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Chapter 39

Somatic diseases and suicidal behaviour

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Abstract

The association between somatic disorders and suicidal behaviour has been examined in many studies. Despite large variation in quality and study design, recent studies have improved our knowledge substantially, not only regarding the extent of risk but also factors influencing the risk. Most studies have been conducted in European countries, the U.S., Australia, Japan, and South Korea. A series of studies have examined suicide risk in relation to somatic disorders of older persons, while others addressed somatic disorders and attempted suicide in children and youth. Physical conditions may play an important role in medical settings, regardless of whether mental disorders are present or not, though especially when mental disorders are present. This chapter presents a review of present knowledge on suicide and suicidal behaviour in selected somatic disorders and pain syndromes, with a focus on studies from different parts of the world.

Keywords: suicide, somatic disorders, chronic disorders, cancer, pain, neurological disorders, heart disease, lung disorders, bowel disorders, methodology

Suicide, suicide attempts, and somatic disorders

In general, studies investigating the association between somatic disorders and suicide are qualitatively better than those on suicide attempts or ideation. The main reason for this is that suicide attempts are diagnosed and coded in different ways in different countries and areas, making the validity of the registration of suicide attempts poor. However, some large-scale

studies have strived to assess the risk factors for suicide attempts (Christiansen and Stenager 2012; Jeong *et al.* 2014; Fässberg *et al.* 2016). Similar challenges are faced when studying suicidal ideation.

Different types of studies have been conducted: first, on the frequency and diagnosis of somatic disorders in patients who have made suicide attempts (Nielsen *et al.* 1990; Dietzfelbinger *et al.* 1991; Öjehagen *et al.* 1991; Stenager *et al.* 1992b)); second, follow-up studies on patients with suicide attempts and somatic disorders, where the risk of repetition of suicide attempts and suicide has been estimated (Nielsen *et al.* 1990; DeLeo *et al.* 1999); and third, follow-up studies on the risk of suicide and suicide attempt in defined populations compared to a control group, usually large scale register studies (Hawton *et al.* 1988; Erlangsen *et al.* 2015; Christiansen and Stenager 2012; Jeong *et al.* 2014; Crump *et al.* 2014; Webb *et al.* 2012; Singhal *et al.* 2014; Kye and Park 2017). Systematic reviews have been conducted to estimate predictors for repetition of suicide attempts and suicide. These reviews have assessed the literature on adults as well as older populations (Beghi *et al.* 2013; Fässberg *et al.* 2016).

The mentioned studies have shown a prevalence of 27 – 50% of somatic disorders in persons with suicide attempts, differing between inpatients and outpatients, and depending on the definition of the somatic disorder. Painful disorders and disorders involved with an increased risk of depression are most common in suicide attempters. Furthermore, somatic disorders in older people play a significant role for risk of suicidal behaviour Stenager and Stenager 1997).

Causal mechanisms between somatic disorders and suicidal behaviour

Suicidal behaviour of a person can be viewed as a consequence of life becoming unbearable. Reasons for this are manifold, and may be of physical, psychological, and social character, or even a combination of these. The threshold for suicidal behaviour in individuals varies, and a single cause may just be a precipitating factor. The challenge is to predict when a given person reaches their threshold and, before that occurs, provide relevant help. In this context, knowledge about which disorders might entail increased suicidal risks could be helpful.

Having a somatic disorder is likely to lead to perceived problems of physical, psychological, and social character. The disorder may imply pains, functional disability, as well as distress about whether or not it is life-threatening.

Different causal mechanisms have been suggested to link somatic disorders with suicidal behaviour. Firstly, being diagnosed with a potential life-threatening disorder is distressing and stressful life events are linked to a higher risk of suicide. Examples of this are persons diagnosed with cancer, dementia, or HIV. Secondly, many somatic disorders are closely linked to psychiatric disorders, particularly depression; it has been shown that people are more likely to develop depression after onset of certain somatic disorders, hence, if the depression is not identified, this might in worst-case scenarios lead to suicide behaviour. Thirdly, having somatic disorders, for instance chronic disorders, might imply physical limitations and dependency on help from others. The acceptability of these circumstances might also lead to an increasing risk of suicide. Fourthly, pain has been suggested as a mechanism explaining suicidal behaviour. Fifthly, a new stream of research seems to suggest that a biological link between somatic disorders and suicidal behaviour based on neurological pathways may be possible.

The situation might be further complicated by simultaneously present, psychiatric disorders, which can impact social performance, loss of the capability to work, and need for support. The risk of suicidal behaviour may change during a disorder. There may be periods

during the course where the risk may be increased, for instance, before or after the diagnosis is made, or when the patient has had the disease for a long period of time. Age may also be a parameter of importance (Juurlink *et al.* 2004). Other factors influencing the risk of suicide could be depression, cognitive deficits, anxiety, and medically induced abuse of medication due to pains, psychosis, and organic mental disorders (e.g., vascular or Alzheimer's dementia). Attention should be given to psychosomatic disorders that have been increasingly recognized during the last decade.

Methodological aspects

In terms of level of evidence, substantial gains have been achieved since the first pioneering studies of physical disorders and suicide. Early studies tended to rely on reports from small clinical samples for calculating the standardized mortality ratio (SMR) by using the observed suicide rate in the study sample and a national suicide rate as a reference for the expected rate. Although this provided insights into suicide rates among persons with physical disorders, the findings could potentially be flawed due to selection bias, confounding factors, small sample sizes, and comparison groups.

Selection bias arises when findings stem from a subgroup (in this case, patients with a physical disorder) that might not be fully representative for all patients with this disorder; it is possible that financial factors determine which patients might attend the clinic, or that a study sample has an over-representation of well-functioning patients, while those who are suffering more severely, might have been less inclined to enroll in a clinical study.

Also, confounding factors might be present. An example of a confounding factor is age: a person's age affects the probability of having dementia; however, age also has an impact on the likelihood of dying by suicide, as suicide rates generally are higher among

older adults. If one should assess whether people with dementia have a higher suicide rate than people with no dementia, it would be important to compare them to a group of persons in the same age range as those exposed to dementia. Comparing the suicide rate of a sample of older adults with dementia to the rate of a younger sample with no dementia would not produce a correct estimate, as the comparison group would have an over-representation of younger persons who generally have a lower suicide rate. The same type of confounding could arise due to differences by gender, civil status, or socioeconomic status. It is, therefore, important to consider whether one has accounted potential confounding factors when interpreting findings from these types of studies.

Another limitation one should consider is the sample size. We have good statistical tools, such as confidence intervals, to inform us whether a finding may be considered as 'significant' (i.e., not likely to be due to random variation). Statistical tools help us determine whether the suicide rate of persons with dementia differs from the rate of those without dementia. On the other hand, if one finds there is no statistical difference, this cannot always be interpreted as a guarantee that the suicide rate of persons with dementia is the same as for those with none. A lack of difference, also called a negative finding, could be due to small sample sizes, for instance, small numbers of patients with rare diseases, such as Amyotrophic lateral sclerosis (ALS) and Huntington's disease. Many of the earlier, explorative studies assessing whether dementia or Huntington's disease are linked to a higher suicide rate, did not note any difference in the rates because they had a small sample of exposed. Still, this did not imply that there was no excess rate, but simply that the studied sample was not large enough to determine whether there was a difference. If one has basic rates for study samples, it is in principle possible to calculate the needed sample size for being able to assess whether there is a statistical difference (power calculation). Studies have addressed this limitation by

employing larger sample sizes, partially through meta-analysis where several samples are merged.

Lastly, some earlier studies have been based on convenience samples, where the comparison group might have been patients presenting with a different disorder, or people dying by other causes of death. Although findings might provide insights, it should be remembered that they do not give reference to a representative sample of the general population; hence, excess risks might not give a true picture of the actual risk of a patient group.

For the reasons mentioned above, it is relevant to assess the data source used in the reported studies. Studies based on clinical databases often benefit from detailed information on the studied disorders (e.g., scales and other measures of severity of the disorder). This also implies a higher validity of the diagnosis. They might, however, not be fully representative for all persons with the studied disorders; perhaps a severity threshold is introduced by only including patients seen at hospital while, for instance, some persons with dementia only are seen in primary care.

Studies from several countries have used administrative linkage data, which might include national hospital registers, such as the Scandinavian registers (Erlangsen *et al.* 2018). The advantage of these data can be national coverage, implying that they are fully representative for the entire population. In addition, this data source allows for follow-up patients over long-term, as well as being likely to cover a sufficiently large sample to also study rare disorders. Nevertheless, in contrast to the clinical samples, lack of detailed information might hamper the possibility to examine causal mechanisms. In other parts of the world, linkage data are increasingly being explored. Some cohort studies use register data covering a subgroup, such as the Veteran Health Systems databases (Huguet *et al.* 2014), which then are representative for persons who have been enlisted in the armed forces only.

Yet, other places complete hospital data registers, but a lack of national population register implies that persons with dementia have to be compared to persons with other types of disorders, hence, a select comparison group.

When studying somatic disorders, it is relevant to evaluate the selection criteria employed to determine whether persons have a disorder. For instance, in the case of dementia, patients captured in clinical databases are likely to be identified using a diagnostic screening tool, hence, implying a higher validity of the diagnosis. Nevertheless, the diagnostic tools for assessing for dementia or early stages of dementia, such as mild cognitive impairment, have improved radically over recent decades, which is likely to impact the diagnostic validity of the patient population identified. Other studies have used records of diagnoses recorded at hospital contact, typically registered using the International Statistical Classification of Diseases and Related Health Problems (ICD), available in different revisions. Yet, others were based on diagnosis given in general practitioners offices. Studies based on recorded diagnoses are likely to generate a large and representative data sample; however, the validity of the diagnosis might be lower than those seen in clinical data samples.

In the subsequent presentation of studies, limitations related to study designs and data sources were taken into account; there was also a strive to exert caution with interpretation of these studies where bias and confounders cannot be excluded.

Cancer

The diagnosis of cancer can be associated with crisis reaction, troublesome treatments, pains, bad prognosis, financial problems, and, as a possible consequence, depression. Although diagnostics and treatment have made substantial gains over recent years, many cancers are ultimately lethal. Thus, it is not surprising that a diagnosis of cancer is associated with an

increased risk of suicide. Numerous studies have dealt with the association of cancer and risk of suicide. They include autopsy studies and register-based studies in large populations, particularly from Scandinavia and the U.S. (Louhivouri and Hakama 1979; Fox *et al.* 1982; Allebeck *et al.* 1989; Levi *et al.* 1991; Storm *et al.* 1992, Yousaf *et al.* 2005). Studies from Japan demonstrated an increased SMR of suicide in cancer patients compared to the background population (Tanaka *et al.* 1999; Akechi *et al.* 2002). Newer, adjusted findings from Japan showed an excess rate ratio of 1.7 and 2.1 for suicide among men and women, respectively (Yamauchi *et al.* 2014). There are no major differences cross-nationally in the results. Few studies found an elevated risk of suicide in certain types of cancer.

A Swedish study found a 16-fold higher rate suicide in males with cancer during the first year after diagnosis (Allebeck *et al.* 1989). However, Norwegian, Danish, and Japanese studies have not been able to confirm this elevated risk during the first year after the diagnosis (Storm *et al.* 1992; Hem *et al.* 2004; Yousaf *et al.* 2005; Yamauchi *et al.* 2014). In a later study based on the Swedish population (Fang *et al.* 2018), the relative risk for suicide during the first week after diagnosis was 12.6 decreasing, to 3.1 after the first year.

Henson *et al.* (2019) used data from the National Cancer Registration and Analysis Service in England, on 4,722,099 patients with cancer, to calculate the suicide risk. The overall SMR for suicide was 1.2, with the highest risk for patients with mesothelioma, as well as cancer in the pancreas, esophagus, lungs, and stomach. The suicide risk was highest the first six months following cancer diagnosis.

Several reviews have been conducted in recent years, including data from Europe, the U.S., Japan, and Australia, where the consensus from these were that cancer patients have an increased suicide risk. The risk is highest in patients suffering from head and neck cancers, cancer in the digestive system, pancreas cancer, and prostate cancers. Furthermore, older men had the highest increase in risk (Spoletini *et al.* 2011; Robson *et al.* 2010). Klaassen *et*

al. (2018) reviewed the evidence regarding patients with prostate cancer and concluded that these patients had an increased risk for suicidal death, and an excess risk was noted among unmarried and older adults. Time since diagnosis was an important factor, since men were having higher risks of suicide also 15 years after diagnosis. As many as 60% of the men had experienced mental health distress. The study proposed implementing a newly developed screening algorithm for quality of health, depression, and suicidal ideation in patients suffering from prostate cancer. Osazuwa-Peters *et al.* (2018) examined the risk of suicide in a study of 151,567 survivors after head and neck cancers, and found that patients were almost twice as likely to die from suicide when compared to other cancer patients. The risk was found to be higher during more recent periods from 2010 – 2014, compared with 2000 – 2004. It is hypothesized, that the elevated risk in head and neck cancers might be explained through difficulties with vital functions, such as breathing, eating, and pain.

In general, the highest suicide rates were reported during the first three months following the diagnosis, and patients who died by suicide within one year after the diagnoses were found to have rapidly progressing cancers. The prognostic status of the cancer, the impact of recurrence and treatment, and comorbid psychiatric disorders and pain, are important factors in predicting suicide risk (Spoletine *et al.* 2011). Screening instruments have been proposed, albeit the predictive value seems to be poor.

Pain and suicide

Studies concerning the association between pain and suicide are challenged by considerable methodological problems, such as the definition of pain and the selection of a study group. A controlled study in England of 6,569 persons with pain found a five-fold increased risk of suicide, accidents, and violence. The study included persons with extensive pain, among

which many were cancer patients (Macfarlane *et al.* 2001). A British study of 1,665 suicide attempters showed that among 4% of cases, pain was considered as an important problem (Theodoulou *et al.* 2005). These patients differed from those in other studies in that they were older, had a higher suicidal intention score, and were rarely seen in a psychiatric setting.

In recent years, increasing attention has been dedicated to the diagnostics and treatment of chronic pain. Vaegter *et al.* (2019) found an increased suicide risk among 6,142 patients with chronic pain from a regional pain clinic in Denmark, where a SMR of 7.3 was noted in comparison to the general population. Stenager *et al.* (2014) examined suicide attempts in another sample from the pain clinic, and found a 3.7-fold higher rate, compared to the background population.

Based on the Australian National Survey of Mental Health and Wellbeing, Campbell *et al.* (2015) analyzed data of 8,841 people and found a two- to three- fold higher risk of suicidality (i.e., suicide ideation and suicide attempts), among persons acknowledging to have chronic pain, compared to people without, despite controlling for demographic, mental health, and substance use disorder.

Hassett *et al.* (2014) conducted a literature review regarding rates and risk factors for suicide in patients with chronic pain. In general, they noted an increased suicide risk across all studies. Larger studies, such as Kikuchi *et al.* (2009), based on 21,083 Japanese men, found that greater pain severity was significantly associated with death by suicide when controlling for a number of other risk factors. Ilgen *et al.* (2010) noted an elevated risk of suicide among 260,254 veterans, and furthermore, an association between severity of pain and suicide. In studies of specific pain conditions, such as fibromyalgia, an SMR of 10.5 and odds ratio (OR) of 3.3 for suicide has been reported (Dreyer *et al.* 2010; Wolfe *et al.* 2011).

In a systematic review of 32 studies (Spiegel *et al.* 2007), it was found that chronic abdominal pain is linked to an increased risk of suicidal behavior, independently of co-

morbid depression. Hassett *et al.* (2014) further identified the following pain-related risk factors for suicide: pain severity, type, the perception of disabilities, access to analgesics, poor sleep, and desire to escape from pain, avoidance, and problem-solving deficits. Another review (Newton-John 2014) noted other risk factors, such as mental illness in the family, history of suicide attempt, comorbidity of depression, ambiguous diagnosis, and medico-legal issues, related to the pain. In a narrative review, Fishbain *et al.* (2014) made the case that both acute and chronic pain are associated with an increased risk for suicidal behaviour.

In summary, pain conditions are found to be associated with an increased risk of suicidal behaviour also after adjustment for psychiatric disorders. Various pain-related risk factors seem to increase the risk. Clinicians caring for pain patients should be aware of this and could use relevant screening instruments.

Neurological disorders

Next to cancer, neurological disorders are the most thoroughly investigated disorders. This is obvious considering that many neurological disorders are linked to an increased risk of developing psychiatric disorders, such as depression. Some neurological disorders do not have well-defined diagnostic criteria, or remain to be assessed using good quality data. As a consequence, not all disorders have been subjected to analysis in well-designed studies. The majority of studies have been conducted in Europe, Australia, the U.S., and Japan. Across the different geographic areas, the results are consistent. The consensus across several studies is that awareness and careful treatment of depression in these patients might be one of the key measures for preventing suicide in these groups.

Multiple sclerosis

While many earlier studies were based on samples from clinical settings, hence introducing the possibility of selection bias, a stream of linkage data studies have now provided national suicide rates for people with multiple sclerosis (MS). Linking a clinical data base, the Danish Multiple Sclerosis Registry, with 10,174 patients with MS listed on the national register data, Brønnum-Hansen *et al.* (2005) found an SMR of 2.1 for dying by suicide. Earlier studies using Danish data noted slightly higher mortality ratios (Stenager *et al.* 1992b). Swedish researchers using general hospital register data to identify 12,834 patients with MS found an SMR of 2.3 for suicide (Frederikson *et al.* 2003).

With regard to sex, age, and time since diagnosis, analyses have revealed that both men and women with MS have excess suicide mortality, as well as most age groups and most follow-up periods (Frederikson *et al.* 2003; Brønnum-Hansen *et al.* 2005). No statistically significant differences between sexes, age groups, or follow-up time since diagnosis, have been noted; this is probably due to the fact that the two studies observed relatively few events of suicide—115 and 90 suicide deaths, respectively.

Clinical linkage data did not find significant associations to suicide attempt, which might be due to a small sample size (Stenager *et al.* 2011). About 29% of US veterans with MS confirmed to have had suicidal ideation, although the study's response rate of 44% limits the representativeness of these findings (Turner *et al.* 2006). A lower prevalence, 8.3%, was noted in a general MS patient sample with a comparable response rate (Viner *et al.* 2014). Taken together, these studies deliver evidence for the presence of suicidal ideation in persons with MS. Association studies have suggested that social isolation, depression severity, lower levels of task-oriented coping and self-efficacy, as well as bowel disability, are linked to suicidal ideation in this MS patient population (Turner *et al.* 2006; Feinstein *et al.* 2002).

In sum, it is likely that people with MS have a two-fold higher suicide rate than the general population; however, larger data samples and more rigorous analysis would be

recommended. Along those lines, a systematic review recommended attention and risk assessment of people with MS (Pompili *et al.* 2012).

Huntington's disease

Although earlier studies have linked Huntington's disease—or Huntington's chorea—to suicide (Schoenfeld *et al.* 1984; Farrer 1986), the body of evidence is limited by methodological restraints. Furthermore, the relatively low prevalence of Huntington's disease implies few case fatalities by suicide. Huntington's disease is an autosomal dominant disorder that can be diagnosed in healthy family members. A Canadian study (Almquist *et al.* 1999) examined 4,527 persons who had been genetically tested with the purpose of examining whether the test results made a difference in the number of persons who died by suicide, made suicide attempts, or were admitted to a psychiatric ward. The study concluded that the behaviour of the tested persons was not dependent on whether or not they tested positive on the diagnosis. Instead, the findings indicated that suicidal behaviour was dependent on whether the tested persons had previously been diagnosed with psychiatric disorders or were unemployed. Using the Huntington Study Group's database from the U.S., Paulsen *et al.* (2005) found that suicidal thoughts were more prevalent among persons who were being evaluated for having the disorder, rather than those where the disorder had been confirmed. Similarly, a Hungarian study noted that more suicides seemed to occur in the early stages of the disease compared to the later stages (Baliko *et al.* 2004).

Spinal cord lesions

Spinal cord lesions are often the result of accidents in young males, and may cause life-long dependence on a wheelchair. Although relatively few events of suicide (n=12) were observed,

Soden *et al.* (2000) noted a higher SMR for people with spinal cord lesions when compared to the general population and adjusting for age and gender, in a regional Australian study. Analysis of a local Norwegian sample also revealed excess suicide mortality among persons who had suffered spinal cord injury, albeit based on few events (Lidal *et al.* 2007).

Epilepsy

Epilepsy is one of the somatic disorders in which the association to suicide has been examined most thoroughly. This is exemplified by a systematic review, largely based on older studies, which noted a SMR of 3.25 (Bell *et al.* 2009).

Qualitatively better studies based on hospital linkage data from various countries have reported a 1.8 – 3.4 fold higher rate of suicide among persons diagnosed with epilepsy in adjusted analyses (Nilsson *et al.* 1997; Christensen *et al.* 2007; Singhall *et al.* 2014). However, data from primary care in the U.K. did not support a significant effect, but this might be related to a small sample size (Webb *et al.* 2012). Epilepsy is linked to mental disorders; people with epilepsy who are diagnosed with a mental disorder, particularly depression, are found to have a substantially higher risk of suicide (Webb *et al.* 2012). In fact, people with epilepsy who have been diagnosed with a mental disorder within the last year, have a greater than 24-fold higher rate of suicide than those with no epilepsy (Christensen *et al.* 2007). Across all age groups, elevated risks are noted when psychiatric comorbidity is present. More detailed studies have revealed that individuals with epilepsy have a higher risk of suicide, which cannot be explained solely through psychiatric disease or socio-demographic conditions. In fact, an approximately two-fold higher rate ratio of suicide was found in persons with epilepsy, irrespective of age group and psychiatric disorders (Christensen *et al.* 2007). Robust findings also reveal that older adults aged 65 and over, have

an approximately two-fold higher risk of suicide after being diagnosed with epilepsy within the last three years (Erlangsen *et al.* 2015). People with epilepsy who have received surgery, such as temporal lobe excision, might have a particularly high risk of suicide (Bell *et al.* 2009). Furthermore, it is possible that people with epilepsy are more inclined to use poisoning as the method of suicide when compared to people without epilepsy (Tian *et al.* 2016).

With respect to self-harm, the first year of being diagnosed with epilepsy seems to be linked to an almost four-fold increase in risk of deliberate self-harm, which decreases to 2.6 in subsequent years (Singhall *et al.* 2014). Interestingly, midlife seems to be a more critical period: as ages from 25 – 64 have been linked to a rate ratio of 3.7, while those with epilepsy who were either younger (10 – 24 years) or older (65+ years) had a rate ratio of 1.9 (Singhall *et al.* 2014). Initial analysis on rates of suicide attempts in young Danes showed a 1.8-fold higher rate (Christiansen *et al.* 2012); however, when adjusting for own and parents' psychiatric comorbidity and other covariates, findings were no longer significantly different from those in the Danish background population without epilepsy. The relevance of psychiatric comorbidity is emphasized in a Russian study by Kalinin and Polianski (2003) on risk factors for suicidal behaviour, who found that patients with epilepsy and additional organic affective disorders, personality changes, and cognitive deterioration, had substantially increased risks.

There is, thus, substantial documentation for the need to be attentive towards psychiatric comorbidity in people with epilepsy.

Migraine

A systematic review concluded that migraines seem to be linked to suicidal behaviour (Novic *et al.* 2016); although support for an association to suicide deaths is limited. An American study found that veterans diagnosed with migraines had 1.3-fold higher risks of suicide than those who used the Veteran Affairs healthcare system for other disorders (Ilgen *et al.* 2013). Using a large population-based database from England, patients diagnosed with migraines upon hospital contact were reported to have a 1.3-fold higher suicide rate than patients with a variety of other disorders in an adjusted analysis (Singhal *et al.* 2014). In a representative sample, respondents with self-reported migraines were found to have a 4-fold higher risk of suicide attempts than a control group not suffering from migraines or severe headaches, also when adjusting for the presence of mental disorders (Breslau *et al.* 2012).

Brain injuries

Numerous studies have examined traumatic brain injury and outcomes of adverse mental health, such as psychiatric illness, suicidal ideation, suicide attempts and completed suicide (Oquendo *et al.* 2004). Linkage of hospital data has allowed for studies where information for exposed and comparisons stem from the same data source, hence, minimizing bias. Teasdale and Engberg (2001a) noted a significantly higher suicide frequency among Danish people diagnosed with traumatic brain injury. Another study brought further evidence on this association, by showing a 2.4-fold higher suicide rate among those with severe traumatic brain injury (Madsen *et al.* 2018). This study also noted a dose-response relationship in terms of severity, days in treatment, and number of hospital contacts, as well as an elevated risk shortly after the incident, while adjusting for relevant covariates.

Parkinson's disease

Much of the early evidence regarding suicidality in persons with Parkinson's disease (PD) has been based on single observations (i.e., casuistic), due to the rareness of observations. An early Danish study noted a reduced suicide rate among patients with PD; however, as noted by the authors, this could be due to the small sample size (Stenager *et al.* 1994). In an American study, the percentage of suicide deaths among 144,364 deaths of persons with PD, was found to be substantially lower than in a general population sample (Myslobodsky *et al.* 2001). This study, thus, supports the results previously found. Nevertheless, a recent South Korean study found a two-fold higher rate of suicide in a clinical sample of patients with PD when compared to the general population, while adjusting for age and gender differences (Lee *et al.* 2016). Comparable findings have been reported from Serbia, although the analysis was based on two suicide deaths (Kostic *et al.* 2010).

The South Korean study, mentioned above, reported that presence of a psychiatric disorder in people with PD predicted a higher risk of suicide, and that patients where motor symptoms in upper extremities were noted, seemingly had higher risks of suicide than those where motor symptoms were only present in lower extremities. Finnish findings suggest that a preceding suicide attempt in persons with PD might be predictive of later suicidal behaviour (Mainio *et al.* 2009).

Stroke

Danish regional register-based studies have suggested an excess of suicide deaths among persons who had suffered a stroke as measured by SMR (Stenager *et al.* 1998). Later, national findings noted a 1.8-fold higher rate of suicide among patients with stroke (Teasdale and Engberg 2001b). In addition, it was noted that the rate was higher among those with a short hospital stay (i.e., hospitalized for less than two weeks as compared to over three

months). The SMR for suicide was 2.8 among patients below 50 years of age, while those aged 60 – 69 had an SMR of 1.6. Seemingly, the risk is higher during the first five years after a stroke. In support of this, a regional linkage study from Canada noted an odds ratio of 2.4 for suicide among older adults aged 66 years or older recorded with stroke by their physician, in comparison to those without stroke, in an analysis adjusted for demographics and comorbidity (Voaklander *et al.* 2008). Findings from Finland furthermore suggest that not only post-stroke depression, but also relapses of recurrent depression might be an element in the causal mechanism of suicidal behaviour among patients with stroke (Forsstrom *et al.* 2010).

Intellectual disabilities

A study using Swedish data of 987,308 males, showed that those who scored low on intelligence in psychological tests during military service enrollments, had two- to three-fold higher risks of suicide compared to males with high intelligence scores (Gunnell *et al.* 2005). On the other hand, a Finnish population-based study found that the suicide risk of females with intellectual disabilities was comparable to the general Finnish population, while males with intellectual disabilities were found to have a lower risk (Patja *et al.* 2001). Interestingly, persons dying by suicide typically only had mild intellectual disabilities and a psychiatric disorder. Low rates of deliberate self-harm have been reported for people with Down syndrome (Singhall *et al.* 2014). The studies reported here did not adjust for relevant covariates, such as psychiatric comorbidity and severity of disease, which might explain the difference in their findings. Still, caregivers do state that people with intellectual disabilities have suicidal ideation (Wark *et al.* 2018).

Other neurological disorders

Only one study reporting on motor neuron disease has been identified. Bak *et al.* (1994) did not find any elevated risk of suicide among persons with a motor neuron disease; however, only 116 patients were included in the study. Another study noted an almost six-fold higher suicide rate among ALS patients, but the level of evidence was restricted by a small sample size, while not adjusting for important risk factors, such as co-morbidity and mental disorders (Fang *et al.* 2008).

Heart disorders

A number of studies have tried to assess whether patients suffering from hearts diseases have an increased suicide risk. However, the literature is inconsistent, both with respect to the diagnosis (e.g., myocardial infarction, atrial fibrillation, heart failure), as well as with respect to adjusting for covariates. Many studies have defined ischemic heart disease very broadly, making comparisons challenging. However, a few studies from Taiwan and Denmark have examined suicide risks in large population-based studies using relevant diagnostic measures.

Liu *et al.* (2016) compared 41,050 persons who died by suicides and 164,200 controls. The diagnosis studied was acute coronary syndrome, a syndrome associated with an increased risk of depression. While adjusting for relevant confounders, a significantly higher OR of 1.2 was found. The risk was highest during the initial six months after the diagnosis, with an OR of 3.1, and remained elevated for at least four years.

Larsen *et al.* (2010) conducted a population-based case-control study with data linkage of several Danish registers. Here, 19,857 persons who died by suicide were compared to 190,058 controls. Results showed that patients with myocardial infarction had a higher suicide rate than controls, which was highest in the first month after discharge. For patients

with myocardial infarction but no psychiatric illness, the adjusted rate ratio was 3.3, while patients with a psychiatric history had a rate ratio of 64.1. The risk remained high for at least five years after diagnosis. Another Danish population-based study (Qin *et al.* 2013) found an increased suicide risk among all circulatory diseases, including cerebrovascular diseases. Erlangsen *et al.* (2015) noted an increased suicide rate among older adults suffering from heart diseases in another Danish population-based study. However, there remains a need for large scale studies on suicide risk related to specific, well-defined heart diseases, and it would be relevant to take into account whether patients are suffering from both heart diseases and psychiatric disorders.

Earlier studies of cardiac diseases have debated whether cholesterol-reducing medication might be linked to an increased risk of suicide and other types of violent deaths. An American study (Neaton *et al.* 1992) of 350000 males followed for 12 years, found a 1.6-fold higher risk of suicide in males with a low cholesterol count. In a meta-analysis by Jacobs *et al.* (1992), a similar conclusion was reached: people with low cholesterol levels had an increased risk of dying from reasons other than heart disorders, including suicide. However, as other studies did not find support for an association between low cholesterol levels and mortality by other disorders other than heart diseases (La Rosa *et al.* 1995), more studies are needed to reach a reliable conclusion.

Lung Disorders

Asthma and Chronic Obstructive Pulmonary Disorder (COPD)

A number of American studies have estimated the risk of suicide in patients with asthma. One community-based study assessed suicidal thoughts in 1,285 young American patients between 9 – 17 years of age. The patients with asthma had a three-fold higher risk of having

suicidal thoughts than controls (Goodwin and Marusic 2004); the risk remained significant also after controlling for psychiatric comorbidity. Another U.S.-based study, which also adjusted for psychiatric comorbidity, confirmed the association between asthma and suicidal thoughts and suicide attempts (Goodwin and Eaton 2005). Hence, the studies indicate that asthma may increase the risk for suicidal behaviour. Christiansen and Stenager (2012) found in their study of 403,431 children and youth that among the identified risk factors for 3,465 participants who had attempted suicide, was treatment for asthma, with a relative risk for suicide attempts of 1.6 for males and 1.7 for females when compared to a matched control group. However, the risk did not remain statistically significant after controlling for psychiatric comorbidity. A study from Taiwan (Kuo *et al.* 2010) showed that among 162,766 school students aged 11 – 16 years enrolled in the study between 1995 and 1996, those with asthma had a twice as high incidence rate of suicide as those without. However, the study did not adjust for confounders, such as mental disorders. In essence, all studies noted a slightly increased risk for suicidal behaviour among patients suffering from asthma, but the level of risk varies and not all studies adjusted for psychiatric comorbidity. The comprehensive review by Goodwin (2012) confirmed this.

A few studies have assessed risk for suicidal behaviour in patients with chronic obstructive pulmonary disorder (COPD), as reviewed and discussed by Hegerl and Mergl (2014). Webb *et al.* (2012) based their studies on patients from The General Practice Research Database in England in all of approximately 4.7 million patients. They found that coronary heart disease, stroke, COPD, and osteoporosis were linked with elevated suicide risk. However, when adjusting for depression, this association was no longer significant. A national study from Sweden followed 7,140,589 people over eight years with respect to suicide mortality and noted a slightly higher suicide rate for those with COPD and asthma (Crump *et al.* 2014). A Danish linkage study of older adults aged 65 years or older found 1.8-

fold and 2.0 higher rate of suicide among older adult men and women, respectively, who were recently diagnosed with COPD, when compared to those not. Goodwin (2011) examined the risk of suicidal ideation and attempts in an American, community-based study. He found a statistically significant risk of suicidal ideation and attempt in COPD patients, compared to patients without COPD. The elevated risk remained significant for suicide attempts after adjusting for demographic and psychiatric covariates.

Bowel disorders

Disorders, such as Crohn's disease and ulcerative colitis, often affect young people and are associated with pain, surgical procedures, and discomfort. Crohn's disease is also associated with an up to a three-fold higher risk of depression (Fuller-Thomson and Sulman 2006). An Italian study (Palli *et al.* 1998) examined the risk of suicide in patients with Crohn's disease and ulcerative colitis and found a non-significant tendency. A Danish study (Winther *et al.* 2003), however, did find an increased risk of suicide in females with ulcerative colitis. A more recent Danish study, based on 27,053 suicide deaths and 551,060 controls, found an increased suicide risk with an OR of 1.6 and 1.9 for Crohn's disease and ulcerative colitis, respectively (Gradus *et al.* 2010).

An American study (Marchioni Beery *et al.* 2018) compared suicidal ideation and self-inflicted injury/suicide in patients with inflammatory bowel disorder to the general population, and found that suicidal behaviour was more common among those with Crohn's disease when compared to ulcerative colitis, but, in comparison to the American population, patients with inflammatory bowel disorder were less likely to have suicidal behaviour. The results from this study stand in contrast to the solid studies noting an increased suicide risk, but it could be due to differences in the outcomes studied.

Liver transplantations

Liver transplantation implies substantial strain on the patients; in addition, the procedure is expensive and the number of available organs is limited. Candidates for treatment often display symptoms of depression, anxiety, cognitive disorders, and fear of the future.

Furthermore, it is an on-going ethical debate whether patients with acute liver failure (ALF) caused by acetaminophen or paracetamol induced hepatotoxicity, should be offered liver transplantation. Karvellas *et al.* (2010) compared 36 acetaminophen ALF patients with 34 controls, and found no difference in rejection of the graft survival between the two groups. A large study including all liver transplantations to ALF patients in Europe over 20 years (Germani *et al.* 2012) considered suicide and non-adherence to immunosuppressive medication as outcomes after AFL, and found an increased risk of suicide and non-adherence among patients who received transplantation after a paracetamol-induced AFL. The authors recommended psychological/psychiatric and social support to transplanted patients after paracetamol overdose, to lessen graft loss and death.

Kidney disorders

The risk of suicide in patients with kidney disorders, and especially in patients with renal failure and kidney transplants, has been studied. Already in 1980, Haenel *et al.* (1980) concluded that patients with renal failure have an increased risk of suicide. Later studies have confirmed these finding regarding the association between renal failure, transplantations, and risk of suicidal behaviour. Pompili *et al.* (2013) published a comprehensive review based on studies from 1970 – 2011. The review concluded that suicide and suicide attempts were more frequent in patients who undergo dialysis compared to the general population. Furthermore,

there is a higher prevalence of psychiatric disorders in dialysis patients, particularly anxiety and depression, which clinicians ought to be aware of.

Liu *et al.* (2017) followed a total of 55,642 patients in the Taiwan National Health Insurance Research Database, who died from suicide between 2000 and 2012. They found an OR of 3.4 for dying by suicide among end stage renal disease patients on hemodialysis, when adjusting for sociodemographic characteristics, as well as physical and psychiatric comorbidities. Those patients who underwent dialysis within zero to three months had a 20-fold higher risk of dying by suicide. Ghanizadeh *et al.* (2009) conducted a study of 71 children and adolescents in Iran, finding a higher prevalence of depressive disorders and symptoms after renal transplantation. As many as 40% of this group had recurrent thoughts of death and acknowledged suicidal ideation. A Korean study (Jhee *et al.* 2017) looked at depression and suicidal ideation in a large cohort covering 44,938 participants. They concluded that risk of depression and suicidal ideation were closely related to renal dysfunction and increased in a dose-response relation to renal dysfunction. Awareness of psychiatric disorders and suicidal risk are recommended in renal disease patients.

Diabetes mellitus

A number of earlier studies have examined the risk of suicide in diabetes mellitus (DM), but only few, were of satisfactory methodological quality. In a Danish study by Kyvik *et al.* (1994) of 1,682 male patients with DM treated with insulin, it was found that 12 had died by suicide. Furthermore, males in the age interval of 20 – 24 years of age, had a SMR of 3.0. The study concluded, together with other studies, that the number of suicides in this patient population may be underestimated as a large number of patients died for unknown reasons. Three recent systematic reviews (Pompili *et al.* 2014; Conti *et al.* 2017; Sarkar and Balhara

2018) all concluded that DM patients have an increased risk of suicidal ideation, suicide attempt, and suicide. However, the level of methodological quality in the analyses can be improved, for instance by adjusting for psychiatric comorbidity. The reported, unadjusted SMR for suicide range between 1.0 and 2.0. Given that depression is common in DM patients, it is important to consider this risk factor. In this patient population, it is also important to be aware of the toxicity of the medications used for treatment, especially insulin. Myers and Trivedi (2017) presented new recommendations for screening of depression and suicidal ideation in DM patients enabling and evaluate the higher risk and access to potentially lethal medications.

Rheumatic diseases

Risk of suicidal behaviour in patients with rheumatic diseases, primarily arthritis, have been evaluated in several earlier studies. A forensic study of 1000 suicides from England and Wales, did reveal an association between arthritis and suicide (Whitlock 1985). However, the authors compared the frequency of suicides in patients with arthritis with the number of patients with arthritis in the U.K., which might not provide an unbiased result. On the other hand, a Finnish study (Timonen *et al.* 2003) found an association between depression, suicide attempts, and suicide in patients with rheumatoid arthritis, and thus reaffirmed the result of the forensic study. In a review by Calandra *et al.* (2018), an increased risk for suicidal behaviour was found for fibromyalgia and arthritis. In systemic lupus erythematosus (SLE), the size of the risk was not listed appropriately in the studies. Fibromyalgia patients had an SMR for suicidal ideation of 2.3 in one study, and two studies reported a SMR for suicide ranging from 3.1 to 10.9. An increased risk of suicidal ideation and suicide attempts was found for arthritis. However, an increased risk of suicide was not noted. Also, a higher level

of methodological rigorousness is warranted, as studies have yet to differentiate between rheumatoid arthritis and osteoarthritis.

Particularly, comorbid depression played an important role for suicidal behaviour in patients with fibromyalgia and arthritis. Also, neuropsychiatric involvement in SLE was of significance in these patient groups. The findings suggested that psychosocial factors, as well as treatment with corticosteroids, might act as mediators for suicidality, and consequently rheumatologists should be aware of depression and risk factors for suicidality in patients suffering from rheumatic diseases.

Tinnitus

Tinnitus involves an elevated risk of depression. An American study reported a life-time prevalence of depression of 62% among persons with tinnitus, in comparison to 21% in a control group (Harrop-Griffiths *et al.* 1987). A study from the U.K. (Lewis *et al.* 1994) on 28 patients with tinnitus who died by suicide, revealed that they were predominantly males, elderly, and socially isolated. Most had psychiatric disorders (97%), mainly depression (70%). As many as 40% of the suicides took place within one year of onset of tinnitus, and 50% within two years, indicating that tinnitus was an important risk factor. It was estimated that the suicide frequency was increased compared to the background population. However, SMR was not calculated. A newer study from South Korea based on 17,446 Korean individuals, noted a significantly higher risk of suicidal ideation and suicide attempts when comparing persons with tinnitus to a control group in adjusted analyses (Seo *et al.* 2016).

HIV and AIDS

Almost since the beginning of the AIDS epidemic, it has been discussed whether AIDS might be associated with an increased risk of suicide. An early American study (Marzuk *et al.* 1988) noted a 36-fold higher risk of suicide in males with AIDS in comparison to controls. Since then, treatment has improved considerably and social stigmatization has decreased. This could partially explain the slightly lower risk of suicide reported in a study of newer data from the U.S. (Coté *et al.* 1992), where an excess risk of 7.4 was found when compared to controls. With support of an association, a recent Danish study noted a 2.3-fold higher suicide rate among persons diagnosed with HIV or AIDS when compared to the general population, in an adjusted analysis (Lund-Sørensen 2006). It has been suggested that HIV infections are linked to other risk factors for suicide, such as psychiatric disorders, substance misuse, and other social factors (Catalan *et al.* 2011). These were sufficient reasons for a recent systematic review to maintain the recommendation that suicide risk screening ought to be a standard procedure when treating people for HIV (Catalan *et al.* 2011).

Although a substantial body of evidence links HIV/AIDS to suicide deaths, a literature review (Komiti *et al.* 2001) of studies from the U.S., Europe, and Australia, concluded that the risk of suicidal behaviour in this patient population is of the same order as in other chronic somatic disorders. Still, the distress of not knowing might lead to suicidal behaviour, as shown in the American study (Perry *et al.* 1990) on HIV, where both patients who tested zero-positive and zero-negative had suicidal thoughts during the period of awaiting the test results; these thoughts were resolved in the following two months.

Conclusion

In this chapter, a number of somatic disorders associated with an increased risk of suicidal behaviour has been reviewed. Suicide can be considered as the final indicator of a

life with insurmountable physical, psychological, and social problems. There are fairly robust findings linking a number of neurological disorders, cancer, and pain to suicide, while the body of evidence is less strong for heart, lung, and rheumatologic disorders, as well as other somatic disorders. However, methodological quality in studies of heart and lung disorders has improved in recent years. One would think that the generally accepted perception that somatic disease is a result of biological, psychological, and social processes, would be reflected in studies on suicidal behaviour. However, this is not the case. Suicidal behaviour is often considered solely as a psychiatric problem, which is a far too a simplistic view (Frederiksen *et al.* 2005). In line with this, many studies that adjust for psychiatric disorders still find an increased risk of suicidal behaviour in patients with somatic disorders. Signs of depression, anxiety, hopelessness, crisis reaction, pain, previous suicide attempts, suicidal thoughts, complicated social conditions (family situation, work, finance, leisure time), and distress over waiting time for somatic diagnosis, can be signs of increased risk in somatic patients. Prophylactic measures are obviously important; identification and treatment of psychiatric disorders (e.g., depression and anxiety disorders) are key measures, as is adequate pain treatment. Actions to ease the social consequences of disease for the patient are important, including involvement of family members, social workers, psychologists, and others. Furthermore, it is important that staff in somatic wards are trained in discussing issues pertaining to mental health and suicidal ideation with their patients; clinicians and nurses should dare to ask about suicidal thoughts and know how to handle these adequately. Staff in wards treating patients with high suicidal risk (e.g., patients with cancer, neurological disorders, or chronic pain), should be trained in identifying and handling psychiatric disorders and suicidal risk.

A final point to be made is that, although the studies were conducted on different continents and in different populations, they show comparable results. While the majority of

studies were conducted in Western Europe, the U.S., and Australia, South Eastern countries, such as South Korea and Taiwan, have also contributed substantially to generate evidence on this association. The differences in risk of suicidal behaviour in relation to somatic disorders were relatively small and, although cultural differences might play a role, it is clear that certain somatic disorders are linked to elevated risks of suicidal behaviour also on a global level.

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