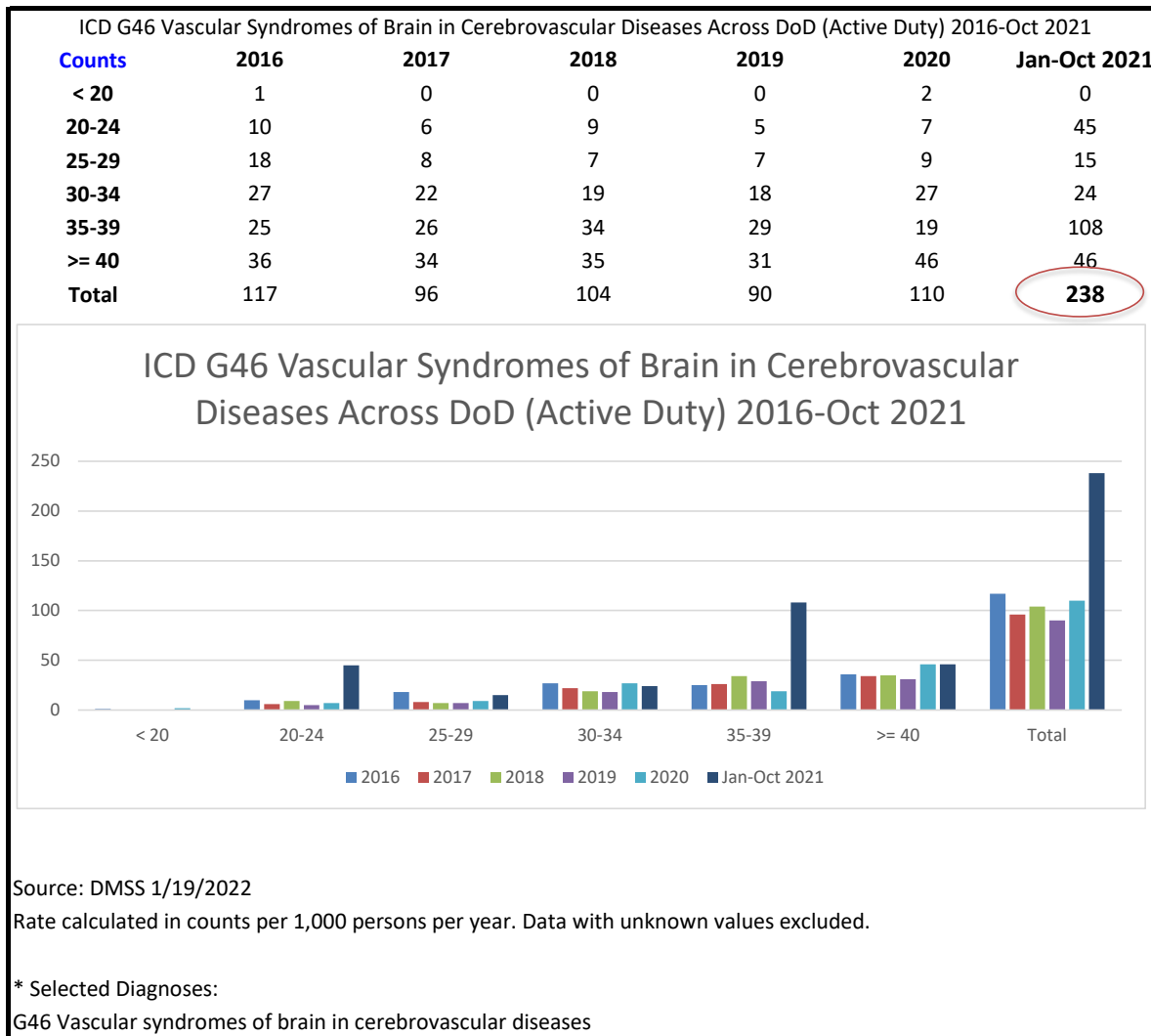
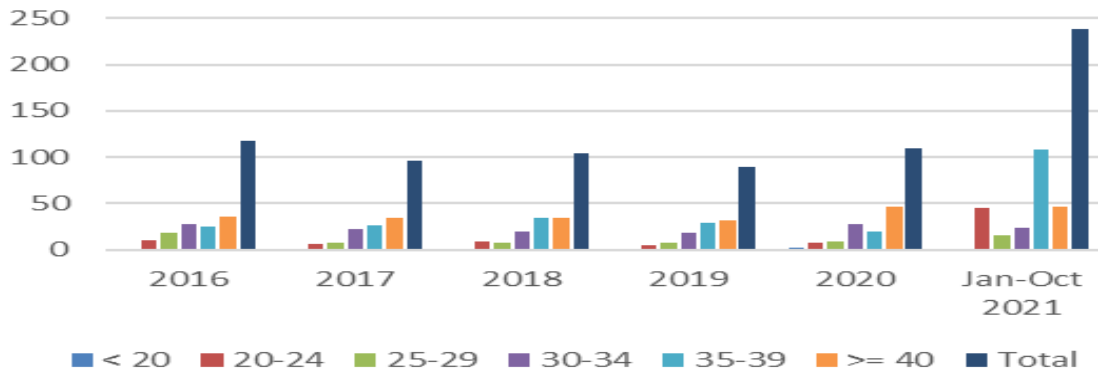


Ambulatory Data - Cases of Selected Diagnoses \*

Service: All  
 Age: All  
 Grade: All  
 Time: 2016, 2017, 2018, 2019, 2020  
 Data Sources: Hospitalizations, Ambulatory Data, Reportable Events  
 Condition: Primary Diagnosis  
 Gender: All  
 Race: All  
 Marital Status: All  
 Occurrence: All Occurrences  
 Occupation: ALL OCCUPATION GROUPS  
 Location: ALL LOCATIONS



## ICD G46 Vascular Syndromes of Brain in Cerebrovascular Diseases Across DoD (Active Duty) 2016-Oct 2021



Population	2016	2017	2018	2019	2020
< 20	89,960.22	97,211.06	101,742.92	103,979.52	99,700.77
20-24	407,896.25	408,673.02	416,571.93	423,448.74	426,856.25
25-29	301,023.73	295,861.48	298,208.35	303,986.22	307,502.33
30-34	210,243.28	206,598.27	205,040.00	206,150.65	209,127.84
35-39	147,076.90	147,648.83	150,119.41	153,231.54	156,973.87
>= 40	132,655.89	127,672.92	124,588.75	124,232.43	126,871.55
<b>Total</b>	<b>1,288,856.27</b>	<b>1,283,665.58</b>	<b>1,296,271.36</b>	<b>1,315,029.10</b>	<b>1,327,032.61</b>

Rate	2016	2017	2018	2019	2020
< 20	0.01	0.00	0.00	0.00	0.02
20-24	0.02	0.01	0.02	0.01	0.02
25-29	0.06	0.03	0.02	0.02	0.03
30-34	0.13	0.11	0.09	0.09	0.13
35-39	0.17	0.18	0.23	0.19	0.12
>= 40	0.27	0.27	0.28	0.25	0.36
<b>Total</b>	<b>0.09</b>	<b>0.07</b>	<b>0.08</b>	<b>0.07</b>	<b>0.08</b>

Source: DMSS 1/19/2022

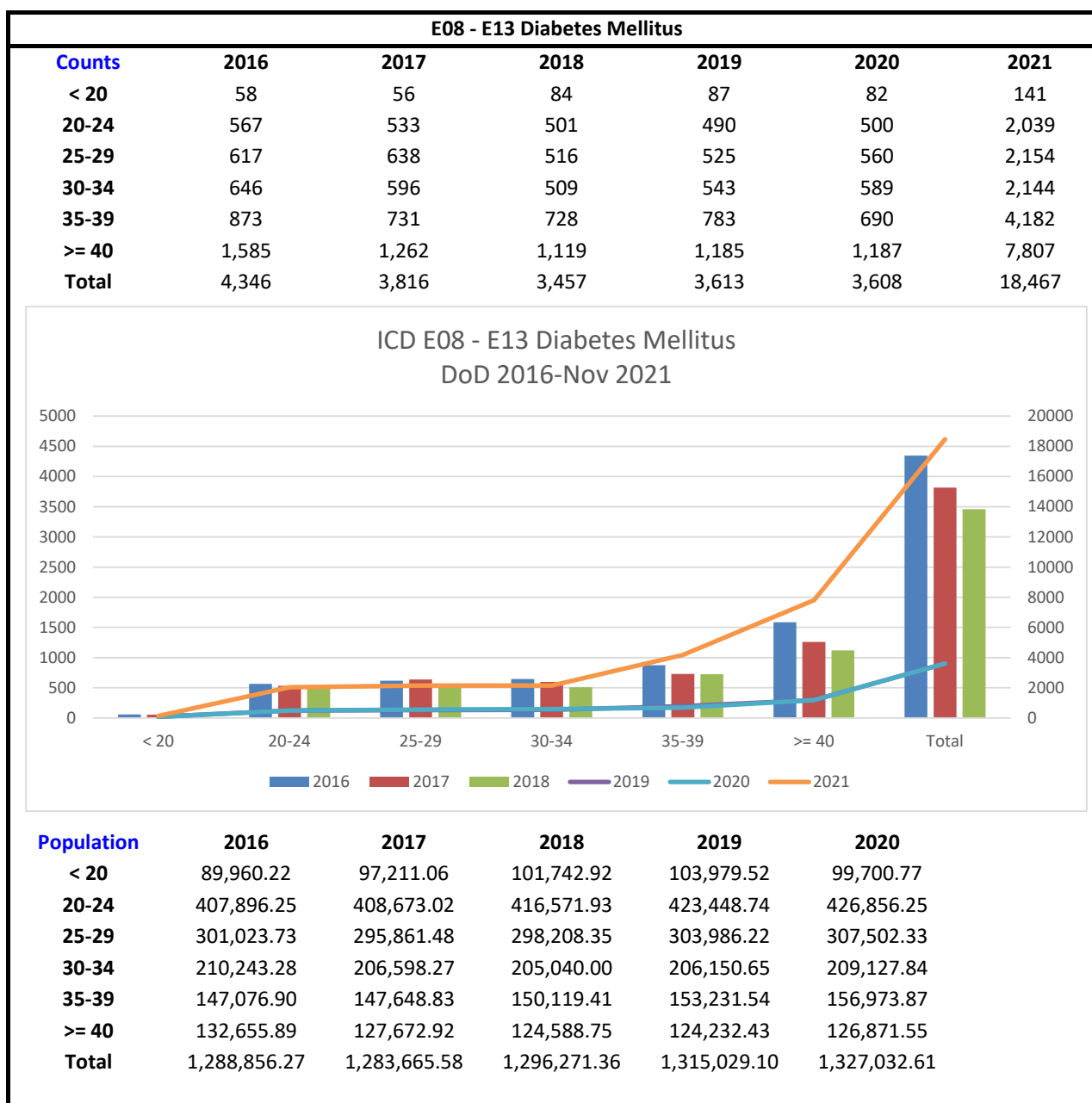
Rate calculated in counts per 1,000 persons per year. Data with unknown values excluded.

\* Selected Diagnoses:

G46 Vascular syndromes of brain in cerebrovascular diseases

Ambulatory Data - Cases of Selected Diagnoses \*

Service: All  
 Age: All  
 Grade: All  
 Time: 2016, 2017, 2018, 2019, 2020  
 Data Sources: Hospitalizations, Ambulatory Data, Reportable Events  
 Condition: Primary Diagnosis  
 Gender: All  
 Race: All  
 Marital Status: All  
 Occurrence: All Occurrences  
 Occupation: ALL OCCUPATION GROUPS  
 Location: ALL LOCATIONS



<b>Rate</b>	<b>2016</b>	<b>2017</b>	<b>2018</b>	<b>2019</b>	<b>2020</b>
<b>&lt; 20</b>	0.64	0.58	0.83	0.84	0.82
<b>20-24</b>	1.39	1.30	1.20	1.16	1.17
<b>25-29</b>	2.05	2.16	1.73	1.73	1.82
<b>30-34</b>	3.07	2.88	2.48	2.63	2.82
<b>35-39</b>	5.94	4.95	4.85	5.11	4.40
<b>&gt;= 40</b>	11.95	9.88	8.98	9.54	9.36
<b>Total</b>	<b>3.37</b>	<b>2.97</b>	<b>2.67</b>	<b>2.75</b>	<b>2.72</b>

Source: DMSS 1/19/2022

Rate calculated in counts per 1,000 persons per year. Data with unknown values excluded.

\* Selected Diagnoses:

E08 - E13 Diabetes mellitus

Ambulatory Data - Cases of Selected Diagnoses \*

Service: All

Age: All

Grade: All

Time: 2016, 2017, 2018, 2019, 2020

Data Sources: Hospitalizations, Ambulatory Data, Reportable Events

Condition: Primary Diagnosis

Gender: All

Race: All

Marital Status: All

Occurrence: All Occurrences

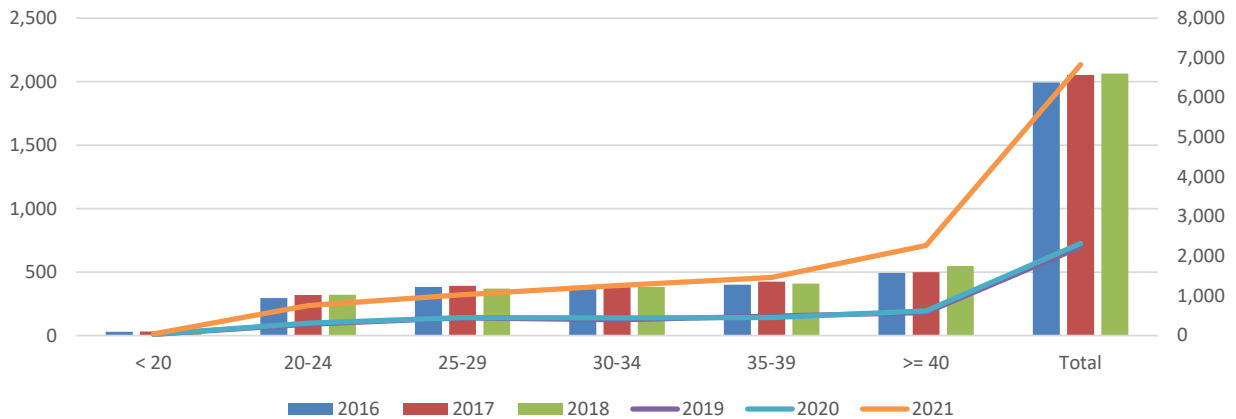
Occupation: ALL OCCUPATION GROUPS

Location: ALL LOCATIONS

K70 - K77 Diseases of liver

Counts	2016	2017	2018	2019	2020	2021
< 20	29	33	31	32	32	43
20-24	295	320	322	289	312	756
25-29	384	393	370	445	453	1,029
30-34	393	382	383	395	444	1,260
35-39	401	425	410	491	457	1,468
>= 40	492	500	547	582	624	2,274
<b>Total</b>	<b>1,994</b>	<b>2,053</b>	<b>2,063</b>	<b>2,234</b>	<b>2,322</b>	<b>6,830</b>

ICD K70 - K77 Diseases of Liver  
DoD Jan 2016 -Nov 2021



Population	2016	2017	2018	2019	2020
< 20	89,960.22	97,211.06	101,742.92	103,979.52	99,700.77
20-24	407,896.25	408,673.02	416,571.93	423,448.74	426,856.25
25-29	301,023.73	295,861.48	298,208.35	303,986.22	307,502.33
30-34	210,243.28	206,598.27	205,040.00	206,150.65	209,127.84
35-39	147,076.90	147,648.83	150,119.41	153,231.54	156,973.87
>= 40	132,655.89	127,672.92	124,588.75	124,232.43	126,871.55
<b>Total</b>	<b>1,288,856.27</b>	<b>1,283,665.58</b>	<b>1,296,271.36</b>	<b>1,315,029.10</b>	<b>1,327,032.61</b>

<b>Rate</b>	<b>2016</b>	<b>2017</b>	<b>2018</b>	<b>2019</b>	<b>2020</b>
<b>&lt; 20</b>	0.32	0.34	0.30	0.31	0.32
<b>20-24</b>	0.72	0.78	0.77	0.68	0.73
<b>25-29</b>	1.28	1.33	1.24	1.46	1.47
<b>30-34</b>	1.87	1.85	1.87	1.92	2.12
<b>35-39</b>	2.73	2.88	2.73	3.20	2.91
<b>&gt;= 40</b>	3.71	3.92	4.39	4.68	4.92
<b>Total</b>	1.55	1.60	1.59	1.70	1.75

Source: DMSS 1/19/2022

Rate calculated in counts per 1,000 persons per year. Data with unknown values excluded.

\* Selected Diagnoses:

K70 - K77 Diseases of liver

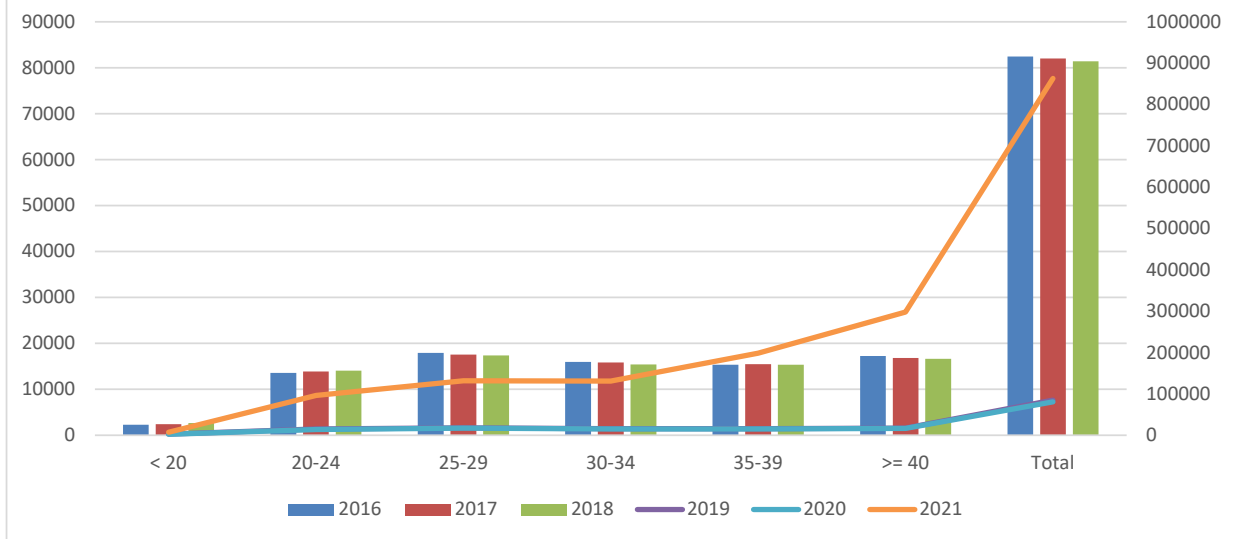
Ambulatory Data - Cases of Selected Diagnoses \*

Service: All  
 Age: All  
 Grade: All  
 Time: 2016, 2017, 2018, 2019, 2020  
 Data Sources: Hospitalizations, Ambulatory Data, Reportable Events  
 Condition: Primary Diagnosis  
 Gender: All  
 Race: All  
 Marital Status: All  
 Occurrence: All Occurrences  
 Occupation: ALL OCCUPATION GROUPS  
 Location: ALL LOCATIONS

**G00 - G99 Diseases of the Nervous System**

Counts	2016	2017	2018	2019	2020	2021
< 20	2,307	2,385	2,630	2,755	2,425	7,287
20-24	13,593	13,882	14,048	14,899	14,023	96,511
25-29	17,939	17,570	17,358	18,105	17,366	131,509
30-34	15,986	15,862	15,383	16,005	15,189	131,236
35-39	15,362	15,487	15,326	16,115	15,285	198,524
>= 40	17,248	16,812	16,637	17,133	16,498	297,946
<b>Total</b>	<b>82,435</b>	<b>81,998</b>	<b>81,382</b>	<b>85,012</b>	<b>80,786</b>	<b>863,013</b>

ICD G00 - G99 Diseases of the Nervous System  
 DoD 2016 to Nov 2021



Population	2016	2017	2018	2019	2020
< 20	89,960.22	97,211.06	101,742.92	103,979.52	99,700.77
20-24	407,896.25	408,673.02	416,571.93	423,448.74	426,856.25
25-29	301,023.73	295,861.48	298,208.35	303,986.22	307,502.33
30-34	210,243.28	206,598.27	205,040.00	206,150.65	209,127.84

<b>35-39</b>	147,076.90	147,648.83	150,119.41	153,231.54	156,973.87
<b>&gt;= 40</b>	132,655.89	127,672.92	124,588.75	124,232.43	126,871.55
<b>Total</b>	1,288,856.27	1,283,665.58	1,296,271.36	1,315,029.10	1,327,032.61

<b>Rate</b>	<b>2016</b>	<b>2017</b>	<b>2018</b>	<b>2019</b>	<b>2020</b>
<b>&lt; 20</b>	25.64	24.53	25.85	26.50	24.32
<b>20-24</b>	33.32	33.97	33.72	35.18	32.85
<b>25-29</b>	59.59	59.39	58.21	59.56	56.47
<b>30-34</b>	76.04	76.78	75.02	77.64	72.63
<b>35-39</b>	104.45	104.89	102.09	105.17	97.37
<b>&gt;= 40</b>	130.02	131.68	133.54	137.91	130.04
<b>Total</b>	63.96	63.88	62.78	64.65	60.88

Source: DMSS 1/19/2022

Rate calculated in counts per 1,000 persons per year. Data with unknown values excluded.

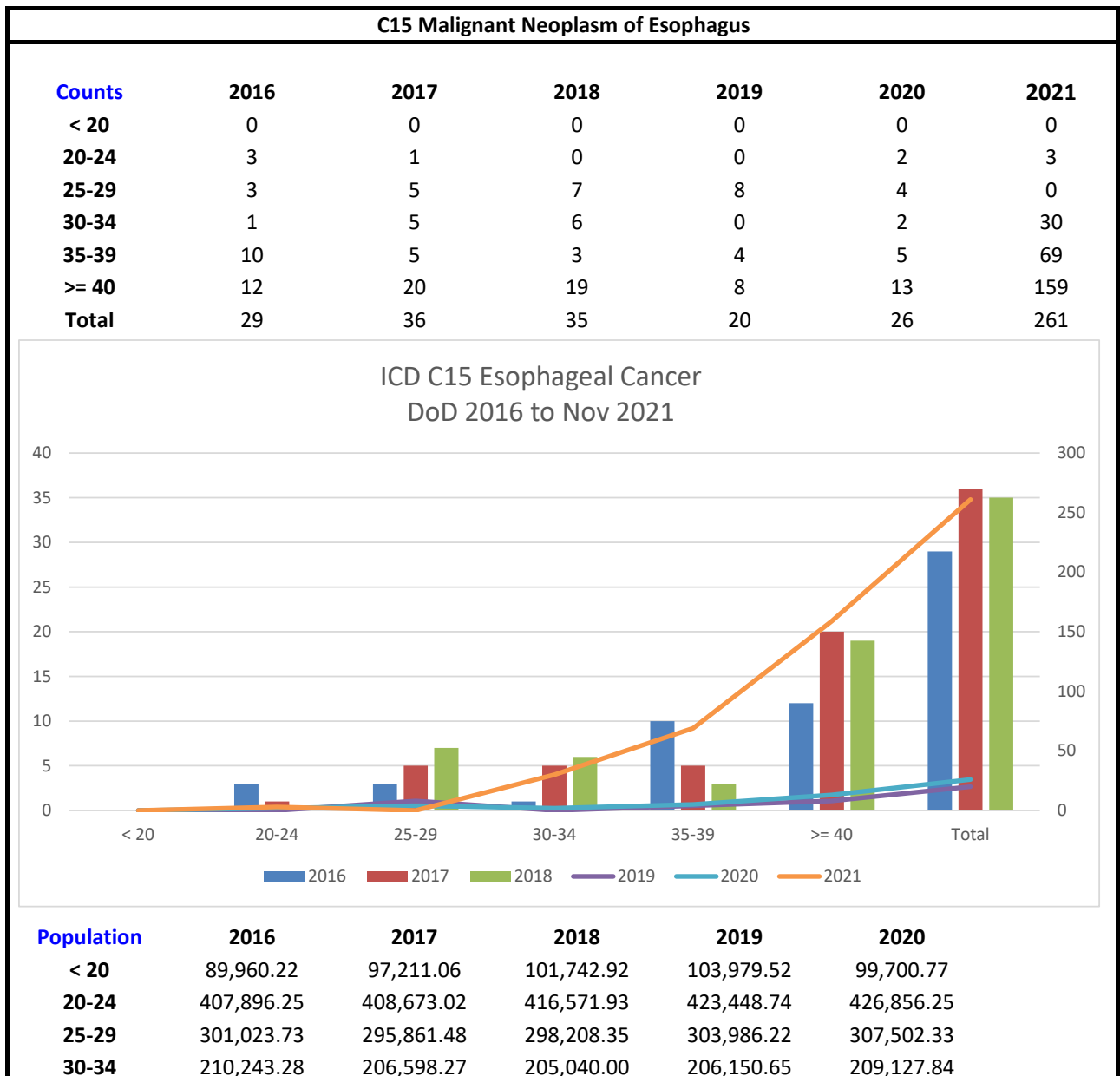
\* Selected Diagnoses:

G00 - G99 Diseases of the nervous system



Ambulatory Data - Cases of Selected Diagnoses \*

Service: All  
 Age: All  
 Grade: All  
 Time: 2016, 2017, 2018, 2019, 2020  
 Data Sources: Hospitalizations, Ambulatory Data, Reportable Events  
 Condition: Primary Diagnosis  
 Gender: All  
 Race: All  
 Marital Status: All  
 Occurrence: All Occurrences  
 Occupation: ALL OCCUPATION GROUPS  
 Location: ALL LOCATIONS



<b>35-39</b>	147,076.90	147,648.83	150,119.41	153,231.54	156,973.87
<b>&gt;= 40</b>	132,655.89	127,672.92	124,588.75	124,232.43	126,871.55
<b>Total</b>	1,288,856.27	1,283,665.58	1,296,271.36	1,315,029.10	1,327,032.61

<b>Rate</b>	<b>2016</b>	<b>2017</b>	<b>2018</b>	<b>2019</b>	<b>2020</b>
<b>&lt; 20</b>	0.00	0.00	0.00	0.00	0.00
<b>20-24</b>	0.01	0.00	0.00	0.00	0.00
<b>25-29</b>	0.01	0.02	0.02	0.03	0.01
<b>30-34</b>	0.00	0.02	0.03	0.00	0.01
<b>35-39</b>	0.07	0.03	0.02	0.03	0.03
<b>&gt;= 40</b>	0.09	0.16	0.15	0.06	0.10
<b>Total</b>	0.02	0.03	0.03	0.02	0.02

Source: DMSS 1/19/2022

Rate calculated in counts per 1,000 persons per year. Data with unknown values excluded.

\* Selected Diagnoses:

C15 Malignant neoplasm of esophagus

# FDA Begins Releasing Pfizer COVID Vax Documents

— Court-ordered release runs risk of "cherry picking and taking things out of context"

by [Amanda D'Ambrosio](#), Enterprise & Investigative Writer, MedPage Today

March 7, 2022

The FDA turned over thousands of documents related to its review of Pfizer-BioNTech's COVID-19 vaccine last week, marking the first of several releases mandated by a court in Texas earlier this year.

The agency released 55,000 pages of COVID-19 vaccine review documents last Tuesday, following a loss in court months earlier that forced it to expedite its process to make the information available to the public. In a January [court order](#), U.S. District Judge Mark Pittman of the Northern District of Texas required the FDA to release around 12,000 documents immediately, and then 55,000 pages a month until all documents are released -- totaling more than 300,000 pages.

The nonprofit that won the case, Public Health and Medical Professionals for Transparency, [sued the FDA](#) last September, claiming that the agency denied its request to expedite the release of COVID-19 vaccine review documents via the Freedom of Information Act (FOIA). In a November joint status report, the FDA [proposed](#) releasing around 500 pages of the documents each month -- which would fulfill the organization's FOIA request in about 55 to 75 years.

The agency must redact confidential business and trade secret information from Pfizer and BioNTech, as well as any private information on patients in the clinical trial. In its proposal for a 55-year timeline, the FDA noted that the branch that would handle the request has only 10 employees, and is currently processing around 400 other FOIA requests.

Although the court recognized the "unduly burdensome challenges" that this request imposed on the FDA, it concluded that the release of these documents is of "paramount public importance," stating that expediting the process is "not only practicable, but necessary." Both the FDA and the nonprofit will submit a joint status report by April 1 detailing the progress of the request.

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After the FDA distributed the first batch of the documents last week, Public Health and Medical Professionals for Transparency posted the files on its own website. The content of the documents ranges widely, with no real explanation of what the files entail. One listed de-identified data on clinical trial patient demographics and medical history, while another detailed the FDA's response to Pfizer's request for fast track review. One included postmarketing safety data based on voluntarily reported adverse events.

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#### Medical News from Around the Web

##### NEUROSURGERY

Acute Postoperative Seizures and Engel Class Outcome at 1 Year Postselective Laser Amygdalohippocampal Ablation for Mesial Temporal Lobe Epilepsy.

##### BLOOD

Bortezomib and high-dose melphalan conditioning regimen in frontline multiple myeloma: an IFM randomized phase 3 study.

##### HYPERTENSION

Midgestation Leptin Infusion Induces Characteristics of Clinical Preeclampsia in Mice, Which Is Ablated by Endothelial Mineralocorticoid Receptor Deletion.

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Zach Zalewski, PhD, JD, a regulatory strategy consultant at Avalere Health, said that many of the documents that will be released were submitted to the FDA up through the vaccine's emergency use authorization and full approval, and may not be material to an overall analysis of the vaccine's safety and efficacy. The FDA already published a [drug approval package](#) for Pfizer-BioNTech's COVID-19 vaccine, which consists of summaries of the FDA-reviewed data. The documents that the agency is required to release will likely comprise the unabridged version of this report, Zalewski said.

"This will literally include every scrap of paper that was submitted to FDA for the entirety of the pandemic," Zalewski told *MedPage Today*. "If transparency is what they want, transparency is what they'll get."

Anti-vaccine advocates have already capitalized on the release of these documents to further call COVID-19 vaccines into question. Children's Health Defense, a nonprofit that has taken a stance against the use of COVID vaccines in kids, highlighted a list of adverse

events reported in the documents -- a list that includes any adverse events that occurred in people who participated in the clinical trial, even those who received placebo, and is misleading, experts have said.

"There's a risk of cherry picking and taking things out of context," Zalewski said. "Just because you will have all the data in front of you, that doesn't mean you'll reach any different conclusions."

Public Health and Medical Professionals for Transparency includes several physicians known for spreading false or misleading information during the pandemic, including [Aaron Kheriaty, MD](#), [Harvey Risch, MD, PhD](#), and [Peter McCullough, MD](#).

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[Amanda D'Ambrosio](#) is a reporter on MedPage Today's enterprise & investigative team. She covers obstetrics-gynecology and other clinical news, and writes features about the U.S. healthcare system. Follow

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# FDA Safety Surveillance of COVID-19 Vaccines :

## DRAFT Working list of possible adverse event outcomes

\*\*\*Subject to change\*\*\*

This side effects appeared for a split second at 2:33:40 in an FDA presentation on October 22, 2020

- Guillain-Barré syndrome
- Acute disseminated encephalomyelitis
- Transverse myelitis
- Encephalitis/myelitis/encephalomyelitis/meningoencephalitis/meningitis/encepholopathy
- Convulsions/seizures
- Stroke
- Narcolepsy and cataplexy
- Anaphylaxis
- Acute myocardial infarction
- Myocarditis/pericarditis
- Autoimmune disease
- Deaths
- Pregnancy and birth outcomes
- Other acute demyelinating diseases
- Non-anaphylactic allergic reactions
- Thrombocytopenia
- Disseminated intravascular coagulation
- Venous thromboembolism
- Arthritis and arthralgia/joint pain
- Kawasaki disease
- Multisystem Inflammatory Syndrome in Children
- Vaccine enhanced disease

# VAERS COVID Vaccine Adverse Event Reports

Reports from the Vaccine Adverse Events Reporting System. Our default data reflects all VAERS data including the "nondomestic" reports. [?](#)

All VAERS COVID Reports  US/Territories/Unknown

1,247,129 Reports  
Through April 22, 2022 [?](#)

27,532  
DEATHS

152,946  
HOSPITALIZATIONS

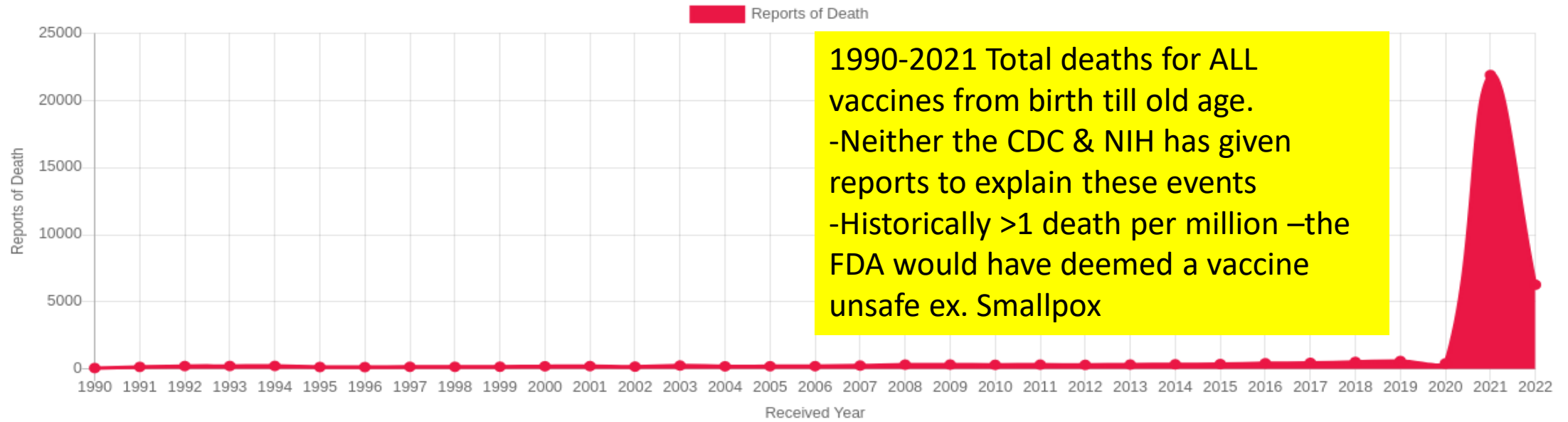
128,134  
URGENT CARE

189,907  
DOCTOR OFFICE VISITS

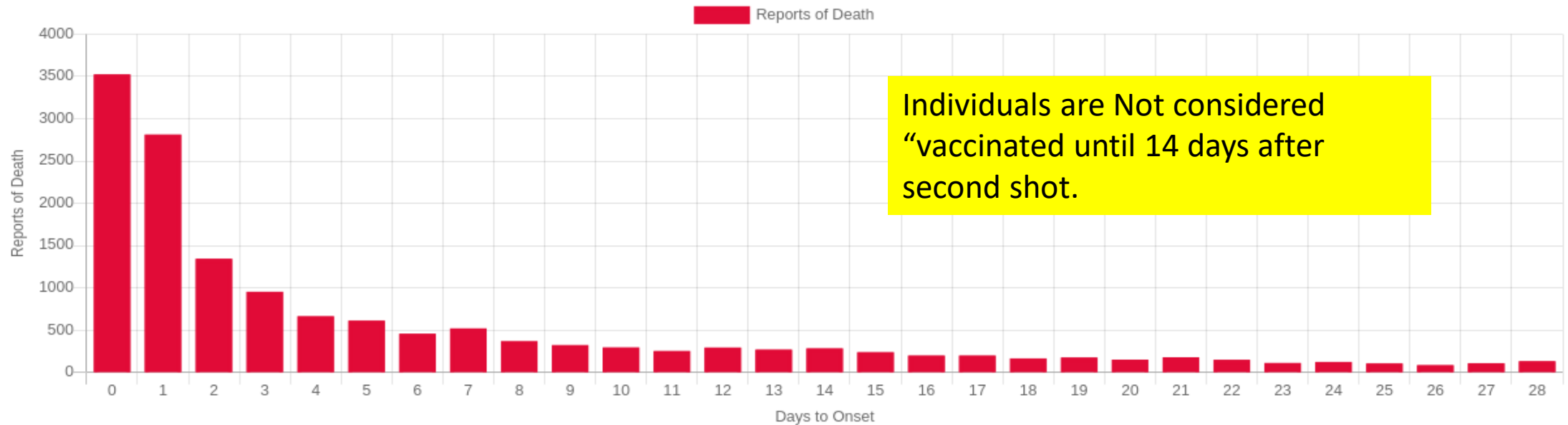
9,643  
ANAPHYLAXIS

15,327  
BELL'S PALSY

All Deaths Reported to VAERS by Year



VAERS COVID Vaccine Reports of Deaths by Days to Onset-All Ages





# Data from openvaers.com

**4,570**  
Miscarriages

**14,096**  
Heart Attacks

**39,639**  
Myocarditis/Pericarditis

**51,163**  
Permanently  
Disabled

**6,494**  
Thrombocytopenia/  
Low Platelet

**30,748**  
Life Threatening

**41,595**  
Severe Allergic  
Reaction

**13,599**  
Shingles

# Reports on Children in VAERS

## COVID Vaccine Reports in Children (Ages 5-17)

Through April 22, 2022 ●

Deaths

**101**

Permanently  
Disabled

**422**

Myocarditis

**1,289**

47,475

Total Reports

589

Life Threatening

3,675

Hospitalized

4,703

ER Visit

8,491

Not Recovered

# Reports on Children in VAERS

**78**

**Encephalitis/  
Encephalopathy**

Encephalitis,  
Encephalopathy,  
AntiNMDA Antibodies,  
AntiMyelin Antibodies

**204**

**Bell's Palsy**

Bell's Palsy, Facial Paralysis,  
Facial Palsy, Facial Nerve  
Disorder

**1,476**

**Severe Allergy**

Epi Pen, Epinephrine,  
Rashes/Hives, Swelling,  
Anaphylaxis

**3,796**

**Migraine/Headache**

Migraine, Headache

**24**

**Aneurysm/Cerebral  
Haemorrhage**

Brain Haemorrhage,  
Aneurysm, Cerebral  
Infarction, CVST

**171**

**Thrombocytopenia/  
Low Platelets**

Thrombocytopenia, Platelet  
Count Decreased

**64**

**Guillain Barre/  
Paralysis**

Guillain Barre, Transverse  
Myelitis, Acute  
Disseminated  
Encephalomyelitis

**102**

**Diabetes**

Diabetes, High Blood  
Sugar, Diabetic  
Ketoacidosis

**107**

**Appendicitis**

Appendicitis,  
Appendicectomy

# Reports on Children in VAERS

47,475

Total Reports

589

Life Threatening

3,675

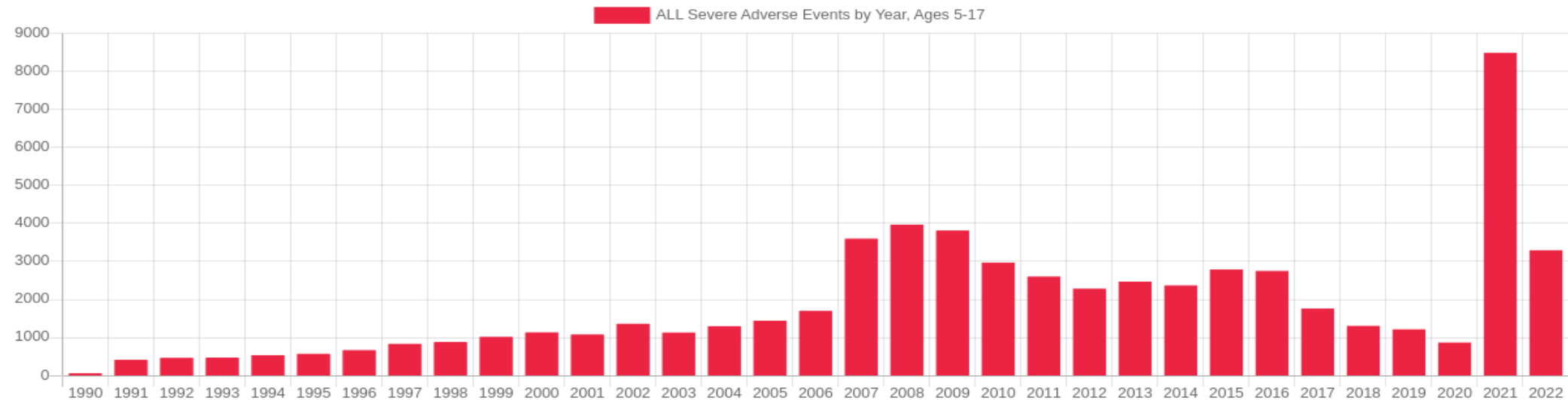
Hospitalized

4,703

ER Visit

8,491

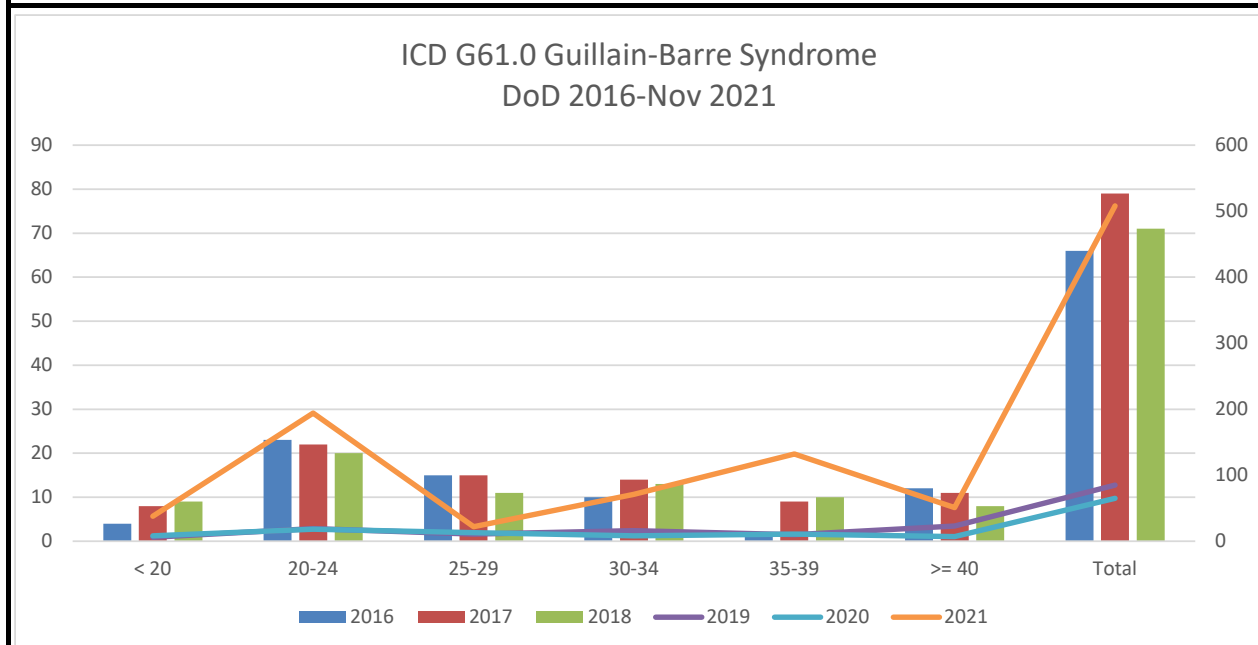
Not Recovered



Ambulatory Data - Cases of Selected Diagnoses \*

Service: All  
 Age: All  
 Grade: All  
 Time: 2016, 2017, 2018, 2019, 2020  
 Data Sources: Hospitalizations, Ambulatory Data, Reportable Events  
 Condition: Primary Diagnosis  
 Gender: All  
 Race: All  
 Marital Status: All  
 Occurrence: All Occurrences  
 Occupation: ALL OCCUPATION GROUPS  
 Location: ALL LOCATIONS

G61.0 Guillain-Barre syndrome						
Counts	2016	2017	2018	2019	2020	2021
< 20	4	8	9	6	8	38
20-24	23	22	20	19	18	194
25-29	15	15	11	11	13	22
30-34	10	14	13	16	8	71
35-39	2	9	10	10	11	132
>= 40	12	11	8	23	7	51
<b>Total</b>	<b>66</b>	<b>79</b>	<b>71</b>	<b>85</b>	<b>65</b>	<b>508</b>



Population	2016	2017	2018	2019	2020
< 20	89,960.22	97,211.06	101,742.92	103,979.52	99,700.77
20-24	407,896.25	408,673.02	416,571.93	423,448.74	426,856.25
25-29	301,023.73	295,861.48	298,208.35	303,986.22	307,502.33
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<b>35-39</b>	147,076.90	147,648.83	150,119.41	153,231.54	156,973.87
<b>&gt;= 40</b>	132,655.89	127,672.92	124,588.75	124,232.43	126,871.55
<b>Total</b>	1,288,856.27	1,283,665.58	1,296,271.36	1,315,029.10	1,327,032.61

<b>Rate</b>	<b>2016</b>	<b>2017</b>	<b>2018</b>	<b>2019</b>	<b>2020</b>
<b>&lt; 20</b>	0.04	0.08	0.09	0.06	0.08
<b>20-24</b>	0.06	0.05	0.05	0.04	0.04
<b>25-29</b>	0.05	0.05	0.04	0.04	0.04
<b>30-34</b>	0.05	0.07	0.06	0.08	0.04
<b>35-39</b>	0.01	0.06	0.07	0.07	0.07
<b>&gt;= 40</b>	0.09	0.09	0.06	0.19	0.06
<b>Total</b>	0.05	0.06	0.05	0.06	0.05

Source: DMSS 1/19/2022

Rate calculated in counts per 1,000 persons per year. Data with unknown values excluded.

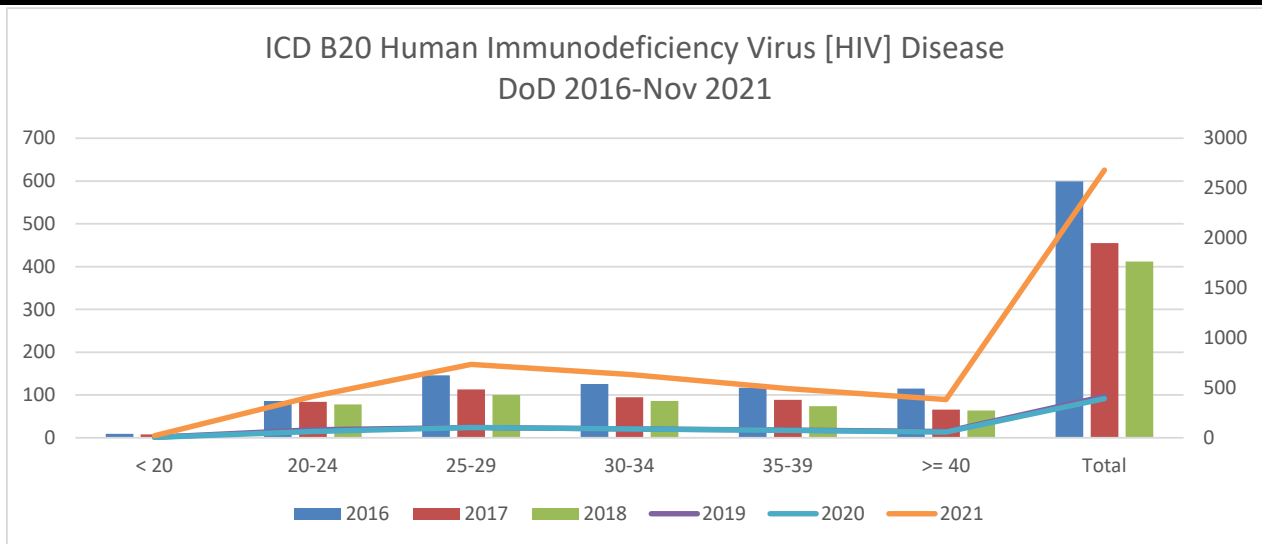
\* Selected Diagnoses:

G61.0 Guillain-Barre syndrome

Ambulatory Data - Cases of Selected Diagnoses \*

Service: All  
 Age: All  
 Grade: All  
 Time: 2016, 2017, 2018, 2019, 2020  
 Data Sources: Hospitalizations, Ambulatory Data, Reportable Events  
 Condition: Primary Diagnosis  
 Gender: All  
 Race: All  
 Marital Status: All  
 Occurrence: All Occurrences  
 Occupation: ALL OCCUPATION GROUPS  
 Location: ALL LOCATIONS

B20 Human Immunodeficiency Virus [HIV] Disease						
Counts	2016	2017	2018	2019	2020	2021
< 20	9	8	10	5	4	21
20-24	86	84	78	79	63	415
25-29	146	113	100	104	102	735
30-34	126	95	86	89	90	634
35-39	117	89	74	76	75	494
>= 40	115	66	64	62	58	382
<b>Total</b>	<b>599</b>	<b>455</b>	<b>412</b>	<b>415</b>	<b>392</b>	<b>2,681</b>



Population	2016	2017	2018	2019	2020
< 20	89,960.22	97,211.06	101,742.92	103,979.52	99,700.77
20-24	407,896.25	408,673.02	416,571.93	423,448.74	426,856.25
25-29	301,023.73	295,861.48	298,208.35	303,986.22	307,502.33
30-34	210,243.28	206,598.27	205,040.00	206,150.65	209,127.84
35-39	147,076.90	147,648.83	150,119.41	153,231.54	156,973.87
>= 40	132,655.89	127,672.92	124,588.75	124,232.43	126,871.55
<b>Total</b>	<b>1,288,856.27</b>	<b>1,283,665.58</b>	<b>1,296,271.36</b>	<b>1,315,029.10</b>	<b>1,327,032.61</b>

<b>Rate</b>	<b>2016</b>	<b>2017</b>	<b>2018</b>	<b>2019</b>	<b>2020</b>
<b>&lt; 20</b>	0.10	0.08	0.10	0.05	0.04
<b>20-24</b>	0.21	0.21	0.19	0.19	0.15
<b>25-29</b>	0.49	0.38	0.34	0.34	0.33
<b>30-34</b>	0.60	0.46	0.42	0.43	0.43
<b>35-39</b>	0.80	0.60	0.49	0.50	0.48
<b>&gt;= 40</b>	0.87	0.52	0.51	0.50	0.46
<b>Total</b>	0.46	0.35	0.32	0.32	0.30

Source: DMSS 1/19/2022

Rate calculated in counts per 1,000 persons per year. Data with unknown values excluded.

\* Selected Diagnoses:

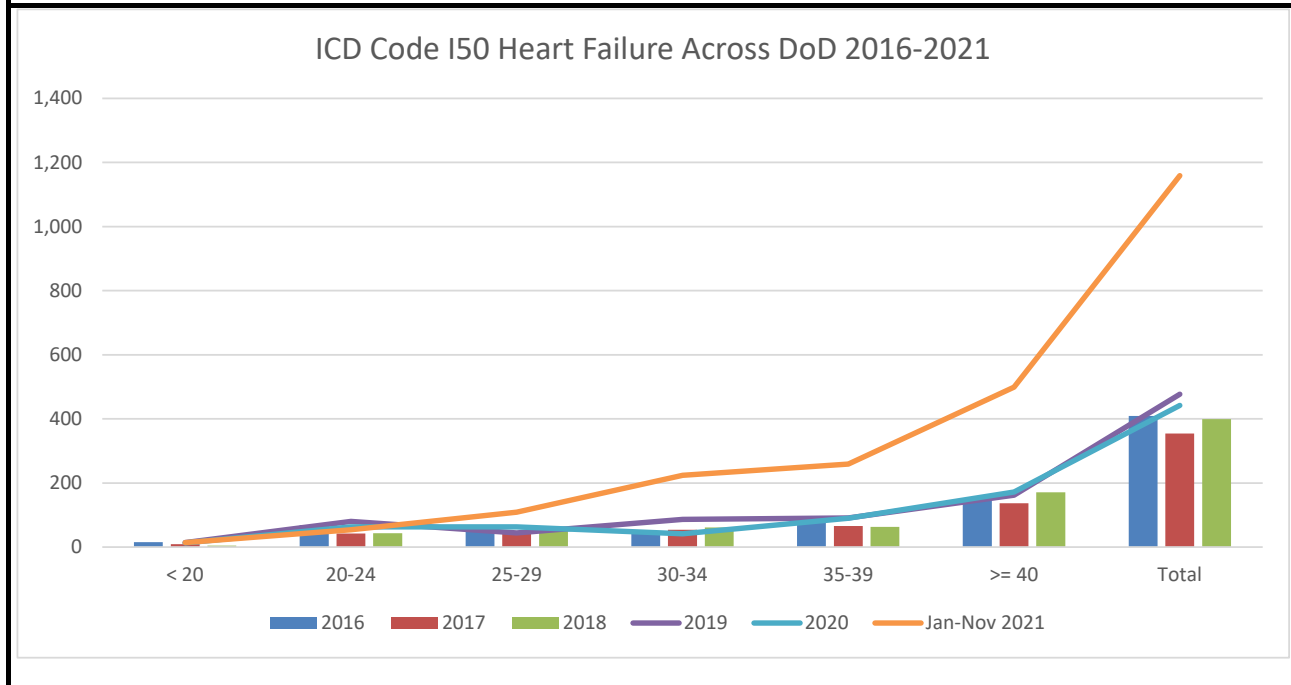
B20 Human immunodeficiency virus [HIV] disease



Ambulatory Data - Cases of Selected Diagnoses \*

Service: All  
 Age: All  
 Grade: All  
 Time: 2016, 2017, 2018, 2019, 2020  
 Data Sources: Hospitalizations, Ambulatory Data, Reportable Events  
 Condition: Primary Diagnosis  
 Gender: All  
 Race: All  
 Marital Status: All  
 Occurrence: All Occurrences  
 Occupation: ALL OCCUPATION GROUPS  
 Location: ALL LOCATIONS

I50 Heart failure							
Counts	2016	2017	2018	2019	2020	Jan-Nov 2021	
< 20	15	9	5	14	13	14	
20-24	68	42	43	80	63	54	
25-29	56	46	56	44	63	109	
30-34	47	54	61	86	41	224	
35-39	76	66	63	91	90	259	
>= 40	147	137	171	162	172	499	
<b>Total</b>	<b>409</b>	<b>354</b>	<b>399</b>	<b>477</b>	<b>442</b>	<b>1,159</b>	



Population	2016	2017	2018	2019	2020
< 20	89,960.22	97,211.06	101,742.92	103,979.52	99,700.77
20-24	407,896.25	408,673.02	416,571.93	423,448.74	426,856.25
25-29	301,023.73	295,861.48	298,208.35	303,986.22	307,502.33
30-34	210,243.28	206,598.27	205,040.00	206,150.65	209,127.84

<b>35-39</b>	147,076.90	147,648.83	150,119.41	153,231.54	156,973.87
<b>&gt;= 40</b>	132,655.89	127,672.92	124,588.75	124,232.43	126,871.55
<b>Total</b>	1,288,856.27	1,283,665.58	1,296,271.36	1,315,029.10	1,327,032.61

<b>Rate</b>	<b>2016</b>	<b>2017</b>	<b>2018</b>	<b>2019</b>	<b>2020</b>
<b>&lt; 20</b>	0.17	0.09	0.05	0.13	0.13
<b>20-24</b>	0.17	0.10	0.10	0.19	0.15
<b>25-29</b>	0.19	0.16	0.19	0.14	0.20
<b>30-34</b>	0.22	0.26	0.30	0.42	0.20
<b>35-39</b>	0.52	0.45	0.42	0.59	0.57
<b>&gt;= 40</b>	1.11	1.07	1.37	1.30	1.36
<b>Total</b>	0.32	0.28	0.31	0.36	0.33

Source: DMSS 1/24/2022

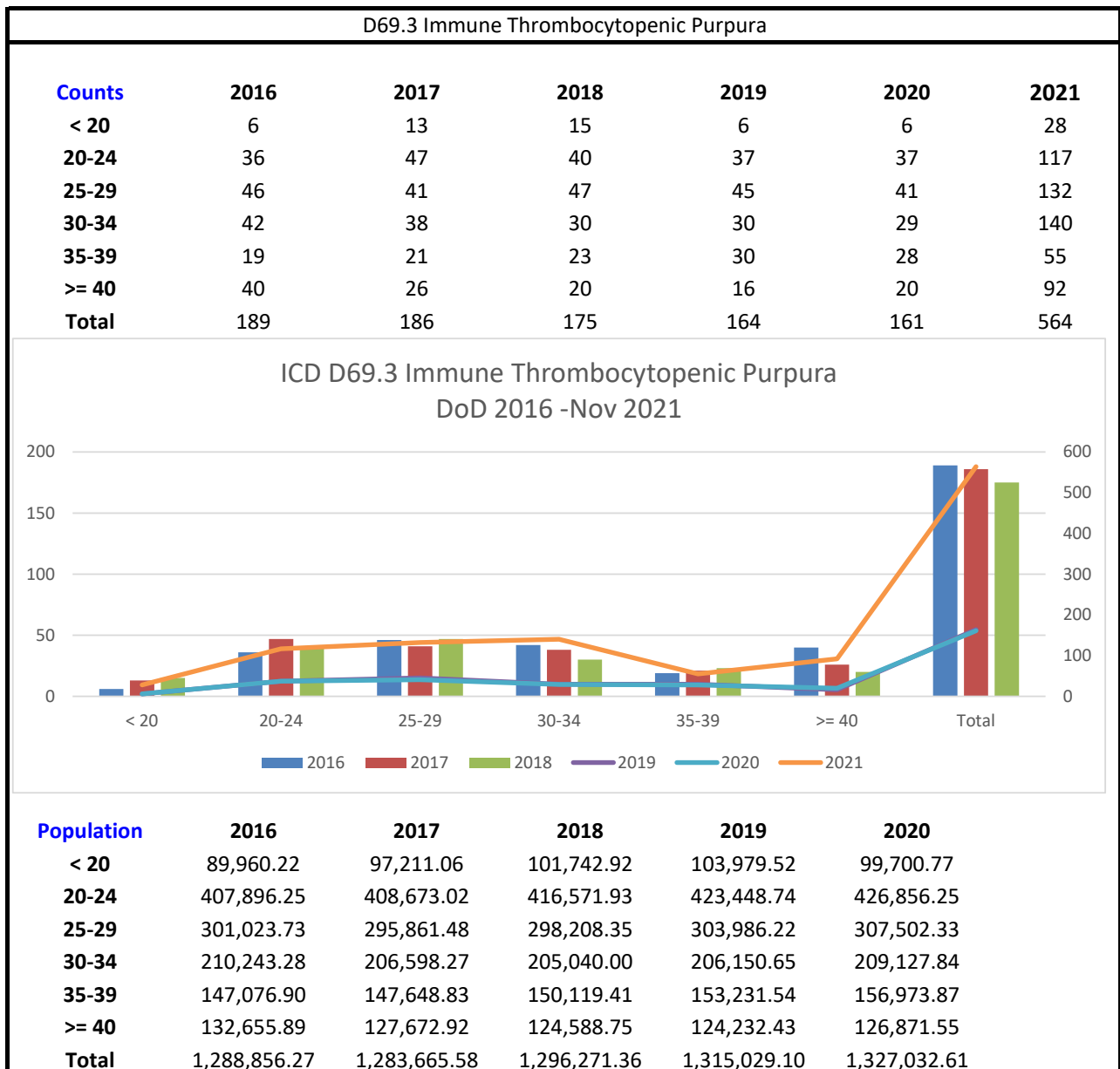
Rate calculated in counts per 1,000 persons per year. Data with unknown values excluded.

\* Selected Diagnoses:

I50 Heart failure

Ambulatory Data - Cases of Selected Diagnoses \*

Service: All  
 Age: All  
 Grade: All  
 Time: 2016, 2017, 2018, 2019, 2020  
 Data Sources: Hospitalizations, Ambulatory Data, Reportable Events  
 Condition: Primary Diagnosis  
 Gender: All  
 Race: All  
 Marital Status: All  
 Occurrence: All Occurrences  
 Occupation: ALL OCCUPATION GROUPS  
 Location: ALL LOCATIONS



<b>Rate</b>	<b>2016</b>	<b>2017</b>	<b>2018</b>	<b>2019</b>	<b>2020</b>
<b>&lt; 20</b>	0.07	0.13	0.15	0.06	0.06
<b>20-24</b>	0.09	0.12	0.10	0.09	0.09
<b>25-29</b>	0.15	0.14	0.16	0.15	0.13
<b>30-34</b>	0.20	0.18	0.15	0.15	0.14
<b>35-39</b>	0.13	0.14	0.15	0.20	0.18
<b>&gt;= 40</b>	0.30	0.20	0.16	0.13	0.16
<b>Total</b>	0.15	0.14	0.14	0.12	0.12

Source: DMSS 1/19/2022

Rate calculated in counts per 1,000 persons per year. Data with unknown values excluded.

\* Selected Diagnoses:

D69.3 Immune thrombocytopenic purpura

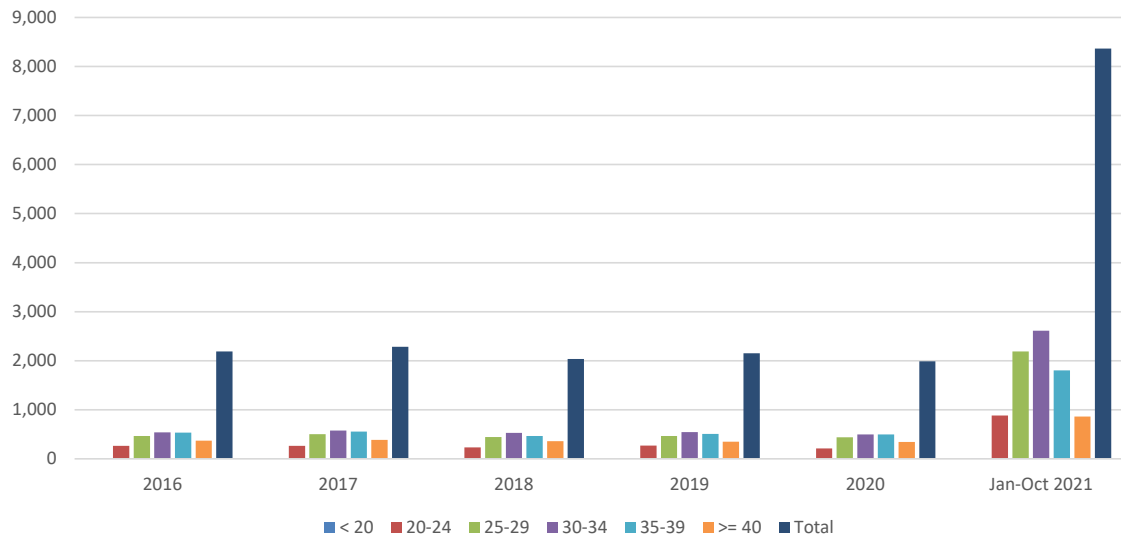
Ambulatory Data - Cases of Selected Diagnoses \*

Service: All  
 Age: All  
 Grade: All  
 Time: 2016, 2017, 2018, 2019, 2020  
 Data Sources: Hospitalizations, Ambulatory Data, Reportable Events  
 Condition: Primary Diagnosis  
 Gender: All  
 Race: All  
 Marital Status: All  
 Occurrence: All Occurrences  
 Occupation: ALL OCCUPATION GROUPS  
 Location: ALL LOCATIONS

ICD N46 Male Infertility across the DoD (Active duty) 2016 to Oct 2021

Counts	2016	2017	2018	2019	2020	Jan-Oct 2021
< 20	8	6	8	13	2	10
20-24	265	263	233	268	212	882
25-29	466	500	444	466	438	2,191
30-34	540	575	527	547	499	2,615
35-39	536	556	466	507	495	1,805
>= 40	372	387	359	351	344	862
<b>Total</b>	<b>2,187</b>	<b>2,287</b>	<b>2,037</b>	<b>2,152</b>	<b>1,990</b>	<b>8,365</b>

ICD N46 Male Infertility across the DoD (Active duty) 2016 to Oct 2021



Source: DMSS 1/19/2022

Rate calculated in counts per 1,000 persons per year. Data with unknown values excluded.

\* Selected Diagnoses:  
 N46 Male infertility

<b>Population</b>	<b>2016</b>	<b>2017</b>	<b>2018</b>	<b>2019</b>	<b>2020</b>
< 20	89,960.22	97,211.06	101,742.92	103,979.52	99,700.77
20-24	407,896.25	408,673.02	416,571.93	423,448.74	426,856.25
25-29	301,023.73	295,861.48	298,208.35	303,986.22	307,502.33
30-34	210,243.28	206,598.27	205,040.00	206,150.65	209,127.84
35-39	147,076.90	147,648.83	150,119.41	153,231.54	156,973.87
>= 40	132,655.89	127,672.92	124,588.75	124,232.43	126,871.55
<b>Total</b>	<b>1,288,856.27</b>	<b>1,283,665.58</b>	<b>1,296,271.36</b>	<b>1,315,029.10</b>	<b>1,327,032.61</b>

<b>Rate</b>	<b>2016</b>	<b>2017</b>	<b>2018</b>	<b>2019</b>	<b>2020</b>
< 20	0.09	0.06	0.08	0.13	0.02
20-24	0.65	0.64	0.56	0.63	0.50
25-29	1.55	1.69	1.49	1.53	1.42
30-34	2.57	2.78	2.57	2.65	2.39
35-39	3.64	3.77	3.10	3.31	3.15
>= 40	2.80	3.03	2.88	2.83	2.71
<b>Total</b>	<b>1.70</b>	<b>1.78</b>	<b>1.57</b>	<b>1.64</b>	<b>1.50</b>

Source: DMSS 1/19/2022

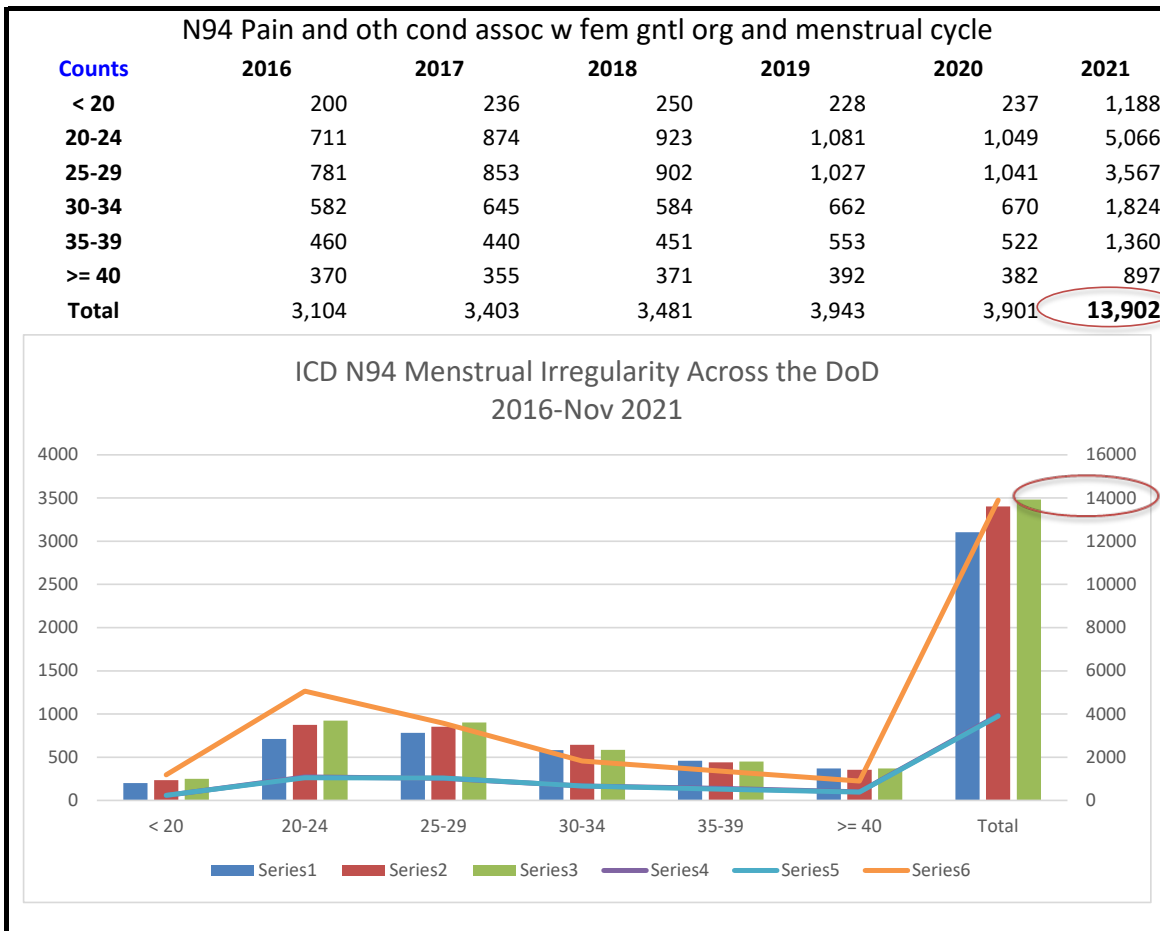
Rate calculated in counts per 1,000 persons per year. Data with unknown values excluded.

\* Selected Diagnoses:

N46 Male infertility

Ambulatory Data - Cases of Selected Diagnoses \*

Service: All  
 Age: All  
 Grade: All  
 Time: 2016, 2017, 2018, 2019, 2020, Jan to Nov 2021  
 Data Sources: Hospitalizations, Ambulatory Data, Reportable Events  
 Condition: Primary Diagnosis  
 Gender: All  
 Race: All  
 Marital Status: All  
 Occurrence: All Occurrences  
 Occupation: ALL OCCUPATION GROUPS  
 Location: ALL LOCATIONS



Population	2016	2017	2018	2019	2020
< 20	89,960.22	97,211.06	101,742.92	103,979.52	99,700.77
20-24	407,896.25	408,673.02	416,571.93	423,448.74	426,856.25
25-29	301,023.73	295,861.48	298,208.35	303,986.22	307,502.33
30-34	210,243.28	206,598.27	205,040.00	206,150.65	209,127.84
35-39	147,076.90	147,648.83	150,119.41	153,231.54	156,973.87
>= 40	132,655.89	127,672.92	124,588.75	124,232.43	126,871.55
<b>Total</b>	<b>1,288,856.27</b>	<b>1,283,665.58</b>	<b>1,296,271.36</b>	<b>1,315,029.10</b>	<b>1,327,032.61</b>

<b>Rate</b>	<b>2016</b>	<b>2017</b>	<b>2018</b>	<b>2019</b>	<b>2020</b>
< 20	2.22	2.43	2.46	2.19	2.38
20-24	1.74	2.14	2.22	2.55	2.46
25-29	2.59	2.88	3.02	3.38	3.39
30-34	2.77	3.12	2.85	3.21	3.20
35-39	3.13	2.98	3.00	3.61	3.33
>= 40	2.79	2.78	2.98	3.16	3.01
<b>Total</b>	2.41	2.65	2.69	3.00	2.94

Source: DMSS 1/19/2022

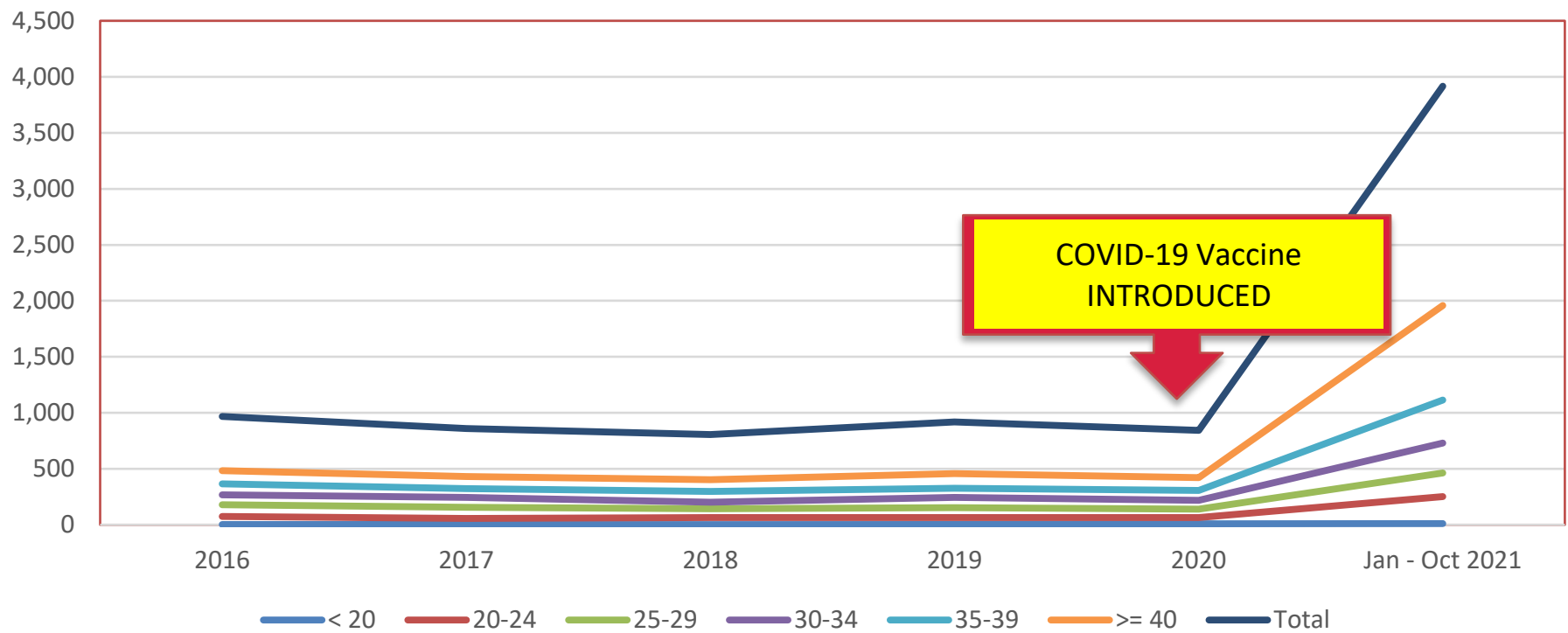
Rate calculated in counts per 1,000 persons per year. Data with unknown values excluded.

\* Selected Diagnoses:

N94 Pain and oth cond assoc w fem gntl org and menstrual cycle



### ICD G31.84 Mild Cognitive Impairment DoD (Active duty) 2016-Oct 2021



Ambulatory Data - Cases of Selected Diagnoses \*

Service: All  
 Age: All  
 Grade: All  
 Time: 2016, 2017, 2018, 2019, 2020  
 Data Sources: Hospitalizations, Ambulatory Data, Reportable Events  
 Condition: Primary Diagnosis  
 Gender: All  
 Race: All  
 Marital Status: All  
 Occurrence: All Occurrences  
 Occupation: ALL OCCUPATION GROUPS  
 Location: ALL LOCATIONS

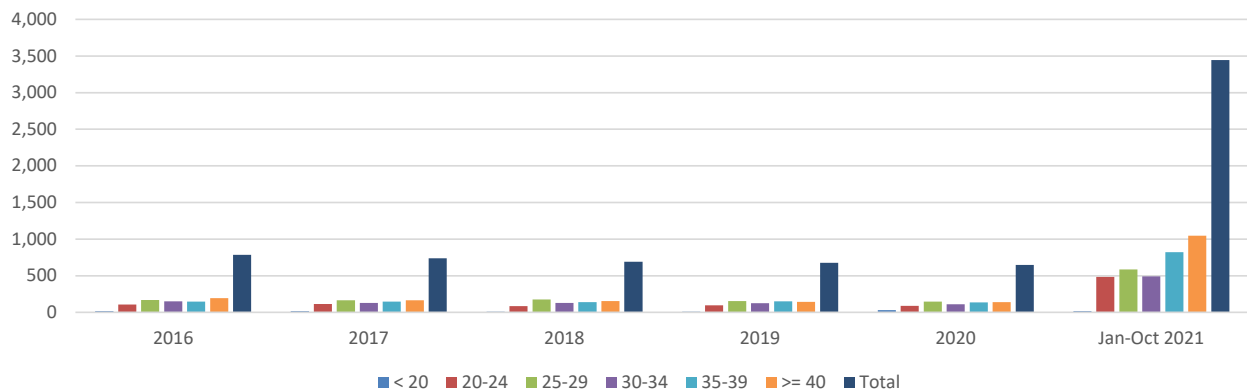
ICD G35 - G37 Demyelinating Diseases of the Central Nervous System

DoD (Active Duty) 2016 to Oct 2021

Counts	2016	2017	2018	2019	2020	Jan-Oct 2021
< 20	15	16	8	8	30	15
20-24	107	115	86	96	87	484
25-29	170	164	175	155	146	585
30-34	152	128	129	124	111	492
35-39	148	148	139	151	134	822
>= 40	193	166	153	143	140	1,046
<b>Total</b>	<b>785</b>	<b>737</b>	<b>690</b>	<b>677</b>	<b>648</b>	<b>3,444</b>

ICD G35 - G37 Demyelinating Diseases of the Central Nervous System

DoD (Active Duty) 2016 to Oct 2021



Source: DMSS 1/19/2022

Rate calculated in counts per 1,000 persons per year. Data with unknown values excluded.

\* Selected Diagnoses:

G35 - G37 Demyelinating diseases of the central nervous system

<b>Population</b>	<b>2016</b>	<b>2017</b>	<b>2018</b>	<b>2019</b>	<b>2020</b>
< 20	89,960.22	97,211.06	101,742.92	103,979.52	99,700.77
20-24	407,896.25	408,673.02	416,571.93	423,448.74	426,856.25
25-29	301,023.73	295,861.48	298,208.35	303,986.22	307,502.33
30-34	210,243.28	206,598.27	205,040.00	206,150.65	209,127.84
35-39	147,076.90	147,648.83	150,119.41	153,231.54	156,973.87
>= 40	132,655.89	127,672.92	124,588.75	124,232.43	126,871.55
<b>Total</b>	<b>1,288,856.27</b>	<b>1,283,665.58</b>	<b>1,296,271.36</b>	<b>1,315,029.10</b>	<b>1,327,032.61</b>

<b>Rate</b>	<b>2016</b>	<b>2017</b>	<b>2018</b>	<b>2019</b>	<b>2020</b>
< 20	0.17	0.16	0.08	0.08	0.30
20-24	0.26	0.28	0.21	0.23	0.20
25-29	0.56	0.55	0.59	0.51	0.47
30-34	0.72	0.62	0.63	0.60	0.53
35-39	1.01	1.00	0.93	0.99	0.85
>= 40	1.45	1.30	1.23	1.15	1.10
<b>Total</b>	<b>0.61</b>	<b>0.57</b>	<b>0.53</b>	<b>0.51</b>	<b>0.49</b>

Source: DMSS 1/19/2022

Rate calculated in counts per 1,000 persons per year. Data with unknown values excluded.

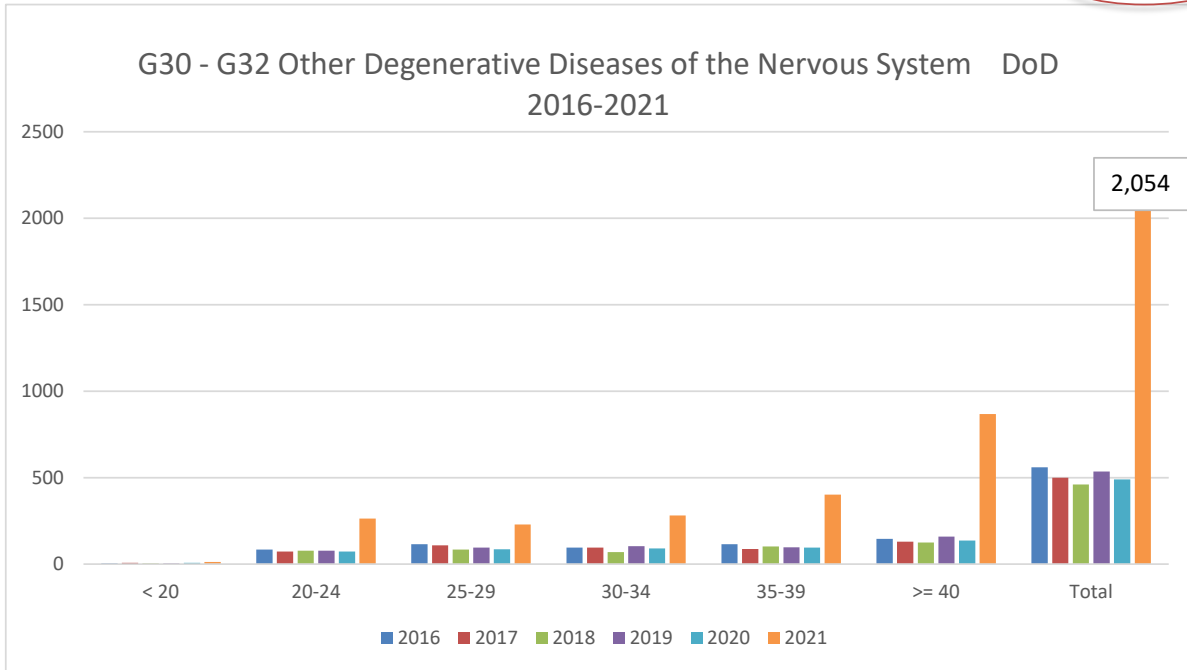
\* Selected Diagnoses:

G35 - G37 Demyelinating diseases of the central nervous system

Ambulatory Data - Cases of Selected Diagnoses \*

Service: All  
 Age: All  
 Grade: All  
 Time: 2016, 2017, 2018, 2019, 2020  
 Data Sources: Hospitalizations, Ambulatory Data, Reportable Events  
 Condition: Primary Diagnosis  
 Gender: All  
 Race: All  
 Marital Status: All  
 Occurrence: All Occurrences  
 Occupation: ALL OCCUPATION GROUPS  
 Location: ALL LOCATIONS

Counts	2016	2017	2018	2019	2020	2021
< 20	4	7	4	5	8	12
20-24	84	73	78	77	72	263
25-29	115	109	84	95	86	229
30-34	96	95	69	103	90	281
35-39	115	87	102	97	96	401
>= 40	146	129	124	159	137	868
<b>Total</b>	<b>560</b>	<b>500</b>	<b>461</b>	<b>536</b>	<b>489</b>	<b>2,054</b>



<b>Population</b>	<b>2016</b>	<b>2017</b>	<b>2018</b>	<b>2019</b>	<b>2020</b>
< 20	89,960.22	97,211.06	101,742.92	103,979.52	99,700.77
20-24	407,896.25	408,673.02	416,571.93	423,448.74	426,856.25
25-29	301,023.73	295,861.48	298,208.35	303,986.22	307,502.33
30-34	210,243.28	206,598.27	205,040.00	206,150.65	209,127.84
35-39	147,076.90	147,648.83	150,119.41	153,231.54	156,973.87
>= 40	132,655.89	127,672.92	124,588.75	124,232.43	126,871.55
<b>Total</b>	<b>1,288,856.27</b>	<b>1,283,665.58</b>	<b>1,296,271.36</b>	<b>1,315,029.10</b>	<b>1,327,032.61</b>

<b>Rate</b>	<b>2016</b>	<b>2017</b>	<b>2018</b>	<b>2019</b>	<b>2020</b>
< 20	0.04	0.07	0.04	0.05	0.08
20-24	0.21	0.18	0.19	0.18	0.17
25-29	0.38	0.37	0.28	0.31	0.28
30-34	0.46	0.46	0.34	0.50	0.43
35-39	0.78	0.59	0.68	0.63	0.61
>= 40	1.10	1.01	1.00	1.28	1.08
<b>Total</b>	<b>0.43</b>	<b>0.39</b>	<b>0.36</b>	<b>0.41</b>	<b>0.37</b>

Source: DMSS 1/19/2022

Rate calculated in counts per 1,000 persons per year. Data with unknown values excluded.

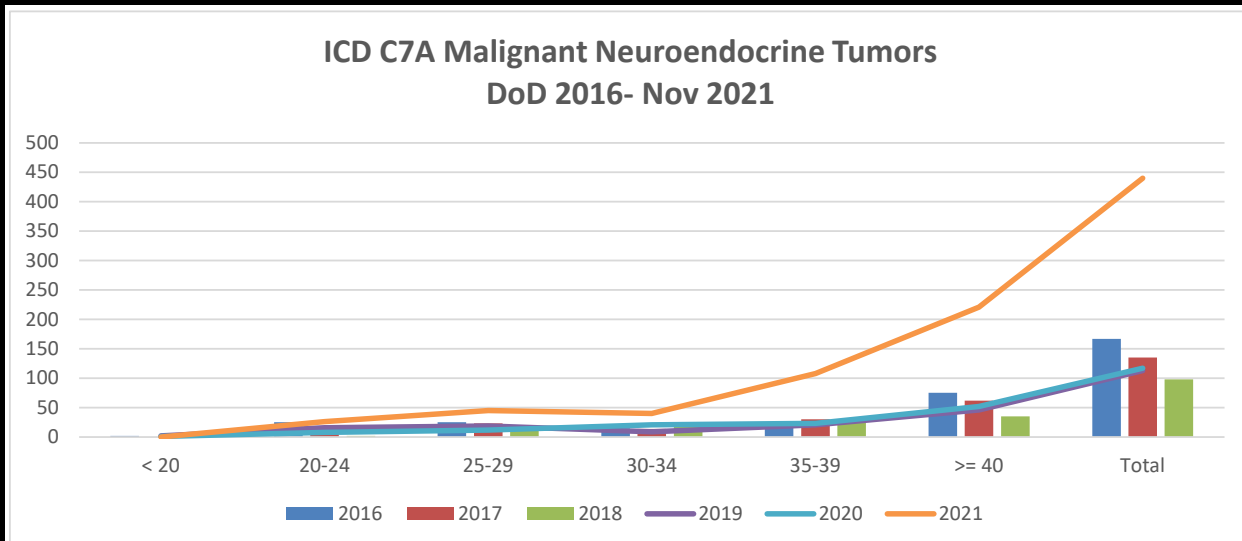
\* Selected Diagnoses:

G30 - G32 Other degenerative diseases of the nervous system

Ambulatory Data - Cases of Selected Diagnoses \*

Service: All  
 Age: All  
 Grade: All  
 Time: 2016, 2017, 2018, 2019, 2020  
 Data Sources: Hospitalizations, Ambulatory Data, Reportable Events  
 Condition: Primary Diagnosis  
 Gender: All  
 Race: All  
 Marital Status: All  
 Occurrence: All Occurrences  
 Occupation: ALL OCCUPATION GROUPS  
 Location: ALL LOCATIONS

C7A Malignant Neuroendocrine Tumors						
Counts	2016	2017	2018	2019	2020	2021
< 20	2	0	0	2	1	0
20-24	25	6	2	16	8	26
25-29	25	23	18	19	12	45
30-34	15	14	18	9	21	40
35-39	25	30	25	21	23	108
>= 40	75	62	35	46	52	221
<b>Total</b>	<b>167</b>	<b>135</b>	<b>98</b>	<b>113</b>	<b>117</b>	<b>440</b>



Population	2016	2017	2018	2019	2020
< 20	89,960.22	97,211.06	101,742.92	103,979.52	99,700.77
20-24	407,896.25	408,673.02	416,571.93	423,448.74	426,856.25
25-29	301,023.73	295,861.48	298,208.35	303,986.22	307,502.33
30-34	210,243.28	206,598.27	205,040.00	206,150.65	209,127.84
35-39	147,076.90	147,648.83	150,119.41	153,231.54	156,973.87
>= 40	132,655.89	127,672.92	124,588.75	124,232.43	126,871.55
<b>Total</b>	<b>1,288,856.27</b>	<b>1,283,665.58</b>	<b>1,296,271.36</b>	<b>1,315,029.10</b>	<b>1,327,032.61</b>

<b>Rate</b>	<b>2016</b>	<b>2017</b>	<b>2018</b>	<b>2019</b>	<b>2020</b>
<b>&lt; 20</b>	0.02	0.00	0.00	0.02	0.01
<b>20-24</b>	0.06	0.01	0.00	0.04	0.02
<b>25-29</b>	0.08	0.08	0.06	0.06	0.04
<b>30-34</b>	0.07	0.07	0.09	0.04	0.10
<b>35-39</b>	0.17	0.20	0.17	0.14	0.15
<b>&gt;= 40</b>	0.57	0.49	0.28	0.37	0.41
<b>Total</b>	0.13	0.11	0.08	0.09	0.09

Source: DMSS 1/19/2022

Rate calculated in counts per 1,000 persons per year. Data with unknown values excluded.

\* Selected Diagnoses:

C7A Malignant neuroendocrine tumors

# Neurologic Dysfunction Following Vaccination Algorithm

Vaccine Administered Within Previous 42 Days

- Symptoms suggesting Neurologic Dysfunction
- Encephalopathy
  - Flaccid limb weakness/paralysis
  - Sensory abnormalities
  - Autonomic dysfunction
  - Other neurologic signs/symptoms (TBD)

- History and physical examination
- Determine signs, symptoms
  - Elicit time course and extent of deficit(s)
  - Determine if history suggests infection, inflammatory disease, vascular/ischemia, neoplasia, multiple sclerosis, alcoholism, radiation exposure, or trauma

H/P suggestive of compressive myelopathy

Yes → If gadolinium enhanced MRI of the spinal cord shows spinal mass, obtain urgent neurosurgical consultation

No

H/P suggestive of Central Process [1]

- Yes →
- Obtain MRI - If diffuse or multifocal brain &/or cord white matter lesions evaluate for the following...
  - CBC with differential, ESR, CRP
  - Lumbar puncture [3]
  - R/O infectious etiology [4]
  - R/O other factors [5]

No

H/P suggestive of Peripheral Process [2]

- Yes →
- Obtain electrophysiologic (NCS/EMG) studies to evaluate for the following...
  - CBC with differential, ESR, CRP
  - Consider LP if sx origin unclear [3]
  - R/O infectious etiology [4]
  - R/O other factors [5]

**Footnote [1]** Suggests a central process

- Encephalopathy
- Focal cortical signs (e.g., aphasia)
- Cranial nerve abnormality(ies)
- Visual field defect/defects
- Presence of primitive reflexes (Babinski's sign, glabellar reflex, snout/sucking reflex)
- Weakness (diffuse or focal)
- Sensory abnormalities
- Altered deep tendon reflexes (hypo- or hyperreflexia, asymmetry of reflexes)
- Cerebellar dysfunction (e.g., ataxia, dysmetria, nystagmus)

**Footnote [2]** Suggests a peripheral process

- Limb weakness following an acute severe pain in the shoulder girdle and upper arm with no apparent cause
- Focal facial weakness/paresthesia
- Acute onset of bilateral relatively symmetric flaccid weakness/paralysis of the limbs with or without involvement of respiratory or cranial nerve-innervated muscles
- Decreased or absent deep tendon reflexes
- Monophasic illness pattern, with weakness nadir reached between 12 hours and 28 days, followed by clinical plateau and subsequent improvement, or death

Click on representative diagnosis (based upon H/P, imaging, & labs) for further diagnostic and therapeutic suggestions.

- ADEM
- Transverse Myelitis
- Encephalopathy
- Guillain-Barre Syndrome
- Brachial Plexus Neuritis
- Bell's Palsy

Contact the Immunization Healthcare Division and your Neurology consultant for specific guidance

**Footnote [3]** Lumbar puncture

- CSF lymphocytic pleocytosis or polymorphonuclear leucocytosis
- Myelin Basic Protein
- Oligoclonal bands
- CSF IgG index

**Footnote [4]** Infectious causes

Influenza, HSV 1 & 2, EBV, CMV, HIV, HHV6, Coxsackie, Coronavirus, West Nile virus; Streptococcus, Chlamydiae, Campylobacter, Syphilis, Mycoplasma pneumoniae, Varicella Zoster, Lyme

**Footnote [5]** Other Labs

- Comp Metabolic Screen
- Hgb A1c
- B12/Folate
- Thyroid profile/TSH
- SPEP - r/o monoclonal abs
- Urinalysis, UPEP - if protein incr
- Urine heavy metals
- ANA/ENA/RF

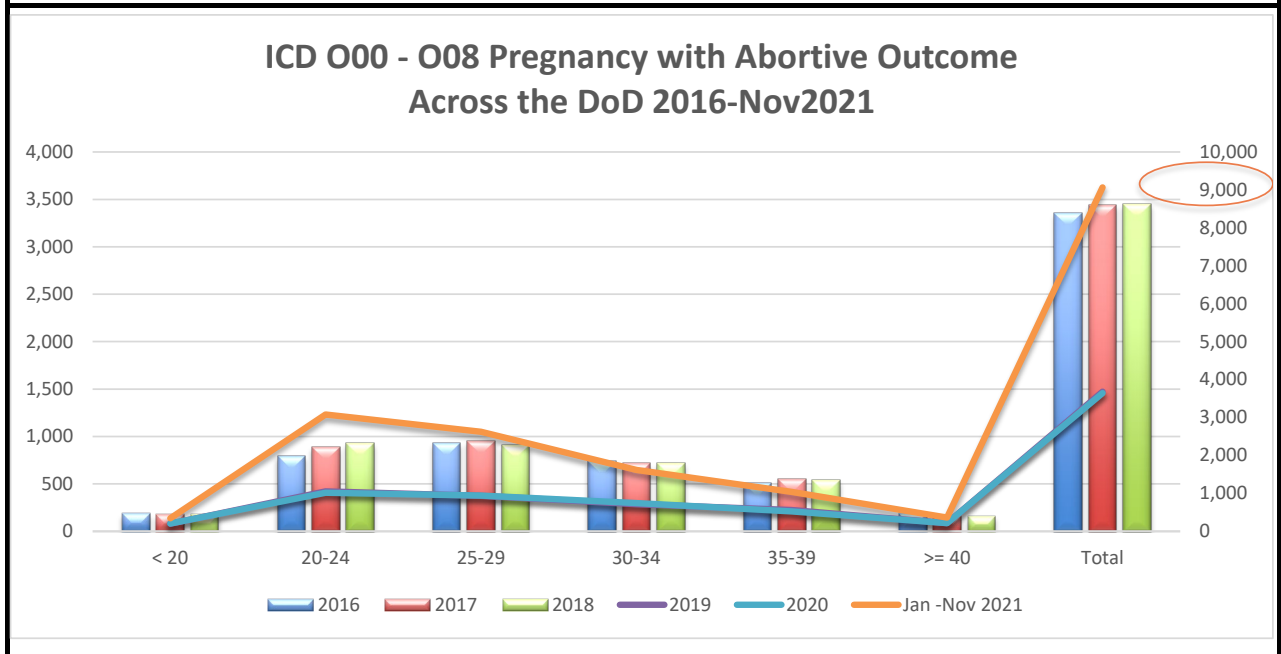


Ambulatory Data - Cases of Selected Diagnoses \*

Service: All  
 Age: All  
 Grade: All  
 Time: 2016, 2017, 2018, 2019, 2020  
 Data Sources: Hospitalizations, Ambulatory Data, Reportable Events  
 Condition: Primary Diagnosis  
 Gender: All  
 Race: All  
 Marital Status: All  
 Occurrence: All Occurrences  
 Occupation: ALL OCCUPATION GROUPS  
 Location: ALL LOCATIONS

O

ICD O00 - O08 Pregnancy with Abortive Outcome						
Counts	2016	2017	2018	2019	2020	Jan -Nov 2021
< 20	187	176	177	201	206	343
20-24	794	888	931	1,052	1,013	3,079
25-29	934	949	913	935	941	2,625
30-34	741	715	721	715	744	1,620
35-39	509	553	543	561	525	1,037
>= 40	192	161	164	218	214	362
<b>Total</b>	<b>3,357</b>	<b>3,442</b>	<b>3,449</b>	<b>3,682</b>	<b>3,643</b>	<b>9,066</b>



Population	2016	2017	2018	2019	2020
< 20	89,960.22	97,211.06	101,742.92	103,979.52	99,700.77
20-24	407,896.25	408,673.02	416,571.93	423,448.74	426,856.25
25-29	301,023.73	295,861.48	298,208.35	303,986.22	307,502.33
30-34	210,243.28	206,598.27	205,040.00	206,150.65	209,127.84
35-39	147,076.90	147,648.83	150,119.41	153,231.54	156,973.87
>= 40	132,655.89	127,672.92	124,588.75	124,232.43	126,871.55

<b>Total</b>	1,288,856.27	1,283,665.58	1,296,271.36	1,315,029.10	1,327,032.61
<b>Rate</b>	<b>2016</b>	<b>2017</b>	<b>2018</b>	<b>2019</b>	<b>2020</b>
< 20	2.08	1.81	1.74	1.93	2.07
20-24	1.95	2.17	2.23	2.48	2.37
25-29	3.10	3.21	3.06	3.08	3.06
30-34	3.52	3.46	3.52	3.47	3.56
35-39	3.46	3.75	3.62	3.66	3.34
>= 40	1.45	1.26	1.32	1.75	1.69
<b>Total</b>	2.60	2.68	2.66	2.80	2.75

Source: DMSS 1/24/2022

Rate calculated in counts per 1,000 persons per year. Data with unknown values excluded.

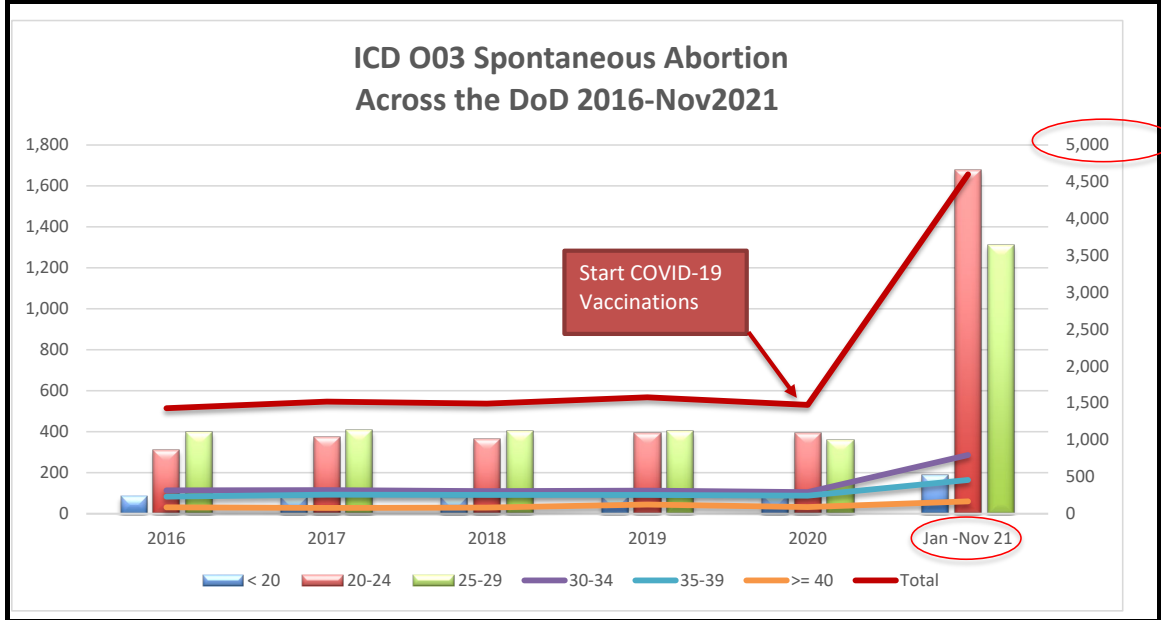
\* Selected Diagnoses:

O00 - O08 Pregnancy with abortive outcome

Ambulatory Data - Cases of Selected Diagnoses \*

Service: All  
 Age: All  
 Grade: All  
 Time: 2016, 2017, 2018, 2019, 2020  
 Data Sources: Hospitalizations, Ambulatory Data, Reportable Events  
 Condition: Primary Diagnosis  
 Gender: All  
 Race: All  
 Marital Status: All  
 Occurrence: All Occurrences  
 Occupation: ALL OCCUPATION GROUPS  
 Location: ALL LOCATIONS

ICD O03 Spontaneous Abortion						
Counts	2016	2017	2018	2019	2020	Jan -Nov 21
< 20	86	83	80	88	94	189
20-24	310	373	364	394	392	1,679
25-29	399	406	403	405	362	1,312
30-34	317	320	307	313	293	796
35-39	232	258	254	256	244	458
>= 40	87	79	85	124	92	168
<b>Total</b>	<b>1,431</b>	<b>1,519</b>	<b>1,493</b>	<b>1,580</b>	<b>1,477</b>	<b>4,602</b>



Population	2016	2017	2018	2019	2020
< 20	89,960.22	97,211.06	101,742.92	103,979.52	99,700.77
20-24	407,896.25	408,673.02	416,571.93	423,448.74	426,856.25
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>= 40	132,655.89	127,672.92	124,588.75	124,232.43	126,871.55
<b>Total</b>	<b>1,288,856.27</b>	<b>1,283,665.58</b>	<b>1,296,271.36</b>	<b>1,315,029.10</b>	<b>1,327,032.61</b>

Rate	2016	2017	2018	2019	2020
< 20	0.96	0.85	0.79	0.85	0.94

<b>20-24</b>	0.76	0.91	0.87	0.93	0.92
<b>25-29</b>	1.33	1.37	1.35	1.33	1.18
<b>30-34</b>	1.51	1.55	1.50	1.52	1.40
<b>35-39</b>	1.58	1.75	1.69	1.67	1.55
<b>&gt;= 40</b>	0.66	0.62	0.68	1.00	0.73
<b>Total</b>	1.11	1.18	1.15	1.20	1.11

Source: DMSS 1/24/2022

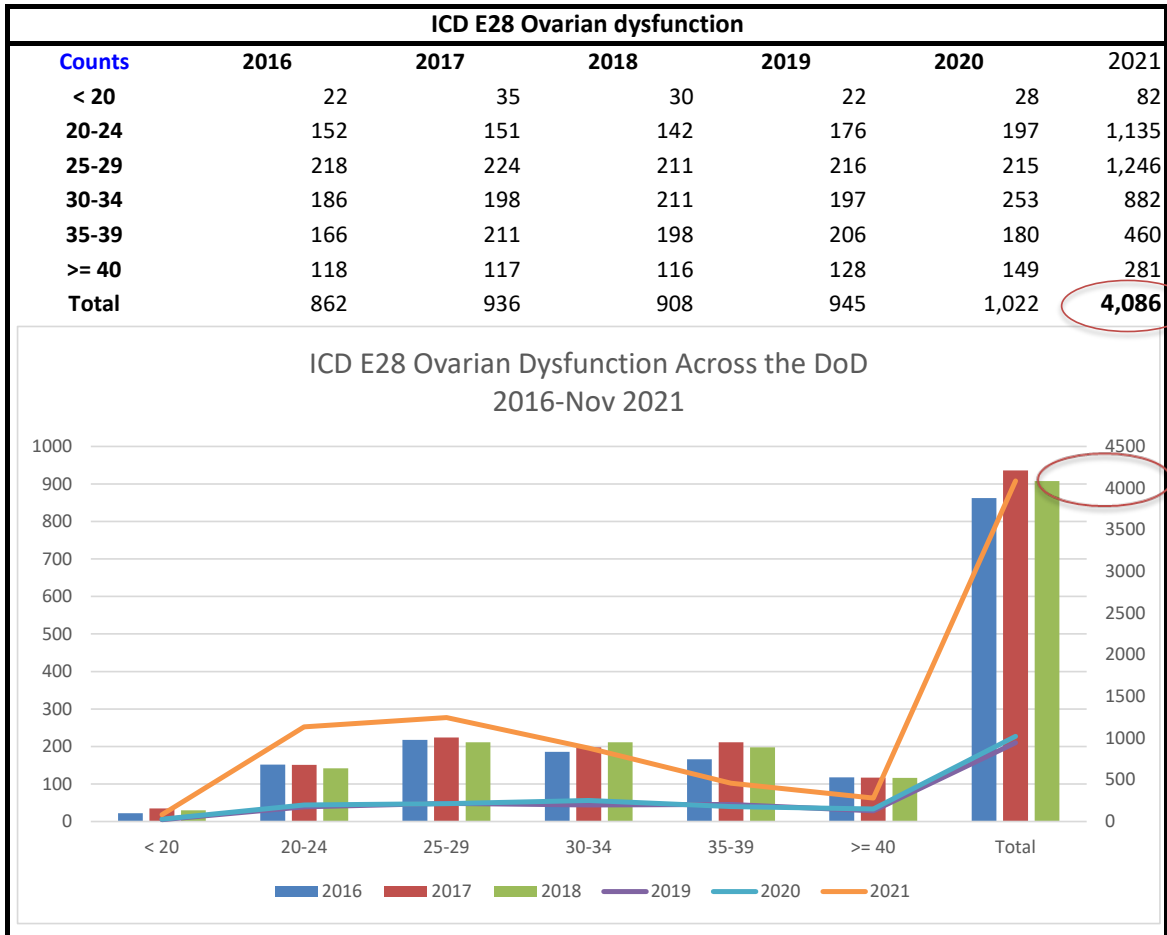
Rate calculated in counts per 1,000 persons per year. Data with unknown values excluded.

\* Selected Diagnoses:

O03 Spontaneous abortion

Ambulatory Data - Cases of Selected Diagnoses \*

Service: All  
 Age: All  
 Grade: All  
 Time: 2016, 2017, 2018, 2019, 2020  
 Data Sources: Hospitalizations, Ambulatory Data, Reportable Events  
 Condition: Primary Diagnosis  
 Gender: All  
 Race: All  
 Marital Status: All  
 Occurrence: All Occurrences  
 Occupation: ALL OCCUPATION GROUPS  
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<b>Total</b>	<b>1,288,856.27</b>	<b>1,283,665.58</b>	<b>1,296,271.36</b>	<b>1,315,029.10</b>	<b>1,327,032.61</b>

<b>Rate</b>	<b>2016</b>	<b>2017</b>	<b>2018</b>	<b>2019</b>	<b>2020</b>
< 20	0.24	0.36	0.29	0.21	0.28
20-24	0.37	0.37	0.34	0.42	0.46
25-29	0.72	0.76	0.71	0.71	0.70
30-34	0.88	0.96	1.03	0.96	1.21
35-39	1.13	1.43	1.32	1.34	1.15
>= 40	0.89	0.92	0.93	1.03	1.17
<b>Total</b>	<b>0.67</b>	<b>0.73</b>	<b>0.70</b>	<b>0.72</b>	<b>0.77</b>

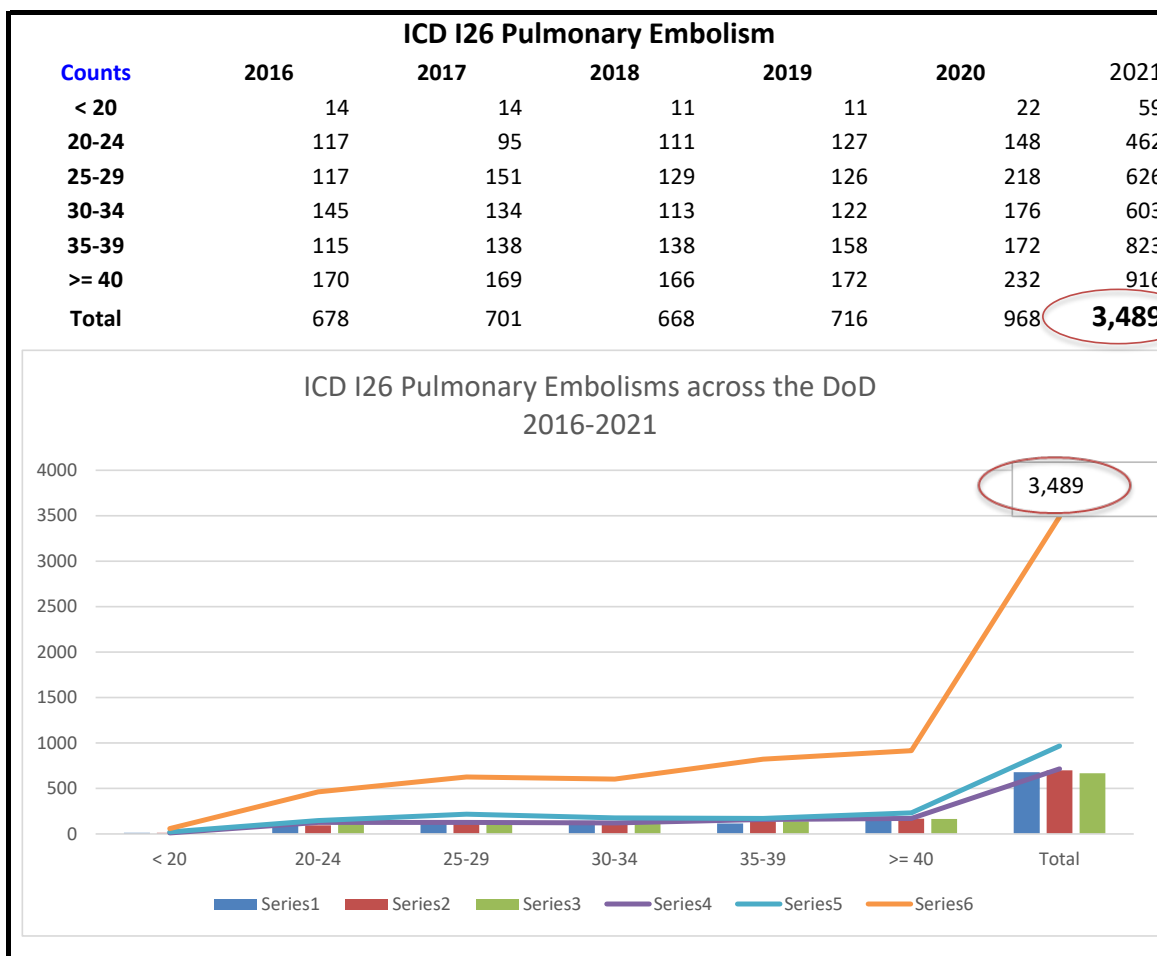
Source: DMSS 1/19/2022

Rate calculated in counts per 1,000 persons per year. Data with unknown values excluded.

\* Selected Diagnoses:  
E28 Ovarian dysfunction

Ambulatory Data - Cases of Selected Diagnoses \*

Service: All  
 Age: All  
 Grade: All  
 Time: 2016, 2017, 2018, 2019, 2020, 2021  
 Data Sources: Hospitalizations, Ambulatory Data, Reportable Events  
 Condition: Primary Diagnosis  
 Gender: All  
 Race: All  
 Marital Status: All  
 Occurrence: All Occurrences  
 Occupation: ALL OCCUPATION GROUPS  
 Location: ALL LOCATIONS



<b>Population</b>	<b>2016</b>	<b>2017</b>	<b>2018</b>	<b>2019</b>	<b>2020</b>
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<b>Rate</b>	<b>2016</b>	<b>2017</b>	<b>2018</b>	<b>2019</b>	<b>2020</b>
< 20	0.16	0.14	0.11	0.11	0.22
20-24	0.29	0.23	0.27	0.30	0.35
25-29	0.39	0.51	0.43	0.41	0.71
30-34	0.69	0.65	0.55	0.59	0.84
35-39	0.78	0.93	0.92	1.03	1.10
>= 40	1.28	1.32	1.33	1.38	1.83
<b>Total</b>	<b>0.53</b>	<b>0.55</b>	<b>0.52</b>	<b>0.54</b>	<b>0.73</b>

Source: DMSS 1/19/2022

Rate calculated in counts per 1,000 persons per year. Data with unknown values excluded.

\* Selected Diagnoses:

I26 Pulmonary embolism



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## Terms and abbreviations used in this section

Terms and abbreviations not omitted or defined ALC-0159 Added	
to this drug	PEG lipid
ALC-0315.	Aminolipids added to this drug
[3h] -the	RadioLabeled [Cholesteryl-1,2-3H (N)] -Cholesteryl Hexadecyl Ether: Radioactive Signs [Cholesteryl-1, 2-3H (N)] Hexadecyl ether
DSPC	1,2-Distearoyl-Sn-Glycero-3-Phosphocholine: 1,2-Distearoyl-Sn-Glycero-3-Phosphocholine
GLP	Good Laboratory Practice: Standard of implementation of non-clinical trials on drug safety
LNP	Lipid-nanoparticle: Lipid nanoparticles
modrna	Nucleoside-Modified mRNA: Modified nucleoside mRNA
mRNA	Messenger RNA: Messenger RNA
m/z	M / Z (M Over Z): Give the weight of ions by unified atomic mass unit (= Dalton) A dimensionless amount obtained by dividing the amount of the number of ions by the absolute value of the number of ions.
PEG	Polyethylene Glycol: Polyethylene glycol
PK	Pharmacokinetics: Pharmacokinetics
Rna	Ribonucleic Acid: ribonucleic acid
There	Supernatant fraction obtained from liver homogenate by centrifuging at 9000 g T <sub>0</sub> A supernatant dispatched with 9000 g centrifuged
WHO	World Health Organization: World Health Organization

## 1. Summary

BNT162B2 (BionTech Code Number: BNT162, PFIZER Code Number: PF-07302048) is a heavy acute call Susing syndrome coronavirus 2 (SARS-COV-2) spike glycoprotein (S protein) total length Code modified nucleoside MRNA (MODRNA) and for infectious diseases with SARS-COV-2 Development has been developed as the essence of mRNA vaccines. In formulation of BNT162B2, two Functional lipid ALC-0315 (amino lipid) and ALC-0159 (PEG lipid) and two structural lipids As By mixing with DSPC (1,2-Distearoyl-Sn-Glycero-3-Phosphocholine) and cholesterol Lipid nanoparticles (LNP) which encapsulate BNT162B2 are formed (hereinafter, "BNT162B2 encapsulated LNP").

ALC-0315 contained in LNP and ALC-0315 and

In vivo and in vitro tests and BNT162B2 to evaluate ALC-0159 absorption (PK), metabolism and excretion

In-vivo distribution test using luciferase or radiolabeled lipid as an alternative reporter

Conducted.

Based on the development of vaccines for the prevention of infections, based on the need to evaluate systemic exposure ( WHO, 2005; Infectious disease prevention vaccine non-clinical trial guidelines) 1, 2, BNT162B2 Encapsulated LNP muscles

By admission PK test did not conduct. Also, the other he contained in this drug is two lipids (cholester

Roll and DSPC is a naturally occurring lipid, and is considered to be metabolism as well as endogenous lipids.

available. In addition, BNT162B2 is degraded by ribonuclease in captured cells and nucleic acid

Thank you, S-protein derived from BNT162B2 is expected to be subject to proteolysis. From the above,

It was thought that no need to evaluate metabolism and excretion of these components.

LNP enclosed RNA encoding luciferase as an alternative reporter of BNT162B2 (Lucife

Laze RNA is enclosed in LNP with the same lipid configuration as BNT162B2 encapsulated LNP: Since then, "Lucifer

Zere In the PK test, which was administered intravenously to Wistar Han rats), plasma, urine, feces and

Collect liver samples over time and in each sample ALC-0315 and ALC-0159 concentrations were measured. That

fruit, ALC-0315 and ALC-0159 have been shown to be promptly distributed from blood to the liver. Also,

ALC-0315 and ALC-0159 excreted about 1% and about 50% of doses as unchanged

In urine, all were less than the detection limit.

In vivo distribution test, luciferase RNA encapsulated LNP was intramuscularly administered to BALB / C mice. That

As a result, the expression of luciferase was found at the site of administration, and the expression level was low in the liver.

Also recognized. Expression at the administration site of luciferase is after administration. It is recognized from 6 hours, and after administration 9 days

Was disappeared. After administration of the liver expression It was observed for 6 hours and disappeared by 48 hours after administration. Also,

Luciferase RNA encapsulated LNP radiolabeled body is intramuscularly administered into rats to quantitatively in vivo distribution.

When evaluated, the radioactivity concentration was the highest at the site of administration. The liver is the highest outside the administration site

It was (maximum of dose 18%).

Metabolism of ALC-0315 and ALC-0159 CD-1 / ICR mouse, Wistar Han or Sprague Dawley rats,

Cynomolgus monkeys or human blood, liver microsomes, liver In vitro using S9 fractions and hepatocytes

evaluated. Also, the above-mentioned rat intravenous administration For plasma, urine, feces and liver samples collected in PK test

In IN VIVO metabolism was also examined. From these in vitro and in vivo tests, ALC-0315 and

ALC-0159 is an ester bond and an amide bond hydration, respectively, in any animal species of testing

It has been shown to be slowly metabolized by solution.

SARS-COV-2 mRNA Vaccine (BNT162, PF-07302048)  
2.6.4 Overview of Pharmacokinetic Test

From the above non-clinical pharmacokinetic evaluation, the circulating LNP was shown to be distributed in the liver. Also, Metabolism and feces excretion is involved in the disappearance of ALC-0315 and ALC-0159, respectively. It was suggested.

## 2. Analysis Method

Report number: PF-07302048\_06 [REDACTED]\_072424

ALC-0315 and ALC-0159, which is a LNP constituent lipid in rat intravenous administration PK test (M2.6.4.3) of GLP non-application ALC-0159 Developed LC / MS method with appropriate performance to quantify concentrations. That is, 20 µl Plasma, liver homogenate (liver A homogenate is prepared using sections collected from three places. Suitable for pooling, dilute with blank matrix), urine and feces homogenate (as appropriate, Blanc Cumatrix diluted) Samples Internal standards ( Removed by acetonitrile containing PEG-2000) After protein, centrifuge and the supernatant We subjected to LC-MS / MS measurement.

## 3. Absorption

Report number: PF-07302048\_06 [REDACTED]\_072424, Overview Table: 2.6.5.3

### Luciferase RNA encapsulated LNP is male to consider the in-vibration condition of ALC-0315 and ALC-0159

Wistar Han rats are administered in a single intravenous administration at a dose of 1 mg RNA / kg, with time (before administration, 0.1, 0.25, Sparse plasma and liver on 0.5, 1, 3, 6 and 24 hours and 2, 4, 8 and 14 days after administration. Collected by sampling Three / time pointed). ALC-0315 and ALC-0159 in plasma and liver Measure the concentration, PK parameters were calculated (Table 1). Blood ALC-0315 and ALC-0159 After giving Slightly distributed to the liver by 24 hours. Also, 24 hours plasma concentration after administration is in the highest plasma Density It was less than 1% (Figure 1). Close-end phase disappearance half-life (T2) is in plasma and in liver The same level, ALC-0315 was 6 to 8 days, and ALC-0159 was 2-3 days. From the results of this test, the liver is in blood from It was suggested that it is one of the major organizations that take ALC-0315 and ALC-0159.

Conducted in this study On the examination results of Urinary and feces concentration of ALC-0315 and ALC-0159 It is Section M2.6.4.6.

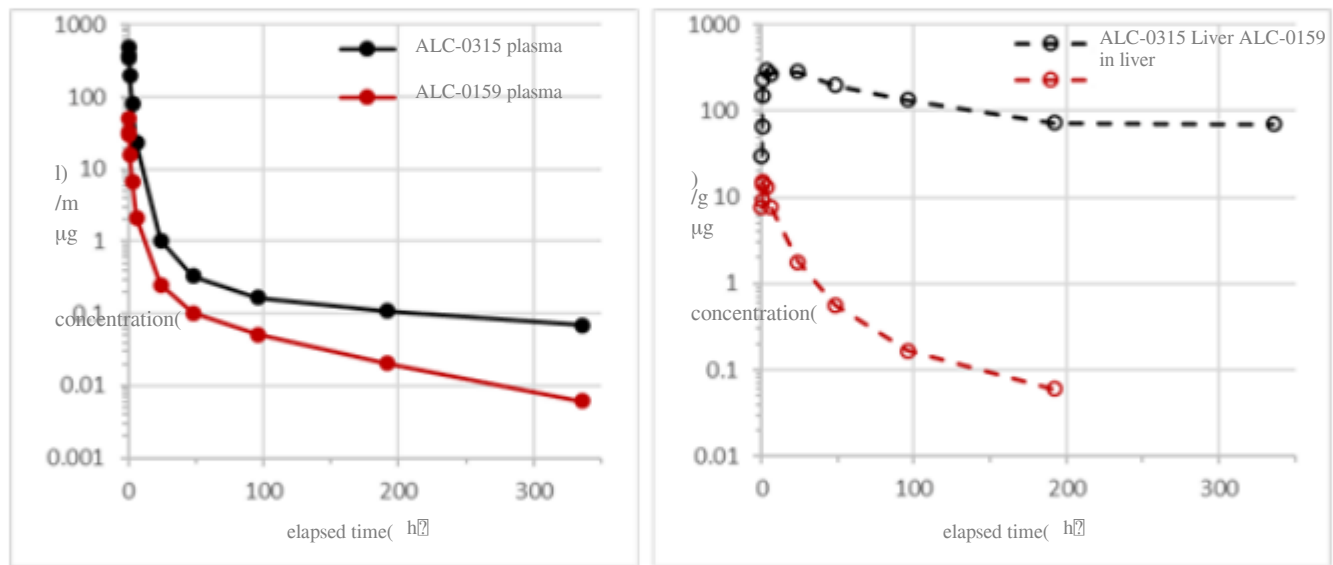
Table 1 luciferase RNA encapsulated LNP in Wistar Han rats at a dose of 1 mg RNA / kg

Analyte	Analyze dose (mg/kg)	Pharmacokinetics of ALC-0315 and ALC-0159		AUCinf (µg•h/mL)	AUClast (µg•h/mL)	To the liver Distribution ratio <sup>a</sup>
		sex/Nt <sup>b</sup>	t <sub>1/2</sub> (h)			
ALC-0315.	15.3	Male	139	1030	1020	60
ALC-0159.	1.96	Male	72.7	99.2	98.6	20

a. Calculated as the highest liver distribution amount (µg) / [dose (µg)]. b. Each time point. Sparse sampling.

Figure 1 luciferase RNA encapsulated LNP in Wistar Han rats at a dose of 1 mg RNA / kg

When given Plasma and liver concentrations of ALC-0315 and ALC-0159

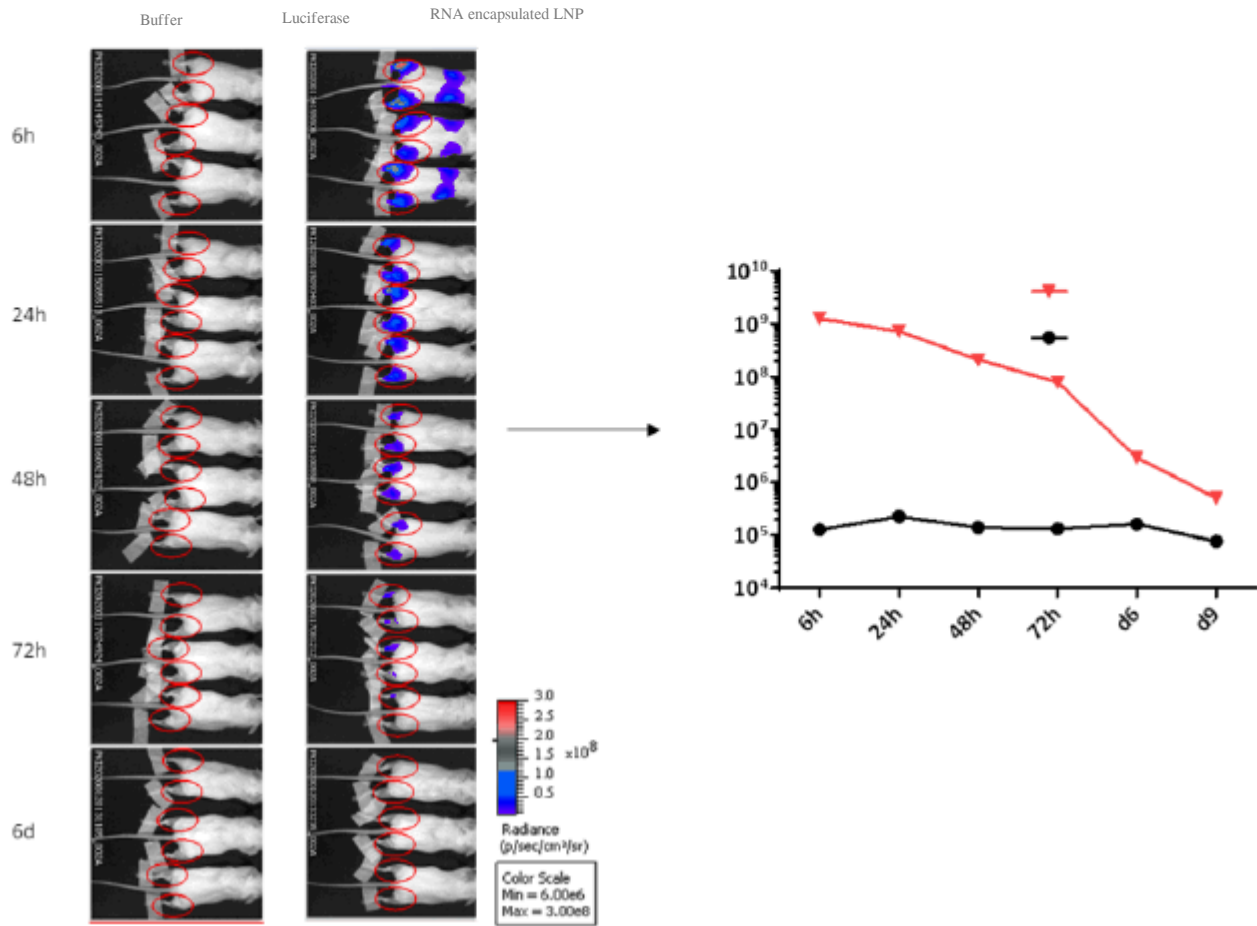


4. Distribution

Report number: R-72, 185350, Overview Table: 2.6.5.5a, 2.6.5.5b

female Administer luciferase RNA encapsulated LNP to BALB / C mice (3 animals) and luciferase emission  
As an alternative marker The vivo distribution of BNT162B2 was examined. That is, luciferase RNA encapsulation  
LNP was administered intramuscularly at a dose of 1 µg RNA (total 2 µg RNA) in the left and right hindlimbs of mice. Then  
Cypherase emission detection Luciferin, which is a light emitting substrate 5 minutes ago, is administered intraperitoneally, isoflurane hemp  
Downward 6 and 24 hours after administration using Xenogen IVIS Spectrum in vivo, 6 and 24 hours and 2,  
By measuring it on 3, 6 and 9 days, it is recommended with time with the same individual of luciferase protein  
I was evaluated. As a result, expression at the site of administration of luciferase is administered Recognized from 6 hours,  
After giving It disappeared on the 9th. Liver expression was also from 6 hours after administration, and disappeared by 48 hours after administration  
I was. Distribution to the liver is a luciferase where topically administered Some of the RNA encapsulated LNP reaches circulating blood and liver  
It was considered to indicate that it was incorporated in the needs. As detailed in M2.6.4.3, rats are  
Laze When RNA encapsulated LNP is administered intravenously, the liver is the main of ALC-0315 and ALC-0159  
It is suggested that it is a distributed organ, this is the finding of the test results that were intramuscularly administered to mice  
The mixture was. In addition, a toxic finding finding of liver disorder is recognized in rat repeated dose toxicity test  
Absent( M2.6.6.3).

Figure 2 Luciferase RNA encapsulated LNP in vivo luminescence in BALB / C mice administered intramuscularly



male and female Wistar Han rats, LNP labeled with [<sup>3</sup>H]-cholesterol hexadecyl ether ([<sup>3</sup>H]-CHE) using the same method as the RNA encapsulated LNP. The RNA encapsulated LNP is intramuscularly administered at a dose of 50 µg RNA and 15 minutes after administration. Plasma and tissues from 3 males and 3 females at each time of 1, 2, 4, 8, 24 and 48 hours were collected. By measuring the radioactivity concentration by liquid scintillation counting method, the in vivo distribution of LNP was reviewed. Both male and female, the radioactivity concentration was the highest at the dosing site at any measurement. After administration of radioactivity concentration in plasma, the highest value was shown for 1 to 4 hours. In addition, liver, spleen, adrenal and ovary were observed, and after administration that the radioactivity was the highest in these tissues 8 to 48 hours. Total radiation recovery rate for doses other than the site of administration is the highest in the liver (maximum 1.8%), spleen (1.0% or less), adrenal (less than 0.11%) and ovary (0.095% or less) significantly lower than the liver. In addition, the average concentration and tissue distribution pattern of radioactivity were roughly similar to male and female.

It is believed that the in vivo expression distribution of the antigen encoded by BNT162B2 depends on the LNP distribution. For this test, the lipid configuration of RNA encapsulated LNP is identical to the application formulation of BNT162B2. The results of this test show that the distribution of BNT162B2 encapsulated LNP is as follows.

## 5. Metabolism

Report number: 01049-01049-020, 01049-021, 01049-022, [REDACTED], [REDACTED], [REDACTED]  
PF-07302048\_05 [REDACTED]\_043725, Overview Table: 2.6.5.10a, 2.6.5.10b, 2.6.5.10c, 2.6.5.10d

CD-1 / ICR mouse, Wistar Han or Sprague Dawley rats, cynomolgus monkeys and humans

Chrome, liver In vitro metabolic stability of ALC-0315 and ALC-0159 using S9 fractions and hepatocytes

The sex was evaluated. ALC-0315 or ALC-0159 for each animal species Microsomer or liver S9 fraction (120

Interceding incubation) or hepatocytes ( Add to 240 minutes incubation)

The proportion of unconstructed unaccurations after bath was measured. resulting in, ALC-0315 and ALC-0159

It is metabolically stable in animal species and test systems, and the ultimate percentage of unaccurate is 82%. More than

further Metabolic pathways of ALC-0315 and ALC-0159 were evaluated in vitro and in vivo.this

In the test, CD-1 mouse, Wistar Han rats, cynomolgus monkey and human blood, liver S9 fraction

And using hepatocytes IN Vitro metabolism was evaluated.In addition, plasma, urine, feces collected in rat PK test

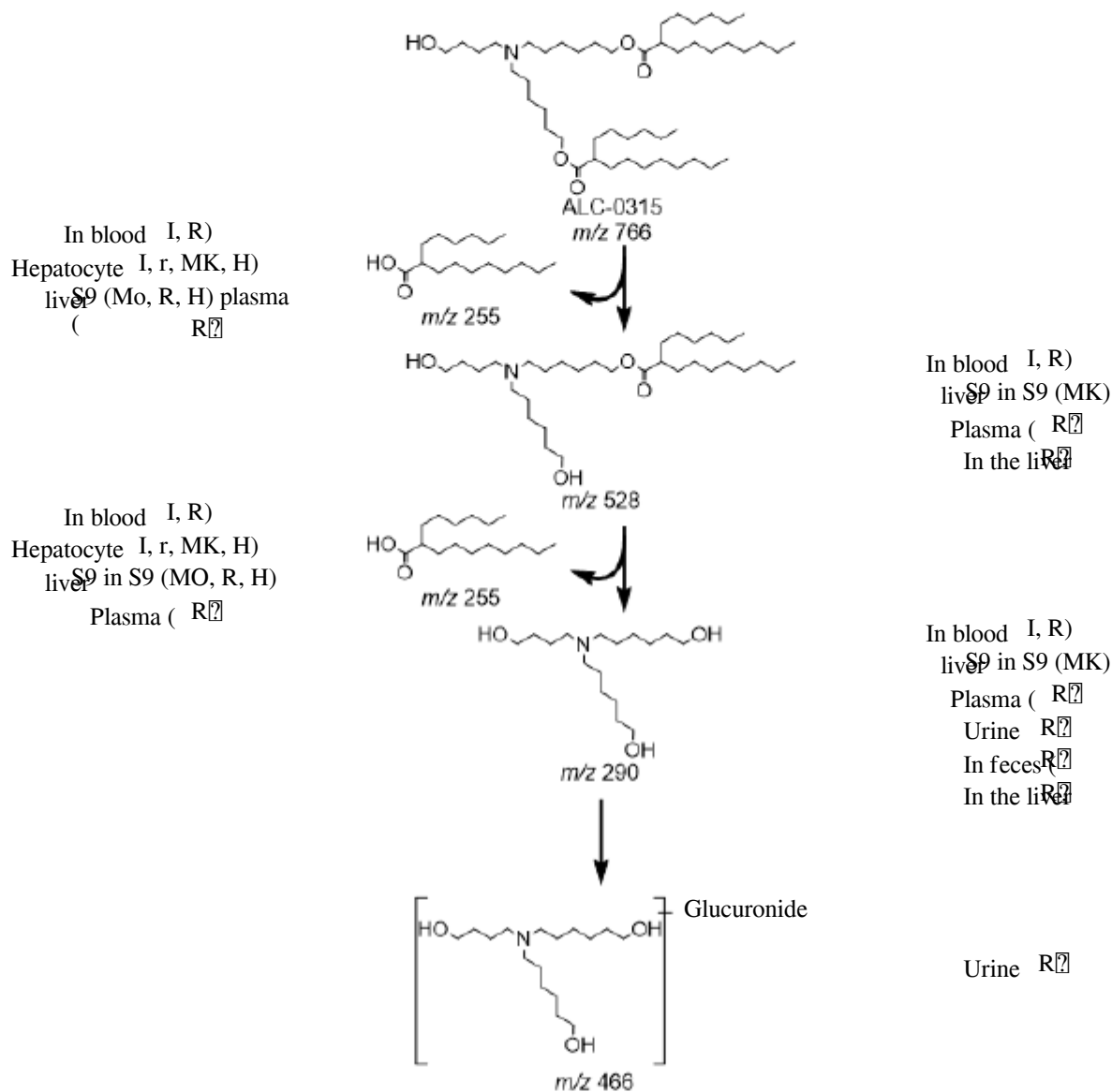
And liver samples, IN VIVO metabolism was evaluated (M2.6.4.3).From the test results, ALC-0315

When Metabolism of ALC-0159 is all slowly slow, and hydrolysis of ester bonds and amide bonds, respectively

It became clear that it is metabolized by. Metabolism by hydrolysis shown in Figure 3 and Figure 4

Was found in all animal species evaluated.

Figure 3 Estimated in vivo metabolic pathway of ALC-0315 in various animal species

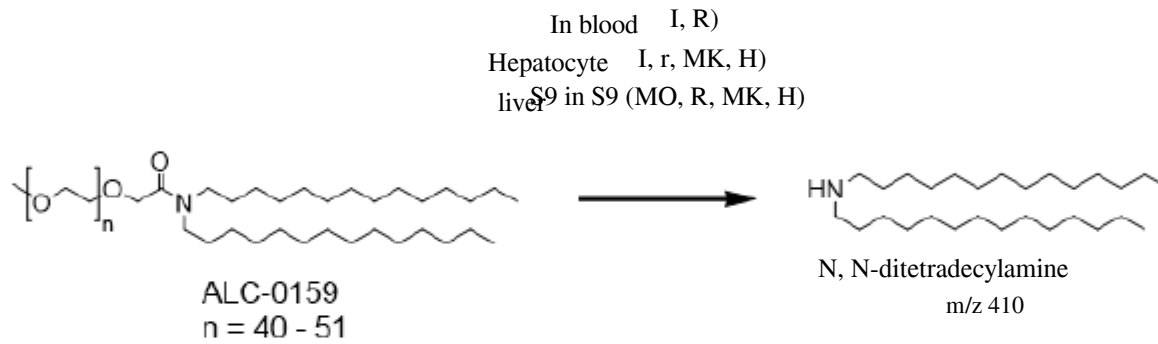


H: Human, MK: Monkey, MO: Mouse, R: Rat

ALC-0315 is metabolized by receiving ester hydrolysis twice in succession. This two hydrolysis  
 By first, monoester metabolites (M / Z 528), then a dual-dose esterification metabolite (M / z 290) is formed  
 It is done. This double-dose esterification metabolite is further metabolized and glucuronic acid conjugate (M / Z 466)  
 However, this glucuronic acid conjugate is rats PK test was only detected in urine. In addition, two hydrolysis  
 Any acidic product of It was also confirmed that 6-hexyl decanoic acid (m / z 255).



Figure 4 Estimated in vivo metabolism pathway of ALC-0159 in various animal species



H: Human, MK: Monkey, MO: Mouse, R: Rat

ALC-0159 produces N, N-ditetradecylamine (M / Z 410) by hydrolysis of amide bonds

The pathway was the main metabolic pathway. This metabolite is blood and mice rats of mouse rats.

Sal-human hepatocytes and liver It was detected in the S9 fraction. Metabolites of ALC-0159 from in vivo samples  
It was not confirmed.

#### 6. Excretion

Luciferase PK test with intravenous administered intravenously to rats at a dose of 1 mg RNA / kg of RNA encapsulated LNP  
( M2.6.4.3, ALC-0315 and ALC-0159 in urine and feces collected over time were measured.

None of the unchangeable bodies of ALC-0315 and ALC-0159 were not detected in urine. On the other hand, in the feces  
ALC-0315 and ALC-0159 unchanged substances are detected, and the percentage per dose is about 1% and  
about 50%. Also, as shown in Figure 3, the metabolites of ALC-0315 were detected in urine.

#### 7. Pharmacokinetic drug interaction

The pharmacokinetic drug interaction test of this vaccine has not been conducted.

#### 8. Other pharmacokinetic tests

Other pharmacokinetic tests of this vaccine have not been conducted.

#### 9. Consideration and conclusion

Rats In the PK test, the concentration of ALC-0315 in plasma and liver is the highest concentration for 2 weeks after administration.  
Every Decreased to 1/7000 and about 1/2-sq, and the ALC-0159 concentration is about 8000 minutes, respectively.  
And about It decreased to one of 250 minutes. T-13 is the same in plasma and liver, ALC-0315, he is 6 to 8 days,  
ALC-0159 was 2-3 days. Plasma T-13 values are distributed in tissues as LNP, each lipid.  
It is then considered to indicate that it has been redistributed in plasma during the disappearance process.

Although the unchangeable body of ALC-0315 was hardly detected in any of urine and feces, rat PK test

Monomeric metabolites and dual esterification metabolites from feces and plasma samples collected 6-Hexy

Radecanoic acid detected glucuronic acid conjugate of dual-dose-esterified metabolites from urine. This metabolism

Process Although it is considered as the main loss mechanism of ALC-0315, quantitative data to verify this hypothesis is obtained

Absent. on the other hand, ALC-0159 was excreted in feces as an unchangeable body of dose. In vitro metabolic experiment

In the hydrolysis of the amide bond, it was slowly metabolized.

Because the in-vivo expression distribution of the antigen encoded by BNT162B2 is considered to depend on the LNP distribution, BALB / C mice are intramuscularly administered luciferase RNA encapsulated LNP and alternative reporter protein

In-vivo distribution was examined. As a result, expression of luciferase is found at the site of administration,

The expression level was also observed in the liver but was also observed. Expression at the site of administration of luciferase was observed from 6 hours after administration and disappeared on 9 days after administration. The expression in the liver is observed from 6 hours after administration.

After giving it disappeared by 48 hours. Distribution to the liver is a circular luciferase RNA encapsulated LNP

It was considered to indicate that it was reached and taken up in the liver. Also, Lucifer in rats

Zero. When the radiolabel of RNA encapsulated LNP was administered intramuscularly, the radioactivity concentration is the highest value at the dosing site.

Indicated. Other than the site of administration, the liver was the highest and then detected in the spleen, adrenal and ovaries,

Total radioactivity recovery for dosages in these tissues was significantly lower than the liver. This result is

In-mouse biological distribution tests were encoded by luciferase expression in liver. In addition,

No toxic findings were observed showing liver injury in rat repeated dose toxicity tests ( M2.6.6.3).

From the above non-clinical pharmacokinetic evaluation, the circulating LNP was shown to be distributed in the liver.

Also, Metabolism and feces excretion is involved in the disappearance of ALC-0315 and ALC-0159, respectively.

It was suggested.

## 10. Charts

The chart is shown in the text and outline table.

## references

- 1 World Health Organization. Annex 1. Guidelines on the nonclinical evaluation of vaccines. In: WHO Technical Report Series No. 927, Geneva, Switzerland. World Health Organization; 2005:31-63.
- 2 Non-clinical trial guidelines for infection prevention vaccine (Medicine dike examination 0527) 1, May 27, 2010)

SARS-COV-2 mRNA Vaccine (BNT162, PF-07302048)  
2.6.5 Overview of Pharmacokinetic Test

## 2.6.5.1. PHARMACOKINETICS OVERVIEW

Test Article: BNT162b2

Type of Study	Test System	Test item	Method of Administration	Testing Facility	Report Number
Single Dose Pharmacokinetics					
Single Dose Pharmacokinetics and Excretion in Urine and Feces of ALC-0159 and ALC-0315	Rat (Wistar Han)	modRNA encoding luciferase formulated in LNP comparable to BNT162b2	IV bolus	Pfizer yet	PF-07302048_06 [REDACTED]_072424
Distribution					
In Vivo Distribution	Mice BALB/c	modRNA encoding luciferase formulated in LNP comparable to BNT162b2	IM Injection	[REDACTED] b	R- [REDACTED] -0072
In Vivo Distribution	Rat (Wistar Han)	modRNA encoding luciferase formulated in LNP comparable to BNT162b2 with trace amounts of [3H]-CHE as non- diffusible label	IM Injection	[REDACTED] c	185350
Metabolism In Vitro and In Vivo Metabolism					
In Vitro Metabolic Stability of ALC-0315 in Liver Microsomes	Mouse (CD-1/ICR), rat (Sprague Dawley and Wistar Han), monkey (Cynomolgus), and	ALC-0315.	In vitro	[REDACTED] d	01049-008 [REDACTED]
In Vitro Metabolic Stability of ALC-0315 in Liver S9	human liver microsomes Mouse (CD-1/ICR), rat (Sprague Dawley), monkey (Cynomolgus), and human S9 liver fractions	ALC-0315.	In vitro	[REDACTED] d	01049-009 [REDACTED]

SARS-COV-2 mRNA Vaccine (BNT162, PF-07302048)  
2.6.5 Overview of Pharmacokinetic Test

## 2.6.5.1. PHARMACOKINETICS OVERVIEW

Test Article: BNT162b2

Type of Study	Test System	Test item	Method of Administration	Testing Facility	Report Number
In Vitro Metabolic Stability of ALC-0315 in Hepatocytes	Mouse (CD-1/ICR), rat (Sprague Dawley and Wistar Han), monkey (Cynomolgus), and human hepatocytes	ALC-0315.	In vitro	[REDACTED] [REDACTED] d	01049-0 [REDACTED]
In Vitro Metabolic Stability of ALC-0159 in Liver Microsomes	Mouse (CD-1/ICR), rat (Sprague Dawley and Wistar Han), monkey (Cynomolgus), and	ALC-0159.	In vitro	[REDACTED] [REDACTED] d	01049-0 [REDACTED]
In Vitro Metabolic Stability of ALC-0159 in Liver S9	human liver microsomes Mouse (CD-1/ICR), rat (Sprague Dawley), monkey (Cynomolgus), and human S9 fractions	ALC-0159.	In vitro	[REDACTED] [REDACTED] d	01049-0 [REDACTED]
In Vitro Metabolic Stability of ALC-0159 in Hepatocytes	Mouse (CD-1/ICR), rat (Sprague Dawley and Wistar Han), monkey (Cynomolgus), and human hepatocytes	ALC-0159.	In vitro	[REDACTED] [REDACTED] d	01049-0 [REDACTED]
Biotransformation of ALC-0159 and ALC-0315 In Vitro and In Vivo in Rats	In vitro: CD-1 mouse, Wistar Han rat, cynomolgus monkey, and human blood, liver S9 fractions and hepatocytes In vivo: male Wistar Han rats	ALC-0315 and ALC-0159	In vitro or IV (in vivo in rats)	Pfizer thin	PF-07302048_05 [REDACTED]_043725

2.6.5.1. PHARMACOKINETICS OVERVIEW

Test Article: BNT162b2

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Type of Study	Test System	Test item	Method of Administration	Testing Facility	Report Number
<p>ALC-0159 = 2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide), a proprietary polyethylene glycol-lipid included as an excipient in the LNP formulation used in BNT162b2; ALC-0315 = (4-hydroxybutyl)azanediyl)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), a proprietary aminolipid included as an excipient in the LNP formulation used in BNT162b2; IM = Intramuscular; IV = Intravenous; LNP = lipid nanoparticles; S9 = Supernatant fraction obtained from liver homogenate by centrifuging at 9000 g. a. La Jolla, California. b. , Germany. c. [REDACTED] , U [REDACTED] Ch [REDACTED]roton, Connecticut.</p>					

SARS-COV-2 mRNA Vaccine (BNT162, PF-07302048)

## 2.6.5 Overview of Pharmacokinetic Test

2.6.5.3. PHARMACOKINETICS:  
PHARMACOKINETICS AFTER A SINGLE DOSETest Article: modRNA encoding luciferase in LNP Report  
Number: PF-07302048\_06\_072424

Species (Strain)	Rat (Wistar Han)	
Sex/Number of Animals	Male/ 3 animals per timepointa	
Feeding Condition	Fasted	
Method of Administration	IV	
Dose modRNA (mg/kg)	1	
How to LC-0159 (MG / KG)	1.96	
How do you have LC-0315 (MG / KG)	15.3	
Sample Matrix	Plasma, liver, urine and feces	
Sampling Time Points (h post dose):	Predose, 0.1, 0.25, 0.5, 1, 3, 6, 24, 48, 96, 192, 336	
Analyte	ALC-0315.	ALC-0159.
PK Parameters:	Meanb	Meanb
AUCinf ( $\mu\text{g}\cdot\text{h}/\text{mL}$ )c	1030	99.2
Aaclast ( $\mu\text{g}\cdot\text{h}/\text{ml}$ )	1020	98.6
Initial $t_{1/2}$ (h)d	1.62	1.74
Terminal elimination $t_{1/2}$ (h)e	139	72.7
Estimated fraction of dose distributed to liver (%)f	59.5	20.3
Dose in Urine (%)	Neg	Neg
Dose in Feces (%)h	1.05	47.2

ALC-0159 = 2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, a proprietary polyethylene glycol-lipid included as an excipient in the LNP formulation used in BNT162b2; ALC-0315 = (4-hydroxybutyl)azanediy)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), a proprietary aminolipid included as an excipient in the LNP formulation used in BNT162b2; AUCinf = Area under the plasma drug concentration-time curve from 0 to infinite time; AUClast = Area under the plasma drug concentration-time curve from 0 to the last quantifiable time point; BLQ = Below the limit of quantitation; LNP = Lipid nanoparticle; modRNA = Nucleoside modified messenger RNA; PK = Pharmacokinetics;  $t_{1/2}$  = Half-life.

a. Non-serial sampling, 36 animals total.

b. Only mean PK parameters are reported due to non-serial sampling.

c. Calculated using the terminal log-linear phase (determined using 48, 96, 192, and 336 h for regression calculation).

d.  $\ln(2)$ /initial elimination rate constant (determined using 1, 3, and 6 h for regression calculation).

e.  $\ln(2)$ /terminal elimination rate constant (determined using 48, 96, 192, and 336 h for regression calculation).

f. Calculated as follows: highest mean amount in the liver ( $\mu\text{g}$ )/total mean dose ( $\mu\text{g}$ ) of ALC-0315 or

ALC-0159. g. Not calculated due to

BLQ data. h. Fecal excretion, calculated as: (mean  $\mu\text{g}$  of analyte in feces/ mean  $\mu\text{g}$  of analyte administered)  $\times$  100

SARS-COV-2 mRNA Vaccine (BNT162, PF-07302048)

## 2.6.5 Overview of Pharmacokinetic Test

## 2.6.5.5A. PHARMACOKINETICS: ORGAN DISTRIBUTION

Test Article: modRNA encoding luciferase in LNP Report Number: R- -0072

Species (Strain):	Mice (BALB/c)		
Sex/Number of Animals:	Female/3 per group		
Feeding Condition:	Fed ad libitum		
Vehicle/Formulation:	Phosphate-buffered saline		
Method of Administration:	Intramuscular injection		
Dose (mg/kg):	1 µg/hind leg in gastrocnemius muscle (2 µg total)		
Number of Doses:	1		
Detection:	Bioluminescence measurement		
Sampling Time (hour):	6, 24, 48, 72 hours; 6 and 9 days post-injection		
Time point	Total Mean Bioluminescence signal (photons/second)		Mean Bioluminescence signal in the liver (photons/second)
	Buffer control	modRNALuciferase in LNP	modRNALuciferase in LNP
6 hours	1.28 x 10 <sup>5</sup>	1.26 x 10 <sup>9</sup>	4.94 x 10 <sup>7</sup>
24 hours	2.28 x 10 <sup>5</sup>	7.31 x 10 <sup>8</sup>	2.4 x 10 <sup>6</sup>
48 hours	1.40 x 10 <sup>5</sup>	2.10 x 10 <sup>8</sup>	Below detection <sup>a</sup>
72 hours	1.33 x 10 <sup>5</sup>	7.87 x 10 <sup>7</sup>	Below detection <sup>a</sup>
6 days	1.62 x 10 <sup>5</sup>	2.92 x 10 <sup>6</sup>	Below detection <sup>a</sup>
9 days	7.66 x 10 <sup>4</sup>	5.09 x 10 <sup>5</sup>	Below detection <sup>a</sup>

LNP = Lipid nanoparticle; modRNA = Nucleoside modified messenger RNA.

a. At or below the background level of the buffer control.

SARS-COV-2 mRNA Vaccine (BNT162, PF-07302048)

## 2.6.5 Overview of Pharmacokinetic Test

## 2.6.5.5B. PHARMACOKINETICS: ORGAN DISTRIBUTION CONTINUED

Test Article: [3H]-Labelled LNP-mRNA formulation containing ALC-0315 and ALC-0159

Report Number: 185350

Species (Strain):								Rat (Wistar Han)						
Sex/Number of Animals:								Male and female/3 animals/sex/timepoint (21 animals/sex total for the 50 µg dose)						
Feeding Condition:								Fed ad libitum						
Method of Administration:								Intramuscular injection						
Please:								50 µg [3H]-08-A01-C0 (lot # NC-0552-1)						
Number of Doses:								1						
Detection:								Radioactivity quantitation using liquid scintillation counting						
Sampling Time (hour):								0.25, 1, 2, 4, 8, 24, and 48 hours post-injection						
Sample	Mean total lipid concentration (µg lipid equivalent/g (or mL) (males and females combined))							% of administered dose (males and females combined)						
	0.25 h	1 h	2 h	4 h	8 h	24 h	48 h	0.25 h	1 h	2 h	4 h	8 h	24 h	48 h
Adipose tissue	0.057	0.100	0.126	0.128	0.093	0.084	0.181	-	-	-	-	-	-	-
Adrenal glands	0.271	1.48	2.72	2.89	6.80	13.8	18.2	0.001	0.007	0.010	0.015	0.035	0.066	0.106
Bladder	0.041	0.130	0.146	0.167	0.148	0.247	0.365	0.000	0.001	0.001	0.001	0.001	0.002	0.002
Bone (femur)	0.091	0.195	0.266	0.276	0.340	0.342	0.687	-	-	-	-	-	-	-
Bone marrow (femur)	0.479	0.960	1.24	1.24	1.84	2.49	3.77	-	-	-	-	-	-	-
Brain	0.045	0.100	0.138	0.115	0.073	0.069	0.068	0.007	0.013	0.020	0.016	0.011	0.010	0.009
Eyes	0.010	0.035	0.052	0.067	0.059	0.091	0.112	0.000	0.001	0.001	0.002	0.002	0.002	0.003
Heart	0.282	1.03	1.40	0.987	0.790	0.451	0.546	0.018	0.056	0.084	0.060	0.042	0.027	0.030
Injection site	128	394	311	338	213	195	165	19.9	52.6	31.6	28.4	21.9	29.1	24.6
Kidneys	0.391	1.16	2.05	0.924	0.590	0.426	0.425	0.050	0.124	0.211	0.109	0.075	0.054	0.057
Large intestine	0.013	0.048	0.093	0.287	0.649	1.10	1.34	0.008	0.025	0.065	0.192	0.405	0.692	0.762
Liver	0.737	4.63	11.0	16.5	26.5	19.2	24.3	0.602	2.87	7.33	11.9	18.1	15.4	16.2
Lung	0.492	1.21	1.83	1.50	1.15	1.04	1.09	0.052	0.101	0.178	0.169	0.122	0.101	0.101

The Highest concentrations in Adrenals and Liver- may explain numerous abnormal liver function tests and intermittent spiking blood pressures



SARS-COV-2 mRNA Vaccine (BNT162, PF-07302048)

## 2.6.5 Overview of Pharmacokinetic Test

2.6.5.5B. PHARMACOKINETICS: ORGAN  
DISTRIBUTION CONTINUED

Test Article: [3H]-Labelled LNP-mRNA formulation containing

ALC-0315 and ALC-0159 Report  
Number: 185350

Sample	Total Lipid concentration (µg lipid equivalent/g [or mL]) (males and females combined)							% of Administered Dose (males and females combined)						
	0.25 h	1 h	2 h	4 h	8 h	24 h	48 h	0.25 h	1 h	2 h	4 h	8 h	24 h	48 h
Lymph (mandibular)	0.064	0.189	0.290	0.408	0.534	0.554	0.727	-	-	-	-	-	-	-
Lymph node (mesenteric)	0.050	0.146	0.530	0.489	0.689	0.985	1.37	-	-	-	-	-	-	-
Muscle	0.021	0.061	0.084	0.103	0.096	0.095	0.192	-	-	-	-	-	-	-
Ovaries (females)	0.104	1.34	1.64	2.34	3.09	5.24	12.3	0.001	0.009	0.008	0.016	0.025	0.037	0.095
Pancreas	0.081	0.207	0.414	0.380	0.294	0.358	0.599	0.003	0.007	0.014	0.015	0.015	0.011	0.019
Pituitary gland	0.339	0.645	0.868	0.854	0.405	0.478	0.694	0.000	0.001	0.001	0.001	0.000	0.000	0.001
Prostate (males)	0.061	0.091	0.128	0.157	0.150	0.183	0.170	0.001	0.001	0.002	0.003	0.003	0.004	0.003
Salivary glands	0.084	0.193	0.255	0.220	0.135	0.170	0.264	0.003	0.007	0.008	0.008	0.005	0.006	0.009
Skin	0.013	0.208	0.159	0.145	0.119	0.157	0.253	-	-	-	-	-	-	-
Small intestine	0.030	0.221	0.476	0.879	1.28	1.30	1.47	0.024	0.130	0.319	0.543	0.776	0.906	0.835
Spinal cord	0.043	0.097	0.169	0.250	0.106	0.085	0.112	0.001	0.002	0.002	0.003	0.001	0.001	0.001
Spleen	0.334	2.47	7.73	10.3	22.1	20.1	23.4	0.013	0.093	0.325	0.385	0.982	0.821	1.03
Stomach	0.017	0.065	0.115	0.144	0.268	0.152	0.215	0.006	0.019	0.034	0.030	0.040	0.037	0.039
Tests (Males)	0.031	0.042	0.079	0.129	0.146	0.304	0.320	0.007	0.010	0.017	0.030	0.034	0.074	0.074
Thymus	0.088	0.243	0.340	0.335	0.196	0.207	0.331	0.004	0.007	0.010	0.012	0.008	0.007	0.008
Thyroid	0.155	0.536	0.842	0.851	0.544	0.578	1.00	0.000	0.001	0.001	0.001	0.001	0.001	0.001
Uterus (females)	0.043	0.203	0.305	0.140	0.287	0.289	0.456	0.002	0.011	0.015	0.008	0.016	0.018	0.022
Whole blood	1.97	4.37	5.40	3.05	1.31	0.909	0.420	-	-	-	-	-	-	-
Plasma	3.97	8.13	8.90	6.50	2.36	1.78	0.805	-	-	-	-	-	-	-
Blood: plasma ratio	0.815	0.515	0.550	0.510	0.555	0.530	0.540	-	-	-	-	-	-	-

WE Were told the mRNA stayed in the muscle- clearly crosses the blood-brain barrier, with highest concentration in OVARIES = menstrual irregularities and infertility risk

2.6.5.5B. PHARMACOKINETICS: ORGAN  
DISTRIBUTION CONTINUED

Test Article: [3H]-Labelled LNP-mRNA formulation containing

ALC-0315 and ALC-0159 Report  
Number: 185350

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-- = Not applicable, partial tissue taken; [3H]-08-A01-C0 = An aqueous dispersion of LNPs, including ALC-0315, ALC-0159, distearoylphosphatidylcholine, cholesterol, mRNA encoding luciferase and trace amounts of radiolabeled [Cholesteryl-1,2-3H(N)]-Cholesteryl Hexadecyl Ether, a nonexchangeable, non-metabolizable lipid marker used to monitor the disposition of the LNPs; ALC-0159 = 2-[(polyethylene glycol)-2000]-N,N--ditetradecylacetamide, a proprietary polyethylene glycol-lipid included as an excipient in the LNP formulation used in BNT162b2; ALC-0315 = (4--hydroxybutyl)azanediy)bis(hexane-6,1-diyl)bis(2-hexyldecanoate), a proprietary aminolipid included as an excipient in the LNP formulation used in BNT162b2; LNP = Lipid nanoparticle; mRNA = messenger RNA.

a. The mean male and female blood:plasma values were first calculated separately and this value represents the mean of the two values.

SARS-COV-2 mRNA Vaccine (BNT162, PF-07302048)

## 2.6.5 Overview of Pharmacokinetic Test

## 2.6.5.9. PHARMACOKINETICS: METABOLISM IN VIVO, RAT

Test Article: modRNA encoding luciferase in LNP Report

Number: PF-07302048\_05\_043725



Species (Strain):		Rat (Wistar Han)			
Sex/ Number of animals		Male/ 36 animals total for plasma and liver, 3 animals for urine and feces			
Method of Administration:		Intravenous			
Dose (mg/kg):		1			
Test System:		Plasma, Urine, Feces, Liver			
Analysis Method:		Ultrahigh performance liquid chromatography/ mass spectrometry			
Biotransformation	m/z	Metabolites of ALC-0315 Detected			
		Plasma	Urine	Feces	Liver
N-dealkylation, oxidation	102.0561a	ND	ND	ND	ND
N-Dealkylation, oxidation	104.0706 b	ND	ND	ND	ND
N-dealkylation, oxidation	130.0874	ND	ND	ND	ND
N-Dealkylation, oxidation	132.1019b	ND	ND	ND	ND
N-dealkylation, hydrolysis, oxidation	145.0506a	ND	ND	ND	ND
Hydrolysis (acid)	Brother .2330	+	ND	ND	ND
Hydrolysis, hydroxylation	271. Investing	ND	ND	ND	ND
Bis-Hydrolysis (Amine)	290.2690 b	+	+	+	+
Hydrolysis, glucuronidation	431.2650a	ND	ND	ND	ND
Bis-hydrolysis (amines), glucuronidation	464.2865a	ND	ND	ND	ND
Bis-hydrolysis (amines), glucuronidation	466.3011b	ND	+	ND	ND
Hydrolysis (amine)	528.4986 b	+	ND	ND	+
Hydrolysis (amine), Glucuronidation	704.5307 b	ND	ND	ND	ND
Otachi and Ashi D	778.6930a	ND	ND	ND	ND
Otachi and Ashi D	780.7076 b	ND	ND	ND	ND
Hydroxylation	Achieve.	ND	ND	ND	ND
Sulfation	844.6706	ND	ND	ND	ND
Sulfation	846.6851b	ND	ND	ND	ND
Glucuronidation	940.7458	ND	ND	ND	ND
Glucuronidation	942.7604 b	ND	ND	ND	ND

Note: Both theoretical and observed metabolites are included.

m/z = mass to charge ratio; ND = Not detected; + = minor metabolite as assessed by ultraviolet detection.

a. Negative ion mode.

b. Positive ion mode.

2.6.5.10A. PHARMACOKINETICS: METABOLISM IN VITRO

Test article: alc-0315  
Report Numbers: 01049- 008

01049-00  
01049-01

Type of Study:	Liver Microsomes + NADPH					Stability of ALC-0315 In Vitro S9 Fraction + NADPH, UDPGA, and alamethicin					Hepatocytes					
Study System:																
ALC-0315 Concentration:	1 µM					1 µM					1 µM					
Duration of Incubation (min):	120 min					120 min					240 min					
Analysis Method:	Ultra-high performance liquid chromatography-tandem mass spectrometry															
Incubation time (min)	Percent ALC-0315 remaining															
	Liver Microsomes					Liver Said Frazy					Hepatocytes					
	Mouse (CD-Rat (SD) 1/ICR)	Rat (WH)	Monkey (Cyno)	Human	Mouse (CD-1 / ICR) (SD)	Rat (SD)	Monkey (Cyno)	Human	Mouse (CD-1 / ICR) (SD)	Rat (WH)	Monkey (Cyno)	Human	Mouse (CD-1 / ICR) (SD)	Rat (WH)	Monkey (Cyno)	Human
0	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00
15	98.77	94.39	96.34	97.96	100.24	97.69	98.85	99.57	95.99	-	-	-	-	-	-	-
30	97.78	96.26	97.32	96.18	99.76	97.22	99.62	96.96	97.32	101.15	97.75	102.70	96.36	100.72	-	-
60	100.49	99.73	98.54	100.00	101.45	98.61	99.62	99.13	94.98	100.77	98.50	102.32	98.21	101.44	-	-
90	97.78	98.66	94.15	97.96	100.48	98.15	98.85	98.70	98.33	101.92	99.25	103.09	100.01	100.36	-	-
120	96.54	95.99	93.66	97.71	98.31	96.76	98.46	99.57	99.33	98.85	97.38	99.61	96.36	100.72	-	-
180	-	-	-	-	-	-	-	-	-	101.15	98.88	103.47	95.64	98.92	-	-
240	-	-	-	-	-	-	-	-	-	99.62	101.12	100.00	93.82	99.64	-	-
t½ (min)	> 120	> 120	> 120	> 120	> 120	> 120	> 120	> 120	> 120	> 240	> 240	> 240	> 240	> 240	> 240	> 240

-- = Data not available; ALC-0315 = (4-hydroxybutyl)azanediylbis(hexane-6,1-diyl)bis(2-hexyldecanoate), a proprietary aminolipid included as an excipient in the lipid nanoparticle formulation used in BNT162b2; Cyno = Cynomolgus; NADPH = Reduced form of nicotinamide adenine dinucleotide phosphate; NC = not calculated; SD = Sprague Dawley; t½ = half-life; WH = Wistar-Han; UDPGA= uridine-diphosphate-glucuronic acid trisodium salt.

2.6.5.10B. PHARMACOKINETICS: METABOLISM IN VITRO

CONTINUED

Test article: alc-0159

Report Numbers: 01049- 020 01049- 21

01049-02

Type of Study:	Stability of ALC-0159 In Vitro										Hepatocytes				
Study System:	Liver Microsomes + NADPH					S9 Fraction + NADPH, UDPGA, and alamethicin									
ALC-0159 Concentration:	1 µM					1 µM					1 µM				
Duration of Incubation (min):	120 min					120 min					240 min				
Analysis Method:	Ultra-high performance liquid chromatography-tandem mass spectrometry														
Incubation time (min)	Percent ALC-0159 remaining														
	Liver Microsomes					Liver Said Frazy					Hepatocytes				
	Mouse (CD-1 / ICR) (SD)	Rat (WH)	Monkey (Cyno)	Human	Mouse (CD-1 / ICR) (SD)	Monkey (Cyno)	Human	Mouse (CD-1 / ICR) (SD)	Rat (WH)	Monkey (Cyno)	Human	Mouse (CD-1 / ICR) (SD)	Rat (WH)	Monkey (Cyno)	Human
0	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00	100.00
15	82.27	101.24	112.11	100.83	99.59	98.93	84.38	91.30	106.73	-	-	-	-	-	-
30	86.40	93.78	102.69	85.12	92.28	91.10	90.87	97.96	107.60	100.85	93.37	113.04	90.23	106.34	-
60	85.54	98.34	105.38	86.36	95.53	102.85	97.97	105.56	104.97	94.92	91.81	105.07	92.93	101.58	-
90	85.41	95.44	100.90	94.63	97.97	90.75	93.51	108.33	109.36	94.28	90.25	112.80	94.59	92.67	-
120	95.87	97.10	108.97	93.39	93.09	106.76	92.70	105.74	119.59	87.08	89.47	104.11	97.51	96.04	-
180	-	-	-	-	-	-	-	-	-	94.92	93.96	102.90	89.81	93.66	-
240	-	-	-	-	-	-	-	-	-	102.75	94.93	98.79	92.93	102.57	-
t½ (min)	> 120	> 120	> 120	> 120	> 120	> 120	> 120	> 120	> 120	> 240	> 240	> 240	> 240	> 240	> 240

-- = Data not available; ALC-0159 = 2-[(polyethylene glycol)-2000]-N,N-ditetradecylacetamide, a proprietary polyethylene glycol-lipid included as an excipient in the lipid nanoparticle formulation used in BNT162b2; Cyno = Cynomolgus; NADPH = Reduced form of nicotinamide adenine dinucleotide phosphate; NC = not calculated; SD = Sprague Dawley; WH = Wistar-Han; UDPGA= uridine-diphosphate-glucuronic acid trisodium salt.

SARS-COV-2 mRNA Vaccine (BNT162, PF-07302048)

## 2.6.5 Overview of Pharmacokinetic Test

## 2.6.5.10C. PHARMACOKINETICS: METABOLISM IN VITRO CONTINUED

Test article: alc-0315

Report Number: OF-07302048\_05

[REDACTED] 043725

Type of study		Metabolism of ALC-0315 In Vitro												
Study system		Blood				Hepatocytes				Liver Said Frazy				
ALC-0315 concentration		10 µM				10 µM				10 µM				
Duration of incubation		24 h				4 h				24 h				
Analysis Method:		Ultrahigh performance liquid chromatography/ mass spectrometry												
Biotransformation	m/z	Blood				Hepatocytes				Liver Said Frazy				
		Mouse	Rat	Monkey	Human	Mouse		Rat	Monkey	Human	Mouse	Rat	Monkey	Human
N-dealkylation, oxidation	102.0561a	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
N-Dealkylation, oxidation	104.0706 b	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
N-dealkylation, oxidation	130.0874	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
N-Dealkylation, oxidation	132.1019b	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
N-dealkylation, hydrolysis, oxidation	145.0506a	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Hydrolysis (acid)	Brother .2330	+	+	ND	ND	+	+	+	+	+	+	ND	+	+
Hydrolysis, hydroxylation	271. Investing	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Bis-Hydrolysis (Amine)	290.2690 b	+	+	ND	ND	ND	ND	ND	ND	ND	ND	+	ND	ND
Hydrolysis, glucuronidation	431.2650a	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Bis-hydrolysis (amines), glucuronidation	464.2865a	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Bis-hydrolysis (amines), glucuronidation	466.3011b	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Hydrolysis (amine)	528.4986 b	ND	+	ND	ND	ND	ND	ND	ND	ND	ND	+	ND	ND
Hydrolysis (amine), glucuronidation	704.5307 b	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Otachi and Ashi D	778.6930a	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Otachi and Ashi D	780.7076 b	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Hydroxylation	Achieve.	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Sulfation	844.6706	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Sulfation	846.6851b	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Glucuronidation	940.7458	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Glucuronidation	942.7604 b	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND

Note: Both theoretical and observed metabolites are included.

m/z = mass to charge ratio; ND = Not detected; + = metabolite present.

a. Negative ion mode.

b. Positive ion mode.

SARS-COV-2 mRNA Vaccine (BNT162, PF-07302048)

## 2.6.5 Overview of Pharmacokinetic Test

## 2.6.5.10D. PHARMACOKINETICS: METABOLISM IN VITRO CONTINUED

Test article: alc-0159

Report Number: OF-07302048\_05

[REDACTED] 043725

Type of study		Metabolism of ALC-0159 In Vitro														
Study system		Blood				Hepatocytes				Liver Said Frazy						
ALC-0159 concentration		10 µM				10 µM				10 µM						
Duration of incubation		24 h				4 h				24 h						
Analysis Method:		Ultrahigh performance liquid chromatography/ mass spectrometry														
Biotransformation	m/z	Blood				Hepatocytes				Liver Said Frazy						
		Mouse	Rat	Monkey	Human	Mouse	Rat	Monkey	Human	Mouse	Rat	Monkey	Human			
Oh, it's THY ACON, LKY	107.0703 b	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Oh, it's THY ACON, LKY	151.0965b	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Oh, it's THY ACON, LKY	195.1227 b	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Hydrolysis, N-Dealkylation	214. Stere	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
N-Dealkylation, oxidation	227.2017	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Hydrolysis (amine)	410.4720b	+	+	ND	ND	+	+	+	+	+	+	+	+	+	+	+
N, Lky	531.5849 b	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
N-Dealkylation	580. Step	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Oh, THY AICO, OY	629. Greatness	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Hydroxylation	633.6931 b	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
ω-Hydroxylation, Oxidation	637.1880b	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Hydrolysis (acid)	708.7721 b	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND

Note: Both theoretical and observed metabolites are included.

m/z = mass to charge ratio; ND = Not detected; + = metabolite present.

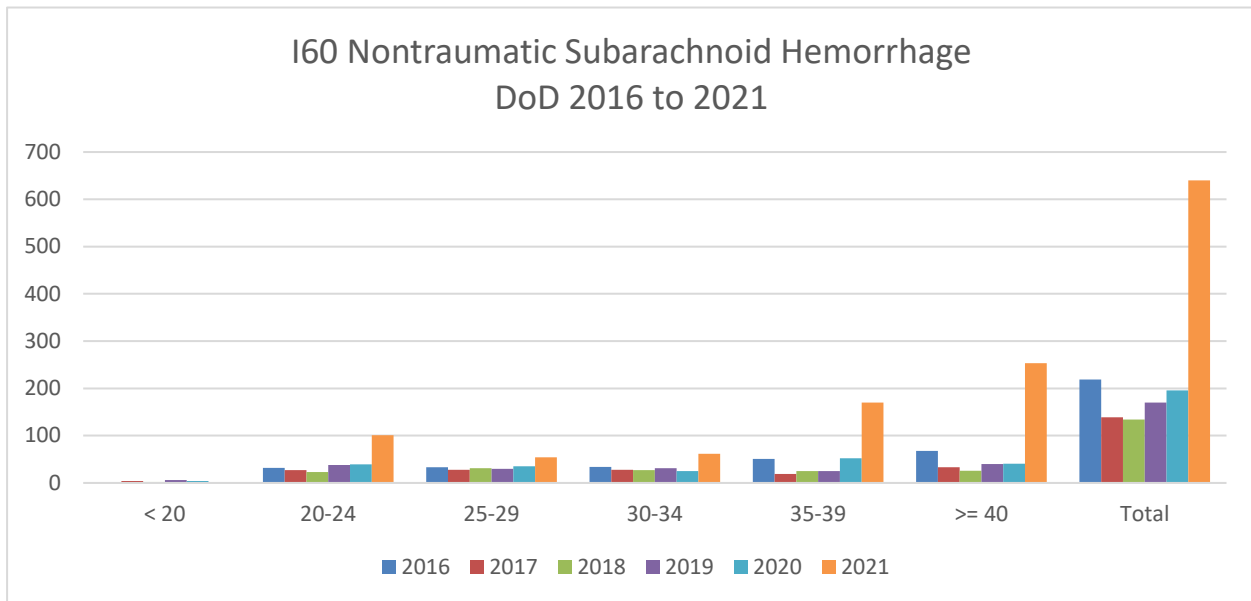
a. Negative ion mode.

b. Positive ion mode.

Ambulatory Data - Cases of Selected Diagnoses \*

Service: All  
 Age: All  
 Grade: All  
 Time: 2016, 2017, 2018, 2019, 2020  
 Data Sources: Hospitalizations, Ambulatory Data, Reportable Events  
 Condition: Primary Diagnosis  
 Gender: All  
 Race: All  
 Marital Status: All  
 Occurrence: All Occurrences  
 Occupation: ALL OCCUPATION GROUPS  
 Location: ALL LOCATIONS

Counts	2016	2017	2018	2019	2020	2021
< 20	1	4	2	6	4	0
20-24	32	27	23	38	39	101
25-29	33	28	31	30	35	54
30-34	34	28	27	31	25	62
35-39	51	19	25	25	52	170
>= 40	68	33	26	40	41	253
Total	219	139	134	170	196	640



Population	2016	2017	2018	2019	2020
< 20	89,960.22	97,211.06	101,742.92	103,979.52	99,700.77
20-24	407,896.25	408,673.02	416,571.93	423,448.74	426,856.25
25-29	301,023.73	295,861.48	298,208.35	303,986.22	307,502.33
30-34	210,243.28	206,598.27	205,040.00	206,150.65	209,127.84



<b>35-39</b>	147,076.90	147,648.83	150,119.41	153,231.54	156,973.87
<b>&gt;= 40</b>	132,655.89	127,672.92	124,588.75	124,232.43	126,871.55
<b>Total</b>	1,288,856.27	1,283,665.58	1,296,271.36	1,315,029.10	1,327,032.61

<b>Rate</b>	<b>2016</b>	<b>2017</b>	<b>2018</b>	<b>2019</b>	<b>2020</b>
<b>&lt; 20</b>	0.01	0.04	0.02	0.06	0.04
<b>20-24</b>	0.08	0.07	0.06	0.09	0.09
<b>25-29</b>	0.11	0.09	0.10	0.10	0.11
<b>30-34</b>	0.16	0.14	0.13	0.15	0.12
<b>35-39</b>	0.35	0.13	0.17	0.16	0.33
<b>&gt;= 40</b>	0.51	0.26	0.21	0.32	0.32
<b>Total</b>	0.17	0.11	0.10	0.13	0.15

Source: DMSS 1/19/2022

Rate calculated in counts per 1,000 persons per year. Data with unknown values excluded.

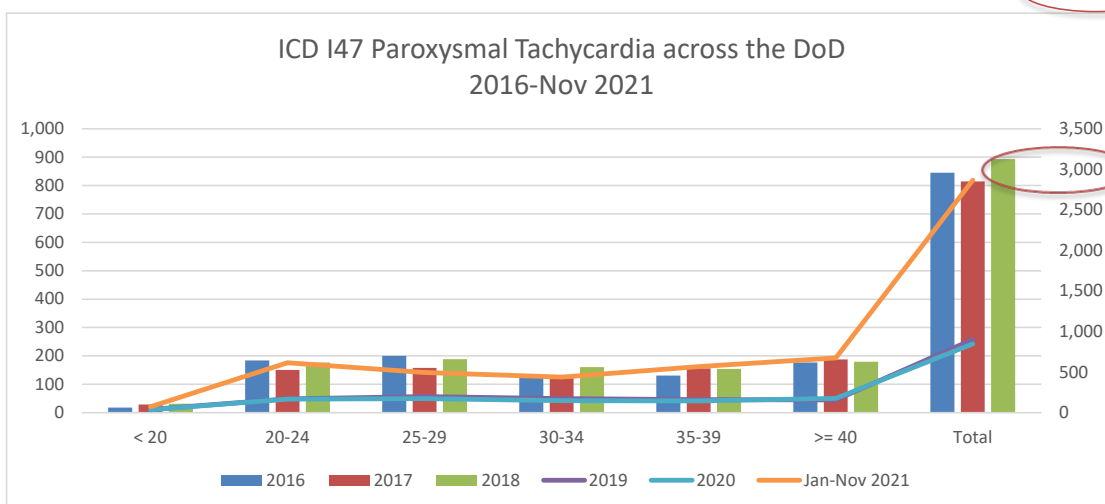
\* Selected Diagnoses:

I60 Nontraumatic subarachnoid hemorrhage

Ambulatory Data - Cases of Selected Diagnoses \*

Service: All  
 Age: All  
 Grade: All  
 Time: 2016, 2017, 2018, 2019, 2020  
 Data Sources: Hospitalizations, Ambulatory Data, Reportable Events  
 Condition: Primary Diagnosis  
 Gender: All  
 Race: All  
 Marital Status: All  
 Occurrence: All Occurrences  
 Occupation: ALL OCCUPATION GROUPS  
 Location: ALL LOCATIONS

ICD I47 Paroxysmal tachycardia							
Counts	2016	2017	2018	2019	2020	Jan-Nov 2021	
< 20	18	29	32	40	36	74	
20-24	184	151	177	170	169	615	
25-29	200	158	189	199	174	496	
30-34	135	133	161	173	148	439	
35-39	131	156	154	162	145	567	
>= 40	177	188	180	159	177	675	
<b>Total</b>	<b>845</b>	<b>815</b>	<b>893</b>	<b>903</b>	<b>849</b>	<b>2,866</b>	



Population	2016	2017	2018	2019	2020
< 20	89,960.22	97,211.06	101,742.92	103,979.52	99,700.77
20-24	407,896.25	408,673.02	416,571.93	423,448.74	426,856.25
25-29	301,023.73	295,861.48	298,208.35	303,986.22	307,502.33
30-34	210,243.28	206,598.27	205,040.00	206,150.65	209,127.84
35-39	147,076.90	147,648.83	150,119.41	153,231.54	156,973.87
>= 40	132,655.89	127,672.92	124,588.75	124,232.43	126,871.55
<b>Total</b>	<b>1,288,856.27</b>	<b>1,283,665.58</b>	<b>1,296,271.36</b>	<b>1,315,029.10</b>	<b>1,327,032.61</b>

Rate	2016	2017	2018	2019	2020
< 20	0.20	0.30	0.31	0.38	0.36
20-24	0.45	0.37	0.42	0.40	0.40
25-29	0.66	0.53	0.63	0.65	0.57
30-34	0.64	0.64	0.79	0.84	0.71

<b>35-39</b>	0.89	1.06	1.03	1.06	0.92
<b>&gt;= 40</b>	1.33	1.47	1.44	1.28	1.40
<b>Total</b>	0.66	0.63	0.69	0.69	0.64

Source: DMSS 1/19/2022

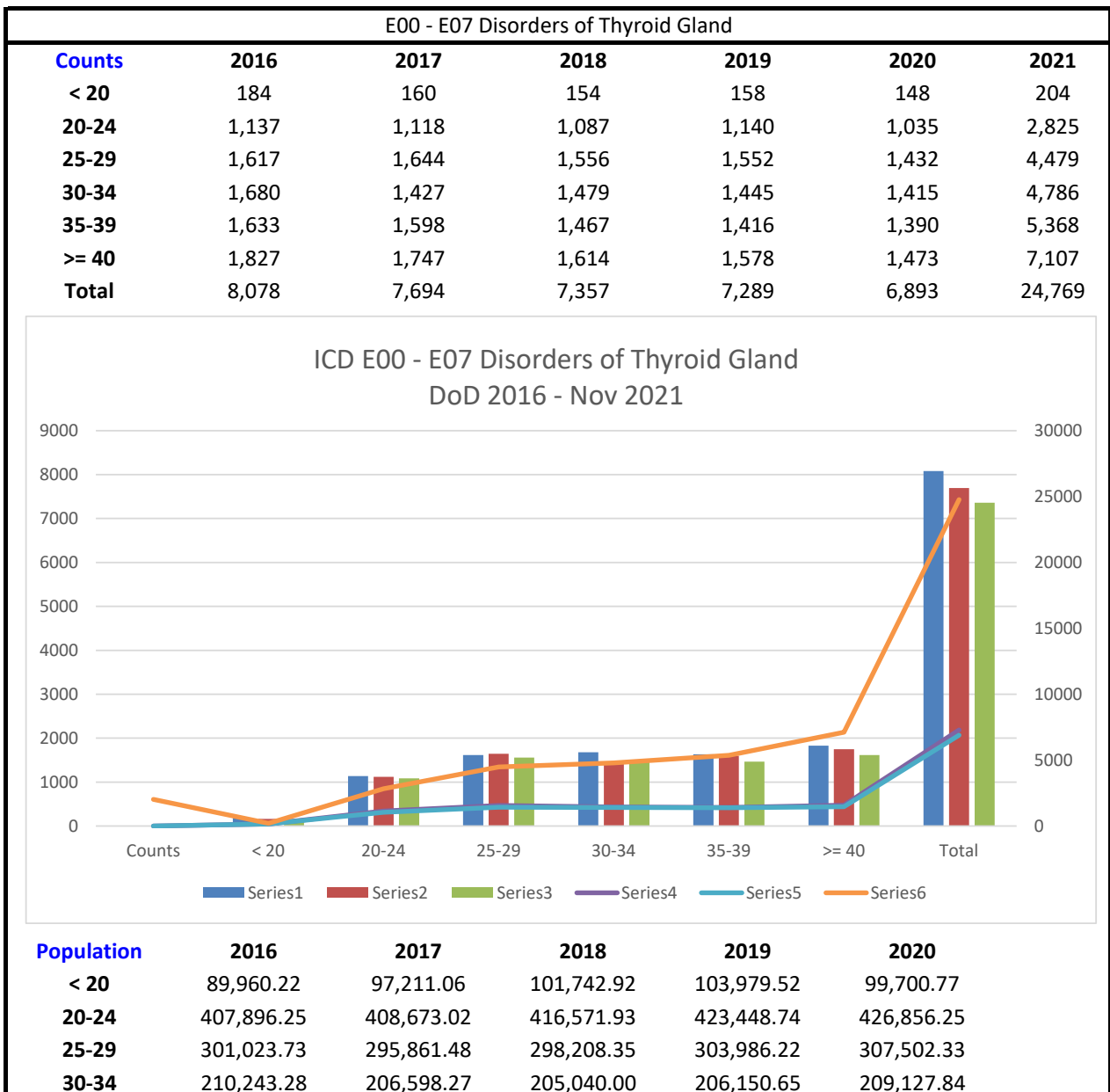
Rate calculated in counts per 1,000 persons per year. Data with unknown values excluded.

\* Selected Diagnoses:

I47 Paroxysmal tachycardia

Ambulatory Data - Cases of Selected Diagnoses \*

Service: All  
 Age: All  
 Grade: All  
 Time: 2016, 2017, 2018, 2019, 2020  
 Data Sources: Hospitalizations, Ambulatory Data, Reportable Events  
 Condition: Primary Diagnosis  
 Gender: All  
 Race: All  
 Marital Status: All  
 Occurrence: All Occurrences  
 Occupation: ALL OCCUPATION GROUPS  
 Location: ALL LOCATIONS



<b>35-39</b>	147,076.90	147,648.83	150,119.41	153,231.54	156,973.87
<b>&gt;= 40</b>	132,655.89	127,672.92	124,588.75	124,232.43	126,871.55
<b>Total</b>	1,288,856.27	1,283,665.58	1,296,271.36	1,315,029.10	1,327,032.61

<b>Rate</b>	<b>2016</b>	<b>2017</b>	<b>2018</b>	<b>2019</b>	<b>2020</b>
<b>&lt; 20</b>	2.05	1.65	1.51	1.52	1.48
<b>20-24</b>	2.79	2.74	2.61	2.69	2.42
<b>25-29</b>	5.37	5.56	5.22	5.11	4.66
<b>30-34</b>	7.99	6.91	7.21	7.01	6.77
<b>35-39</b>	11.10	10.82	9.77	9.24	8.85
<b>&gt;= 40</b>	13.77	13.68	12.95	12.70	11.61
<b>Total</b>	6.27	5.99	5.68	5.54	5.19

Source: DMSS 1/19/2022

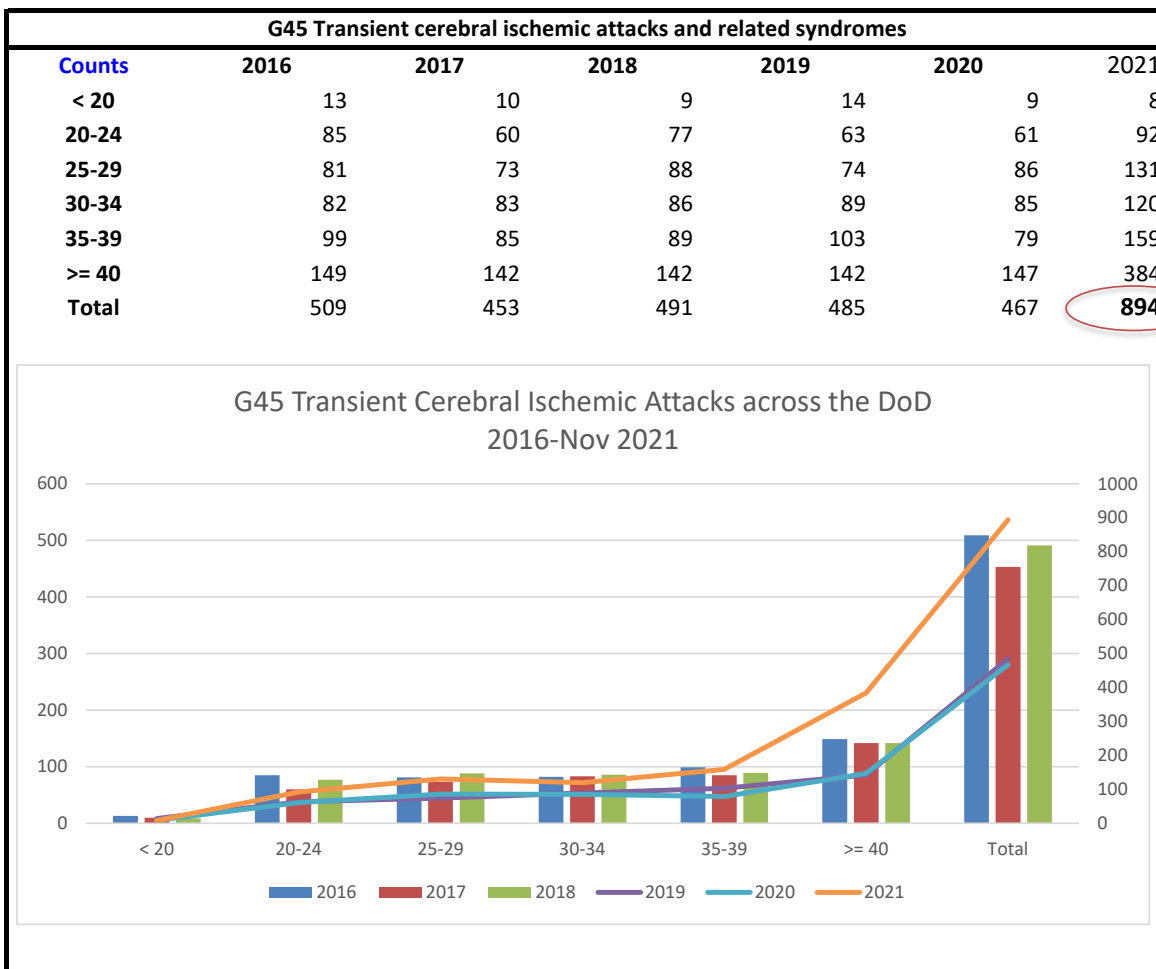
Rate calculated in counts per 1,000 persons per year. Data with unknown values excluded.

\* Selected Diagnoses:

E00 - E07 Disorders of thyroid gland

Ambulatory Data - Cases of Selected Diagnoses \*

Service: All  
 Age: All  
 Grade: All  
 Time: 2016, 2017, 2018, 2019, 2020, Jan -Nov 2021  
 Data Sources: Hospitalizations, Ambulatory Data, Reportable Events  
 Condition: Primary Diagnosis  
 Gender: All  
 Race: All  
 Marital Status: All  
 Occurrence: All Occurrences  
 Occupation: ALL OCCUPATION GROUPS  
 Location: ALL LOCATIONS



<b>Population</b>	<b>2016</b>	<b>2017</b>	<b>2018</b>	<b>2019</b>	<b>2020</b>
< 20	89,960.22	97,211.06	101,742.92	103,979.52	99,700.77
20-24	407,896.25	408,673.02	416,571.93	423,448.74	426,856.25
25-29	301,023.73	295,861.48	298,208.35	303,986.22	307,502.33
30-34	210,243.28	206,598.27	205,040.00	206,150.65	209,127.84
35-39	147,076.90	147,648.83	150,119.41	153,231.54	156,973.87
>= 40	132,655.89	127,672.92	124,588.75	124,232.43	126,871.55
<b>Total</b>	<b>1,288,856.27</b>	<b>1,283,665.58</b>	<b>1,296,271.36</b>	<b>1,315,029.10</b>	<b>1,327,032.61</b>

<b>Rate</b>	<b>2016</b>	<b>2017</b>	<b>2018</b>	<b>2019</b>	<b>2020</b>
< 20	0.14	0.10	0.09	0.13	0.09
20-24	0.21	0.15	0.18	0.15	0.14
25-29	0.27	0.25	0.30	0.24	0.28
30-34	0.39	0.40	0.42	0.43	0.41
35-39	0.67	0.58	0.59	0.67	0.50
>= 40	1.12	1.11	1.14	1.14	1.16
<b>Total</b>	<b>0.39</b>	<b>0.35</b>	<b>0.38</b>	<b>0.37</b>	<b>0.35</b>

Source: DMSS 1/19/2022

Rate calculated in counts per 1,000 persons per year. Data with unknown values excluded.

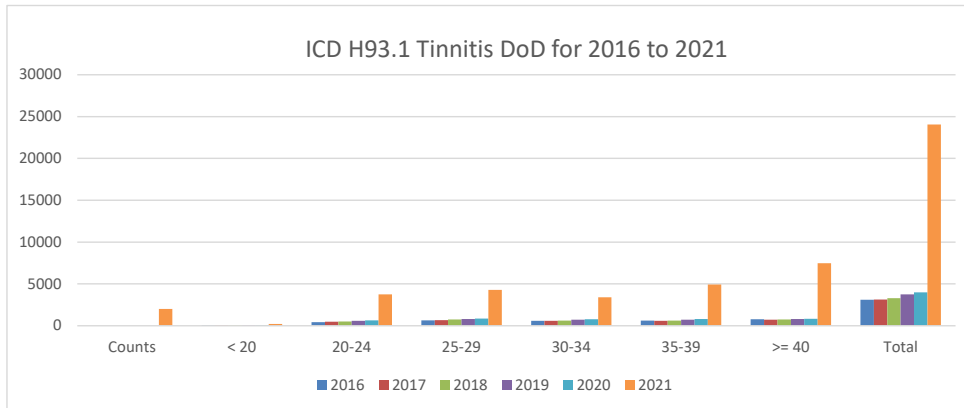
\* Selected Diagnoses:

G45 Transient cerebral ischemic attacks and related syndromes

Ambulatory Data - Cases of Selected Diagnoses \*

Service: All  
 Age: All  
 Grade: All  
 Time: 2016, 2017, 2018, 2019, 2020  
 Data Sources: Hospitalizations, Ambulatory Data, Reportable Events  
 Condition: Primary Diagnosis  
 Gender: All  
 Race: All  
 Marital Status: All  
 Occurrence: All Occurrences  
 Occupation: ALL OCCUPATION GROUPS  
 Location: ALL LOCATIONS

Counts	2016	2017	2018	2019	2020	2021
< 20	72	71	75	81	78	205
20-24	425	481	500	590	637	3,743
25-29	650	682	740	813	863	4,290
30-34	578	587	612	733	789	3,392
35-39	612	580	621	731	793	4,941
>= 40	775	731	754	811	825	7,484
<b>Total</b>	<b>3,112</b>	<b>3,132</b>	<b>3,302</b>	<b>3,759</b>	<b>3,985</b>	<b>24,055</b>



Population	2016	2017	2018	2019	2020
< 20	89,960.22	97,211.06	101,742.92	103,979.52	99,700.77
20-24	407,896.25	408,673.02	416,571.93	423,448.74	426,856.25
25-29	301,023.73	295,861.48	298,208.35	303,986.22	307,502.33
30-34	210,243.28	206,598.27	205,040.00	206,150.65	209,127.84
35-39	147,076.90	147,648.83	150,119.41	153,231.54	156,973.87
>= 40	132,655.89	127,672.92	124,588.75	124,232.43	126,871.55
<b>Total</b>	<b>1,288,856.27</b>	<b>1,283,665.58</b>	<b>1,296,271.36</b>	<b>1,315,029.10</b>	<b>1,327,032.61</b>

Rate	2016	2017	2018	2019	2020
< 20	0.80	0.73	0.74	0.78	0.78
20-24	1.04	1.18	1.20	1.39	1.49
25-29	2.16	2.31	2.48	2.67	2.81
30-34	2.75	2.84	2.98	3.56	3.77
35-39	4.16	3.93	4.14	4.77	5.05
>= 40	5.84	5.73	6.05	6.53	6.50
<b>Total</b>	<b>2.41</b>	<b>2.44</b>	<b>2.55</b>	<b>2.86</b>	<b>3.00</b>

Source: DMSS 1/19/2022

Rate calculated in counts per 1,000 persons per year. Data with unknown values excluded.

\* Selected Diagnoses:

H93.1 Tinnitus



Ambulatory Data - Cases of Selected Diagnoses \*

Service: All

Age: All

Grade: All

Time: 2016, 2017, 2018, 2019, 2020

Data Sources: Hospitalizations, Ambulatory Data, Reportable Events

Condition: Primary Diagnosis

Gender: All

Race: All

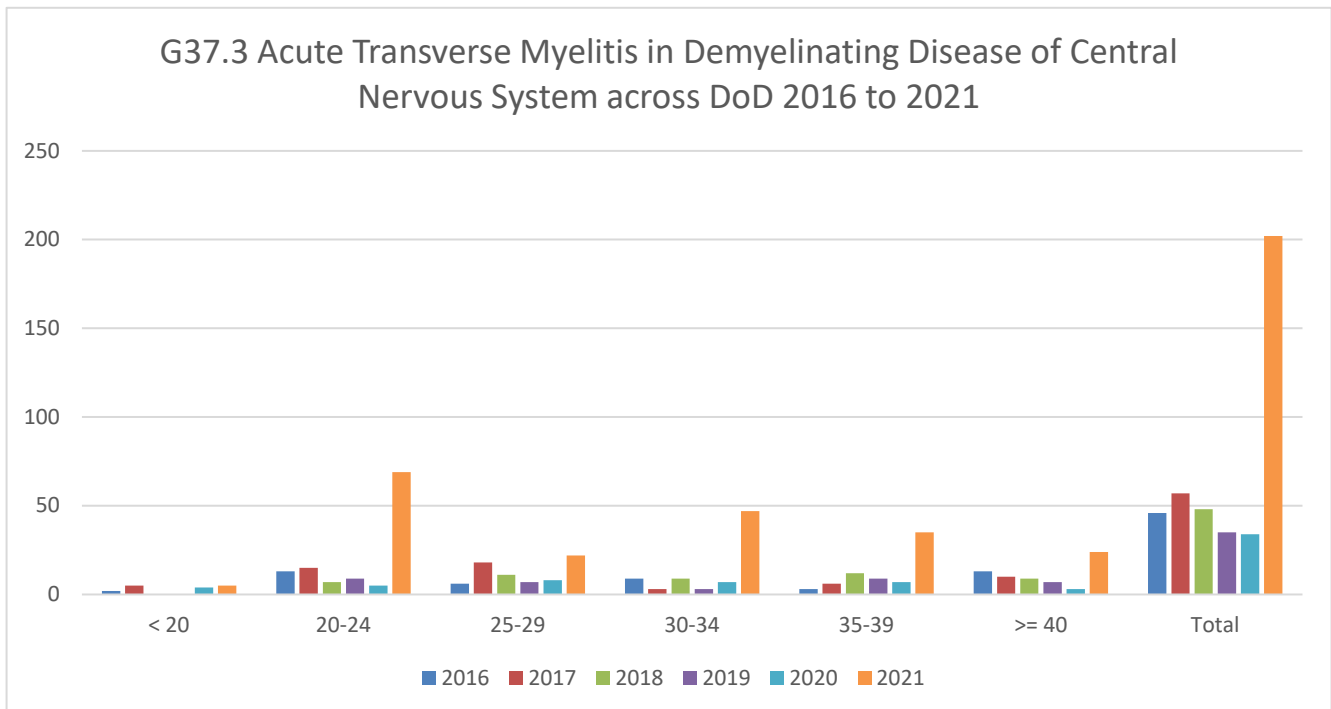
Marital Status: All

Occurrence: All Occurrences

Occupation: ALL OCCUPATION GROUPS

Location: ALL LOCATIONS

Counts	2016	2017	2018	2019	2020	2021
< 20	2	5	0	0	4	5
20-24	13	15	7	9	5	69
25-29	6	18	11	7	8	22
30-34	9	3	9	3	7	47
35-39	3	6	12	9	7	35
>= 40	13	10	9	7	3	24
<b>Total</b>	<b>46</b>	<b>57</b>	<b>48</b>	<b>35</b>	<b>34</b>	<b>202</b>



Population	2016	2017	2018	2019	2020
< 20	89,960.22	97,211.06	101,742.92	103,979.52	99,700.77
20-24	407,896.25	408,673.02	416,571.93	423,448.74	426,856.25

<b>25-29</b>	301,023.73	295,861.48	298,208.35	303,986.22	307,502.33
<b>30-34</b>	210,243.28	206,598.27	205,040.00	206,150.65	209,127.84
<b>35-39</b>	147,076.90	147,648.83	150,119.41	153,231.54	156,973.87
<b>&gt;= 40</b>	132,655.89	127,672.92	124,588.75	124,232.43	126,871.55
<b>Total</b>	1,288,856.27	1,283,665.58	1,296,271.36	1,315,029.10	1,327,032.61

<b>Rate</b>	<b>2016</b>	<b>2017</b>	<b>2018</b>	<b>2019</b>	<b>2020</b>
<b>&lt; 20</b>	0.02	0.05	0.00	0.00	0.04
<b>20-24</b>	0.03	0.04	0.02	0.02	0.01
<b>25-29</b>	0.02	0.06	0.04	0.02	0.03
<b>30-34</b>	0.04	0.01	0.04	0.01	0.03
<b>35-39</b>	0.02	0.04	0.08	0.06	0.04
<b>&gt;= 40</b>	0.10	0.08	0.07	0.06	0.02
<b>Total</b>	0.04	0.04	0.04	0.03	0.03

Source: DMSS 1/19/2022

Rate calculated in counts per 1,000 persons per year. Data with unknown values excluded.

\* Selected Diagnoses:

G37.3 Acute transverse myelitis in demyelinating disease of CNS