Lesson 3

Vaccine Efficacy

Hilleman & Vaccines

Student Pages

MMR and Varicella ProQuad Vaccine

Measles, mumps, rubella, and varicella vaccination data for babies vaccinated at 12 months old and again at 15 months old, with the ProQuad Vaccine (Merck Sharp & Dohme Corp., 2018).

Initial Study Data

Note: The final data only included babies for whom they could collect all of the safety data.

Number Who Received Dose 1	470
Number Who Received Dose 2	462
Percentage Who Were Female	47.9
Percentage Who Were Male	52.1

Dose 1 efficacy based on immunogenicity response criteria (must have a certain amount of or antibodies/mL of blood. Antibody production): for measles, mumps, rubella, and varicella (chicken pox) vaccinations

Note: Confidence interval is 95%

Measles	
Number of Participants	438
Percentage of showing Immunogenicity (mean)	90.2
Mumps	
Number of Participants	417
Percentage Showing Immunogenicity (mean)	98.3
Rubella	
Number of Participants	447
Percentage Showing Immunogenicity	98
Varicella	
Number of Participants	353
Percentage Showing Immunogenicity (mean)	97.5

Bibliography

Merck Sharp & Dohme Corp. Comparative Study of Immunogenicity and Safety of a 2-Dose Regimen of ProQuad Manufactured with rHA (V221-038). clinicaltrials.gov. https://clinicaltrials.gov/ct2/show/results/NCT00566527?term=proquad&draw=2&rank=4&view=results. Updated January 30, 2018.

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Dose 2 efficacy based on immunogenicity response criteria (must have a certain amount of antibody production): for measles, mumps, rubella, and varicella (chicken pox) vaccinations

Note: Confidence interval is 95%

Measles	
Number of Participants	434
Percentage of showing Immunogenicity (mean)	98.8
Mumps	
Number of Participants	414
Percentage Showing Immunogenicity (mean)	99.5
Rubella	
Number of Participants	443
Percentage Showing Immunogenicity	99.5
Varicella	
Number of Participants	347
Percentage Showing Immunogenicity (mean)	100

Bibliography

Merck Sharp & Dohme Corp. Comparative Study of Immunogenicity and Safety of a 2-Dose Regimen of ProQuad Manufactured with rHA (V221-038). clinicaltrials.gov. https://clinicaltrials.gov/ct2/show/results/NCT00566527?term=proquad&draw=2&rank=4&view=results. Updated January 30, 2018.

Haemophilus influenzae type b Vaccine Data

In the United States, Haemophilus influenzae type b is the top cause of invasive bacterial issues for kids and causes what we typically hear of, meningitis. Type b is the kind of polysaccharide capsule surrounding the bacteria. Before the use of vaccinations, one in 200 children were affected with 60% of them developing meningitis, 3-6% died, and 20-30% had hearing loss and mental retardation. Two thirds of the children affected are under 15 months of age in the U.S. The original vaccines, from the 1970s, showed 90% efficacy but only in children who were older than 18 months. Conjugate vaccines link a T-cell dependent antigen to the bacterial capsule to elicit an immune response in younger children. Now, there are two conjugate vaccines licensed for infants at 2 months of age. The two vaccines are HbOC and PRP-OMP. For these, it is believed that 1 microgram/mL is an indication of long-term immunity (MMWR Recommendations and Reports, 1991).

Vaccine Type and Participants	Percent Efficacy After the Required Regimen
HbOC (3 doses)	100
Number of Participants	60,000
PRP-OMP (2 doses)	93
Number of Participants (All Navajo infants)	3,486

Bibliography

MMWR Recommendations and Reports. Haemophilus b Conjugate Vaccines for Prevention of Haemophilus influenzae type b Disease Among Infants and Children Two Months of Age and Older Recommendations of the ACIP. cdc.gov. https://www.cdc.gov/mmwr/preview/mmwrhtml/00041736.htm. Published January 11, 1991.

Hepatitis B Vaccine Data

Hepatitis B Virus (HBV) affects 850,000 people in the United States, and based on data from the countries of immigrants to the U.S., the number is estimated at 2.2 million people in the U.S. who live with HBV. The CDC was told of 3,370 cases of acute HBV in the year 2015, but it was estimated that the number was 6.5 times higher. Since the HepB vaccination recommendations were issued in 1982, there has been an 88.5% decrease in HBV infections. Injection-drug use has caused spikes in HBV infections. To prevent the spread of HBV, in 1991, the Advisory Committee on Immunization Practices (ACIP) began requiring the testing of all pregnant women, the vaccination of all children and adolescents who had not been vaccinated, vaccination of at-risk adults, and vaccination of all infants at birth within the first 24 hours. People who have antibodies to the hepatitis B surface antigen (anti-HBs) at levels grater than or equal to 10 mIU/mL 1-2 months after the series of 3 doses are considered immune. Seroprotection decreases with increasing age at which people receive the vaccine, it is better to receive this vaccine while young (Schillie, Vellozzi, Reingold, Harris, Haber, et al., 2018).

Dose Number in Different Age Groups	**Percent Efficacy After Each Dose**
Ages 19-35 Months	
Dose Number 1	25
Dose Number 2	63
Dose Number 3	95
Adults Under Age 40	
Dose 1	30-55
Dose 2	75
Dose 3	90

Bibliography

Schillie, S., Vellozzi, C., Reingold, A., Harris, A. Haber, P. et al. Centers for Disease Control and Prevention. Prevention of hepatitis B virus infection in the United States: Recommendations of the Advisory Committee on Immunization Practices. https://www.cdc.gov/mmwr/volumes/67/rr/rr6701a1.htm . Published January 12, 2018.

Pfizer COVID-19 Vaccine - Phase 3 Data (Polack, et. al., 2020)

Initial Study Data

Age	**Greater than or equal to 16 years**
Number of Participants	45348
Number Who Received Dose 1	21720
Number Who Received Dose 2	21728
Days Before Receiving Dose 2	21
Percentage of Males	52.7
Percentage of Females	47.3
Median Age (years)	52
Age Range in Years	**18-95**
Percentage Aged Greater than 55 Years	52
Participants with No Current or Prior COVID-19 infection	36523
Confidence Interval Percentage	95

Note: Efficacy was based on confirmed cases per 1000 person-years in the vaccine group compared to the placebo group.)

Efficacy Percentage	95
Dosage micrograms/dose	30

Primary End Point: Prevent symptomatic COVID-19 7 days after the second dose was given, for patients who were seronegative at baseline (no traces of COVID-19 infection). Secondary End Point: Prevent Severe COVID-19

Treatment Group Participants Positive After Day 7	8
Placebo Group Participants Positive After Day 7	162

Primary End Point Null Hypothesis	Efficacy is 30% or less	(Rejected)
Percent Efficacy Between Doses 1 and 2		52

Bibliography

Polack, P.F., Thomas, S.J., Kitchin, N., Absalon, J., Gurtman, A., Lockhart, S., Perez, J.L., M.D., Marc, G.P., Moreira, E.D., Zerbini, C., Bailey, R., Swanson, K.A., et.al. (2020) Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. The New England Journal of Medicine, 383, 2603-2615. doi: 10.1056/NEJMoa2034577

Moderna COVID-19 Vaccine- Phase 3 Data (Baden, et al., 2021)

Initial Study Data

Age	**Greater than or equal to 18 years**
Number of Participants	30420
Number Who Received Dose 1	15210
Number Who Received Placebo Dose 1	15210
Days Before Receiving Dose 2	28
Percentage of Males	52.7
Percentage of Females	47.3
Median Age (years)	51.4
Age Range in Years	**18-95**
Ages 18-65 percentage	75.2
Percentage Aged Greater than 65 Years	24.8
Confidence Interval Percentage	95
Placebo Participants with Confirmed COVID	185
Treatment Participants with Confirmed COVID	11

Note: Efficacy was based on percentage reduction in the hazard ratio for the primary end point (mRNA-1273 vs. placebo)

Efficacy Percentage After Dose 2	94.1
Dosage micrograms/dose	100
Efficacy Percentage After Dose 1	95.2

Primary End Point: Prevent symptomatic COVID-19 7 days after the second dose was given, for patients who were seronegative at baseline (no traces of COVID-19 infection). Secondary End Point Goal: Prevent Severe COVID-19. Secondary End Point: Prevent COVID-19 after the first dose.

Primary End Point Null Hypothesis	Efficacy is 30% or less (Rejected)
Secondary End Point Efficacy Percentage for preventing Severe COVID	100

Bibliography

Baden, L.R., El Sahly, H.M., Essing, B., Kotloff, K., Frey, S., Novak, R., Diemert, D., Spector, S.A., Rouphael, N., Creech, C.B., McGettigan, J., Khetan, S., et al. (2020). Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. The New England Journal of Medicine, 384, 403-416. doi: 10.1056/NEJMoa2035389

Polio Vaccine Data for Inactivated Polio Vaccine (IPV) and Oral Polio Vaccine (OPV)

There are three serotypes of poliovirus, types 1, 2, and 3 (P1, P2, & P3). Paralytic disease is caused least frequently by poliovirus type 2 and most frequently by type 1. OPV was the second form of vaccine and contained the live attenuated Sabin strain. New recommendations from the Advisory Committee on poliovirus type 2 and most frequently by type 1. OPV was the second form of vaccine and contained the live attenuated Sabin strain. New recommendations from the Advisory Committee on Immunization Practices (ACIP) require two doses of IPV followed by two doses of OPV, because OPV causes vaccine-associated paralytic poliomyelitis (VAPP) and has been the only cause of paralytic poliomyelitis in the United States since 1979. Cases occur only once per 2.4 million doses, but this is enough for the recommended changes and VAPP is currently estimated to occur once per 750,000 people receiving the first dose. People can be reinfected and secrete wild or vaccine strains in their feces when using only IPV even in the newer, more potent vaccine (enhanced IPV). Gastrointestinal immunity occurs more effectively after two doses of OPV, and if two doses of IPV are given first, then patients are antibody-protected against developing VAPP from the OPV. Currently in the United States, IPOL is an IPV and is the only one used. The IPV-OPV schedules are an ongoing study. Children receive 4 doses of IPV, scheduled at 2 months, 4 months, 6 months, and 4 years of age or Kindergarten shots.

Some countries already use IPV-OPV schedules in part to control the spread of the wild polio virus in feces. Some countries only use OPV, especially where there are still outbreaks and in places where it could be more difficult to stick to a schedule like that which is required for IPV alone. The enhanced potency IPV was licensed in the U.S. in 1987 and is used because the U.S. has eradicated the wild polio virus. Therefore, there is no risk of polio virus spreading through feces. Some other countries do still have this risk, so they do use OPV (MMWR Recommendations and Reports, 1997).

Note: This data comes from studies in the United States using different combinations of IPV, OPV, or IPV-OPV schedules.

	Ages and Types of Injections (months)				Efficacy For Each Polio Type After Dose 2			Efficacy For Each Polio Type After Dose 3			Efficacy For Each Polio Type After Dose 4			Number of Participants
Studies	2	4	6	12-15	P1	P2	P3	P1	P2	P3	P1	P2	P3	
1: Enhance IPV and Live OPV	IPV	IPV		IPV	99	99	99	99	100	100				331
	IPV	IPV		IPV	99	100	100	100	100	100				332
	Live OPV	OPV		OPV	92	100	96	97	100	100				337
2: IPV Grown in vero cells	IPV	IPV		IPV	96	100	96	96	100	100				91
	OPV	OPV		OPV	100	100	100	100	100	100				22
	IPV	OPV		OPV	94	100	94	100	100	100				29
	IPV	IPV		OPV	100	100	100	100	100	100				29
3: IPV + DTP	IPV	IPV		IPV	97	92	75	100	100	100				101
	OPV	OPV		OPV	95	100	90	95	100	100				98
	IPV	IPV		OPV	90	93	74	97	100	85				98
	IPV	IPV	OPV	OPV	89	96	71	94	100	81	95	100	98	106
	IPV	IPV/ OVP	OPV	OPV	96	100	85	93	99	97	95	100	100	101

4: IPV Grown in Vero, IPV + DTP	IPV	IPV		IPV	97	96	95	100	100	100				94
	IPV	IPV		IPV	98	100	98	100	100	100				68
	IPV	IPV		OPV	94	95	96	100	100	96				75
	IPV	IPV		OPV	99	99	95	100	100	100				99
5: IPV + DTP	IPV	IPV	IPV	OPV	98	98	100	100	100	100	100	100	100	97
	IPV	IPV	OPV	OPV	100	97	99	100	100	100	100	100	100	96
	IPV	IPV	IPV/ OPV	OPV	95	96	100	100	100	100	100	100	100	91

Bibliography

MMWR Recommendations and Reports. Poliomyelitis Prevention in the United States: Introduction of a Sequential Vaccination Schedule of Inactivated Poliovirus Vaccine Followed by Oral Poliovirus Vaccine; Recommendations of the Advisory Committee on Immunization Practices (ACIP). cdc.gov. https://www.cdc.gov/mmwr/preview/mmwrhtml/00046568.htm. Published January 24, 1997.

DTP Vaccine Data

The original DTP vaccines included diphtheria and tetanus toxoids and inactivated, whole-cell Bordetalla pertussis bacterial cells. This form of the vaccine has been used since the 1940s, and is 70-90% effective at preventing severe disease. However, the risk for severe events following vaccination was enough to begin the search for a better form of the pertussis portion of the vaccine. Acellular pertussis vaccines use inactivated pertussis toxin (PT) and other bacterial parts to create the vaccine. The aP in the DTaP vaccine indicates that the pertussis portion does not include whole cells (acellular). Tripedia was the first DTaP vaccine licensed in the United States in 1996. Other bacterial parts of the pertussis vaccine include filamentous hemagglutinin (FHA), pertactin (Pn), and fimbriae (Fim). Currently, Tripedia, ACEL-IMUNE, and INFANRIX TM are licensed in the U.S., but only ACEL-IMUNE is licensed for the fifth dose. There are four whole-cell DTP vaccines licensed in the U.S. and they can still be used and can be combined with the Hib vaccine for the first four doses. When using DTaP, it must have a separate injection site than that of Hib. In the U.S., the whole-cell DTP is shown to be 70-90% effective a preventing severe pertussis disease (MMWR Recommendations and Reports, 1997).

Efficacy Data for Tripedia, ACEL-IMUNE, and Whole-Cell DTP

Note: The confidence interval was 95% for all studies.

Studies	Ages at Which Vaccinations Were Administered
Acellular Pertussis in the Tripedia Vaccine	2, 4 and 6 months
Percent Efficacy	81
Percent Who Developed Immunogenicity to Pertussis Toxin (PT)	99
Percent Who Developed Immunogenicity to Filamentous Hemagglutinin (FHA) for Pertussis	86
Percent Who Developed Immunogenicity to Tetanus	90
Percent Who Developed Immunogenicity to Diphtheria	90
In Germany, Percent Efficacy for Pertussis	80
Acellular Pertussis in the ACEL-IMUNE Vaccine	
Percent Efficacy	81
Percent Who Developed Immunogenicity to Pertussis Toxin (PT)	67
Percent Who Developed Immunogenicity to Filamentous Hemagglutinin (FHA) for Pertussis	80
Percent Who Developed Immunogenicity to Tetanus	100
Percent Who Developed Immunogenicity to Diphtheria	86
Whole-Cell Pertussis in the DTP Vaccine	
In Germany, Percent Efficacy for whole-cell DTP in the Tripedia Study	95
In Germany, Percent Efficacy for whole-cell DTP in the ACEL-IMUNE Study	91

Bibliography

MMWR Recommendations and Reports. Perussis Vaccination: Use of Acellular Pertussis Vaccines Among Infants and Young Children Recommendations of the Advisory Committee on Immunization Practices (ACIP). cdc.gov. https://www.cdc.gov/mmwr/preview/mmwrhtml/00048610.htm Published March 28, 1997.

Student Worksheet

Study the provided data sets and write down three statistical questions.

1.

2.

3.

Now, choose one question and use the provided data sets to create a graph that answers your question.