postulated that the ICER was less than zero.

H_4: ICER < 0

4.1.4.1. ARMY, NAVY, MARINE CORPS, AND AIR FORCE

Before calculating the ICER, annual number of FRI hospitalizations prevented was calculated in each service branch for each vaccination strategy. Adenovirus vaccination prevented 1,221, 543, 317, 677, and 13 FRI hospitalizations annually in the Army, Navy, Marine Corps, Air Force, and Coast Guard respectively. This number was then divided by annual number of basic trainees to determine the average number of FRI hospitalizations prevented. Table 4.2 shows the base case results of the decision analysis in terms of incremental cost – effectiveness. The ICER was negative in all service branches but the Coast Guard. These resulting ICER values indicate that adenovirus vaccination is the dominant strategy compared with no adenovirus vaccination when measured by hospitalizations for FRI prevented. Therefore, hypothesis 4 is not rejected in all service branches but the Coast Guard.

4.1.4.2. COAST GUARD

The Coast Guard was the only service branch in the military that resulted in a positive ICER. Implementation of the adenovirus vaccination program costs the

Coast Guard $10,187 per case of FRI hospitalization prevented, which was greater than the WTP threshold of $1,625 per case of FRI hospitalization.

4.1.4.3. SUMMARY HYPOTHESIS 4

The ICER as measured by hospitalizations prevented was less than 0 in the Army, Navy, Marine Corps, and Air Force. However, the Coast Guard's ICER was greater than 0. These results indicate that the adenovirus vaccination strategy is the dominant strategy when compared to a no vaccination strategy in the Army, Navy, Marine Corps, and Air Force.

TABLE 4.2. BASE CASE COST – EFFECTIVENESS OF ADENOVIRUS VACCINATION STRATEGIES

ALTERNATIVE	COST ($)†	EFF	IC ($)	IE	ICER ($/case prevented)
ARMY					
AdV Vaccination	$150	0.0019			
No Vaccination	$228	0.0181	$78	-0.0162	-4,815
NAVY					
AdV Vaccination	$146	0.0018			
No Vaccination	$176	0.0167	$30	-0.0149	-2,013
MARINE CORPS					
AdV Vaccination	$139	0.0010			
No Vaccination	$147	0.0117	$8	-0.0107	-748
AIR FORCE					
AdV Vaccination	$166	0.0028			
No Vaccination	$309	0.0214	$142	-0.0186	-7,634
COAST GUARD					
AdV Vaccination	$136	0.0009			
No Vaccination	$74	0.0070	- $62	-0.0061	-10,163

EFF = Effectiveness in terms of cases of FRI hospitalization; IC = Incremental Cost; IE = Incremental Effectiveness; ICER = Incremental Cost – Effectiveness Ratio; AdV = Adenovirus; † = All costs are rounded to the nearest dollar; ICER is interpreted as cost per hospitalization prevented

4.2. SENSITIVITY ANALYSIS FOR PART 1 TORNADO DIAGRAMS

Tornado diagrams show which model parameters have the largest impact on the decision analysis model. For each service branch, a tornado diagram was produced for all cost and probability parameters.

4.2.1. ARMY

The cost and probability parameter tornado diagrams for the Army are shown in Figures 4.1 and 4.2. Figure 4.1 indicates that the cost of the adenovirus vaccine has the largest impact on the model, while results from Figure 4.2 show that probability of hospitalization due to FRI also has a large impact on the model.

FIGURE 4.1. ARMY: TORNADO DIAGRAM - COSTS

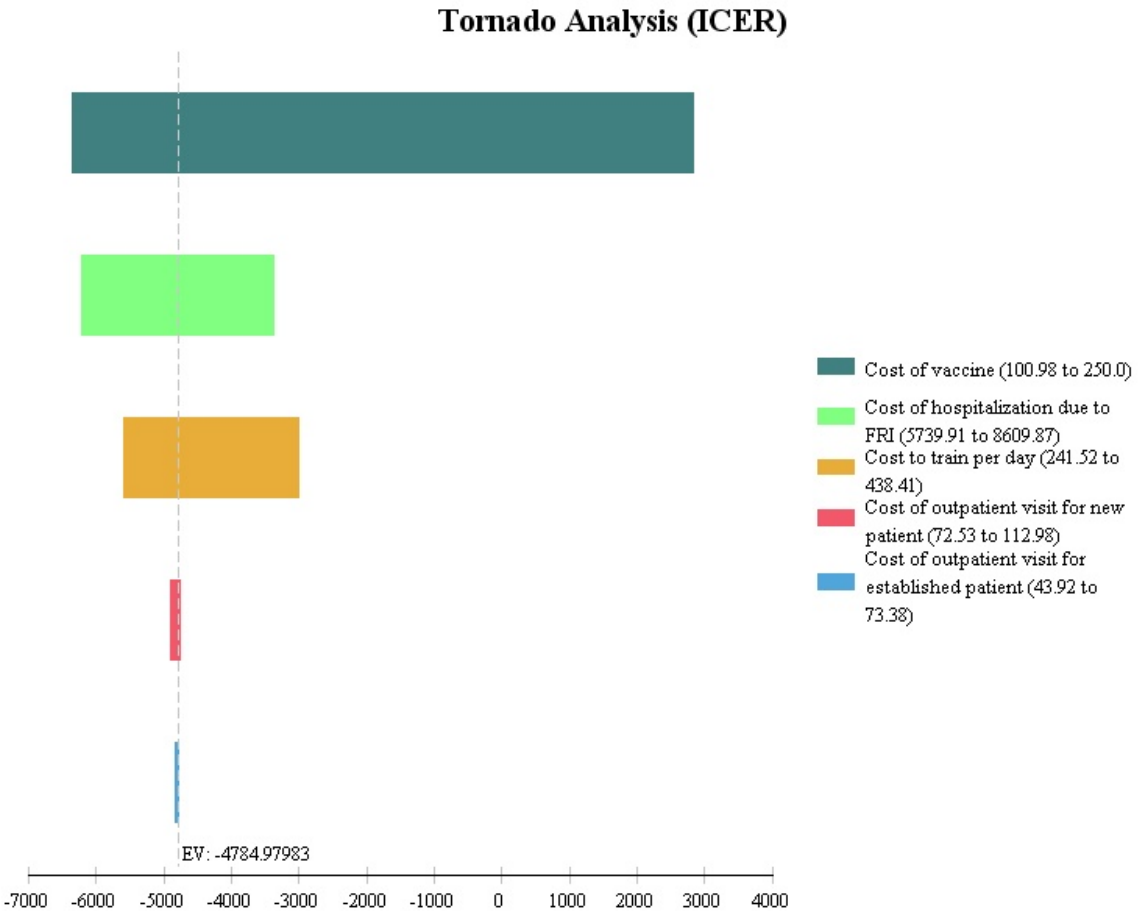
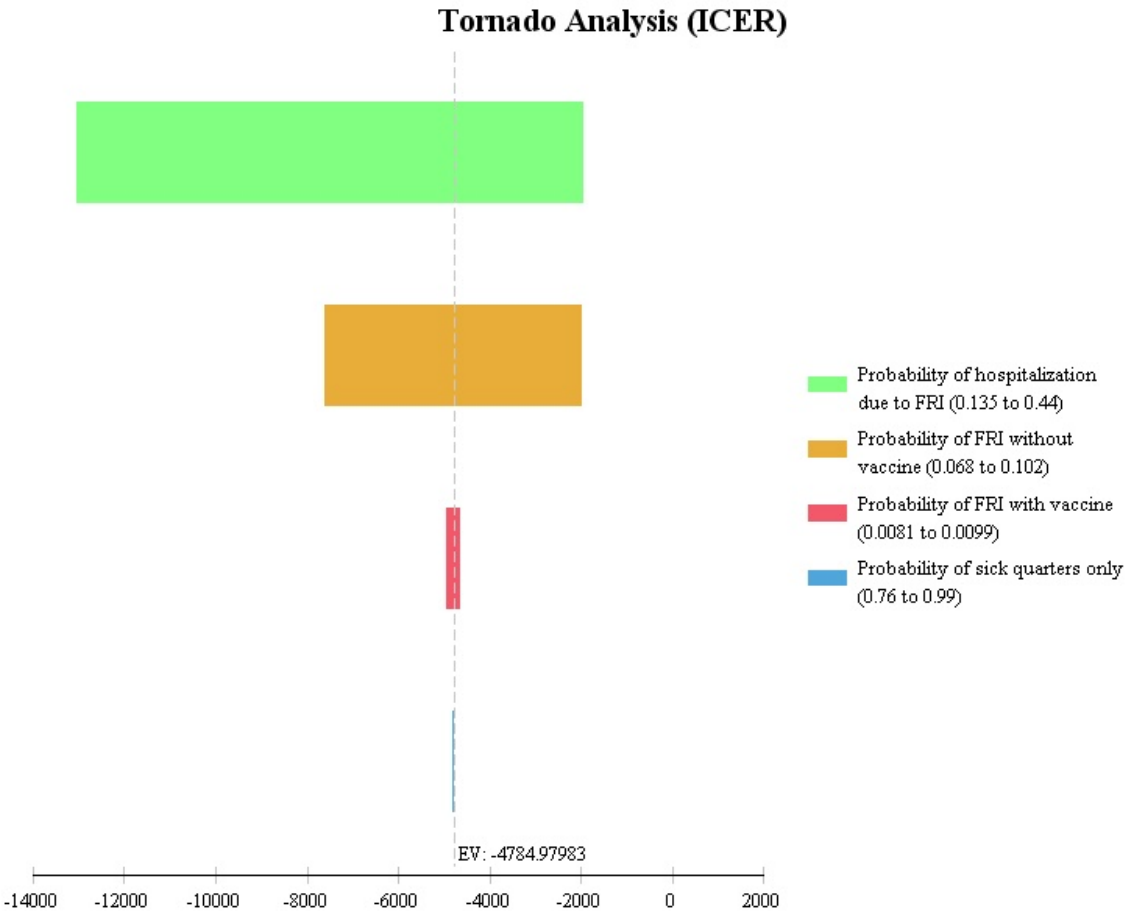


FIGURE 4.2. ARMY: TORNADO DIAGRAM – PROBABILITIES



4.2.2. NAVY

Cost and probability tornado diagrams for the Navy are shown in Figures 4.3 and 4.4. Like with the Army, Figure 4.3 shows that the cost of the adenovirus vaccine had the largest impact on the model. Figure 4.4 shows that the probability of FRI during times without the adenovirus vaccination has a large impact on the Navy model.

FIGURE 4.3. NAVY: TORNADO DIAGRAM – COSTS

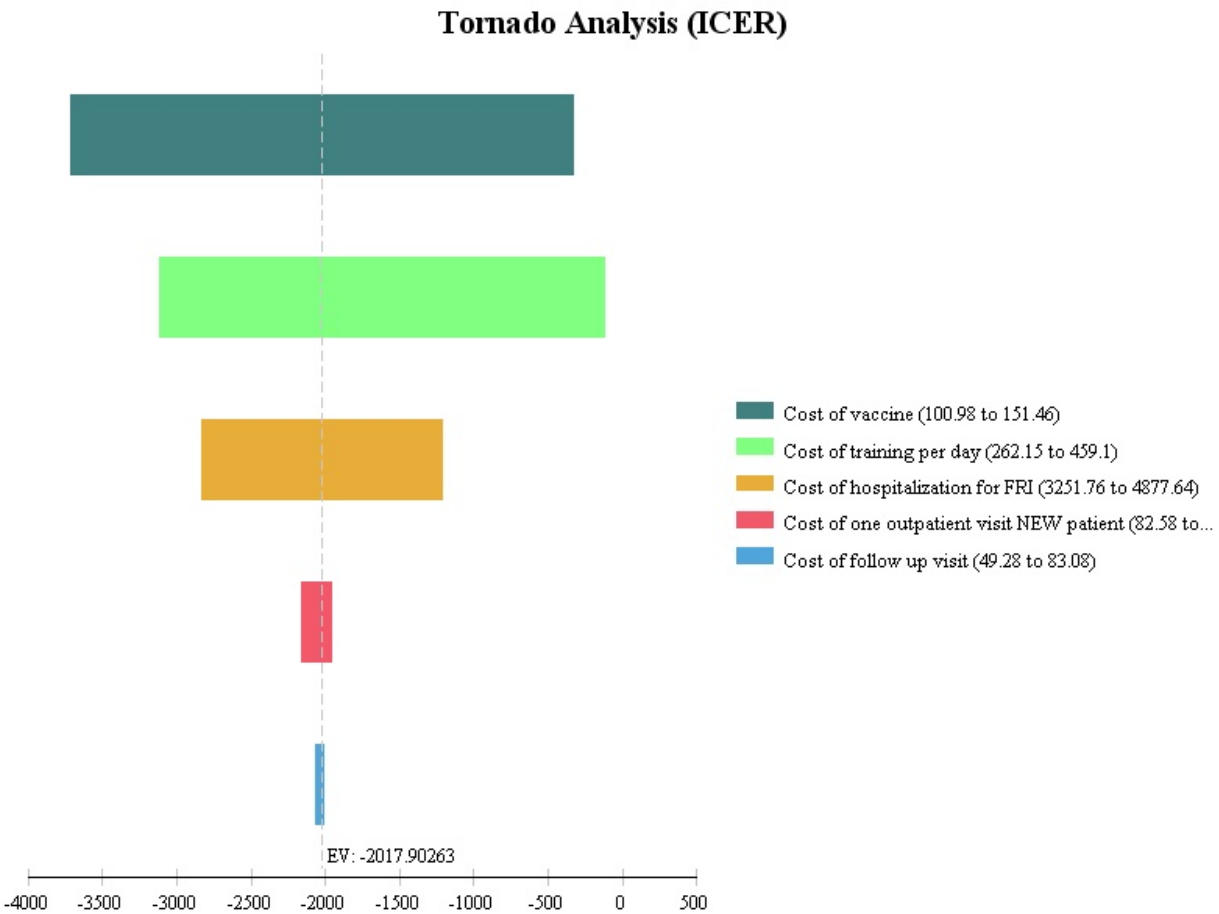
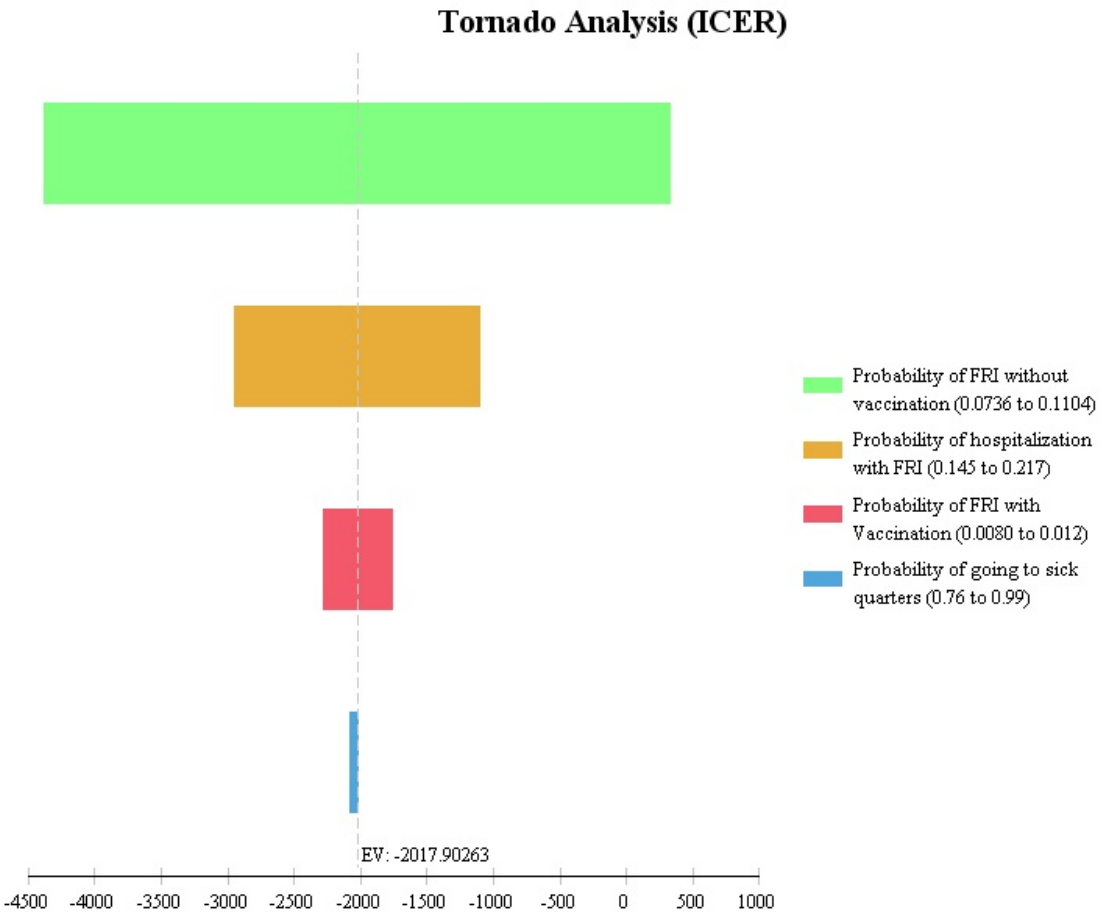


FIGURE 4.4. NAVY: TORNADO DIAGRAM – PROBABILITIES



4.2.3. MARINE CORPS

Figures 4.5 and 4.6 show cost and probability tornado diagrams for the Marine Corps. Just like the Army and Navy, the cost diagram, Figure 4.5, indicates that cost of vaccine has the largest impact on the model. The probability with the largest impact was the probability of FRI when adenovirus vaccination is not available, which is shown in Figure 4.6. The variable, cost of the adenovirus vaccine, had a threshold value of $134.

FIGURE 4.5. MARINE CORPS: TORNADO DIAGRAM – COSTS

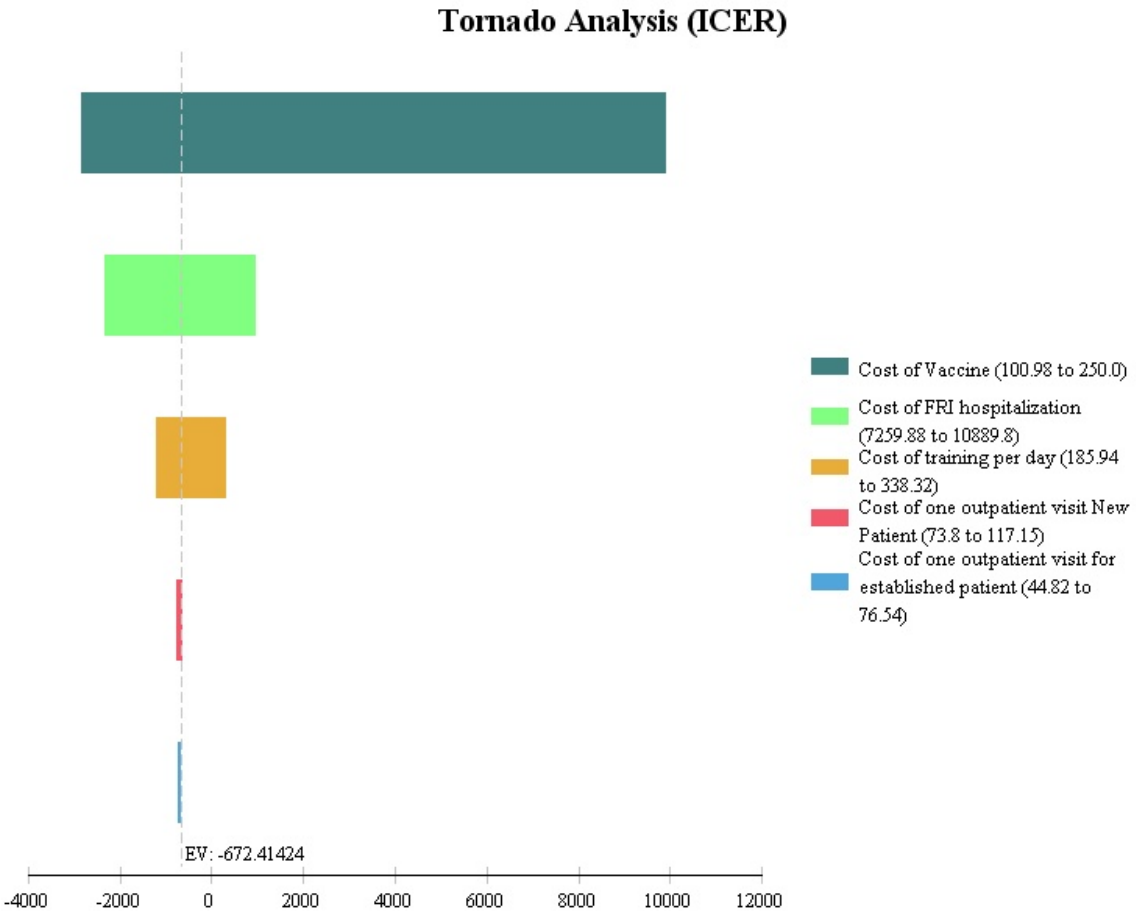
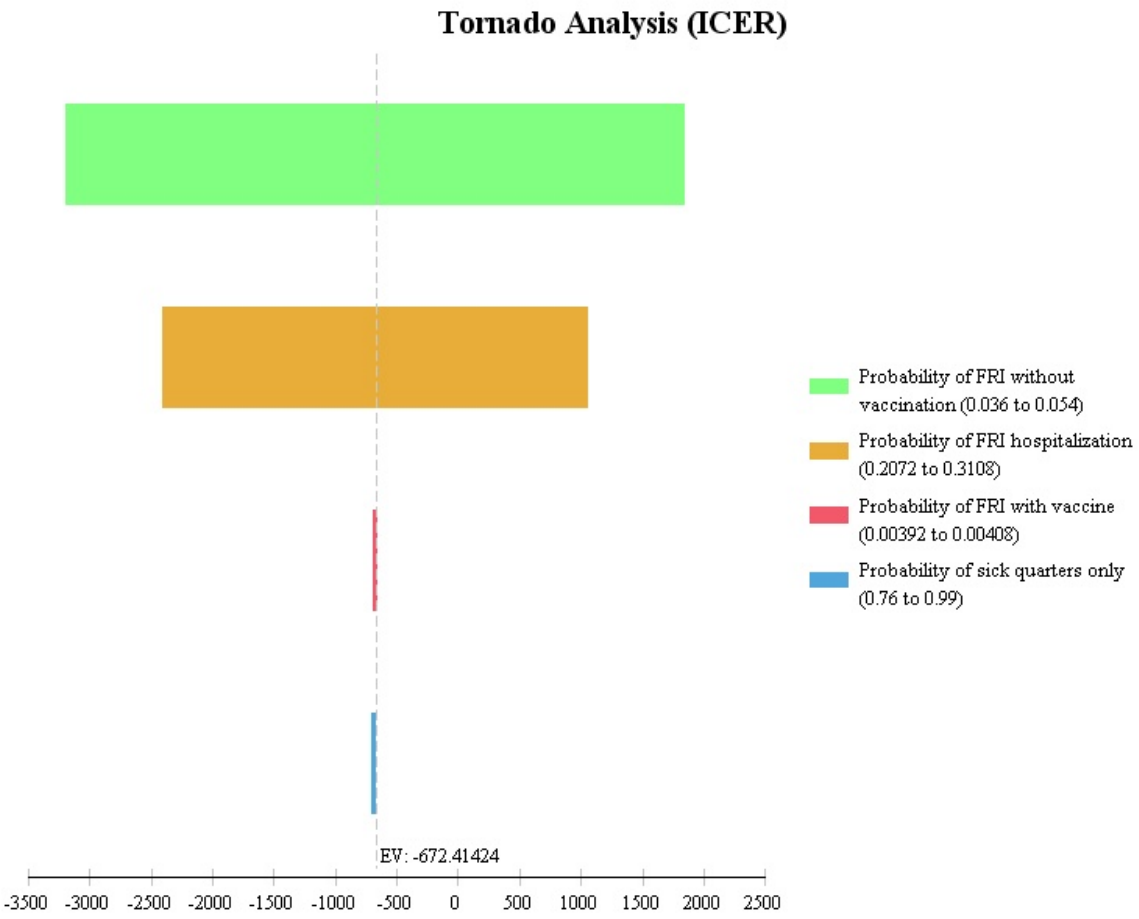


FIGURE 4.6. MARINE CORPS: TORNADO DIAGRAM – PROBABILITIES



4.2.4. AIR FORCE

Figures 4.7 and 4.8 show tornado diagrams for costs and probabilities for the Air Force. Like with the Army, Navy, and Marine Corps, the tornado diagram shows that the cost with the largest impact on the model was the cost of the adenovirus vaccine. The cost tornado diagram is shown in Figure 4.7. In addition, like the Navy and Marine Corps, the tornado diagram in Figure 4.8 indicates that the probability with the largest impact is the probability of FRI when an adenovirus vaccine is not available.

FIGURE 4.7. AIR FORCE: TORNADO DIAGRAM – COSTS

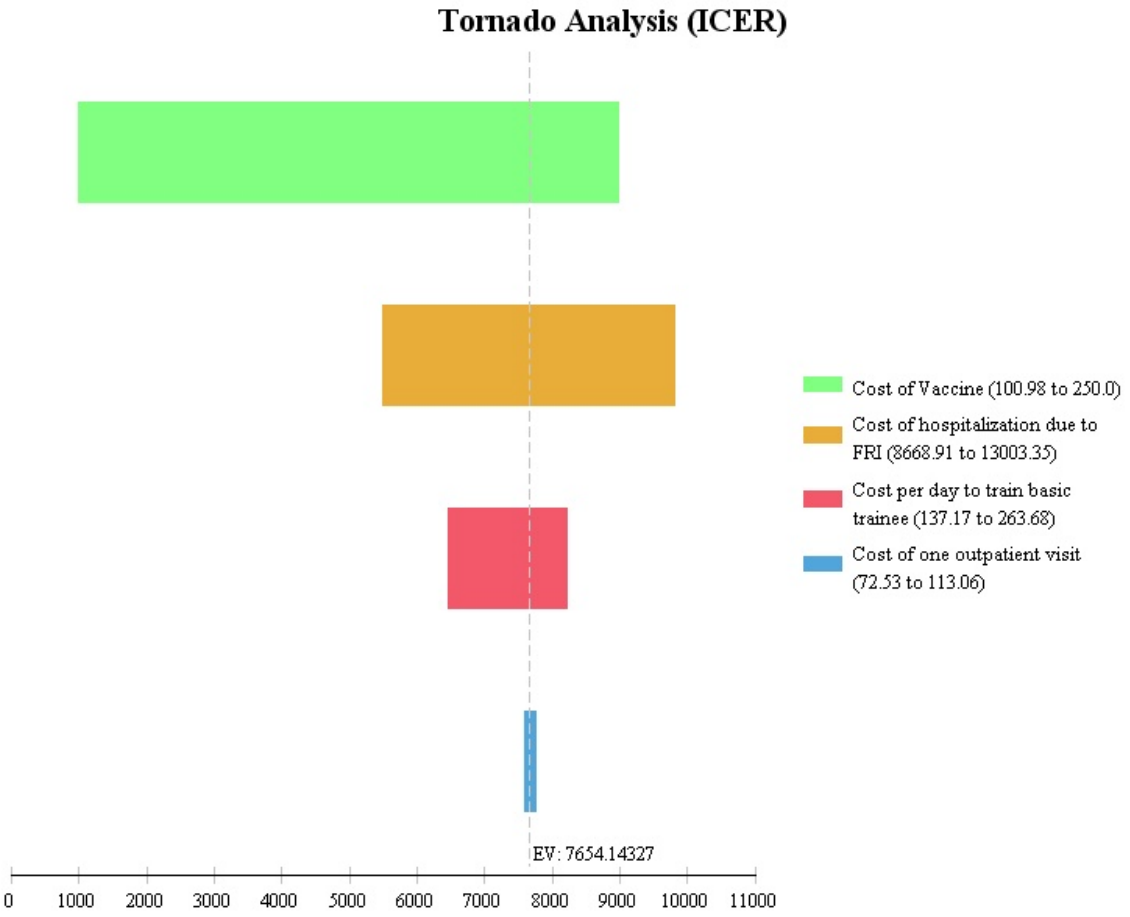
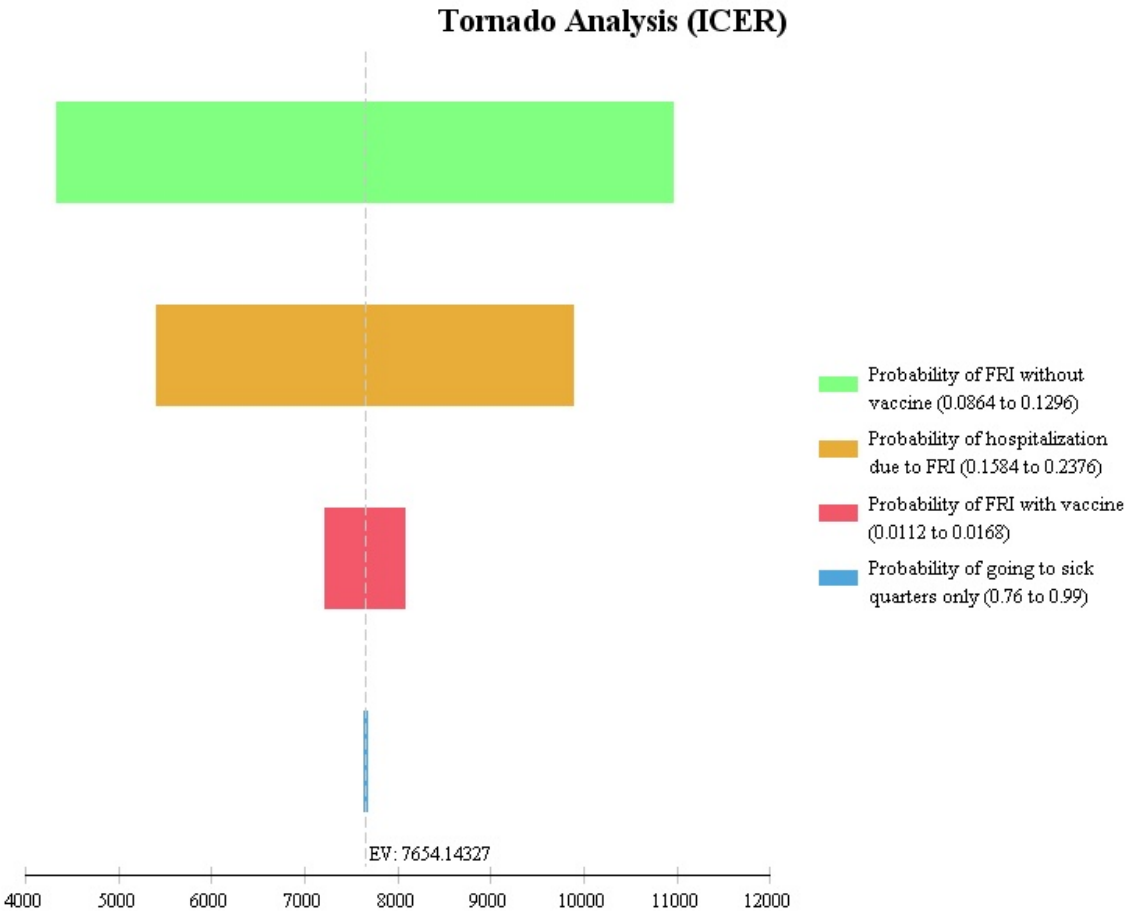


FIGURE 4.8. AIR FORCE: TORNADO DIAGRAM – PROBABILITIES



4.2.5. COAST GUARD

The tornado diagrams for the Coast Guard model are shown in Figures 4.9 and 4.10. Figure 4.9 shows that like all other service branches, the cost with the largest impact on the model is the cost of the vaccine. The probability tornado diagram also indicates that the probability with the largest impact is the probability of FRI when the adenovirus vaccine is not available. The probability tornado diagram is shown in Figure 4.10. This is the same result seen in all previous probability tornado diagrams except for the Army.

FIGURE 4.9. COAST GUARD: TORNADO DIAGRAM – COSTS

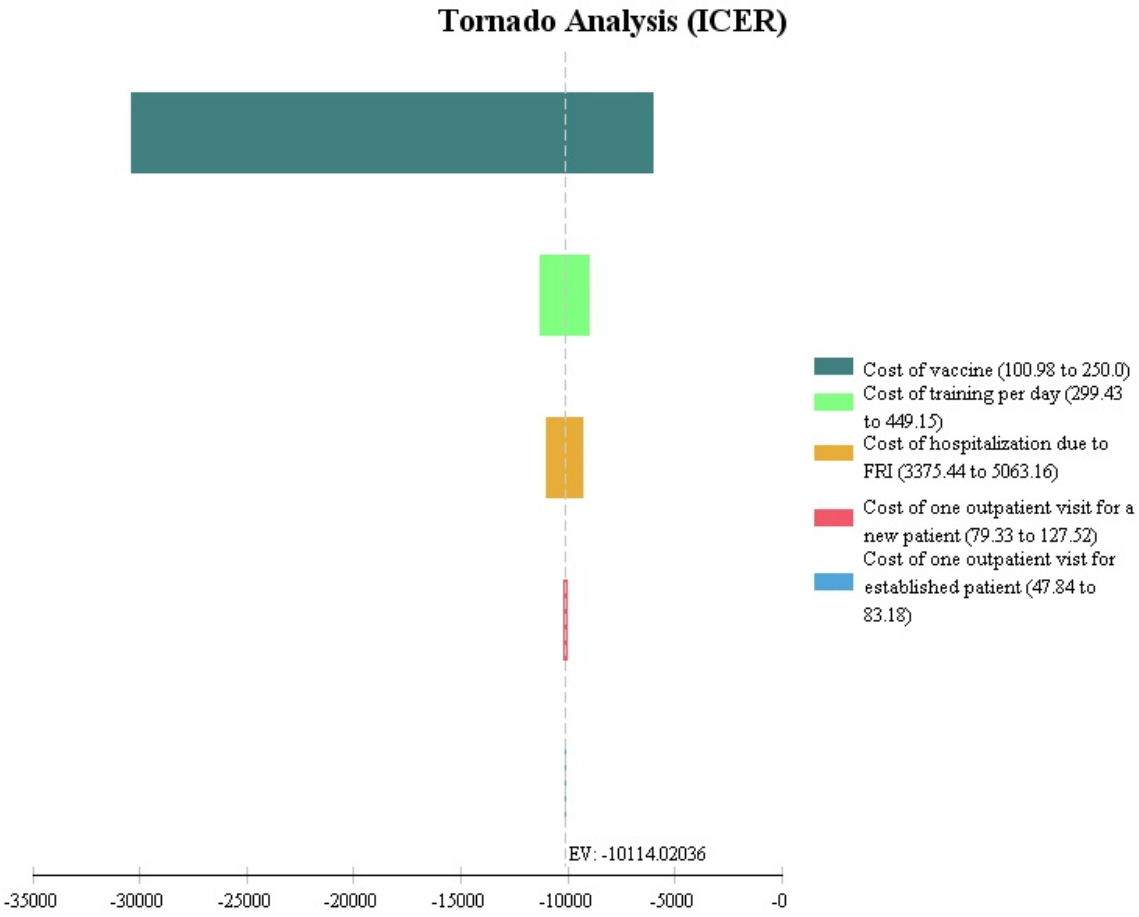
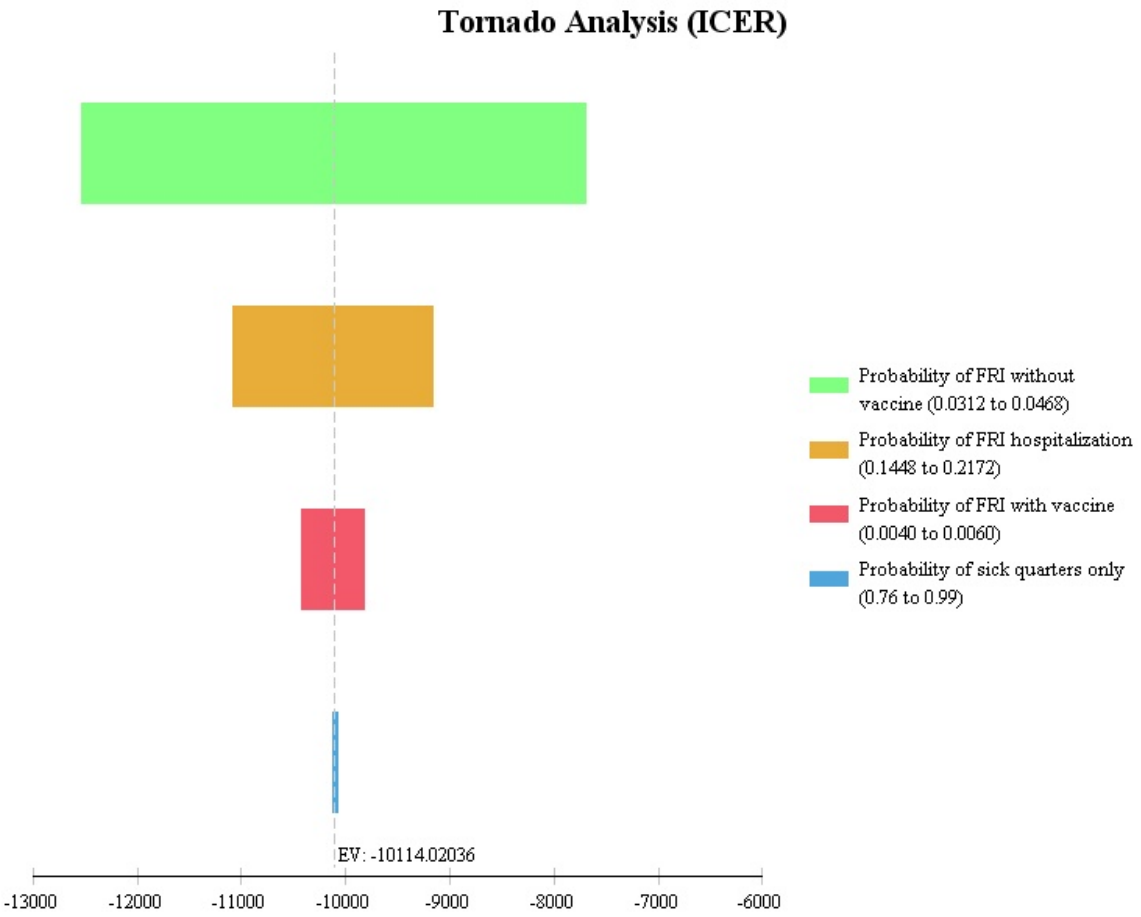


FIGURE 4.10. COAST GUARD – TORNADO DIAGRAM – PROBABILITIES



4.3. ONE – WAY SENSITIVITY ANALYSES – PART I

One – way sensitivity analyses were conducted on all cost (+/- 20%) and probability parameters (+/- 20%). The threshold value represents the point at which changes in the variable cause the vaccination strategy to no longer be cost – saving. If a variable was sensitive to changes in value, it was discussed below.

4.3.1. ARMY

The adenovirus vaccine strategy was the dominant strategy. Results were insensitive to variations in all cost estimates but the cost of the adenovirus vaccine. The threshold value was $204. Therefore, if the vaccine price increased to above $204, the no adenovirus vaccine strategy would be dominant.

4.3.2. NAVY

The adenovirus vaccine strategy was the dominant strategy. Results were insensitive to all variations in all cost estimates but the cost of the adenovirus vaccine. The threshold value was $156. If the price of the adenovirus vaccine was more than $156, the adenovirus vaccination strategy would not be the dominant strategy anymore.

4.3.3. MARINE CORPS

The adenovirus vaccine strategy was the dominant strategy for the Marine Corps. Results were insensitive to all variations in all cost estimates but the cost of the adenovirus vaccine and all probability values but the probability of FRI without

vaccination. The threshold value for cost of the vaccines was $134. If the price of the adenovirus vaccine was more than $134, the adenovirus vaccination strategy would not be the dominant strategy anymore. Further analysis of the variable, probability of FRI without vaccination, showed that when this value decreased below 0.0076, the adenovirus vaccination strategy ceased to be the dominant vaccination strategy.

4.3.4. AIR FORCE

The adenovirus vaccine strategy was the dominant strategy in Air Force basic trainees. Results were insensitive to variations in all cost and probability estimates.

4.3.5. COAST GUARD

Neither the adenovirus vaccine strategy nor the no vaccine strategy was dominant. Results were insensitive to variations in all cost and probability estimates.

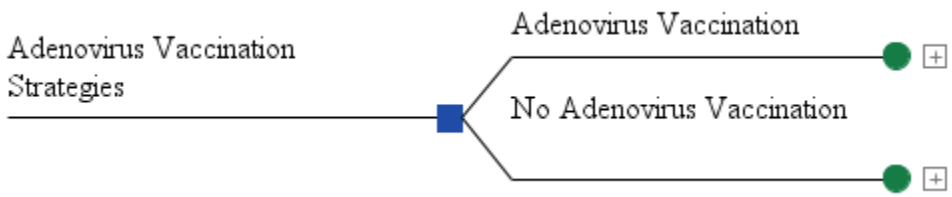
4.4. OBJECTIVES FOR PART II

4.4.1. OBJECTIVE 5 involved the development of a decision analysis model using military - specific data collected from the literature and experts on the military's adenovirus vaccine. No hypothesis was developed for this objective.

The final decision tree was developed using data collected from the literature and experts on the military's adenovirus vaccine. The decision tree is mainly based on Howell et al.'s

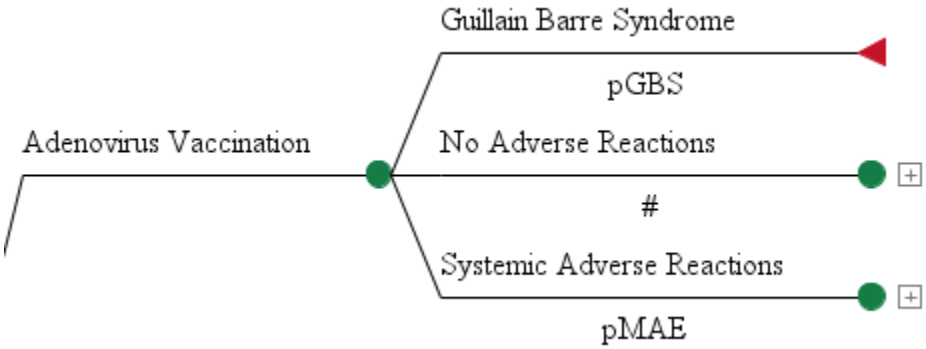
and Hyer et al.'s decision tree used in part 1 of this study. The model was assessed by estimating the average cost per training day lost. Figure 4.11 illustrates the two vaccination strategies compared. A description of model parameters is shown in appendix A.

FIGURE 4.11. ADENOVIRUS VACCINATION ALTERNATIVES



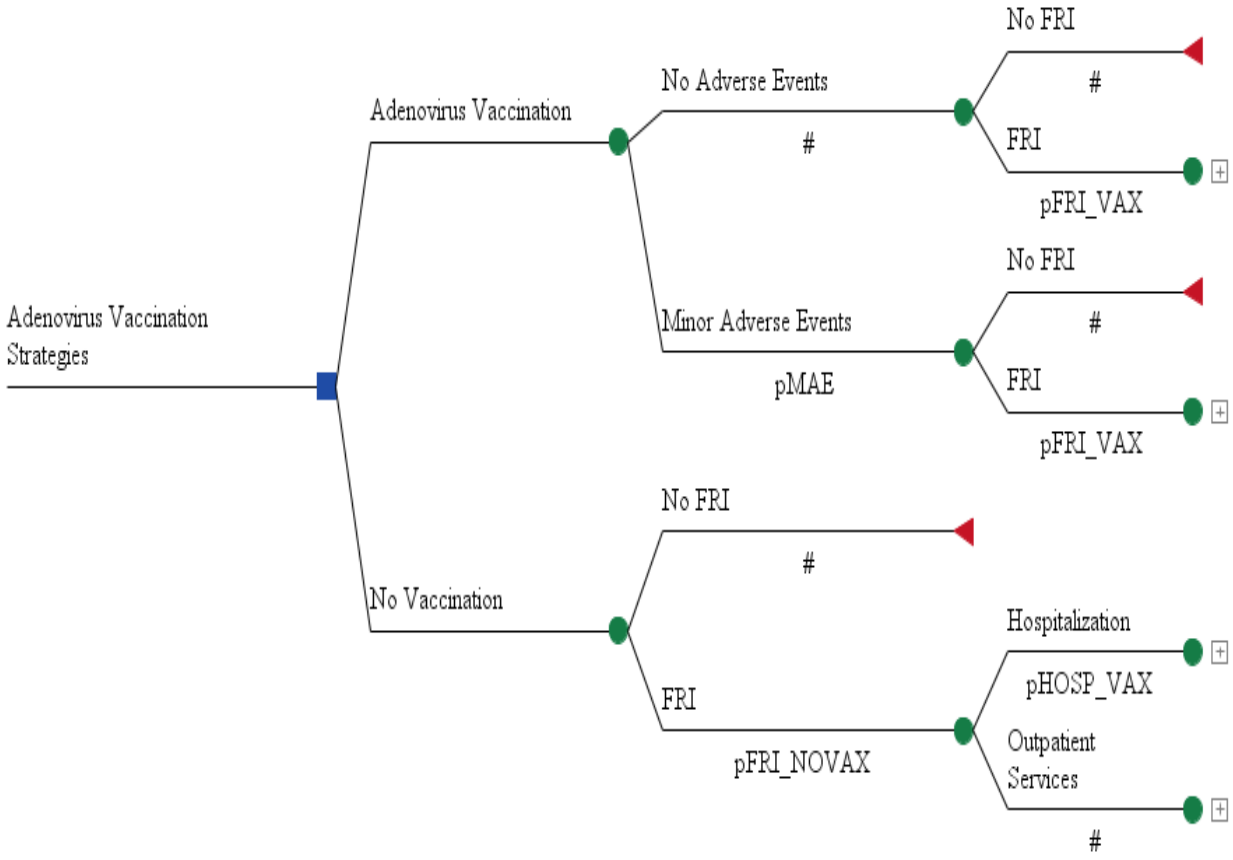
For the adenovirus vaccination branch, there are three possible adverse reaction pathways that are assessed: no adverse reactions, minor adverse reactions, and Guillain – Barre Syndrome. The GBS pathway is a terminal pathway because a basic trainee developing GBS will not return to basic training. The three pathways attached to the adenovirus vaccination branch are shown in Figure 4.12.

FIGURE 4.12. ADENOVIRUS VACCINE ADVERSE REACTION BRANCH



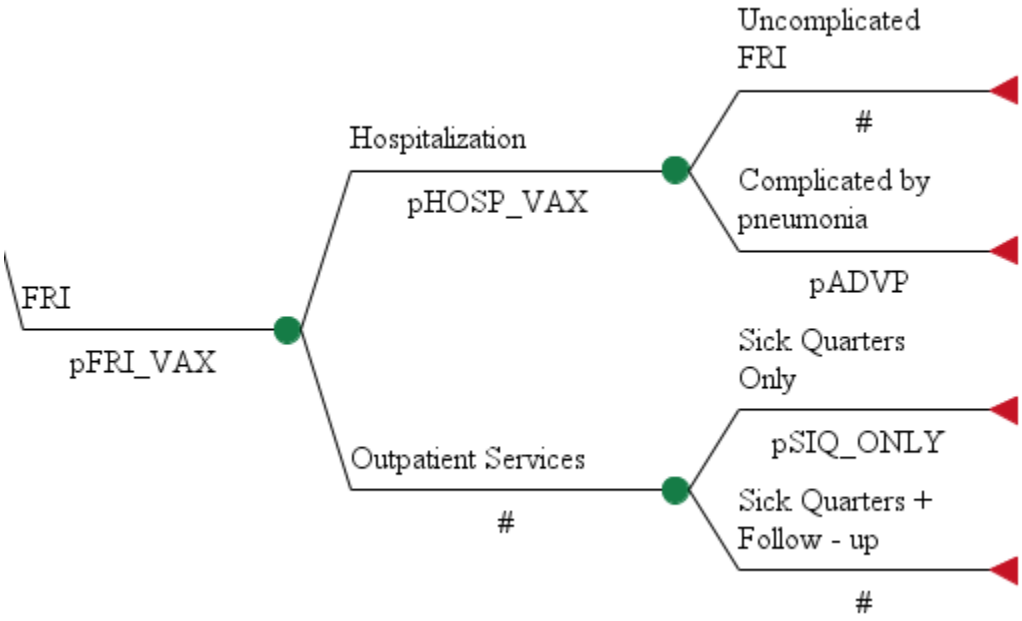
Two pathways are connected to the adverse reaction branches and are assessed. These pathways include a develop FRI branch and not develop FRI branch. The no FRI branch ends with a terminal node. From this point on, the branches for both vaccination strategies are identical. This is illustrated in figure 4.13.

FIGURE 4.13. FRI PATHWAYS FROM ALL BRANCHES



If a trainee develops FRI, he/she either receives outpatient treatment only, outpatient treatment with follow – up, or hospitalization. Two possible pathways diverge from the FRI branch. These pathways include outpatient treatment or hospitalization. This is shown in Figure 4.14.

FIGURE 4.14. DECISION TREE TERMINAL BRANCHES



The outpatient service branch terminates with sick quarters only or sick quarters plus a follow – up outpatient visit. The hospitalization branch terminates with uncomplicated FRI or FRI complicated by pneumonia.

4.4.2. OBJECTIVE 6 was to estimate and compare training days lost (TDL) associated with each adenovirus vaccination strategy. Hypothesis 5 postulates that TDL associated with adenovirus vaccination is less than TDL associated with no vaccination.

$$H_5: TDL_{\text{AdV Vaccination}} < TDL_{\text{No Vaccination}}$$

The average TDL is less than one day, so it is difficult to see the impact of the vaccination strategies. For clarity, the average TDL and annual TDL are reported for each service branch.

4.4.2.1. ARMY

For the Army, the average TDL for the adenovirus vaccination strategy was 0.05 TDL (1 hour, 12 minutes), while the average TDL for the no adenovirus vaccination strategy was 0.35 TDL (8 hours, 40 minutes). Annual TDL for the adenovirus vaccine strategy was 3,768.65, while the no vaccination strategy resulted in 26,380.55 TDL. When comparing the two adenovirus vaccination strategies, the average TDL averted was 0.30 and the annual TDL averted was 22,611.9. These results illustrate that TDL with the adenovirus vaccination strategy is less than TDL with the no vaccination strategy, which leads the researcher to not reject hypothesis 5.

4.4.2.2. NAVY

Results for the Navy show that the average TDL for the adenovirus vaccination strategy was 0.06 TDL (1 hour, 26 minutes), while the average TDL for the no adenovirus vaccination strategy was 0.38 TDL (9 hours). Annual TDL for the adenovirus vaccination strategy was 2,193.9 TDL, while the no vaccination strategy resulted in an annual TDL of 13,894.7 TDL. When comparing the two strategies, the average TDL averted (net outcome) was 0.32 and the annual TDL averted was 11,700.8. These results demonstrate that TDL with the adenovirus vaccination strategy is less than TDL with the no vaccination strategy in the Navy, which led the researcher to not reject hypothesis 5.

4.4.2.3. MARINE CORPS

Results for the Marine Corps show that average TDL for the adenovirus vaccination strategy was 0.02 TDL (30 minutes), while the average TDL for the no adenovirus vaccination strategy was 0.19 TDL (4 hours, 32 minutes). Annual TDL for the adenovirus vaccination strategy was 595.14 TDL and 5653.83 TDL for the no vaccination strategy. When comparing the two strategies, the average TDL averted was 0.17 and the annual TDL averted was 5,058.69. These results illustrate that TDL with the adenovirus vaccination strategy is less than TDL with the no vaccination strategy in the Marine Corps, which leads the researcher to not reject hypothesis 5.

4.4.2.4. AIR FORCE

Results for the Air Force show that average TDL for the adenovirus vaccination strategy is 0.06 TDL (1 hour, 26 minutes) and 0.45 TDL (10 hours, 40 minutes) for the no adenovirus vaccination strategy. Annual TDL for the adenovirus vaccination strategy is 2,183.52 TDL, while the annual TDL for the no vaccination strategy is 16,376.4 TDL. When comparing the two vaccination strategies, average TDL averted 0.39 and annual TDL averted was 14,192.88. These results show that TDL for the adenovirus vaccination strategy is less than TDL for the no vaccination

strategy, which leads the researcher to not reject hypothesis 5.

4.4.2.5. COAST GUARD

Results for the Coast Guard show that average TDL for the adenovirus vaccination strategy is 0.02 TDL (30 minutes) and 0.16 TDL (3 hours, 50 minutes) for the no vaccination strategy. Annual TDL for the adenovirus vaccination strategy is 42.72 TDL, while annual TDL for the no vaccination strategy is 341.76 TDL. When comparing the two adenovirus vaccination strategies, average TDL averted was 0.14 and annual TDL averted was 299.04. These Coast Guard results show that TDL for the adenovirus vaccination strategy is less than TDL for the no vaccination strategy, which leads the researcher to not reject hypothesis 5.

4.4.2.6. SUMMARY HYPOTHESIS 5

Average TDL for the adenovirus vaccination strategy were less than TDL for the no vaccination strategy in all service branches. Therefore, hypothesis 5 was not rejected for all service branches.

4.4.3. OBJECTIVE 7 was to estimate and compare the average total cost resulting from the adenovirus vaccination strategy and the no vaccination strategy. The hypothesis for this objective was that the average total cost for the adenovirus vaccination strategy was less than the average total cost for the no vaccination strategy.

H_6: Avg. Total Cost $_{\text{AdV Vaccination}}$ < Avg. Total Cost $_{\text{No Vaccination}}$

4.4.3.1. ARMY

Results for the Army show that the average total cost for the adenovirus vaccination strategy is $162.74, while the average total cost for the no adenovirus vaccination strategy is $221.29. When comparing the two strategies, the incremental cost shows that the no vaccination group's average total costs are $58.55 more than the adenovirus' group. This indicates the adenovirus vaccination strategy costs less than the no adenovirus vaccination strategy in the Army, which leads the researcher to not reject hypothesis 6.

4.4.3.2. NAVY

Navy results indicate that the average total cost for the adenovirus vaccination strategy is $157.27, while the average total cost for the no vaccination strategy is $166.80. The incremental cost when comparing the two strategies is $9.53, which means the average total cost in the no adenovirus group is $9.53.more than the average total cost in the adenovirus group. These results show that the adenovirus vaccination

strategy costs less than the no vaccination strategy in the Navy, which leads the researcher to not reject hypothesis 6.

4.4.3.3. MARINE CORPS

Marine Corps results suggest that the average total cost of the adenovirus vaccination strategy is $152.25, while the average total cost for the no vaccination strategy is $145.90. The incremental cost when comparing the two strategies is - $6.35, which means that the adenovirus vaccination strategy costs more than the no adenovirus vaccination strategy. Therefore, hypothesis 6 was rejected.

4.4.3.4. AIR FORCE

Air Force results indicate that the average total cost for the adenovirus vaccination strategy is $178.89 and the average total cost for the no vaccination strategy is $309.14. When comparing the two strategies, the incremental cost is $130.25, which indicates the adenovirus vaccination strategy cost less than the no vaccination strategy. The positive incremental cost shows that the adenovirus vaccination strategy costs less than the no adenovirus vaccination strategy in the Air Force, leading the researcher to not reject hypothesis 6.

4.4.3.5. COAST GUARD

Coast Guard results demonstrate that the average total cost for the adenovirus vaccination strategy is $148.11, while the average total cost for the no adenovirus vaccination strategy is $70.13. When comparing the two strategies, the incremental cost is - $77.98. The negative incremental cost shows that the adenovirus vaccination strategy costs more than the no adenovirus vaccination strategy in the Coast Guard, leading to the rejection of hypothesis 6.

4.4.3.6. SUMMARY FOR HYPOTHESIS 6

The hypothesis tested for objective 7 was that the average total cost for the adenovirus vaccination strategy was less than the average cost for the no adenovirus vaccination strategy. Army, Navy, and Air Force results led the researcher to not reject hypothesis 6, whereas Marine Corps and Coast Guard results led to the rejection of hypothesis 6.

4.4.4. OBJECTIVE 8 was to evaluate the cost – effectiveness of adenovirus vaccines as measured by TDL averted by computing an incremental cost – effective ratio (ICER). The hypothesis tested for this objective is that the ICER is negative, meaning the adenovirus vaccination strategy is cost saving.

H_7: ICER < 0

4.4.4.1. ARMY, NAVY, AND AIR FORCE

Incremental cost- effectiveness ratios for all service branches are shown in Table 4.3. The cost – effectiveness ratios for the Army, Navy, and Air Force are all negative. The negative ICER indicates that the adenovirus vaccination strategy is the dominant strategy or the most cost – effective strategy when compared with the no vaccination strategy. The negative ICER led the researcher to not reject hypothesis 7.

4.4.4.2. MARINE CORPS AND COAST GUARD

The cost – effectiveness ratio for the Marine Corps and Coast Guard are both positive. Neither strategy is dominant, so the decision to use the adenovirus vaccine depends on what the service branch is willing – to – pay per TDL avoided. The interpretation of the cost – effectiveness ratio for the Marine Corps is that they pay $37.35 per TDL averted. The interpretation of the cost – effectiveness ratio for the Coast Guard is $557.00 per TDL averted. The positive ICERs led to the rejection of hypothesis 7 for the Marine Corps and Coast Guard.

TABLE 4.3. BASE CASE COST – EFFECTIVENESS OF ADENOVIRUS STRATEGIES FOR U.S. SERVICE BRANCHES

ALTERNATIVE	COST ($)	EFF	IC ($)	IE	ICER ($/TDL)
ARMY					
AdV Vaccination	$162.74	0.05			
No Vaccination	$221.29	0.35	$58.55	-0.30	-$195.17
NAVY					
AdV Vaccination	$157.27	0.06			
No Vaccination	$166.80	0.38	$9.53	-0.32	-$29.78
MARINE CORPS					
AdV Vaccination	$152.25	0.02			
No Vaccination	$145.90	0.19	-$6.35	-0.17	$37.35
AIR FORCE					
AdV Vaccination	$178.89	0.06			
No Vaccination	$309.14	0.45	$130.25	-0.39	-$333.97
COAST GUARD					
AdV Vaccination	$148.11	0.02			
No Vaccination	$70.13	0.16	-$77.98	-0.14	$557.00

AdV = Adenovirus; Eff = Effectiveness as defined by training days lost ; IC = Incremental Cost; IE = Incremental Effect; ICER = Incremental Cost – effectiveness Ratio; TDL= Training Days Lost

4.5. SENSITIVITY ANALYSES – PART II

This section reports the results of one – way sensitivity analyses performed on the study variables. Tables 4.4 through 4.6 show the variables that had the largest relative impact on the results of the cost – effectiveness analysis in the Army, Navy, and Marine Corps respectively. All results of the one – way sensitivity analyses are shown in Appendix B. Findings were robust across all variables in the Air Force and Coast Guard. The adenovirus vaccination strategy was dominant in the Air Force, while no strategy was dominant in the Coast Guard.

4.5.1. ARMY ONE - WAY SENSITIVITY ANALYSES RESULTS

Table 4.4 shows the two variables that had the largest impact on the results of the cost – effectiveness analysis in Army basic trainees. The conclusion that adenovirus vaccination is more cost – effective than no adenovirus vaccination is sensitive to the cost of the adenovirus vaccine and the probability of developing GBS after vaccination. The optimal strategy would change from the adenovirus strategy to the no adenovirus strategy if the cost of the adenovirus vaccine was greater than $184.77 and the probability of developing GBS after vaccination was greater than 0.00027. Findings were robust across all other variables with the adenovirus vaccination strategy being the dominant strategy.

TABLE 4.4. ARMY ONE –WAY SENSITIVITY ANALYSES RESULTS

	ICER ($/TDL averted)		
	BASE	**LOW**	**HIGH**
Cost of adenovirus vaccine (cADV_VAX)	**126.22**	**100.98**	**250.00**
AdV Vaccination vs. No Vaccination	-198.91	-284.66	221.61
[P] of developing GBS after AdV vaccination (pGBS)	**0.00005**	**0.000005**	**0.0005**
AdV Vaccination vs. No Vaccination	-19.49	-237.15	217.55

ICER = Incremental Cost – effectiveness Ratio; TDL = Training Days Lost; [P] = Probability; AdV = Adenovirus

4.5.2. NAVY ONE – WAY SENSITIVITY ANALYSES RESULTS

Table 4.5 shows the variables that had the largest impact on the cost – effectiveness analysis in Navy basic trainees. Cost of the adenovirus vaccine, cost of FRI hospitalization, and cost of basic training are the cost variables that had the largest impact on cost – effectiveness. Threshold values were $135.75, $3,366.70, and $338.35 for cost of adenovirus vaccine, cost of FRI hospitalization and cost of basic training respectively. Training days lost to FRI hospitalization and sick quarters were the two effectiveness variables that the largest impact on cost – effectiveness. Threshold values were 1.19 and 1.93 for training days lost to FRI hospitalizations and sick quarters respectively. Probability of FRI without vaccine usage, probability of GBS after vaccination, and probability of FRI hospitalization were the probability variables that had an impact on cost – effectiveness. Threshold values were 0.087, 0.00009, and 0.115 for probability of FRI without vaccine usage, probability of GBS after vaccination, and probability of FRI hospitalization respectively. Threshold values represent the point at which the optimal strategy changes. Cost – effectiveness conclusions are sensitive to several variables when analyzing Navy basic trainees. Findings were robust across all other variables with the adenovirus vaccination strategy being the dominant strategy.

TABLE 4.5. NAVY ONE – WAY SENSITIVITY ANALYSES RESULTS

	ICER ($/TDL averted)		
COST VARIABLES ($)			
	BASE	**LOW**	**HIGH**
Cost of adenovirus vaccine (cADV_VAX)	**126.22**	**100.98**	**250.00**
AdV Vaccination vs. No Vaccination	-29.65	-108.17	355.43
Cost of FRI hospitalization (cHOSP)	**4,067.70**	**3,257.76**	**4,877.64**
AdV Vaccination vs. No Vaccination	-29.78	4.63	-64.18
Cost of training (cTRAIN)	**360.63**	**262.15**	**459.10**
AdV Vaccination vs. No Vaccination	-13.74	47.00	-74.46
EFFECTIVENESS VARIABLES (TDL)			
	BASE	**LOW**	**HIGH**
Training days lost to FRI hospitalization (effFRI_HOSP)	**3**	**1**	**12**
AdV Vaccination vs. No Vaccination	-40.67	3.48	-128.30
Training days lost to sick quarters (effSIQ)	**2.30**	**1**	**3**
AdV Vaccination vs. No Vaccination	-5.79	103.39	-75.17
PROBABAILITY VARIABLES			
	BASE	**LOW**	**HIGH**
[P] of FRI without vaccine (pFRI_NOVAX)	**0.370**	**0.074**	**0.667**
AdV Vaccination vs. No Vaccination	-349.60	97.06	-390.40
[P] of GBS after vaccination (pGBS)	**0.00028**	**0.00005**	**0.0005**
AdV Vaccination vs. No Vaccination	155.46	-29.65	351.24
[P] of FRI hospitalization (pHOSP_VAX)	**0.181**	**0.145**	**0.217**
AdV Vaccination vs. No Vaccination	-29.65	12.26	-70.92

[P] = Probability; ICER = Incremental Cost – effectiveness Ratio; TDL = Training Days Lost; FRI = Febrile Respiratory Illness; GBS = Guillain – Barre Syndrome

4.5.3. MARINE CORPS ONE – WAY SENSITIVITY ANALYSES RESULTS

Table 4.6 displays results from one – way sensitivity analyses on variables that impacted the findings of the cost – effectiveness analysis in Marine Corps basic trainees. Conclusions about cost – effectiveness were sensitive to the following variables: cost of adenovirus vaccine, cost of FRI hospitalization, cost of basic training, and training days lost due to FRI hospitalization. Threshold values were $119.87, $9,724.69, $348.91, and 5.28 for the cost of the adenovirus vaccine, cost FRI hospitalization, cost of basic training, and training days lost due to FRI hospitalization respectively. Findings were robust across all other variables where the no adenovirus vaccination strategy was the dominant strategy.

TABLE 4.6. MARINE CORPS ONE – WAY SENSITIVITY ANALYSES RESULTS

	ICER ($/TDL averted)		
	BASE	**LOW**	**HIGH**
Cost of adenovirus vaccine (cADV_VAX)	**150.65**	**100.98**	**250**
AdV Vaccination vs. No Vaccination	182.44	-111.97	771.25
Cost of FRI hospitalization (cHOSP)	**9,074.84**	**7,259.88**	**10,889.80**
AdV Vaccination vs. No Vaccination	37.63	142.72	-67.46
Cost of training (cTRAIN)	**360.63**	**262.15**	**459.10**
AdV Vaccination vs. No Vaccination	-6.90	51.13	-64.94
Training days lost due to FRI hospitalization (effFRI_HOSP)	**6.5**	**1**	**12**
AdV Vaccination vs. No Vaccination	-16.75	79.89	-72.92

ICER = Incremental Cost – effectiveness Ratio; TDL = Training Days Lost; FRI = Febrile Respiratory Illness; AdV = Adenovirus

4.6. PROBABLISTIC SENSITIVITY ANALYSIS

A probabilistic sensitivity analysis was conducted using a Monte Carlo simulation. Triangular, gamma, and beta distributions were created for TDL, costs, and probabilities respectively. Ranges for variables are shown in tables 3.13 through 3.17. Table 4.7 summarizes results from the Monte Carlo sensitivity analysis. The mean costs for the adenovirus vaccination strategy for each service branch were $163.71 (SD $70.28, Range: $129.38 – $2,411.88), $158.31 (SD $79.28, Range: $64.55 - $3,117.77), $154.12 (SD $94.15, Range: $62.25 - $3,715.07), $180.00 (SD $75.70, Range: $76.16 - $2,648.14), and $144.41 (SD $73.67, Range: $55.37 - $1,874.48) for Army, Navy, Marine Corps, Air Force, and Coast Guard respectively. Mean costs for the no vaccination strategy for each service branch were $233.16 (SD $136.99, Range: $22.54 - $1,375.43), $174.73 (SD $52.18, Range: $44.12 - $545.45), $151.60 (SD $46.50, Range: $39.82 - $401.62), $316.56 (SD $96.48, Range: $76.64 - $1,132.56), and $46.10 (SD $14.99, Range:$13.27 – $145.53) for Army, Navy, Marine Corps, Air Force, and Coast Guard respectively. Mean TDL values for the adenovirus vaccination strategy were 0.05 (SD 0.01), 0.06 (SD 0.02), 0.03 (SD 0.02), 0.08 (SD 0.02), and 0.04 (SD 0.01) for Army, Navy, Marine Corps, Air Force, and Coast Guard respectively. Mean TDL values for the no vaccination strategy were 0.40 (SD 0.12), 0.39 (SD 0.10), 0.20 (SD 0.05), 0.47 (SD 0.12), and 0.17 (SD 0.04) for the Army, Navy, Marine Corps, Air Force, and Coast Guard respectively.

Figures 4.15 through 4.19 display the incremental cost – effectiveness scatter plots comparing the adenovirus vaccination strategy and the no vaccination strategy in each

service branch. The outcome of this analysis, training days lost, is a negative value, which means training days lost without the adenovirus vaccine is greater than training days lost with the adenovirus vaccine. Essentially, the adenovirus vaccine is more effective than no adenovirus vaccine in terms of training days lost. Therefore, when interpreting the incremental cost – effectiveness scatter plots for this analysis, one must remember that the quadrants are reversed. To help with interpretation, scatter plots are clearly labeled. For a more extensive explanation of TreeAge ICER scatter plots, see Appendix C.

Each scatter plot is labeled with the percentage of iterations that fall in quadrant four, which represents the proportion of iterations where the adenovirus vaccination strategy is the dominant strategy over the no vaccination strategy. Those proportions are 68%, 65%, 53%, 95%, and 0% for the Army, Navy, Marine Corps, Air Force, and Coast Guard. Including the areas where the ICER is less than a willingness – to – pay threshold of $200 (section C2), results in increasing proportions where the adenovirus vaccine strategy is more cost – effective to 98%, 90%, 75%, 98%, and 3% for the Army, Navy, Marine Corps, Air Force, and Coast Guard, respectively.

TABLE 4.7. SUMMARY OF RESULTS FROM MONTE CARLO ANALYSIS

ALTERNATIVE	COST ($)	EFF	IC ($)	IE	ICER ($/TDL)
ARMY					
AdV Vaccination	$163.71	0.05			
No Vaccination	$233.16	0.40	$69.45	-0.35	-$198.43
NAVY					
AdV Vaccination	$158.31	0.06			
No Vaccination	$174.73	0.39	$16.42	-0.33	-$49.76
MARINE CORPS					
AdV Vaccination	$152.12	0.03			
No Vaccination	$151.60	0.29	-$0.52	-0.26	$2.00
AIR FORCE					
AdV Vaccination	$180.00	0.08			
No Vaccination	$316.56	0.47	$136.56	-0.39	-$350.15
COAST GUARD					
AdV Vaccination	$144.41	0.04			
No Vaccination	$46.10	0.17	-$98.31	-0.13	$756.23

AdV = Adenovirus; EFF = Effectiveness as measured by training days lost; IC = Incremental Cost; IE = Incremental Effectiveness; ICER = Incremental Cost – effectiveness Ratio; TDL = Training Days Lost

FIGURE 4.15. ARMY INCREMENTAL CE SCATTER PLOT – ADENOVIRUS VACCINATION VERSUS NO VACCINATION

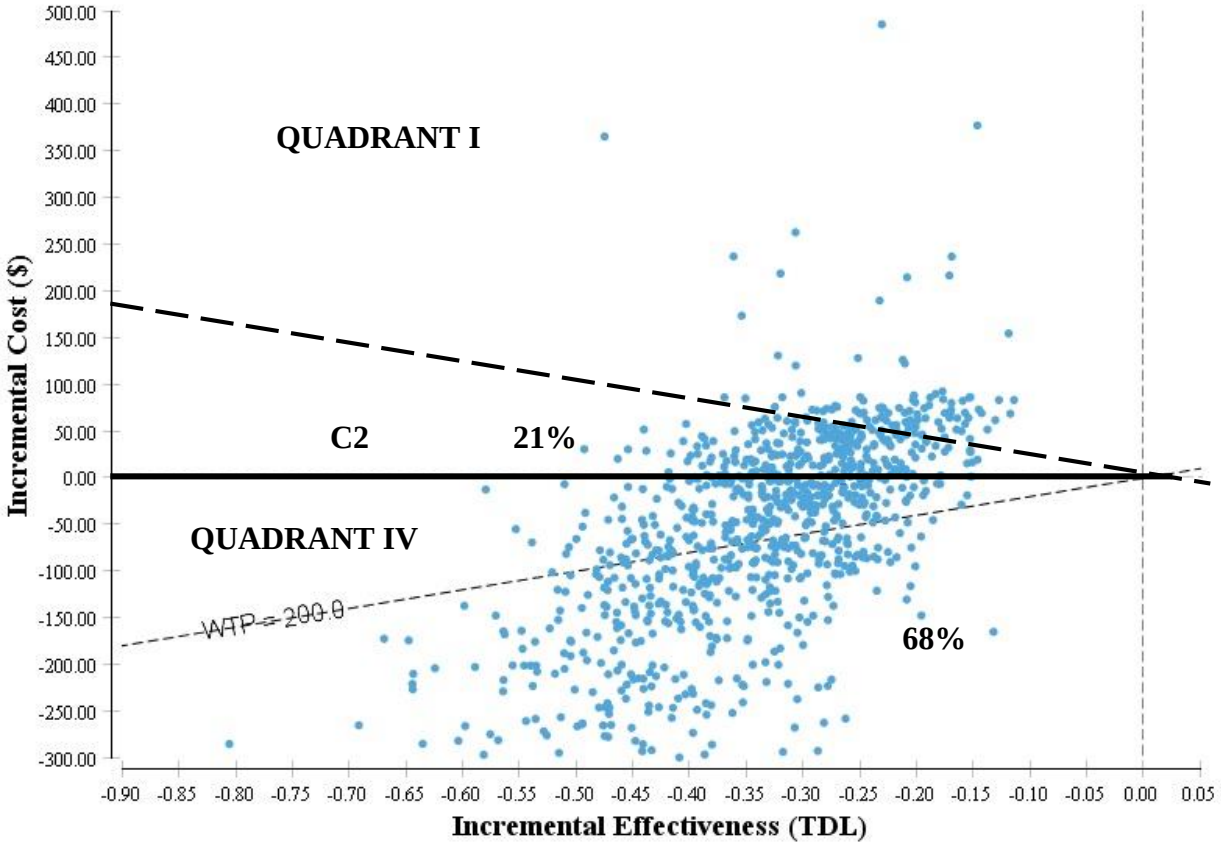


FIGURE 4.16. NAVY INCREMENTAL CE SCATTER PLOT – ADENOVIRUS VACCINATION VERSUS NO VACCINATION

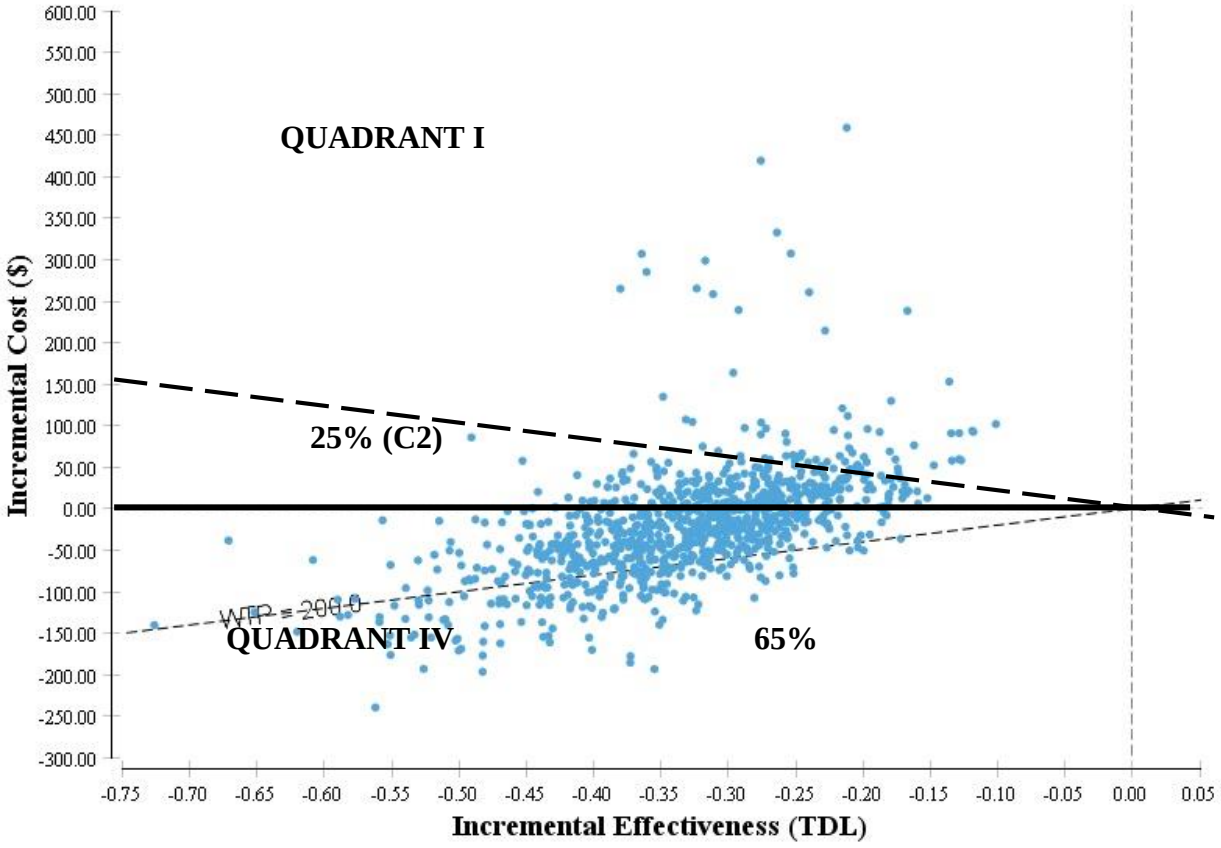


FIGURE 4.17. MARINE CORPS INCREMENTAL CE SCATTER PLOT – ADENOVIRUS VACCINATION VERSUS NO VACCINATION

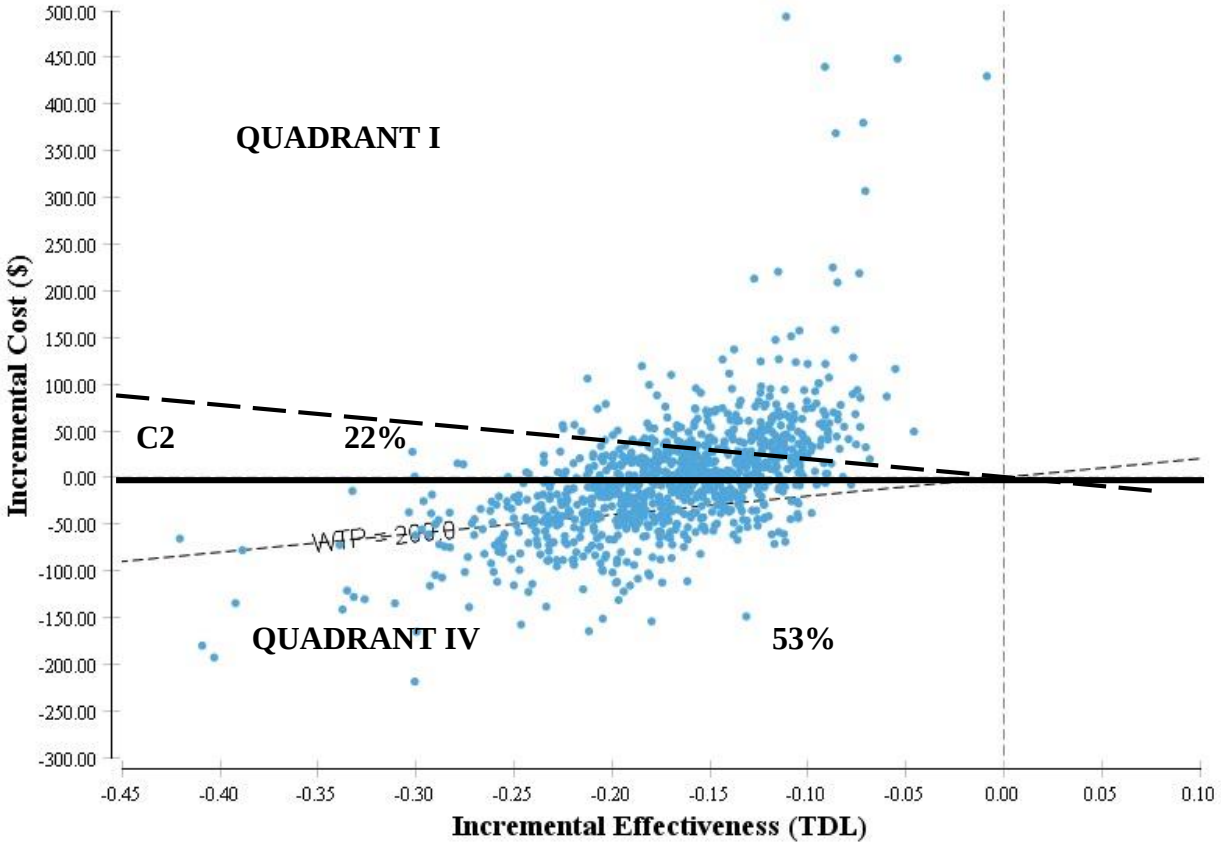


FIGURE 4.18. AIR FORCE INCREMENTAL CE SCATTER PLOT – ADENOVIRUS VACCINATION VERSUS NO VACCINATION

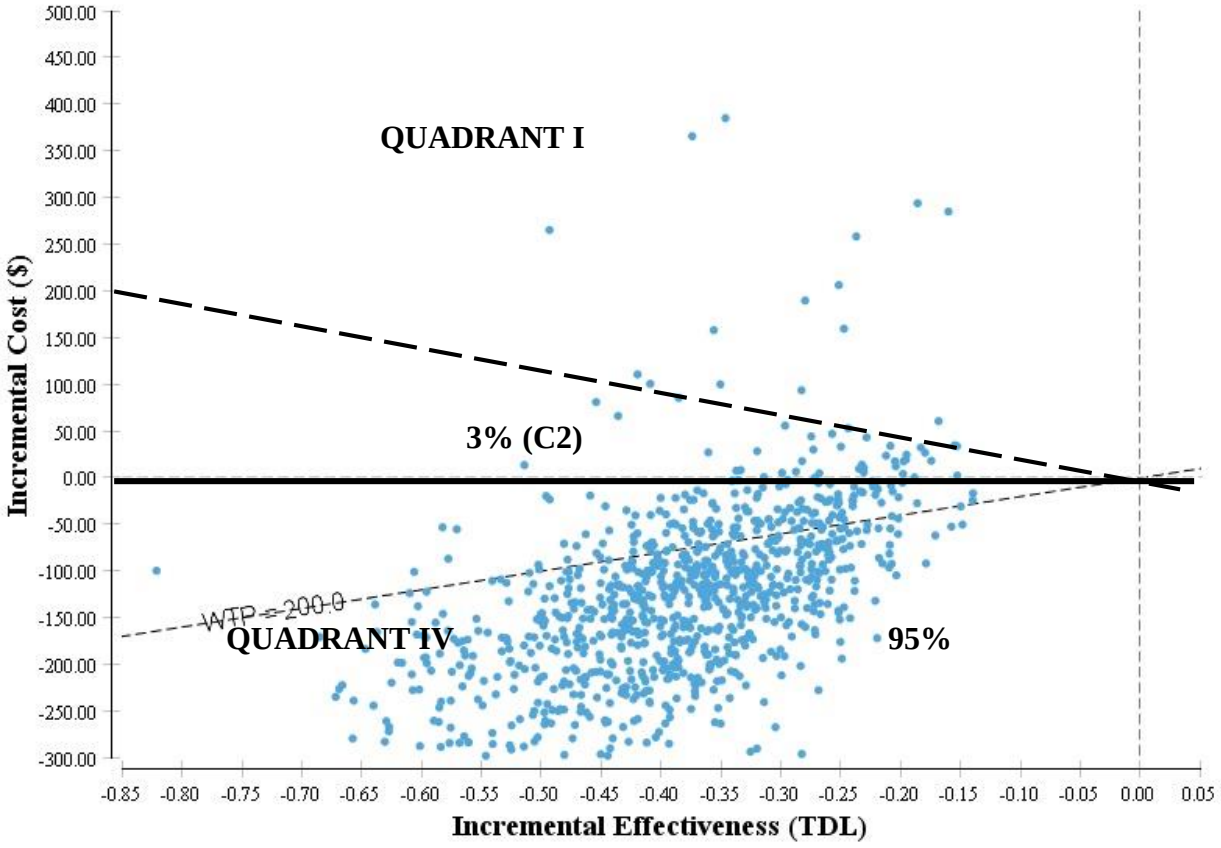
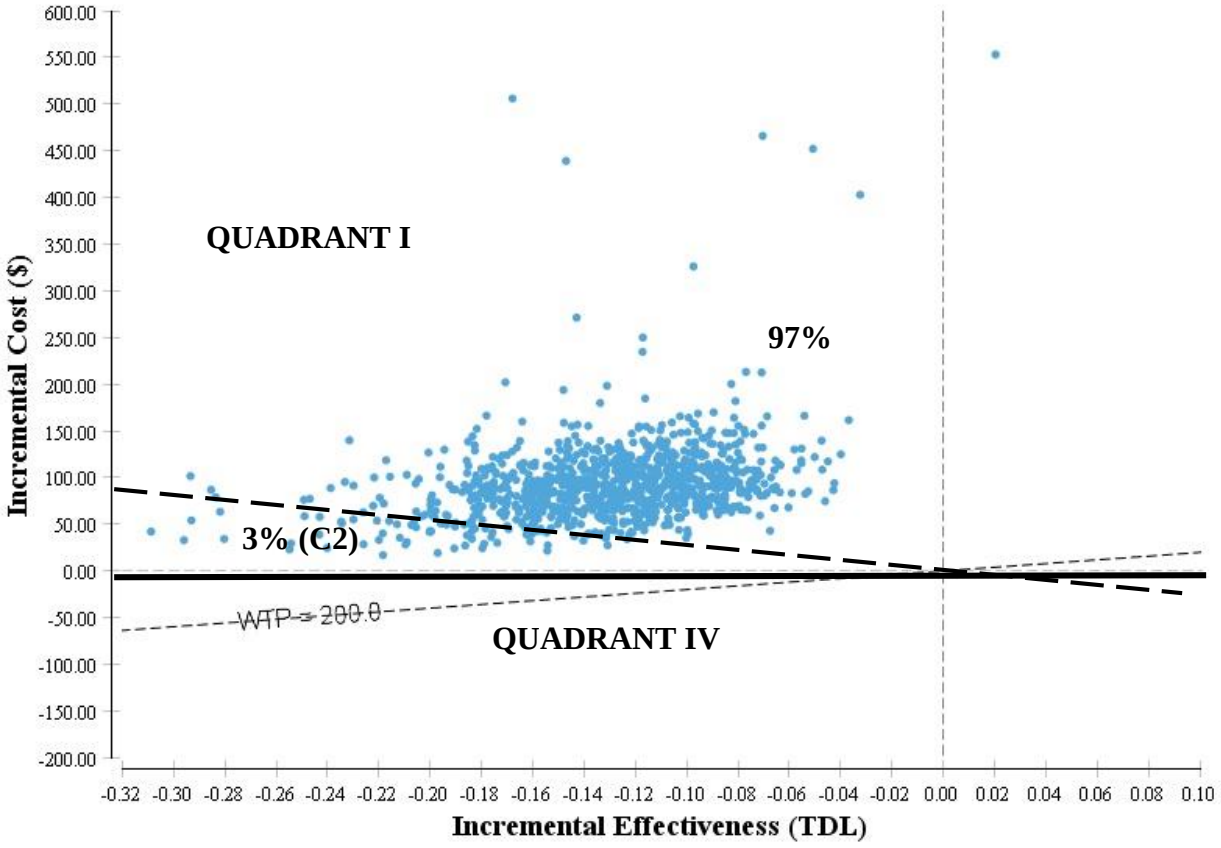


FIGURE 4.19. COAST GUARD INCREMENTAL CE SCATTER PLOT – ADENOVIRUS VACCINATION VERSUS NO VACCINATION



CHAPTER 5: DISCUSSION AND CONCLUSIONS

5.1. INTRODUCTION

Chapter 5 includes a discussion of base – case results, results from sensitivity analyses, and an interpretation of the results from part I and part II of this study. In addition, a comparison of results to current literature, study limitations, and suggestions for future research are discussed.

5.2. BASE – CASE AND SENSITIVITY ANALYSES RESULTS

In part I of this study, adenovirus vaccination of basic trainees was cost – effective as measured by FRI hospitalization cases prevented in all US military service branches but the Coast Guard. The model showed that introducing the adenovirus vaccine to basic trainees saved the Army, 5.8 million, the Navy, $1 million, Marine Corps, $238,000, and the Air Force $5.2 million, annually. In addition, AdV vaccination prevented 1,221, 543, 317, 677, and 13 cases of FRI hospitalization annually in the Army, Navy, Marine Corps, Air Force, and Coast Guard respectively. Cost – effectiveness ratios were negative in all branches but the Coast Guard. In general, the cost – effectiveness of AdV vaccination was robust in the Army, Navy, Marine Corps, and Air Force. One – way sensitivity analyses showed that the majority of results of the Part I model were insensitive to changes in all variables but the cost of the vaccine. The Army's tornado diagram indicates that the probability of hospitalization due to FRI had a huge impact on the model. However, the one – way sensitivity analysis showed that changes in this

parameter would not change the ICER. The average threshold value for the cost of the adenovirus vaccine in the Army, Navy, and Marine Corps was approximately $164.

In part II of this study, adenovirus vaccination of basic trainees was cost – effective as measured by training days lost (TDL) averted in all US military service branches but the Marine Corps and the Coast Guard. The ICER for the Marine Corps was $37.63, which is interpreted as a cost of $37.63 per TDL averted. The ICER for the Coast Guard indicated that it would cost the Coast Guard $563.78 per TDL averted. Probabilistic sensitivity analyses showed that the adenovirus vaccination strategy was cost – effective in 98%, 90%, 75%, 98%, and 3% for the Army, Navy, Marine Corps, Air Force and Coast Guard respectively at the $200 WTP threshold.

5.3. COMPARISON TO LITERATURE

Before this study, only three published studies examined the cost – effectiveness of the adenovirus vaccine in US military basic trainees. [7, 9 – 10] Howell et al. looked at the use of the adenovirus vaccine in male Army basic trainees and found that a year – round vaccine program would prevent 7,800 hospitalized cases of FRI and save the Army $15.5 million over no vaccination. [9] The economic analysis for the first part of this dissertation used the same model Howell used with current data and found that the adenovirus vaccine would prevent 6,030 hospitalized cases of FRI and save the Army $5.8 million over no vaccination in US Army basic trainees. The difference between results is likely due to the high incidence used in the previous study. The incidence of FRI used in Howell et al.'s study was 4.06 cases per 100 trainee-weeks, which is four times the incidence used in this

current study. The Army uses a FRI threshold rate of 1.5 FRI admissions per 100 trainee – weeks to indicate an epidemic that needs to be investigated. [9] The incidence used by Howell et al. is almost three times the epidemic threshold and indicates that all Army basic training sites experience an epidemic for half of the year. Therefore, results from Howell et al.'s study may be overestimated due to the inflated incidence rate. However, both studies showed that an adenovirus vaccination program is cost – effective when compared to no vaccination in Army basic trainees in terms of hospital admissions for FRI prevented.

In 2000, Hyer et al. did a cost – effectiveness study on the adenovirus vaccine in male and female Navy basic trainees. Hyer's study showed that a year – round adenovirus vaccination program would prevent 4,555 hospital admissions for FRI and save the Navy $2.6 million. [10] The analysis done in this dissertation in Navy basic trainees found that use of the adenovirus vaccine prevented 3,591 hospital admissions for FRI and saved the Navy $1.1 million. Hyer et al. also used an incidence that was above the FRI epidemic threshold. Results from both of the studies on Navy basic trainees showed that an adenovirus vaccination is cost – effective when compared to no vaccination in terms of hospital admissions for FRI prevented.

The study presented here is the first to determine the cost – effectiveness of the adenovirus vaccine in US service branches besides the Army and Navy. As shown in the presented study, results vary greatly between service branches in terms of cost - effectiveness because incidence and cost estimates differ between service branches.

5.4. STUDY LIMITATIONS

Economic modelling and specifically this study have several limitations. One of the biggest limitations to this study is limited data on adenovirus transmission and the adenovirus vaccine for all service branches. The adenovirus vaccine is only used in US military basic trainees, so all research was performed by the US military in the late 1950s to early 1960s, before the original adenovirus vaccine was used. The majority of this early research focused on one service branch, the Army. No further research was performed on adenovirus in basic trainees until adenovirus vaccination ceased in the late 1990s. Research in the late 1990s focused on the need for a new adenovirus vaccine manufacturer and the increase in adenovirus incidence. Research focusing on the Air Force, Marine Corps, and Coast Guard is limited, so collecting data specific to their service branches for this analysis was difficult. Since the Coast Guard is not part of the Department of Defense, average values for the other service branches were used for several variables in the model. In addition, the number of basic trainees in the US Coast Guard may not be large enough to adequately determine the cost – effectiveness in this service branch.

The model did not include the cost of recycling a basic trainee due to missed training days. If a basic trainee misses too many training days, he/she has to restart basic training. Epidemiologic investigations at Army basic training sites during FRI epidemics showed that no basic trainees were recycled due to FRI. [49] Conversely, a study in Navy basic trainees estimated that up to 200 basic trainees with adenovirus had to be recycled after an outbreak in 2001. [61] Taking into consideration the results from these two studies, it is

difficult to determine the impact basic trainee recycling has on the cost – effectiveness of the adenovirus vaccine.

Two limitations of the study have to do with the manufacturing and shipping of the adenovirus vaccine. The military has a contract with Teva to buy 250,000 doses (type 4 + 7) of the adenovirus vaccine annually, whether it is used or not (Personal communication, Dr. Snyder). This model did not take into account those doses that were bought by the DoD and not distributed. Adenovirus vaccine type 4 and type 7 are each manufactured in bottles of 100 doses. Adenovirus vaccines must remain refrigerated and not exposed to any moisture during transport to the basic training facility. Loss or destruction of vaccines during transport were not considered.

This analysis used average incidence rates for a five – year period when the adenovirus vaccine was not available to estimate incidence for the no vaccination arm of the analysis. One limitation of this measurement is that it assumes that the incidence rate remains constant throughout the year. However, research shows that adenovirus incidence depends on several factors like season, basic training population size, and serotype, and varies throughout the year. Incidence can either be over or underestimated but both models were robust when varying this parameter.

Cost estimates used in this analysis are TRICARE reimbursement amounts for the FY 2013. This analysis assumed that the reimbursement amount was the actual amount paid by the DoD, but rebates or other discounts may impact the final price the DoD pays.

Several assumptions were made about CPT codes and DRG groups that can lead to overestimation of costs.

5.5. CONCLUSION AND DIRECTIONS FOR FUTURE RESEARCH

As mentioned above, health economics research, specifically on the adenovirus vaccine, focusing on the separate military service branches is rarely found in the literature. Either the research is not being performed or the US military is not publishing their research. Future research should focus on service branch - specific health economics research, adenovirus serotype distribution and changes in distribution, and the impact of herd immunity due to adenovirus vaccination of basic trainees. Performing cost analyses on each service branch can highlight areas where costs are not used efficiently, which can eventually result in cost savings to the DoD. Too many differences exist between military service branches, especially in terms of serotype distribution and health care costs, to analyze the entire military as one combined population. As shown in this analysis, a vaccine may cost the same for all basic trainees but that does not mean it is cost – effective in all service branches.

For years, military physicians considered risk of FRI in all service branches to be equal. With current information on serotype variation and antigenic drift, assuming that all service branches and basic training sites have the same risk of FRI is misleading. Adenovirus serotype and genome type distribution is another area where more research needs to be performed. An article published in 2006 showed that adenoviral co – infections (simultaneous infection by multiple pathogenic adenovirus species) emerged in

previously vaccinated military basic trainees. Many of the co – infections were species not generally associated with FRI in the military. In addition, co – infections can lead to recombination which plays a major role in creating new, more virulent strains of adenovirus. Since the adenovirus vaccine is specific to serotypes 4 and 7, changes in adenovirus serotypes can impact adenovirus vaccine cost – effectiveness. The Navy and Army currently perform adenovirus serotype surveillance, but this surveillance must continue and concentrate on changes in adenovirus serotypes since redeployment of the adenovirus vaccine because these changes can impact the cost – effectiveness of the adenovirus vaccine.

Lastly, more research needs to focus on adenovirus transmission and herd immunity in US military basic trainees. Literature shows that adenovirus transmission includes person – to – person contact and environmental exposure, but which transmission route is most significant is unclear. Unsuspected environmental routes of transmission may contribute significantly to transmission, while suspected routes of person – to – person transmission may be non - significant. Transmission dynamics of adenovirus are very complex and serotypes differ in terms of infectiousness and survival of the pathogen, so transmission for all serotypes needs to be understood. Understanding adenovirus transmission dynamics allows for more complex economic models that include herd immunity to be built.

This study provides evidence supporting the cost – effectiveness of using the adenovirus vaccine in US basic trainees in all service branches but the Coast Guard. Results from the part I and part II cost – effectiveness analyses show that an adenovirus vaccination

strategy is favorable when compared to no vaccination. The probabilistic sensitivity analysis provides additional evidence on the cost – effectiveness of the adenovirus vaccine in terms of training days lost averted as the results were insensitive to varying estimates. Results from these analyses are a compelling reason to continue adenovirus vaccination in US basic trainees.

APPENDIX A. MODEL VARIABLE DESCRIPTIONS

PART I MODELVARIABLE DESCRIPTIONS

VARIABLE	DESCRIPTION
cVAX	Cost of adenovirus vaccine per basic trainee
cHOSP_FRI	Cost of inpatient hospitalization due to FRI
cOUTPT	Cost of one outpatient visit, new patient
cOUTPT_FLLWUP	Cost of one outpatient visit, established patient
cTRAIN	Cost to train basic trainee per day
effNOVAX	Expected number of admissions to hospital due to FRI when vaccine not in use
effVAX	Expected number of admissions to hospital due to FRI when vaccine in use
pFRI_NOVAX	Probability of developing FRI during basic training when adenovirus vaccine not in use
pFRIVAX	Probability of developing FRI during basic training after receiving adenovirus vaccine
pHOSP	Probability of being admitted to the hospital for FRI
pSIQ	Probability of being sent to sick quarters after outpatient visit for FRI

PART II MODEL VARIABLE DESCRIPTIONS

VARIABLE	DESCRIPTION
cADV_VAX	Cost of adenovirus vaccine per basic trainee
cADVP	Cost of hospitalization due to adenoviral pneumonia
cFLLW_UP	Cost out one outpatient visit, established patient
cGBS	Cost to treat Guillain - Barre Syndrome in basic trainees
cHOSP	Cost of hospitalization due to FRI
cOUTPT	Cost of one outpatient visit, new patient
cTRAIN	Cost to train basic trainee per day
effAdV_HOSP	Training days lost due to time spent in hospital because of adenoviral pneumonia
effFRI_HOSP	Training days lost due to time spent in hospital because of FRI
effGBS	Training days lost due to Guillain - Barre Syndrome
effLP	Training days lost due to lost productivity
effMAE	Training days lost as a result of minor systemic reactions to adenovirus vaccine
effNOFRI	Training days lost due to no FRI
effOUTPT	Training days lost due to time spent at outpatient visit
effSIQ	Training days lost due to time spent in sick quarters
pADVP	Probability of developing adenoviral pneumonia as complication of FRI
pFRI_NOVAX	Probability of developing FRI when adenovirus vaccine is not available
pFRI_VAX	Probability of developing FRI after receiving an adenovirus vaccine
pGBS	Probability of developing Guillain - Barre Syndrome after adenovirus vaccination
pHOSP_VAX	Probability of hospitalization as a result of FRI
pMAE	Probability of experiencing a minor systemic reaction to adenovirus vaccine
pSIQ_ONLY	Probability of being sent to sick quarters after outpatient visit because of FRI diagnosis

APPENDIX B. ONE – WAY SENSITIVITY ANALYSES RESULTS

VARIABLE: cADV_VAX – Cost of adenovirus vaccine

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
100.98	Adenovirus Vaccination	137.50	0.05	2564.78	0.00	0.00	0.00	
100.98	No Vaccination	221.29	0.35	635.96	83.79	-0.29	-284.66	(Dominated)
138.235	Adenovirus Vaccination	174.75	0.05	3259.70	0.00	0.00	0.00	
138.235	No Vaccination	221.29	0.35	635.96	46.53	-0.29	-158.09	(Dominated)
175.49	Adenovirus Vaccination	212.01	0.05	3954.62	0.00	0.00	0.00	
175.49	No Vaccination	221.29	0.35	635.96	9.28	-0.29	-31.52	(Dominated)
212.745	No Vaccination	221.29	0.35	635.96	0.00	0.00	0.00	
212.745	Adenovirus Vaccination	249.26	0.05	4649.55	27.98	0.29	95.05	Not Dominated
250	No Vaccination	221.29	0.35	635.96	0.00	0.00	0.00	
250	Adenovirus Vaccination	286.52	0.05	5344.47	65.23	0.29	221.61	Not Dominated

VARIABLE: cADVP – Cost of adenoviral pneumonia hospitalization

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
5598.3	Adenovirus Vaccination	161.98	0.05	3021.40	0.00	0.00	0.00	
5598.3	No Vaccination	214.11	0.35	615.33	52.13	-0.29	-177.11	(Dominated)
6298.09	Adenovirus Vaccination	162.09	0.05	3023.41	0.00	0.00	0.00	
6298.09	No Vaccination	215.12	0.35	618.25	53.04	-0.29	-180.19	(Dominated)
6997.88	Adenovirus Vaccination	162.19	0.05	3025.41	0.00	0.00	0.00	
6997.88	No Vaccination	216.14	0.35	621.16	53.94	-0.29	-183.27	(Dominated)
7697.67	Adenovirus Vaccination	162.30	0.05	3027.41	0.00	0.00	0.00	
7697.67	No Vaccination	217.15	0.35	624.07	54.85	-0.29	-186.34	(Dominated)
8397.46	Adenovirus Vaccination	162.41	0.05	3029.41	0.00	0.00	0.00	
8397.46	No Vaccination	218.16	0.35	626.99	55.76	-0.29	-189.42	(Dominated)

VARIABLE: cFLLW_UP – Cost of follow – up outpatient visits

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
43.92	Adenovirus Vaccination	162.71	0.05	3034.98	0.00	0.00	0.00	
43.92	No Vaccination	220.98	0.35	635.08	58.27	-0.29	-197.98	(Dominated)
51.285	Adenovirus Vaccination	162.74	0.05	3035.55	0.00	0.00	0.00	
51.285	No Vaccination	221.27	0.35	635.92	58.54	-0.29	-198.87	(Dominated)
58.65	Adenovirus Vaccination	162.77	0.05	3036.13	0.00	0.00	0.00	
58.65	No Vaccination	221.56	0.35	636.76	58.80	-0.29	-199.75	(Dominated)
66.015	Adenovirus Vaccination	162.80	0.05	3036.70	0.00	0.00	0.00	
66.015	No Vaccination	221.85	0.35	637.59	59.06	-0.29	-200.64	(Dominated)
73.38	Adenovirus Vaccination	162.83	0.05	3037.28	0.00	0.00	0.00	
73.38	No Vaccination	222.15	0.35	638.43	59.32	-0.29	-201.52	(Dominated)

VARIABLE: cGBS – Cost of Guillain – Barre Syndrome

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
194674.13	Adenovirus Vaccination	160.30	0.05	2990.19	0.00	0.00	0.00	
194674.13	No Vaccination	221.29	0.35	635.96	60.98	-0.29	-207.18	(Dominated)
219008.42	Adenovirus Vaccination	161.52	0.05	3012.89	0.00	0.00	0.00	
219008.42	No Vaccination	221.29	0.35	635.96	59.77	-0.29	-203.05	(Dominated)
243342.71	Adenovirus Vaccination	162.74	0.05	3035.58	0.00	0.00	0.00	
243342.71	No Vaccination	221.29	0.35	635.96	58.55	-0.29	-198.91	(Dominated)
267677	Adenovirus Vaccination	163.95	0.05	3058.28	0.00	0.00	0.00	
267677	No Vaccination	221.29	0.35	635.96	57.33	-0.29	-194.78	(Dominated)
292011.29	Adenovirus Vaccination	165.17	0.05	3080.97	0.00	0.00	0.00	
292011.29	No Vaccination	221.29	0.35	635.96	56.12	-0.29	-190.64	(Dominated)

VARIABLE: cHOSP – Cost of FRI hospitalization

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
5379.91	Adenovirus Vaccination	159.57	0.05	2976.53	0.00	0.00	0.00	
5379.91	No Vaccination	191.39	0.35	550.04	31.82	-0.29	-108.09	(Dominated)
6187.4	Adenovirus Vaccination	161.00	0.05	3003.10	0.00	0.00	0.00	
6187.4	No Vaccination	204.84	0.35	588.69	43.84	-0.29	-148.95	(Dominated)
6994.89	Adenovirus Vaccination	162.42	0.05	3029.66	0.00	0.00	0.00	
6994.89	No Vaccination	218.29	0.35	627.35	55.87	-0.29	-189.80	(Dominated)
7802.38	Adenovirus Vaccination	163.84	0.05	3056.22	0.00	0.00	0.00	
7802.38	No Vaccination	231.74	0.35	666.00	67.89	-0.29	-230.66	(Dominated)
8609.87	Adenovirus Vaccination	165.27	0.05	3082.79	0.00	0.00	0.00	
8609.87	No Vaccination	245.19	0.35	704.65	79.92	-0.29	-271.52	(Dominated)

VARIABLE: cOUTPT – Cost of outpatient visits (New patient)

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
72.53	Adenovirus Vaccination	162.66	0.05	3034.16	0.00	0.00	0.00	
72.53	No Vaccination	220.57	0.35	633.89	57.90	-0.29	-196.72	(Dominated)
82.6425	Adenovirus Vaccination	162.73	0.05	3035.49	0.00	0.00	0.00	
82.6425	No Vaccination	221.24	0.35	635.83	58.51	-0.29	-198.78	(Dominated)
92.755	Adenovirus Vaccination	162.81	0.05	3036.83	0.00	0.00	0.00	
92.755	No Vaccination	221.92	0.35	637.78	59.11	-0.29	-200.83	(Dominated)
102.8675	Adenovirus Vaccination	162.88	0.05	3038.16	0.00	0.00	0.00	
102.8675	No Vaccination	222.60	0.35	639.72	59.72	-0.29	-202.89	(Dominated)
112.98	Adenovirus Vaccination	162.95	0.05	3039.50	0.00	0.00	0.00	
112.98	No Vaccination	223.27	0.35	641.67	60.32	-0.29	-204.94	(Dominated)

VARIABLE: cTRAIN – Cost to train basic trainee per day

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
241.52	Adenovirus Vaccination	159.42	0.05	2973.64	0.00	0.00	0.00	
241.52	No Vaccination	193.04	0.35	554.78	33.62	-0.29	-114.23	(Dominated)
290.7425	Adenovirus Vaccination	160.63	0.05	2996.26	0.00	0.00	0.00	
290.7425	No Vaccination	203.36	0.35	584.44	42.73	-0.29	-145.16	(Dominated)
339.965	Adenovirus Vaccination	161.84	0.05	3018.89	0.00	0.00	0.00	
339.965	No Vaccination	213.68	0.35	614.09	51.83	-0.29	-176.10	(Dominated)
389.1875	Adenovirus Vaccination	163.06	0.05	3041.52	0.00	0.00	0.00	
389.1875	No Vaccination	223.99	0.35	643.74	60.94	-0.29	-207.03	(Dominated)
438.41	Adenovirus Vaccination	164.27	0.05	3064.15	0.00	0.00	0.00	
438.41	No Vaccination	234.31	0.35	673.40	70.04	-0.29	-237.96	(Dominated)

VARIABLE: effADVP_HOSP – Training days lost to adenoviral pneumonia hospitalization

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
3	Adenovirus Vaccination	162.68	0.05	3043.21	0.00	0.00	0.00	
3	No Vaccination	220.74	0.35	637.05	58.06	-0.29	-198.13	(Dominated)
4	Adenovirus Vaccination	162.74	0.05	3035.58	0.00	0.00	0.00	
4	No Vaccination	221.29	0.35	635.96	58.55	-0.29	-198.91	(Dominated)
5	Adenovirus Vaccination	162.80	0.05	3028.00	0.00	0.00	0.00	
5	No Vaccination	221.83	0.35	634.89	59.04	-0.30	-199.69	(Dominated)
6	Adenovirus Vaccination	162.85	0.05	3020.45	0.00	0.00	0.00	
6	No Vaccination	222.38	0.35	633.82	59.52	-0.30	-200.46	(Dominated)
7	Adenovirus Vaccination	162.91	0.05	3012.95	0.00	0.00	0.00	
7	No Vaccination	222.92	0.35	632.76	60.01	-0.30	-201.22	(Dominated)

VARIABLE: effFRI_HOSP – Training days lost due to FRI hospitalization

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
1	Adenovirus Vaccination	161.41	0.05	3030.77	0.00	0.00	0.00	
1	No Vaccination	208.75	0.31	663.46	47.34	-0.26	-181.12	(Dominated)
3.75	Adenovirus Vaccination	163.24	0.05	3037.37	0.00	0.00	0.00	
3.75	No Vaccination	225.99	0.36	626.96	62.75	-0.31	-204.60	(Dominated)
6.5	Adenovirus Vaccination	165.06	0.05	3043.86	0.00	0.00	0.00	
6.5	No Vaccination	243.22	0.41	598.70	78.16	-0.35	-222.03	(Dominated)
9.25	Adenovirus Vaccination	166.89	0.05	3050.23	0.00	0.00	0.00	
9.25	No Vaccination	260.46	0.45	576.16	93.57	-0.40	-235.49	(Dominated)
12	Adenovirus Vaccination	168.71	0.06	3056.48	0.00	0.00	0.00	
12	No Vaccination	277.69	0.50	557.77	108.98	-0.44	-246.20	(Dominated)

VARIABLE: effGBS – Training days lost due to Guillain – Barre Syndrome

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
39	Adenovirus Vaccination	162.55	0.05	3060.62	0.00	0.00	0.00	
39	No Vaccination	221.29	0.35	635.96	58.74	-0.29	-199.21	(Dominated)
44	Adenovirus Vaccination	162.64	0.05	3048.04	0.00	0.00	0.00	
44	No Vaccination	221.29	0.35	635.96	58.64	-0.29	-199.06	(Dominated)
49	Adenovirus Vaccination	162.74	0.05	3035.58	0.00	0.00	0.00	
49	No Vaccination	221.29	0.35	635.96	58.55	-0.29	-198.91	(Dominated)
54	Adenovirus Vaccination	162.83	0.05	3023.24	0.00	0.00	0.00	
54	No Vaccination	221.29	0.35	635.96	58.45	-0.29	-198.76	(Dominated)
59	Adenovirus Vaccination	162.93	0.05	3011.01	0.00	0.00	0.00	
59	No Vaccination	221.29	0.35	635.96	58.36	-0.29	-198.61	(Dominated)

VARIABLE: effLOST_PRO – Training days lost due to lost productivity

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.93	Adenovirus Vaccination	162.74	0.05	3420.27	0.00	0.00	0.00	
0.93	No Vaccination	221.29	0.29	754.61	58.55	-0.25	-238.33	(Dominated)
1.24	Adenovirus Vaccination	162.74	0.05	3230.83	0.00	0.00	0.00	
1.24	No Vaccination	221.29	0.32	694.65	58.55	-0.27	-218.31	(Dominated)
1.55	Adenovirus Vaccination	162.74	0.05	3061.28	0.00	0.00	0.00	
1.55	No Vaccination	221.29	0.34	643.51	58.55	-0.29	-201.40	(Dominated)
1.86	Adenovirus Vaccination	162.74	0.06	2908.63	0.00	0.00	0.00	
1.86	No Vaccination	221.29	0.37	599.39	58.55	-0.31	-186.92	(Dominated)
2.17	Adenovirus Vaccination	162.74	0.06	2770.48	0.00	0.00	0.00	
2.17	No Vaccination	221.29	0.39	560.93	58.55	-0.34	-174.38	(Dominated)

VARIABLE: effMAE – Training days lost due to minor systemic reactions

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.03	Adenovirus Vaccination	162.74	0.04	3911.01	0.00	0.00	0.00	
0.03	No Vaccination	221.29	0.35	635.96	58.55	-0.31	-191.12	(Dominated)
0.0675	Adenovirus Vaccination	162.74	0.05	3587.68	0.00	0.00	0.00	
0.0675	No Vaccination	221.29	0.35	635.96	58.55	-0.30	-193.49	(Dominated)
0.105	Adenovirus Vaccination	162.74	0.05	3313.73	0.00	0.00	0.00	
0.105	No Vaccination	221.29	0.35	635.96	58.55	-0.30	-195.92	(Dominated)
0.1425	Adenovirus Vaccination	162.74	0.05	3078.65	0.00	0.00	0.00	
0.1425	No Vaccination	221.29	0.35	635.96	58.55	-0.30	-198.41	(Dominated)
0.18	Adenovirus Vaccination	162.74	0.06	2874.71	0.00	0.00	0.00	
0.18	No Vaccination	221.29	0.35	635.96	58.55	-0.29	-200.96	(Dominated)

VARIABLE: effOUTPT – Training days lost due to outpatient visits

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.084	Adenovirus Vaccination	162.74	0.05	3027.92	0.00	0.00	0.00	
0.084	No Vaccination	221.29	0.35	633.17	58.55	-0.30	-197.97	(Dominated)
0.203	Adenovirus Vaccination	162.74	0.05	2964.37	0.00	0.00	0.00	
0.203	No Vaccination	221.29	0.36	610.35	58.55	-0.31	-190.30	(Dominated)
0.322	Adenovirus Vaccination	162.74	0.06	2903.42	0.00	0.00	0.00	
0.322	No Vaccination	221.29	0.38	589.12	58.55	-0.32	-183.21	(Dominated)
0.441	Adenovirus Vaccination	162.74	0.06	2844.94	0.00	0.00	0.00	
0.441	No Vaccination	221.29	0.39	569.32	58.55	-0.33	-176.62	(Dominated)
0.56	Adenovirus Vaccination	162.74	0.06	2788.76	0.00	0.00	0.00	
0.56	No Vaccination	221.29	0.40	550.80	58.55	-0.34	-170.50	(Dominated)

VARIABLE: effSIQ – Training days lost due to time spent in sick quarters

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
1	Adenovirus Vaccination	159.27	0.04	3761.83	0.00	0.00	0.00	
1	No Vaccination	188.57	0.26	722.49	29.29	-0.22	-133.96	(Dominated)
1.5	Adenovirus Vaccination	160.61	0.05	3440.99	0.00	0.00	0.00	
1.5	No Vaccination	201.15	0.29	683.16	40.54	-0.25	-163.64	(Dominated)
2	Adenovirus Vaccination	161.94	0.05	3174.69	0.00	0.00	0.00	
2	No Vaccination	213.74	0.33	651.86	51.80	-0.28	-187.08	(Dominated)
2.5	Adenovirus Vaccination	163.27	0.06	2950.10	0.00	0.00	0.00	
2.5	No Vaccination	226.32	0.36	626.35	63.05	-0.31	-206.05	(Dominated)
3	Adenovirus Vaccination	164.60	0.06	2758.15	0.00	0.00	0.00	
3	No Vaccination	238.91	0.39	605.16	74.30	-0.34	-221.73	(Dominated)

VARIABLE: pFRI_NOVAX – Probability of FRI when vaccine not available

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.068	Adenovirus Vaccination	162.74	0.05	3035.58	0.00	0.00	0.00	
0.068	No Vaccination	177.03	0.28	635.96	14.29	-0.22	-63.59	(Dominated)
0.0765	Adenovirus Vaccination	162.74	0.05	3035.58	0.00	0.00	0.00	
0.0765	No Vaccination	199.16	0.31	635.96	36.42	-0.26	-140.32	(Dominated)
0.085	Adenovirus Vaccination	162.74	0.05	3035.58	0.00	0.00	0.00	
0.085	No Vaccination	221.29	0.35	635.96	58.55	-0.29	-198.91	(Dominated)
0.0935	Adenovirus Vaccination	162.74	0.05	3035.58	0.00	0.00	0.00	
0.0935	No Vaccination	243.42	0.38	635.96	80.68	-0.33	-245.12	(Dominated)
0.102	Adenovirus Vaccination	162.74	0.05	3035.58	0.00	0.00	0.00	
0.102	No Vaccination	265.54	0.42	635.96	102.81	-0.36	-282.48	(Dominated)

VARIABLE: pFRIVAX – Probability of FRI after receiving adenovirus vaccine

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.0081	Adenovirus Vaccination	160.40	0.05	3208.28	0.00	0.00	0.00	
0.0081	No Vaccination	221.29	0.35	635.96	60.89	-0.30	-204.36	(Dominated)
0.00855	Adenovirus Vaccination	161.57	0.05	3118.92	0.00	0.00	0.00	
0.00855	No Vaccination	221.29	0.35	635.96	59.72	-0.30	-201.65	(Dominated)
0.009	Adenovirus Vaccination	162.74	0.05	3035.58	0.00	0.00	0.00	
0.009	No Vaccination	221.29	0.35	635.96	58.55	-0.29	-198.91	(Dominated)
0.00945	Adenovirus Vaccination	163.91	0.06	2957.68	0.00	0.00	0.00	
0.00945	No Vaccination	221.29	0.35	635.96	57.38	-0.29	-196.14	(Dominated)
0.0099	Adenovirus Vaccination	165.08	0.06	2884.71	0.00	0.00	0.00	
0.0099	No Vaccination	221.29	0.35	635.96	56.21	-0.29	-193.33	(Dominated)

VARIABLE: pGBS – Probability of developing Guillain – Barre Syndrome after receiving adenovirus vaccine

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0	Adenovirus Vaccination	150.96	0.05	2936.56	0.00	0.00	0.00	
0	No Vaccination	221.29	0.35	635.96	70.33	-0.30	-237.15	(Dominated)
1.30E-04	Adenovirus Vaccination	183.35	0.06	3190.60	0.00	0.00	0.00	
1.30E-04	No Vaccination	221.29	0.35	635.96	37.94	-0.29	-130.59	(Dominated)
2.50E-04	Adenovirus Vaccination	215.74	0.06	3396.18	0.00	0.00	0.00	
2.50E-04	No Vaccination	221.29	0.35	635.96	5.54	-0.28	-19.49	(Dominated)
3.80E-04	No Vaccination	221.29	0.35	635.96	0.00	0.00	0.00	
3.80E-04	Adenovirus Vaccination	248.14	0.07	3565.96	26.85	0.28	96.45	Not Dominated
5.00E-04	No Vaccination	221.29	0.35	635.96	0.00	0.00	0.00	
5.00E-04	Adenovirus Vaccination	280.53	0.08	3708.54	59.24	0.27	217.55	Not Dominated

VARIABLE: pHOSP_VAX – Probability of hospitalization with FRI

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.135	Adenovirus Vaccination	157.29	0.05	2942.07	0.00	0.00	0.00	
0.135	No Vaccination	169.86	0.34	496.92	12.57	-0.29	-43.59	(Dominated)
0.21125	Adenovirus Vaccination	162.62	0.05	3033.49	0.00	0.00	0.00	
0.21125	No Vaccination	220.13	0.35	632.90	57.52	-0.29	-195.50	(Dominated)
0.2875	Adenovirus Vaccination	167.94	0.05	3124.42	0.00	0.00	0.00	
0.2875	No Vaccination	270.40	0.35	764.28	102.46	-0.30	-341.49	(Dominated)
0.36375	Adenovirus Vaccination	173.26	0.05	3214.86	0.00	0.00	0.00	
0.36375	No Vaccination	320.67	0.36	891.29	147.41	-0.31	-481.91	(Dominated)
0.44	Adenovirus Vaccination	178.58	0.05	3304.83	0.00	0.00	0.00	
0.44	No Vaccination	370.94	0.37	1014.15	192.36	-0.31	-617.07	(Dominated)

VARIABLE: pMAE – Probability of minor systemic adverse reactions

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.08	Adenovirus Vaccination	162.74	0.05	3217.25	0.00	0.00	0.00	
0.08	No Vaccination	221.29	0.35	635.96	58.55	-0.30	-196.89	(Dominated)
0.09	Adenovirus Vaccination	162.74	0.05	3123.77	0.00	0.00	0.00	
0.09	No Vaccination	221.29	0.35	635.96	58.55	-0.30	-197.89	(Dominated)
0.1	Adenovirus Vaccination	162.74	0.05	3035.58	0.00	0.00	0.00	
0.1	No Vaccination	221.29	0.35	635.96	58.55	-0.29	-198.91	(Dominated)
0.11	Adenovirus Vaccination	162.74	0.06	2952.23	0.00	0.00	0.00	
0.11	No Vaccination	221.29	0.35	635.96	58.55	-0.29	-199.94	(Dominated)
0.12	Adenovirus Vaccination	162.74	0.06	2873.33	0.00	0.00	0.00	
0.12	No Vaccination	221.29	0.35	635.96	58.55	-0.29	-200.98	(Dominated)

VARIABLE: pSIQ_ONLY – Probability of outpatient visit resulting in sick quarters

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.76	Adenovirus Vaccination	162.81	0.05	3031.55	0.00	0.00	0.00	
0.76	No Vaccination	221.94	0.33	673.78	59.14	-0.28	-214.50	(Dominated)
0.8175	Adenovirus Vaccination	162.79	0.05	3032.77	0.00	0.00	0.00	
0.8175	No Vaccination	221.74	0.34	661.90	58.96	-0.28	-209.56	(Dominated)
0.875	Adenovirus Vaccination	162.77	0.05	3033.99	0.00	0.00	0.00	
0.875	No Vaccination	221.55	0.34	650.40	58.78	-0.29	-204.82	(Dominated)
0.9325	Adenovirus Vaccination	162.74	0.05	3035.21	0.00	0.00	0.00	
0.9325	No Vaccination	221.35	0.35	639.28	58.60	-0.29	-200.26	(Dominated)
0.99	Adenovirus Vaccination	162.72	0.05	3036.43	0.00	0.00	0.00	
0.99	No Vaccination	221.15	0.35	628.51	58.43	-0.30	-195.88	(Dominated)

VARIABLE: pADVP – Probability of developing adenoviral pneumonia

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.072	Adenovirus Vaccination	162.68	0.05	3035.98	0.00	0.00	0.00	
0.072	No Vaccination	220.74	0.35	634.66	58.06	-0.29	-197.34	(Dominated)
0.092	Adenovirus Vaccination	162.82	0.05	3034.99	0.00	0.00	0.00	
0.092	No Vaccination	222.10	0.35	637.91	59.28	-0.29	-201.27	(Dominated)
0.112	Adenovirus Vaccination	162.97	0.05	3034.00	0.00	0.00	0.00	
0.112	No Vaccination	223.46	0.35	641.15	60.49	-0.29	-205.19	(Dominated)
0.132	Adenovirus Vaccination	163.11	0.05	3033.02	0.00	0.00	0.00	
0.132	No Vaccination	224.82	0.35	644.38	61.71	-0.30	-209.10	(Dominated)
0.152	Adenovirus Vaccination	163.26	0.05	3032.03	0.00	0.00	0.00	
0.152	No Vaccination	226.18	0.35	647.61	62.93	-0.30	-213.01	(Dominated)

NAVY ONE – WAY SENSITIVITY ANALYSES RESULTS

VARIABLE: cADVP – Cost of adenoviral pneumonia hospitalization

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
3171.54	Adenovirus Vaccination	156.83	0.06	2693.94	0.00	0.00	0.00	
3171.54	No Vaccination	162.75	0.38	428.68	5.92	-0.32	-18.43	(Dominated)
3567.9775	Adenovirus Vaccination	156.89	0.06	2694.92	0.00	0.00	0.00	
3567.9775	No Vaccination	163.28	0.38	430.07	6.40	-0.32	-19.90	(Dominated)
3964.415	Adenovirus Vaccination	156.94	0.06	2695.91	0.00	0.00	0.00	
3964.415	No Vaccination	163.81	0.38	431.46	6.87	-0.32	-21.36	(Dominated)
4360.8525	Adenovirus Vaccination	157.00	0.06	2696.90	0.00	0.00	0.00	
4360.8525	No Vaccination	164.34	0.38	432.85	7.34	-0.32	-22.82	(Dominated)
4757.29	Adenovirus Vaccination	157.06	0.06	2697.88	0.00	0.00	0.00	
4757.29	No Vaccination	164.86	0.38	434.25	7.81	-0.32	-24.29	(Dominated)

VARIABLE: cADV_VAX – Cost of adenovirus vaccine

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
100.98	Adenovirus Vaccination	132.03	0.06	2267.93	0.00	0.00	0.00	
100.98	No Vaccination	166.80	0.38	439.34	34.77	-0.32	-108.17	(Dominated)
138.235	No Vaccination	166.80	0.38	439.34	0.00	0.00	0.00	
138.235	Adenovirus Vaccination	169.28	0.06	2907.88	2.48	0.32	7.73	Not Dominated
175.49	No Vaccination	166.80	0.38	439.34	0.00	0.00	0.00	
175.49	Adenovirus Vaccination	206.54	0.06	3547.84	39.74	0.32	123.63	Not Dominated
212.745	No Vaccination	166.80	0.38	439.34	0.00	0.00	0.00	
212.745	Adenovirus Vaccination	243.79	0.06	4187.79	76.99	0.32	239.53	Not Dominated
250	No Vaccination	166.80	0.38	439.34	0.00	0.00	0.00	
250	Adenovirus Vaccination	281.05	0.06	4827.75	114.25	0.32	355.43	Not Dominated

VARIABLE: cFLLW_UP – Cost of outpatient visits for established patient

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
49.28	Adenovirus Vaccination	157.23	0.06	2700.90	0.00	0.00	0.00	
49.28	No Vaccination	166.48	0.38	438.49	9.24	-0.32	-28.76	(Dominated)
57.73	Adenovirus Vaccination	157.27	0.06	2701.48	0.00	0.00	0.00	
57.73	No Vaccination	166.79	0.38	439.32	9.52	-0.32	-29.63	(Dominated)
66.18	Adenovirus Vaccination	157.30	0.06	2702.06	0.00	0.00	0.00	
66.18	No Vaccination	167.10	0.38	440.14	9.80	-0.32	-30.50	(Dominated)
74.63	Adenovirus Vaccination	157.33	0.06	2702.63	0.00	0.00	0.00	
74.63	No Vaccination	167.42	0.38	440.97	10.08	-0.32	-31.37	(Dominated)
83.08	Adenovirus Vaccination	157.37	0.06	2703.21	0.00	0.00	0.00	
83.08	No Vaccination	167.73	0.38	441.79	10.36	-0.32	-32.23	(Dominated)

VARIABLE: cGBS – Cost of Guillain – Barre Syndrome

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
194674.13	Adenovirus Vaccination	154.83	0.06	2659.69	0.00	0.00	0.00	
194674.13	No Vaccination	166.80	0.38	439.34	11.96	-0.32	-37.22	(Dominated)
219008.395	Adenovirus Vaccination	156.05	0.06	2680.59	0.00	0.00	0.00	
219008.395	No Vaccination	166.80	0.38	439.34	10.75	-0.32	-33.44	(Dominated)
243342.66	Adenovirus Vaccination	157.27	0.06	2701.49	0.00	0.00	0.00	
243342.66	No Vaccination	166.80	0.38	439.34	9.53	-0.32	-29.65	(Dominated)
267676.925	Adenovirus Vaccination	158.48	0.06	2722.39	0.00	0.00	0.00	
267676.925	No Vaccination	166.80	0.38	439.34	8.31	-0.32	-25.87	(Dominated)
292011.19	Adenovirus Vaccination	159.70	0.06	2743.29	0.00	0.00	0.00	
292011.19	No Vaccination	166.80	0.38	439.34	7.10	-0.32	-22.08	(Dominated)

VARIABLE: cHOSP – Cost of FRI hospitalization

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
3257.76	No Vaccination	154.44	0.38	406.78	0.00	0.00	0.00	
3257.76	Adenovirus Vaccination	155.92	0.06	2678.41	1.49	0.32	4.63	Not Dominated
3662.73	Adenovirus Vaccination	156.60	0.06	2690.00	0.00	0.00	0.00	
3662.73	No Vaccination	160.64	0.38	423.12	4.04	-0.32	-12.57	(Dominated)
4067.7	Adenovirus Vaccination	157.27	0.06	2701.58	0.00	0.00	0.00	
4067.7	No Vaccination	166.84	0.38	439.46	9.57	-0.32	-29.78	(Dominated)
4472.67	Adenovirus Vaccination	157.95	0.06	2713.16	0.00	0.00	0.00	
4472.67	No Vaccination	173.05	0.38	455.80	15.10	-0.32	-46.98	(Dominated)
4877.64	Adenovirus Vaccination	158.62	0.06	2724.75	0.00	0.00	0.00	
4877.64	No Vaccination	179.25	0.38	472.14	20.63	-0.32	-64.18	(Dominated)

VARIABLE: cOUTPT – Cost of outpatient visit for new patient

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
82.58	Adenovirus Vaccination	157.15	0.06	2699.44	0.00	0.00	0.00	
82.58	No Vaccination	165.70	0.38	436.45	8.55	-0.32	-26.61	(Dominated)
94.2125	Adenovirus Vaccination	157.24	0.06	2701.08	0.00	0.00	0.00	
94.2125	No Vaccination	166.58	0.38	438.76	9.33	-0.32	-29.04	(Dominated)
105.845	Adenovirus Vaccination	157.34	0.06	2702.72	0.00	0.00	0.00	
105.845	No Vaccination	167.45	0.38	441.06	10.11	-0.32	-31.47	(Dominated)
117.4775	Adenovirus Vaccination	157.43	0.06	2704.35	0.00	0.00	0.00	
117.4775	No Vaccination	168.33	0.38	443.37	10.90	-0.32	-33.90	(Dominated)
129.11	Adenovirus Vaccination	157.53	0.06	2705.99	0.00	0.00	0.00	
129.11	No Vaccination	169.21	0.38	445.68	11.68	-0.32	-36.33	(Dominated)

VARIABLE: cTRAIN – Cost of training basic trainee per day

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
262.15	No Vaccination	138.89	0.38	365.82	0.00	0.00	0.00	
262.15	Adenovirus Vaccination	153.99	0.06	2645.22	15.10	0.32	46.99	Not Dominated
311.3875	No Vaccination	149.94	0.38	394.95	0.00	0.00	0.00	
311.3875	Adenovirus Vaccination	155.29	0.06	2667.51	5.34	0.32	16.63	Not Dominated
360.625	Adenovirus Vaccination	156.59	0.06	2689.81	0.00	0.00	0.00	
360.625	No Vaccination	161.00	0.38	424.07	4.42	-0.32	-13.74	(Dominated)
409.8625	Adenovirus Vaccination	157.89	0.06	2712.10	0.00	0.00	0.00	
409.8625	No Vaccination	172.06	0.38	453.20	14.18	-0.32	-44.10	(Dominated)
459.1	Adenovirus Vaccination	159.18	0.06	2734.40	0.00	0.00	0.00	
459.1	No Vaccination	183.12	0.38	482.33	23.94	-0.32	-74.46	(Dominated)

VARIABLE: effAdV_HOSP – Training days lost due to adenoviral pneumonia

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
3	Adenovirus Vaccination	157.21	0.06	2707.27	0.00	0.00	0.00	
3	No Vaccination	166.28	0.38	439.53	9.07	-0.32	-28.33	(Dominated)
4	Adenovirus Vaccination	157.27	0.06	2701.49	0.00	0.00	0.00	
4	No Vaccination	166.80	0.38	439.34	9.53	-0.32	-29.65	(Dominated)
5	Adenovirus Vaccination	157.32	0.06	2695.75	0.00	0.00	0.00	
5	No Vaccination	167.31	0.38	439.15	9.99	-0.32	-30.96	(Dominated)
6	Adenovirus Vaccination	157.38	0.06	2690.03	0.00	0.00	0.00	
6	No Vaccination	167.83	0.38	438.97	10.45	-0.32	-32.27	(Dominated)
7	Adenovirus Vaccination	157.44	0.06	2684.35	0.00	0.00	0.00	
7	No Vaccination	168.34	0.38	438.79	10.91	-0.33	-33.56	(Dominated)

VARIABLE: effFRI_HOSP – Training days lost due to FRI hospitalization

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
1	No Vaccination	154.96	0.35	443.98	0.00	0.00	0.00	
1	Adenovirus Vaccination	155.98	0.05	2841.96	1.02	0.29	3.48	Not Dominated
3.75	Adenovirus Vaccination	157.75	0.06	2652.87	0.00	0.00	0.00	
3.75	No Vaccination	171.24	0.39	437.78	13.49	-0.33	-40.67	(Dominated)
6.5	Adenovirus Vaccination	159.52	0.06	2490.82	0.00	0.00	0.00	
6.5	No Vaccination	187.52	0.43	432.79	28.00	-0.37	-75.83	(Dominated)
9.25	Adenovirus Vaccination	161.29	0.07	2350.40	0.00	0.00	0.00	
9.25	No Vaccination	203.80	0.48	428.68	42.51	-0.41	-104.50	(Dominated)
12	Adenovirus Vaccination	163.06	0.07	2227.54	0.00	0.00	0.00	
12	No Vaccination	220.08	0.52	425.24	57.02	-0.44	-128.33	(Dominated)

VARIABLE: effGBS – Training days lost due to Guillain – Barre Syndrome

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
31	Adenovirus Vaccination	157.11	0.06	2717.51	0.00	0.00	0.00	
31	No Vaccination	166.80	0.38	439.34	9.69	-0.32	-30.09	(Dominated)
35	Adenovirus Vaccination	157.19	0.06	2709.47	0.00	0.00	0.00	
35	No Vaccination	166.80	0.38	439.34	9.61	-0.32	-29.87	(Dominated)
39	Adenovirus Vaccination	157.27	0.06	2701.49	0.00	0.00	0.00	
39	No Vaccination	166.80	0.38	439.34	9.53	-0.32	-29.65	(Dominated)
43	Adenovirus Vaccination	157.34	0.06	2693.57	0.00	0.00	0.00	
43	No Vaccination	166.80	0.38	439.34	9.45	-0.32	-29.43	(Dominated)
47	Adenovirus Vaccination	157.42	0.06	2685.69	0.00	0.00	0.00	
47	No Vaccination	166.80	0.38	439.34	9.38	-0.32	-29.21	(Dominated)

VARIABLE: effLP – Training days lost due to lost productivity

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.93	Adenovirus Vaccination	157.27	0.05	3052.83	0.00	0.00	0.00	
0.93	No Vaccination	166.80	0.32	524.49	9.53	-0.27	-35.76	(Dominated)
1.24	Adenovirus Vaccination	157.27	0.05	2879.55	0.00	0.00	0.00	
1.24	No Vaccination	166.80	0.35	481.33	9.53	-0.29	-32.65	(Dominated)
1.55	Adenovirus Vaccination	157.27	0.06	2724.90	0.00	0.00	0.00	
1.55	No Vaccination	166.80	0.38	444.73	9.53	-0.32	-30.03	(Dominated)
1.86	Adenovirus Vaccination	157.27	0.06	2586.00	0.00	0.00	0.00	
1.86	No Vaccination	166.80	0.40	413.30	9.53	-0.34	-27.81	(Dominated)
2.17	Adenovirus Vaccination	157.27	0.06	2460.58	0.00	0.00	0.00	
2.17	No Vaccination	166.80	0.43	386.02	9.53	-0.37	-25.89	(Dominated)

VARIABLE: effMAE – Training days lost due to minor vaccine systemic reactions

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.03	Adenovirus Vaccination	157.27	0.05	3402.95	0.00	0.00	0.00	
0.03	No Vaccination	166.80	0.38	439.34	9.53	-0.33	-28.58	(Dominated)
0.0675	Adenovirus Vaccination	157.27	0.05	3147.55	0.00	0.00	0.00	
0.0675	No Vaccination	166.80	0.38	439.34	9.53	-0.33	-28.91	(Dominated)
0.105	Adenovirus Vaccination	157.27	0.05	2927.81	0.00	0.00	0.00	
0.105	No Vaccination	166.80	0.38	439.34	9.53	-0.33	-29.24	(Dominated)
0.1425	Adenovirus Vaccination	157.27	0.06	2736.75	0.00	0.00	0.00	
0.1425	No Vaccination	166.80	0.38	439.34	9.53	-0.32	-29.58	(Dominated)
0.18	Adenovirus Vaccination	157.27	0.06	2569.10	0.00	0.00	0.00	
0.18	No Vaccination	166.80	0.38	439.34	9.53	-0.32	-29.93	(Dominated)

VARIABLE: effOUTPT – Training days lost due to outpatient visits

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.056	Adenovirus Vaccination	157.27	0.06	2709.45	0.00	0.00	0.00	
0.056	No Vaccination	166.80	0.38	441.17	9.53	-0.32	-29.78	(Dominated)
0.063	Adenovirus Vaccination	157.27	0.06	2705.47	0.00	0.00	0.00	
0.063	No Vaccination	166.80	0.38	440.25	9.53	-0.32	-29.72	(Dominated)
0.07	Adenovirus Vaccination	157.27	0.06	2701.49	0.00	0.00	0.00	
0.07	No Vaccination	166.80	0.38	439.34	9.53	-0.32	-29.65	(Dominated)
0.077	Adenovirus Vaccination	157.27	0.06	2697.53	0.00	0.00	0.00	
0.077	No Vaccination	166.80	0.38	438.43	9.53	-0.32	-29.59	(Dominated)
0.084	Adenovirus Vaccination	157.27	0.06	2693.58	0.00	0.00	0.00	
0.084	No Vaccination	166.80	0.38	437.53	9.53	-0.32	-29.52	(Dominated)

VARIABLE: effSIQ – Training days lost due to time in sick quarters

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
1	No Vaccination	128.95	0.28	457.74	0.00	0.00	0.00	
1	Adenovirus Vaccination	153.15	0.05	3219.63	24.21	0.23	103.39	Not Dominated
1.5	No Vaccination	143.51	0.32	449.32	0.00	0.00	0.00	
1.5	Adenovirus Vaccination	154.74	0.05	2995.08	11.23	0.27	41.95	Not Dominated
2	Adenovirus Vaccination	156.32	0.06	2803.50	0.00	0.00	0.00	
2	No Vaccination	158.06	0.36	442.69	1.75	-0.30	-5.79	(Dominated)
2.5	Adenovirus Vaccination	157.90	0.06	2638.14	0.00	0.00	0.00	
2.5	No Vaccination	172.62	0.39	437.32	14.72	-0.33	-43.96	(Dominated)
3	Adenovirus Vaccination	159.48	0.06	2493.95	0.00	0.00	0.00	
3	No Vaccination	187.18	0.43	432.89	27.70	-0.37	-75.17	(Dominated)

VARIABLE: pADVP – Probability of developing adenoviral pneumonia

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.064	Adenovirus Vaccination	157.19	0.06	2701.58	0.00	0.00	0.00	
0.064	No Vaccination	166.12	0.38	437.87	8.93	-0.32	-27.80	(Dominated)
0.086	Adenovirus Vaccination	157.30	0.06	2701.46	0.00	0.00	0.00	
0.086	No Vaccination	167.05	0.38	439.89	9.76	-0.32	-30.34	(Dominated)
0.108	Adenovirus Vaccination	157.40	0.06	2701.34	0.00	0.00	0.00	
0.108	No Vaccination	167.98	0.38	441.90	10.58	-0.32	-32.88	(Dominated)
0.13	Adenovirus Vaccination	157.50	0.06	2701.23	0.00	0.00	0.00	
0.13	No Vaccination	168.91	0.38	443.92	11.41	-0.32	-35.41	(Dominated)
0.152	Adenovirus Vaccination	157.60	0.06	2701.11	0.00	0.00	0.00	
0.152	No Vaccination	169.83	0.38	445.92	12.24	-0.32	-37.94	(Dominated)

VARIABLE: pFRI_NOVAX – Probability of FRI when vaccine not available

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.0736	No Vaccination	133.44	0.30	439.34	0.00	0.00	0.00	
0.0736	Adenovirus Vaccination	157.27	0.06	2701.49	23.83	0.25	97.06	Not Dominated
0.2217	Adenovirus Vaccination	157.27	0.06	2701.49	0.00	0.00	0.00	
0.2217	No Vaccination	401.95	0.91	439.34	244.68	-0.86	-285.62	(Dominated)
0.3698	Adenovirus Vaccination	157.27	0.06	2701.49	0.00	0.00	0.00	
0.3698	No Vaccination	670.46	1.53	439.34	513.19	-1.47	-349.62	(Dominated)
0.5179	Adenovirus Vaccination	157.27	0.06	2701.49	0.00	0.00	0.00	
0.5179	No Vaccination	938.97	2.14	439.34	781.70	-2.08	-376.00	(Dominated)
0.666	Adenovirus Vaccination	157.27	0.06	2701.49	0.00	0.00	0.00	
0.666	No Vaccination	1207.48	2.75	439.34	1050.21	-2.69	-390.39	(Dominated)

VARIABLE: pFRI_VAX – Probability of FRI after vaccination

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.008	Adenovirus Vaccination	153.64	0.05	3075.18	0.00	0.00	0.00	
0.008	No Vaccination	166.80	0.38	439.34	13.16	-0.33	-39.90	(Dominated)
0.009	Adenovirus Vaccination	155.45	0.05	2874.08	0.00	0.00	0.00	
0.009	No Vaccination	166.80	0.38	439.34	11.34	-0.33	-34.84	(Dominated)
0.01	Adenovirus Vaccination	157.27	0.06	2701.49	0.00	0.00	0.00	
0.01	No Vaccination	166.80	0.38	439.34	9.53	-0.32	-29.65	(Dominated)
0.011	Adenovirus Vaccination	159.08	0.06	2551.75	0.00	0.00	0.00	
0.011	No Vaccination	166.80	0.38	439.34	7.72	-0.32	-24.32	(Dominated)
0.012	Adenovirus Vaccination	160.89	0.07	2420.61	0.00	0.00	0.00	
0.012	No Vaccination	166.80	0.38	439.34	5.91	-0.31	-18.86	(Dominated)

VARIABLE: pGBS – Probability of Guillain – Barre Syndrome after adenovirus vaccination

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
5.00E-05	Adenovirus Vaccination	157.27	0.06	2701.49	0.00	0.00	0.00	
5.00E-05	No Vaccination	166.80	0.38	439.34	9.53	-0.32	-29.65	(Dominated)
1.60E-04	No Vaccination	166.80	0.38	439.34	0.00	0.00	0.00	
1.60E-04	Adenovirus Vaccination	186.34	0.06	2976.73	19.54	0.32	61.62	Not Dominated
2.80E-04	No Vaccination	166.80	0.38	439.34	0.00	0.00	0.00	
2.80E-04	Adenovirus Vaccination	215.41	0.07	3215.94	48.61	0.31	155.46	Not Dominated
3.90E-04	No Vaccination	166.80	0.38	439.34	0.00	0.00	0.00	
3.90E-04	Adenovirus Vaccination	244.48	0.07	3425.78	77.68	0.31	251.96	Not Dominated
5.00E-04	No Vaccination	166.80	0.38	439.34	0.00	0.00	0.00	
5.00E-04	Adenovirus Vaccination	273.55	0.08	3611.33	106.75	0.30	351.24	Not Dominated

VARIABLE: pHOSP_VAX – Probability of hospitalization due to FRI

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.145	No Vaccination	151.72	0.38	402.59	0.00	0.00	0.00	
0.145	Adenovirus Vaccination	155.63	0.06	2687.40	3.91	0.32	12.26	Not Dominated
0.163	Adenovirus Vaccination	156.45	0.06	2694.47	0.00	0.00	0.00	
0.163	No Vaccination	159.26	0.38	421.03	2.81	-0.32	-8.78	(Dominated)
0.181	Adenovirus Vaccination	157.27	0.06	2701.49	0.00	0.00	0.00	
0.181	No Vaccination	166.80	0.38	439.34	9.53	-0.32	-29.65	(Dominated)
0.199	Adenovirus Vaccination	158.09	0.06	2708.48	0.00	0.00	0.00	
0.199	No Vaccination	174.34	0.38	457.51	16.25	-0.32	-50.36	(Dominated)
0.217	Adenovirus Vaccination	158.91	0.06	2715.44	0.00	0.00	0.00	
0.217	No Vaccination	181.88	0.38	475.55	22.97	-0.32	-70.92	(Dominated)

VARIABLE: pMAE – Probability of minor systemic reactions after adenovirus vaccination

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.08	Adenovirus Vaccination	157.27	0.06	2848.28	0.00	0.00	0.00	
0.08	No Vaccination	166.80	0.38	439.34	9.53	-0.32	-29.37	(Dominated)
0.09	Adenovirus Vaccination	157.27	0.06	2772.95	0.00	0.00	0.00	
0.09	No Vaccination	166.80	0.38	439.34	9.53	-0.32	-29.51	(Dominated)
0.1	Adenovirus Vaccination	157.27	0.06	2701.49	0.00	0.00	0.00	
0.1	No Vaccination	166.80	0.38	439.34	9.53	-0.32	-29.65	(Dominated)
0.11	Adenovirus Vaccination	157.27	0.06	2633.63	0.00	0.00	0.00	
0.11	No Vaccination	166.80	0.38	439.34	9.53	-0.32	-29.79	(Dominated)
0.12	Adenovirus Vaccination	157.27	0.06	2569.09	0.00	0.00	0.00	
0.12	No Vaccination	166.80	0.38	439.34	9.53	-0.32	-29.93	(Dominated)

VARIABLE: pSIQ_ONLY – Probability of outpatient visit resulting in sick quarters

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.76	Adenovirus Vaccination	157.35	0.06	2697.84	0.00	0.00	0.00	
0.76	No Vaccination	167.63	0.38	440.36	10.28	-0.32	-31.89	(Dominated)
0.8175	Adenovirus Vaccination	157.32	0.06	2698.94	0.00	0.00	0.00	
0.8175	No Vaccination	167.38	0.38	440.05	10.05	-0.32	-31.21	(Dominated)
0.875	Adenovirus Vaccination	157.30	0.06	2700.05	0.00	0.00	0.00	
0.875	No Vaccination	167.13	0.38	439.74	9.83	-0.32	-30.54	(Dominated)
0.9325	Adenovirus Vaccination	157.28	0.06	2701.16	0.00	0.00	0.00	
0.9325	No Vaccination	166.88	0.38	439.43	9.60	-0.32	-29.86	(Dominated)
0.99	Adenovirus Vaccination	157.25	0.06	2702.26	0.00	0.00	0.00	
0.99	No Vaccination	166.62	0.38	439.12	9.37	-0.32	-29.18	(Dominated)

MARINE CORPS ONE – WAY SENSITIVITY ANALYSIS RESULTS

VARIABLE: cADVP – Cost of hospitalization due to adenoviral pneumonia

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
10557.89	No Adenovirus Vaccines	143.45	0.19	760.31	0.00	0.00	0.00	
10557.89	Adenovirus Vaccine	152.04	0.02	7620.95	8.58	0.17	50.88	Not Dominated
11875.38	No Adenovirus Vaccines	144.68	0.19	766.82	0.00	0.00	0.00	
11875.38	Adenovirus Vaccine	152.14	0.02	7626.42	7.47	0.17	44.25	Not Dominated
13192.86	No Adenovirus Vaccines	145.91	0.19	773.34	0.00	0.00	0.00	
13192.86	Adenovirus Vaccine	152.25	0.02	7631.90	6.35	0.17	37.61	Not Dominated
14510.35	No Adenovirus Vaccines	147.14	0.19	779.85	0.00	0.00	0.00	
14510.35	Adenovirus Vaccine	152.36	0.02	7637.37	5.23	0.17	30.98	Not Dominated
15827.83	No Adenovirus Vaccines	148.36	0.19	786.36	0.00	0.00	0.00	
15827.83	Adenovirus Vaccine	152.47	0.02	7642.84	4.11	0.17	24.35	Not Dominated

VARIABLE: cADV_VAX – Cost of adenovirus vaccine

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
100.98	Adenovirus Vaccine	127.01	0.02	6366.70	0.00	0.00	0.00	
100.98	No Adenovirus Vaccines	145.90	0.19	773.32	18.89	-0.17	-111.97	(Dominated)
138.24	No Adenovirus Vaccines	145.90	0.19	773.32	0.00	0.00	0.00	
138.24	Adenovirus Vaccine	164.27	0.02	8234.15	18.36	0.17	108.84	Not Dominated
175.49	No Adenovirus Vaccines	145.90	0.19	773.32	0.00	0.00	0.00	
175.49	Adenovirus Vaccine	201.52	0.02	10101.60	55.62	0.17	329.64	Not Dominated
212.75	No Adenovirus Vaccines	145.90	0.19	773.32	0.00	0.00	0.00	
212.75	Adenovirus Vaccine	238.78	0.02	11969.04	92.87	0.17	550.45	Not Dominated
250.00	No Adenovirus Vaccines	145.90	0.19	773.32	0.00	0.00	0.00	
250.00	Adenovirus Vaccine	276.03	0.02	13836.49	130.13	0.17	771.25	Not Dominated

VARIABLE: cFLLW_UP – Cost of outpatient visit for established patient

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
41.95	No Adenovirus Vaccines	145.64	0.19	771.89	0.00	0.00	0.00	
41.95	Adenovirus Vaccine	152.23	0.02	7630.68	6.59	0.17	39.08	Not Dominated
49.55	No Adenovirus Vaccines	145.83	0.19	772.90	0.00	0.00	0.00	
49.55	Adenovirus Vaccine	152.25	0.02	7631.53	6.42	0.17	38.06	Not Dominated
57.14	No Adenovirus Vaccines	146.02	0.19	773.90	0.00	0.00	0.00	
57.14	Adenovirus Vaccine	152.26	0.02	7632.38	6.25	0.17	37.03	Not Dominated
64.74	No Adenovirus Vaccines	146.20	0.19	774.91	0.00	0.00	0.00	
64.74	Adenovirus Vaccine	152.28	0.02	7633.22	6.08	0.17	36.01	Not Dominated
72.33	No Adenovirus Vaccines	146.39	0.19	775.91	0.00	0.00	0.00	
72.33	Adenovirus Vaccine	152.30	0.02	7634.07	5.90	0.17	34.98	Not Dominated

VARIABLE: cGBS – Cost of Guillain – Barre Syndrome

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
194674.13	No Adenovirus Vaccines	145.90	0.19	773.32	0.00	0.00	0.00	
194674.13	Adenovirus Vaccine	149.82	0.02	7509.91	3.92	0.17	23.21	Not Dominated
219008.40	No Adenovirus Vaccines	145.90	0.19	773.32	0.00	0.00	0.00	
219008.40	Adenovirus Vaccine	151.04	0.02	7570.90	5.13	0.17	30.42	Not Dominated
243342.66	No Adenovirus Vaccines	145.90	0.19	773.32	0.00	0.00	0.00	
243342.66	Adenovirus Vaccine	152.25	0.02	7631.88	6.35	0.17	37.63	Not Dominated
267676.93	No Adenovirus Vaccines	145.90	0.19	773.32	0.00	0.00	0.00	
267676.93	Adenovirus Vaccine	153.47	0.02	7692.87	7.57	0.17	44.84	Not Dominated
292011.19	No Adenovirus Vaccines	145.90	0.19	773.32	0.00	0.00	0.00	
292011.19	Adenovirus Vaccine	154.69	0.02	7753.86	8.78	0.17	52.05	Not Dominated

VARIABLE: cHOSP – Cost of hospitalization due to FRI

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
7259.88	No Adenovirus Vaccines	126.44	0.19	670.17	0.00	0.00	0.00	
7259.88	Adenovirus Vaccine	150.52	0.02	7545.18	24.08	0.17	142.72	Not Dominated
8167.36	No Adenovirus Vaccines	136.17	0.19	721.75	0.00	0.00	0.00	
8167.36	Adenovirus Vaccine	151.39	0.02	7588.53	15.21	0.17	90.17	Not Dominated
9074.84	No Adenovirus Vaccines	145.90	0.19	773.32	0.00	0.00	0.00	
9074.84	Adenovirus Vaccine	152.25	0.02	7631.88	6.35	0.17	37.63	Not Dominated
9982.32	Adenovirus Vaccine	153.12	0.02	7675.24	0.00	0.00	0.00	
9982.32	No Adenovirus Vaccines	155.64	0.19	824.89	2.52	-0.17	-14.92	(Dominated)
10889.80	Adenovirus Vaccine	153.98	0.02	7718.59	0.00	0.00	0.00	
10889.80	No Adenovirus Vaccines	165.37	0.19	876.47	11.38	-0.17	-67.46	(Dominated)

VARIABLE: cOUTPT – Cost of outpatient visit for new patient

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
73.80	No Adenovirus Vaccines	145.48	0.19	771.05	0.00	0.00	0.00	
73.80	Adenovirus Vaccine	152.22	0.02	7629.98	6.74	0.17	39.94	Not Dominated
84.64	No Adenovirus Vaccines	145.84	0.19	772.97	0.00	0.00	0.00	
84.64	Adenovirus Vaccine	152.25	0.02	7631.59	6.41	0.17	37.99	Not Dominated
95.48	No Adenovirus Vaccines	146.20	0.19	774.88	0.00	0.00	0.00	
95.48	Adenovirus Vaccine	152.28	0.02	7633.20	6.08	0.17	36.04	Not Dominated
106.31	No Adenovirus Vaccines	146.56	0.19	776.80	0.00	0.00	0.00	
106.31	Adenovirus Vaccine	152.31	0.02	7634.81	5.75	0.17	34.08	Not Dominated
117.15	No Adenovirus Vaccines	146.92	0.19	778.71	0.00	0.00	0.00	
117.15	Adenovirus Vaccine	152.34	0.02	7636.42	5.42	0.17	32.13	Not Dominated

VARIABLE: cTRAIN – Cost of training basic trainee per day

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
262.15	No Adenovirus Vaccines	143.33	0.19	759.65	0.00	0.00	0.00	
262.15	Adenovirus Vaccine	151.95	0.02	7616.77	8.63	0.17	51.13	Not Dominated
311.39	No Adenovirus Vaccines	148.87	0.19	789.03	0.00	0.00	0.00	
311.39	Adenovirus Vaccine	152.60	0.02	7649.25	3.73	0.17	22.11	Not Dominated
360.63	Adenovirus Vaccine	153.25	0.02	7681.72	0.00	0.00	0.00	
360.63	No Adenovirus Vaccines	154.41	0.19	818.41	1.16	-0.17	-6.90	(Dominated)
409.86	Adenovirus Vaccine	153.90	0.02	7714.20	0.00	0.00	0.00	
409.86	No Adenovirus Vaccines	159.96	0.19	847.80	6.06	-0.17	-35.92	(Dominated)
459.10	Adenovirus Vaccine	154.54	0.02	7746.67	0.00	0.00	0.00	
459.10	No Adenovirus Vaccines	165.50	0.19	877.18	10.96	-0.17	-64.94	(Dominated)

VARIABLE: effADV_HOSP – Training days lost due to adenoviral pneumonia hospitalization

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
3	No Adenovirus Vaccines	145.64	0.19	775.75	0.00	0.00	0.00	
3	Adenovirus Vaccine	152.23	0.02	7662.53	6.59	0.17	39.26	Not Dominated
4	No Adenovirus Vaccines	145.90	0.19	773.32	0.00	0.00	0.00	
4	Adenovirus Vaccine	152.25	0.02	7631.88	6.35	0.17	37.63	Not Dominated
5	No Adenovirus Vaccines	146.17	0.19	770.92	0.00	0.00	0.00	
5	Adenovirus Vaccine	152.28	0.02	7601.49	6.11	0.17	36.01	Not Dominated
6	No Adenovirus Vaccines	146.44	0.19	768.54	0.00	0.00	0.00	
6	Adenovirus Vaccine	152.30	0.02	7571.35	5.86	0.17	34.41	Not Dominated
7	No Adenovirus Vaccines	146.70	0.19	766.19	0.00	0.00	0.00	
7	Adenovirus Vaccine	152.32	0.02	7541.45	5.62	0.17	32.83	Not Dominated

VARIABLE: effFRI_HOSP – Training days lost due to FRI hospitalization

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
1.00	No Adenovirus Vaccines	139.79	0.17	835.93	0.00	0.00	0.00	
1.00	Adenovirus Vaccine	151.71	0.02	8408.01	11.92	0.15	79.89	Not Dominated
3.75	No Adenovirus Vaccines	148.20	0.20	753.36	0.00	0.00	0.00	
3.75	Adenovirus Vaccine	152.46	0.02	7377.75	4.26	0.18	24.20	Not Dominated
6.50	Adenovirus Vaccine	153.20	0.02	6579.42	0.00	0.00	0.00	
6.50	No Adenovirus Vaccines	156.60	0.23	692.31	3.40	-0.20	-16.75	(Dominated)
9.25	Adenovirus Vaccine	153.95	0.03	5942.62	0.00	0.00	0.00	
9.25	No Adenovirus Vaccines	165.01	0.26	645.35	11.06	-0.23	-48.12	(Dominated)
12.00	Adenovirus Vaccine	154.70	0.03	5422.83	0.00	0.00	0.00	
12.00	No Adenovirus Vaccines	173.41	0.29	608.09	18.72	-0.26	-72.92	(Dominated)

VARIABLE: effGBS – Training days lost due to Guillain – Barre Syndrome

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
50.00	No Adenovirus Vaccines	145.90	0.19	773.32	0.00	0.00	0.00	
50.00	Adenovirus Vaccine	152.07	0.02	7879.32	6.16	0.17	36.39	Not Dominated
56.50	No Adenovirus Vaccines	145.90	0.19	773.32	0.00	0.00	0.00	
56.50	Adenovirus Vaccine	152.16	0.02	7753.55	6.26	0.17	37.01	Not Dominated
63.00	No Adenovirus Vaccines	145.90	0.19	773.32	0.00	0.00	0.00	
63.00	Adenovirus Vaccine	152.25	0.02	7631.88	6.35	0.17	37.63	Not Dominated
69.50	No Adenovirus Vaccines	145.90	0.19	773.32	0.00	0.00	0.00	
69.50	Adenovirus Vaccine	152.35	0.02	7514.12	6.44	0.17	38.25	Not Dominated
76.00	No Adenovirus Vaccines	145.90	0.19	773.32	0.00	0.00	0.00	
76.00	Adenovirus Vaccine	152.44	0.02	7400.06	6.53	0.17	38.88	Not Dominated

VARIABLE: effLP – Training days lost due to lost productivity

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.93	No Adenovirus Vaccines	145.90	0.16	920.40	0.00	0.00	0.00	
0.93	Adenovirus Vaccine	152.25	0.02	8816.17	6.35	0.14	44.95	Not Dominated
1.24	No Adenovirus Vaccines	145.90	0.17	845.96	0.00	0.00	0.00	
1.24	Adenovirus Vaccine	152.25	0.02	8225.59	6.35	0.15	41.24	Not Dominated
1.55	No Adenovirus Vaccines	145.90	0.19	782.65	0.00	0.00	0.00	
1.55	Adenovirus Vaccine	152.25	0.02	7709.17	6.35	0.17	38.09	Not Dominated
1.86	No Adenovirus Vaccines	145.90	0.20	728.17	0.00	0.00	0.00	
1.86	Adenovirus Vaccine	152.25	0.02	7253.76	6.35	0.18	35.39	Not Dominated
2.17	No Adenovirus Vaccines	145.90	0.21	680.77	0.00	0.00	0.00	
2.17	Adenovirus Vaccine	152.25	0.02	6849.15	6.35	0.19	33.05	Not Dominated

VARIABLE: effMAE – Training days lost due to minor systemic reactions to adenovirus vaccine

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.03	No Adenovirus Vaccines	145.90	0.19	773.32	0.00	0.00	0.00	
0.03	Adenovirus Vaccine	152.25	0.02	7642.61	6.35	0.17	37.62	Not Dominated
0.07	No Adenovirus Vaccines	145.90	0.19	773.32	0.00	0.00	0.00	
0.07	Adenovirus Vaccine	152.25	0.02	7636.86	6.35	0.17	37.63	Not Dominated
0.11	No Adenovirus Vaccines	145.90	0.19	773.32	0.00	0.00	0.00	
0.11	Adenovirus Vaccine	152.25	0.02	7631.12	6.35	0.17	37.63	Not Dominated
0.14	No Adenovirus Vaccines	145.90	0.19	773.32	0.00	0.00	0.00	
0.14	Adenovirus Vaccine	152.25	0.02	7625.39	6.35	0.17	37.63	Not Dominated
0.18	No Adenovirus Vaccines	145.90	0.19	773.32	0.00	0.00	0.00	
0.18	Adenovirus Vaccine	152.25	0.02	7619.66	6.35	0.17	37.64	Not Dominated

VARIABLE: effOUPT – Training days lost due to outpatient office visits

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.056	No Adenovirus Vaccines	145.90	0.19	776.68	0.00	0.00	0.00	
0.056	Adenovirus Vaccine	152.25	0.02	7658.95	6.35	0.17	37.80	Not Dominated
0.063	No Adenovirus Vaccines	145.90	0.19	775.00	0.00	0.00	0.00	
0.063	Adenovirus Vaccine	152.25	0.02	7645.39	6.35	0.17	37.71	Not Dominated
0.07	No Adenovirus Vaccines	145.90	0.19	773.32	0.00	0.00	0.00	
0.07	Adenovirus Vaccine	152.25	0.02	7631.88	6.35	0.17	37.63	Not Dominated
0.077	No Adenovirus Vaccines	145.90	0.19	771.65	0.00	0.00	0.00	
0.077	Adenovirus Vaccine	152.25	0.02	7618.43	6.35	0.17	37.55	Not Dominated
0.084	No Adenovirus Vaccines	145.90	0.19	769.99	0.00	0.00	0.00	
0.084	Adenovirus Vaccine	152.25	0.02	7605.01	6.35	0.17	37.46	Not Dominated

VARIABLE: effSIQ – Training days lost due to time spend in sick quarters

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
1	No Adenovirus Vaccines	133.55	0.15	918.96	0.00	0.00	0.00	
1	Adenovirus Vaccine	151.16	0.02	9390.47	17.61	0.13	136.25	Not Dominated
1.5	No Adenovirus Vaccines	138.30	0.16	853.72	0.00	0.00	0.00	
1.5	Adenovirus Vaccine	151.58	0.02	8622.86	13.28	0.14	91.93	Not Dominated
2	No Adenovirus Vaccines	143.05	0.18	800.66	0.00	0.00	0.00	
2	Adenovirus Vaccine	152.00	0.02	7974.61	8.95	0.16	56.05	Not Dominated
2.5	No Adenovirus Vaccines	147.81	0.20	756.65	0.00	0.00	0.00	
2.5	Adenovirus Vaccine	152.42	0.02	7419.89	4.62	0.17	26.41	Not Dominated
3	No Adenovirus Vaccines	152.56	0.21	719.57	0.00	0.00	0.00	
3	Adenovirus Vaccine	152.85	0.02	6939.81	0.29	0.19	1.51	Not Dominated

VARIABLE: pADVP – Probability of developing adenoviral pneumonia

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.067	No Adenovirus Vaccines	145.24	0.19	770.41	0.00	0.00	0.00	
0.067	Adenovirus Vaccine	152.19	0.02	7633.42	6.96	0.17	41.26	Not Dominated
0.08825	No Adenovirus Vaccines	146.33	0.19	775.17	0.00	0.00	0.00	
0.08825	Adenovirus Vaccine	152.29	0.02	7630.91	5.96	0.17	35.32	Not Dominated
0.1095	No Adenovirus Vaccines	147.42	0.19	779.92	0.00	0.00	0.00	
0.1095	Adenovirus Vaccine	152.39	0.02	7628.41	4.97	0.17	29.40	Not Dominated
0.13075	No Adenovirus Vaccines	148.51	0.19	784.65	0.00	0.00	0.00	
0.13075	Adenovirus Vaccine	152.49	0.02	7625.92	3.98	0.17	23.50	Not Dominated
0.152	No Adenovirus Vaccines	149.60	0.19	789.38	0.00	0.00	0.00	
0.152	Adenovirus Vaccine	152.58	0.02	7623.42	2.98	0.17	17.61	Not Dominated

VARIABLE: pFRI_NOVAX – Probability of FRI when adenovirus vaccine not available

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.07	Adenovirus Vaccine	152.25	0.02	7631.88	0.00	0.00	0.00	
0.07	No Adenovirus Vaccines	238.64	0.31	773.32	86.38	-0.29	-299.28	(Dominated)
0.08	Adenovirus Vaccine	152.25	0.02	7631.88	0.00	0.00	0.00	
0.08	No Adenovirus Vaccines	268.47	0.35	773.32	116.21	-0.33	-355.16	(Dominated)
0.09	Adenovirus Vaccine	152.25	0.02	7631.88	0.00	0.00	0.00	
0.09	No Adenovirus Vaccines	298.29	0.39	773.32	146.04	-0.37	-399.26	(Dominated)
0.10	Adenovirus Vaccine	152.25	0.02	7631.88	0.00	0.00	0.00	
0.10	No Adenovirus Vaccines	328.12	0.42	773.32	175.87	-0.40	-434.94	(Dominated)
0.11	Adenovirus Vaccine	152.25	0.02	7631.88	0.00	0.00	0.00	
0.11	No Adenovirus Vaccines	357.95	0.46	773.32	205.70	-0.44	-464.41	(Dominated)

VARIABLE: pFRI_VAX – Probability of FRI after receiving adenovirus vaccine

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.008	No Adenovirus Vaccines	145.90	0.19	773.32	0.00	0.00	0.00	
0.008	Adenovirus Vaccine	165.22	0.04	4495.92	19.32	0.15	127.15	Not Dominated
0.009	No Adenovirus Vaccines	145.90	0.19	773.32	0.00	0.00	0.00	
0.009	Adenovirus Vaccine	168.46	0.04	4113.98	22.56	0.15	152.71	Not Dominated
0.01	No Adenovirus Vaccines	145.90	0.19	773.32	0.00	0.00	0.00	
0.01	Adenovirus Vaccine	171.71	0.05	3803.09	25.80	0.14	179.77	Not Dominated
0.011	No Adenovirus Vaccines	145.90	0.19	773.32	0.00	0.00	0.00	
0.011	Adenovirus Vaccine	174.95	0.05	3545.13	29.04	0.14	208.46	Not Dominated
0.012	No Adenovirus Vaccines	145.90	0.19	773.32	0.00	0.00	0.00	
0.012	Adenovirus Vaccine	178.19	0.05	3327.62	32.29	0.14	238.94	Not Dominated

VARIABLE: pGBS – Probability of developing Guillain – Barre Syndrome after vaccination

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0	Adenovirus Vaccine	140.50	0.02	8208.71	0.00	0.00	0.00	
0	No Adenovirus Vaccines	145.90	0.19	773.32	5.41	-0.17	-31.53	(Dominated)
0.00013	No Adenovirus Vaccines	145.90	0.19	773.32	0.00	0.00	0.00	
0.00013	Adenovirus Vaccine	172.83	0.02	6938.29	26.93	0.16	164.41	Not Dominated
0.00025	No Adenovirus Vaccines	145.90	0.19	773.32	0.00	0.00	0.00	
0.00025	Adenovirus Vaccine	205.16	0.03	6273.42	59.26	0.16	379.94	Not Dominated
0.00038	No Adenovirus Vaccines	145.90	0.19	773.32	0.00	0.00	0.00	
0.00038	Adenovirus Vaccine	237.50	0.04	5864.47	91.59	0.15	618.15	Not Dominated
0.0005	No Adenovirus Vaccines	145.90	0.19	773.32	0.00	0.00	0.00	
0.0005	Adenovirus Vaccine	269.83	0.05	5587.52	123.93	0.14	882.80	Not Dominated

VARIABLE: pHOSP_VAX – Probability of hospitalization due to FRI

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.145	No Adenovirus Vaccines	96.44	0.18	523.18	0.00	0.00	0.00	
0.145	Adenovirus Vaccine	147.86	0.02	7555.94	51.42	0.16	312.08	Not Dominated
0.163	No Adenovirus Vaccines	104.25	0.19	563.46	0.00	0.00	0.00	
0.163	Adenovirus Vaccine	148.55	0.02	7568.13	44.30	0.17	267.87	Not Dominated
0.181	No Adenovirus Vaccines	112.06	0.19	603.44	0.00	0.00	0.00	
0.181	Adenovirus Vaccine	149.25	0.02	7580.24	37.19	0.17	223.99	Not Dominated
0.199	No Adenovirus Vaccines	119.87	0.19	643.12	0.00	0.00	0.00	
0.199	Adenovirus Vaccine	149.94	0.02	7592.28	30.07	0.17	180.45	Not Dominated
0.217	No Adenovirus Vaccines	127.68	0.19	682.51	0.00	0.00	0.00	
0.217	Adenovirus Vaccine	150.63	0.02	7604.25	22.95	0.17	137.23	Not Dominated

VARIABLE: pMAE – Probability of minor systemic reactions due to adenovirus vaccine

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.08	No Adenovirus Vaccines	145.90	0.19	773.32	0.00	0.00	0.00	
0.08	Adenovirus Vaccine	152.25	0.02	7635.04	6.35	0.17	37.63	Not Dominated
0.09	No Adenovirus Vaccines	145.90	0.19	773.32	0.00	0.00	0.00	
0.09	Adenovirus Vaccine	152.25	0.02	7633.46	6.35	0.17	37.63	Not Dominated
0.1	No Adenovirus Vaccines	145.90	0.19	773.32	0.00	0.00	0.00	
0.1	Adenovirus Vaccine	152.25	0.02	7631.88	6.35	0.17	37.63	Not Dominated
0.11	No Adenovirus Vaccines	145.90	0.19	773.32	0.00	0.00	0.00	
0.11	Adenovirus Vaccine	152.25	0.02	7630.31	6.35	0.17	37.63	Not Dominated
0.12	No Adenovirus Vaccines	145.90	0.19	773.32	0.00	0.00	0.00	
0.12	Adenovirus Vaccine	152.25	0.02	7628.74	6.35	0.17	37.63	Not Dominated

VARIABLE: pSIQ_ONLY – Probability of going to sick quarters after outpatient office visit

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.76	No Adenovirus Vaccines	146.24	0.19	773.27	0.00	0.00	0.00	
0.76	Adenovirus Vaccine	152.28	0.02	7618.32	6.04	0.17	35.74	Not Dominated
0.8175	No Adenovirus Vaccines	146.14	0.19	773.29	0.00	0.00	0.00	
0.8175	Adenovirus Vaccine	152.27	0.02	7622.42	6.14	0.17	36.31	Not Dominated
0.875	No Adenovirus Vaccines	146.04	0.19	773.30	0.00	0.00	0.00	
0.875	Adenovirus Vaccine	152.27	0.02	7626.52	6.23	0.17	36.88	Not Dominated
0.9325	No Adenovirus Vaccines	145.94	0.19	773.32	0.00	0.00	0.00	
0.9325	Adenovirus Vaccine	152.26	0.02	7630.63	6.32	0.17	37.45	Not Dominated
0.99	No Adenovirus Vaccines	145.83	0.19	773.33	0.00	0.00	0.00	
0.99	Adenovirus Vaccine	152.25	0.02	7634.75	6.41	0.17	38.03	Not Dominated

AIR FORCE ONE –WAY SENSITIVITY ANALYSES RESULTS

VARIABLE: cADVP – Cost of hospitalization due to adenoviral pneumonia

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
8455.06	Adenovirus Vaccine	177.23	0.06	2952.17	0.00	0.00	0.00	
8455.06	No Adenovirus Vaccine	296.34	0.45	662.59	119.11	-0.39	-307.60	(Dominated)
9511.94	Adenovirus Vaccine	177.47	0.06	2956.07	0.00	0.00	0.00	
9511.94	No Adenovirus Vaccine	298.15	0.45	666.64	120.68	-0.39	-311.67	(Dominated)
10568.82	Adenovirus Vaccine	177.70	0.06	2959.98	0.00	0.00	0.00	
10568.82	No Adenovirus Vaccine	299.95	0.45	670.68	122.25	-0.39	-315.73	(Dominated)
11625.7	Adenovirus Vaccine	177.94	0.06	2963.88	0.00	0.00	0.00	
11625.7	No Adenovirus Vaccine	301.76	0.45	674.72	123.83	-0.39	-319.80	(Dominated)
12682.58	Adenovirus Vaccine	178.17	0.06	2967.79	0.00	0.00	0.00	
12682.58	No Adenovirus Vaccine	303.57	0.45	678.77	125.40	-0.39	-323.86	(Dominated)

VARIABLE: cADV_VAX – Cost of adenovirus vaccine

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
100.98	Adenovirus Vaccine	153.65	0.06	2559.39	0.00	0.00	0.00	
100.98	No Adenovirus Vaccine	309.14	0.45	691.22	155.49	-0.39	-401.57	(Dominated)
138.235	Adenovirus Vaccine	190.91	0.06	3179.95	0.00	0.00	0.00	
138.235	No Adenovirus Vaccine	309.14	0.45	691.22	118.24	-0.39	-305.36	(Dominated)
175.49	Adenovirus Vaccine	228.16	0.06	3800.51	0.00	0.00	0.00	
175.49	No Adenovirus Vaccine	309.14	0.45	691.22	80.98	-0.39	-209.14	(Dominated)
212.745	Adenovirus Vaccine	265.42	0.06	4421.07	0.00	0.00	0.00	
212.745	No Adenovirus Vaccine	309.14	0.45	691.22	43.73	-0.39	-112.93	(Dominated)
250	Adenovirus Vaccine	302.67	0.06	5041.62	0.00	0.00	0.00	
250	No Adenovirus Vaccine	309.14	0.45	691.22	6.47	-0.39	-16.71	(Dominated)

VARIABLE: cFLLW_UP – Cost of outpatient office visit for established patient

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
43.91	Adenovirus Vaccine	178.84	0.06	2979.03	0.00	0.00	0.00	
43.91	No Adenovirus Vaccine	308.78	0.45	690.41	129.93	-0.39	-335.57	(Dominated)
51.2925	Adenovirus Vaccine	178.89	0.06	2979.78	0.00	0.00	0.00	
51.2925	No Adenovirus Vaccine	309.13	0.45	691.18	130.24	-0.39	-336.35	(Dominated)
58.675	Adenovirus Vaccine	178.94	0.06	2980.53	0.00	0.00	0.00	
58.675	No Adenovirus Vaccine	309.47	0.45	691.96	130.54	-0.39	-337.13	(Dominated)
66.0575	Adenovirus Vaccine	178.98	0.06	2981.28	0.00	0.00	0.00	
66.0575	No Adenovirus Vaccine	309.82	0.45	692.74	130.84	-0.39	-337.91	(Dominated)
73.44	Adenovirus Vaccine	179.03	0.06	2982.03	0.00	0.00	0.00	
73.44	No Adenovirus Vaccine	310.17	0.45	693.52	131.14	-0.39	-338.69	(Dominated)

VARIABLE: cGBS – Cost of Guillain – Barre Syndrome

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
194674.13	Adenovirus Vaccine	176.46	0.06	2939.28	0.00	0.00	0.00	
194674.13	No Adenovirus Vaccine	309.14	0.45	691.22	132.68	-0.39	-342.67	(Dominated)
219008.395	Adenovirus Vaccine	177.68	0.06	2959.55	0.00	0.00	0.00	
219008.395	No Adenovirus Vaccine	309.14	0.45	691.22	131.47	-0.39	-339.53	(Dominated)
243342.66	Adenovirus Vaccine	178.89	0.06	2979.82	0.00	0.00	0.00	
243342.66	No Adenovirus Vaccine	309.14	0.45	691.22	130.25	-0.39	-336.39	(Dominated)
267676.925	Adenovirus Vaccine	180.11	0.06	3000.08	0.00	0.00	0.00	
267676.925	No Adenovirus Vaccine	309.14	0.45	691.22	129.03	-0.39	-333.24	(Dominated)
292011.19	Adenovirus Vaccine	181.33	0.06	3020.35	0.00	0.00	0.00	
292011.19	No Adenovirus Vaccine	309.14	0.45	691.22	127.82	-0.39	-330.10	(Dominated)

VARIABLE: cHOSP – Cost of hospitalization for FRI

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
8668.91	Adenovirus Vaccine	173.37	0.06	2887.76	0.00	0.00	0.00	
8668.91	No Adenovirus Vaccine	266.51	0.45	595.89	93.14	-0.39	-240.55	(Dominated)
9752.52	Adenovirus Vaccine	176.13	0.06	2933.79	0.00	0.00	0.00	
9752.52	No Adenovirus Vaccine	287.82	0.45	643.56	111.70	-0.39	-288.47	(Dominated)
10836.13	Adenovirus Vaccine	178.89	0.06	2979.82	0.00	0.00	0.00	
10836.13	No Adenovirus Vaccine	309.14	0.45	691.22	130.25	-0.39	-336.39	(Dominated)
11919.74	Adenovirus Vaccine	181.66	0.06	3025.84	0.00	0.00	0.00	
11919.74	No Adenovirus Vaccine	330.46	0.45	738.89	148.81	-0.39	-384.31	(Dominated)
13003.35	Adenovirus Vaccine	184.42	0.06	3071.87	0.00	0.00	0.00	
13003.35	No Adenovirus Vaccine	351.78	0.45	786.56	167.36	-0.39	-432.23	(Dominated)

VARIABLE: cOUTPT – Cost of outpatient visit for new patient

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
72.53	Adenovirus Vaccine	178.75	0.06	2977.42	0.00	0.00	0.00	
72.53	No Adenovirus Vaccine	308.03	0.45	688.75	129.29	-0.39	-333.90	(Dominated)
82.6625	Adenovirus Vaccine	178.86	0.06	2979.32	0.00	0.00	0.00	
82.6625	No Adenovirus Vaccine	308.91	0.45	690.71	130.05	-0.39	-335.87	(Dominated)
92.795	Adenovirus Vaccine	178.98	0.06	2981.21	0.00	0.00	0.00	
92.795	No Adenovirus Vaccine	309.79	0.45	692.67	130.81	-0.39	-337.84	(Dominated)
102.9275	Adenovirus Vaccine	179.09	0.06	2983.11	0.00	0.00	0.00	
102.9275	No Adenovirus Vaccine	310.67	0.45	694.63	131.58	-0.39	-339.81	(Dominated)
113.06	Adenovirus Vaccine	179.20	0.06	2985.00	0.00	0.00	0.00	
113.06	No Adenovirus Vaccine	311.55	0.45	696.60	132.34	-0.39	-341.79	(Dominated)

VARIABLE: cTRAIN – Cost to train basic trainee per day

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
262.15	Adenovirus Vaccine	180.35	0.06	3004.05	0.00	0.00	0.00	
262.15	No Adenovirus Vaccine	319.76	0.45	714.97	139.42	-0.39	-360.06	(Dominated)
311.3875	Adenovirus Vaccine	182.14	0.06	3033.83	0.00	0.00	0.00	
311.3875	No Adenovirus Vaccine	332.82	0.45	744.16	150.68	-0.39	-389.15	(Dominated)
360.625	Adenovirus Vaccine	183.92	0.06	3063.61	0.00	0.00	0.00	
360.625	No Adenovirus Vaccine	345.87	0.45	773.34	161.95	-0.39	-418.24	(Dominated)
409.8625	Adenovirus Vaccine	185.71	0.06	3093.39	0.00	0.00	0.00	
409.8625	No Adenovirus Vaccine	358.92	0.45	802.52	173.21	-0.39	-447.33	(Dominated)
459.1	Adenovirus Vaccine	187.50	0.06	3123.17	0.00	0.00	0.00	
459.1	No Adenovirus Vaccine	371.97	0.45	831.71	184.47	-0.39	-476.42	(Dominated)

VARIABLE: effADV_HOSP – Training days lost due to adenoviral pneumonia hospitalization

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
3	Adenovirus Vaccine	178.84	0.06	2990.04	0.00	0.00	0.00	
3	No Adenovirus Vaccine	308.76	0.45	693.02	129.92	-0.39	-336.83	(Dominated)
4	Adenovirus Vaccine	178.89	0.06	2979.82	0.00	0.00	0.00	
4	No Adenovirus Vaccine	309.14	0.45	691.22	130.25	-0.39	-336.39	(Dominated)
5	Adenovirus Vaccine	178.94	0.06	2969.67	0.00	0.00	0.00	
5	No Adenovirus Vaccine	309.52	0.45	689.44	130.58	-0.39	-335.95	(Dominated)
6	Adenovirus Vaccine	178.99	0.06	2959.59	0.00	0.00	0.00	
6	No Adenovirus Vaccine	309.90	0.45	687.66	130.91	-0.39	-335.51	(Dominated)
7	Adenovirus Vaccine	179.04	0.06	2949.59	0.00	0.00	0.00	
7	No Adenovirus Vaccine	310.28	0.45	685.90	131.24	-0.39	-335.08	(Dominated)

VARIABLE: effFRI_HOSP – Training days lost due to FRI hospitalization

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
1	Adenovirus Vaccine	177.76	0.05	3235.85	0.00	0.00	0.00	
1	No Adenovirus Vaccine	300.40	0.41	736.48	122.64	-0.35	-347.48	(Dominated)
3.75	Adenovirus Vaccine	179.32	0.06	2894.67	0.00	0.00	0.00	
3.75	No Adenovirus Vaccine	312.42	0.46	676.24	133.10	-0.40	-332.72	(Dominated)
6.5	Adenovirus Vaccine	180.87	0.07	2622.89	0.00	0.00	0.00	
6.5	No Adenovirus Vaccine	324.43	0.52	628.63	143.56	-0.45	-321.07	(Dominated)
9.25	Adenovirus Vaccine	182.43	0.08	2401.28	0.00	0.00	0.00	
9.25	No Adenovirus Vaccine	336.45	0.57	590.06	154.02	-0.49	-311.63	(Dominated)
12	Adenovirus Vaccine	183.99	0.08	2217.12	0.00	0.00	0.00	
12	No Adenovirus Vaccine	348.46	0.62	558.17	164.47	-0.54	-303.84	(Dominated)

VARIABLE: effGBS – Training days lost due to Guillain – Barre Syndrome

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
31	Adenovirus Vaccine	178.80	0.06	2998.31	0.00	0.00	0.00	
31	No Adenovirus Vaccine	309.14	0.45	691.22	130.34	-0.39	-336.27	(Dominated)
35	Adenovirus Vaccine	178.85	0.06	2989.03	0.00	0.00	0.00	
35	No Adenovirus Vaccine	309.14	0.45	691.22	130.29	-0.39	-336.33	(Dominated)
39	Adenovirus Vaccine	178.89	0.06	2979.82	0.00	0.00	0.00	
39	No Adenovirus Vaccine	309.14	0.45	691.22	130.25	-0.39	-336.39	(Dominated)
43	Adenovirus Vaccine	178.94	0.06	2970.66	0.00	0.00	0.00	
43	No Adenovirus Vaccine	309.14	0.45	691.22	130.21	-0.39	-336.45	(Dominated)
47	Adenovirus Vaccine	178.98	0.06	2961.56	0.00	0.00	0.00	
47	No Adenovirus Vaccine	309.14	0.45	691.22	130.16	-0.39	-336.50	(Dominated)

VARIABLE: effLP – Training days lost due to lost productivity

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.93	Adenovirus Vaccine	178.89	0.05	3531.57	0.00	0.00	0.00	
0.93	No Adenovirus Vaccine	309.14	0.37	824.64	130.25	-0.32	-401.73	(Dominated)
1.24	Adenovirus Vaccine	178.89	0.05	3252.89	0.00	0.00	0.00	
1.24	No Adenovirus Vaccine	309.14	0.41	757.04	130.25	-0.35	-368.60	(Dominated)
1.55	Adenovirus Vaccine	178.89	0.06	3014.97	0.00	0.00	0.00	
1.55	No Adenovirus Vaccine	309.14	0.44	699.67	130.25	-0.38	-340.52	(Dominated)
1.86	Adenovirus Vaccine	178.89	0.06	2809.48	0.00	0.00	0.00	
1.86	No Adenovirus Vaccine	309.14	0.48	650.39	130.25	-0.41	-316.41	(Dominated)
2.17	Adenovirus Vaccine	178.89	0.07	2630.22	0.00	0.00	0.00	
2.17	No Adenovirus Vaccine	309.14	0.51	607.59	130.25	-0.44	-295.50	(Dominated)

VARIABLE: effMAE – Training days lost due to minor systemic reactions

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.03	Adenovirus Vaccine	178.89	0.06	2984.69	0.00	0.00	0.00	
0.03	No Adenovirus Vaccine	309.14	0.45	691.22	130.25	-0.39	-336.30	(Dominated)
0.0675	Adenovirus Vaccine	178.89	0.06	2982.08	0.00	0.00	0.00	
0.0675	No Adenovirus Vaccine	309.14	0.45	691.22	130.25	-0.39	-336.35	(Dominated)
0.105	Adenovirus Vaccine	178.89	0.06	2979.47	0.00	0.00	0.00	
0.105	No Adenovirus Vaccine	309.14	0.45	691.22	130.25	-0.39	-336.39	(Dominated)
0.1425	Adenovirus Vaccine	178.89	0.06	2976.87	0.00	0.00	0.00	
0.1425	No Adenovirus Vaccine	309.14	0.45	691.22	130.25	-0.39	-336.44	(Dominated)
0.18	Adenovirus Vaccine	178.89	0.06	2974.27	0.00	0.00	0.00	
0.18	No Adenovirus Vaccine	309.14	0.45	691.22	130.25	-0.39	-336.48	(Dominated)

VARIABLE: effOUTPT – Training days lost due to outpatient visits

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.056	Adenovirus Vaccine	178.89	0.06	2991.63	0.00	0.00	0.00	
0.056	No Adenovirus Vaccine	309.14	0.45	694.13	130.25	-0.39	-337.81	(Dominated)
0.063	Adenovirus Vaccine	178.89	0.06	2985.71	0.00	0.00	0.00	
0.063	No Adenovirus Vaccine	309.14	0.45	692.67	130.25	-0.39	-337.10	(Dominated)
0.07	Adenovirus Vaccine	178.89	0.06	2979.82	0.00	0.00	0.00	
0.07	No Adenovirus Vaccine	309.14	0.45	691.22	130.25	-0.39	-336.39	(Dominated)
0.077	Adenovirus Vaccine	178.89	0.06	2973.94	0.00	0.00	0.00	
0.077	No Adenovirus Vaccine	309.14	0.45	689.78	130.25	-0.39	-335.68	(Dominated)
0.084	Adenovirus Vaccine	178.89	0.06	2968.10	0.00	0.00	0.00	
0.084	No Adenovirus Vaccine	309.14	0.45	688.34	130.25	-0.39	-334.97	(Dominated)

VARIABLE: effSIQ – Training days lost due to time spent in sick quarters

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
1	Adenovirus Vaccine	175.65	0.05	3865.64	0.00	0.00	0.00	
1	No Adenovirus Vaccine	284.14	0.33	849.08	108.49	-0.29	-375.12	(Dominated)
1.5	Adenovirus Vaccine	176.90	0.05	3465.00	0.00	0.00	0.00	
1.5	No Adenovirus Vaccine	293.75	0.38	777.24	116.86	-0.33	-357.47	(Dominated)
2	Adenovirus Vaccine	178.14	0.06	3143.73	0.00	0.00	0.00	
2	No Adenovirus Vaccine	303.37	0.42	720.16	125.23	-0.36	-343.48	(Dominated)
2.5	Adenovirus Vaccine	179.39	0.06	2880.39	0.00	0.00	0.00	
2.5	No Adenovirus Vaccine	312.99	0.46	673.73	133.60	-0.40	-332.10	(Dominated)
3	Adenovirus Vaccine	180.64	0.07	2660.59	0.00	0.00	0.00	
3	No Adenovirus Vaccine	322.61	0.51	635.22	141.97	-0.44	-322.68	(Dominated)

VARIABLE: pFRI_NOVAX – Probability of FRI when vaccine not available

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.0864	Adenovirus Vaccine	178.89	0.06	2979.82	0.00	0.00	0.00	
0.0864	No Adenovirus Vaccine	247.31	0.36	691.22	68.42	-0.30	-229.79	(Dominated)
0.0972	Adenovirus Vaccine	178.89	0.06	2979.82	0.00	0.00	0.00	
0.0972	No Adenovirus Vaccine	278.23	0.40	691.22	99.34	-0.34	-290.05	(Dominated)
0.108	Adenovirus Vaccine	178.89	0.06	2979.82	0.00	0.00	0.00	
0.108	No Adenovirus Vaccine	309.14	0.45	691.22	130.25	-0.39	-336.39	(Dominated)
0.1188	Adenovirus Vaccine	178.89	0.06	2979.82	0.00	0.00	0.00	
0.1188	No Adenovirus Vaccine	340.06	0.49	691.22	161.16	-0.43	-373.13	(Dominated)
0.1296	Adenovirus Vaccine	178.89	0.06	2979.82	0.00	0.00	0.00	
0.1296	No Adenovirus Vaccine	370.97	0.54	691.22	192.08	-0.48	-402.97	(Dominated)

VARIABLE: pADVP – Probability of adenoviral pneumonia hospitalization

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.072	Adenovirus Vaccine	178.77	0.06	2978.81	0.00	0.00	0.00	
0.072	No Adenovirus Vaccine	308.23	0.45	689.45	129.46	-0.39	-334.47	(Dominated)
0.092	Adenovirus Vaccine	179.07	0.06	2981.32	0.00	0.00	0.00	
0.092	No Adenovirus Vaccine	310.51	0.45	693.88	131.44	-0.39	-339.26	(Dominated)
0.112	Adenovirus Vaccine	179.36	0.06	2983.83	0.00	0.00	0.00	
0.112	No Adenovirus Vaccine	312.79	0.45	698.30	133.42	-0.39	-344.04	(Dominated)
0.132	Adenovirus Vaccine	179.66	0.06	2986.34	0.00	0.00	0.00	
0.132	No Adenovirus Vaccine	315.06	0.45	702.72	135.40	-0.39	-348.81	(Dominated)
0.152	Adenovirus Vaccine	179.96	0.06	2988.84	0.00	0.00	0.00	
0.152	No Adenovirus Vaccine	317.34	0.45	707.12	137.39	-0.39	-353.57	(Dominated)

VARIABLE: pFRI_VAX – Probability of FRI after vaccination

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.0112	Adenovirus Vaccine	170.88	0.05	3529.24	0.00	0.00	0.00	
0.0112	No Adenovirus Vaccine	309.14	0.45	691.22	138.26	-0.40	-346.68	(Dominated)
0.0126	Adenovirus Vaccine	174.89	0.05	3225.10	0.00	0.00	0.00	
0.0126	No Adenovirus Vaccine	309.14	0.45	691.22	134.26	-0.39	-341.61	(Dominated)
0.014	Adenovirus Vaccine	178.89	0.06	2979.82	0.00	0.00	0.00	
0.014	No Adenovirus Vaccine	309.14	0.45	691.22	130.25	-0.39	-336.39	(Dominated)
0.0154	Adenovirus Vaccine	182.90	0.07	2777.81	0.00	0.00	0.00	
0.0154	No Adenovirus Vaccine	309.14	0.45	691.22	126.24	-0.38	-331.00	(Dominated)
0.0168	Adenovirus Vaccine	186.91	0.07	2608.55	0.00	0.00	0.00	
0.0168	No Adenovirus Vaccine	309.14	0.45	691.22	122.24	-0.38	-325.45	(Dominated)

VARIABLE: pGBS – Probability of Guillain – Barre Syndrome after adenovirus vaccination

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0	Adenovirus Vaccine	167.55	0.06	2874.87	0.00	0.00	0.00	
0	No Adenovirus Vaccine	309.14	0.45	691.22	141.59	-0.39	-364.02	(Dominated)
1.30E-04	Adenovirus Vaccine	198.73	0.06	3149.45	0.00	0.00	0.00	
1.30E-04	No Adenovirus Vaccine	309.14	0.45	691.22	110.41	-0.38	-287.42	(Dominated)
2.50E-04	Adenovirus Vaccine	229.91	0.07	3385.06	0.00	0.00	0.00	
2.50E-04	No Adenovirus Vaccine	309.14	0.45	691.22	79.23	-0.38	-208.87	(Dominated)
3.80E-04	Adenovirus Vaccine	261.10	0.07	3589.46	0.00	0.00	0.00	
3.80E-04	No Adenovirus Vaccine	309.14	0.45	691.22	48.05	-0.37	-128.30	(Dominated)
5.00E-04	Adenovirus Vaccine	292.28	0.08	3768.45	0.00	0.00	0.00	
5.00E-04	No Adenovirus Vaccine	309.14	0.45	691.22	16.87	-0.37	-45.62	(Dominated)

VARIABLE: pHOSP_VAX – Probability of hospitalization due to FRI

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.1584	Adenovirus Vaccine	172.55	0.06	2896.61	0.00	0.00	0.00	
0.1584	No Adenovirus Vaccine	260.25	0.44	586.64	87.69	-0.38	-228.33	(Dominated)
0.1782	Adenovirus Vaccine	175.72	0.06	2938.38	0.00	0.00	0.00	
0.1782	No Adenovirus Vaccine	284.69	0.45	639.15	108.97	-0.39	-282.58	(Dominated)
0.198	Adenovirus Vaccine	178.89	0.06	2979.82	0.00	0.00	0.00	
0.198	No Adenovirus Vaccine	309.14	0.45	691.22	130.25	-0.39	-336.39	(Dominated)
0.2178	Adenovirus Vaccine	182.06	0.06	3020.94	0.00	0.00	0.00	
0.2178	No Adenovirus Vaccine	333.59	0.45	742.88	151.53	-0.39	-389.75	(Dominated)
0.2376	Adenovirus Vaccine	185.23	0.06	3061.74	0.00	0.00	0.00	
0.2376	No Adenovirus Vaccine	358.04	0.45	794.13	172.81	-0.39	-442.69	(Dominated)

VARIABLE: pMAE – Probability of minor systemic reactions due to adenovirus vaccine

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.08	Adenovirus Vaccine	178.89	0.06	2981.24	0.00	0.00	0.00	
0.08	No Adenovirus Vaccine	309.14	0.45	691.22	130.25	-0.39	-336.36	(Dominated)
0.09	Adenovirus Vaccine	178.89	0.06	2980.53	0.00	0.00	0.00	
0.09	No Adenovirus Vaccine	309.14	0.45	691.22	130.25	-0.39	-336.37	(Dominated)
0.1	Adenovirus Vaccine	178.89	0.06	2979.82	0.00	0.00	0.00	
0.1	No Adenovirus Vaccine	309.14	0.45	691.22	130.25	-0.39	-336.39	(Dominated)
0.11	Adenovirus Vaccine	178.89	0.06	2979.11	0.00	0.00	0.00	
0.11	No Adenovirus Vaccine	309.14	0.45	691.22	130.25	-0.39	-336.40	(Dominated)
0.12	Adenovirus Vaccine	178.89	0.06	2978.40	0.00	0.00	0.00	
0.12	No Adenovirus Vaccine	309.14	0.45	691.22	130.25	-0.39	-336.41	(Dominated)

VARIABLE: pSIQ_ONLY – Probability of being in sick quarters

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.76	Adenovirus Vaccine	179.00	0.06	2974.25	0.00	0.00	0.00	
0.76	No Adenovirus Vaccine	309.99	0.45	691.34	130.99	-0.39	-337.42	(Dominated)
0.8175	Adenovirus Vaccine	178.97	0.06	2975.93	0.00	0.00	0.00	
0.8175	No Adenovirus Vaccine	309.74	0.45	691.31	130.77	-0.39	-337.11	(Dominated)
0.875	Adenovirus Vaccine	178.94	0.06	2977.62	0.00	0.00	0.00	
0.875	No Adenovirus Vaccine	309.48	0.45	691.27	130.54	-0.39	-336.80	(Dominated)
0.9325	Adenovirus Vaccine	178.90	0.06	2979.30	0.00	0.00	0.00	
0.9325	No Adenovirus Vaccine	309.22	0.45	691.23	130.32	-0.39	-336.48	(Dominated)
0.99	Adenovirus Vaccine	178.87	0.06	2980.99	0.00	0.00	0.00	
0.99	No Adenovirus Vaccine	308.96	0.45	691.20	130.09	-0.39	-336.17	(Dominated)

COAST GUARD ONE – WAY SENSITIVITY ANALYSES RESULTS

VARIABLE: cADVP – Cost of adenoviral pneumonia hospitalization

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
3292.17	No Adenovirus Vaccine	68.80	0.16	427.47	0.00	0.00	0.00	
3292.17	Adenovirus Vaccine	147.94	0.02	6539.10	79.14	0.14	572.15	Not Dominated
3703.69	No Adenovirus Vaccine	69.03	0.16	428.92	0.00	0.00	0.00	
3703.69	Adenovirus Vaccine	147.97	0.02	6540.42	78.94	0.14	570.68	Not Dominated
4115.21	No Adenovirus Vaccine	69.26	0.16	430.36	0.00	0.00	0.00	
4115.21	Adenovirus Vaccine	148.00	0.02	6541.74	78.73	0.14	569.22	Not Dominated
4526.73	No Adenovirus Vaccine	69.50	0.16	431.81	0.00	0.00	0.00	
4526.73	Adenovirus Vaccine	148.03	0.02	6543.05	78.53	0.14	567.75	Not Dominated
4938.25	No Adenovirus Vaccine	69.73	0.16	433.25	0.00	0.00	0.00	
4938.25	Adenovirus Vaccine	148.06	0.02	6544.37	78.33	0.14	566.29	Not Dominated

VARIABLE: cADV_VAX – Cost of adenovirus vaccine

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
100.98	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
100.98	Adenovirus Vaccine	122.87	0.02	5430.96	52.74	0.14	381.30	Not Dominated
113.60	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
113.60	Adenovirus Vaccine	135.49	0.02	5988.79	65.36	0.14	472.54	Not Dominated
126.22	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
126.22	Adenovirus Vaccine	148.11	0.02	6546.62	77.98	0.14	563.78	Not Dominated
138.84	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
138.84	Adenovirus Vaccine	160.73	0.02	7104.45	90.60	0.14	655.02	Not Dominated
151.46	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
151.46	Adenovirus Vaccine	173.35	0.02	7662.28	103.22	0.14	746.26	Not Dominated

VARIABLE: cFLLW_UP – Cost of outpatient visit for established patient

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
47.84	No Adenovirus Vaccine	69.99	0.16	434.90	0.00	0.00	0.00	
47.84	Adenovirus Vaccine	148.09	0.02	6545.87	78.10	0.14	564.62	Not Dominated
56.68	No Adenovirus Vaccine	70.13	0.16	435.76	0.00	0.00	0.00	
56.68	Adenovirus Vaccine	148.11	0.02	6546.66	77.98	0.14	563.74	Not Dominated
65.51	No Adenovirus Vaccine	70.27	0.16	436.62	0.00	0.00	0.00	
65.51	Adenovirus Vaccine	148.13	0.02	6547.44	77.85	0.14	562.87	Not Dominated
74.35	No Adenovirus Vaccine	70.41	0.16	437.48	0.00	0.00	0.00	
74.35	Adenovirus Vaccine	148.14	0.02	6548.23	77.73	0.14	561.99	Not Dominated
83.18	No Adenovirus Vaccine	70.55	0.16	438.35	0.00	0.00	0.00	
83.18	Adenovirus Vaccine	148.16	0.02	6549.02	77.61	0.14	561.12	Not Dominated

VARIABLE: cGBS – Cost of Guillain – Barre Syndrome

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
194674.13	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
194674.13	Adenovirus Vaccine	145.67	0.02	6439.06	75.55	0.14	546.19	Not Dominated
219008.40	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
219008.40	Adenovirus Vaccine	146.89	0.02	6492.84	76.76	0.14	554.98	Not Dominated
243342.66	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
243342.66	Adenovirus Vaccine	148.11	0.02	6546.62	77.98	0.14	563.78	Not Dominated
267676.93	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
267676.93	Adenovirus Vaccine	149.32	0.02	6600.40	79.20	0.14	572.58	Not Dominated
292011.19	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
292011.19	Adenovirus Vaccine	150.54	0.02	6654.18	80.41	0.14	581.37	Not Dominated

VARIABLE: cHOSP – Cost of hospitalization due to FRI

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
3375.44	No Adenovirus Vaccine	64.65	0.16	401.67	0.00	0.00	0.00	
3375.44	Adenovirus Vaccine	147.40	0.02	6515.57	82.76	0.14	598.32	Not Dominated
3797.37	No Adenovirus Vaccine	67.39	0.16	418.70	0.00	0.00	0.00	
3797.37	Adenovirus Vaccine	147.76	0.02	6531.09	80.37	0.14	581.05	Not Dominated
4219.30	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
4219.30	Adenovirus Vaccine	148.11	0.02	6546.62	77.98	0.14	563.78	Not Dominated
4641.23	No Adenovirus Vaccine	72.87	0.16	452.75	0.00	0.00	0.00	
4641.23	Adenovirus Vaccine	148.46	0.02	6562.15	75.59	0.14	546.51	Not Dominated
5063.16	No Adenovirus Vaccine	75.61	0.16	469.77	0.00	0.00	0.00	
5063.16	Adenovirus Vaccine	148.81	0.02	6577.68	73.20	0.14	529.24	Not Dominated

VARIABLE: cOUTPT – Cost of outpatient visit for new patient

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
79.33	No Adenovirus Vaccine	69.64	0.16	432.71	0.00	0.00	0.00	
79.33	Adenovirus Vaccine	148.04	0.02	6543.87	78.40	0.14	566.84	Not Dominated
91.38	No Adenovirus Vaccine	70.03	0.16	435.10	0.00	0.00	0.00	
91.38	Adenovirus Vaccine	148.09	0.02	6546.05	78.07	0.14	564.41	Not Dominated
103.43	No Adenovirus Vaccine	70.41	0.16	437.49	0.00	0.00	0.00	
103.43	Adenovirus Vaccine	148.14	0.02	6548.23	77.73	0.14	561.99	Not Dominated
115.47	No Adenovirus Vaccine	70.80	0.16	439.88	0.00	0.00	0.00	
115.47	Adenovirus Vaccine	148.19	0.02	6550.41	77.40	0.14	559.56	Not Dominated
127.52	No Adenovirus Vaccine	71.18	0.16	442.27	0.00	0.00	0.00	
127.52	Adenovirus Vaccine	148.24	0.02	6552.59	77.06	0.14	557.14	Not Dominated

VARIABLE: cTRAIN – Cost to train basic trainee per day

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
299.43	No Adenovirus Vaccine	63.00	0.16	391.44	0.00	0.00	0.00	
299.43	Adenovirus Vaccine	147.05	0.02	6499.78	84.05	0.14	607.65	Not Dominated
336.86	No Adenovirus Vaccine	66.56	0.16	413.58	0.00	0.00	0.00	
336.86	Adenovirus Vaccine	147.58	0.02	6523.20	81.02	0.14	585.71	Not Dominated
374.29	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
374.29	Adenovirus Vaccine	148.11	0.02	6546.62	77.98	0.14	563.78	Not Dominated
411.72	No Adenovirus Vaccine	73.69	0.16	457.86	0.00	0.00	0.00	
411.72	Adenovirus Vaccine	148.64	0.02	6570.04	74.95	0.14	541.85	Not Dominated
449.15	No Adenovirus Vaccine	77.25	0.16	480.00	0.00	0.00	0.00	
449.15	Adenovirus Vaccine	149.17	0.02	6593.46	71.91	0.14	519.91	Not Dominated

VARIABLE: effADV_HOSP – Training days lost due to hospitalization for adenoviral pneumonia

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
3.00	No Adenovirus Vaccine	69.91	0.16	435.94	0.00	0.00	0.00	
3.00	Adenovirus Vaccine	148.08	0.02	6566.44	78.17	0.14	567.13	Not Dominated
4.00	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
4.00	Adenovirus Vaccine	148.11	0.02	6546.62	77.98	0.14	563.78	Not Dominated
5.00	No Adenovirus Vaccine	70.34	0.16	435.51	0.00	0.00	0.00	
5.00	Adenovirus Vaccine	148.13	0.02	6526.93	77.80	0.14	560.45	Not Dominated
6.00	No Adenovirus Vaccine	70.55	0.16	435.29	0.00	0.00	0.00	
6.00	Adenovirus Vaccine	148.16	0.02	6507.37	77.61	0.14	557.15	Not Dominated
7.00	No Adenovirus Vaccine	70.76	0.16	435.08	0.00	0.00	0.00	
7.00	Adenovirus Vaccine	148.19	0.02	6487.93	77.43	0.14	553.87	Not Dominated

VARIABLE: effFRI_HOSP – Training days lost due to FRI hospitalization

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
1.00	No Adenovirus Vaccine	65.26	0.15	441.11	0.00	0.00	0.00	
1.00	Adenovirus Vaccine	147.48	0.02	7037.01	82.22	0.13	647.42	Not Dominated
3.75	No Adenovirus Vaccine	71.95	0.17	433.92	0.00	0.00	0.00	
3.75	Adenovirus Vaccine	148.34	0.02	6380.84	76.39	0.14	535.84	Not Dominated
6.50	No Adenovirus Vaccine	78.63	0.18	428.12	0.00	0.00	0.00	
6.50	Adenovirus Vaccine	149.20	0.03	5842.33	70.56	0.16	446.23	Not Dominated
9.25	No Adenovirus Vaccine	85.32	0.20	423.35	0.00	0.00	0.00	
9.25	Adenovirus Vaccine	150.05	0.03	5392.43	64.74	0.17	372.68	Not Dominated
12.00	No Adenovirus Vaccine	92.00	0.22	419.35	0.00	0.00	0.00	
12.00	Adenovirus Vaccine	150.91	0.03	5010.94	58.91	0.19	311.24	Not Dominated

VARIABLE: effGBS – Training days lost due to Guillain – Barre Syndrome

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
31.00	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
31.00	Adenovirus Vaccine	147.96	0.02	6657.72	77.83	0.14	561.08	Not Dominated
35.00	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
35.00	Adenovirus Vaccine	148.03	0.02	6601.67	77.91	0.14	562.43	Not Dominated
39.00	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
39.00	Adenovirus Vaccine	148.11	0.02	6546.62	77.98	0.14	563.78	Not Dominated
43.00	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
43.00	Adenovirus Vaccine	148.18	0.02	6492.53	78.06	0.14	565.14	Not Dominated
47.00	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
47.00	Adenovirus Vaccine	148.26	0.02	6439.39	78.13	0.14	566.50	Not Dominated

VARIABLE: effLP – Training days lost due to lost productivity

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.93	No Adenovirus Vaccine	70.13	0.13	520.17	0.00	0.00	0.00	
0.93	Adenovirus Vaccine	148.11	0.02	7684.45	77.98	0.12	674.94	Not Dominated
1.24	No Adenovirus Vaccine	70.13	0.15	477.36	0.00	0.00	0.00	
1.24	Adenovirus Vaccine	148.11	0.02	7112.49	77.98	0.13	618.51	Not Dominated
1.55	No Adenovirus Vaccine	70.13	0.16	441.06	0.00	0.00	0.00	
1.55	Adenovirus Vaccine	148.11	0.02	6619.77	77.98	0.14	570.80	Not Dominated
1.86	No Adenovirus Vaccine	70.13	0.17	409.90	0.00	0.00	0.00	
1.86	Adenovirus Vaccine	148.11	0.02	6190.89	77.98	0.15	529.91	Not Dominated
2.17	No Adenovirus Vaccine	70.13	0.18	382.84	0.00	0.00	0.00	
2.17	Adenovirus Vaccine	148.11	0.03	5814.21	77.98	0.16	494.50	Not Dominated

VARIABLE: effMAE – Training days lost due to minor systemic reactions

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.03	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
0.03	Adenovirus Vaccine	148.11	0.02	6556.77	77.98	0.14	563.64	Not Dominated
0.07	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
0.07	Adenovirus Vaccine	148.11	0.02	6551.33	77.98	0.14	563.71	Not Dominated
0.11	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
0.11	Adenovirus Vaccine	148.11	0.02	6545.90	77.98	0.14	563.79	Not Dominated
0.14	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
0.14	Adenovirus Vaccine	148.11	0.02	6540.48	77.98	0.14	563.87	Not Dominated
0.18	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
0.18	Adenovirus Vaccine	148.11	0.02	6535.07	77.98	0.14	563.94	Not Dominated

VARIABLE: effOUTPT – Training days lost due to outpatient visits

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.06	No Adenovirus Vaccine	70.13	0.16	437.53	0.00	0.00	0.00	
0.06	Adenovirus Vaccine	148.11	0.02	6570.93	77.98	0.14	566.17	Not Dominated
0.06	No Adenovirus Vaccine	70.13	0.16	436.63	0.00	0.00	0.00	
0.06	Adenovirus Vaccine	148.11	0.02	6558.76	77.98	0.14	564.97	Not Dominated
0.07	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
0.07	Adenovirus Vaccine	148.11	0.02	6546.62	77.98	0.14	563.78	Not Dominated
0.08	No Adenovirus Vaccine	70.13	0.16	434.82	0.00	0.00	0.00	
0.08	Adenovirus Vaccine	148.11	0.02	6534.53	77.98	0.14	562.59	Not Dominated
0.08	No Adenovirus Vaccine	70.13	0.16	433.92	0.00	0.00	0.00	
0.08	Adenovirus Vaccine	148.11	0.02	6522.49	77.98	0.14	561.41	Not Dominated

VARIABLE: effSIQ – Training days lost due to time spent in sick quarters

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
1.00	No Adenovirus Vaccine	54.58	0.12	457.08	0.00	0.00	0.00	
1.00	Adenovirus Vaccine	146.11	0.02	8445.84	91.53	0.10	896.32	Not Dominated
1.50	No Adenovirus Vaccine	60.56	0.14	447.32	0.00	0.00	0.00	
1.50	Adenovirus Vaccine	146.88	0.02	7591.69	86.32	0.12	743.87	Not Dominated
2.00	No Adenovirus Vaccine	66.54	0.15	439.61	0.00	0.00	0.00	
2.00	Adenovirus Vaccine	147.65	0.02	6901.02	81.11	0.13	624.08	Not Dominated
2.50	No Adenovirus Vaccine	72.52	0.17	433.38	0.00	0.00	0.00	
2.50	Adenovirus Vaccine	148.41	0.02	6330.99	75.90	0.14	527.47	Not Dominated
3.00	No Adenovirus Vaccine	78.49	0.18	428.23	0.00	0.00	0.00	
3.00	Adenovirus Vaccine	149.18	0.03	5852.54	70.69	0.16	447.91	Not Dominated

VARIABLE: pADVP – Probability of developing adenoviral pneumonia

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.07	No Adenovirus Vaccine	70.02	0.16	435.24	0.00	0.00	0.00	
0.07	Adenovirus Vaccine	148.09	0.02	6547.88	78.07	0.14	564.62	Not Dominated
0.09	No Adenovirus Vaccine	70.28	0.16	436.44	0.00	0.00	0.00	
0.09	Adenovirus Vaccine	148.13	0.02	6544.74	77.85	0.14	562.51	Not Dominated
0.11	No Adenovirus Vaccine	70.53	0.16	437.63	0.00	0.00	0.00	
0.11	Adenovirus Vaccine	148.16	0.02	6541.60	77.63	0.14	560.41	Not Dominated
0.13	No Adenovirus Vaccine	70.79	0.16	438.82	0.00	0.00	0.00	
0.13	Adenovirus Vaccine	148.19	0.02	6538.47	77.41	0.14	558.31	Not Dominated
0.15	No Adenovirus Vaccine	71.04	0.16	440.01	0.00	0.00	0.00	
0.15	Adenovirus Vaccine	148.22	0.02	6535.35	77.18	0.14	556.21	Not Dominated

VARIABLE: pFRI_NOVAX – Probability of developing FRI when adenovirus vaccine is not available

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.03	No Adenovirus Vaccine	56.10	0.13	435.72	0.00	0.00	0.00	
0.03	Adenovirus Vaccine	148.11	0.02	6546.62	92.01	0.11	866.92	Not Dominated
0.04	No Adenovirus Vaccine	63.11	0.14	435.72	0.00	0.00	0.00	
0.04	Adenovirus Vaccine	148.11	0.02	6546.62	84.99	0.12	695.39	Not Dominated
0.04	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
0.04	Adenovirus Vaccine	148.11	0.02	6546.62	77.98	0.14	563.78	Not Dominated
0.04	No Adenovirus Vaccine	77.14	0.18	435.72	0.00	0.00	0.00	
0.04	Adenovirus Vaccine	148.11	0.02	6546.62	70.97	0.15	459.60	Not Dominated
0.05	No Adenovirus Vaccine	84.15	0.19	435.72	0.00	0.00	0.00	
0.05	Adenovirus Vaccine	148.11	0.02	6546.62	63.96	0.17	375.09	Not Dominated

VARIABLE: pFRI_VAX – Probability of developing FRI after adenovirus vaccination

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.00	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
0.00	Adenovirus Vaccine	146.31	0.02	7913.41	76.18	0.14	534.80	Not Dominated
0.00	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
0.00	Adenovirus Vaccine	147.21	0.02	7161.29	77.08	0.14	549.07	Not Dominated
0.01	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
0.01	Adenovirus Vaccine	148.11	0.02	6546.62	77.98	0.14	563.78	Not Dominated
0.01	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
0.01	Adenovirus Vaccine	149.01	0.02	6034.89	78.88	0.14	578.93	Not Dominated
0.01	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
0.01	Adenovirus Vaccine	149.91	0.03	5602.23	79.78	0.13	594.55	Not Dominated

VARIABLE: pGBS – Probability of developing Guillain – Barre Syndrome after adenovirus vaccine

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.00	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
0.00	Adenovirus Vaccine	136.50	0.02	6540.70	66.37	0.14	473.86	Not Dominated
0.00	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
0.00	Adenovirus Vaccine	168.42	0.03	6555.04	98.29	0.14	726.76	Not Dominated
0.00	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
0.00	Adenovirus Vaccine	200.34	0.03	6564.85	130.21	0.13	998.37	Not Dominated
0.00	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
0.00	Adenovirus Vaccine	232.26	0.04	6571.99	162.13	0.13	1290.84	Not Dominated
0.00	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
0.00	Adenovirus Vaccine	264.18	0.04	6577.41	194.05	0.12	1606.67	Not Dominated

VARIABLE: pHOSP_VAX – Probability of being hospitalized due to FRI

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.14	No Adenovirus Vaccine	63.57	0.16	397.97	0.00	0.00	0.00	
0.14	Adenovirus Vaccine	147.27	0.02	6553.35	83.69	0.14	609.67	Not Dominated
0.16	No Adenovirus Vaccine	66.85	0.16	416.92	0.00	0.00	0.00	
0.16	Adenovirus Vaccine	147.69	0.02	6549.97	80.84	0.14	586.64	Not Dominated
0.18	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
0.18	Adenovirus Vaccine	148.11	0.02	6546.62	77.98	0.14	563.78	Not Dominated
0.20	No Adenovirus Vaccine	73.40	0.16	454.39	0.00	0.00	0.00	
0.20	Adenovirus Vaccine	148.53	0.02	6543.29	75.13	0.14	541.09	Not Dominated
0.22	No Adenovirus Vaccine	76.68	0.16	472.91	0.00	0.00	0.00	
0.22	Adenovirus Vaccine	148.95	0.02	6539.98	72.27	0.14	518.58	Not Dominated

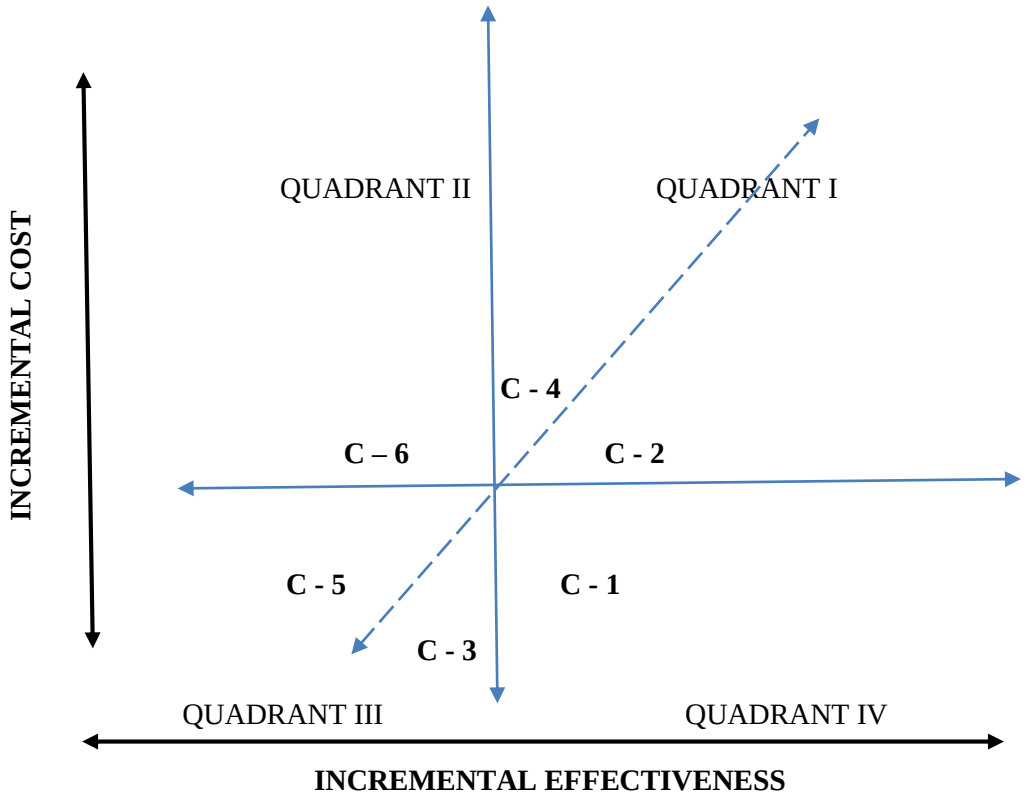
VARIABLE: pMAE – Probability of minor systemic reactions after adenovirus vaccination

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.08	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
0.08	Adenovirus Vaccine	148.11	0.02	6549.58	77.98	0.14	563.74	Not Dominated
0.09	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
0.09	Adenovirus Vaccine	148.11	0.02	6548.10	77.98	0.14	563.76	Not Dominated
0.10	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
0.10	Adenovirus Vaccine	148.11	0.02	6546.62	77.98	0.14	563.78	Not Dominated
0.11	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
0.11	Adenovirus Vaccine	148.11	0.02	6545.15	77.98	0.14	563.80	Not Dominated
0.12	No Adenovirus Vaccine	70.13	0.16	435.72	0.00	0.00	0.00	
0.12	Adenovirus Vaccine	148.11	0.02	6543.67	77.98	0.14	563.82	Not Dominated

VARIABLE: pSIQ_ONLY – Probability of spending time in sick quarters

VARIABLE	STRATEGY	COST	EFF	CE	INCRCOST	INCREFF	INCRCE	DOMINATED
0.76	No Adenovirus Vaccine	70.47	0.16	436.69	0.00	0.00	0.00	
0.76	Adenovirus Vaccine	148.15	0.02	6532.83	77.68	0.14	560.13	Not Dominated
0.82	No Adenovirus Vaccine	70.36	0.16	436.40	0.00	0.00	0.00	
0.82	Adenovirus Vaccine	148.14	0.02	6537.00	77.77	0.14	561.23	Not Dominated
0.88	No Adenovirus Vaccine	70.26	0.16	436.10	0.00	0.00	0.00	
0.88	Adenovirus Vaccine	148.12	0.02	6541.17	77.86	0.14	562.34	Not Dominated
0.93	No Adenovirus Vaccine	70.16	0.16	435.81	0.00	0.00	0.00	
0.93	Adenovirus Vaccine	148.11	0.02	6545.35	77.95	0.14	563.44	Not Dominated
0.99	No Adenovirus Vaccine	70.05	0.16	435.52	0.00	0.00	0.00	
0.99	Adenovirus Vaccine	148.10	0.02	6549.53	78.04	0.14	564.55	Not Dominated

APPENDIX C.



- **C – 1** – Comparator is less costly and more effective. Comparator is recommended because it absolutely dominates baseline
- **C – 2** – Comparator is more costly and more effective. Comparator is recommended because the ICER does not exceed the WTP
- **C – 3** – Comparator is less costly and less effective. Comparator is recommended because the ICER does not exceed the WTP
- **C – 4** – Comparator is more costly and more effective. Comparator is not recommended because the ICER exceeds the WTP
- **C – 5** – Comparator is less costly and less effective. Comparator is not recommended because the ICER exceeds the WTP
- **C – 6** – Comparator is more costly and less effective. Comparator is not recommended because it is absolutely dominated by the baseline.

Source: TreeAge Software Inc.. Williamstown, MA: TreeAge Pro User Manual;

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