Rare Diseases in Pennsylvania

Comprehensive Report Issued by the Pennsylvania Rare Disease Advisory Council Pursuant to Act 14 of 2017

July 2019

PENNSYLVANIA
RARE DISEASE
ADVISORY COUNCIL

Letter from the Chair

July 2019

Health and Human Services Committee, Pennsylvania Senate
Health Committee, Pennsylvania House of Representatives

On behalf of the Pennsylvania Rare Disease Advisory Council (Council), it remains my distinct honor and privilege to submit the comprehensive report as required by Section 6(b) of Act 14 of 2017. One year ago, the Council delivered the initial report establishing its priorities through 2025, along with approaches for achieving those goals. The Council has remained steadfast in its mission: **to improve the quality of life for all those affected by rare diseases in Pennsylvania,** by acknowledging and addressing their unique needs and taking meaningful actions to uncomplicate their journey.

Representatives of the Council discussed the challenge of achieving a complete understanding of the incidence and prevalence of rare diseases in Pennsylvania with you and your staff this past January. While that challenge is formidable, the Council's dedication and progress are evident in this report. The Council, for example, has identified protocols for mining multiple, current and future data sets which are beginning to provide a glimpse into the counts of those Pennsylvanians with a rare disease. The Council continues to push forward with multiple initiatives to address the true impact of rare disease on Pennsylvanians.

This report does not, nor could any report, fully address the needs of the rare disease community. As you will read, the needs are nearly as varied as the more than 7,000 known rare diseases. There is, however, a consistent theme with respect to needs: The rare disease community is highly motivated, highly dedicated, and resilient. They work daily to overcome the direct impact of the diseases on their health, as well as the indirect emotional, physical, financial and professional burdens.

The Council does not pursue the identification and understanding of the needs of the rare disease community based only on their own experiences. Rather, they are striving to engage every individual with a personal or professional connection to rare disease. This ongoing assessment is a significant undertaking and will inform the Council's work for years to come. That, in turn, will benefit many organizations and individuals across Pennsylvania.

Nearly two years ago, this Council formed, hoping to become a voice for the approximately 1.2 million Pennsylvanians affected by rare disease. This report advances that effort with sincerity and humility, while doing so with a keen sense of the work that remains. I look forward to the continued work of its members and with each of you. Thank you for your leadership and involvement.

Very Respectfully,

Tomas J. Aguilar
Chairman, Pennsylvania Rare Disease Advisory Council
Director, Bureau of Health Promotion & Risk Reduction
Pennsylvania Department of Health

Council Agreement Update

We, the undersigned, as members of the Pennsylvania Rare Disease Advisory Council, by our signatures below, hereby forward this report pursuant to Act 14 of 2017. The report contains a discussion of the investigation into the incidence and prevalence as well as the beginning of the assessment of the needs of the rare disease community in the Commonwealth of Pennsylvania. As a body, we agree with the conclusions, assessments, and goal statuses contained within the report.

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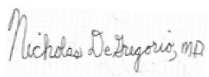

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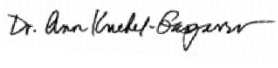

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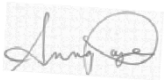

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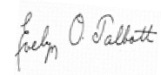

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Executive Summary

As specified in the authorizing legislation creating the Pennsylvania Rare Disease Advisory Council (Act 14 of 2017), the Council is tasked with submitting a year two comprehensive report identifying, as best as possible, the incidence and prevalence of rare disease in Pennsylvania, the needs of the rare disease community, and feasible actions to address those needs.

Incidence and Prevalence

With the passage of the Orphan Drug Act in 1983, the U.S. Congress defined a rare disease as a condition affecting less than 200,000 U.S. residents. In the initial report of the Council (2018), an estimated 10 percent of the U.S. population (as identified by the National Organization for Rare Disorders) is cited as living with a rare disease. In the absence of a known published estimate of the incidence or prevalence of rare disease in Pennsylvania, the Council applied this national percentage (as a proxy for prevalence) to Pennsylvania's population to estimate incidence. This resulted in an estimate of approximately 1.2 million residents living with a rare disease in Pennsylvania.

In year two, the Council developed a methodology for identifying rare disease incidence and prevalence within the Commonwealth that compares existing coding data (ICD-10 codes) to blinded data from Pennsylvania's major hospital systems, claims data from commercial insurers, managed care organizations, Medicare, Medicaid and Department of Health data. A number of factors limit the resolution of this estimate, most notably the fact that only 1,494 recognized rare disease codes are in use compared to the approximately 7,000 known rare diseases.

An initial data run from the Pennsylvania Health Care Cost Containment Council (PHC4) found 28,739 primary diagnoses of rare disease among hospitalized Pennsylvania residents in 2016 and 27,865 such diagnoses in 2017. Neoplasms deemed rare accounted for 40.41 percent of diagnoses in 2016 and 40.69 percent in 2017. Tables 1 and 2 of the report highlight the diagnoses made through hospitalization with very little variation from 2016-17. For both years, the initial diagnosis of a rare disease upon hospitalization skewed heavily toward the aged, with over 70 percent in both years being comprised of those aged 50 and over (as illustrated in Tables 4 and 5).

For calendar year 2018, the top 20 rare diseases were identified for Pennsylvania Medicaid beneficiaries based on claims data. Overall, there were 215,922 Medicaid claims specific to rare disease among the approximately 3.4 million unique individuals eligible for Medicaid in 2018. Table 3 in the report highlights the top 20 (Atrial Septal Defect being the most common of the rare diseases with 8,615 claims).

Now, with the ability to make comparisons beyond hospitalization, using commercial and public payer information, an estimate of rare disease in Pennsylvania can be derived. Many rare diseases are chronic in nature and diagnosed without an initial hospitalization.

Additionally, the number of rare disease specific codes is expected to exceed 5,000 with the release of ICD-11 codes, tentatively scheduled for 2022, providing much more clarity around incidence and prevalence.

Needs of the Rare Disease Community in Pennsylvania

This report shares powerful testimonials from patients living with one or more rare diseases that underscore the magnitude and complexity of the true needs in the rare disease community in Pennsylvania. Their individual stories illustrate perseverance, strength and resolve. Notably, the life stories of these individuals reveal common challenges, often monumental, associated with inadequate availability of critical resources, programs and support.

In order to understand these needs, the Council has developed and will administer a rare disease community needs assessment survey – the first of its kind in the nation. The survey will explore topics such as:

- Diagnostic delay;
- Access to diagnostic and specialty care;
- Access to treatment and support, including emergency medical care; inpatient care and psychosocial support;
- Costs, including treatment, care, travel, time away from work or school;
- Insurance coverage and disability benefits; and
- Barriers and other difficulties.

The survey results will raise awareness of these issues among the citizens of the Commonwealth through the Council's website and social media platforms. They will also inform the Council's future policy and resource recommendations.

Goals and Objectives

The report concludes with an update on the Council's goals and objectives to date, including the status of the following initiatives:

- Logo development;
- User-friendly website;
- Epidemiological instrument and data-mining program;
- Needs assessment survey of individuals with rare diseases;
- Centralized database of rare disease information;
- Rare disease navigation service;
- Marketing resources;
- Best practices and policy recommendations;
- Information technology infrastructure and expertise; and
- Council governance.

Introduction

In 2017, Governor Tom Wolf signed Act 14 creating the Pennsylvania Rare Disease Advisory Council. The Council was established to:

- Coordinate statewide efforts to study the incidence and prevalence of rare diseases within Pennsylvania and the status of the rare disease community;
- Serve as an advisory body on rare diseases to the General Assembly and to all relevant state and private agencies that provide services to, or are charged with the care of, individuals with rare diseases; and
- Coordinate the performance of the Council's duties with those of other rare disease advisory bodies, community-based organizations, and other public and private organizations within the state to ensure greater cooperation between entities within the state and federal agencies regarding the research, diagnosis and treatment of rare diseases.

Since the Council's inception in 2017, it has sought to determine the incidence and prevalence of rare diseases throughout the Commonwealth in term of the lives affected. It has progressed from the estimated population delivered in the year one report to a methodology for analyzing patient records. Determining an actual count of rare disease patients will require collaboration with additional stakeholders to obtain and analyze data.

The Council has prepared a survey to compile the needs of the rare disease community, rather than theorizing what may be needed. This will be the first statewide survey of the needs of the rare disease community. The Council plans to partner with stakeholders to reach a broad audience of patients and families. The survey results will help shape future Council initiatives and will strengthen its advocacy for the rare disease community.

Earlier this year, the Council launched https://pardac.org/, a website to share news and events for and about the rare disease community. Together with its Facebook and Twitter accounts, the Council aims to raise awareness for and engagement in its varied initiatives.

Having a rare disease impacts every facet of the daily lives of patients and their families throughout the Commonwealth. This Council is committed to help inform the state about ways to improve these lives.

Follow the Rare Disease Advisory Council:

www.facebook.com/PARareDiseaseAdvisoryCouncil/
@PARareDiseaseAdvisoryCouncil

@PARareDisease

Incidence and Prevalence of Rare Disease

The purpose of this section is to define incidence (new cases per a defined time period) and prevalence (existing cases regardless of onset) initially by broad category and, in the future, by specific disease breakdown and to establish the methodology for estimating incidence and prevalence of rare diseases in the Commonwealth. Knowledge of the prevalence is essential in planning resource allocation and state budgeting to provide optimal medical care, as well as to improve the experience of care for the rare disease population.

Disclaimer: The data presented in this report represent early estimates of the incidence and prevalence of rare diseases in Pennsylvania. The data should therefore only be used as a means to better understand basic trends within the limitations described in this report and to support the development of policies and resources that will allow for a more accurate determination of the incidence and prevalence of rare disease in Pennsylvania.

Definitions and Importance of Incidence and Prevalence

In epidemiologic terms, the definition of incidence is the measure of the probability of occurrence of a given medical condition in a population within a specified period. Although sometimes loosely expressed simply as the number of new cases during a specified period, it is better expressed as a proportion or a rate with a denominator. The challenge in determining incidence is the ability to identify a new case during a specified time period. This has been difficult historically, given limited resources and non-electronic record keeping. New technologies that make reporting less onerous present an opportunity for Pennsylvania to develop a system of reporting that could be modeled nationwide.

The definition of prevalence is the total number of individuals in a population who have a disease or health condition during a specific period, usually expressed as a percentage of the population.

Careful estimates of incidence and prevalence of rare diseases will allow many important stakeholders (patients, state, payers, et al) to develop plans for how best to provide and finance care for rare disease patients in Pennsylvania by weighing the short-term budgetary costs of therapies versus the long-term value of potential financial savings and better health outcomes.

I have tried very hard not to let my rare disease define who I am. I do not want to be know as 'that sick person'. **Still, my rare disease affects me every day. It affects my wife and children, it affects me financially, it affects my quality of life, and it affects my ability to have long-term plans or stability.**

Tom - Homozygous Familial Hypercholesterolemia Patient Advocate
Bellefonte, Pennsylvania

Toward A Better Estimate of Rare Disease Patients

With the passage of the Orphan Drug Act in 1983, the U.S. Congress defined a rare disease as a condition, whether hereditary or spontaneous in nature, affecting fewer than 200,000 individuals in the United States. The European Orphanet report series defines a rare disease by a prevalence of not more than five affected persons per 10,000 individuals.[1] Rare Disease Europe (EURODIS) uses a similar definition: a disease or disorder that affects fewer than one in 2,000 citizens.[2]

There is currently no known published estimate of the incidence or prevalence of rare disease in Pennsylvania and no rare disease registry. In the initial report of the Pennsylvania Rare Disease Advisory Council, an estimated 10 percent of the U.S. population was cited as living with a rare disease. Applying this percentage to the census of Pennsylvania, there are an estimated 1.2 million residents living with a rare disease in Pennsylvania.

As stated in the authorizing legislation, the Council is required to begin the process of estimating the incidence and prevalence of rare disease in Pennsylvania in year two. To do this, the Council has explored potential methods to identify processes and data that can more accurately determine the Pennsylvania rare disease population. There are many questions related to this task, such as:

- Is the estimate of 1.2 million Pennsylvania residents living with a rare disease accurate?
- Are there areas of increased risk for rare disease among residents within the Commonwealth?
- Do certain rare diseases have higher or lower rates in the Commonwealth than the national average?
- Are there regions within the Commonwealth where certain rare diseases are more common?
- What groups within Commonwealth are most affected?
- What initiatives can Pennsylvania implement statewide that will improve the accuracy and resolution of incidence and prevalence of rare diseases going forward?

It's important to consider that there are multiple hospital and physician networks that serve rare disease patients in the Commonwealth and that influence state residency by the rare disease community. Patients and their families may choose to live in or relocate to Pennsylvania to

> For the three years prior to my diagnosis, I was fully aware of the changes and problems I was experiencing and reported them to medical professionals as they occurred. I can't help but feel that **I could have been diagnosed sooner if there were more awareness of the disease and advocacy for patients who present with symptoms.**
>
> **DaVita** – Cushing's Disease
> Philadelphia, Pennsylvania

obtain treatment for their disease. For example, rare bleeding disorders such as hemophilia have a disproportionately larger population in Pennsylvania compared to the national average, which is due, in part, to the network of seven hemophilia treatment centers within the state. By using ICD-10 data from multiple sources, the Council aims to establish an accurate count of the rare disease population within the state, both for rare diseases in general and specific diseases.

ICD-10 Data

ICD-10 is a clinical cataloging system used by the health care industry, providers, coders, IT professionals, insurance carriers, government agencies and researchers. ICD-10 codes are used to note diseases on health records, to track epidemiological trends and to assist in medical reimbursement decisions**.**

The World Health Organization (WHO) owns, develops and publishes ICD codes, and national governments (including the U.S.) and other regulating bodies have adopted the system. WHO publishes minor updates every year and major updates every three years.

The Council has begun the work of obtaining ICD-10 codes for specific rare diseases and will seek assistance from insurers (both commercial and government) and health care providers in sharing their blinded data for Pennsylvania residents. As mentioned, there are challenges and limitations. Most notably, there are 1,494 identified ICD-10 codes for rare disease in contrast to approximately 7,000 rare diseases identified according to the National Organization for Rare Disorders (NORD).

Despite these challenges, the initial findings from an ICD-10 frequency analysis should provide the first data analysis of individuals hospitalized with rare disease in Pennsylvania. Additionally, the Council recognizes the data is not finite and there will be a continual need for additional data analysis. With the launch of the ICD-11 codes, there will be more than 5,000 codes for specific rare diseases. The Council's analysis will always be retrospective and never complete.

ICD-10 Data to Estimate Incidence and Prevalence

There are currently two ways of capturing overall incidence or prevalence of rare diseases that have an assigned ICD-10 code:

- The use of de-duplicated Medicaid MCO, Medicaid Fee for Services, and commercial health insurance visits and claims for the diagnosis and treatment of a rare disease; and
- Hospital visit for a diagnosis or exacerbation related to a rare disease requiring medical attention.

The former might be expected to be more complete, as it would cover all locations of care and identify individuals with rare diseases who have not been hospitalized. However, it may involve more duplication from multiple claims of primary and

specialty care received over time, which would require correction. There are also self-report mechanisms, which include a verification of diagnosis via websites sponsored by rare disease organizations, such as Amyotrophic Lateral Sclerosis Association, Multiple Sclerosis Association, Sickle Cell Society, Cystic Fibrosis Foundation and American Lung Association.

Hospitalizations of state residents in Pennsylvania are captured over time and are collected by PHC4. For each hospitalization, PHC4 assigns a unique anonymized ID to an individual. This unique code can be used to determine repeat visits and can capture an individual's health care experience for persons with and without a rare disease. Coding for these diseases has not kept up with discovery, however, and will be discussed later in this section.

Other examples of the ability to capture rare disease include the Pennsylvania Cancer Registry and newborn screening. The registry was established in 1982 and registers the incidence and prevalence of all cancers, including rare cancers. Newborn screening, which began in 1965, detects certain defects present at birth, including rare treatable genetic disorders which, when treated promptly, can dramatically improve outcomes.

In Pennsylvania, all babies are screened, within 24 to 48 hours of birth, for certain conditions through dried blood spot screening, hearing screening, and pulse oximetry screening to detect critical congenital heart defects (CCHD). The federal Recommended Uniform Screening Panel (RUSP) includes 35 core conditions and 26 secondary conditions that the U.S. Department of Health and Human Services advises states to include in newborn screening.[3] Pennsylvania currently screens newborns for 37 conditions, while Delaware (52), New Jersey (57) and New York (60) screen for additional conditions.[4] Next-generation DNA sequencing approaches hold great promise in further advancing newborn screening. A statewide birth defects registry is being considered to centralize newborn screening data.

My son Pete passed away in 2018 of spinal muscular atrophy (SMA). **Early diagnosis of rare disease is essential for successful treatment. Before he passed, Pete advocated for adding SMA to the newborn screening panel.** His impact has helped shape how we think about and prepare for life with a rare disease. We will continue to promote awareness of SMA and advocate for those affected with this rare disease.

Allyson, Parent of child who had SMA

Montgomery County, Pennsylvania

Methodology

Through the auspices of the Pennsylvania Department of Health's bureaus of Epidemiology and Health Promotion and Risk Reduction, a request was made to establish rare disease baseline rates for hospitalized patients in Pennsylvania. The analysis will give an estimate

of patients who were hospitalized with a rare disease as the primary or secondary diagnosis by age; an analysis by gender and race/ethnicity may be possible in the future. A request was made for a standard dataset of inpatient discharge data by quarter for 2013 thorough 2017 for each of the nine health regions and all 67 counties in Pennsylvania. The data describes the distribution of cases of rare diseases with an ICD-10 code for Pennsylvania within the total number of hospitalized patients. Data for 2013-2015 were not coded with ICD-10 codes; therefore, data is presented for 2016-2017 only.

Each person's record was assigned a unique, anonymized pseudo identifier. Information was provided on age, race, gender, and primary and secondary diagnoses. ICD-10 codes for rare diseases were obtained from Orphanet.com and compiled. Code was then written using SAS 9.4 Software and applied to the primary diagnosis codes within the PHC4 data set of over 1.58 million individual records (estimated annually) on all hospitalizations. The 1,494 codes deemed rare were matched to a specific ICD-10 code. From this, the number of individuals hospitalized with and without a rare disease primary diagnosis was determined. Records were de-duplicated for those individuals with more than one rare disease, maintaining the first hospitalization. The remaining hospitalizations without a primary diagnosis of a rare disease were included in the non-rare disease hospitalization group.

An additional analysis considered any secondary diagnoses of rare disease within the 2017 1.58+ million hospitalization records where the primary diagnosis was not a rare disease. Secondary conditions are those that coexist at the time of admission, or develop subsequently, and that affect the patient care during the current episode; they may be known or diagnosed specifically or generally, as "other diagnoses." PHC4 allows a maximum of 17 secondary diagnoses. This analysis accounted for individuals hospitalized in an emergent situation (e.g., pneumonia, sepsis, etc.) that can overshadow an underlying cause or secondary diagnosis.

Important Limitations to the Council's 2019 Estimates

The estimates of the incidence and prevalence of rare diseases in Pennsylvania in this report are derived from records from Pennsylvania's major hospital systems/managed care organizations, Pennsylvania Medicare, Medicaid and Department of Health data, a database of hospitalizations in

> Having a rare disease can be a challenge for the medical profession; the patient becomes the educator and medications are often limited. **In the case of an emergency, doctors and nurses are usually hesitant to believe what the patient is telling them and can delay proper care.** If the rare disease is also a known incurable disease, it is like having an alarm clock without an off switch for the snooze.
>
> **Paul** – Cystinuria
> Lancaster, Pennsylvania

Pennsylvania (PHC4), and a limited number of other sources. The estimates represent a first attempt at using secondary data sources to develop a methodology going forward to estimate the burden of disease and provide an estimate of specific disease outcomes for the citizens of Pennsylvania.

A number of factors limit the resolution and accuracy of the estimated incidence and prevalence of rare diseases in Pennsylvania; therefore, the estimates should be considered preliminary.

- Individuals with rare diseases not diagnosed or treated by the major hospital systems or insured through managed care organizations, Medicare or Medicaid may not have been captured in the data sets used to form the estimates, especially if they were not hospitalized during the periods assessed. This may be especially acute for Pennsylvania's rural communities and special populations (e.g., the Plain communities).
- The estimates are limited by the current diagnostic coding, specifically, the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10), which accounts for only 1,494 of the roughly 7,000 rare diseases identified to date (a nearly 80 percent gap in known diseases to available codes). In addition, ICD-10 codes lack the specificity necessary to resolve many rare diseases from existing medical records/databases.
- According to the International Rare Diseases Research Consortium, researchers are identifying 250 to 280 new rare diseases annually.[5] Diagnostic coding — even the anticipated ICD-11 diagnostic code system — is not keeping pace with the rate of discovery of new rare diseases.
- Secondary diagnoses are not always immediately verified by medical records that are "on hand."[6]
- There is not a registry or reporting system for individuals with undiagnosed diseases in Pennsylvania and, therefore, no straightforward way to include them in the estimate.

The U.S. transition from ICD-10 to ICD-11 will not begin until 2022.[7] Given the gap in codes between ICD-10 and ICD-11, the Council believes any preliminary estimate may underestimate rare diseases in Pennsylvania. Data do not need to be complete to be useful; much can be learned from the information the Council has obtained to

I don't like it when kids are scared to play with me because they think I'm contagious. I don't like being the sick one. **In my eyes, I'm just a normal kid.** I can do anything and everything a normal person can. If you didn't know I had a rare disease, you would just think I'm a normal kid and nothing about me was different.

Audrianna (11 years old) – Autosomal Dominant Polycystic Kidney Disease (ADPKD)
Plymouth Meeting, Pennsylvania

date. Over time, as the code set expands, the data, analyses and resulting estimates will become more accurate.

As the code set expands, health informatics approaches that mine electronic medical records for data that is consistent with diagnosis of a rare disease could be used to refine estimates of the incidence and prevalence of rare diseases. This intensive process would require substantial resources.

Results

Table 1 shows the distribution of the frequency of hospital visits by major ICD-10 disease groupings from highest to lowest proportion of cases. Neoplasms deemed rare account for the greatest number of hospital visits (40.41 percent), followed by diseases of the nervous system (9.81 percent), diseases of the blood and blood-forming organs, and certain disorders involving immune mechanisms (9.28 percent), endocrinological, nutritional and metabolic disease (8.09 percent), and diseases of the musculoskeletal system and connective tissue conditions (8.09 percent).

The specific rare diseases of each ICD-10 grouping are shown in Appendix 1.

Table 1: Primary Diagnoses of Rare Disease Among Hospitalized Pennsylvania Residents, 2016

Rare Disease by ICD-10 Grouping	Frequency	Percentage
For an expanded list of specific rare diseases within each group, see Appendix 1		
Neoplasms (C00-D49)	11,614	40.41
Diseases of the nervous system (G00-G99)	2,820	9.81
Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism (D50-D89)	2,667	9.28
Endocrine, nutritional and metabolic diseases (E00-E89)	2,325	8.09
Diseases of the musculoskeletal system and connective tissue (M00-M99)	1,650	5.74
Injury, poisoning and certain other consequences of external causes (S00-T88)	1,594	5.55
Congenital malformations, deformations and chromosomal abnormalities (Q00-Q99)	1,539	5.36
Certain infections and parasitic diseases (A00-B99)	1,466	5.10
Diseases of the genitourinary system (N00-N99)	706	2.46
Diseases of the circulatory system (I00-I99)	571	1.99
Diseases of the digestive system (K00-K95)	516	1.80
Mental, behavioral and neurodevelopmental disorders (F01-F99)	489	1.70
Diseases of the respiratory system (J00-J99)	381	1.33
Diseases of the skin and subcutaneous tissue (L00-L99)	136	0.47
Symptoms, signs and abnormal clinical laboratory findings not elsewhere classified (R00-R99)	107	0.37
Pregnancy, childbirth and the puerperium (O00-O9A)	65	0.23
Diseases of the eye and adnexa (H00-H59) and of the ear and mastoid process (H60-H95)	57	0.19
Certain conditions originating in the perinatal period (P00-P96)	36	0.13
Total Rare	28,739	
Not Rare (Never rare disease hospitalization in 2016)	912,145	

Source: Pennsylvania Health Care Cost Containment Council (PHC4)
Data limited due to primary diagnosis only; not representative of statewide frequency
See Appendix 3 for secondary diagnosis of rare disease.

Table 2 shows a similar frequency distribution of hospital visits by major ICD-10 disease groupings for 2017. Neoplasms deemed rare still account for the greatest number of hospital visits, however the percentage increased to 40.69 percent.

Table 2: Primary Diagnoses of Rare Disease Among Hospitalized Pennsylvania Residents, 2017

Rare Disease by ICD-10 Grouping	Frequency	Percentage
For an expanded list of specific rare diseases within each group, see Appendix 1		
Neoplasms (C00-D49)	11,338	40.69
Diseases of the nervous system (G00-G99)	2,851	10.23
Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism (D50-D89)	2,661	9.55
Endocrine, nutritional and metabolic diseases (E00-E89)	2,255	8.09
Diseases of the musculoskeletal system and connective tissue (M00-M99)	1,561	5.60
Injury, poisoning and certain other consequences of external causes (S00-T88)	1,555	5.58
Congenital malformations, deformations and chromosomal abnormalities (Q00-Q99)	1,421	5.10
Certain infections and parasitic diseases (A00-B99)	1,389	4.98
Diseases of the circulatory system (I00-I99)	635	2.28
Diseases of the genitourinary system (N00-N99)	577	2.07
Diseases of the digestive system (K00-K95)	489	1.75
Mental, behavioral and neurodevelopmental disorders (F01-F99)	415	1.49
Diseases of the respiratory system (J00-J99)	337	1.21
Diseases of the skin and subcutaneous tissue (L00-L99)	167	0.60
Symptoms, signs and abnormal clinical laboratory findings not elsewhere classified (R00-R99)	96	0.34
Diseases of the eye and adnexa (H00-H59) and of the ear and mastoid process (H60-H95)	56	0.20
Pregnancy, childbirth and the puerperium (O00-O9A)	37	0.13
Certain conditions originating in the perinatal period (P00-P96)	25	0.09
Total Rare	27,865	
Not Rare (Never rare disease hospitalization in 2017)	900,218	

Source: Pennsylvania Health Care Cost Containment Council (PHC4)
Data limited due to primary diagnosis only; not representative of statewide frequency
See Appendix 3 for secondary diagnosis of rare disease.

Using an alternate data set for hospital visits, namely medical claims data from the Pennsylvania Department of Human Services, Table 3 shows the top 20 rare diseases by code among approved Pennsylvania Medicaid Claims from Calendar Year 2018. Each of the 773 rare diseases comprises See Appendix 3 for full data set. The data imply a significant burden of disease associated with having a rare disease.

Table 3: Top 20 Rare Disease Cases from Pennsylvania Medicaid Claims, Calendar Year 2018

Diagnosis Code	Diagnosis Level Name	Count
Q211	Atrial septal defect	8,615
E781	Pure hyperglyceridemia	8,119
M722	Plantar fascial fibromatosis	7,407
Q909	Down syndrome, unspecified	6,484
E784	Other hyperlipidemia	5,871
I420	Dilated cardiomyopathy	5,388
D573	Sickle cell trait	5,268
N800	Endometriosis of uterus	3,980
D571	Sickle cell disease without crisis	3,885
N809	Endometriosis, unspecified	3,409
D869	Sarcoidosis, unspecified	3,319
D473	Essential thrombocythemia	3,300
H905	Unspecified sensorineural hearing loss	3,179
D751	Secondary polycythemia	2,892
D550	Anemia due to G6pd deficiency	2,812
P220	Respiratory distress syndrome of newborn	2,810
E230	Hypopituitarism	2,728
D519	Vitamin B12 deficiency anemia, unspecified	2,693
Q231	Congenital insufficiency aortic valve	2,587
E806	Other disorders of bilirubin metabolism	2,341
	All other diagnoses* **	128,835
	Total	215,922

Source: Pennsylvania Department of Human Services

* “Other diagnoses” is interpreted as additional conditions that affect patient care in terms of requiring one of the following:

1. Clinical evaluation
2. Therapeutic treatment
3. Diagnostic studies
4. An extended length of stay
5. Increased nursing care and/or monitoring

** All other diagnoses includes 509 Codes with 11+ Claims, does not include 239 ICD-10 Codes with 1 to 10 counts. See Appendix 2.

The age distribution of the first rare disease primary diagnosis hospitalization in 2016 or 2017 is shown in Tables 4 and 5. The greatest proportion of hospitalizations for rare diseases is among individuals 50 years of age and older (70.25 percent in 2016 and 72.12 percent in 2017).

The frequency data for children 5 years of age or younger is likely much higher than shown in Tables 4 and 5. Orphanet estimates that roughly 80% of rare diseases have a genetic origin. Half of those affected by a genetic disorder are children.[8]

Table 4: Age Distribution at First Rare Disease Visit, 2016

Age Group	Frequency	Percent
≤ 5 years of age*	633	2.20
6-19 years old	1,398	4.86
20-49 years old	6,516	22.67
≥50 years of age	20,192	70.26
Source: Pennsylvania Health Care Cost Containment Council (PHC4) Data limited due to primary diagnosis only; not representative of statewide frequency *The frequency data for children 5 years of age or younger is likely much higher.		

Table 5: Age Distribution at First Rare Disease Visit, 2017

Age Group	Frequency	Percent
≤ 5 years of age*	465	1.67
6-19 years old	1,110	3.98
20-49 years old	6,194	22.23
≥50 years of age	20,096	72.12
Source: Pennsylvania Health Care Cost Containment Council (PHC4) Data limited due to primary diagnosis only; not representative of statewide frequency *The frequency data for children 5 years of age or younger is likely much higher.		

Future Work with Pennsylvania Health Datasets

A request match for rare disease codes against anonymized medical record information will be made to commercial health care insurers in Pennsylvania. Prevalence of rare diseases in Pennsylvania may then be estimated by:

1. Identifying the total number of unique individuals with Medicare Advantage insurance and a rare disease diagnosis in both inpatient and outpatient settings;

2. Identifying the total number of unique individuals with commercial insurance and a rare disease diagnosis in both inpatient and outpatient settings;
3. Adding together the Medicare Advantage and commercial insureds with rare diseases;
4. Eliminating individuals with primary commercial and secondary Medical Assistance insurance to avoid counting these individuals twice; and
5. Comparing the number of total unique individuals with rare diseases to the overall population in Pennsylvania to determine prevalence as a percentage of the population or as the number of cases per 10,000 or 100,000 Pennsylvanians.
    a. Subsequently, prevalence may also be estimated for rare diseases categories or for individual rare diseases.
    b. More specificity in coding diseases can be applied given the cell sizes adhere to rules to protect confidentiality.

Future work will also include determining hospitalization rates for specific rare diseases by year by age, gender, race and ethnicity. The Council will de-duplicate records for the secondary diagnoses to determine the number of individuals who reported a rare disease or multiple rare diseases over time both for primary and secondary ICD-10 codes to determine a better estimate of rare disease medical encounters in the population.

Needs of the Rare Disease Community

The approximately 1.2 million Pennsylvanians living with a rare disease and their families deal with profound challenges and barriers, burdens of needs, and uncertainty every single day.

Several people graciously shared their stories as examples of what the rare disease community faces every day in Pennsylvania.

Anna Payne, an individual living with a rare disease:

> "I was never supposed to be an adult with a rare disease. When I was born, the life expectancy of a patient with Cystic Fibrosis was 17 years. I have fought to survive this long. Every day, I spend four hours doing breathing treatments and take about 50 pills. These treatments and medications help me breathe and digest my food—two simple things most people take for granted. The older I get, the more time I spend doing breathing treatments, including in the middle of the night. This disease affects every facet of my life and as I have gotten older, that has only intensified. **My life revolves around ensuring I have time to complete my treatments and planning when I have to take time from work for medical appointments or hospitalizations, which might mean I don't get paid or cannot take a vacation that year.**"

Joe Coyne, a parent with a child affected with a rare terminal illness:

> "Navigating the system has been very difficult. **When we started our journey, we had to not only withstand the impact of receiving a devastating diagnosis, but we also had to find doctors while in shock. The time needed to do this was very great and resources were few.** In time, we came to terms with our diagnosis and were able to focus on finding treatments, working with legislators and living meaningful lives. Today we continue to struggle with our future but find purpose in helping others by creating a resource to connect rare disease patients, families, and needed related service providers."

Sharon O'Shaughnessy, a parent navigating the transition from childhood to adulthood:

> "At 16, our daughter's ultra-rare illness suddenly took the form of transient psychosis. We knew it was metabolic, but **the local waits for pediatric metabolic specialist appointments were so long that the five-month phase passed before we ever got an appointment.** At 20, when it happened again, we were confronted with the fact that our local pediatric hospitals would not see a new patient after age 18. **We ended up having to seek care in another state 10 hours away.** My hope is that we can streamline this process so other parents seeking team-based multi-specialist appointments through the pediatric to adult transition can be quickly seen and followed here in Pennsylvania."

Dr. Gerard Vockley, Chief Division of Medical Genetics, Director, Center of Rare Disease Therapy:

> "We see patients with rare disease from all walks of life—from Pennsylvania and across the country. Recognizing one of the >7,000 known rare diseases is a challenge for busy physicians in a general clinical setting, and thus many patients and families face a significant therapeutic odyssey, going from one care provider to another looking for answers for unexplained medical problems. Reaching a diagnosis allows care providers, patients, and families to focus on therapy and improving life. However, rare disease therapies are often complicated, expensive and bring a new set of challenges for care providers, patients, and families. Rare diseases require an integrated approach to diagnosis, treatment, and support that integrates all aspects of patient care from primary care physicians to highly specialized medical services. **Financial concerns, including the high cost of therapy, and the need for life long treatment lead to financial stresses on patients and families that require special attention from health care providers, hospitals, and insurers.** Diagnosis and treatment of rare diseases is likely to be a signature effort of medicine in the coming years and requires thoughtful and concerted action from across the health care, advocacy, and government spheres."

These are just a few stories of perseverance, strength and resolve in the face of great needs and inadequacies in critical resources, programs and support.

The Upcoming Needs Assessment Survey

It is of critical importance that the Council receives broad statewide input from those affected to better understand and quantify the needs of the rare disease community. To this end, the Council has developed a survey for the rare disease community.

The Council is not aware of any other state that has administered a statewide survey to assess the difficulties and needs of those affected by rare disorders. However, a national survey published by the Canadian Organization for Rare Disorders (CORD) in 2015 provides a useful model for questions about diagnostic delay, access to diagnostics and specialty care, access to treatment and support (including psychosocial

When you have a rare disease, finding the right combination of treatments is often done by trial and error. Since there is no cure, you wonder how long the medication will continue to be effective and how the disease will progress. **We need government support to increase the amount of research and to subsidize the cost of treatments.**

Terry – Pulmonary Fibrosis, Northampton County, Pennsylvania

support), and costs related to care[9]. Additionally, with input from individuals with rare disorders, as well as other organizations such as NORD in the U.S., the Council's survey includes questions regarding insurance coverage, time, and costs related to travel and taking time away from work or school, challenges associated with emergency medical care and inpatient care, and questions regarding disability benefits.

The survey is currently undergoing beta-testing. With Institutional Review Board approval and funding for marketing of this survey across the state, the Council intends to conduct the survey in Fall 2019. Informed by robust needs assessment data, the Council will revisit its goals, objectives and activities to improve the quality of life for those affected by rare diseases in Pennsylvania.

Implications

The realization that there are approximately 7,000 rare disorders, each with its own manifestation, prognosis, and management, might initially inhibit attempts to define common needs among them. The assumptions underlying Act 14 are that while there are properties unique to specific rare disorders, there are common challenges to daily life and we all place high value on life, liberty, and the pursuit of happiness. The Needs Assessment Survey will enable the Council to investigate the impact of rare disease and offer the opportunity for the rare disease community across the Commonwealth to provide input that will shape future focus and initiatives. The survey results may also serve as a benchmark, allowing for the study of the impact of future programs.

As a parent of a child with a rare disease, I struggle to maintain order. My school-age daughter needs a home health aide to watch her after school and on breaks. I constantly worry as **the aide turnover and callout rate is high due to the low pay**. We must negotiate multiple medical specialist visits (that will only increase as her degenerative condition worsens) and which parent will take time off to take her. **Although we are thankful to be living in a state that provides guaranteed medical assistance to our disabled child**, the ability to raise her at home with two parents working full-time is challenging. **There will come a point where one of us has to either work part-time or quit entirely to keep up this routine and it will hurt us mentally and financially**.

Kathy - Mucopolysaccharidosis IIIB parent (aka Sanfilippo Syndrome)
Bucks County, PA

Goals and Objectives Update

The Council is working diligently to fulfill the statutory requirements of Act 14:

1. Coordinate a statewide effort to fully understand the incidence, prevalence, status, and needs of individuals and the rare disease community in Pennsylvania;
2. Serve as an advisory board to the General Assembly and to other relevant state and private agencies charged with care and service to the rare disease community;
3. Coordinate efforts among other rare disease private and public bodies to advance research, diagnosis and treatment of rare disease; and
4. Fulfill the Council's ability to accept grants from the federal government, private foundations and other appropriate sources to develop and support programs related to rare diseases in Pennsylvania.

Recommended efforts, initiatives and services include the following:

A. Logo development;
B. User-friendly website;
C. Epidemiological instrument and data-mining program;
D. Needs assessment survey of individuals with rare diseases;
E. Centralized database of rare disease information;
F. Rare disease navigation service;
G. Best practices and policy recommendations;
H. Marketing resources;
I. Information technology infrastructure and expertise; *
J. Council governance; *
K. Council restructure; * and
L. Pennsylvania Rare Disease Stakeholder Summit. *

* These initiatives are additional activities the Council has incorporated into the existing objectives from the year one report.

The detailed table that follows describes recommended projects and initiatives, why they are important, and what they will accomplish. It also reports what has been completed, what is in progress, and what is recommended to accomplish the statutory requirements. The Council recognizes there are significant resource constraints to these goals and will continue to pursue every opportunity to ensure their success, including those outlined in Act 14, as well as the identification of potential commonwealth funding.

Project/Initiative	Brief Rationale/Need/Benefit	Progress and Pending Activity Resource requirements to be determined
A. Design and adopt a logo for the Rare Disease Advisory Council	The logo provides brand identity for the Council as a trusted agent and source of accurate information for the rare disease community.	• Develop logo – complete
B. Create and maintain a user-friendly website	The website will serve as a centralized source of information and available resources for rare diseases in the Commonwealth. It will serve to educate and help residents, health officials and individuals with rare diseases.	• Secure website developer – complete • URL acquisition – complete • Web development – in progress • Annual website maintenance (updating) – future
C. Develop and maintain an epidemiological instrument and program for data mining to characterize the incidence and prevalence of rare diseases in Pennsylvania	The epidemiological instrument and data mining program are necessary to provide an initial estimate of rare disease, incidence and prevalence. It must also support an ongoing reporting mechanism for annual updates. This will require modification to account for newly identified rare disease diagnoses and ICD-10 codes, as well as the projected transition to ICD-11 codes over the next few years. It will be a key data source to understand the current and future burden and projected costs of caring for those with rare diseases in the Commonwealth.	• Develop the epidemiological instrument and data mining program • Maintain the epidemiological instrument and data mining program
D. Develop and implement a needs	The survey is necessary to determine the types, locations, burdens of need, and barriers to care for	• Develop the survey – in process • Conduct the survey

Project/Initiative	Brief Rationale/Need/Benefit	Progress and Pending Activity Resource requirements to be determined
assessment survey to assess the needs of individuals with rare diseases geographically within Pennsylvania	individuals with rare diseases in Pennsylvania. Identifying key issues confronting the rare disease community will help guide improvement through policy changes and resource allocation.	• Analyze survey results
E. Develop and maintain a centralized and searchable database or registry of information for rare diseases in Pennsylvania	An informational database is necessary to house, maintain integrity, and report on all rare disease data collected. It will be the ultimate source of reliable information to understand incidence and prevalence trends, provide support for research and policy decisions, and gauge improvement in the diagnosis and care of individuals with rare diseases in Pennsylvania.	• Develop a centralized rare disease database • Maintain the database
F. Plan for a Rare Disease Navigation Service	Much like the Pennsylvania Telepsychiatry Line (TiPS) is available to support providers and patients/families with consultations and resources for behavioral health conditions, a similar program could be developed to support providers and patients with rare diseases. Centralized rare disease knowledge and expertise would assist and guide physicians, patients and families through the diagnostic maze, connect them to appropriate centers/providers, streamline diagnostic testing and link them to supportive resources. It would include professionals	• Hiring, salaries, benefits, office location, telephone, computers, training and other supplies

Project/Initiative	Brief Rationale/Need/Benefit	Progress and Pending Activity Resource requirements to be determined
	experienced in managing rare diseases, including specialized navigators, care coordinators and physician support.	
G. Best practices and policy recommendations	Work of the Council will include research and development of best practices and policy to promote the optimal diagnosis and management of rare diseases. Potential areas of focus may include but are not limited to: • Rare disease registries and data collection; • Genetic testing and newborn screening; • Codification of rare diseases; • Integrated care for rare disease patients; • Rare disease diagnostic/treatment pathways; • Orphan drugs; • Gene therapy; • Reimbursement and access to services; • Criteria for rare disease centers of excellence; and • Integration with social service policy designed to address and meet the unmet unique social needs of complex rare disease patients.	• Policy research, planning and program specialists
H. Marketing resources	Marketing resources and materials will enable the promotion of rare diseases needs and services in Pennsylvania. This may range from an awareness of	• Marketing resources and materials

Project/Initiative	Brief Rationale/Need/Benefit	Progress and Pending Activity Resource requirements to be determined
	support available for individuals and families, appropriate diagnostic services and providers with rare disease expertise. More efficient diagnoses and management may reduce the diagnostic odyssey and cost by avoiding unnecessary diagnostic testing.	
I. Information technology infrastructure and expertise	This will be needed to connect, collect and enable sharing of rare disease data among key stake-holders, including health insurance organizations, academic medical centers, cancer centers, rare disease clinics, etc.	• IT infrastructure and staff services
J. Council governance	To function as a decision-making, accountable and fiduciary entity, having a governmental structure is advised, e.g., chair, vice chair, secretary and treasurer.	• Develop structure and procedures
K. Restructuring the Council as a charitable foundation • Private 501(c)(3) • Public 509(a) • Other	Adopting a foundational structure would enable the Council to raise and receive funds, contract for services and disperse funds as appropriate to accomplish its goals. This would require both legal and accounting/tax advice if deemed appropriate by the General Assembly. It is assumed that this will be well received as a charitable contribution by donors and by policy makers as an innovative approach to addressing the need.	• Restructuring activity, including legal and accounting/tax consulting • Maintenance activity, including legal and accounting/tax consulting

Project/Initiative	Brief Rationale/Need/Benefit	Progress and Pending Activity Resource requirements to be determined
	Legal and accounting/tax consulting services will be essential to help design the appropriate structure and function of the Council to meet its current and future requirements to meet the needs of the rare disease community.	
L. Pennsylvania Rare Disease Stakeholder Summit	Establish a Pennsylvania Rare Disease Stakeholder Summit bringing together multiple stakeholders with an interest in rare diseases. The summit would support updates in research, identification of best practices, support information exchange, and networking among key representatives of the Commonwealth, patients and patient advocacy groups, providers, insurers, policy analysts, biopharmaceutical companies, etc.	• Facility • Speakers • Program/handouts • Food
* These initiatives are additional activities the Council has incorporated into the existing objectives from the year one report.		

Closing

The Council is prepared to delve much deeper into analysis to generate greater confidence in the identification of the incidence and prevalence of rare diseases in Pennsylvania. The preliminary data provides a snapshot based on diagnoses present upon discharge after hospitalization in a given year and rare disease claims filed on behalf of state Medicaid beneficiaries. The methodology and protocols employed in this analysis should assist in building upon this information as commercial insurance and potentially Medicare claims are reviewed.

Additionally, the Council looks forward to the completion of the needs assessment survey and collaboration with stakeholders throughout the Commonwealth. Doing so will result in a greater understanding of the range of needs from which to develop policy recommendations for the General Assembly and the administration. The issues impacting the rare disease community are not solely health care or insurance-related. They impact all aspects of society, including government and non-governmental policies, systems and programs. This complexity and scope underscore the importance of creating not only advocacy and awareness but also a recognition of the need for sufficient resources to effect these changes. The Council believes such investments will yield vast benefits.

The Council's resolve to work toward making Pennsylvania a national leader in transforming the lives of those affected by rare diseases has been reflected by numerous states modeling the efforts of this Council in Pennsylvania. This Council's members are proudly representing themselves across the Commonwealth and across the nation. In a few short years, Act 14 has positioned Pennsylvania as a leader in this profoundly important cause.

In the upcoming months, the Council looks forward to a collaborative approach to fulfill its mission to be an advocate for the rare disease community in Pennsylvania and provide unique and critical input regarding this community to both the General Assembly and the Wolf administration. Knowledge is power, and the Council is committed to continuing to provide this indispensable knowledge to both the Commonwealth's policy makers and its citizens. The Council strongly believes it has made significant first steps by acting on a common phrase within the rare disease community: "Out of the darkness … into the light."

Appendices

Appendix 1 Major Rare Conditions by Category (ICD-10)

Infections and parasitic diseases (A00-B99)

Cholera
Rare form of salmonellosis
Typhoid
Paratyphoid fever
Invasive non-typhoidal salmonellosis
Shigellosis
Botulism
Amoebiasis due to Entamoeba histolytica
Balantidiasis
Cryptosporidiosis
Isosporiasis
Plague
Tularemia
Brucellosis
Melioidosis
Rat-bite fever
Spirillary rat-bite fever
Streptobacillary rat-bite fever
Leptospirosis
Cat-scratch disease
Leprosy
Pulmonary non-tuberculous mycobacterial infection
Listeriosis
Tetanus
Diphtheria
Whooping cough
Meningococcal meningitis
Waterhouse-Friderichsen syndrome
Actinomycosis
Nocardiosis
Oroya fever
Legionellosis
Pontiac fever
Bacterial toxic-shock syndrome
Gonococcal conjunctivitis
Relapsing fever
Noma
Lyme disease
Epidemic typhus
Typhus-group rickettsiosis
Brill-Zinsser disease
Murine typhus
Scrub typhus
Rocky Mountain spotted fever
Spotted fever rickettsiosis
Q fever
Trench fever
Rickettsialpox
Poliomyelitis
Human prion disease
Progressive multifocal leukoencephalopathy
Rabies
Japanese encephalitis
Tick-borne encephalitis
Chikungunya
Rift valley fever
Yellow fever
Argentine hemorrhagic fever
Bolivian hemorrhagic fever
Lassa fever
Dengue fever
Crimean-Congo hemorrhagic fever
Omsk hemorrhagic fever
Kyasanur forest disease
Marburg hemorrhagic fever
Ebola hemorrhagic fever
Hemorrhagic fever-renal syndrome

Infections and parasitic diseases (A00-B99) [continued]

Herpes simplex virus encephalitis
Herpes simplex virus keratitis
Human infection by orthopoxvirus
Hepatitis delta
AIDS wasting syndrome
Hantavirus pulmonary syndrome
Coccidioidomycosis
Histoplasmosis
Paracoccidioidomycosis
Sporotrichosis
Chromomycosis
Aspergillosis
Cryptococcosis
Zygomycosis
Mycetoma
Malaria
Leishmaniasis
African trypanosomiasis
American trypanosomiasis
Pneumocystosis
Babesiosis
Amoebiasis due to free-living amoebae
Schistosomiasis
Cystic echinococcosis
Alveolar echinococcosis
Cysticercosis
Diphyllobothriasis
Hymenolepiasis
Dracunculiasis
Onchocerciasis
Filariasis
Lymphatic filariasis
Loiasis
Mansonelliasis
Trichinellosis
Ankylostomiasis
Strongyloidiasis
Anisakiasis
Angiostrongyliasis
Toxocariasis
Myiasis
Tungiasis

Neoplasms (C00-D49)

Malignant epithelial tumor of salivary glands
Squamous cell carcinoma of the esophagus
Adenocarcinoma of the esophagus
Leiomyosarcoma of small intestine
Hepatocellular carcinoma
Cholangiocarcinoma
Hepatoblastoma
Well-differentiated fetal adenocarcinoma of the lung
Familial melanoma
Multiple self-healing squamous epithelioma
Cutaneous neuroendocrine carcinoma
Pleural mesothelioma
Malignant peritoneal mesothelioma
Kaposi sarcoma
Salivary gland type cancer of the breast
Metaplastic carcinoma of the breast
Rare adenocarcinoma of the breast
Adenocarcinoma of the cervix uteri
Squamous cell carcinoma of the cervix uteri
Adenosarcoma of the cervix uteri
Malignant mixed epithelial and mesenchymal tumor of cervix uteri
High-grade neuroendocrine carcinoma of the cervix uteri

Neoplasms (C00-D49) [continued]

Primitive neuroectodermal tumor of the cervix uteri

Leiomyosarcoma of the cervix uteri

Rhabdomyosarcoma of the cervix uteri

Sarcoma of cervix uteri

Glassy cell carcinoma of the cervix uteri

Adenoid basal carcinoma of the cervix uteri

Adenoid cystic carcinoma of the cervix uteri

Papillary carcinoma of the cervix uteri

Malignant germ cell tumor of the cervix uteri

Carcinofibroma of the corpus uteri

Malignant mixed epithelial and mesenchymal tumor of corpus uteri

Primitive neuroectodermal tumor of the corpus uteri

Adenoid cystic carcinoma of the corpus uteri

High-grade neuroendocrine carcinoma of the corpus uteri

Low-grade neuroendocrine tumor of the corpus uteri

Malignant germ cell tumor of the corpus uteri

Malignant tumor of fallopian tubes

Paratesticular adenocarcinoma

Non-papillary transitional cell carcinoma of the bladder

Small cell carcinoma of the bladder

Retinoblastoma

Adrenocortical carcinoma

Rare parathyroid tumor

Classic Hodgkin lymphoma

Classic Hodgkin lymphoma, nodular sclerosis type

Classic Hodgkin lymphoma, mixed cellularity type

Classic Hodgkin lymphoma, lymphocyte-depleted type

Classic Hodgkin lymphoma, lymphocyte-rich type

Follicular lymphoma

Primary cutaneous follicle center lymphoma

Mantle cell lymphoma

Diffuse large B-cell lymphoma

Subcutaneous panniculitis-like T-cell lymphoma

Burkitt lymphoma

ALK-positive anaplastic large cell lymphoma

Anaplastic large cell lymphoma

ALK-negative anaplastic large cell lymphoma

Extranodal nasal NK/T cell lymphoma

Hepatosplenic T-cell lymphoma

Enteropathy-associated T-cell lymphoma

CD4+/CD56+ hematodermic neoplasm

Angioimmunoblastic T-cell lymphoma

Primary cutaneous CD30+ T-cell lymphoproliferative disease

Lymphomatoid papulosis

Waldenström macroglobulinemia

Heavy chain disease

MALT lymphoma

Multiple myeloma

Plasma cell leukemia

Plasmacytoma

Primary plasmacytoma of the bone

Acute lymphoblastic leukemia

T-cell prolymphocytic leukemia

Acute myeloid leukemia

Chronic myeloid leukemia

Atypical chronic myeloid leukemia

Acute promyelocytic leukemia

Acute myelomonocytic leukemia

Neoplasms (C00-D49) [continued]

Acute myeloid leukemia with abnormal bone marrow eosinophils inv(16)(p13q22) or t(16;16)(p13;q22)

Acute myeloid leukemia with 11q23 abnormalities

Acute myeloid leukaemia with myelodysplasia-related features

Chronic myelomonocytic leukemia

Juvenile myelomonocytic leukemia

Mast cell leukemia

Acute panmyelosis with myelofibrosis

Langerhans cell histiocytosis

Letterer-Siwe disease

Mastocytosis

Dendritic cell tumor

Histiocytic sarcoma

Benign epithelial tumor of salivary glands

Rare lymphatic malformation

Vestibular schwannoma

Thymoma

Craniopharyngioma

Multiple polyglandular tumor

Polycythemia vera

Essential thrombocythemia

Hypereosinophilic syndrome

Chronic eosinophilic leukemia

Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism (D50-D89)

Constitutional megaloblastic anemia due to vitamin B12 metabolism disorder

Rare constitutional hemolytic anemia due to an enzyme disorder

Hemolytic anemia due to hexose monophosphate shunt and glutathione metabolism anomalies

Hemolytic anemia due to a disorder of glycolytic enzymes

Hemolytic anemia due to an erythrocyte nucleotide metabolism disorder

Alpha-thalassemia

Hemoglobinopathy

Beta-thalassemia

Delta-beta-thalassemia

Hereditary persistence of fetal hemoglobin-beta-thalassemia syndrome

Sickle cell anemia

Sickle cell disease and related diseases

Sickle cell disease associated with another hemoglobin anomaly

Hereditary spherocytosis

Hereditary elliptocytosis

Hereditary stomatocytosis

Rare acquired hemolytic anemia

Typical hemolytic-uremic syndrome

Paroxysmal nocturnal hemoglobinuria

Transient erythroblastopenia of childhood

Aplastic anemia

Idiopathic aplastic anemia

Rare acquired aplastic anemia

Sideroblastic anemia

Constitutional sideroblastic anemia

Congenital dyserythropoietic anemia

Hemophilia A

Hemophilia B

Von Willebrand disease

Congenital factor XI deficiency

Acquired hemophilia

Secondary polycythemia

Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism (D50-D89) [continued]

Immunodeficiency predominantly affecting antibody production

Selective IgM deficiency

Specific antibody deficiency with normal immunoglobulin concentrations and normal numbers of B cells

Transient hypogammaglobulinemia of infancy

Other immunodeficiency syndrome with predominantly antibody defects

Severe combined immunodeficiency

Reticular dysgenesis

Combined T and B cell immunodeficiency

T-B- severe combined immunodeficiency

T-B+ severe combined immunodeficiency

Severe combined immunodeficiency due to adenosine deaminase deficiency

Thymic aplasia

Purine nucleoside phosphorylase deficiency

Immunodeficiency by defective expression of HLA class 1

Immunodeficiency by defective expression of HLA class 2

Wiskott-Aldrich syndrome

22q11.2 deletion syndrome

Short-limb skeletal dysplasia with severe combined immunodeficiency

X-linked lymphoproliferative disease

Hyper-IgE syndrome

Common variable immunodeficiency

Immunodeficiency due to a complement cascade protein anomaly

Sarcoidosis

Endocrine, nutritional and metabolic diseases (E00-E89)

Congenital hypothyroidism

Permanent congenital hypothyroidism

Rare hyperthyroidism

Rare hypoparathyroidism

Pseudohypoparathyroidism

Rare hyperparathyroidism

Acromegaly

Pituitary gigantism

Pituitary deficiency

Hereditary central diabetes insipidus

Cushing syndrome

Cushing disease

Nelson syndrome

Congenital adrenal hyperplasia

Peripheral precocious puberty

Autoimmune polyendocrinopathy type 2

Polyendocrinopathy

Carcinoid syndrome

Androgen insensitivity syndrome

Pellagra

Disorder of phenylalanine metabolism

Classic phenylketonuria

Disorder of tyrosine metabolism

Oculocutaneous or ocular albinism

Maple syrup urine disease

Disorder of branched-chain amino acid metabolism

Disorder of amino acid absorption and transport

Disorder of lysine and hydroxylysine metabolism

Disorder of ornithine metabolism

Congenital lactase deficiency

Glycogen storage disease

Disorder of fructose metabolism

Endocrine, nutritional and metabolic diseases (E00-E89) [continued]

Disorder of galactose metabolism
Gangliosidosis
GM2 gangliosidosis
Sphingolipidosis
Neuronal ceroid lipofuscinosis
Mucopolysaccharidosis type 1
Mucopolysaccharidosis
Mucopolysaccharidosis type 2
Glycoproteinosis
Rare hyperlipidemia
Rare dyslipidemia
Combined hyperlipidemia
Disorder of purine or pyrimidine metabolism
Lesch-Nyhan syndrome
Porphyria
Isolated agammaglobulinemia
Disorder of porphyrin and heme metabolism
Porphyria cutanea tarda
Acatalasemia
Crigler-Najjar syndrome
Disorder of copper metabolism
Disorder of mineral absorption and transport
Disorder of iron metabolism and transport
Disorder of zinc metabolism and transport
Cystic fibrosis
Amyloidosis
Primary systemic amyloidosis
AA amyloidosis
Primary localized amyloidosis
Primary cutaneous amyloidosis

Mental, behavioral and neurodevelopmental disorders (F01-F99)

Idiopathic hypersomnia
Landau-Kleffner syndrome
Rare pervasive developmental disorder
Atypical autism
Rett syndrome
Childhood disintegrative disorder

Diseases of the nervous system (G00-G99)

Pneumococcal meningitis
Tropical spastic paraparesis
Huntington disease
Autosomal recessive cerebellar ataxia due to a DNA repair defect
Hereditary spastic paraplegia
Proximal spinal muscular atrophy type 1
Motor neuron disease
Postpoliomyelitis syndrome
Neuroleptic malignant syndrome
Postencephalitic parkinsonism
Pantothenate kinase-associated neurodegeneration
Progressive supranuclear palsy
Multiple system atrophy, parkinsonian type
Early-onset generalized limb-onset dystonia
Oromandibular dystonia
Neuromyelitis optica
Schilder disease
Marchiafava-Bignami disease
Baló concentric sclerosis
Pyridoxine-dependent epilepsy
Narcolepsy type 1
Trigeminal neuralgia
Persistent idiopathic facial pain
Melkersson-Rosenthal syndrome
Hemifacial spasm
Isolated facial myokymia

Diseases of the nervous system (G00-G99) [continued]

Complex regional pain syndrome type 2
Refsum disease
Cerebellar ataxia with peripheral neuropathy
Guillain-Barré syndrome
Myasthenia gravis
Congenital myasthenic syndrome
Muscular dystrophy
Myotonic syndrome
Congenital myopathy
Periodic paralysis
Lambert-Eaton myasthenic syndrome
Familial dysautonomia
Multiple system atrophy
Normal pressure hydrocephalus
Idiopathic intracranial hypertension
Syringomyelia
Spontaneous intracranial hypotension

Diseases of the eye and adnexa (H00-H59)

Ocular cicatricial pemphigoid
Corneal dystrophy
Anterior uveitis
Phacoanaphylactic uveitis
Posterior uveitis
Retinopathy of prematurity
Endophthalmitis
Mitochondrial DNA-related progressive external ophthalmoplegia

Diseases of the ear and mastoid process (H60-H95)

Non-syndromic genetic deafness

Diseases of the circulatory system (I00-I99)

Rheumatic fever
Idiopathic and/or familial pulmonary arterial hypertension
Dilated cardiomyopathy
Endomyocardial fibroelastosis
Familial isolated restrictive cardiomyopathy
Moyamoya disease
Buerger disease
Celiac artery compression syndrome
Hereditary hemorrhagic telangiectasia
Primitive portal vein thrombosis
Budd-Chiari syndrome

Diseases of the respiratory system (J00-J99)

Chronic beryllium disease
Hypersensitivity pneumonitis
Farmer's lung disease
Drug or radiation exposure-related interstitial lung disease
Adult acute respiratory distress syndrome
Idiopathic Pulmonary Fibrosis

Diseases of the digestive system (K00-K95)

Anodontia
Dental ankylosis
Oral submucous fibrosis
Idiopathic achalasia
Undetermined colitis
Anal fistula
Radiation proctitis
Primary biliary cholangitis
Autoimmune hepatitis
Hepatic veno-occlusive disease

Diseases of the skin and subcutaneous tissue (L00-L99)

Staphylococcal scalded skin syndrome
Pemphigus vulgaris
Pemphigus vegetans
Bullous pemphigoid
Acquired epidermolysis bullosa
Dermatitis herpetiformis
Subcorneal pustular dermatosis
Generalized pustular psoriasis
Pustulosis palmaris et plantaris
Rare lichen planus
Bullous lichen planus
Pityriasis rubra pilaris
Stevens-Johnson syndrome/toxic epidermal necrolysis spectrum
Solar urticaria
Alopecia totalis
Alopecia universalis
Lichen planopilaris
Quinquaud's folliculitis decalvans
Acquired hypertrichosis lanuginosa
Sebocystomatosis
Neurofibromatosis type 6
Acquired ichthyosis
Pyoderma gangrenosum
Primary anetoderma
Rare cutaneous lupus erythematosus
Discoid lupus erythematosus
Subacute cutaneous lupus erythematosus
Localized scleroderma
Erythema elevatum diutinum
Sweet syndrome
Wells syndrome

Diseases of the musculoskeletal system and connective tissue (M00-M99)

Reactive arthritis
Adult-onset Still disease
Juvenile idiopathic arthritis
Systemic-onset juvenile idiopathic arthritis
Oligoarticular juvenile idiopathic arthritis
Familial calcium pyrophosphate deposition
Pigmented villonodular synovitis
Intermittent hydrarthrosis
Polyarteritis nodosa
Primary polyarteritis nodosa
Eosinophilic granulomatosis with polyangiitis
Kawasaki disease
Anti-glomerular basement membrane disease
Granulomatosis with polyangiitis
Takayasu arteritis
Microscopic polyangiitis
Drug-induced lupus erythematosus
Juvenile dermatomyositis
Polymyositis
Systemic sclerosis

Diseases of the musculoskeletal system and connective tissue (M00-M99) [continued]

CREST syndrome
Overlapping connective tissue disease
Mixed connective tissue disease
Behçet disease
Polymyalgia rheumatica
Eosinophilic fasciitis
Nodular non-suppurative panniculitis
Infectious, fungal or parasitic myopathy
Fibrodysplasia ossificans progressiva
Ledderhose disease
Monostotic fibrous dysplasia
Solitary bone cyst
Chronic nonbacterial osteomyelitis/Chronic recurrent multifocal osteomyelitis
Idiopathic avascular necrosis
Avascular necrosis
Traumatic avascular necrosis
Legg-Calvé-Perthes disease
Osteochondritis dissecans
Relapsing polychondritis

Diseases of the genitourinary system (N00-N99)

Dense deposit disease
Nephrogenic diabetes insipidus
Interstitial cystitis
Extrapelvic endometriosis
Asherman syndrome
Ovarian hyperstimulation syndrome

Pregnancy, childbirth and the puerperium (O00-O9A)

Complete hydatidiform mole
Hydatidiform mole
Partial hydatidiform mole
Preeclampsia
HELLP syndrome
Peripartum cardiomyopathy

Certain conditions originating in the perinatal period (P00-P96)

Infant acute respiratory distress syndrome
Meconium aspiration syndrome
Bronchopulmonary dysplasia
Congenital rubella syndrome
Fetal cytomegalovirus syndrome
Congenital varicella syndrome
Congenital toxoplasmosis
Hemolytic disease due to fetomaternal alloimmunization
Hydrops fetalis
Immune hydrops fetalis
Non-immune hydrops fetalis
Neonatal diabetes mellitus
Transient tyrosinemia of the newborn
Necrotizing enterocolitis
Transient neonatal myasthenia gravis

Congenital malformations, deformations and chromosomal abnormalities (Q00-Q99)

Isolated anencephaly/exencephaly
Craniorachischisis
Iniencephaly
Frontal encephalocele
Isolated encephalocele
Nasal encephalocele
Occipital encephalocele
Congenital hydrocephalus
Congenital non-communicating hydrocephalus
Isolated arhinencephaly
Holoprosencephaly
Septo-optic dysplasia spectrum
Megalencephaly
Isolated spina bifida
Isolated amyelia
Diastematomyelia
Arnold-Chiari malformation type II
Congenital ptosis
Isolated congenital ectropion
Congenital ectropion
Isolated microphthalmia-anophthalmia-coloboma
Microphthalmia-anophthalmia-coloboma
Nanophthalmia
Early-onset non-syndromic cataract
Isolated ectopia lentis
Coloboma of eye lens
Congenital primary aphakia
Coloboma of iris
Isolated congenital sclerocornea
Congenital glaucoma
Anotia
External auditory canal aplasia/hypoplasia
Middle ear anomaly
Isolated congenital auditory ossicle malformation
Microtia
Truncus arteriosus
Double outlet right ventricle
Double outlet left ventricle
Transposition of the great arteries
Univentricular heart
Congenitally corrected transposition of the great arteries
Interatrial communication
Atrioventricular canal defect
Tetralogy of Fallot
Congenital aortopulmonary window
Congenital pulmonary valve stenosis
Congenital tricuspid stenosis
Congenital tricuspid malformation
Ebstein malformation
Hypoplastic right heart syndrome
Congenital aortic valve stenosis
Congenital aortic valve insufficiency
Congenital mitral valve insufficiency and/or stenosis
Congenital mitral stenosis
Hypoplastic left heart syndrome
Dextrocardia
Levocardia
Triatrial heart
Subpulmonary stenosis
Fixed subaortic stenosis
Coronary artery congenital malformation
Congenital heart block
Aorta coarctation
Peripheral pulmonary stenosis
Congenital pulmonary venous return anomaly
Congenital total pulmonary venous return anomaly

Congenital malformations, deformations and chromosomal abnormalities (Q00-Q99) [continued]

Congenital partial pulmonary venous return anomaly
Congenital renal artery stenosis
Rare arteriovenous malformation
Choanal atresia
Nose and cavum anomaly
Congenital laryngeal web
Larynx anomaly
Congenital subglottic stenosis
Laryngocele
Congenital laryngomalacia
Congenital tracheomalacia
Congenital pulmonary sequestration
Pulmonary agenesis
Cleft palate
Cleft hard palate
Cleft velum
Bifid uvula
Cleft lip with or without cleft palate
Isolated cleft lip
Cleft lip and alveolus
Cleft lip/palate
Macroglossia
Esophageal atresia
Isolated tracheoesophageal fistula
Atresia of small intestine
Isolated anorectal malformation
Low anorectal malformation
Hirschsprung disease
Isolated biliary atresia
Isolated polycystic liver disease
Congenital pancreatic cyst
Agenesis and aplasia of uterine body
Didelphys uterus
Bicornuate uterus
Unilateral aplasia of the Müllerian ducts
Uterine cervical aplasia and agenesis
Posterior hypospadias
Testicular regression syndrome
Penile agenesis
Renal agenesis
Renal agenesis, unilateral
Renal agenesis, bilateral
Renal hypoplasia
Renal hypoplasia, unilateral
Renal hypoplasia, bilateral
Autosomal recessive polycystic kidney disease
Renal dysplasia
Autosomal dominant tubulointerstitial kidney disease
Congenital hydronephrosis
Congenital primary megaureter
Epispadias
Bladder exstrophy
Atresia of urethra
Isolated plagiocephaly
Congenital bowing of long bones
Non-syndromic polydactyly
Polydactyly of a biphalangeal thumb
Non-syndromic syndactyly
Polysyndactyly
Amelia of upper limb
Non-syndromic limb reduction defect
Congenital absence of upper arm and forearm with hand present
Congenital absence of both forearm and hand
Acheiria
Radial hemimelia
Ulnar hemimelia

Congenital malformations, deformations and chromosomal abnormalities (Q00-Q99) [continued]

Isolated split hand-split foot malformation
Amelia of lower limb
Congenital absence of thigh and lower leg with foot present
Congenital absence of both lower leg and foot
Apodia
Femoral agenesis/hypoplasia
Tibial hemimelia
Fibular hemimelia
Amelia
Arthrogryposis multiplex congenita
Craniosynostosis
Mandibulofacial dysostosis
Isolated Klippel-Feil syndrome
Achondrogenesis
Thanatophoric dysplasia
Ciliopathies with major skeletal involvement
Chondrodysplasia punctata
Achondroplasia
Diastrophic dwarfism
Spondyloepiphyseal dysplasia and spondyloepimetaphyseal dysplasia
Osteogenesis imperfecta
Fibrous dysplasia of bone
Osteopetrosis and related disorders
Camurati-Engelmann disease
Enchondromatosis
Multiple osteochondromas
Congenital diaphragmatic hernia
Gastroschisis
Ehlers-Danlos syndrome
Recessive X-linked ichthyosis
Lamellar ichthyosis
Autosomal dominant epidermolytic ichthyosis
Harlequin ichthyosis
Epidermolysis bullosa simplex
Junctional epidermolysis bullosa, generalized severe
Dystrophic epidermolysis bullosa
Xeroderma pigmentosum
Cutaneous mastocytosis
Incontinentia pigmenti
Hypohidrotic ectodermal dysplasia
Isolated congenital breast hypoplasia/aplasia
Supernumerary breasts
Isolated congenital anonychia
Tuberous sclerosis complex
Fetal alcohol syndrome
Fetal hydantoin syndrome
Acromegaloid facial appearance syndrome
Syndrome with limb malformations as a major feature
Overgrowth syndrome
Marfan syndrome
Dahlberg-Borer-Newcomer syndrome
Down syndrome
Trisomy 18
Trisomy 13
Polyploidy
Total autosomal monosomy
Autosomal monosomy
Partial deletion of the short arm of chromosome 4
Partial autosomal monosomy
Partial deletion of the short arm of chromosome 5
Turner syndrome
Turner syndrome due to structural X chromosome anomalies

Congenital malformations, deformations and chromosomal abnormalities (Q00-Q99) [continued]

Mosaic monosomy X
Trisomy X
47,XYY syndrome
Tetragametic chimerism
46,XX gonadal dysgenesis
Fragile X syndrome

Symptoms, signs and abnormal clinical laboratory findings, not elsewhere classified (R00-R99)

Cardiogenic shock

Injury, poisoning and certain other consequences of external causes (S00-T88)

Acute opioid poisoning
Cocaine intoxication
Methanol poisoning
Lead poisoning
Mercury poisoning
Manganese poisoning
Snakebite envenomation
Scorpion envenomation
Cyanide poisoning
Acute radiation syndrome
Acquired angioedema
Malignant hyperthermia of anesthesia

Provisional assignment of new diseases of uncertain etiology or emergency use

Acute respiratory coronavirus infection
Zika virus disease

Appendix 2 Methodology for Analysis of Medicaid Claims for Rare Disease Diagnoses

The Pennsylvania Department of Human Services was presented a list of 1,494 rare disease that had been linked and identified to ICD-10 codes. This list of rare diseases was compared to the Pennsylvania Medicaid data for the calendar year 2018 to yield cases in which physicians submitted claims that were approved for over one-half of the procedures (773 of the 1,494 or 51.7 percent).

To determine if each claim met the criteria for this request, a query was run in SAS. Data was taken from both the T_CLAIM_DIM (fee-for-service claims) and T_ENC DIM (HealthChoices claims).

For fee-for-service claims, the tables T_CLAIM_DIM and T_DX_DIM (Diagnosis code table) were joined by the Diagnosis EDW Identifier (IND_EDW_DX). The request using the criteria below was run for all nine diagnosis codes:

1. The date the claim was loaded into the database (DTE_RA) was after the initial date of service (DTE_BEGIN_SERV).
2. Date of Service was in 2018 (DTE_BEGIN_SERVICE between '2018-01-01' and '2018-12-31').
3. The diagnosis code was in the list of 1,494 presented to us by the requester.
4. Verification was made if the claim was paid or adjusted (CDE_ADJMT_CLAIM in C,A,N).
5. The claim was PAID (CDE_STATUS_HEADER_CLAIM = P).

For PROMISe claims, the tables T_ENC_DIM and T_DX_DIM were joined by the Diagnosis EDW Identifier. The request using the criteria below was run for all nine diagnosis codes:

1. The date the claim was loaded into the database (DTE_ACCPTD_DPW) was after the initial date of service (DTE_BEGIN_SERV).
2. Date of Service was in 2018 (DTE_BEGIN_SERVICE between '2018-01-01' and '2018-12-31').
3. The diagnosis code was in the list of 1,494 presented to us by the requester.
4. Verification was made if the claim was paid or adjusted (CDE_ADJMT_CLAIM in C,A,N).
5. The claim was PAID (CDE_STATUS_HEADER_CLAIM = P).
6. The claim was Accepted in the MCO system (CDE_REJD_ACCPTED_MCO = ?,9).

Once the runs were completed, the data from all data runs was brought together, duplicates at the recipient, diagnosis code, claim type level were removed and then identified as Inpatient (Facility or Hospital), Outpatient (usually a Facility or Hospital where the patient does not stay overnight after the procedure) or Professional (usually a physician visit). Long-term living and pharmacy data were removed from the resulting dataset. The data was then summed at the diagnosis code/diagnosis name level for the inpatient, outpatient and professional data. Any total for a procedure that was zero was eliminated and the totals

were added together to get the results. If any of these results were 10 or less, the total was replaced with '*' for the privacy of the recipients with the diagnosis.

Appendix 3 Rare and Not Rare Secondary Diagnoses

Rare/Not Rare Secondary Diagnoses (PHC4) Among Pennsylvania Hospitalizations, for Those Not Reporting a Primary Dx of Rare Disease in 2017

	Frequency	Percent
Secondary Dx1	1,518,358	
Not Rare	1,459,652	96.13
Rare	58,706	3.87
No Secondary Dx1	65,372	
Secondary Dx2	1,453,901	
Not Rare	1,395,571	95.99
Rare	58,330	4.01
No Secondary Dx2	129,829	
Secondary Dx3	1,377,087	
Not Rare	1,309,908	95.12
Rare	67,179	4.88
No Secondary Dx3	206,643	
Secondary Dx4	1,297,652	
Not Rare	1,226,902	94.55
Rare	70,750	5.45
No Secondary Dx4	286,078	
Secondary Dx5	1,214,379	
Not Rare	1,143,773	94.19
Rare	70,606	5.81
No Secondary Dx5	369,351	
Secondary Dx6	1,135,387	
Not Rare	1,067,677	94.04
Rare	67,710	5.96
No Secondary Dx6	448,343	
Secondary Dx7	1,053,000	
Not Rare	990,593	94.07
Rare	62,407	5.93
No Secondary Dx7	530,730	
Secondary Dx8	971,319	
Not Rare	914,866	94.19
Rare	56,453	5.81
No Secondary Dx8	612,411	
Secondary Dx9	891,419	
Not Rare	841,196	94.36
Rare	50,223	5.64
No Secondary Dx9	692,301	

	Frequency	Percent
Secondary Dx10	813,154	
Not Rare	768,788	94.54
Rare	44,366	5.46
No Secondary Dx10	770,756	
Secondary Dx11	737,917	
Not Rare	699,269	94.76
Rare	38,648	5.24
No Secondary Dx11	845,813	
Secondary Dx12	665,715	
Not Rare	632,144	94.96
Rare	33,571	5.04
No Secondary Dx12	918,015	
Secondary Dx13	597,678	
Not Rare	568,807	95.17
Rare	28,871	4.83
No Secondary Dx13	986,052	
Secondary Dx14	533,354	
Not Rare	509,119	95.46
Rare	24,235	4.54
No Secondary Dx14	1,050,376	
Secondary Dx15	473,746	
Not Rare	452,653	95.55
Rare	21,093	4.45
No Secondary Dx15	1,109,984	
Secondary Dx16	418,752	
Not Rare	401,337	95.84
Rare	17,415	4.16
No Secondary Dx16	1,164,978	
Secondary Dx17	368,396	
Not Rare	353,717	96.02
Rare	14,679	3.98
No Secondary Dx17	1,215,334	

Appendix 4 Council Membership

Council members come from myriad backgrounds across the Commonwealth, as demonstrated through their biographies.

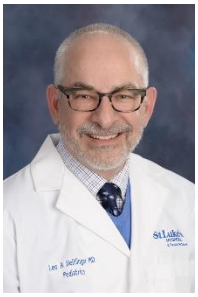
CHAIRMAN: Tomas J. Aguilar, Director, Bureau of Health Promotion and Risk Reduction, Pennsylvania Department of Health – Mr. Aguilar joined the Department of Health in 2012 and leads the Department's Chronic Disease and Injury Prevention efforts, driven by dedicated public health education and interventions experts. The Bureau's programs use evidence-based interventions to implement policy, health system and environmental changes to impact health outcomes. He previously served as the chair of the Task Force on Lyme Disease and Related Tick-Borne Diseases and is a member of the board of directors for the National Association of Chronic Disease Directors.

Dr. David Kelley, Chief Medical Officer for the Pennsylvania Department of Human Services' Office of Medical Assistance Programs – Dr. Kelley oversees the clinical and quality aspects of the Medical Assistance Programs that provide health benefits to over 2.5 million recipients. The office includes oversight of eight managed care organizations and the access fee-for-service program. In the past 10 years, the office has led multiple, significant processes and patient-oriented improvements to maximize efficiencies and improve the health of the health benefits recipients. Prior to joining the department, Dr. Kelley worked for Aetna Health Inc. as the medical director responsible for utilization and quality management in Pennsylvania, served as assistant professor and director of Clinical Quality Improvement at Penn State University's College of Medicine, and clinically practiced at an FQHC, private practice and a community-based team approach to diabetes care in a Medicaid hospital clinic. Dr. Kelley received his B.S. degree at Elizabethtown College, completed medical school at the University of Pittsburgh and his residency training at Baylor College of Medicine in Houston, obtained his MPA at Penn State University, and is board certified in internal medicine and geriatrics.

Nick Slotterback, Health and Physical Education Advisor, Pennsylvania Department of Education – As the representative from the Department of Education, he has a personal, common interest with the council in that his godson has a rare disease and his wife's cousin is the state ambassador for Rare Action Network in South Carolina. Their son was born with a rare disease and Mr. Slotterback is working to include rare disease education in the upcoming standard revision for Academic Standards for Health, Safety and Physical Education.

Megan Barbour, Policy Director, Pennsylvania Insurance Department (PID) – Ms. Barbour is responsible for supporting the Insurance Commissioner and Department staff with the development and execution of strategic objectives that advance the goals of the Department and adhere to the policy principles and mission of the Wolf administration. Prior to her time at PID,

Megan worked as an Executive Policy Specialist at the Pennsylvania Department of Health, advancing tactical program and policy development for the Pennsylvania Rural Health Model, an innovative value-based payment program. Before working in state government, Megan completed her Master's in Public Health, with a concentration in health systems organization and policy at the Pennsylvania State University and produced several health services research publications examining the impact of behavioral health comorbidities on clinical, quality and cost measures. Passionate about ensuring affordable, comprehensive insurance access and public service, Megan is committed to developing and implementing effective evidence-based policies to improve the lives of Pennsylvanians.



Leo Heitlinger, MD, FAAP, St Luke's Pediatric Gastroenterology – Dr. Heitlinger earned his medical degree from New York Medical College and continued his training at the University of California at Irvine and the Children's Hospital of Buffalo. Dr. Heitlinger has held positions at the Children's Hospital of Buffalo, Columbus Children's Hospital and St Luke's Hospital and Health Network, where he served as Chief of Pediatrics and as a Pediatric Gastroenterologist. Dr. Heitlinger has served on numerous boards and committees of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition, the Crohn's and Colitis Foundation, and the American Academy of Pediatrics.

William C. Welch, M.D., FACS, FICS, Chair, Department of Neurosurgery at Pennsylvania Hospital – Dr. Welch received his medical degree from SUNY/Downstate, School of Medicine and completed his residency at the University of Rochester Medical Center and a fellowship at Montefiore Medical Center. Dr. Welch's memberships include multiple international and national boards, as well as colleges and associations, including the National American Association of Orthopedic and Neurological Surgeons and the International Neurosurgical Society of America. Dr. Welch was named to the Philadelphia magazine's 2013 Super Doctors list and has been recognized as one of America's "Top Doctors" and one of the "Best Doctors in America" on multiple occasions**.**

Ann Marie Kriebel-Gasparro, DrNP, MSN, CRNP, FNP-BC, GNP-BC, Assistant Professor in Nursing, Director, DNP Program Alvernia University – Dr. Kriebel-Gasparro is dually credentialed as a family and gerontological nurse practitioner and has her Doctor of Nursing Practice (DrNP) degree from Drexel University. Her practice began seeing medically underserved patients in a HPSA in North Philadelphia as a primary care provider in the National Health Service Corps for four years, then as coordinator of the Penn Hemophilia and Thrombosis Center for four years; she also practiced in neurology, oncology and nursing homes in Pa. and N.J. for many years. Her clinical practice is as a family and gerontological nurse practitioner in home health and occupational medicine. Her interest in rare diseases is based on her practice and management of patients for many years with hemophilia, rare genetic thrombotic diseases and rare genetic neurologic diseases. Dr. Kriebel-Gasparro has taught in ADN, pre-licensure BSN, RN-BSN, accelerated BSN, BSN to

DNP and post MSN to DNP programs. Previously, she was the director of the DNP Program at Temple University. Her teaching and practice centers on the development of innovative models of health care delivery; including the implementation of a didactic and immersion clinical experience in palliative care for nursing students.

Evelyn O. Talbott, DrPH, MPH, epidemiologist and professor, Department of Epidemiology, Graduate School of Public Health, University of Pittsburgh – Dr. Talbott has conducted numerous epidemiologic investigations and provided teaching in environmental epidemiology and has served on numerous committees at the Pennsylvania Department of Health. She is a founding member of the international Society for Environmental Epidemiology, serving as its secretary treasurer for four years, and is a fellow of the American Heart Association Council on Epidemiology and Prevention. She recently served as director of the CDC-funded Academic Center of Excellence in Environmental Public Health Tracking. She is dedicated to furthering ALS research in both treatment and identification of potential risk factors, as well as for all rare diseases. Most recently, she has focused on air pollution and neuro-cognitive and neurodegenerative diseases. These diseases include childhood autism and neurotoxic exposures, risk factors for ALS, and the risk of childhood lead poisoning.

Can (John) Ficicioglu, M.D., Ph.D., associate professor of pediatrics at the Children's Hospital of Philadelphia, Perelman School of Medicine at the University of Pennsylvania – Dr. Ficicioglu is director of the Newborn Metabolic Screening Program and Lysosomal Storage Disease Center at The Children's Hospital of Philadelphia with expertise in newborn metabolic screening, lysosomal storage disorders, intermediary metabolism defects, galactosemia and PKU. He is developing best practices in diagnostic algorithms and outcomes of inborn errors of metabolism detected through newborn screening. Dr. Ficicioglu received his M.D. from the University of Istanbul, Cerrahpasa Medical School, completing his internship and residency in pediatrics and his Ph.D. in histology and embryology from the University of Marmara, Istanbul. Previously an associate professor in pediatrics at the Cerrahpasa Medical School, he completed his genetics fellowship at the Children's Hospital of Boston, Harvard Medical School.

Nicholas DeGregorio, M.D., FACP, MMM, Senior Medical Director, UPMC *for You* – Dr. DeGregorio is currently the Senior Medical Director for UPMC *for You* and provides support for UPMC Health Plan provider credentialing, opioid management and value-based payment/shared savings programs. He practiced general internal medicine for approximately 20 years before joining UPMC Health Plan in 2004, where he previously worked as medical director in the areas of medical management, network development and quality improvement. Dr. DeGregorio's areas of special interest include developing patient-centered process improvement strategies to reduce disparities while improving efficiencies and improving the health of members. In his work as a Medicaid medical director he developed experience and interest in the many issues and problems faced by members with rare conditions. In his role on the Pennsylvania Rare Disease Advisory Council, his goal is to help advance knowledge and

reduce both medical and social barriers to timely diagnoses and treatment for patients with rare diseases.

Bret Yarczower M.D., MBA, Senior Medical Director, Health Services Operations – Dr. Yarczower responsibilities with Geisinger Health Plan include health care services and technology. In his role, he chairs committees evaluating the safety and efficacy of new and evolving medical and surgical technologies and pharmaceuticals. Dr. Yarczower has been with Geisinger Health System for more than 24 years, beginning as a pediatrician. He joined Geisinger Health Plan as an assistant medical director in 2001. Dr. Yarczower earned his B.A. from Temple University and received his M.D. from the Medical College of Pennsylvania, interned and completed his residency at the University of Michigan and received his MBA from the University of Massachusetts. He is a fellow and board certified by the American Academy of Pediatrics. Dr. Yarczower completed the Executive Leadership Program from AHIP, America's Health Insurance Plans. He has received awards for outstanding patient satisfaction and community service.

Patrick Collins, Senior Director for North American Healthcare Policy and External Affairs at CSL Behring – CSL Behring is a King of Prussia-based manufacturer of therapies for the treatment of multiple rare diseases. Mr. Collins has direct responsibility for CSL Behring's North American government affairs program and has been employed with the company for 17 years in positions of growing public policy responsibility. Prior to joining CSL Behring, Mr. Collins served as director of government relations for the National Hemophilia Foundation. He has also worked in New York City and state government. Mr. Collins lives in Exton, Pennsylvania with his wife and daughter.

Robert (Rob) Jinks, Ph.D., Professor of Neuroscience in the Department of Biology and the Biological Foundations of Behavior Program at Franklin & Marshall College (F&M) – Dr. Jinks earned his B.S. in bioengineering and his Ph.D. in neuroscience from Syracuse University. He has held faculty positions at the University of Pennsylvania School of Medicine and Swarthmore College in addition to F&M. For the first two decades of his career, Dr. Jinks' research focused on the cellular and molecular signaling between the brain and the retina necessary to promote normal, healthy vision. In 2009-10, as a visiting associate professor at the F.M. Kirby Center for Molecular Ophthalmology at the University of Pennsylvania School of Medicine, Dr. Jinks and the Clinic for Special Children in Strasburg, Pa. developed a collaboration focused on the use of next-generation DNA sequencing approaches to identify the genetic basis of rare neurodevelopmental disorders. The collaboration resulted in several publications that have characterized multiple neurodevelopmental disorders, many of which are now studied in U.S. and foreign labs.

Joseph Coyne, M.Ed., LBSC, Executive Director, Garrett the Grand – Batten Fighter – First and foremost, Mr. Coyne is a father and advocate for his son Garrett who is affected by Batten Disease. They started a non-profit to fund research, raise awareness and support others in the community with rare disease. Current projects consist of beginning a wellness program to run with or for those who are unable to run themselves due to disabilities. He is passionate about progressing rare disease and making Pennsylvania the leader for the rare disease community.

Sharon O'Shaughnessy, Narcolepsy Patient with Cataplexy, Advocacy Chair, Narcolepsy Network (National Non-profit); Member, Avadel Pharmaceuticals Patient Advisory Group – Sharon is a parent to Rachel, 23, who has an undiagnosed genetic syndrome, despite exome sequencing. Ms. O'Shaughnessy earned her B.A. in psychology and education from Bucknell, and a M.A. in communication disorders and speech science from University of Colorado-Boulder. Using spectrographic speech analysis, her research employed reflexive vocal closure to improve vocal quality despite previous vocal failure through the course of neuro-degenerative diseases. As an advocate, Ms. O'Shaughnessy wrote legislation regarding students with special educational needs that was passed in Virginia, testified at FDA in 2013 and 2018 for treatments that are now making their way through approval, started a school for children with special needs learning alongside typical peers, and, for 15 years, served as a parent mentor for a CHOP support group for parents of children who are medically fragile. Ms. O'Shaughnessy has seen rare diseases from just about all angles, and she is thrilled to be serving on the Pa. Rare Disease Advisory Council.

Elizabeth Rementer, Parent Advocate and Communications Professional – A mother of twin sons with apraxia of speech, a rare neurological speech disorder, Ms. Rementer is also an advocate and volunteer for numerous Central Pennsylvania organizations and activities that support children and adults with special needs and their families. She has more than a decade of experience in public relations, working for the Commonwealth and in the state legislature, and is a graduate of Penn State University with a bachelor's degree in journalism.

Connie Deline, M.D., Vice-President, Chair, Medical Advisory Board, Spinal CSF Leak Foundation – Dr. Deline's interest in participation with the Council is three-fold: a patient with a rare disorder (spontaneous intracranial hypotension); a family medicine and integrative medicine physician, now retired from clinical medicine due to disability; and a representative of a rare disease health advocacy non-profit organization.

Anna Payne, Cystic Fibrosis Patient – As a patient with a rare disease, this is personal to Ms. Payne. She knows firsthand the struggles our community faces. She advocates at the federal, state and local levels to help legislators and other leaders to understand how legislation will impact our community. Ms. Payne wants to improve the lives of as many patients as possible, and, for those living with a rare disease, this is a time-sensitive matter. She most recently ran for local office and was elected in November 2017 as the auditor of Middletown Township. Ms. Payne believes it is well past the time that those who are capable step up and make their voices heard.

Marie Conley, Conley Consulting, LLC – Marie Conley is the founder of The Conley Cushing's Disease Fund, which was established on July 17, 2014, and is a project of The Foundation for Enhancing Communities, fiscal sponsor. The funds raised are used in part to create awareness, advocacy and support for patients with this disease and their loved ones, as well as support institutions and organizations focused on research and treatment surrounding Cushing's Disease. In 2012, Marie was diagnosed with Cushing's Disease – a disease so rare it affects less than 10 people per million each year. She is also adrenal insufficient. She is a consultant focusing on engagement and stakeholder strategies for a variety of clients through her company Conley Consulting, LLC. Marie hails from Bucks County, Pennsylvania, and lives in Elizabethtown, Pennsylvania with her husband Chris Lammando and their son Carter.

Stephanie Fischer, Executive Committee, Rare Advocacy Movement, and Bensalem – Ms. Fischer is a rare disease patient and stroke survivor from Bucks County. She serves on the Executive Committee of the Rare Advocacy Movement and on the Advisory Board of the Rare and Undiagnosed Network. Stephanie consulted for Global Genes for a year after serving as the Chief Patient Engagement and Communications Officer at the EveryLife Foundation for Rare Diseases. She previously spent more than 10 years focused on health policy communication at the Biotechnology Innovation Organization (BIO) and Pharmaceutical Research and Manufacturers of America (PhRMA). She worked for U.S. Representative Jim Greenwood (PA-8) for nine years until his retirement in 2004.

Jennifer H. Wescoe, M.Ed., NCC, Executive Director, Founder, Wescoe Foundation for Pulmonary Fibrosis – Ms. Wescoe's father, Ron Wescoe, was diagnosed with Idiopathic Pulmonary Fibrosis (IPF) in November 2003. He passed away 11 months later. There was no support, resources or education regarding this incurable lung disease. As a family, they felt lost, alone, confused and, frankly, scared of what her Dad had to endure, struggling to breathe every day. Not only did he struggle to breathe and deal with this serious lung disease, it affected the entire family dynamic as family absorbed roles of caregiver, educator, leader and observer. Ms. Wescoe and her family know how vital education and support is with any disease, let alone a rare disease. She has made it her mission to provide support, education and resources for patients and their families living with pulmonary fibrosis and created the non-profit 501(c)3 organization, Wescoe Foundation for

Pulmonary Fibrosis. Today, Ms. Wescoe has the privilege of working with Pennsylvania Department of Health and an incredible group of people who have the same drive and determination to help others in Pennsylvania living with a rare disease. She believes the Council will have a profound and effective impact on patients and their families coping with a rare disease.

Jessica L. Deary – Ms. Deary is a patient speaker, individual patient advocate, legislative ambassador, patient advisor to organizations and a writer. Ms. Deary's education and professional experience began in the corporate sector, during which time she obtained an M.B.A. and worked in strategic management. Drawn to patient advocacy through her own experiences as a long-standing patient with a rare, complicated and incurable medical condition, her diverse background, experience and unconventional journey has blessed her with numerous opportunities to act in many differing roles -- from provider to patient and many points in between. These differing perspectives and her own experiences as a patient in need have resulted in an unyielding passion to improve patient care and promote a more positive workplace culture. This passion helped her to redirect her professional endeavors toward aiding other patients to obtain adequate medical care and to helping organizations create fiscally advantageous operational strategies to improve care for patients. Ms. Deary continues to expand her knowledge in patient experience and patient-centered care and recently received a certificate in patient advocacy. She is currently working towards her RN degree.

Endnotes

[1] *Orphanet*. www.orpha.net.

[2] "FAQs About Rare Diseases." *NIH: National Center for Advancing Translational Science, Genetic and Rare Diseases Information Center.* https://rarediseases.info.nih.gov/diseases/pages/31/faqs-about-rare-diseases

[3] "Recommended Uniform Screening Panel." *Health Resources and Services Administration.* https://www.hrsa.gov/advisory-committees/heritable-disorders/rusp/index.html.

[4] "RUSP Conditions By State." *Baby's First Test.* https://babysfirsttest.org/newborn-screening/states.

[5] Dawkins, H.J.S., Draghia-Akli, R., Lasko, P., Lau, L.P.L., Jonker, A.H., Cutillo, C.M., Rath, A., Boycott, K.M., Baynam, G., Lochmuller, H., et al. (2018). Progress in Rare Diseases Research 2010-2016: An IRDiRC Perspective*. Clin Transl Sci* 11: 11-20.

[6] Settling on a Secondary Diagnosis: Part I. *ICD10monitor.* https://www.icd10monitor.com/settling-on-a-secondary-diagnosis-part-i

[7] The World Health Organization effective date for ICD-11 is January 1, 2022, so the U.S will not be able to implement any earlier than that. ICD-10 implementation was delayed so it is possible ICD-11 implementation may also face delay.

[8] Bick D, Jones M, Taylor SL, et al. (2019). Case for genome sequencing in infants and children with rare, undiagnosed or genetic diseases. *Journal of Medical Genetics* Published Online First: 25 April 2019. doi: 10.1136/jmedgenet-2019-106111

[9] https://www.raredisorders.ca/content/uploads/CORD-Patient-Survey-Summary.pdf