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Complete List of Authors:	Whitney, Daniel Kamdar, Neil Ng, Sophia Hirth, Richard A. Hurvitz, Edward Peterson, Mark
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The economic burden of pediatric-onset disabilities among young and middle-aged adults

Daniel G. Whitney,[1] Neil S. Kamdar,[2,3,4,5] Sophia Ng,[2] Richard A. Hirth,[6] Edward A. Hurvitz,[1] Mark D. Peterson[2]

[1]Department of Physical Medicine and Rehabilitation, University of Michigan, Ann Arbor, USA

[2]Institute for Healthcare Policy and Innovation, University of Michigan, Ann Arbor, USA

[3]Department of Obstetrics and Gynecology, University of Michigan, Ann Arbor, USA

[4]Department of Surgery, University of Michigan, Ann Arbor, USA

[5]Department of Emergency Medicine, University of Michigan, Ann Arbor, USA

[6]Department of Health Policy and Management, University of Michigan School of Public Health, Ann Arbor, USA

Corresponding author:

Daniel G. Whitney, PhD

325 E. Eisenhower Pkwy, Ann Arbor, MI, USA 48108

Phone: 734-936-7175

E-mail: danielwhitney8@gmail.com

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Abstract

Objective: Individuals with pediatric-onset disabilities (PoDs) have complex healthcare needs and are susceptible to adverse health outcomes, which may impose a higher strain on healthcare resources. The burden of healthcare resource utilization and costs attributed to the population of adults with PoDs is not clearly established. The objective here was to compare healthcare resource utilization and costs between adults with vs. without PoDs.

Design: Cohort.

Setting: Data were from the 2016 Optum Clinformatics® Data Mart, a de-identified nationwide claims database of beneficiaries from a single private payer.

Participants: ICD-10-CM diagnosis codes were used to identify beneficiaries with PoDs that were between 18 and 64 years of age.

Primary and secondary outcome measures: Annual all-cause healthcare resource utilization was compared between adults with and without PoDs. Annual all-cause total healthcare costs were compared between adults with and without PoDs before and after adjusting for sociodemographics and several costly noncommunicable diseases.

Results: Adults with PoDs (n=121,446) had greater annual mean counts of service utilization for all service types (e.g., inpatient, outpatient, emergency visits) compared to adults without PoDs (n=5,415,475; all p<0.001). Adults with PoDs had greater unadjusted total standardized reimbursement costs (mean difference=$18,238; cost ratio [CR]=3.16; 95% confidence interval [CI]=3.13-3.18) and total patient out-of-pocket costs (mean difference=$1,069; CR=1.88; 95%CI=1.86-1.89). After adjusting for sociodemographics and noncommunicable diseases, total standardized reimbursement costs were 2.32 times higher (95%CI=2.30-2.34) and total patient

out-of-pocket costs were 1.65 times higher (95%CI=1.64-1.66) compared to adults without PoDs.

Conclusion: Adults with PoDs had greater healthcare utilization and costs, even after accounting for costly diseases. Future research is needed to identify the cost drivers for adults with PoDs.

Trial registration: None, this is not a trial.

Keywords: pediatric-onset disabilities; economics; healthcare utilization

Strengths and limitations of this study

- This is the largest study to date to examine health economics on adults with pediatric-onset disabilities, which allowed us to assess healthcare utilization across the different types of pediatric-onset disabilities.
- We examined the healthcare-related economic burden after accounting for costly noncommunicable diseases that are more prevalent among adults with pediatric-onset disabilities.
- This study leveraged administrative claims data, and are therefore subject to limitations that are inherent to claims data, such as inaccurate coding of medical conditions.
- We were unable to determine specific cost drivers.

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Competing interest: None declared.

Patient consent for publication: Not required.

INTRODUCTION

Pediatric-onset disabilities (PoDs) refer to a group of congenital or acquired conditions that originate at conception, during pregnancy, or in childhood, and consist of impairments in behavioral, intellectual, and/or physical functioning, or are associated with abnormal developmental or metabolic processes. While clinical care and coordinated healthcare management for children with PoDs is a large focus of pediatric clinicians and researchers, far less attention on the topic has been given to these individuals as they become adults. The complex healthcare needs and health complications born out of direct (e.g., genetic) and resulting (e.g., delayed growth) consequences associated with PoDs during growth and development, have lasting ramifications on the health and functional status across the lifespan. Research has shown that individuals with PoDs are susceptible to early development of chronic, noncommunicable diseases and early mortality,[1-13] thus placing a high strain on the patients, caregivers, and healthcare resources. Importantly, the population of adults with PoDs is projected to expand over the coming decades,[14-16] which may lead to a noticeable increase in the national healthcare economic burden, and should be considered an urgent public health issue. However, healthcare resource utilization and costs directly attributable to adults with PoDs has not been extensively studied.

The current U.S. healthcare system may not be capable of meeting the high demands of healthcare needs for many individuals with PoDs in terms of knowledge of the life-course health development, care coordination, and healthcare accessibility.[17-20] A comprehensive understanding of healthcare resource utilization and costs among adults with PoDs is crucial for public health, healthcare policy reform, and implementing better clinical practice guidelines for

cost-effective care. Further, understanding the healthcare economic burden among at-risk populations prior to reaching the elderly years could inform public health efforts, policymakers, and early patient- and clinical-decision making processes and strategies (e.g., surgeries, medications) to maximize resource- and cost-effective treatment. Therefore, the primary aim of this study was to characterize healthcare resource utilization and costs among young and middle-aged adults with PoDs, as compared to young and middle-aged adults without PoDs, before and after adjusting for costly comorbid noncommunicable diseases. We hypothesized that adults with PoDs would have higher healthcare resource utilization and costs compared to adults without PoDs, even after adjusting for noncommunicable diseases.

METHODS

Data source

Data were from the 2016 Clinformatics® Data Mart Database (OptumInsight™, Eden Prairie, MN, USA), which is a nationwide, de-identified single private payer administrative claims database. This database contains over 16 million beneficiaries in 2016 who have either commercial or Medicare Advantage health plans, and includes all the inpatient, outpatient, pharmacy, emergency visit, office visit, and other ancillary service utilization throughout their enrollment on the insurance plan. Since data are de-identified, the University Institutional Review Board approved this study as non-regulated.

Sample selection

Beneficiaries that were 18 to 64 years of age, had 12 full months of continuous enrollment, and had at least one service utilization in 2016 were considered for this investigation.

Beneficiaries were excluded if they did not have known data for sex (n=991, <0.01%). All PoDs and noncommunicable diseases were identified using the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10) codes, and are presented in **Supplementary Table 1**. Since it is not possible to determine if some conditions developed in childhood or adulthood (e.g., spinal cord injury, cancer), conditions were included in the group representing PoDs if there were known childhood origins. These conditions were then grouped into the following PoD subcategories: PoDs of the musculoskeletal system; PoDs of the circulatory system; neurodevelopmental PoDs; PoDs of the urinary system; PoDs of the respiratory system and digestive system; PoDs of the nervous system; PoDs of the genital organs; PoDs of malformations of the eye, ear, face, and neck; and other chromosomal abnormalities.

Noncommunicable diseases

Prevalent noncommunicable diseases, as individual dichotomous variables (present vs. not present), were ascertained by at least 1 medical claim in 2016, and were selected with guidance from the literature on disease, disability, and mortality among adults.[2,3,21-26] Noncommunicable diseases were represented as categories across multiple biological systems as follows: ischemic heart diseases (e.g., atherosclerotic heart disease); cerebrovascular diseases (e.g., cerebral infarction); hypertensive and other cardiovascular diseases (e.g., hypertension, heart failure); type 2 diabetes mellitus; malignant cancer; osteoporosis; mood affective disorders (e.g., depression); chronic obstructive pulmonary diseases (e.g., emphysema); chronic kidney diseases (e.g., kidney disease stages I-V); and liver diseases (e.g., cirrhosis).

Healthcare resource utilization

Annual all-cause healthcare resource utilization was identified using medical claims and was categorized into the following service types: inpatient; outpatient, ambulatory, and other (herein referred to as "outpatient and other"); emergency department; and office. Specific services per service category are presented in **Supplementary Table 2**. Measures to assess healthcare resource utilization included the percentage of patients per group (with PoDs, without PoDs) that had at least one service utilization for each service category, and the annual mean count of service utilization per group for each service category. To limit extreme values and to reduce the effect of possible spurious outliers, winsorization of data to the upper 99.0% was performed for each service category.

Healthcare costs

Annual all-cause healthcare costs were identified using medical and outpatient pharmacy (herein referred to as "pharmacy") claims, and were from the paid amounts of adjudicated (final action) claims, which included insurer and health plan payments and patient copayments, deductibles, and coinsurance. Total (medical + pharmacy), medical, and pharmacy all-cause healthcare costs were represented as standardized reimbursement cost (i.e., sum of all health plan and patient paid amounts) and patient out-of-pocket cost (i.e., sum of copayment, deductible, and coinsurance).

To account for differences in pricing across health plans and provider contracts, the standardized cost field utilized algorithms that reflect the allowed payments across all provider services. This allows comparisons across patients, data sources, and geographic areas, and accounts for contractual payer and provider differences. Price standardization accounts for quantity of services provided, relative resource costs involved in providing the services, and the

nature of the service which can be defined as the CPT/HCPCS codes for professional services, NDC for pharmacy service, or type of admission for inpatient stay.

Sociodemographic variables

Age, sex, ethnicity, education level, household annual income, and insurance coverage (i.e., commercial only, Medicare Advantage) were considered for risk adjustment.

Statistical analysis

Descriptive characteristics and healthcare resource utilization and cost measures were summarized using mean (SD) for continuous variables and percentage for categorical variables. Group differences for healthcare resource utilization measures were examined using Chi-Square tests for binary data and generalized linear models assuming a zero-inflated Poisson distribution (for non-utilization) and log-link function for count data (i.e., number of visits per service type). As recommended for healthcare cost data analysis,[27,28] generalized linear models with gamma distribution and log-link function were performed to estimate the cost ratios (CR; exponentiated form of parameter estimate) for explanatory variables, while controlling for age, sex, education, insurance coverage, and all noncommunicable diseases. Ethnicity and household annual income were not initially included as covariates because of the extent of unknown/missingness. However, we conducted a sensitivity analysis using the fully adjusted generalized linear models that included ethnicity and household annual income to determine if these variables biased the estimated CR for group (reference: without PoDs) for healthcare cost measures.

Healthcare resource utilization and total cost measures were then summarized using mean (SD) after stratifying the type of PoD (e.g., musculoskeletal system, neurodevelopmental).

Comparisons between each of the PoD categories with the sample without PoDs were examined for healthcare resource utilization and cost measures, but statistical comparisons were not performed since these analyses were exploratory. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA). Effect estimates were reported as CRs with 95% confidence intervals (CI), and $p \leq 0.05$ (two-tailed) was used to determine statistical significance.

Patient and public involvement

Patient were not directly involved in the design or conduct of this study.

RESULTS

Descriptive characteristics of individuals with PoDs (n=121,446) and without PoDs (n=5,415,475) are presented in **Table 1**. Individuals with PoDs had a similar age as individuals without PoDs, and a similar distribution of sex, ethnicity, education level, and household annual income. Individuals with PoDs had higher prevalence of noncommunicable diseases compared to individuals without PoDs, including: ischemic heart disease (8.7%, 3.5%); cerebrovascular disease (6.3%, 1.5%); hypertensive or other cardiovascular disease (37.8%, 25.4%); type 2 diabetes (14.5%, 10.0%); malignant cancer (6.6%, 3.8%); osteoporosis (3.4%, 1.3%); mood affective disorders (20.8%, 11.0%); chronic obstructive pulmonary disease (1.8%, 0.7%); chronic kidney disease (6.6%, 1.8%); and liver disease (7.3%, 2.9%).

Table 1. Descriptive characteristics and prevalence of noncommunicable diseases among adults (18-64 years) with and without pediatric-onset disabilities (PoDs).

	PoD (n=121,446)	Without PoD (n=5,415,475)
	Point estimate	Point estimate

Descriptive characteristics		
Age, mean (SD)	44.3 (13.6)	43.8 (12.9)
18-40 years, %	38.8	40.3
41-64 years, %	61.2	59.7
Sex, %		
Female	55.6	53.8
Male	44.4	46.2
Ethnicity, %		
White	55.7	53.4
Black	7.9	7.4
Hispanic	8.3	9.4
Asian	3.0	4.3
Unknown/missing	25.0	25.5
Education, %		
Less than high school	0.4	0.5
High school diploma	25.1	24.0
More than high school	71.9	73.5
Unknown/missing	2.6	2.1
Household annual income, %		
<$40K	15.2	13.1
$40K to 59.9K	9.9	10.0
$60K to 99.9K	19.0	20.0
≥$100K	32.6	34.1
Unknown/missing	23.4	22.8
Insurance coverage, %		
Commercial only	78.9	93.4
Medicare Advantage	21.1	6.6
Noncommunicable diseases		
Ischemic heart disease, %	8.7	3.5
Cerebrovascular disease, %	6.3	1.5
Hypertensive/other cardiovascular disease, %	37.8	25.4
Type 2 diabetes, %	14.5	10.0
Malignant cancer, %	6.6	3.8
Osteoporosis, %	3.4	1.3
Mood affective disorders, %	20.8	11.0
Chronic obstructive pulmonary disease, %	1.8	0.7
Chronic kidney disease, %	6.6	1.8
Liver disease, %	7.3	2.9

Individuals with PoDs had higher prevalence of patients with at least one service utilized compared to individuals without PoDs for inpatient visits (22.5% vs. 7.0%), outpatient and other visits (98.9% vs. 94.8%), emergency department visits (33.6% vs. 18.6%), and office visits (96.4% vs. 85.6%) (all p<0.001). Individuals with PoDs had greater annual mean count of

service utilization compared to individuals without PoDs for inpatient visits (1.0 ± 2.4 vs. 0.2 ± 1.2), outpatient and other visits (14.7 ± 13.4 vs. 7.1 ± 8.9), emergency department visits (0.6 ± 1.1 vs. 0.3 ± 0.7), and office visits (7.4 ± 5.8 vs. 3.8 ± 4.2) (all p<0.001) (data not shown).

Unadjusted annual all-cause healthcare costs for individuals with and without PoDs are presented in **Figure 1**. The standardized reimbursement costs (**Figure 1A**) were higher for individuals with PoDs compared to individuals without PoDs for total (mean difference=$18,238; cost ratio [CR]=3.16; 95% confidence interval [CI]=3.13-3.18), medical (mean difference=$16,445; CR=3.39; 95% CI=3.36-3.42), and pharmacy (mean difference=$1,793; CR=1.95; 95% CI=1.93-1.97) costs. The patient out-of-pocket costs (**Figure 1B**) were higher for individuals with PoDs compared to individuals without PoDs for total (mean difference=$1,069; CR=1.88; 95% CI=1.86-1.89), medical (mean difference=$937; CR=1.96; 95% CI=1.95-1.98), and pharmacy (mean difference=$132; CR=1.39; 95% CI=1.38-1.40) costs.

Annual all-cause standardized reimbursement healthcare costs after adjusting for age, sex, education, insurance coverage, and noncommunicable diseases are presented in **Table 2**. Individuals with PoDs had higher total (CR=2.32; 95% CI=2.30-2.34), medical (CR=2.47; 95% CI=2.45-2.49), and pharmacy (CR=1.65; 95% CI=1.63-1.66) standardized reimbursement costs. All-cause patient out-of-pocket healthcare costs after adjusting for age, sex, education, and noncommunicable diseases are presented in **Table 3**. Individuals with PoDs had higher total (CR=1.65; 95% CI=1.64-1.66), medical (CR=1.72; 95% CI=1.71-1.73), and pharmacy (CR=1.30; 95% CI=1.29-1.31) patient out-of-pocket costs. The sensitivity analysis revealed that ethnicity and household annual income did not affect the results (n=3,545,206) for total (CR=2.35; 95% CI=2.33-2.38), medical (CR=2.48; 95% CI=2.45-2.50), and pharmacy (CR=1.79; 95% CI=1.76-1.81) standardized reimbursement costs, or for total (CR=1.62; 95%

CI=1.61-1.64), medical (CR=1.68; 95% CI=1.67-1.70), and pharmacy (CR=1.34; 95% CI=1.32-1.35) patient out-of-pocket costs.

Table 2. Annual adjusted cost ratios (CR) for total, medical, and pharmacy standardized reimbursement costs for year 2016 among adults (18-64 years) with and without pediatric-onset disabilities (PoDs).

	Total	Medical	Pharmacy
	CR (95% CI)	CR (95% CI)	CR (95% CI)
With PoDs (ref: without PoDs)	2.32 (2.30, 2.34)	2.47 (2.45, 2.49)	1.65 (1.63, 1.66)
Age (continuous)	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)	1.02 (1.02, 1.02)
Sex (ref: female)	0.75 (0.75, 0.76)	0.71 (0.71, 0.71)	1.10 (1.10, 1.10)
Education (ref: less than high school)			
High school diploma	1.10 (1.08, 1.12)	1.06 (1.05, 1.08)	1.32 (1.29, 1.35)
More than high school	1.13 (1.11, 1.15)	1.07 (1.05, 1.09)	1.55 (1.52, 1.58)
Unknown/missing	1.04 (1.03, 1.06)	1.02 (1.00, 1.04)	1.39 (1.36, 1.42)
Insurance coverage (ref: commercial only)	1.49 (1.48, 1.49)	1.26 (1.26, 1.27)	2.42 (2.40, 2.43)
Noncommunicable diseases (ref: without)			
Ischemic heart disease	2.00 (1.99, 2.01)	2.25 (2.24, 2.27)	1.20 (1.19, 1.21)
Cerebrovascular disease	2.05 (2.03, 2.07)	2.31 (2.29, 2.33)	1.13 (1.12, 1.14)
Hypertensive/other cardiovascular disease	1.58 (1.57, 1.58)	1.62 (1.62, 1.63)	1.24 (1.23, 1.24)
Type 2 diabetes	1.38 (1.38, 1.39)	1.21 (1.20, 1.21)	1.96 (1.95, 1.97)
Malignant cancer	3.48 (3.46, 3.50)	3.79 (3.77, 3.81)	2.19 (2.18, 2.21)
Osteoporosis	1.59 (1.58, 1.61)	1.54 (1.52, 1.55)	1.81 (1.79, 1.83)
Mood affective disorders	2.03 (2.02, 2.04)	2.05 (2.04, 2.06)	1.82 (1.81, 1.83)
Chronic obstructive pulmonary disease	1.85 (1.83, 1.87)	1.95 (1.92, 1.98)	1.48 (1.46, 1.51)
Chronic kidney disease	2.92 (2.90, 2.94)	3.41 (3.38, 3.44)	1.60 (1.58, 1.62)
Liver disease	2.38 (2.37, 2.40)	2.44 (2.42, 2.46)	1.98 (1.96, 2.00)

CI, confidence interval. Generalized linear models with gamma distribution and log-link function were performed to estimate the cost ratio and 95% CI, which is the exponentiated form of the parameter estimate.

Table 3. Annual adjusted cost ratios (CR) for total, medical, and pharmacy patient out-of-pocket costs for year 2016 among adults (18-64 years) with and without pediatric-onset disabilities (PoDs).

	Total	Medical	Pharmacy
	CR (95% CI)	CR (95% CI)	CR (95% CI)

With PoDs (ref: without PoDs)	1.65 (1.64, 1.66)	1.72 (1.71, 1.73)	1.30 (1.29, 1.31)
Age (continuous)	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)	1.02 (1.02, 1.02)
Sex (ref: female)	0.80 (0.80, 0.81)	0.79 (0.79, 0.79)	0.91 (0.91, 0.91)
Education (ref: less than high school)			
High school diploma	1.23 (1.21, 1.24)	1.06 (1.05, 1.08)	1.35 (1.33, 1.37)
More than high school	1.26 (1.24, 1.28)	1.05 (1.04, 1.07)	1.63 (1.61, 1.66)
Unknown/missing	1.17 (1.15, 1.19)	1.04 (1.02, 1.06)	1.55 (1.53, 1.58)
Insurance coverage (ref: commercial only)	0.81 (0.81, 0.81)	0.70 (0.70, 0.70)	1.31 (1.30, 1.31)
Noncommunicable diseases (ref: without)			
Ischemic heart disease	1.54 (1.53, 1.55)	1.64 (1.63, 1.65)	1.22 (1.21, 1.22)
Cerebrovascular disease	1.46 (1.44, 1.47)	1.61 (1.60, 1.63)	1.01 (1.00, 1.01)
Hypertensive/other cardiovascular disease	1.34 (1.34, 1.35)	1.27 (1.27, 1.27)	1.40 (1.40, 1.40)
Type 2 diabetes	1.24 (1.24, 1.24)	1.10 (1.10, 1.10)	1.63 (1.63, 1.64)
Malignant cancer	1.78 (1.77, 1.79)	1.93 (1.92, 1.94)	1.16 (1.15, 1.16)
Osteoporosis	1.28 (1.27, 1.30)	1.27 (1.26, 1.29)	1.29 (1.28, 1.30)
Mood affective disorders	1.64 (1.63, 1.64)	1.58 (1.58, 1.59)	1.69 (1.68, 1.69)
Chronic obstructive pulmonary disease	1.45 (1.44, 1.47)	1.53 (1.51, 1.55)	1.23 (1.22, 1.25)
Chronic kidney disease	1.45 (1.44, 1.46)	1.66 (1.65, 1.67)	1.16 (1.15, 1.16)
Liver disease	1.61 (1.60, 1.62)	1.74 (1.73, 1.75)	1.14 (1.13, 1.14)

CI, confidence interval. Generalized linear models with gamma distribution and log-link function were performed to estimate the cost ratio and 95% CI, which is the exponentiated form of the parameter estimate.

Unadjusted healthcare resource utilization for each PoD category is presented in **Supplementary Table 3**. All PoD categories tended to have higher healthcare resource utilization compared to individuals without PoDs, which was 2.5 (PoDs of malformations of the eye, ear, face, and neck) to 7.5 (PoDs of the circulatory and nervous systems) times higher for inpatient visits, 1.6 (PoDs of malformations of the eye, ear, face, and neck) to 2.3 (PoDs of the urinary system) times higher for outpatient and other visits, 1.3 (PoDs of malformations of the eye, ear, face, and neck) to 2.7 (neurodevelopmental PoDs and PoDs of the urinary and nervous systems) times higher for emergency department visits, and 1.6 (PoDs of malformations of the eye, ear, face, and neck) to 2.2 (PoDs of the urinary system) times higher for office visits.

Unadjusted all-cause total healthcare costs for each PoD category are presented in **Figure 2**. All PoD categories tended to have higher total all-cause healthcare costs compared to individuals without PoDs, which was 1.9 (PoDs of malformations of the eye, ear, face, and neck) to 4.3 (PoDs of the urinary system) times higher for standardized reimbursement costs and 1.5 (PoDs of malformations of the eye, ear, face, and neck) to 2.2 (PoDs of the circulatory, urinary, respiratory, and digestive systems) times higher for patient out-of-pockets costs.

DISCUSSION

The principal finding of this investigation is that young and middle-aged privately-insured adults with PoDs had higher healthcare resource utilization across all medical services, and higher all-cause healthcare costs compared to young and middle-aged privately-insured adults without PoDs. Moreover, these findings were evident across all PoD categories when compared to individuals without PoDs, suggesting that there was not a single PoD diagnosis or subset of PoDs (e.g., musculoskeletal) that were driving the elevated healthcare resource utilization or cost measures. While previous studies examining adverse health complications among populations with PoDs have suggested earlier screening strategies for disease prevention and healthcare management,[3,13] the findings from the current study could inform decision making processes regarding private health benefit plan design and healthcare resource allocation for services and treatments by administrators and policymakers.

Individuals with PoDs have complex healthcare needs and may require extensive medical services as part of their routine clinical care. While still in its infancy, the current state of the literature about the aging process for individuals with PoDs suggests a greater risk for developing several noncommunicable diseases compared to the general population.[2-4,6,10,11,13]

This may help to explain, in part, the higher healthcare resource utilization and costs from the current study, as these diseases incur high medical and pharmacy costs. Other non-health factors may play a role in the excess healthcare utilization and costs attributable to PoDs. Care coordination, knowledge transfer, and access to healthcare resources may not be sufficient for many individuals with PoDs to meet the high demands of their specific healthcare needs.[17-20] Importantly, disparities between healthcare needs due to health complications (e.g., noncommunicable diseases) and healthcare delivery can lead to uninformed patient- and clinical-decision making processes for healthcare management and intervention.

In the current study, we found substantial mean differences for all-cause healthcare costs and large unadjusted cost ratios for the standardized reimbursement and patient out-of-pocket costs between individuals with vs. without PoDs. After adjusting for sociodemographics, insurance coverage, and the presence of several costly noncommunicable diseases, total standardized reimbursement costs were still 2.3 times higher and patient out-of-pocket costs were 1.7 times higher for individuals with PoDs compared to individuals without PoDs. These results suggest a few things. First, costly noncommunicable diseases only account for a small portion of the excess healthcare costs attributable to PoDs; however, there may be other costly diseases not examined in this study that are more prevalent among individuals with PoDs. Second, the findings that patient out-of-pocket costs were elevated for individuals with PoDs compared to individuals without PoDs, but to a lesser extent than for standardized reimbursement costs, suggests that health plans are accommodating some, but not all, of the medical needs by individuals with PoDs. This is supported by the higher prevalence of Medicare Advantage health plans among individuals with PoDs compared to individuals without PoDs (21.1% vs. 6.6%). Further, the CR for Medicare Advantage was higher compared to commercial

alone for standardized reimbursement costs, but lower for patient out-of-pocket costs for the entire sample, suggesting greater cost reduction plans. Nevertheless, identifying and delineating other "cost drivers" for populations with PoDs is needed.

The sample size for the group with PoDs was very large, which allowed us to examine healthcare resource utilization and costs after stratifying by the type of PoD, with sample sizes ranging from 5,518 (PoDs with chromosomal abnormalities) to 33,566 (PoDs of the musculoskeletal system). Our exploratory analyses suggest that all PoD categories have higher healthcare resource utilization and costs compared to adults without PoDs. Moreover, there was a considerable range of excess healthcare utilization and costs across PoD categories. In general, PoD categories with the highest healthcare resource utilization and costs were PoDs of the urinary, circulatory, respiratory and digestive, and nervous systems. While different types of PoDs should not be assumed to have the same set of health complications, as most have very specific etiologies and comorbidities, there are overlapping risk factors across various types of PoDs that may impede healthful transition into and throughout adulthood, thus leading to similar health outcomes and healthcare needs. These factors may manifest as a direct consequence of the condition (e.g., impaired executive functioning) or as an indirect consequence of a condition (e.g., chronic pain, low societal integration). On the other hand, individuals with specific PoDs may be more susceptible to certain adverse health outcomes and reliantly on specific healthcare services. For example, children and adolescents with PoDs have higher prevalence of mental health disorders compared to the general population of children,[29,30] but the prevalence is greater among children and adolescents with neurodevelopmental PoDs than nervous system PoDs.[29,31] Future research is needed to parse out the PoD-specific factors contributing to excess healthcare utilization and costs to lessen the healthcare economic burden attributable to various PoDs.

The limitations of the study must be discussed. It is important to note that the findings from the current investigation are likely underreporting the extent of healthcare resource utilization and costs associated with U.S. populations with PoDs. To be enrolled with a private health insurance plan, individuals must be able to afford the costs or be covered through their employer, their parents (up to 26 years of age), or their spouse. Individuals with PoDs tend to have lower employment and marriage rates compared to the general population,[32] which is likely to be more problematic with more medically complex forms of PoDs. Furthermore, individuals with more severe forms of PoDs are likely to be covered, or co-covered, by public health insurance due to medical circumstances. Therefore, our sample of adults with PoDs likely reflects a higher functioning and healthier segment of the U.S. population with PoDs; however, this is only speculation.

In conclusion, young and middle-aged adults with PoDs have higher healthcare resource utilization and costs compared to young and middle-aged adults without PoDs. These higher costs come along with higher out-of-pocket burden, which can affect the individual's financial well-being, thus further contributing to health disparities. The elevated healthcare costs were evident even after adjusting for several costly noncommunicable diseases that are more prevalent among populations with PoDs. Furthermore, each PoD category had higher healthcare resource utilization and costs compared to individuals without PoDs. Future research is needed to identify specific cost drivers for the healthcare economic disparity for individuals with PoDs, and by the type of PoD, as well as year to year healthcare costs, which may provide insight into the long-term financial burden.

Contributors: D. Whitney conceived and designed the study, analyzed the data, and wrote the first draft of the manuscript. S. Ng and N. Kamdar assisted in statistical analysis and interpretation. E. Hurvitz, R. Hirth, and M. Peterson assisted in interpretation of data. All authors approved the final manuscript for submission, and agree to be accountable for all aspects of the work.

Data sharing: As part of our Data Use Agreements, raw data will not be shared. We will share statistical code or data summary upon reasonable request.

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Figure legends

Figure 1. Annual mean all-cause total, medical, and pharmacy standardized reimbursement costs (**A**) and annual mean all-cause total, medical, and pharmacy patient out-of-pocket costs (**B**) among adults (18-64 years) with and without pediatric-onset disabilities (PoDs).

Figure 2. Annual mean all-cause total standardized reimbursement costs (**A**) and annual mean all-cause total patient out-of-pocket costs (**B**) among adults (18-64 years) with and without pediatric-onset disabilities (PoDs), stratified by the type of PoD. Individuals may have more than one PoD and can be represented across multiple PoD categories.

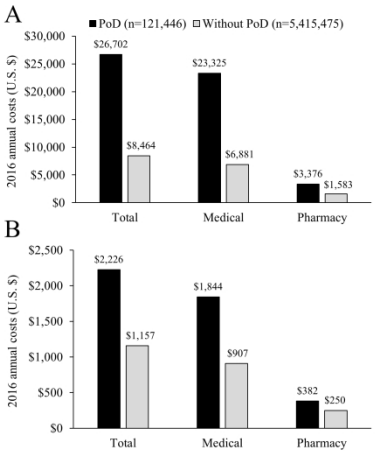

Figure 1. Annual mean all-cause total, medical, and pharmacy standardized reimbursement costs (A) and annual mean all-cause total, medical, and pharmacy patient out-of-pocket costs (B) among adults (18-64 years) with and without pediatric-onset disabilities (PoDs).

338x190mm (300 x 300 DPI)

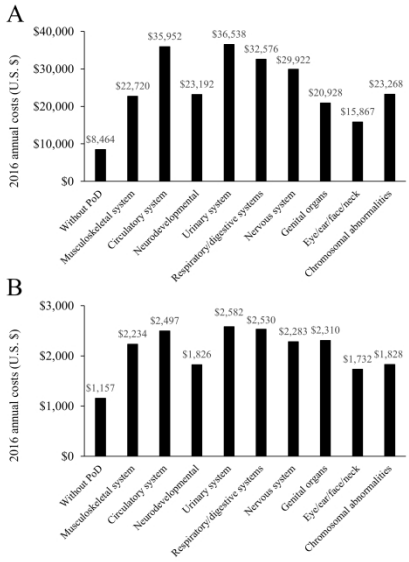

Figure 2. Annual mean all-cause total standardized reimbursement costs (A) and annual mean all-cause total patient out-of-pocket costs (B) among adults (18-64 years) with and without pediatric-onset disabilities (PoDs), stratified by the type of PoD. Individuals may have more than one PoD and can be represented across multiple PoD categories.

338x190mm (300 x 300 DPI)

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5-9
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5-6
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-8
Bias	9	Describe any efforts to address potential sources of bias	5, 6, 7, 8
Study size	10	Explain how the study size was arrived at	5-6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8-9
		(*b*) Describe any methods used to examine subgroups and interactions	8-9
		(*c*) Explain how missing data were addressed	5
		(*d*) If applicable, explain how loss to follow-up was addressed	NA
		(*e*) Describe any sensitivity analyses	8
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9, Table 1
		(b) Indicate number of participants with missing data for each variable of interest	NA
		(c) Summarise follow-up time (eg, average and total amount)	11, 12, 14
Outcome data	15*	Report numbers of outcome events or summary measures over time	9-14

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	9-14 and tables/figures Tables
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	13-14
Discussion			
Key results	18	Summarise key results with reference to study objectives	14-17
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	17
Generalisability	21	Discuss the generalisability (external validity) of the study results	15-16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	No funding reported

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

Supplementary Table 1. Diagnostic codes for all pediatric-onset disabilities (PoDs) and noncommunicable diseases using the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10) codes.

Pediatric-onset disability categories and specific conditions	ICD-10 codes
Musculoskeletal system	
Congenital deformities of hip or feet; congenital musculoskeletal deformities of head, face, spine and chest; other congenital musculoskeletal deformities; polydactyly; syndactyly; reduction defects of upper, lower, or unspecified limb; other congenital malformations of limb(s); other congenital malformations of skull and face bones; congenital malformations of spine and bony thorax; osteochondrodysplasia with defects of growth of tubular bones and spine; other osteochondrodysplasias; congenital malformations of musculoskeletal system, not elsewhere classified	Q65-79 families
Juvenile arthritis	M08 family
Other disorders of bone	
Physeal arrest	M89.1 family
Other disorders of bone development and growth	M89.2 family
Circulatory system	
Congenital malformations of the cardiac chambers, cardiac septa, pulmonary and tricuspid valves, aortic and mitral valves; other congenital malformations of the heart; congenital malformations of great arteries, great veins; other congenital malformations of peripheral vascular system or circulatory system	Q20-28 families
Neurodevelopmental	
Intellectual disabilities, mild, moderate, severe, profound, other, and unspecified	F70-73, F78, F79
Specific developmental disorders of speech and language, scholastic skills, motor function; pervasive developmental disorders; other and unspecified disorders of psychological development	F80 family, F81 family, F82, F84 family, F88, F99
Urinary system	
Renal agenesis and other reduction defects of kidney; cystic kidney disease; congenital obstructive defects of renal pelvis and congenital malformations of ureter; other congenital malformations of kidney	Q60-63 families
Respiratory and digestive systems	
Congenital malformations of nose, larynx, trachea or bronchus, lung; other congenital malformations of respiratory system; cleft lip and/or palate; other congenital malformations of tongue, mouth, or pharynx; congenital malformations of esophagus; other congenital malformations of upper alimentary tract; congenital absence, atresia and stenosis of small or large intestine; other congenital malformations of intestine; congenital malformations of gallbladder, bile ducts, or liver; other congenital malformations of digestive system	Q30-45 families

Nervous system	
Encephalocele; microcephaly; congenital hydrocephalus; spina bifida; other congenital malformations of brain, spinal cord, or nervous system	Q01 family, Q02, Q03-7 families
Cerebral palsy	G80 family
Juvenile epilepsy	G40.B family
Genital organs	
Congenital malformations of ovaries, fallopian tubes, broad ligaments, uterus, and cervix; undescended and ectopic testicle; hypospadias; other congenital malformations of female or male genital organs; indeterminate sex and pseudohermaphroditism	Q50-56 families
Malformations of the eye, ear, face, and neck	
Congenital malformations of eyelid, lacrimal apparatus, or orbit; anophthalmos, microphthalmos, or macrophthalmos; congenital lens malformations; congenital malformations of anterior or posterior segment of eye; other congenital malformations of eye; congenital malformations of ear causing impairment of hearing; other congenital malformations of ear, face, or neck	Q10-18 families
Other chromosomal abnormalities, not classified elsewhere	
Down syndrome; Trisomy 18 and Trisomy 13; other trisomies and partial trisomies of the autosomies, not elsewhere classified; monosomies and deletions from the autosomes, not elsewhere classified; balanced rearrangements and structural markers, not elsewhere classified; Turner's syndrome; other sex chromosome abnormalities, female or male phenotype, not elsewhere classified; other chromosome abnormalities	Q90-93 families, Q95-99 families
<u>Noncommunicable diseases</u>	
Ischemic heart disease	
Angina pectoris; acute myocardial infarction; subsequent ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction; other acute ischemic heart diseases; chronic ischemic heart disease	I20-22 families, I24 family, I25 family
Cerebrovascular disease	
Nontraumatic subarachnoid or intracerebral hemorrhage; other and unspecified nontraumatic intracranial hemorrhage; cerebral infarction; occlusion and stenosis of precerebral or cerebral arteries, not resulting in cerebral infarction; other cerebrovascular diseases; cerebrovascular disorders in diseases classified elsewhere; sequelae of cerebrovascular disease	I60-63 families, I65-69 families
Hypertensive and other cardiovascular disease	
Essential (primary) hypertension; hypertensive heart, chronic kidney disease, or heart and chronic kidney disease; secondary hypertension; hypertensive crisis; heart failure; peripheral atherosclerosis	I10-13 families, I15 family, I16 family, I50 family, I70 family
Type II diabetes mellitus	E11 family
Malignant cancer	

Malignant neoplasms of lip, oral cavity, or pharynx, digestive organs, respiratory and intrathoracic organs, bone and articular cartilage, mesothelial and soft tissue, breast, female or male genital organs, urinary tract, eye, brain, or other parts of central nervous system, thyroid or other endocrine glands, ill-defined, other secondary, or unspecified sites, neuroendocrine tumors, lymphoid, hematopoietic, or related tissue; melanoma and other malignant neoplasms of skin	C00-26 families, C30-41 families, C43-58 families, C60-80 families, C7A family, C7B family, C81-96 families
Osteoporosis	
With or without current pathological fracture	M80 family, M81 family
Mood affective disorders	
Manic episode; bipolar disorder; major depressive disorder, single episode or recurrent; persistent mood [affective] disorders; unspecified mood [affective] disorders	F30-34 families, F39
Chronic obstructive pulmonary disease	
Simple and mucopurulent chronic bronchitis; unspecified chronic bronchitis; emphysema; other chronic obstructive pulmonary disease	J41-44 families
Chronic kidney disease	
Stage I-V; end stage renal disease; chronic kidney disease, unspecified	N18 family
Liver disease	
Alcoholic liver disease; toxic liver disease; hepatic failure, not elsewhere classified; chronic hepatitis, not elsewhere classified; fibrosis and cirrhosis of liver; other inflammatory liver diseases; other diseases of liver; liver disorders in diseases classified elsewhere	K70-76 families, K77

Supplementary Table 2. Healthcare resource utilization by service type.

Healthcare service type	Level 1 Description: Level 2 Description
Inpatient services	Facility Inpatient: Acute and Rehab/Skilled Nursing Facility; Professional Services: Inpatient Visits
Outpatient, ambulatory, and other services	Facility Outpatient: OP Facility Diagnostic, Laboratory, Other, Radiology, and Surgery; Professional Services: Allergy Tests and Injections, Anesthesia, Consultations, Diagnostic Testing, Immunizations and Injections, Laboratory, Mental Health, Obstetrics, Pathology, Physical Medicine/Rehab, Professional Other, Preventive Medicine, Radiology, Surgery, Vision, Hearing, and Speech
Emergency department services	Facility Outpatient: Emergency Room; Professional Services: Emergency Room
Office services	Professional Services: Office Visits

Supplementary Table 3. Annual healthcare resource utilization in 2016 among adults (18-64 years) by the type of pediatric-onset disability (PoD).*

	Inpatient	Outpatient and other	Emergency department	Office
PoD categories	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Musculoskeletal system (n=33,566)	0.7 (1.9)	15.2 (13.2)	0.5 (1.0)	8.0 (5.9)
Circulatory system (n= 24,393)	1.5 (2.9)	15.8 (13.7)	0.7 (1.1)	7.6 (5.9)
Neurodevelopmental (n=17,149)	1.3 (2.9)	13.9 (14.5)	0.8 (1.2)	6.5 (5.5)
Urinary system (n=12,477)	1.2 (2.6)	16.2 (13.4)	0.8 (1.2)	8.2 (6.0)
Respiratory or digestive systems (n=12,190)	1.2 (2.6)	15.2 (13.1)	0.7 (1.2)	7.8 (6.1)
Nervous system (n=11,021)	1.5 (2.9)	15.4 (14.5)	0.8 (1.2)	7.4 (6.0)
Genital organs (n=6,164)	0.6 (1.7)	13.5 (11.8)	0.5 (0.9)	6.3 (5.3)
Eye/ear/face/neck (n=5,811)	0.5 (1.7)	11.5 (11.8)	0.4 (0.9)	5.9 (5.3)
Chromosomal abnormalities (n=5,518)	0.9 (2.3)	14.6 (13.9)	0.5 (1.0)	6.7 (5.7)

*Individuals may have more than one PoD and can be represented across multiple PoD categories.

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The economic burden of pediatric-onset disabilities among young and middle-aged adults in the United States: A cohort study of privately insured beneficiaries

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The economic burden of pediatric-onset disabilities among young and middle-aged adults in the United States: A cohort study of privately insured beneficiaries

Daniel G. Whitney,[1,2] Neil S. Kamdar,[2,3,4,5] Richard A. Hirth,[6,7] Edward A. Hurvitz,[1] Mark D. Peterson[2]

[1]Department of Physical Medicine and Rehabilitation, University of Michigan, Ann Arbor, USA

[2]Institute for Healthcare Policy and Innovation, University of Michigan, Ann Arbor, USA

[3]Department of Obstetrics and Gynecology, University of Michigan, Ann Arbor, USA

[4]Department of Surgery, University of Michigan, Ann Arbor, USA

[5]Department of Emergency Medicine, University of Michigan, Ann Arbor, USA

[6]Department of Health Management and Policy, University of Michigan School of Public Health, Ann Arbor, USA

[7]Department of Internal Medicine, University of Michigan, Ann Arbor, USA

Corresponding author:

Daniel G. Whitney, PhD

325 E. Eisenhower Pkwy, Ann Arbor, MI, USA 48108

Phone: 734-936-7175

E-mail: danielwhitney8@gmail.com

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Abstract

Objective: Individuals with pediatric-onset disabilities (PoDs) have complex healthcare needs and are susceptible to adverse health outcomes, which may impose a higher strain on healthcare resources. The burden of healthcare resource utilization and costs attributed to the population of adults with PoDs is not clearly established. The objective here was to compare healthcare resource utilization and costs between adults with vs. without PoDs.

Design: Cohort.

Setting: Data were from the 2016 Optum Clinformatics® Data Mart, a de-identified nationwide claims database of beneficiaries from a single private payer in the U.S.

Participants: ICD-10-CM diagnosis codes were used to identify beneficiaries with PoDs that were between 18 and 64 years of age.

Primary and secondary outcome measures: Annual all-cause healthcare resource utilization was compared between adults with and without PoDs. Annual all-cause total healthcare costs were compared between adults with and without PoDs before and after adjusting for sociodemographics and several costly noncommunicable diseases.

Results: Adults with PoDs (n=121,446) had greater annual mean counts of service utilization for all service types (e.g., inpatient, outpatient, emergency visits) compared to adults without PoDs (n=5,415,475; all p<0.001). Adults with PoDs had greater unadjusted total standardized reimbursement costs ($26,702 vs. $8,464; mean difference=$18,238; cost ratio [CR]=3.16; 95% confidence interval [CI]=3.13-3.18) and total patient out-of-pocket costs ($2,226 vs. $1,157; mean difference=$1,069; CR=1.88; 95%CI=1.86-1.89). After adjusting for sociodemographics and noncommunicable diseases, total standardized reimbursement costs were 2.32 times higher

(95%CI=2.30-2.34) and total patient out-of-pocket costs were 1.65 times higher (95%CI=1.64-1.66) compared to adults without PoDs.

Conclusion: Adults with PoDs had greater healthcare utilization and costs, even after accounting for costly diseases. Future research is needed to identify the cost drivers for adults with PoDs.

Trial registration: None, this is not a trial.

Keywords: pediatric-onset disabilities; economics; healthcare utilization

Strengths and limitations of this study

- This is the largest study to date to examine healthcare utilization and associated costs of adults with different types of pediatric-onset disabilities.
- We examined the healthcare-related economic burden after accounting for costly noncommunicable diseases that are more prevalent among adults with pediatric-onset disabilities.
- This study leveraged administrative claims data, and are therefore subject to limitations that are inherent to claims data, such as inaccurate coding of medical conditions.
- We were unable to determine specific cost drivers.

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Competing interest: None declared.

Patient consent for publication: Not required.

INTRODUCTION

Pediatric-onset disabilities (PoDs) refer to a group of congenital or acquired conditions that originate at conception, during pregnancy, or in childhood, and consist of impairments in behavioral, intellectual, and/or physical functioning, or are associated with abnormal developmental or metabolic processes. While clinical care and coordinated healthcare management (e.g., specialist referral) for children with PoDs is a large focus of pediatric clinicians and researchers, far less attention on the topic has been given to these individuals as they become adults. The complex healthcare needs and health complications born out of direct (e.g., genetic) and resulting (e.g., delayed growth) consequences associated with PoDs during growth and development, have lasting ramifications on the health and functional status across the lifespan. Research has shown that individuals with PoDs are susceptible to early development of chronic, noncommunicable diseases and early mortality,[1-13] thus placing a high strain on the patients, caregivers, and healthcare resources. Importantly, the population of adults with PoDs is projected to expand over the coming decades,[14-16] which may lead to a noticeable increase in the national healthcare economic burden, and should be considered an urgent public health issue. However, healthcare resource utilization and costs directly attributable to adults with PoDs has not been extensively studied.

The current U.S. healthcare system may not be adequately prepared to care for adults with PoDs.[17-20] To date, little is known about the natural trajectory of adverse health complications across the lifespan for these populations, best practices for coordinating healthcare services between general physicians and specialists (e.g., pediatricians), and how to provide adequate resources for preventive and treatment services to these populations. A comprehensive understanding of healthcare resource utilization and costs among adults with PoDs is crucial for

public health, healthcare policy reform, and implementing better clinical practice guidelines for cost-effective care. Further, understanding the healthcare economic burden among at-risk populations prior to reaching the elderly years could inform public health efforts, policymakers, and early patient- and clinical-decision making processes and strategies (e.g., surgeries, medications) to maximize comorbidity management and prevention. Therefore, the primary aim of this study was to characterize healthcare resource utilization and costs among young and middle-aged adults with PoDs, as compared to young and middle-aged adults without PoDs, before and after adjusting for costly comorbid noncommunicable diseases. We hypothesized that adults with PoDs would have higher healthcare resource utilization and costs compared to adults without PoDs, even after adjusting for noncommunicable diseases.

METHODS

Data source

Data were from the 2016 Clinformatics® Data Mart Database (OptumInsight™, Eden Prairie, MN, USA), which is a nationwide, de-identified single private payer administrative claims database. This database contains over 16 million beneficiaries in 2016 who have either commercial or Medicare Advantage health plans, and includes all the inpatient, outpatient, pharmacy, emergency visit, office visit, and other ancillary service utilization throughout their enrollment on the insurance plan. Medicare beneficiaries can opt to enroll in a private Medicare Advantage health plan in lieu of participating in the traditional public Medicare program. Such plans can offer extra coverage not available in the traditional Medicare program, such as vision, hearing, dental, and/or health and wellness programs. To be enrolled in a private payer health plan, beneficiaries of any age, income, or disability status either pay for coverage or are covered

through their employer. Administrative claims data are primarily used for billing reimbursement purposes, and health conditions are identified using specific codes attached to individual claims. Since data are de-identified, the University Institutional Review Board approved this study as non-regulated.

Sample selection

Beneficiaries that were 18 to 64 years of age, had 12 full months of continuous enrollment, and had at least one service utilization in 2016 (to make a diagnosis of PoDs and noncommunicable diseases) were considered for this investigation. Beneficiaries were excluded if they did not have known data for sex (n=991, <0.01%). All PoDs and noncommunicable diseases were identified using the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10) codes, and are presented in **Supplementary Table 1**. Since it is not possible to determine if some conditions developed in childhood or adulthood (e.g., spinal cord injury, cancer), conditions were included in the group representing PoDs if there were known childhood origins. These conditions were then grouped into the following PoD subcategories: PoDs of the musculoskeletal system; PoDs of the circulatory system; neurodevelopmental PoDs; PoDs of the urinary system; PoDs of the respiratory system and digestive system; PoDs of the nervous system; PoDs of the genital organs; PoDs of malformations of the eye, ear, face, and neck; and other chromosomal abnormalities.

Noncommunicable diseases

Prevalent noncommunicable diseases, as individual dichotomous variables (present vs. not present), were ascertained by at least 1 medical claim in 2016, and were selected with

guidance from the literature on disease, disability, and mortality among adults.[2,3,21-26] Noncommunicable diseases were represented as categories across multiple biological systems as follows: ischemic heart diseases (e.g., atherosclerotic heart disease); cerebrovascular diseases (e.g., cerebral infarction); hypertensive and other cardiovascular diseases (e.g., hypertension, heart failure); type 2 diabetes mellitus; malignant cancer; osteoporosis; mood affective disorders (e.g., depression); chronic obstructive pulmonary diseases (e.g., emphysema); chronic kidney diseases (e.g., kidney disease stages I-V); and liver diseases (e.g., cirrhosis).

Healthcare resource utilization

Annual all-cause healthcare resource utilization was identified using medical claims and was categorized into the following service types: inpatient; outpatient, ambulatory, and other (herein referred to as "outpatient and other"); emergency department; and office. Specific services per service category are presented in **Table 1**. Measures to assess healthcare resource utilization included the percentage of patients per group (with PoDs, without PoDs) that had at least one service utilization within each service category, and the annual mean count of service utilization per group for each service category.

Table 1. Healthcare resource utilization by service type.

Healthcare service type	Level 1 Description: Level 2 Description
Inpatient services	Facility Inpatient: Acute and Rehab/Skilled Nursing Facility; Professional Services: Inpatient Visits
Outpatient, ambulatory, and other services	Facility Outpatient: OP Facility Diagnostic, Laboratory, Other, Radiology, and Surgery; Professional Services: Allergy Tests and Injections, Anesthesia, Consultations, Diagnostic Testing, Immunizations and Injections, Laboratory, Mental Health, Obstetrics, Pathology, Physical Medicine/Rehab, Professional Other, Preventive Medicine, Radiology, Surgery, Vision, Hearing, and Speech
Emergency department services	Facility Outpatient: Emergency Room; Professional Services: Emergency Room
Office services	Professional Services: Office Visits

Healthcare costs

Annual all-cause healthcare costs were identified using medical and outpatient pharmacy (herein referred to as "pharmacy") claims, and were from the paid amounts of adjudicated (final action) claims, which included insurer and health plan payments and patient copayments, deductibles, and coinsurance. Total (medical + pharmacy), medical, and pharmacy all-cause healthcare costs were represented as standardized reimbursement cost (i.e., sum of all health plan and patient paid amounts) and patient out-of-pocket cost (i.e., sum of copayment, deductible, and coinsurance).

Clinformatics® Data Mart Database accounts for differences in pricing across health plans and provider contracts by standardizing cost field utilized algorithms that reflect the allowed payments across all provider services. This allows comparisons across patients, data sources, and geographic areas, and accounts for contractual payer and provider differences. Price standardization accounts for quantity of services provided, relative resource costs involved in providing the services, and the nature of the service which can be defined as the CPT/HCPCS codes for professional services, NDC for pharmacy service, or type of admission for inpatient stay.

Sociodemographic variables

Age, sex, ethnicity, education level, household annual income, and insurance coverage (i.e., commercial only, Medicare Advantage) were considered for risk adjustment to differentiate the effect of potential confounders from the effect of PoDs on the outcome.

Statistical analysis

To limit extreme values and to reduce the effect of possible spurious outliers, winsorization of healthcare resource utilization data to the upper 99.0% was performed for each service category.

Descriptive characteristics and healthcare resource utilization and cost measures were summarized using mean (SD) for continuous variables and percentage for categorical variables. Group differences for healthcare resource utilization measures were examined using Chi-Square tests for binary data (e.g., sex, education level, noncommunicable diseases) and generalized linear models assuming a zero-inflated Poisson distribution (for non-utilization) and log-link function for count data (i.e., number of visits per service type), while controlling for age, sex, education, insurance coverage, and all noncommunicable diseases. As recommended for healthcare cost data analysis,[27,28] generalized linear models with gamma distribution and log-link function were performed to estimate the cost ratios (CR; exponentiated form of variable estimate) for explanatory variables (e.g., PoD group), while controlling for age, sex, education, insurance coverage, and all noncommunicable diseases. For the generalized linear models, the main effect for PoD group was interpreted. We adjusted the models for the noncommunicable diseases because these diseases can incur excess healthcare utilization and costs, which may explain any differences in costs between groups. Ethnicity and household annual income were not initially included as covariates because of the extent of unknown/missingness. However, because these variables can be associated with healthcare delivery and noncommunicable diseases, we conducted a sensitivity analysis using the fully adjusted generalized linear models that included ethnicity and household annual income to determine if these variables biased the estimated CR for group (reference: without PoDs) for healthcare cost measures.

Healthcare resource utilization and total cost measures were then summarized using mean (SD) after stratifying the type of PoD (e.g., musculoskeletal system, neurodevelopmental). Comparisons between each of the PoD categories with the sample without PoDs were examined for healthcare resource utilization and cost measures using the same procedures and models noted above.

Finally, to determine if age differentially associated with healthcare costs for adults with and without PoDs, we examined the age (young, 18-40 years; middle-aged, 41-64 years) by group interaction for all individuals with PoDs compared to the sample without PoDs, and then for each of the PoD categories compared to the sample without PoDs. The outcome measures were total standardized reimbursement costs and patient out-of-pocket costs, as these were the primary outcome measures of interest. If the interaction was significant, subsequent analyses were performed after stratifying by age group.

All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA). Effect estimates were reported as CRs with 95% confidence intervals (CI), and $p \leq 0.05$ (two-tailed) was used to determine statistical significance.

Patient and public involvement

Patient were not directly involved in the design or conduct of this study.

RESULTS

Descriptive characteristics of individuals with PoDs (n=121,446) and without PoDs (n=5,415,475) are presented in **Table 2**. Notably, individuals with PoDs had a higher proportion enrolled in the Medicare Advantage health plan compared to individuals without PoDs. Further,

individuals with PoDs had higher prevalence of noncommunicable diseases compared to individuals without PoDs, including: ischemic heart disease (8.7%, 3.5%); cerebrovascular disease (6.3%, 1.5%); hypertensive or other cardiovascular disease (37.8%, 25.4%); type 2 diabetes (14.5%, 10.0%); malignant cancer (6.6%, 3.8%); osteoporosis (3.4%, 1.3%); mood affective disorders (20.8%, 11.0%); chronic obstructive pulmonary disease (1.8%, 0.7%); chronic kidney disease (6.6%, 1.8%); and liver disease (7.3%, 2.9%) (all p<0.001).

Table 2. Descriptive characteristics and prevalence of noncommunicable diseases among adults (18-64 years) with and without pediatric-onset disabilities (PoDs).

	PoD (n=121,446)	Without PoD (n=5,415,475)	
	Point estimate	Point estimate	
Descriptive characteristics			p-value
Age, mean (SD)	44.3 (13.6)	43.8 (12.9)	<0.001
18-40 years, %	38.8	40.3	
41-64 years, %	61.2	59.7	
Sex, %			<0.001
Female	55.6	53.8	
Male	44.4	46.2	
Ethnicity, %			<0.001
White	55.7	53.4	
Black	7.9	7.4	
Hispanic	8.3	9.4	
Asian	3.0	4.3	
Unknown/missing	25.0	25.5	
Education, %			<0.001
Less than high school	0.4	0.5	
High school diploma	25.1	24.0	
More than high school	71.9	73.5	
Unknown/missing	2.6	2.1	
Household annual income, %			<0.001
<$40K	15.2	13.1	
$40K to 59.9K	9.9	10.0	
$60K to 99.9K	19.0	20.0	
≥$100K	32.6	34.1	
Unknown/missing	23.4	22.8	
Insurance coverage, %			<0.001
Commercial only	78.9	93.4	
Medicare Advantage	21.1	6.6	

Noncommunicable diseases			
Ischemic heart disease, %	8.7	3.5	<0.001
Cerebrovascular disease, %	6.3	1.5	<0.001
Hypertensive/other cardiovascular disease, %	37.8	25.4	<0.001
Type 2 diabetes, %	14.5	10.0	<0.001
Malignant cancer, %	6.6	3.8	<0.001
Osteoporosis, %	3.4	1.3	<0.001
Mood affective disorders, %	20.8	11.0	<0.001
Chronic obstructive pulmonary disease, %	1.8	0.7	<0.001
Chronic kidney disease, %	6.6	1.8	<0.001
Liver disease, %	7.3	2.9	

Healthcare resource utilization for adults with and without PoDs

Individuals with PoDs had higher prevalence of patients with at least one service utilized compared to individuals without PoDs for inpatient visits (22.5% vs. 7.0%), outpatient and other visits (98.9% vs. 94.8%), emergency department visits (33.6% vs. 18.6%), and office visits (96.4% vs. 85.6%) (all p<0.001). Individuals with PoDs had greater unadjusted annual mean count of service utilization compared to individuals without PoDs for inpatient visits (1.0 ± 2.4 vs. 0.2 ± 1.2), outpatient and other visits (14.7 ± 13.4 vs. 7.1 ± 8.9), emergency department visits (0.6 ± 1.1 vs. 0.3 ± 0.7), and office visits (7.4 ± 5.8 vs. 3.8 ± 4.2) (all p<0.001) (data not shown). The higher service utilization was present even after adjusting for age, sex, education, insurance coverage, and all noncommunicable diseases for each service category (all p<0.001).

Healthcare costs for adults with and without PoDs

Unadjusted annual all-cause healthcare costs for individuals with and without PoDs are presented in **Figure 1**. The standardized reimbursement costs (**Figure 1A**) were higher for individuals with PoDs compared to individuals without PoDs for total (mean difference=$18,238; cost ratio [CR]=3.16; 95% confidence interval [CI]=3.13-3.18), medical

(mean difference=$16,445; CR=3.39; 95% CI=3.36-3.42), and pharmacy (mean difference=$1,793; CR=1.95; 95% CI=1.93-1.97) costs. The patient out-of-pocket costs (**Figure 1B**) were higher for individuals with PoDs compared to individuals without PoDs for total (mean difference=$1,069; CR=1.88; 95% CI=1.86-1.89), medical (mean difference=$937; CR=1.96; 95% CI=1.95-1.98), and pharmacy (mean difference=$132; CR=1.39; 95% CI=1.38-1.40) costs.

Annual all-cause standardized reimbursement healthcare costs after adjusting for age, sex, education, insurance coverage, and noncommunicable diseases are presented in **Table 3**. Individuals with PoDs had higher total (CR=2.32; 95% CI=2.30-2.34), medical (CR=2.47; 95% CI=2.45-2.49), and pharmacy (CR=1.65; 95% CI=1.63-1.66) standardized reimbursement costs. All-cause patient out-of-pocket healthcare costs after adjusting for age, sex, education, insurance coverage, and noncommunicable diseases are presented in **Table 4**. Individuals with PoDs had higher total (CR=1.65; 95% CI=1.64-1.66), medical (CR=1.72; 95% CI=1.71-1.73), and pharmacy (CR=1.30; 95% CI=1.29-1.31) patient out-of-pocket costs. The sensitivity analysis revealed that ethnicity and household annual income did not affect the results (n=3,545,206) for total (CR=2.35; 95% CI=2.33-2.38), medical (CR=2.48; 95% CI=2.45-2.50), and pharmacy (CR=1.79; 95% CI=1.76-1.81) standardized reimbursement costs, or for total (CR=1.62; 95% CI=1.61-1.64), medical (CR=1.68; 95% CI=1.67-1.70), and pharmacy (CR=1.34; 95% CI=1.32-1.35) patient out-of-pocket costs.

Table 3. Annual adjusted cost ratios (CR) for total, medical, and pharmacy standardized reimbursement costs for year 2016 among adults (18-64 years) with and without pediatric-onset disabilities (PoDs).

	Total	Medical	Pharmacy
	CR (95% CI)	CR (95% CI)	CR (95% CI)
With PoDs (ref: without PoDs)	2.32 (2.30, 2.34)	2.47 (2.45, 2.49)	1.65 (1.63, 1.66)
Age (continuous)	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)	1.02 (1.02, 1.02)
Sex (ref: female)	0.75 (0.75, 0.76)	0.71 (0.71, 0.71)	1.10 (1.10, 1.10)

Education (ref: less than high school)			
High school diploma	1.10 (1.08, 1.12)	1.06 (1.05, 1.08)	1.32 (1.29, 1.35)
More than high school	1.13 (1.11, 1.15)	1.07 (1.05, 1.09)	1.55 (1.52, 1.58)
Unknown/missing	1.04 (1.03, 1.06)	1.02 (1.00, 1.04)	1.39 (1.36, 1.42)
Insurance coverage (ref: commercial only)	1.49 (1.48, 1.49)	1.26 (1.26, 1.27)	2.42 (2.40, 2.43)
Noncommunicable diseases (ref: without)			
Ischemic heart disease	2.00 (1.99, 2.01)	2.25 (2.24, 2.27)	1.20 (1.19, 1.21)
Cerebrovascular disease	2.05 (2.03, 2.07)	2.31 (2.29, 2.33)	1.13 (1.12, 1.14)
Hypertensive/other cardiovascular disease	1.58 (1.57, 1.58)	1.62 (1.62, 1.63)	1.24 (1.23, 1.24)
Type 2 diabetes	1.38 (1.38, 1.39)	1.21 (1.20, 1.21)	1.96 (1.95, 1.97)
Malignant cancer	3.48 (3.46, 3.50)	3.79 (3.77, 3.81)	2.19 (2.18, 2.21)
Osteoporosis	1.59 (1.58, 1.61)	1.54 (1.52, 1.55)	1.81 (1.79, 1.83)
Mood affective disorders	2.03 (2.02, 2.04)	2.05 (2.04, 2.06)	1.82 (1.81, 1.83)
Chronic obstructive pulmonary disease	1.85 (1.83, 1.87)	1.95 (1.92, 1.98)	1.48 (1.46, 1.51)
Chronic kidney disease	2.92 (2.90, 2.94)	3.41 (3.38, 3.44)	1.60 (1.58, 1.62)
Liver disease	2.38 (2.37, 2.40)	2.44 (2.42, 2.46)	1.98 (1.96, 2.00)

CI, confidence interval. Generalized linear models with gamma distribution and log-link function were performed to estimate the cost ratio and 95% CI, which is the exponentiated form of the parameter estimate. N=5,536,921.

Table 4. Annual adjusted cost ratios (CR) for total, medical, and pharmacy patient out-of-pocket costs for year 2016 among adults (18-64 years) with and without pediatric-onset disabilities (PoDs).

	Total	Medical	Pharmacy
	CR (95% CI)	CR (95% CI)	CR (95% CI)
With PoDs (ref: without PoDs)	1.65 (1.64, 1.66)	1.72 (1.71, 1.73)	1.30 (1.29, 1.31)
Age (continuous)	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)	1.02 (1.02, 1.02)
Sex (ref: female)	0.80 (0.80, 0.81)	0.79 (0.79, 0.79)	0.91 (0.91, 0.91)
Education (ref: less than high school)			
High school diploma	1.23 (1.21, 1.24)	1.06 (1.05, 1.08)	1.35 (1.33, 1.37)
More than high school	1.26 (1.24, 1.28)	1.05 (1.04, 1.07)	1.63 (1.61, 1.66)
Unknown/missing	1.17 (1.15, 1.19)	1.04 (1.02, 1.06)	1.55 (1.53, 1.58)
Insurance coverage (ref: commercial only)	0.81 (0.81, 0.81)	0.70 (0.70, 0.70)	1.31 (1.30, 1.31)
Noncommunicable diseases (ref: without)			
Ischemic heart disease	1.54 (1.53, 1.55)	1.64 (1.63, 1.65)	1.22 (1.21, 1.22)
Cerebrovascular disease	1.46 (1.44, 1.47)	1.61 (1.60, 1.63)	1.01 (1.00, 1.01)
Hypertensive/other cardiovascular disease	1.34 (1.34, 1.35)	1.27 (1.27, 1.27)	1.40 (1.40, 1.40)

Type 2 diabetes	1.24 (1.24, 1.24)	1.10 (1.10, 1.10)	1.63 (1.63, 1.64)
Malignant cancer	1.78 (1.77, 1.79)	1.93 (1.92, 1.94)	1.16 (1.15, 1.16)
Osteoporosis	1.28 (1.27, 1.30)	1.27 (1.26, 1.29)	1.29 (1.28, 1.30)
Mood affective disorders	1.64 (1.63, 1.64)	1.58 (1.58, 1.59)	1.69 (1.68, 1.69)
Chronic obstructive pulmonary disease	1.45 (1.44, 1.47)	1.53 (1.51, 1.55)	1.23 (1.22, 1.25)
Chronic kidney disease	1.45 (1.44, 1.46)	1.66 (1.65, 1.67)	1.16 (1.15, 1.16)
Liver disease	1.61 (1.60, 1.62)	1.74 (1.73, 1.75)	1.14 (1.13, 1.14)

CI, confidence interval. Generalized linear models with gamma distribution and log-link function were performed to estimate the cost ratio and 95% CI, which is the exponentiated form of the parameter estimate. N=5,536,921.

Healthcare resource utilization and costs by PoD category

Unadjusted healthcare resource utilization for each PoD category is presented in **Supplementary Table 2**. After adjusting for age, sex, education, insurance coverage, and noncommunicable diseases, all PoD categories had higher healthcare resource utilization compared to individuals without PoDs (all $p<0.001$), except for PoDs of the genital organs for inpatient visits ($p=0.44$) and PoDs of malformations of the eye, ear, face, and neck for emergency department visits ($p=0.33$). Unadjusted all-cause total healthcare costs for each PoD category are presented in **Figure 2**. After adjusting for age, sex, education, insurance coverage, and noncommunicable diseases, all PoD categories had higher standardized reimbursement costs and patient out-of-pockets costs (all $p<0.001$).

Age by group interaction for healthcare costs for all adults with PoDs and by PoD category

There were significant age group (18-40 years; 41-64 years) by group (with PoDs; without PoDs) interactions for all individuals with PoDs and for each of the PoD categories for total standardized reimbursement and patient out-of-pocket costs (all $p<0.001$). After stratifying by young and middle-aged, all individuals with PoDs and each PoD category had higher CRs

compared to individuals without PoDs, with the magnitude of the CR being greater for young than middle-aged individuals with PoDs (**Supplementary Table 3**).

DISCUSSION

The principal finding of this investigation is that young and middle-aged privately-insured adults with PoDs had higher healthcare resource utilization across all medical services, and higher all-cause healthcare costs compared to young and middle-aged privately-insured adults without PoDs. These findings were evident across all PoD categories when compared to individuals without PoDs. Moreover, the differences in costs were greater for younger than middle-aged adults with PoDs, and for each PoD category, compared to adults without PoDs. While previous studies examining adverse health complications among populations with PoDs have suggested earlier screening strategies for disease prevention and healthcare management,[3,13] the findings from the current study could inform decision making processes regarding private health benefit plan design and healthcare resource allocation for services and treatments by administrators and policymakers.

In the current study, we found substantial mean differences for all-cause healthcare costs and large unadjusted cost ratios for the standardized reimbursement and patient out-of-pocket costs between individuals with vs. without PoDs. After adjusting for sociodemographics, insurance coverage, and the presence of several costly noncommunicable diseases, total standardized reimbursement costs were still 2.3 times higher and patient out-of-pocket costs were 1.7 times higher for individuals with PoDs compared to individuals without PoDs. These results suggest a few things. First, costly noncommunicable diseases only account for a small portion of the excess healthcare costs attributable to PoDs; however, there may be other costly

diseases not examined in this study that are more prevalent among individuals with PoDs. Second, the findings that patient out-of-pocket costs were elevated for individuals with PoDs compared to individuals without PoDs, but to a lesser extent than for standardized reimbursement costs, suggests that health plans are accommodating some, but not all, of the medical needs by individuals with PoDs. This is supported by the higher prevalence of Medicare Advantage health plans among individuals with PoDs compared to individuals without PoDs (21.1% vs. 6.6%). Further, the CR for Medicare Advantage was higher compared to commercial alone for standardized reimbursement costs, but lower for patient out-of-pocket costs for the entire sample, suggesting greater cost reduction plans. Nevertheless, identifying and delineating other "cost drivers" for populations with PoDs is needed.

The sample size for the group with PoDs was very large, which allowed us to examine healthcare resource utilization and costs after stratifying by the type of PoD, with sample sizes ranging from 5,518 (PoDs with chromosomal abnormalities) to 33,566 (PoDs of the musculoskeletal system). Our analyses suggest that all PoD categories have higher healthcare resource utilization and costs compared to adults without PoDs. Moreover, there was a considerable range of excess healthcare utilization and costs across PoD categories. In general, PoD categories with the highest healthcare resource utilization and costs were PoDs of the urinary, circulatory, respiratory and digestive, and nervous systems. While different types of PoDs should not be assumed to have the same set of health complications, as most have very specific etiologies and comorbidities, there are overlapping risk factors across various types of PoDs that may impede healthful transition into and throughout adulthood, thus leading to similar health outcomes and healthcare needs. These factors may manifest as a direct consequence of the condition (e.g., impaired executive functioning) or as an indirect consequence of a condition

(e.g., chronic pain, low societal integration). On the other hand, individuals with specific PoDs may be more susceptible to certain adverse health outcomes and reliantly on specific healthcare services. For example, children and adolescents with PoDs have higher prevalence of mental health disorders compared to the general population of children,[29,30] but the prevalence is greater among children and adolescents with neurodevelopmental PoDs than nervous system PoDs.[29,31] Future research is needed to parse out the PoD-specific factors contributing to excess healthcare utilization and costs to lessen the healthcare economic burden attributable to various PoDs.

A major strength of the study included the large sample size for adults with PoDs. Gathering data on clinical populations is challenging and very little is known about health disparities among individuals with PoDs across the lifespan. Another major strength of this study is the comprehensive assessment of several costly noncommunicable diseasese which allowed for cost adjustment.

The limitations of the study must also be discussed. First, it is important to note that the findings from the current investigation are likely underreporting the extent of healthcare resource utilization and costs associated with U.S. populations with PoDs. To be enrolled with a private health insurance plan, individuals must be able to afford the costs or be covered through their employer, their parents (up to 26 years of age), or their spouse. Individuals with PoDs tend to have lower employment and marriage rates compared to the general population,[32] which is likely to be more problematic with more medically complex forms of PoDs. Furthermore, individuals with more severe forms of PoDs are likely to be covered, or co-covered, by public health insurance due to medical circumstances. Therefore, our sample of adults with PoDs likely reflects a higher functioning and healthier segment of the U.S. population with PoDs;[33] however, this is only speculation. Second, the present study excluded individuals that did not have service

utilization in 2016, which may have biased results. However, these excluded individuals that had insurance coverage may be somewhat healthier since they did not require a medical encounter in 2016, thus potentially biasing results in the present study to be more conservative estimates. Third, data were from a single year and longer study periods and longitudinal research designs could provide more robust findings and implications for research, practice, and policy. Fourth, we were only able to adjust for a limited set of covariates, and we are unable to rule out other potential confounding factors. Fifth, we used a single claim to identify PoDs and noncommunicable diseases. Validation studies tend to show that two or more claims for a medical condition improves ability to identify individuals with that condition.[34,35] However, single claim-based algorithms using claims data have moderate-to-high positive predictive value (~80%) and high sensitivity (99%) to detect PoDs,[34] and moderate-to-high sensitivity (up to 99%) and specificity (up to 87%) to detect a variety of costly noncommunicable diseases;[36,37] although, the accuracy of medical condition identification using claims data depends on the length of the study period[38] and the condition examined.[34,36,38,39] Given the short study period of 12 months to extract data and the large and robust effect sizes, the selected methodology to identify associations is likely sufficient to provide evidence of health and economic disparities.

In conclusion, young and middle-aged adults with PoDs have higher healthcare resource utilization and costs compared to young and middle-aged adults without PoDs. These higher costs come along with higher out-of-pocket burden, which can affect the individual's financial well-being, thus further contributing to health disparities. The elevated healthcare costs were evident even after adjusting for several costly noncommunicable diseases that are more prevalent among populations with PoDs. Furthermore, each PoD category had higher healthcare resource utilization and costs compared to individuals without PoDs. Future research is needed to identify

specific cost drivers for the healthcare economic disparity for individuals with PoDs, and by the type of PoD, as well as year to year healthcare costs, which may provide insight into the long-term financial burden. Future research is also needed to develop algorithms and strategies for disease and cost prediction for these populations, which may significantly enhance preventive and personalized medicine, improve healthful aging, and reduce long-term costs.[40]

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Data sharing: As part of our Data Use Agreements, raw data will not be shared. We will share statistical code or data summary upon reasonable request.

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Figure legends

Figure 1. Annual mean all-cause total, medical, and pharmacy standardized reimbursement costs (**A**) and annual mean all-cause total, medical, and pharmacy patient out-of-pocket costs (**B**) among adults (18-64 years) with and without pediatric-onset disabilities (PoDs).

Figure 2. Annual mean all-cause total standardized reimbursement costs (**A**) and annual mean all-cause total patient out-of-pocket costs (**B**) among adults (18-64 years) with and without pediatric-onset disabilities (PoDs), stratified by the type of PoD. Individuals may have more than one PoD and can be represented across multiple PoD categories. All PoD categories had higher costs compared to individuals without PoDs after adjusting for age, sex, education, insurance coverage, and several noncommunicable diseases (all $p<0.001$).

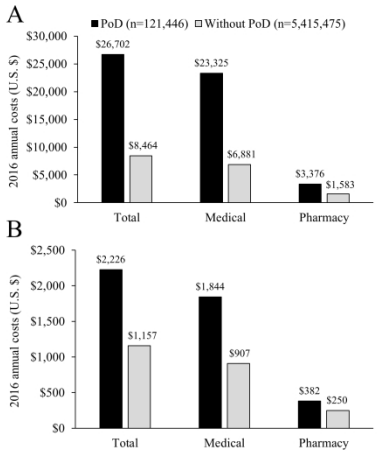

Figure 1. Annual mean all-cause total, medical, and pharmacy standardized reimbursement costs (A) and annual mean all-cause total, medical, and pharmacy patient out-of-pocket costs (B) among adults (18-64 years) with and without pediatric-onset disabilities (PoDs).

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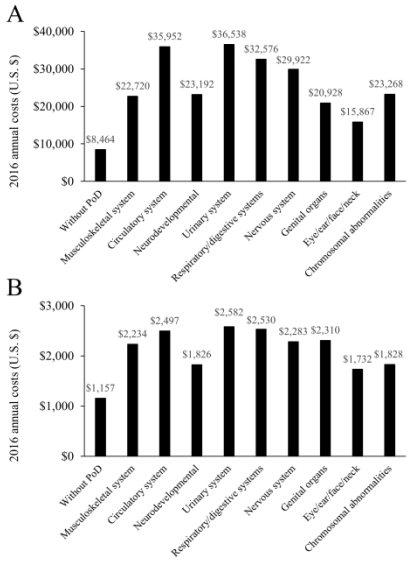

Figure 2. Annual mean all-cause total standardized reimbursement costs (A) and annual mean all-cause total patient out-of-pocket costs (B) among adults (18-64 years) with and without pediatric-onset disabilities (PoDs), stratified by the type of PoD. Individuals may have more than one PoD and can be represented across multiple PoD categories.

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Supplementary Table 1. Diagnostic codes for all pediatric-onset disabilities (PoDs) and noncommunicable diseases using the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10) codes.

Pediatric-onset disability categories and specific conditions	ICD-10 codes
Musculoskeletal system	
Congenital deformities of hip or feet; congenital musculoskeletal deformities of head, face, spine and chest; other congenital musculoskeletal deformities; polydactyly; syndactyly; reduction defects of upper, lower, or unspecified limb; other congenital malformations of limb(s); other congenital malformations of skull and face bones; congenital malformations of spine and bony thorax; osteochondrodysplasia with defects of growth of tubular bones and spine; other osteochondrodysplasias; congenital malformations of musculoskeletal system, not elsewhere classified	Q65-79 families
Juvenile arthritis	M08 family
Other disorders of bone	
Physeal arrest	M89.1 family
Other disorders of bone development and growth	M89.2 family
Circulatory system	
Congenital malformations of the cardiac chambers, cardiac septa, pulmonary and tricuspid valves, aortic and mitral valves; other congenital malformations of the heart; congenital malformations of great arteries, great veins; other congenital malformations of peripheral vascular system or circulatory system	Q20-28 families
Neurodevelopmental	
Intellectual disabilities, mild, moderate, severe, profound, other, and unspecified	F70-73, F78, F79
Specific developmental disorders of speech and language, scholastic skills, motor function; pervasive developmental disorders; other and unspecified disorders of psychological development	F80 family, F81 family, F82, F84 family, F88, F99
Urinary system	
Renal agenesis and other reduction defects of kidney; cystic kidney disease; congenital obstructive defects of renal pelvis and congenital malformations of ureter; other congenital malformations of kidney	Q60-63 families
Respiratory and digestive systems	
Congenital malformations of nose, larynx, trachea or bronchus, lung; other congenital malformations of respiratory system; cleft lip and/or palate; other congenital malformations of tongue, mouth, or pharynx; congenital malformations of esophagus; other congenital malformations of upper alimentary tract; congenital absence, atresia and stenosis of small or large intestine; other congenital malformations of intestine; congenital malformations of gallbladder, bile ducts, or liver; other congenital malformations of digestive system	Q30-45 families

Nervous system	
Encephalocele; microcephaly; congenital hydrocephalus; spina bifida; other congenital malformations of brain, spinal cord, or nervous system	Q01 family, Q02, Q03-7 families
Cerebral palsy	G80 family
Juvenile epilepsy	G40.B family
Genital organs	
Congenital malformations of ovaries, fallopian tubes, broad ligaments, uterus, and cervix; undescended and ectopic testicle; hypospadias; other congenital malformations of female or male genital organs; indeterminate sex and pseudohermaphroditism	Q50-56 families
Malformations of the eye, ear, face, and neck	
Congenital malformations of eyelid, lacrimal apparatus, or orbit; anophthalmos, microphthalmos, or macrophthalmos; congenital lens malformations; congenital malformations of anterior or posterior segment of eye; other congenital malformations of eye; congenital malformations of ear causing impairment of hearing; other congenital malformations of ear, face, or neck	Q10-18 families
Other chromosomal abnormalities, not classified elsewhere	
Down syndrome; Trisomy 18 and Trisomy 13; other trisomies and partial trisomies of the autosomies, not elsewhere classified; monosomies and deletions from the autosomes, not elsewhere classified; balanced rearrangements and structural markers, not elsewhere classified; Turner's syndrome; other sex chromosome abnormalities, female or male phenotype, not elsewhere classified; other chromosome abnormalities	Q90-93 families, Q95-99 families
<u>Noncommunicable diseases</u>	
Ischemic heart disease	
Angina pectoris; acute myocardial infarction; subsequent ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction; other acute ischemic heart diseases; chronic ischemic heart disease	I20-22 families, I24 family, I25 family
Cerebrovascular disease	
Nontraumatic subarachnoid or intracerebral hemorrhage; other and unspecified nontraumatic intracranial hemorrhage; cerebral infarction; occlusion and stenosis of precerebral or cerebral arteries, not resulting in cerebral infarction; other cerebrovascular diseases; cerebrovascular disorders in diseases classified elsewhere; sequelae of cerebrovascular disease	I60-63 families, I65-69 families
Hypertensive and other cardiovascular disease	
Essential (primary) hypertension; hypertensive heart, chronic kidney disease, or heart and chronic kidney disease; secondary hypertension; hypertensive crisis; heart failure; peripheral atherosclerosis	I10-13 families, I15 family, I16 family, I50 family, I70 family
Type II diabetes mellitus	E11 family
Malignant cancer	

Malignant neoplasms of lip, oral cavity, or pharynx, digestive organs, respiratory and intrathoracic organs, bone and articular cartilage, mesothelial and soft tissue, breast, female or male genital organs, urinary tract, eye, brain, or other parts of central nervous system, thyroid or other endocrine glands, ill-defined, other secondary, or unspecified sites, neuroendocrine tumors, lymphoid, hematopoietic, or related tissue; melanoma and other malignant neoplasms of skin	C00-26 families, C30-41 families, C43-58 families, C60-80 families, C7A family, C7B family, C81-96 families
Osteoporosis	
With or without current pathological fracture	M80 family, M81 family
Mood affective disorders	
Manic episode; bipolar disorder; major depressive disorder, single episode or recurrent; persistent mood [affective] disorders; unspecified mood [affective] disorders	F30-34 families, F39
Chronic obstructive pulmonary disease	
Simple and mucopurulent chronic bronchitis; unspecified chronic bronchitis; emphysema; other chronic obstructive pulmonary disease	J41-44 families
Chronic kidney disease	
Stage I-V; end stage renal disease; chronic kidney disease, unspecified	N18 family
Liver disease	
Alcoholic liver disease; toxic liver disease; hepatic failure, not elsewhere classified; chronic hepatitis, not elsewhere classified; fibrosis and cirrhosis of liver; other inflammatory liver diseases; other diseases of liver; liver disorders in diseases classified elsewhere	K70-76 families, K77

Supplementary Table 2. Annual healthcare resource utilization in 2016 among adults (18-64 years) by the type of pediatric-onset disability (PoD).

	Inpatient	Outpatient and other	Emergency department	Office
PoD categories	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Musculoskeletal system (n=33,566)	0.7 (1.9)*	15.2 (13.2)*	0.5 (1.0)*	8.0 (5.9)*
Circulatory system (n= 24,393)	1.5 (2.9)*	15.8 (13.7)*	0.7 (1.1)*	7.6 (5.9)*
Neurodevelopmental (n=17,149)	1.3 (2.9)*	13.9 (14.5)*	0.8 (1.2)*	6.5 (5.5)*
Urinary system (n=12,477)	1.2 (2.6)*	16.2 (13.4)*	0.8 (1.2)*	8.2 (6.0)*
Respiratory or digestive systems (n=12,190)	1.2 (2.6)*	15.2 (13.1)*	0.7 (1.2)*	7.8 (6.1)*
Nervous system (n=11,021)	1.5 (2.9)*	15.4 (14.5)*	0.8 (1.2)*	7.4 (6.0)*
Genital organs (n=6,164)	0.6 (1.7)	13.5 (11.8)*	0.5 (0.9)*	6.3 (5.3)*
Eye/ear/face/neck (n=5,811)	0.5 (1.7)*	11.5 (11.8)*	0.4 (0.9)	5.9 (5.3)*
Chromosomal abnormalities (n=5,518)	0.9 (2.3)*	14.6 (13.9)*	0.5 (1.0)*	6.7 (5.7)*
Without PoDs (n=5,415,475)	0.2 (1.2)	7.1 (8.9)	0.3 (0.7)	3.8 (4.2)

Individuals may have more than one PoD and can be represented across multiple PoD categories.

*Indicates significantly different, $p<0.001$, compared to individuals without PoDs after adjusting for age, sex, education, insurance coverage, and several noncommunicable diseases.

Supplementary Table 3. Annual adjusted cost ratios (CR) for total standardized reimbursement and patient out-of-pocket costs for year 2016 among young (18-40 years) and middle-aged (41-64 years) adults with pediatric-onset disabilities compared to adults without PoDs (reference).

	Standardized reimbursement costs		Patient out-of-pocket costs	
	Young	Middle-aged	Young	Middle-aged
	CR (95% CI)	CR (95% CI)	CR (95% CI)	CR (95% CI)
All PoDs	2.73 (2.69, 2.76)	2.03 (2.01, 2.05)	1.84 (1.82, 1.86)	1.52 (1.5, 1.53)
PoD categories				
Musculoskeletal system	2.92 (2.84, 2.99)	2.26 (2.22, 2.30)	1.93 (1.89, 1.97)	1.68 (1.65, 1.70)
Circulatory system	3.16 (3.06, 3.25)	2.22 (2.18, 2.27)	1.86 (1.81, 1.90)	1.51 (1.48, 1.54)
Neurodevelopmental	2.44 (2.37, 2.51)	1.46 (1.42, 1.50)	1.71 (1.66, 1.75)	1.18 (1.15, 1.21)
Urinary system	2.60 (2.47, 2.73)	1.80 (1.75, 1.84)	1.78 (1.70, 1.86)	1.44 (1.41, 1.47)
Respiratory or digestive systems	3.82 (3.63, 4.02)	2.21 (2.15, 2.27)	2.17 (2.07, 2.27)	1.61 (1.57, 1.65)
Nervous system	3.67 (3.54, 3.81)	2.08 (2.01, 2.15)	2.21 (2.14, 2.29)	1.51 (1.47, 1.55)
Genital organs	2.98 (2.86, 3.11)	2.35 (2.22, 2.48)	2.09 (2.01, 2.17)	1.78 (1.70, 1.86)
Eye/ear/face/neck	1.98 (1.87, 2.09)	1.44 (1.38, 1.50)	1.50 (1.42, 1.58)	1.31 (1.26, 1.35)
Chromosomal abnormalities	2.90 (2.77, 3.04)	1.81 (1.71, 1.91)	1.82 (1.75, 1.90)	1.24 (1.19, 1.30)

The models are adjusted for age (as continuous), sex, education, insurance coverage, and all noncommunicable diseases. All age*group interactions were significant, $p<0.001$.

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5-9
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5-6
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-8
Bias	9	Describe any efforts to address potential sources of bias	5, 6, 7, 8
Study size	10	Explain how the study size was arrived at	5-6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8-9
		(*b*) Describe any methods used to examine subgroups and interactions	8-9
		(*c*) Explain how missing data were addressed	5
		(*d*) If applicable, explain how loss to follow-up was addressed	NA
		(*e*) Describe any sensitivity analyses	8
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9, Table 1
		(b) Indicate number of participants with missing data for each variable of interest	NA
		(c) Summarise follow-up time (eg, average and total amount)	11, 12, 14
Outcome data	15*	Report numbers of outcome events or summary measures over time	9-14

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	9-14 and tables/figures Tables
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	13-14
Discussion			
Key results	18	Summarise key results with reference to study objectives	14-17
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	17
Generalisability	21	Discuss the generalisability (external validity) of the study results	15-16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	No funding reported

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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The economic burden of pediatric-onset disabilities among young and middle-aged adults in the United States: A cohort study of privately insured beneficiaries

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The economic burden of pediatric-onset disabilities among young and middle-aged adults in the United States: A cohort study of privately insured beneficiaries

Daniel G. Whitney,[1,2] Neil S. Kamdar,[2,3,4,5] Richard A. Hirth,[6,7] Edward A. Hurvitz,[1] Mark D. Peterson[2]

[1]Department of Physical Medicine and Rehabilitation, University of Michigan, Ann Arbor, USA

[2]Institute for Healthcare Policy and Innovation, University of Michigan, Ann Arbor, USA

[3]Department of Obstetrics and Gynecology, University of Michigan, Ann Arbor, USA

[4]Department of Surgery, University of Michigan, Ann Arbor, USA

[5]Department of Emergency Medicine, University of Michigan, Ann Arbor, USA

[6]Department of Health Management and Policy, University of Michigan School of Public Health, Ann Arbor, USA

[7]Department of Internal Medicine, University of Michigan, Ann Arbor, USA

Corresponding author:

Daniel G. Whitney, PhD

325 E. Eisenhower Pkwy, Ann Arbor, MI, USA 48108

Phone: 734-936-7175

E-mail: danielwhitney8@gmail.com

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Abstract

Objective: Individuals with pediatric-onset disabilities (PoDs) have complex healthcare needs and are susceptible to adverse health outcomes, which may impose a higher strain on healthcare resources. The burden of healthcare resource utilization and costs attributed to the population of adults with PoDs is not clearly established. The objective here was to compare healthcare resource utilization and costs between adults with vs. without PoDs.

Design: Cohort.

Setting: Data were from the 2016 Optum Clinformatics® Data Mart, a de-identified nationwide claims database of beneficiaries from a single private payer in the U.S.

Participants: ICD-10-CM diagnosis codes were used to identify beneficiaries with PoDs that were between 18 and 64 years of age.

Primary and secondary outcome measures: Annual all-cause healthcare resource utilization and total healthcare costs were compared between adults with and without PoDs before and after adjusting for sociodemographics and several costly noncommunicable diseases.

Results: Adults with PoDs (n=121,446) had greater annual mean counts of service utilization for all service types (e.g., inpatient, outpatient, emergency visits) compared to adults without PoDs (n=5,415,475) before and after adjustments (all p<0.001). Adults with PoDs had greater unadjusted total standardized reimbursement costs ($26,702 vs. $8,464; mean difference=$18,238; cost ratio [CR]=3.16; 95% confidence interval [CI]=3.13-3.18) and total patient out-of-pocket costs ($2,226 vs. $1,157; mean difference=$1,069; CR=1.88; 95%CI=1.86-1.89). After adjustments, total standardized reimbursement costs were 2.32 times higher (95%CI=2.30-2.34) and total patient out-of-pocket costs were 1.65 times higher (95%CI=1.64-1.66) compared to adults without PoDs.

Conclusion: Adults with PoDs had greater healthcare utilization and costs, even after accounting for costly diseases. Future research is needed to identify the cost drivers for adults with PoDs.

Trial registration: None, this is not a trial.

Keywords: pediatric-onset disabilities; economics; healthcare utilization

Strengths and limitations of this study

- This is the largest study to date to examine healthcare utilization and associated costs of adults with different types of pediatric-onset disabilities.
- We examined the healthcare-related economic burden after accounting for costly noncommunicable diseases that are more prevalent among adults with pediatric-onset disabilities.
- This study leveraged administrative claims data, and are therefore subject to limitations that are inherent to claims data, such as inaccurate coding of medical conditions.
- We were unable to determine specific cost drivers.

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Competing interest: None declared.

Patient consent for publication: Not required.

INTRODUCTION

Pediatric-onset disabilities (PoDs) refer to a group of congenital or acquired conditions that originate at conception, during pregnancy, or in childhood, and consist of impairments in behavioral, intellectual, and/or physical functioning, or are associated with abnormal developmental or metabolic processes. While clinical care and coordinated healthcare management (e.g., specialist referral) for children with PoDs is a large focus of pediatric clinicians and researchers, far less attention on the topic has been given to these individuals as they become adults. The complex healthcare needs and health complications born out of direct (e.g., genetic) and resulting (e.g., delayed growth) consequences associated with PoDs during growth and development, have lasting ramifications on the health and functional status across the lifespan. Research has shown that individuals with PoDs are susceptible to early development of chronic, noncommunicable diseases and early mortality,[1-13] thus placing a high strain on the patients, caregivers, and healthcare resources. Importantly, the population of adults with PoDs is projected to expand over the coming decades,[14-16] which may lead to a noticeable increase in the national healthcare economic burden, and should be considered an urgent public health issue. However, healthcare resource utilization and costs directly attributable to adults with PoDs has not been extensively studied.

The current U.S. healthcare system may not be adequately prepared to care for adults with PoDs.[17-20] To date, little is known about the natural trajectory of adverse health complications across the lifespan for these populations, best practices for coordinating healthcare services between general physicians and specialists (e.g., pediatricians), and how to provide adequate resources for preventive and treatment services to these populations. A comprehensive understanding of healthcare resource utilization and costs among adults with PoDs is crucial for

public health, healthcare policy reform, and implementing better clinical practice guidelines for cost-effective care. Further, understanding the healthcare economic burden among at-risk populations prior to reaching the elderly years could inform public health efforts, policymakers, and early patient- and clinical-decision making processes and strategies (e.g., surgeries, medications) to maximize comorbidity management and prevention. Therefore, the primary aim of this study was to characterize healthcare resource utilization and costs among young and middle-aged adults with PoDs, as compared to young and middle-aged adults without PoDs, before and after adjusting for costly comorbid noncommunicable diseases. We hypothesized that adults with PoDs would have higher healthcare resource utilization and costs compared to adults without PoDs, even after adjusting for noncommunicable diseases.

METHODS

Data source

Data were from the 2016 Clinformatics® Data Mart Database (OptumInsight™, Eden Prairie, MN, USA), which is a nationwide, de-identified single private payer administrative claims database. This database contains over 16 million beneficiaries in 2016 who have either commercial or Medicare Advantage health plans, and includes all the inpatient, outpatient, pharmacy, emergency visit, office visit, and other ancillary service utilization throughout their enrollment on the insurance plan. Medicare beneficiaries can opt to enroll in a private Medicare Advantage health plan in lieu of participating in the traditional public Medicare program. Such plans can offer extra coverage not available in the traditional Medicare program, such as vision, hearing, dental, and/or health and wellness programs. To be enrolled in a private payer health plan, beneficiaries of any age, income, or disability status either pay for coverage or are covered

through their employer. Administrative claims data are primarily used for billing reimbursement purposes, and health conditions are identified using specific codes attached to individual claims. Since data are de-identified, the University Institutional Review Board approved this study as non-regulated.

Sample selection

Beneficiaries that were 18 to 64 years of age, had 12 full months of continuous enrollment, and had at least one service utilization in 2016 (to make a diagnosis of PoDs and noncommunicable diseases) were considered for this investigation. Beneficiaries were excluded if they did not have known data for sex (n=991, <0.01%). All PoDs and noncommunicable diseases were identified using the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10) codes, and are presented in **Supplementary Table 1**. Since it is not possible to determine if some conditions developed in childhood or adulthood (e.g., spinal cord injury, cancer), conditions were included in the group representing PoDs if there were known childhood origins. These conditions were then grouped into the following PoD subcategories: PoDs of the musculoskeletal system; PoDs of the circulatory system; neurodevelopmental PoDs; PoDs of the urinary system; PoDs of the respiratory system and digestive system; PoDs of the nervous system; PoDs of the genital organs; PoDs of malformations of the eye, ear, face, and neck; and other chromosomal abnormalities.

Noncommunicable diseases

Prevalent noncommunicable diseases, as individual dichotomous variables (present vs. not present), were ascertained by at least 1 medical claim in 2016, and were selected with

guidance from the literature on disease, disability, and mortality among adults.[2,3,21-26] Noncommunicable diseases were represented as categories across multiple biological systems as follows: ischemic heart diseases (e.g., atherosclerotic heart disease); cerebrovascular diseases (e.g., cerebral infarction); hypertensive and other cardiovascular diseases (e.g., hypertension, heart failure); type 2 diabetes mellitus; malignant cancer; osteoporosis; mood affective disorders (e.g., depression); chronic obstructive pulmonary diseases (e.g., emphysema); chronic kidney diseases (e.g., kidney disease stages I-V); and liver diseases (e.g., cirrhosis).

Healthcare resource utilization

Annual all-cause healthcare resource utilization was identified using medical claims and was categorized into the following service types: inpatient; outpatient, ambulatory, and other (herein referred to as "outpatient and other"); emergency department; and office. Specific services per service category are presented in **Table 1**. Measures to assess healthcare resource utilization included the percentage of patients per group (with PoDs, without PoDs) that had at least one service utilization within each service category, and the annual mean count of service utilization per group for each service category.

Table 1. Healthcare resource utilization by service type.

Healthcare service type	Level 1 Description: Level 2 Description
Inpatient services	Facility Inpatient: Acute and Rehab/Skilled Nursing Facility; Professional Services: Inpatient Visits
Outpatient, ambulatory, and other services	Facility Outpatient: OP Facility Diagnostic, Laboratory, Other, Radiology, and Surgery; Professional Services: Allergy Tests and Injections, Anesthesia, Consultations, Diagnostic Testing, Immunizations and Injections, Laboratory, Mental Health, Obstetrics, Pathology, Physical Medicine/Rehab, Professional Other, Preventive Medicine, Radiology, Surgery, Vision, Hearing, and Speech
Emergency department services	Facility Outpatient: Emergency Room; Professional Services: Emergency Room
Office services	Professional Services: Office Visits

Healthcare costs

Annual all-cause healthcare costs were identified using medical and outpatient pharmacy (herein referred to as "pharmacy") claims, and were from the paid amounts of adjudicated (final action) claims, which included insurer and health plan payments and patient copayments, deductibles, and coinsurance. Total (medical + pharmacy), medical, and pharmacy all-cause healthcare costs were represented as standardized reimbursement cost (i.e., sum of all health plan and patient paid amounts) and patient out-of-pocket cost (i.e., sum of copayment, deductible, and coinsurance).

Clinformatics® Data Mart Database accounts for differences in pricing across health plans and provider contracts by standardizing cost field utilized algorithms that reflect the allowed payments across all provider services. This allows comparisons across patients, data sources, and geographic areas, and accounts for contractual payer and provider differences. Price standardization accounts for quantity of services provided, relative resource costs involved in providing the services, and the nature of the service which can be defined as the CPT/HCPCS codes for professional services, NDC for pharmacy service, or type of admission for inpatient stay.

Sociodemographic variables

Age, sex, ethnicity, education level, household annual income, and insurance coverage (i.e., commercial only, Medicare Advantage) were considered for risk adjustment to differentiate the effect of potential confounders from the effect of PoDs on the outcome.

Statistical analysis

To limit extreme values and to reduce the effect of possible spurious outliers, winsorization of healthcare resource utilization data to the upper 99.0% was performed for each service category.

Descriptive characteristics and healthcare resource utilization and cost measures were summarized using mean ± standard deviation (SD) for continuous variables and percentage for categorical variables. Group differences for healthcare resource utilization measures were examined using Chi-Square tests for unadjusted analyses of binary data (e.g., sex, education level, noncommunicable diseases). Generalized linear models assuming a zero-inflated Poisson distribution (for non-utilization) and log-link function were performed for count data (i.e., number of visits per service type) to estimate the ratio of means (RM; exponentiated form of variable estimate which represents a multiplicative effect on the estimated mean count per one unit change in the explanatory variable[27]) for explanatory variables (e.g., PoD group), while controlling for age, sex, education, insurance coverage, and all noncommunicable diseases. As recommended for healthcare cost data analysis,[28,29] generalized linear models with gamma distribution and log-link function were performed to estimate the cost ratios (CR; exponentiated form of variable estimate) for explanatory variables (e.g., PoD group), while controlling for age, sex, education, insurance coverage, and all noncommunicable diseases. For the generalized linear models, the main effect for PoD group was interpreted. We adjusted the models for the noncommunicable diseases to determine the effect of PoDs on the outcome beyond the presence of these diseases, because they can incur excess healthcare utilization and costs which may explain any differences in costs between groups. Ethnicity and household annual income were not initially included as covariates because of the extent of unknown/missingness. However,

because these variables can be associated with healthcare delivery and noncommunicable diseases, we conducted a sensitivity analysis using the fully adjusted generalized linear models that included ethnicity and household annual income to determine if these variables biased the estimated CR for group (reference: without PoDs) for healthcare cost measures.

To determine whether there is variation in the effect of different PoD categories, healthcare resource utilization and total cost measures were summarized using mean ± SD after stratifying the type of PoD (e.g., musculoskeletal system, neurodevelopmental). Comparisons between each of the PoD categories with the sample without PoDs were examined for healthcare resource utilization and cost measures using the same procedures and models noted above.

Finally, to determine if age was differentially associated with healthcare costs for adults with and without PoDs, we examined the age (young, 18-40 years; middle-aged, 41-64 years) by group interaction for all individuals with PoDs compared to the sample without PoDs, and then for each of the PoD categories compared to the sample without PoDs. The outcome measures were total standardized reimbursement costs and patient out-of-pocket costs, as these were the primary outcome measures of interest. If the interaction was significant, subsequent analyses were performed after stratifying by age group.

All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA). Effect estimates were reported as CRs with 95% confidence intervals (CI), and $p \leq 0.05$ (two-tailed) was used to determine statistical significance.

Patient and public involvement

Patient were not directly involved in the design or conduct of this study.

RESULTS

Descriptive characteristics of individuals with PoDs (n=121,446) and without PoDs (n=5,415,475) are presented in **Table 2**. Notably, individuals with PoDs had a higher proportion enrolled in the Medicare Advantage health plan compared to individuals without PoDs. Further, individuals with PoDs had higher prevalence of noncommunicable diseases compared to individuals without PoDs, including: ischemic heart disease (8.7%, 3.5%); cerebrovascular disease (6.3%, 1.5%); hypertensive or other cardiovascular disease (37.8%, 25.4%); type 2 diabetes (14.5%, 10.0%); malignant cancer (6.6%, 3.8%); osteoporosis (3.4%, 1.3%); mood affective disorders (20.8%, 11.0%); chronic obstructive pulmonary disease (1.8%, 0.7%); chronic kidney disease (6.6%, 1.8%); and liver disease (7.3%, 2.9%) (all p<0.001).

Table 2. Descriptive characteristics and prevalence of noncommunicable diseases among adults (18-64 years) with and without pediatric-onset disabilities (PoDs).

	PoD (n=121,446)	Without PoD (n=5,415,475)	
	Point estimate	Point estimate	
Descriptive characteristics			p-value
Age, mean (SD)	44.3 (13.6)	43.8 (12.9)	<0.001
18-40 years, %	38.8	40.3	
41-64 years, %	61.2	59.7	
Sex, %			<0.001
Female	55.6	53.8	
Male	44.4	46.2	
Ethnicity, %			<0.001
White	55.7	53.4	
Black	7.9	7.4	
Hispanic	8.3	9.4	
Asian	3.0	4.3	
Unknown/missing	25.0	25.5	
Education, %			<0.001
Less than high school	0.4	0.5	
High school diploma	25.1	24.0	
More than high school	71.9	73.5	
Unknown/missing	2.6	2.1	
Household annual income, %			<0.001

<$40K	15.2	13.1	
$40K to 59.9K	9.9	10.0	
$60K to 99.9K	19.0	20.0	
≥$100K	32.6	34.1	
Unknown/missing	23.4	22.8	
Insurance coverage, %			<0.001
Commercial only	78.9	93.4	
Medicare Advantage	21.1	6.6	
Noncommunicable diseases			
Ischemic heart disease, %	8.7	3.5	<0.001
Cerebrovascular disease, %	6.3	1.5	<0.001
Hypertensive/other cardiovascular disease, %	37.8	25.4	<0.001
Type 2 diabetes, %	14.5	10.0	<0.001
Malignant cancer, %	6.6	3.8	<0.001
Osteoporosis, %	3.4	1.3	<0.001
Mood affective disorders, %	20.8	11.0	<0.001
Chronic obstructive pulmonary disease, %	1.8	0.7	<0.001
Chronic kidney disease, %	6.6	1.8	<0.001
Liver disease, %	7.3	2.9	

Healthcare resource utilization for adults with and without PoDs

Individuals with PoDs had higher prevalence of patients with at least one service utilized compared to individuals without PoDs for inpatient visits (22.5% vs. 7.0%), outpatient and other visits (98.9% vs. 94.8%), emergency department visits (33.6% vs. 18.6%), and office visits (96.4% vs. 85.6%) (all p<0.001). Individuals with PoDs had greater unadjusted annual mean count of service utilization compared to individuals without PoDs (presented as mean ± SD) for inpatient visits (1.0 ± 2.4 vs. 0.2 ± 1.2), outpatient and other visits (14.7 ± 13.4 vs. 7.1 ± 8.9), emergency department visits (0.6 ± 1.1 vs. 0.3 ± 0.7), and office visits (7.4 ± 5.8 vs. 3.8 ± 4.2) (all p<0.001) (data not shown). The higher service utilization was present even after adjusting for age, sex, education, insurance coverage, and all noncommunicable diseases for each service category (all p<0.001; **Supplementary Table 2**).

Healthcare costs for adults with and without PoDs

Unadjusted annual all-cause healthcare costs for individuals with and without PoDs are presented in **Figure 1**. The standardized reimbursement costs (**Figure 1A**) were higher for individuals with PoDs compared to individuals without PoDs for total (mean difference=$18,238; cost ratio [CR]=3.16; 95% confidence interval [CI]=3.13-3.18), medical (mean difference=$16,445; CR=3.39; 95% CI=3.36-3.42), and pharmacy (mean difference=$1,793; CR=1.95; 95% CI=1.93-1.97) costs. The patient out-of-pocket costs (**Figure 1B**) were higher for individuals with PoDs compared to individuals without PoDs for total (mean difference=$1,069; CR=1.88; 95% CI=1.86-1.89), medical (mean difference=$937; CR=1.96; 95% CI=1.95-1.98), and pharmacy (mean difference=$132; CR=1.39; 95% CI=1.38-1.40) costs.

Annual all-cause standardized reimbursement healthcare costs after adjusting for age, sex, education, insurance coverage, and noncommunicable diseases are presented in **Table 3**. Individuals with PoDs had higher total (CR=2.32; 95% CI=2.30-2.34), medical (CR=2.47; 95% CI=2.45-2.49), and pharmacy (CR=1.65; 95% CI=1.63-1.66) standardized reimbursement costs. All-cause patient out-of-pocket healthcare costs after adjusting for age, sex, education, insurance coverage, and noncommunicable diseases are presented in **Table 4**. Individuals with PoDs had higher total (CR=1.65; 95% CI=1.64-1.66), medical (CR=1.72; 95% CI=1.71-1.73), and pharmacy (CR=1.30; 95% CI=1.29-1.31) patient out-of-pocket costs. The sensitivity analysis revealed that ethnicity and household annual income did not affect the results (n=3,545,206) for total (CR=2.35; 95% CI=2.33-2.38), medical (CR=2.48; 95% CI=2.45-2.50), and pharmacy (CR=1.79; 95% CI=1.76-1.81) standardized reimbursement costs, or for total (CR=1.62; 95% CI=1.61-1.64), medical (CR=1.68; 95% CI=1.67-1.70), and pharmacy (CR=1.34; 95% CI=1.32-1.35) patient out-of-pocket costs.

Table 3. Annual adjusted cost ratios (CR) for total, medical, and pharmacy standardized reimbursement costs for year 2016 among adults (18-64 years) with and without pediatric-onset disabilities (PoDs).

	Total	Medical	Pharmacy
	CR (95% CI)	CR (95% CI)	CR (95% CI)
With PoDs (ref: without PoDs)	2.32 (2.30, 2.34)	2.47 (2.45, 2.49)	1.65 (1.63, 1.66)
Age (continuous)	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)	1.02 (1.02, 1.02)
Sex (ref: female)	0.75 (0.75, 0.76)	0.71 (0.71, 0.71)	1.10 (1.10, 1.10)
Education (ref: less than high school)			
High school diploma	1.10 (1.08, 1.12)	1.06 (1.05, 1.08)	1.32 (1.29, 1.35)
More than high school	1.13 (1.11, 1.15)	1.07 (1.05, 1.09)	1.55 (1.52, 1.58)
Unknown/missing	1.04 (1.03, 1.06)	1.02 (1.00, 1.04)	1.39 (1.36, 1.42)
Insurance coverage (ref: commercial only)	1.49 (1.48, 1.49)	1.26 (1.26, 1.27)	2.42 (2.40, 2.43)
Noncommunicable diseases (ref: without)			
Ischemic heart disease	2.00 (1.99, 2.01)	2.25 (2.24, 2.27)	1.20 (1.19, 1.21)
Cerebrovascular disease	2.05 (2.03, 2.07)	2.31 (2.29, 2.33)	1.13 (1.12, 1.14)
Hypertensive/other cardiovascular disease	1.58 (1.57, 1.58)	1.62 (1.62, 1.63)	1.24 (1.23, 1.24)
Type 2 diabetes	1.38 (1.38, 1.39)	1.21 (1.20, 1.21)	1.96 (1.95, 1.97)
Malignant cancer	3.48 (3.46, 3.50)	3.79 (3.77, 3.81)	2.19 (2.18, 2.21)
Osteoporosis	1.59 (1.58, 1.61)	1.54 (1.52, 1.55)	1.81 (1.79, 1.83)
Mood affective disorders	2.03 (2.02, 2.04)	2.05 (2.04, 2.06)	1.82 (1.81, 1.83)
Chronic obstructive pulmonary disease	1.85 (1.83, 1.87)	1.95 (1.92, 1.98)	1.48 (1.46, 1.51)
Chronic kidney disease	2.92 (2.90, 2.94)	3.41 (3.38, 3.44)	1.60 (1.58, 1.62)
Liver disease	2.38 (2.37, 2.40)	2.44 (2.42, 2.46)	1.98 (1.96, 2.00)

CI, confidence interval. Generalized linear models with gamma distribution and log-link function were performed to estimate the cost ratio and 95% CI, which is the exponentiated form of the parameter estimate. N=5,536,921.

Table 4. Annual adjusted cost ratios (CR) for total, medical, and pharmacy patient out-of-pocket costs for year 2016 among adults (18-64 years) with and without pediatric-onset disabilities (PoDs).

	Total	Medical	Pharmacy
	CR (95% CI)	CR (95% CI)	CR (95% CI)
With PoDs (ref: without PoDs)	1.65 (1.64, 1.66)	1.72 (1.71, 1.73)	1.30 (1.29, 1.31)
Age (continuous)	1.00 (1.00, 1.00)	1.00 (1.00, 1.00)	1.02 (1.02, 1.02)
Sex (ref: female)	0.80 (0.80, 0.81)	0.79 (0.79, 0.79)	0.91 (0.91, 0.91)
Education (ref: less than high school)			
High school diploma	1.23 (1.21, 1.24)	1.06 (1.05, 1.08)	1.35 (1.33, 1.37)
More than high school	1.26 (1.24, 1.28)	1.05 (1.04, 1.07)	1.63 (1.61, 1.66)

Unknown/missing	1.17 (1.15, 1.19)	1.04 (1.02, 1.06)	1.55 (1.53, 1.58)
Insurance coverage (ref: commercial only)	0.81 (0.81, 0.81)	0.70 (0.70, 0.70)	1.31 (1.30, 1.31)
Noncommunicable diseases (ref: without)			
Ischemic heart disease	1.54 (1.53, 1.55)	1.64 (1.63, 1.65)	1.22 (1.21, 1.22)
Cerebrovascular disease	1.46 (1.44, 1.47)	1.61 (1.60, 1.63)	1.01 (1.00, 1.01)
Hypertensive/other cardiovascular disease	1.34 (1.34, 1.35)	1.27 (1.27, 1.27)	1.40 (1.40, 1.40)
Type 2 diabetes	1.24 (1.24, 1.24)	1.10 (1.10, 1.10)	1.63 (1.63, 1.64)
Malignant cancer	1.78 (1.77, 1.79)	1.93 (1.92, 1.94)	1.16 (1.15, 1.16)
Osteoporosis	1.28 (1.27, 1.30)	1.27 (1.26, 1.29)	1.29 (1.28, 1.30)
Mood affective disorders	1.64 (1.63, 1.64)	1.58 (1.58, 1.59)	1.69 (1.68, 1.69)
Chronic obstructive pulmonary disease	1.45 (1.44, 1.47)	1.53 (1.51, 1.55)	1.23 (1.22, 1.25)
Chronic kidney disease	1.45 (1.44, 1.46)	1.66 (1.65, 1.67)	1.16 (1.15, 1.16)
Liver disease	1.61 (1.60, 1.62)	1.74 (1.73, 1.75)	1.14 (1.13, 1.14)

CI, confidence interval. Generalized linear models with gamma distribution and log-link function were performed to estimate the cost ratio and 95% CI, which is the exponentiated form of the parameter estimate. N=5,536,921.

Healthcare resource utilization and costs by PoD category

Unadjusted healthcare resource utilization for each PoD category is presented in **Supplementary Table 3**. After adjusting for age, sex, education, insurance coverage, and noncommunicable diseases, all PoD categories had higher healthcare resource utilization compared to individuals without PoDs (all $p<0.001$), except for PoDs of the genital organs for inpatient visits ($p=0.44$) and PoDs of malformations of the eye, ear, face, and neck for emergency department visits ($p=0.33$). Unadjusted all-cause total healthcare costs for each PoD category are presented in **Figure 2**. After adjusting for age, sex, education, insurance coverage, and noncommunicable diseases, all PoD categories had higher standardized reimbursement costs and patient out-of-pockets costs (all $p<0.001$).

Age by group interaction for healthcare costs for all adults with PoDs and by PoD category

There were significant age group (18-40 years; 41-64 years) by group (with PoDs; without PoDs) interactions for all individuals with PoDs and for each of the PoD categories for total standardized reimbursement and patient out-of-pocket costs (all $p<0.001$). After stratifying by young and middle-aged, all individuals with PoDs and each PoD category had higher CRs compared to individuals without PoDs, with the magnitude of the CR suggesting costs may be greater for young than middle-aged individuals with PoDs (**Supplementary Table 4**).

DISCUSSION

The principal finding of this investigation is that young and middle-aged privately-insured adults with PoDs had higher healthcare resource utilization across all medical services, and higher all-cause healthcare costs compared to young and middle-aged privately-insured adults without PoDs. These findings were evident across all PoD categories when compared to individuals without PoDs. Moreover, the differences in costs were greater for younger than middle-aged adults with PoDs, and for each PoD category, compared to adults without PoDs. While previous studies examining adverse health complications among populations with PoDs have suggested earlier screening strategies for disease prevention and healthcare management,[3,13] the findings from the current study could inform decision making processes regarding private health benefit plan design and healthcare resource allocation for services and treatments by administrators and policymakers.

In the current study, we found substantial mean differences for all-cause healthcare costs and large unadjusted cost ratios for the standardized reimbursement and patient out-of-pocket costs between individuals with vs. without PoDs. After adjusting for sociodemographics,

insurance coverage, and the presence of several costly noncommunicable diseases, total standardized reimbursement costs were still 2.3 times higher and patient out-of-pocket costs were 1.7 times higher for individuals with PoDs compared to individuals without PoDs. These results suggest a few things. First, costly noncommunicable diseases only account for a small portion of the excess healthcare costs attributable to PoDs; however, there may be other costly diseases not examined in this study that are more prevalent among individuals with PoDs. Second, the findings that patient out-of-pocket costs were elevated for individuals with PoDs compared to individuals without PoDs, but to a lesser extent than for standardized reimbursement costs, suggests that health plans are accommodating some, but not all, of the medical needs by individuals with PoDs. This is supported by the higher prevalence of Medicare Advantage health plans among individuals with PoDs compared to individuals without PoDs (21.1% vs. 6.6%). Further, the CR for Medicare Advantage was higher compared to commercial alone for standardized reimbursement costs, but lower for patient out-of-pocket costs for the entire sample, suggesting greater cost reduction plans. Nevertheless, identifying and delineating other "cost drivers" for populations with PoDs is needed.

The sample size for the group with PoDs was very large, which allowed us to examine healthcare resource utilization and costs after stratifying by the type of PoD, with sample sizes ranging from 5,518 (PoDs with chromosomal abnormalities) to 33,566 (PoDs of the musculoskeletal system). Our analyses suggest that all PoD categories have higher healthcare resource utilization and costs compared to adults without PoDs. Moreover, there was a considerable range of excess healthcare utilization and costs across PoD categories. In general, PoD categories with the highest healthcare resource utilization and costs were PoDs of the urinary, circulatory, respiratory and digestive, and nervous systems. While different types of

PoDs should not be assumed to have the same set of health complications, as most have very specific etiologies and comorbidities, there are overlapping risk factors across various types of PoDs that may impede healthful transition into and throughout adulthood, thus leading to similar health outcomes and healthcare needs. These factors may manifest as a direct consequence of the condition (e.g., impaired executive functioning) or as an indirect consequence of a condition (e.g., chronic pain, low societal integration). On the other hand, individuals with specific PoDs may be more susceptible to certain adverse health outcomes and reliantly on specific healthcare services. For example, children and adolescents with PoDs have higher prevalence of mental health disorders compared to the general population of children,[30,31] but the prevalence is greater among children and adolescents with neurodevelopmental PoDs than nervous system PoDs.[30,32] Future research is needed to parse out the PoD-specific factors contributing to excess healthcare utilization and costs to lessen the healthcare economic burden attributable to various PoDs.

A major strength of the study included the large sample size for adults with PoDs. Gathering data on clinical populations is challenging and very little is known about health disparities among individuals with PoDs across the lifespan. Another major strength of this study is the comprehensive assessment of several costly noncommunicable diseasese which allowed for cost adjustment.

The limitations of the study must also be discussed. First, it is important to note that the findings from the current investigation are likely underreporting the extent of healthcare resource utilization and costs associated with U.S. populations with PoDs. To be enrolled with a private health insurance plan, individuals must be able to afford the costs or be covered through their employer, their parents (up to 26 years of age), or their spouse. Individuals with PoDs tend to have lower employment and marriage rates compared to the general population,[33] which is likely

to be more problematic with more medically complex forms of PoDs. Furthermore, individuals with more severe forms of PoDs are likely to be covered, or co-covered, by public health insurance due to medical circumstances. Therefore, our sample of adults with PoDs likely reflects a higher functioning and healthier segment of the U.S. population with PoDs;[34] however, this is only speculation. Second, the present study excluded individuals that did not have service utilization in 2016, which may have biased results. However, these excluded individuals that had insurance coverage may be somewhat healthier since they did not require a medical encounter in 2016, thus potentially biasing results in the present study to be more conservative estimates. Third, data were from a single year and longer study periods and longitudinal research designs could provide more robust findings and implications for research, practice, and policy. Fourth, we were only able to adjust for a limited set of covariates, and we are unable to rule out other potential confounding factors. Fifth, we used a single claim to identify PoDs and noncommunicable diseases. Validation studies tend to show that two or more claims for a medical condition improves ability to identify individuals with that condition.[35,36] However, single claim-based algorithms using claims data have moderate-to-high positive predictive value (~80%) and high sensitivity (99%) to detect PoDs,[35] and moderate-to-high sensitivity (up to 99%) and specificity (up to 87%) to detect a variety of costly noncommunicable diseases;[37,38] although, the accuracy of medical condition identification using claims data depends on the length of the study period[39] and the condition examined.[35,37,39,40] Given the short study period of 12 months to extract data and the large and robust effect sizes, the selected methodology to identify associations is likely sufficient to provide evidence of health and economic disparities.

In conclusion, young and middle-aged adults with PoDs have higher healthcare resource utilization and costs compared to young and middle-aged adults without PoDs. These higher

costs come along with higher out-of-pocket burden, which can affect the individual's financial well-being, thus further contributing to health disparities. The elevated healthcare costs were evident even after adjusting for several costly noncommunicable diseases that are more prevalent among populations with PoDs. Furthermore, each PoD category had higher healthcare resource utilization and costs compared to individuals without PoDs. Future research is needed to identify specific cost drivers for the healthcare economic disparity for individuals with PoDs, and by the type of PoD, as well as year to year healthcare costs, which may provide insight into the long-term financial burden. Future research is also needed to develop algorithms and strategies for disease and cost prediction for these populations, which may significantly enhance preventive and personalized medicine, improve healthful aging, and reduce long-term costs.[41]

Contributors: D. Whitney conceived and designed the study, analyzed the data, and wrote the first draft of the manuscript. N. Kamdar assisted in statistical analysis and interpretation. E. Hurvitz, R. Hirth, and M. Peterson assisted in interpretation of data. All authors approved the final manuscript for submission, and agree to be accountable for all aspects of the work.

Data sharing: De-identified 2016 data are from Clinformatics® Data Mart Database (OptumInsightTM, Eden Prairie, MN, USA). As part of our Data Use Agreement, we are unable to share raw data. However, upon reasonable request, we can share SAS code and summarized data tables.

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Figure legends

Figure 1. Annual mean all-cause total, medical, and pharmacy standardized reimbursement costs (**A**) and annual mean all-cause total, medical, and pharmacy patient out-of-pocket costs (**B**) among adults (18-64 years) with and without pediatric-onset disabilities (PoDs).

Figure 2. Annual mean all-cause total standardized reimbursement costs (**A**) and annual mean all-cause total patient out-of-pocket costs (**B**) among adults (18-64 years) with and without pediatric-onset disabilities (PoDs), stratified by the type of PoD. Individuals may have more than one PoD and can be represented across multiple PoD categories. All PoD categories had higher costs compared to individuals without PoDs after adjusting for age, sex, education, insurance coverage, and several noncommunicable diseases (all $p<0.001$).

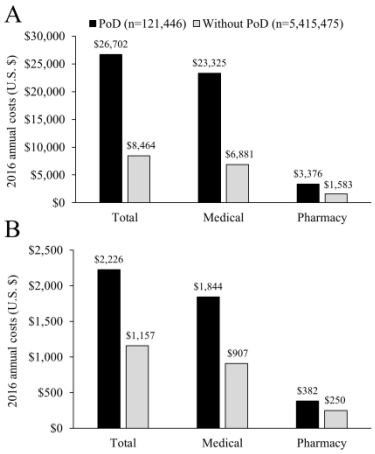

Figure 1. Annual mean all-cause total, medical, and pharmacy standardized reimbursement costs (A) and annual mean all-cause total, medical, and pharmacy patient out-of-pocket costs (B) among adults (18-64 years) with and without pediatric-onset disabilities (PoDs).

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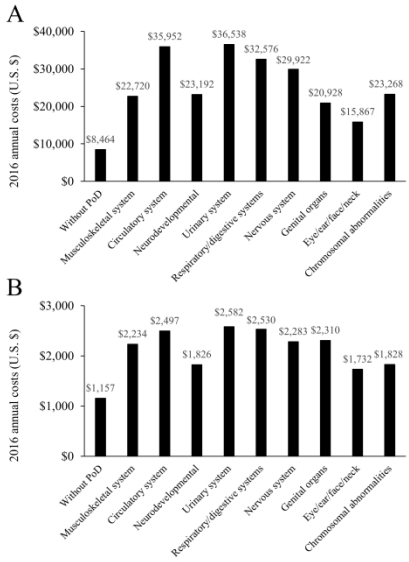

Figure 2. Annual mean all-cause total standardized reimbursement costs (A) and annual mean all-cause total patient out-of-pocket costs (B) among adults (18-64 years) with and without pediatric-onset disabilities (PoDs), stratified by the type of PoD. Individuals may have more than one PoD and can be represented across multiple PoD categories.

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Supplementary Table 1. Diagnostic codes for all pediatric-onset disabilities (PoDs) and noncommunicable diseases using the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10) codes.

Pediatric-onset disability categories and specific conditions	ICD-10 codes
Musculoskeletal system	
Congenital deformities of hip or feet; congenital musculoskeletal deformities of head, face, spine and chest; other congenital musculoskeletal deformities; polydactyly; syndactyly; reduction defects of upper, lower, or unspecified limb; other congenital malformations of limb(s); other congenital malformations of skull and face bones; congenital malformations of spine and bony thorax; osteochondrodysplasia with defects of growth of tubular bones and spine; other osteochondrodysplasias; congenital malformations of musculoskeletal system, not elsewhere classified	Q65-79 families
Juvenile arthritis	M08 family
Other disorders of bone	
Physeal arrest	M89.1 family
Other disorders of bone development and growth	M89.2 family
Circulatory system	
Congenital malformations of the cardiac chambers, cardiac septa, pulmonary and tricuspid valves, aortic and mitral valves; other congenital malformations of the heart; congenital malformations of great arteries, great veins; other congenital malformations of peripheral vascular system or circulatory system	Q20-28 families
Neurodevelopmental	
Intellectual disabilities, mild, moderate, severe, profound, other, and unspecified	F70-73, F78, F79
Specific developmental disorders of speech and language, scholastic skills, motor function; pervasive developmental disorders; other and unspecified disorders of psychological development	F80 family, F81 family, F82, F84 family, F88, F99
Urinary system	
Renal agenesis and other reduction defects of kidney; cystic kidney disease; congenital obstructive defects of renal pelvis and congenital malformations of ureter; other congenital malformations of kidney	Q60-63 families
Respiratory and digestive systems	
Congenital malformations of nose, larynx, trachea or bronchus, lung; other congenital malformations of respiratory system; cleft lip and/or palate; other congenital malformations of tongue, mouth, or pharynx; congenital malformations of esophagus; other congenital malformations of upper alimentary tract; congenital absence, atresia and stenosis of small or large intestine; other congenital malformations of intestine; congenital malformations of gallbladder, bile ducts, or liver; other congenital malformations of digestive system	Q30-45 families

Nervous system	
Encephalocele; microcephaly; congenital hydrocephalus; spina bifida; other congenital malformations of brain, spinal cord, or nervous system	Q01 family, Q02, Q03-7 families
Cerebral palsy	G80 family
Juvenile epilepsy	G40.B family
Genital organs	
Congenital malformations of ovaries, fallopian tubes, broad ligaments, uterus, and cervix; undescended and ectopic testicle; hypospadias; other congenital malformations of female or male genital organs; indeterminate sex and pseudohermaphroditism	Q50-56 families
Malformations of the eye, ear, face, and neck	
Congenital malformations of eyelid, lacrimal apparatus, or orbit; anophthalmos, microphthalmos, or macrophthalmos; congenital lens malformations; congenital malformations of anterior or posterior segment of eye; other congenital malformations of eye; congenital malformations of ear causing impairment of hearing; other congenital malformations of ear, face, or neck	Q10-18 families
Other chromosomal abnormalities, not classified elsewhere	
Down syndrome; Trisomy 18 and Trisomy 13; other trisomies and partial trisomies of the autosomies, not elsewhere classified; monosomies and deletions from the autosomes, not elsewhere classified; balanced rearrangements and structural markers, not elsewhere classified; Turner's syndrome; other sex chromosome abnormalities, female or male phenotype, not elsewhere classified; other chromosome abnormalities	Q90-93 families, Q95-99 families
<u>Noncommunicable diseases</u>	
Ischemic heart disease	
Angina pectoris; acute myocardial infarction; subsequent ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction; other acute ischemic heart diseases; chronic ischemic heart disease	I20-22 families, I24 family, I25 family
Cerebrovascular disease	
Nontraumatic subarachnoid or intracerebral hemorrhage; other and unspecified nontraumatic intracranial hemorrhage; cerebral infarction; occlusion and stenosis of precerebral or cerebral arteries, not resulting in cerebral infarction; other cerebrovascular diseases; cerebrovascular disorders in diseases classified elsewhere; sequelae of cerebrovascular disease	I60-63 families, I65-69 families
Hypertensive and other cardiovascular disease	
Essential (primary) hypertension; hypertensive heart, chronic kidney disease, or heart and chronic kidney disease; secondary hypertension; hypertensive crisis; heart failure; peripheral atherosclerosis	I10-13 families, I15 family, I16 family, I50 family, I70 family
Type II diabetes mellitus	E11 family
Malignant cancer	

Malignant neoplasms of lip, oral cavity, or pharynx, digestive organs, respiratory and intrathoracic organs, bone and articular cartilage, mesothelial and soft tissue, breast, female or male genital organs, urinary tract, eye, brain, or other parts of central nervous system, thyroid or other endocrine glands, ill-defined, other secondary, or unspecified sites, neuroendocrine tumors, lymphoid, hematopoietic, or related tissue; melanoma and other malignant neoplasms of skin	C00-26 families, C30-41 families, C43-58 families, C60-80 families, C7A family, C7B family, C81-96 families
Osteoporosis	
With or without current pathological fracture	M80 family, M81 family
Mood affective disorders	
Manic episode; bipolar disorder; major depressive disorder, single episode or recurrent; persistent mood [affective] disorders; unspecified mood [affective] disorders	F30-34 families, F39
Chronic obstructive pulmonary disease	
Simple and mucopurulent chronic bronchitis; unspecified chronic bronchitis; emphysema; other chronic obstructive pulmonary disease	J41-44 families
Chronic kidney disease	
Stage I-V; end stage renal disease; chronic kidney disease, unspecified	N18 family
Liver disease	
Alcoholic liver disease; toxic liver disease; hepatic failure, not elsewhere classified; chronic hepatitis, not elsewhere classified; fibrosis and cirrhosis of liver; other inflammatory liver diseases; other diseases of liver; liver disorders in diseases classified elsewhere	K70-76 families, K77

Supplementary Table 2. Annual adjusted ratio of means (RM) for healthcare resource utilization for year 2016 among adults (18-64 years) with and without pediatric-onset disabilities (PoDs).

	Inpatient	Outpatient and other	Emergency department	Office
	RM (95% CI)	RM (95% CI)	RM (95% CI)	RM (95% CI)
With PoDs (ref: without PoDs)	1.19 (1.19, 1.20)	1.56 (1.56, 1.56)	1.13 (1.12, 1.14)	1.41 (1.40, 1.41)
Age (continuous)	1.00 (1.00, 1.00)	1.01 (1.01, 1.01)	0.98 (0.98, 0.98)	1.00 (1.00, 1.00)
Sex (ref: female)	1.14 (1.14, 1.14)	0.76 (0.76, 0.76)	0.88 (0.88, 0.89)	0.81 (0.81, 0.81)
Education (ref: less than high school)				
High school diploma	0.97 (0.95, 0.99)	1.08 (1.08, 1.09)	1.11 (1.09, 1.14)	1.01 (1.00, 1.01)
More than high school	0.95 (0.93, 0.97)	1.23 (1.23, 1.24)	0.84 (0.83, 0.86)	1.03 (1.02, 1.04)
Unknown/missing	0.93 (0.91, 0.95)	1.13 (1.12, 1.13)	0.91 (0.89, 0.94)	1.03 (1.02, 1.04)
Insurance coverage (ref: commercial only)	1.22 (1.22, 1.23)	1.21 (1.21, 1.21)	1.86 (1.85, 1.87)	1.32 (1.31, 1.32)
Noncommunicable diseases (ref: without)				
Ischemic heart disease	1.08 (1.07, 1.08)	1.34 (1.33, 1.34)	1.45 (1.44, 1.46)	1.25 (1.25, 1.25)
Cerebrovascular disease	1.21 (1.21, 1.22)	1.34 (1.33, 1.34)	1.39 (1.38, 1.40)	1.17 (1.16, 1.17)
Hypertensive/other cardiovascular disease	1.45 (1.45, 1.46)	1.20 (1.20, 1.20)	1.74 (1.73, 1.75)	1.33 (1.33, 1.33)
Type 2 diabetes	1.11 (1.11, 1.12)	1.18 (1.18, 1.18)	1.14 (1.13, 1.14)	1.20 (1.20, 1.20)
Malignant cancer	1.22 (1.22, 1.23)	1.69 (1.69, 1.69)	1.23 (1.22, 1.24)	1.54 (1.54, 1.55)
Osteoporosis	1.14 (1.13, 1.15)	1.28 (1.28, 1.29)	1.13 (1.12, 1.14)	1.24 (1.24, 1.24)
Mood affective disorders	1.45 (1.45, 1.46)	1.68 (1.68, 1.68)	1.70 (1.69, 1.70)	1.60 (1.60, 1.60)
Chronic obstructive pulmonary disease	1.19 (1.18, 1.2)	1.24 (1.23, 1.24)	1.34 (1.33, 1.35)	1.24 (1.23, 1.24)
Chronic kidney disease	1.27 (1.26, 1.27)	1.44 (1.44, 1.45)	1.21 (1.20, 1.22)	1.19 (1.18, 1.19)
Liver disease	1.28 (1.27, 1.28)	1.42 (1.42, 1.42)	1.67 (1.66, 1.68)	1.34 (1.34, 1.35)

CI, confidence interval. Generalized linear models with Poisson distribution and log-link function were performed to estimate the RM and 95% CI, which is the exponentiated form of the parameter estimate.

N=5,536,921.

Supplementary Table 3. Annual healthcare resource utilization in 2016 among adults (18-64 years) by the type of pediatric-onset disability (PoD).

	Inpatient	Outpatient and other	Emergency department	Office
PoD categories	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Musculoskeletal system (n=33,566)	0.7 (1.9)*	15.2 (13.2)*	0.5 (1.0)*	8.0 (5.9)*
Circulatory system (n= 24,393)	1.5 (2.9)*	15.8 (13.7)*	0.7 (1.1)*	7.6 (5.9)*
Neurodevelopmental (n=17,149)	1.3 (2.9)*	13.9 (14.5)*	0.8 (1.2)*	6.5 (5.5)*
Urinary system (n=12,477)	1.2 (2.6)*	16.2 (13.4)*	0.8 (1.2)*	8.2 (6.0)*
Respiratory or digestive systems (n=12,190)	1.2 (2.6)*	15.2 (13.1)*	0.7 (1.2)*	7.8 (6.1)*
Nervous system (n=11,021)	1.5 (2.9)*	15.4 (14.5)*	0.8 (1.2)*	7.4 (6.0)*
Genital organs (n=6,164)	0.6 (1.7)	13.5 (11.8)*	0.5 (0.9)*	6.3 (5.3)*
Eye/ear/face/neck (n=5,811)	0.5 (1.7)*	11.5 (11.8)*	0.4 (0.9)	5.9 (5.3)*
Chromosomal abnormalities (n=5,518)	0.9 (2.3)*	14.6 (13.9)*	0.5 (1.0)*	6.7 (5.7)*
Without PoDs (n=5,415,475)	0.2 (1.2)	7.1 (8.9)	0.3 (0.7)	3.8 (4.2)

Individuals may have more than one PoD and can be represented across multiple PoD categories.

*Indicates significantly different, $p<0.001$, compared to individuals without PoDs after adjusting for age, sex, education, insurance coverage, and several noncommunicable diseases.

Supplementary Table 4. Annual adjusted cost ratios (CR) for total standardized reimbursement and patient out-of-pocket costs for year 2016 among young (18-40 years) and middle-aged (41-64 years) adults with pediatric-onset disabilities compared to adults without PoDs (reference).

	Standardized reimbursement costs		Patient out-of-pocket costs	
	Young	Middle-aged	Young	Middle-aged
	CR (95% CI)	CR (95% CI)	CR (95% CI)	CR (95% CI)
All PoDs	2.73 (2.69, 2.76)	2.03 (2.01, 2.05)	1.84 (1.82, 1.86)	1.52 (1.5, 1.53)
PoD categories				
Musculoskeletal system	2.92 (2.84, 2.99)	2.26 (2.22, 2.30)	1.93 (1.89, 1.97)	1.68 (1.65, 1.70)
Circulatory system	3.16 (3.06, 3.25)	2.22 (2.18, 2.27)	1.86 (1.81, 1.90)	1.51 (1.48, 1.54)
Neurodevelopmental	2.44 (2.37, 2.51)	1.46 (1.42, 1.50)	1.71 (1.66, 1.75)	1.18 (1.15, 1.21)
Urinary system	2.60 (2.47, 2.73)	1.80 (1.75, 1.84)	1.78 (1.70, 1.86)	1.44 (1.41, 1.47)
Respiratory or digestive systems	3.82 (3.63, 4.02)	2.21 (2.15, 2.27)	2.17 (2.07, 2.27)	1.61 (1.57, 1.65)
Nervous system	3.67 (3.54, 3.81)	2.08 (2.01, 2.15)	2.21 (2.14, 2.29)	1.51 (1.47, 1.55)
Genital organs	2.98 (2.86, 3.11)	2.35 (2.22, 2.48)	2.09 (2.01, 2.17)	1.78 (1.70, 1.86)
Eye/ear/face/neck	1.98 (1.87, 2.09)	1.44 (1.38, 1.50)	1.50 (1.42, 1.58)	1.31 (1.26, 1.35)
Chromosomal abnormalities	2.90 (2.77, 3.04)	1.81 (1.71, 1.91)	1.82 (1.75, 1.90)	1.24 (1.19, 1.30)

The models are adjusted for age (as continuous), sex, education, insurance coverage, and all noncommunicable diseases.

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5-9
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5-6
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-8
Bias	9	Describe any efforts to address potential sources of bias	5, 6, 7, 8
Study size	10	Explain how the study size was arrived at	5-6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8-9
		(*b*) Describe any methods used to examine subgroups and interactions	8-9
		(*c*) Explain how missing data were addressed	5
		(*d*) If applicable, explain how loss to follow-up was addressed	NA
		(*e*) Describe any sensitivity analyses	8
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	9
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9, Table 1
		(b) Indicate number of participants with missing data for each variable of interest	NA
		(c) Summarise follow-up time (eg, average and total amount)	11, 12, 14
Outcome data	15*	Report numbers of outcome events or summary measures over time	9-14

Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (*b*) Report category boundaries when continuous variables were categorized (*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	9-14 and tables/figures Tables
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	13-14
Discussion			
Key results	18	Summarise key results with reference to study objectives	14-17
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	17
Generalisability	21	Discuss the generalisability (external validity) of the study results	15-16
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	No funding reported

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.