

## TOPIC COLLECTION: ASSOCIATED MENTAL DISORDERS AND PHYSICAL CONDITIONS

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### Letter from the Editor

This collection (a seminal study from Denmark and several summaries of related studies along the medical-psychiatric interface) reminds us that the mind and body are continually interacting and affecting one another. We are increasingly recognizing the prevalence and importance of co-occurring medical and mental disorders. An exhaustive literature documents a bidirectional relationship between these two kinds of disorders: Rates of mental disorders are elevated in almost every medical illness category compared with rates in community controls, possibly as a consequence of the burden of medical illness; and, as demonstrated in the *New England Journal of Medicine* article, most mental disorders seem to increase the incidence of many medical illnesses. Even more importantly, evidence not reviewed here shows that mental and medical disorders can have mutually adverse effects on the course that each disorder takes over time, as well as on treatment efficacy and outcome. This reciprocal relationship is thought to exert its effects through mutually reinforcing neurobiological mechanisms involving inflammation and the immune and endocrine systems, and through behaviors (obesity; tobacco, alcohol, and drug use; avoidance of medical care) that increase the risk for medical illness. As the authors note, the relationship between the two entities may not be entirely causal, but may also relate to common environmental exposures, especially early in development, and perhaps also to common genetic factors. That is, when two phenomena appear to be related, this association may be accounted for by an underlying third factor common to both.

These theoretical issues remain to be worked out in subsequent research, but what do we need to know now, as practicing physicians, whether in primary or specialty care, whether working more in the medical or the mental sphere? Interest is growing in psychiatrists taking a primary care role in their patients' global medical condition, guiding them toward necessary evaluations with their providers and providing education and support in this process. Being more vigilant about patients' overall medical status means considering the following questions: Do they have a primary care physician and how often do they have visits? Have they had standard laboratory screening recently? Are they following treatment recommendations? Might medical problems be affecting the course or outcome of their mental disorder? Psychiatrists, who often spend more time with patients during appointments than primary care or specialty physicians, must consider this an opportunity not to be wasted. Conversely, primary and specialty care physicians need to become aware of the increased rates of mental disorders associated with the illnesses they treat and not pass off — for example — a depressive reaction as an expected effect (“who wouldn’t be depressed?”), but rather see to it that these disorders are vigorously addressed and treated.

We hope you enjoy this collection, which provides important information on the mutually reinforcing effects of medical and mental disorders.

Peter Roy-Byrne, MD

Dr. Roy-Byrne is Professor, Department of Psychiatry and Behavioral Sciences, University of Washington, Seattle.

## ORIGINAL ARTICLE

# Association between Mental Disorders and Subsequent Medical Conditions

N.C. Momen, O. Plana-Ripoll, E. Agerbo, M.E. Benros, A.D. Børglum, M.K. Christensen, S. Dalsgaard, L. Degenhardt, P. de Jonge, J.-C.P.G. Debost, M. Fenger-Grøn, J.M. Gunn, K.M. Iburg, L.V. Kessing, R.C. Kessler, T.M. Laursen, C.C.W. Lim, O. Mors, P.B. Mortensen, K.L. Musliner, M. Nordentoft, C.B. Pedersen, L.V. Petersen, A.R. Ribe, A.M. Roest, S. Saha, A.J. Schork, K.M. Scott, C. Sievert, H.J. Sørensen, T.J. Stedman, M. Vestergaard, B. Vilhjalmsen, T. Werge, N. Weye, H.A. Whiteford, A. Prior, and J.J. McGrath

## ABSTRACT

**BACKGROUND**

Persons with mental disorders are at a higher risk than the general population for the subsequent development of certain medical conditions.

**METHODS**

We used a population-based cohort from Danish national registries that included data on more than 5.9 million persons born in Denmark from 1900 through 2015 and followed them from 2000 through 2016, for a total of 83.9 million person-years. We assessed 10 broad types of mental disorders and 9 broad categories of medical conditions (which encompassed 31 specific conditions). We used Cox regression models to calculate overall hazard ratios and time-dependent hazard ratios for pairs of mental disorders and medical conditions, after adjustment for age, sex, calendar time, and previous mental disorders. Absolute risks were estimated with the use of competing-risks survival analyses.

**RESULTS**

A total of 698,874 of 5,940,299 persons (11.8%) were identified as having a mental disorder. The median age of the total population was 32.1 years at entry into the cohort and 48.7 years at the time of the last follow-up. Persons with a mental disorder had a higher risk than those without such disorders with respect to 76 of 90 pairs of mental disorders and medical conditions. The median hazard ratio for an association between a mental disorder and a medical condition was 1.37. The lowest hazard ratio was 0.82 for organic mental disorders and the broad category of cancer (95% confidence interval [CI], 0.80 to 0.84), and the highest was 3.62 for eating disorders and urogenital conditions (95% CI, 3.11 to 4.22). Several specific pairs showed a reduced risk (e.g., schizophrenia and musculoskeletal conditions). Risks varied according to the time since the diagnosis of a mental disorder. The absolute risk of a medical condition within 15 years after a mental disorder was diagnosed varied from 0.6% for a urogenital condition among persons with a developmental disorder to 54.1% for a circulatory disorder among those with an organic mental disorder.

**CONCLUSIONS**

Most mental disorders were associated with an increased risk of a subsequent medical condition; hazard ratios ranged from 0.82 to 3.62 and varied according to the time since the diagnosis of the mental disorder. (Funded by the Danish National Research Foundation and others; COMO-GMC ClinicalTrials.gov number, NCT03847753.)

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Address reprint requests to Dr. McGrath at the National Center for Register-based Research, School of Business and Social Sciences at Aarhus University, 8210 Aarhus V, Denmark, or at [j.mcgrath@uq.edu.au](mailto:j.mcgrath@uq.edu.au).

Drs. Prior and McGrath contributed equally to this article.

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## Anxiety and Depression Can Make You Sick

*Long-term associations between mental and physical health are examined in a prospective study.*

To address the relationship between health and affective symptoms (anxiety or depression), researchers analyzed data from a British prospective study of 3001 people followed repeatedly since birth in 1946. Follow-up beginning at age 53 involved an average of 14 years of complete data. Case-level symptoms (i.e., suggestive of a diagnosis) of anxiety or depression were defined as the highest 16th percentile of rating-scale scores, based on U.K. population estimates.

Risks for death were significantly elevated during follow-up among people with case-level symptoms. If symptoms were found once, risk was increased 76%; if found twice or 3 to 4 times, risks were increased 87% and 134%, respectively, although these last two associations were no longer significant after adjustment for variables including health indicators (e.g., cardiovascular conditions, smoking, diet, exercise). Such individuals were not more likely to die of suicide or accidents than medical illness. Affective symptoms beginning after age 53 were associated with greater risk for death but only during the following 4 years. Affective symptoms in adolescence were associated with heightened mortality risk only in adulthood.

### COMMENT

It remains unclear whether significant symptoms of anxiety or depression are markers of medical risk or have physiologic or behavioral-health consequences. In either case, clinicians should evaluate anxious and depressed patients carefully for medical comorbidity, especially if symptoms are chronic. As potentially fatal illnesses might develop within a few years of later-onset affective symptoms, treating such symptoms early and vigorously and delivering very close medical follow-up could reduce later morbidity and mortality. The same medical benefit might not accrue to treatment of early-onset affective symptoms, which convey continued risk even after they remit. — **Steven Dubovsky, MD**

Archer G et al. Association between lifetime affective symptoms and premature mortality. *JAMA Psychiatry* 2020 Apr 8; [e-pub]. (<https://doi.org/10.1001/jamapsychiatry.2020.0316>)

## Heightened Risks for Suicide in Patients with Neurological Disorders

*The risk is greatest in the initial months after diagnosis and in patients with severe low-frequency illnesses such as Huntington disease.*

Neurological disorders can be disabling and deadly and have been linked to suicide. These researchers used Danish national-registry retrospective data on 7,300,395 individuals to examine associations between neurologic illness and deaths by suicide between 1980 and 2016; 17% of people had neurologic illnesses.

In analyses controlling for demographics, physical comorbidities, prior mental illness, and self-harm history, people with neurologic illnesses were 1.8 times more likely to die by suicide than people without these illnesses. Risks were largest for amyotrophic lateral sclerosis and Huntington disease (incidence rate ratio [IRR] for each, 4.9). Other disorders with heightened risks included multiple sclerosis (IRR, 2.2), head injury (IRR, 1.7), epilepsy (IRR, 1.7), and stroke (IRR, 1.3). The risk was greatest in the first 3 months after diagnosis (IRR, 3.1); at  $\geq 10$  years, the IRR was 1.5. The risk was also elevated in patients with multiple neurological hospitalizations. Dementia was associated with an overall lower risk but with a raised risk in the first month of diagnosis (IRR, 3.0). More-prevalent disorders (head injury, stroke, epilepsy) accounted for the largest proportion of suicide deaths.

### COMMENT

Although cross-sectional data cannot confirm causality, these illnesses' devastating physical, emotional, and social effects, as well as direct neurobiological changes, could facilitate development of severe depressive reactions. Greater immediate effects suggest that with time, individuals adapt to the shock and disability of these illnesses, thereby reducing suicide risk. The most important clinical take-homes are that the period immediately after diagnosis poses greatest risk, even for disorders without heightened risk later on (i.e., dementia), and that clinicians should vigorously pursue aggressive rehabilitative treatments that can ameliorate the associated functional disabilities. — **Peter Roy-Byrne, MD**

Erlangsen A et al. Association between neurological disorders and death by suicide in Denmark. *JAMA* 2020 Feb 4; 323:444. (<https://doi.org/10.1001/jama.2019.21834>)

## Double Jeopardy: Youth with Chronic Physical Conditions Have Higher Mental Health Risk

*Activity limitations explained some but not all of the increased rate of chronic mental health problems.*

Children with chronic physical conditions (CPCs) such as asthma, migraines, and diabetes are known to be at higher risk for chronic mental health disorders. However, most prior studies were cross-sectional and thus unable to examine how mental health problems emerge over time or explain the mechanisms underlying this association.

To address these limitations, researchers analyzed longitudinal data from over 48,000 children and young adults aged 6–25 years participating in a nationally representative study. Participants had no mental health conditions at baseline and were followed for 2 years. Parents and adult children were sequentially interviewed about medical and mental health problems in the family.

Youth with CPCs had a 51% higher risk for developing any chronic mental health condition (11.5%) compared with youth without CPCs (7.1%). This risk was higher in older age groups (12–18 and 19–25 vs. 6–11 years). Fourteen percent of the risk for mental health problems was explained by activity limitations, such as difficulties participating in school or social events.

### COMMENT

Optimizing the management of chronic physical conditions such as asthma and migraines may help improve long-term mental health by allowing children to engage more in school, family, and recreational activities and social life. The fact that risk for mental health conditions rose in adolescence means that early childhood is an important stage for prevention interventions — specifically, addressing school absenteeism, promoting sports inclusion, and advising therapy for maladaptive parent-child interaction patterns.

— **Jenny Radesky, MD**

Adams JS et al. Mental illness among youth with chronic physical conditions. *Pediatrics* 2019 Jun 14; e20181819; [e-pub]. (<https://doi.org/10.1542/peds.2018-1819>)

## Adults with Cerebral Palsy Are at Higher Risk for Depression and Anxiety

*The elevated risk seems to be restricted to patients without intellectual disabilities.*

Although cerebral palsy (CP) is a condition with lifelong neuro-psychiatric and physical comorbidities, research on psychiatric disorders in this population focuses on childhood. These researchers used a U.K. primary care database to identify 1705 adults with a CP diagnosis (mean age, 33; women, 47%). During the 28-year follow-up, the investigators examined records for the diagnosis of a first event of an anxiety or depressive disorder.

Each case was matched to three controls on age, sex, and geographically determined socioeconomic status. The patient cohort was divided into those with and without intellectual disability (ID). In analyses adjusting for chronic conditions and frequency of medical visits, individuals with CP had a higher risk than controls for developing depressive (hazard ratio, 1.28) or anxiety disorders (HR, 1.38). However, the heightened risk occurred entirely in individuals who did not have ID (HRs: depression, 1.44; anxiety, 1.55).

### COMMENT

CP is a heterogeneous disorder, and patients may have multiple comorbidities (mobility, pain, fatigue). Thus, these findings of heightened risks for depression and anxiety are not surprising, and it is difficult to determine the etiology (e.g., coping with physical issues, social issues, or effects of brain functioning). It is interesting that this finding pertains to those without ID, but the study does not clarify whether the risk differs between those with severe IDs and those with milder ones (attention, learning disorders). Diagnosing anxiety and depression in people with severe ID might also be challenging. However, this study highlights our need to be aware that these disorders are common, and we mental health clinicians might receive referrals of patients with these problems.

— **Jonathan Silver, MD**

Smith KJ et al. Risk of depression and anxiety in adults with cerebral palsy. *JAMA Neurol* 2018 Dec 28; [e-pub]. (<http://dx.doi.org/10.1001/jamaneurol.2018.4147>)