DR DANIEL WHITNEY (Orcid ID : 0000-0003-2132-1527)

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Whitney Comorbidity Index to monitor health status for adults with cerebral palsy: validation and thresholds to assist clinical decision making

DANIEL G WHITNEY[1,2]
TANIMA BASU[2]

1 Department of Physical Medicine and Rehabilitation, University of Michigan, Ann Arbor, MI; **2** Institute for Healthcare Policy and Innovation, University of Michigan, Ann Arbor, MI, USA.

Correspondence to Daniel G Whitney, 325 E Eisenhower Parkway, Ann Arbor, MI 48108, USA. E-mail: dgwhit@med.umich.edu

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ABBREVIATION

WCI Whitney Comorbidity Index

AIM To validate the Whitney Comorbidity Index (WCI), which was recently developed to monitor disease status for adults with cerebral palsy (CP), and to identify WCI scores associated with an increased mortality risk using a representative adult CP sample.

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METHOD Data from 2016 to 2018 were used from a random 20% sample from the fee-for-service Medicare database for this retrospective cohort study. The WCI was examined as unweighted (WCI_{unw}) and weighted (WCI_{w}) among adults at least 18 years old with CP. Cox regression models were developed with mortality as the outcome after adjusting for demographics. A concordance statistic (C-statistic) of at least 0.70 was considered as showing sufficient validity. The hazard ratio of mortality for each WCI score was estimated. Secondary analyses were performed for subgroups with co-occurring epilepsy and/or intellectual disabilities.

RESULTS For the entire group (*n*=16 728) and subgroups, the WCI showed sufficient validity (C-statistic 0.73–0.81). For the entire group, the mortality rate was elevated for a score of 1 compared with 0 from the WCI_{unw} (hazard ratio 3.06; 95% confidence interval [CI] 1.52–6.17) and WCI_{w} (hazard ratio 4.08; 95% CI 1.69–9.85), and became larger with each WCI score. Results were similar for the subgroups.

INTERPRETATION The WCI is a valid marker for health/disease status for adults with CP. Several WCI score thresholds were identified to assist in clinical decision making for preventive medicine and intervention implementation.

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What this paper adds

- The Whitney Comorbidity Index (WCI) is valid among 16 728 adults with CP.
- The WCI is valid for those with co-occurring epilepsy and/or intellectual disabilities.
- Thresholds of the WCI score were identified to assist clinical decision making.

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[Main text]

Emerging research shows that adults with cerebral palsy (CP) have an increased risk for a variety of morbidities across biological systems and mental health disorders.[1–13] Importantly, many of these morbidities can be prevented, delayed, or better managed with early clinical intervention.

Primary care physicians are typically the front-line healthcare providers who assess and diagnose the morbidities that are pervasive for adults with CP. Unfortunately, as many healthcare providers are unaware of the medical complexities of aging with CP, delivery of primary care is often suboptimal and may miss indications for preventive medicine or needed referrals to specialists for early intervention.[14–16] Therefore, there is a need for a clinically friendly tool to assist in decision making for clinical management of adults with CP.

The Whitney Comorbidity Index (WCI) was recently developed using administrative claims data to monitor health and disease status specifically for adults with CP.[17] The WCI includes 27 clinically relevant comorbidities that are summed; a higher WCI score corresponds to a higher number of these comorbidities. Comparative assessment to other well-established comorbidity indices used for clinical monitoring, including the Charlson[18] and Elixhauser[19] comorbidity indices, found that the WCI better captured the unique morbidity profiles for adults with CP and was a significantly better predictor of mortality.[17] The WCI is clinically feasible as it requires summing the presence of 27 relevant comorbidities, which is between the number of comorbidities in the Charlson (n=17)[18] and the Elixhauser (n=30)[19] comorbidity indices.

However, the WCI was developed from a privately insured sample of adults with CP, which represents a smaller and less severely impaired segment of the adult population with CP compared with federally subsidized health insurance plans, such as Medicare.[1,20] Therefore, identifying the external validity of the WCI needs to be addressed before translation of the WCI into routine clinical practice. Additionally, there is a need to understand how to utilize the WCI in clinical practice for decision making, such as identifying the thresholds of WCI scores associated with an increased risk of mortality to prompt clinicians for additional screening or intervention implementation.

The primary aim of this study was to validate the WCI using a large representative sample from the Medicare database. The secondary aim was to determine the association between individual WCI scores and mortality. As epilepsy and intellectual disabilities often co-occur with CP, this study first examined the entire group with CP, then for subgroups to examine the effect of these co-occurring neurological conditions.

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METHOD

Data source

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Data were from a 20% random sample of the Medicare fee-for-service administrative claims data source. Data for demographics and all comorbidities in the WCI were ascertained from the calendar year 2016, and the death date was ascertained from the calendar years 2017 and 2018. Medicare is a federal program in the USA that provides health insurance coverage to adults aged at least 65 years or individuals of any age who have one or more chronic disability (including CP) or who have end-stage renal disease. Administrative claims data are used primarily for billing reimbursement from healthcare visits. Medical conditions are identified by searching for specific International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) codes that are attached to individual claims. The ICD-10-CM codes used to identify each medical condition are presented in Table S1 (online supporting information). Since data are de-identified, the University of Michigan Institutional Review Board approved this study as non-regulated.

Study timeline and sample selection

The start date of follow-up for all participants was 1st January 2017. This allowed a 1-year baseline period before the start date of follow-up, as is commonly used for claims-based research studies to ascertain baseline data (e.g. WCI comorbidities),[21] and 2 years of follow-up for mortality. A flow diagram of the inclusion/exclusion criteria is presented in Figure S1 (online supporting information). Adults at least 18 years of age with CP were identified using a claims-based algorithm that required meeting one or both of the following criteria: at least one inpatient claim in 2016 for CP; at least two outpatient claims in 2016 for CP. To be eligible for the analysis, we required adults with CP to have continuous health plan enrollment in parts A and B from 1st January 2016 to 30th January 2017 (1y + 30d) to obtain a full 1-year baseline period and at least 30 days of follow-up for mortality, and complete data on demographics.

For the subgroup analysis, epilepsy and intellectual disabilities were identified in the same manner as CP. Mutually exclusive groups were then stratified as adults with CP only, adults with CP and co-occurring epilepsy but without intellectual disabilities (CP+epilepsy), adults with CP and co-occurring intellectual disabilities but without epilepsy (CP+intellectual disability), and adults with CP, epilepsy, and intellectual disabilities (CP+epilepsy+intellectual disability).

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Mortality

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All-cause mortality from 1st January 2017 to 31st December 2018 (2y period) was derived from the Medicare database where more than 99% of deaths are validated.[22] To be consistent with our previous study,[17] the primary outcome was 2-year mortality and the secondary outcome was 1-year mortality. Individuals who did not die were right-censored as the date of drop in health plan enrollment or end of study period, whichever came first.

WCI

Development of the WCI has been previously described.[17] Briefly, the WCI was developed using an iterative process that harmonized clinical theory of relevant comorbidities, consideration of existing validated measures (e.g. Charlson comorbidity index), and data-driven approaches to select the final 27 comorbidities (Table S1). Two versions of the WCI were created. In the unweighted version (WCI_{unw}), each comorbidity contributes to 1 point if present and 0 points if not present, with the WCI_{unw} total score ranging from 0 to 27 points. In the weighted version (WCI_w), comorbidities were given a weight of 1 to 6 on the basis of the strength of association between the comorbidity and 2-year mortality after adjusting for demographics,[17] with the WCI_w total score ranging from 0 to 59 points. The weight for each comorbidity is presented in Table S1. The weighting algorithm is a numerical approach to give more emphasis to comorbidities that are more strongly associated with the outcome. In our previous study,[17] both the WCI_{unw} and WCI_w were robust predictors of mortality and outperformed the Charlson and Elixhauser comorbidity indices, but the WCI_{unw} and WCI_w were comparable to one another. Therefore, this study examined both the WCI_{unw} and WCI_w. All comorbidities were identified in the same manner as CP.

The WCI includes epilepsy and intellectual disabilities as individual comorbidities. For the subgroup analyses, the WCI score was modified after removing these comorbidities.

Statistical analysis

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To determine the validity of the WCI (as WCI_{unw} and WCI_w) for predicting mortality, Cox proportional hazards regression models were developed after adjusting for age (as continuous), sex, ethnicity, and US region of residence. The WCI variables were treated as discrete variables, but the same conclusions were reached when the WCI variables were treated as continuous (data not presented). The Akaike Information Criterion was used to assess the model's goodness of fit and the concordance statistic (C-statistic) was used to

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assess the discrimination of the model. The C-statistic ranges from 0.50 to 1.00 with a value of at least 0.70 indicating a good model. This study used a value of at least 0.70 to indicate that the WCI has external validity, which is a commonly used threshold (e.g. Sultan et al.[23]). This study computed both the Harrell and Uno C-statistic because of differences in how the censoring is managed.[24] Since the results and conclusions were similar, only the Uno C-statistic and 95% confidence intervals (CI) are reported. The concordance probabilities were compared between the WCI_{unw} and WCI_{w} using the methodology outlined by Uno et al.[24] to determine whether one outperformed the other.

Cox proportional hazards regression models were developed to estimate the hazard ratio (with 95% CI) of each WCI score with mortality as the outcome after adjusting for age, sex, ethnicity, and US region of residence. The hazard ratios with 95% CI were graphically presented to identify which WCI scores were associated with an increased risk of mortality, as well as inflection points where the risk of mortality became exceedingly higher; inflecting points were determined in this study on the basis of a qualitative assessment of the graph. To compare the ability of the two WCI versions for predicting mortality to determine which version was more sensitive for clinical practice, the WCI_{unw} WCI_{w} scores were standardized into quintiles to facilitate the comparison given their different range of scores. Cox proportional hazards regression models estimated the adjusted hazard ratio using the lowest quintile as the reference.

For the subgroup analysis, unadjusted analyses were first performed because of the smaller sample sizes, followed by adjusted analyses as described above for subgroups where the number of deaths per WCI score was sufficient for regression analysis.

Analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA) and $p \leq 0.05$ was considered statistically significant.

RESULTS

Baseline descriptive characteristics for the entire group of adults with CP (*n*=16 728) and the subgroups of CP only (*n*=7542), CP+epilepsy (*n*=2607), CP+intellectual disability (*n*=2781), and CP+epilepsy+intellectual disability (*n*=3798) are presented in Table 1. The mean (standard deviation [SD]) of the WCI_{unw} and WCI_{w} for the entire group were 4.6 (3.3) and 9.4 (7.1) respectively. The prevalence of each WCI comorbidity for the entire group and subgroups is presented in Table S2 (online supporting information).

During the follow-up for a mean (SD) and median (interquartile range) of 696 (126) and 730 (730–730) days respectively, for the entire group, 1486 (8.9%) died with a mean

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(SD) age of 61 years 11 months (15y), 27 (0.1%) were right-censored because of loss of follow-up, and 15 215 (91.0%) were right-censored because of the end of the study period. The follow-up time was similar for each of the subgroups compared with the entire group, and 602 (8.0%) died from CP only with a mean age (SD) of 67 years 4 months (14y 11mo), 203 (7.8%) died from CP+epilepsy with a mean age (SD) of 59 years 5 months (15y 6mo), 260 (9.4%) died from CP+intellectual disability with a mean (SD) age of 62 years (13y 4mo), and 421 (11.1%) died from CP+epilepsy+intellectual disability with a mean (SD) age of 55 years 1 month (12y 8mo). Descriptive characteristics of those who died during the follow-up are presented in Table S3 (online supporting information).

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Validation

For the entire group, the C-statistic (95% CI) for WCI_{unw} predicating 1- and 2-year mortality was 0.78 (0.73–0.83) and 0.77 (0.71–0.83) respectively, indicating sufficient validity (Table 2). While the WCI_w showed slightly better discrimination and model fit statistics (i.e. a lower Akaike Information Criterion indicates improved model fit), the difference was minor and not statistically significant (p>0.70). For the subgroups, the C-statistic ranged from 0.73 to 0.81 for WCI_{unw} and WCI_w for predicting 1- and 2-year mortality. There was no apparent or statistical difference in discrimination between the WCI_{unw} and WCI_w for any model (all p>0.30).

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WCI score thresholds for the entire group

The WCI scores were combined at the upper end to allow for statistical modelling, such that WCI_{unw} scores over 12 were grouped as having 13+ and WCI_w scores over 23 were grouped as 24+. Compared with a score of 0, each score above 0 was associated with a significantly increased 2-year mortality rate for the WCI_{unw} (Fig. 1a) and WCI_w (Fig. 1b) (all p<0.05). It is important to note that the exceedingly large adjusted hazard ratios of 2-year mortality associated with higher WCI scores may diminish, visually, just how detrimental lower WCI scores can be. For example, the adjusted hazard ratio (95% CI) for a WCI_{unw} score of 1 was 3.06 (1.52–6.17) and a WCI_w score of 1 was 4.08 (1.69–9.85) compared with a score of 0. A qualitative assessment of the adjusted hazard ratios (95% CI) suggests that the strength of the association with 2-year mortality became larger with each subsequent WCI score. When the WCI_{unw} or WCI_w were transformed to quintiles, the pattern and extent of the adjusted hazard ratios were similar to one another (Fig. S2, online supporting information). The patterns and conclusions were similar for 1-year mortality (data not shown).

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WCI score thresholds for subgroups

The unadjusted proportion of those who died during the 2-year follow-up regressed on the WCI_{unw} score for each subgroup is presented in Figure 2. In general, the pattern was similar between subgroups, in that a higher WCI_{unw} score corresponded to a higher rate of mortality. There were too few deaths for CP+epilepsy and CP+epilepsy+intellectual disability, and scores of 0 or 1 were combined and set as the reference for the regression analysis. The adjusted hazard ratio for 2-year mortality for each WCI_{unw} score is presented in Figure S3 (online supporting information) for each subgroup, which was similar to the pattern observed for the unadjusted analysis.

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DISCUSSION

This study provides empirical evidence that the WCI, either unweighted or weighted, is a valid tool for assessing health and disease status for adults with CP. The validity was consistent for adults with CP with and without co-occurring epilepsy and/or intellectual disabilities, thus enhancing clinical utility of the WCI for the broader adult population with CP.

This study also identified novel thresholds of WCI scores that can be used to assist in clinical decision making that were generally consistent across the subgroups. For the entire group, the adjusted rate of mortality was more than 3-fold higher with a WCI score of 1 compared with a score of 0, indicating an initial clinical threshold to use. The adjusted rate of mortality continued to climb at an alarming rate with higher WCI scores. For example, a WCI_{unw} score of 4 was associated with a 4.9-fold higher adjusted rate of mortality; a WCI_{unw} score of 4 indicates the presence of four comorbidities, which was the median number of comorbidities among this large sample (Table 1), thus providing a general clinical threshold for the adult population with CP. Finally, 19% of participants from the entire sample had a WCI_{unw} score of at least 6; a WCI_{unw} score of 6 was associated with a 7.1-fold higher adjusted rate of mortality.

Consistent with the study that developed the WCI,[17] neither the unweighted or weighted version in the current study emerged as a stronger predictor of mortality on the basis of the C-statistics and standardized comparison. For example, the quintile patterns for the association with mortality were almost overlaid, suggesting that neither is more sensitive at detecting mortality. We recommend using the unweighted version of the WCI, as this version requires a simple summation of zeros and ones (not present/present) for the 27 WCI

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comorbidities, and does not require knowledge of algorithm weights, thus enhancing interpretability and feasibility.

The WCI can also be used for risk adjustment in outcomes-based research. There is growing recognition in the field for the need of epidemiological investigations to identify health-related problems and opportunities to improve healthful aging for adults with CP. In many outcomes-based research studies, several covariates are needed to adjust statistical models to account for group differences to accomplish the research objective. More variables are often needed for adjustment in studies involving individuals with versus without disabilities given the vast differences in the extent of health and disease status. It can be difficult to obtain a large sample size for clinical populations, thus creating a unique challenge of a need for more covariates for adjustment among a relatively small sample size. This can result in biased regression estimates leading to erroneous interpretation of statistical models.[25] The WCI is a single, valid variable that adequately accounts for health and disease for adults with CP. Comorbidity indices can also be modified to account for a particular study design. For example, if myocardial infarction is an outcome of interest, the WCI can be modified by removing myocardial infarction from the WCI. The current study provides the ICD-10-CM codes for the WCI comorbidities (Table S1), while our previous study provides the ICD-9-CM codes.[17]

Relevant study limitations from using claims-based research for adults with CP have been reported previously.[1,2,6–8,26] It is worth repeating that claims do not contain data on severity of CP, which would provide clinically relevant information. Further, claims data may underestimate the prevalence of comorbidities for adults with CP, as comorbidity diagnoses are probably missed by clinicians who have little experience in clinically managing adult patients with CP. The potential impact on the conclusions from this study is an underestimation of the effects of WCI on mortality. In addition, it is important to note that a claims-based comorbidity index has limitations in detecting the health and disease status for individuals with CP. The scoring system of 0 or 1 for the absence or presence of a comorbidity may not fully capture the impact or physiologic integration that the comorbidity may have on health and function. For example, high blood pressure is positively associated with endothelial cell damage.[27] For those with hypertension, someone with a higher blood pressure (e.g. 190/100mmHg) would probably have more endothelial damage and worse cardiovascular health, despite having the same score as someone with a milder form of hypertension (e.g. 150/90mmHg). While the WCI originally investigated several mental health disorders and substance abuse problems,[17] only depression met the statistical criteria to

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be part of the WCI. However, mental health disorders can be challenging for healthcare providers to accurately diagnose for individuals with CP, especially for those with co-occurring cognitive or communication problems. Psychosocial aspects of health are a major issue for adults with CP.[28,29] Comorbidity indices are not designed to capture psychosocial aspects of health, or other non-morbidity important aspects of health, such as social determinants of health or access to adequate healthcare. Additionally, as eloquently described by Streiner,[30] an index is specific to the construct and method in which it was developed; in this case, to predict mortality among a sample that had to meet specific inclusion criteria. Further, the idea of comorbidities and their impact on aging with CP can be convoluted, considering CP is in part defined by 'accompanying disturbances'.[31] Lastly, as we have previously shown the WCI to outperform other commonly used comorbidity indices, we did not carry this comparative analytical approach forward. Future studies are needed to determine whether other comorbidity indices capture the comorbidity profiles in the Medicare sample of adults with CP.

In conclusion, the WCI is a valid, simple, and clinically friendly tool that can be used to monitor health and disease status for adults with CP with or without co-occurring epilepsy or intellectual disabilities. We encourage the use of the WCI, especially the unweighted version as it is clinically feasible, valid, and easy to calculate and interpret. Several thresholds of WCI_{unw} scores were noted given the strength of the association with mortality, and could be considered to assist in clinical decision making, such as whether to perform additional screening or intervention implementation. A WCI_{unw} score of 1 can be used as an initial threshold indicating poor health; a WCI_{unw} score of 3 may reflect an early inflection point where mortality risk increases with each additional WCI score; a WCI_{unw} score of 4 can be used as the median value for the adult population with CP; and a WCI_{unw} score of 6 can be used as the upper 20% value for the adult population with CP.

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SUPPORTING INFORMATION

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The following additional material may be found online:

Table S1: ICD-10-CM codes and weight for each of the comorbidities in the WCI.

Table S2: Prevalence of individual comorbidities from the WCI.

Table S3: Baseline descriptive characteristics for those that died during the 2-year follow-up.

Figure S1: Flow chart of inclusion/exclusion study criteria.

Figure S2: WCI quintiles with 2-year mortality.

Figure S3: WCI values with 2-year mortality for the subgroups.

REFERENCES

1. French ZP, Caird MS, Whitney DG. Osteoporosis epidemiology among adults with cerebral palsy: findings from private and public administrative claims data. *JBMR Plus* 2019; **3**: e10231.
2. French ZP, Torres RV, Whitney DG. Elevated prevalence of osteoarthritis among adults with cerebral palsy. *J Rehabil Med.* 2019; **51**: 575–81.
3. Whitney DG, Alford AI, Devlin MJ, Caird MS, Hurvitz EA, Peterson MD. Adults with cerebral palsy have higher prevalence of fracture compared with adults without cerebral palsy independent of osteoporosis and cardiometabolic diseases. *J Bone Miner Res* 2019; **34**: 1240–7.
4. Whitney DG, Hurvitz EA, Devlin MJ, et al. Age trajectories of musculoskeletal morbidities in adults with cerebral palsy. *Bone* 2018; **114**: 285–91.
5. Whitney DG, Hurvitz EA, Ryan JM, et al. Noncommunicable disease and multimorbidity in young adults with cerebral palsy. *Clin Epidemiol* 2018; **10**: 511–9.
6. Whitney DG, Kamdar NS, Ng S, Hurvitz EA, Peterson MD. Prevalence of high-burden medical conditions and health care resource utilization and costs among adults with cerebral palsy. *Clin Epidemiol* 2019; **11**: 469–81.
7. Whitney DG, Schmidt M, Bell S, Morgenstern H, Hirth RA. incidence rate of advanced chronic kidney disease among privately insured adults with neurodevelopmental disabilities. *Clin Epidemiol* 2020; **12**: 235–43.
8. Whitney DG, Warschausky SA, Ng S, Hurvitz EA, Kamdar NS, Peterson MD. Prevalence of mental health disorders among adults with cerebral palsy: a cross-sectional analysis. *Ann Intern Med* 2019; **171**: 328–33.

This article is protected by copyright. All rights reserved

Author Manuscript

9. Ryan JM, Peterson MD, Ryan N, et al. Mortality due to cardiovascular disease, respiratory disease, and cancer in adults with cerebral palsy. *Dev Med Child Neurol* 2019; **61**: 924–8.

10. Cremer N, Hurvitz EA, Peterson MD. Multimorbidity in middle-aged adults with cerebral palsy. *Am J Med* 2017; **130**: 744 e749–744 e715.

11. Smith KJ, Peterson MD, O'Connell NE, et al. Risk of depression and anxiety in adults with cerebral palsy. *JAMA Neurol* 2019; **76**: 294–300.

12. van der Slot WM, Roebroeck ME, Nieuwenhuijsen C, et al. Cardiovascular disease risk in adults with spastic bilateral cerebral palsy. *J Rehabil Med* 2013; **45**: 866–72.

13. Van Der Slot WM, Nieuwenhuijsen C, Van Den Berg-Emons RJ, et al. Chronic pain, fatigue, and depressive symptoms in adults with spastic bilateral cerebral palsy. *Dev Med Child Neurol* 2012; **54**: 836–42.

14. Aisen ML, Kerkovich D, Mast J, et al. Cerebral palsy: clinical care and neurological rehabilitation. *Lancet Neurol* 2011; **10**: 844–52.

15. Peterson MD, Hurvitz EA. Cerebral palsy grows up. *Mayo Clin Proc* 2020; Forthcoming https://doi.org/10.1016/j.mayocp.2020.10.006.

16. McColl MA, Forster D, Shortt SE, et al. Physician experiences providing primary care to people with disabilities. *Healthc Policy* 2008; **4**: e129–47.

17. Whitney DG, Kamdar NS. Development of a new comorbidity index for adults with cerebral palsy and comparative assessment with common comorbidity indices. *Dev Med Child Neurol* 2021; **63**: 313–9.

18. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987; **40**: 373–83.

19. Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. *Med Care* 1998; **36**: 8–27.

20. Whitney DG. Prevalence of high-burden medical conditions among young and middle-aged adults with pediatric-onset medical conditions: findings from US private and public administrative claims data. *Int J Health Policy Manag* 2019; **8**: 629–35.

21. Chang HY, Weiner JP, Richards TM, Bleich SN, Segal JB. Validating the adapted Diabetes Complications Severity Index in claims data. *Am J Manag Care* 2012; **18**: 721–6.

22. Jarosek S. Death information in the research identifiable Medicare data [Internet]. 2018. Available at: https://www.resdac.org/articles/death-information-research-identifiable-

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medicare-data#:~:text=Overall%2C%2099%25%20of%20death%20days%20have%20been%20validated.,-The%20most%20common&text=However%2C%20RRB%20beneficiaries%20comprise%20a,and%2098%25%20are%20SSA%20beneficiaries (accessed 14 December 2020).

23. Sultan AA, West J, Grainge MJ, et al. Development and validation of risk prediction model for venous thromboembolism in postpartum women: multinational cohort study. *BMJ* 2016; **355**: i6253.

24. Uno H, Cai T, Pencina MJ, D'Agostino RB, Wei LJ. On the C-statistics for evaluating overall adequacy of risk prediction procedures with censored survival data. *Stat Med* 2011; **30**: 1105–17.

25. Ogundimu EO, Altman DG, Collins GS. Adequate sample size for developing prediction models is not simply related to events per variable. *J Clin Epidemiol* 2016; **76**: 175–82.

26. Whitney DG, Caird MS, Jepsen KJ, et al. Elevated fracture risk for adults with neurodevelopmental disabilities. *Bone* 2020; **130**: 115080.

27. Gkaliagkousi E, Gavriilaki E, Vasileiadis I, et al. Endothelial microvesicles circulating in peripheral and coronary circulation are associated with central blood pressure in coronary artery disease. *Am J Hypertens* 2019; **32**: 1199–205.

28. Balandin S, Berg N, Waller A. Assessing the loneliness of older people with cerebral palsy. *Disabil Rehabil* 2006; **28**: 469–79.

29. Whitney DG, Warschausky SA, Ng S, Hurvitz EA, Kamdar NS, Peterson MD. Prevalence of mental health disorders among adults with cerebral palsy a cross-sectional analysis. *Ann Int Med* 2019; **171**: 328–33.

30. Streiner DL. Comorbidity indices: how should they be developed? *Dev Med Child Neurol* 2021; **63**: 246.

31. Rosenbaum P, Paneth N, Leviton A, et al. A report: the definition and classification of cerebral palsy April 2006. *Dev Med Child Neurol Suppl* 2007; **109**: 8–14.

Table 1: Baseline descriptive characteristics of the entire group of adults with cerebral palsy (CP) and for subgroups on the basis of co-occurring epilepsy (EP) and intellectual disabilities (ID)

	Entire group (*n*=16 728)	CP only (*n*=7542)	CP+EP (*n*=2607)	CP+ID (*n*=2781)	CP+EP+ID (*n*=3798)

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Mean age (SD), y:mo	51:0 (15:4)	53:0 (16:2)	47:2 (15:2)	52:2 (14:4)	49:0 (13:4)
18–40y	27.7 (4633)	25.2 (1901)	38.8 (1012)	23.2 (645)	28.3 (1075)
41–64y	51.6 (8631)	48.1 (3628)	45.5 (1187)	56.4 (1568)	59.2 (2248)
≥65y	20.7 (3464)	26.7 (2013)	15.7 (408)	20.4 (568)	12.5 (3798)
Sex					
Female	48.2 (8066)	51.2 (3858)	52.1 (1359)	51.1 (1421)	53.3 (2024)
Male	51.8 (8662)	48.9 (3684)	47.9 (1248)	48.9 (1360)	46.7 (1774)
Ethnicity					
White	80.5 (13 471)	80.7 (6085)	77.6 (2023)	82 (2280)	81.2 (3083)
Black	13.0 (2180)	13 (977)	13.6 (354)	13.1 (365)	12.7 (484)
Hispanic	3.3 (560)	1.1 (84)	1.4 (37)	1.4 (38)	1.3 (49)
Asian	1.0 (167)	1 (78)	1.4 (36)	0.8 (21)	0.8 (32)
Native American	0.8 (142)	3.3 (251)	4.6 (120)	2.3 (64)	3.3 (125)
Other	1.2 (208)	0.9 (67)	1.4 (37)	0.5 (13)	0.7 (25)
US region of residence					
Midwest	27.7 (4639)	27.5 (2074)	26 (678)	29.1 (810)	28.4 (1077)
Northeast	21.7 (3631)	19.2 (1447)	16.4 (428)	27.6 (767)	26 (989)
South	34.4 (5756)	36 (2718)	39 (1017)	29.9 (830)	31.4 (1191)
West	16.2 (2702)	17.3 (1303)	18.6 (484)	13.5 (374)	14.2 (541)
WCI[a]					
Unweighted					
Mean (SD)	4.6 (3.3)	3.4 (3.0)	3.7 (3.1)	3.7 (2.9)	4.7 (3.1)
Median (IQR)	4 (2–6)	3 (1–5)	3 (1–5)	3 (2–5)	4 (2–6)
Weighted					
Mean (SD)	9.4 (7.1)	6.9 (6.4)	7.6 (6.5)	7.8 (6.3)	9.9 (6.9)
Median (IQR)	8 (4–13)	5 (2–10)	6 (3–11)	6 (3–11)	9 (4–14)
Deaths during follow-up	8.9 (1489)	8.0 (602)	7.8 (203)	9.4 (260)	11.1 (421)

Data are % (*n*) unless otherwise stated. [a]The Whitney Comorbidity Index (WCI) comorbidities, epilepsy and intellectual disabilities, were removed from the WCI for the subgroups. IQR, interquartile range.

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Table 2: Model fit and discrimination statistics for the Whitney Comorbidity Index (WCI) as unweighted (WCI_{unw}) and weighted (WCI_w) for predicting 1- and 2-year mortality[a] for the entire group of adults with cerebral palsy (CP) and for subgroups on the basis of co-occurring epilepsy (EP) and intellectual disabilities (ID)

	1-year mortality		2-year mortality	
	AIC	Uno's C-statistic (95% CI)	AIC	Uno's C-statistic (95% CI)
Entire group (*n*=16 728)				
WCI_{unw}	14 493	0.78 (0.73–0.83)	27 297	0.77 (0.71–0.83)
WCI_w	14 459	0.79 (0.74–0.84)	27 251	0.78 (0.71–0.84)
CP only (*n*=7542)				
WCI_{unw}	5418	0.81 (0.72–0.89)	9937	0.80 (0.73–0.87)
WCI_w	5415	0.81 (0.75–0.88)	9929	0.81 (0.75–0.87)
CP+EP (*n*=2607)				
WCI_{unw}	1630	0.80 (0.74–0.86)	2995	0.78 (0.73–0.83)
WCI_w	1637	0.81 (0.75–0.87)	2987	0.80 (0.76–0.83)
CP+ID (*n*=2781)				
WCI_{unw}	1952	0.76 (0.70–0.82)	3905	0.76 (0.72–0.80)
WCI_w	1951	0.77 (0.71–0.84)	3900	0.77 (0.74–0.81)
CP+EP+ID (*n*=3798)				
WCI_{unw}	3503	0.76 (0.70–0.82)	6629	0.73 (0.67–0.79)
WCI_w	3495	0.77 (0.74–0.81)	6616	0.74 (0.71–0.77)

[a]Adjusted for age, sex, ethnicity, and US region of residence. AIC, Akaike Information Criterion; C-statistic, concordance statistic; CI, confidence interval.

[Figure legends]

Figure 1: Adjusted hazard ratio (HR; filled circle) with 95% confidence intervals (CI; vertical bars) for each of the Whitney Comorbidity Index (WCI) values (reference: no morbidities) as (a) unweighted (WCI_{unw}) and (b) weighted (WCI_w) with 2-year mortality as the outcome for the entire group (*n*=16 728). Models were adjusted for age (continuous), sex, ethnicity, and US region of residence. The dotted horizontal line represents the reference of 1.00 for those with zero morbidities.

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Figure 2: Unadjusted prevalence of those who died during the 2-year follow-up for each of the unweighted Whitney Comorbidity Index (WCI_{unw}) values stratified by adults with cerebral palsy only (CP only) (*n*=7542), adults with CP and co-occurring epilepsy (CP+EP) (*n*=2,607), adults with CP and co-occurring intellectual disabilities (CP+ID) (*n*=2781), and adults with CP and co-occurring EP and ID (CP+EP+ID) (*n*=3798).

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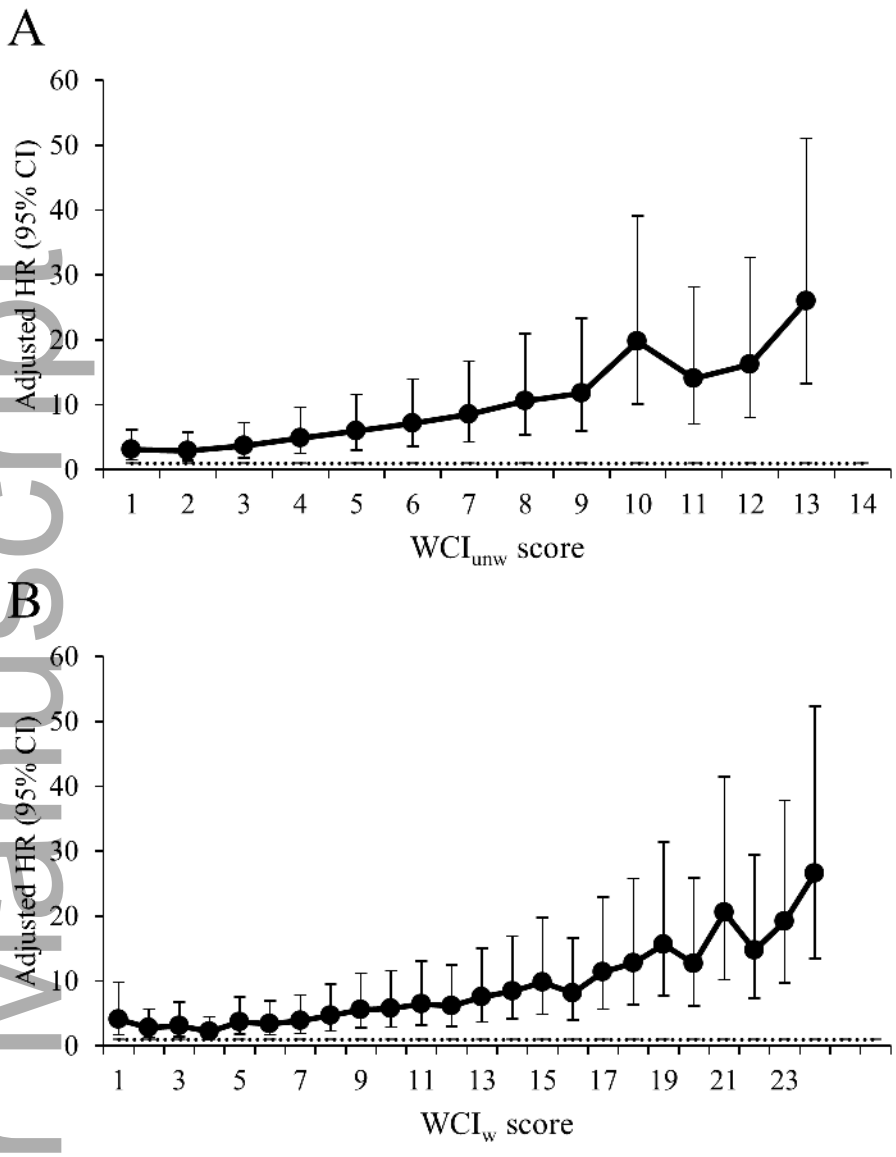

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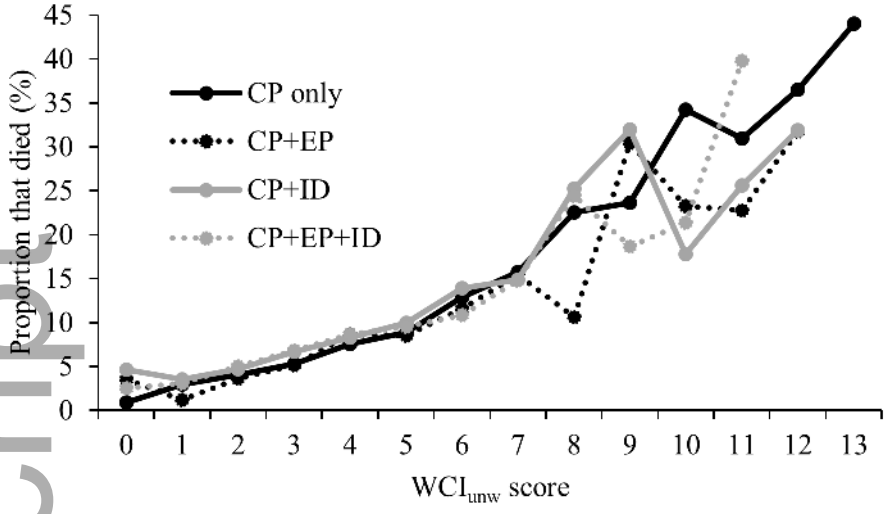

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