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Depression and Anxiety Symptoms in UK Thalidomide Survivors: A Brief Survey

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Abstract: Between 1958 and 1961, the drug Thalidomide was prescribed in the UK as a treatment for morning sickness. It caused severe birth defects. Thalidomide survivors are now experiencing a range of secondary health problems, including depression and anxiety. Internationally, it is estimated that 40% to 50% of Thalidomide survivors have recently experienced common mental health problems. The aim of this study was to gather information about the pattern of symptoms of depression and anxiety amongst UK Thalidomide survivors. A cross-sectional postal survey of 182 UK Thalidomide survivors, which used Patient Health Questionnaire (PHQ-9) and General Anxiety Disorder Scale (GAD-7) to measure self-reported depression and anxiety, was conducted. Data were first analysed using descriptive statistics. A point-biserial correlation was used to examine whether being unable to work was associated with higher depression and anxiety scores. Prevalence of all levels of depression and anxiety was higher amongst the Thalidomide survivors than the general UK population but broadly similar to other groups of adults with disabling conditions. Being unable to work was associated with higher depression and anxiety scores. More research is needed to understand the relationship between early acquired physical disability and depression, in particular the implications, over the life course, of secondary health problems and changing social roles.

Keywords: thalidomide; early acquired physical disability; mental health; depression; life course

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1. Introduction

Between 1958 and 1961, the drug Thalidomide was prescribed in the UK as a supposedly safe treatment for morning sickness. However, when taken in the first trimester, it caused severe birth defects, which together are referred to as Thalidomide Embryopathy (TE). Dysmelia (missing, short and/or deformed limbs) and associated damage to joints are the most common features of TE, but the drug also caused a wide variety of other birth defects, including damage to eyes, ears and internal organs, and facial disfigurement [1]. It is estimated that between 10,000 and 25,000 Thalidomide babies were born worldwide [2,3] (Lenz 1988, Johnson et al. 2018). In the UK, the figure was around 2000. As many as three quarters died soon after birth or in early childhood, but the UK Thalidomide survivors who reached adulthood are expected to have a near normal life expectancy. Across the world, around 5000 Thalidomide survivors are still living with the consequences of the drug, and while TE is regarded as a non-progressive condition, it is not static. Thalidomide survivors are now experiencing a range of Thalidomide-related health problems which are being layered onto, and interacting with, their original impairments, causing further loss of function [4]. This loss of function and the consequences it has for independence have profound implications for Thalidomide survivors' mental well-being [5]. The international literature [4] suggests that common mental health problems are the second most frequently reported health issue for Thalidomide survivors, after musculoskeletal problems.

Although estimates vary, based on the nature of the studies and measures used, the evidence from Germany [6], Brazil [7] and Japan [8] suggests that between 40% and 50% of Thalidomide survivors have recently experienced mental health problems. In 2015, a Health

and Well-being survey of UK Thalidomide survivors found that almost half the respondents reported they were currently or had recently experienced depression and/or anxiety [5], but little is known about the severity of depression and anxiety being experienced.

In the wider disability literature, the link between disability and depression is well established. There is also substantial evidence about the possible reasons for this association, notably that people with disabilities are likely to experience the negative effects of: lower levels of social integration; activity limitations, barriers to employment; financial difficulties; and both structural and interpersonal discrimination [9–12]. However, what is less well understood is the cumulative impact of these disadvantages, especially for those with early acquired impairments, and how this impact might change over the life course [13,14]. Thalidomide survivors are a relatively small group, and the historical and social context of their lives is unique. However, because they are a cohort who are ageing together, understanding their experience may contribute to our broader understanding of disability and depression over the life course.

The aim of this study was to gather information about the pattern of symptoms of depression and generalised anxiety amongst UK Thalidomide survivors, and where possible, make comparisons with both the general population and other groups with early acquired disabilities. It was part of a larger body of work which subsequently developed and tested a peer-led intervention for Thalidomide survivors experiencing low mood.

2. Materials and Methods

The study design was a cross-sectional postal survey of all UK Thalidomide survivors. It received ethical approval from the Department of Health Sciences Research Governance Committee at the University of York, on 2 July 2018. The survey questionnaire was developed in partnership with Thalidomide survivors, and staff and trustees from the UK Thalidomide Trust. The questionnaire had five sections, three of which are relevant to this paper (self-reported health status and open-ended questions related to well-being were not included in the analysis):

Section 1: Biographical Information-Three questions about gender, home circumstances, and work situation. Information about age was not sought because the great majority of Thalidomide survivors were aged between 56 and 59 at the time of the survey.

Section 2: Depression-Self-reported depression severity was measured using the Patient Health Questionnaire (PHQ-9) [15]. PHQ-9 explores how the person has felt in the last two weeks and consists of nine questions with four possible responses to each question. The responses are scored from 0 to 3, giving an overall score range of 0–27. There are five scoring levels indicative of severity of depression symptoms: 0 to 4 = no depression; 5 to 9 = mild depression; 10–14 = moderate depression; 15 to 19 = moderately severe depression; and 20 to 27 = severe depression.

Section 3: Generalised Anxiety-Self-reported anxiety was measured using the General Anxiety Disorder Scale (GAD-7) [16]. This measure explores how the person has felt in the last two weeks and consists of seven questions with the four possible responses scored from 0 to 3, giving an overall score range of 0–21. There are four scoring levels that classify severity of anxiety symptoms reported: 0 to 4 = no anxiety; 5 to 9 = mild anxiety; 10 to 14 = moderate anxiety; and 15 to 21 = severe anxiety.

The survey questionnaire (together with a letter from the Trust, an information sheet and a freepost reply envelope), was sent by the Thalidomide Trust to 413 UK Thalidomide survivors. Those who: lacked capacity; were currently being treated for severe mental illness; or lived outside the UK were excluded (n = 53). The survey was distributed by post in early September 2018. A reminder email was sent in early October. It was also publicised on the Thalidomide Trust website and via social media. When the survey closed in mid-October, 182 completed questionnaires had been received, giving a response rate of 44%.

The survey data were entered into an Excel spreadsheet. Each response was given an identification number. The anonymised data were then transferred to SPSS (IBM, Armonk, NY, USA) for analysis. The data were first analysed using descriptive statistics, and the

results for the three validated questionnaires were then compared, where possible, with the general population or other groups with early acquired disabilities. Previous research [5] had suggested that being unable to work was having a negative impact on the mental well-being of UK Thalidomide survivors. A binary variable (unable to work/working or chosen not to work) was created. We examined (using a point-biserial correlation) whether being unable to work was associated with higher depression (PHQ-9) and anxiety (GAD-7) scores.

3. Results

Of the 182 survey respondents, 92 (50.5%) were women, 80 (44.5%) were men and 10 (5%) did not give their gender. The UK population of thalidomide survivors is equally split between women and men, and so there was a slight bias towards women in the survey sample. In terms of living circumstance, around two-thirds lived with their partner/spouse or their partner/spouse and other family members (117/65.4%), and almost a quarter (42/23.5%) lived alone. Three respondents did not provide data. For work situation, just over a third (61/34.2%) said they were unable to work because of their disability or health problems, and nearly a third said they had chosen not to work in order to preserve their health/functioning (40/22.4%) or for family/personal reasons (12/6.7%). Twenty-two (12.3%) were working full time, 18 (10%) were working part time and six (3.4%) said they were not working but would like to. Nineteen respondents (10.9%) recorded their work situation as "Other", which, from the descriptions provided, included those who were on sick leave, or had retired early or had family caring responsibilities. Four respondents did not provide data. For the further statistical analysis, these work categories were recoded as 0 = unable to work (61/34.1%) and 1 = all other categories (118/65.9%).

3.1. Depression

Analysis of the PHQ-9 scores showed that 75 respondents (43.4%) had no symptoms of depression. Just over a quarter (27.2%, $n = 47$) had symptoms of mild depression. Almost a third reported symptoms of moderate to very severe depression: 23 respondents (13.3%) moderate depression; 16 (9.2%) severe depression; and 12 (6.9%) very severe depression (see Table 1). On average, male respondents had higher PHQ-9 scores (more depression symptoms; $M = 8.08$, $SD = 7.54$) than female respondents ($M = 6.64$, $SD = 6.06$) but this difference was not statistically significant, $F\ (1, 165) = 1.84$, $p = 0.177$ (ten participants who did not give their gender were excluded). The overall mean PHQ-9 score for the sample was 7.32, $SD = 6.85$. Note that due to missing data, PHQ-9 scores were not available for nine participants, who were not included in these analyses. Further analysis also showed that being unable to work was associated with higher depression (PHQ-9) scores ($r_{pb} = -0.463$, $p = 0.000$) (nine respondents had missing data and were excluded).

Although PHQ-9 has been widely used in both clinical and population-based settings, an eight-item version without the final question about self-harm (PHQ-8) has since been developed for use in large epidemiological studies [17] where mental health follow-up is not feasible. A major study by Arias de la Torre et al. (2021) [18] used PHQ-8 to estimate the prevalence and age pattern of depression in the UK population. They found that in the 45-to-59 age group: 12% had mild depressive symptoms; 5.1% had moderate depressive symptoms; and 5.3% had severe depressive symptoms. They also found that depressive symptoms were higher amongst women than men. This suggests that the prevalence of all levels of self-reported depression is likely to be much higher amongst the Thalidomide survivors than the general UK population, but unlike the general population, there was no significant difference between men and women.

It was difficult to find comparative data on PHQ-9 (or PHQ-8) scores for other groups with early acquired disability. However, a German study [19] of depression in the general population, which also used PHQ-9, found a strong positive association between depression and disability. Jensen et al. (2014) [20] used PHQ-9 to measure depression amongst people with Spinal Cord Injury (SCI), Multiple Sclerosis (MS) and Muscular Dystrophy (MD). Whilst this study included adults of all ages, the mean age for their participants was

52.6, i.e., relatively close to the age group for UK Thalidomide survivors (i.e., between 56 and 59 years at the time of the survey). The pattern of PHQ-9 scores in the study is broadly similar to that of Thalidomide survivors, although the proportion of Thalidomide survivors in the "Moderately Severe" and "Severe" groups is almost double (9% compared to 16.1%). Table 1 shows the results for both this study and Jensen et al. (2014).

Table 1. PHQ-9 results for Thalidomide survivors and comparator group.

Level of Depression	Thalidomide Survivors		* Combined % for SCI, MS and MD
	Number	Percentage	
None (0–4)	75	43.4%	44%
Mild (5–9)	47	27.2%	32%
Moderate (10–14)	23	13.3%	15%
Moderately Severe (15–19)	16	9.2%	6%
Severe (20–27)	12	6.9%	3%
Total	173	100%	
Missing	9		

* From Jensen et al. 2014: SCI = Spinal Cord Injury; MS = Multiple Sclerosis; MD = Muscular Dystrophy.

3.2. Generalised Anxiety

Analysis of the GAD-7 scores found that three quarters of respondents had no symptoms of anxiety (n = 91/51.7%) or only mild symptoms (n = 41/23.3%). The remaining quarter had symptoms of moderate to severe anxiety: 26 respondents (14.8%) moderate anxiety; and 18 (10.2%) had severe anxiety (see Table 2). This compares to estimates of 5% and 1%, respectively, for the general UK population [21]. On average, male respondents had higher GAD-7 scores (more anxiety symptoms; M = 6.66, SD = 6.63) than female respondents (M = 5.35, SD = 4.92), but this difference was not statistically significant, F (1, 165) = 2.11, p = 0.148 (excluding the ten participants who did not give their gender). The overall mean GAD-7 score for the sample was 5.95, SD = 5.87. Note that, due to missing data, GAD-7 scores were not available for six participants who were not included in this analysis. Further analysis also showed that being unable to work was associated with higher anxiety (GAD-7) scores (r_{pb} = −0.348/p = 0.000) (nine respondents had missing data and were excluded). Sixty-five participants (38.70%) had no symptoms of either depression or anxiety; 21 had only depressive symptoms and 9 had only anxiety symptoms. The majority of those reporting symptoms were therefore reporting symptoms of both depression and anxiety.

Table 2. GAD-7 results for Thalidomide survivors.

Level of Anxiety	Number	Percentage
None (0–4)	91	51.7%
Mild (5–9)	41	23.3%
Moderate (10–14)	26	14.8%
Severe (15–21)	18	10.2%
Total	176	100%
Missing	6	

4. Discussion

This is the first study of the prevalence and severity of depression and anxiety amongst UK Thalidomide survivors. The findings suggest that the prevalence of all levels of self-reported depression and generalised anxiety are higher amongst the Thalidomide survivors than the general UK population, with more than half reporting symptoms of depression and just under half reporting symptoms of generalised anxiety. However, the prevalence of symptoms of depression is broadly similar to other groups of adults with disabling conditions. Although there is substantial evidence that people with disabilities

are more likely to report depressive symptoms, the relationship between physical disability and depression is complex. Much of the literature focusses on older adults, and our understanding of this relationship in working-age adults, especially those with early acquired impairments, is still developing [9,12,13]. Kemp and Mosqueda (2004) [22] made the point that whilst rates of depression are higher amongst people with disabilities, impairment alone does not cause depression. Rather, it is the social and psychological consequences of impairment that lead to higher levels of depressive symptoms.

A few studies have examined functional impairment (as measured by Activities of Daily Living/Instrumental Activities of Daily Living (ADL/IADL) and prevalence of depression. A UK study by Meltzer et al. (2012) [23] found a higher prevalence of depression and mixed depression/anxiety amongst people with disabilities compared to people who do not have impairments with disabling consequences, a finding supported by a more recent study of middle-aged and older Chinese adults [24]. The literature on ageing with TE also suggests that restricted physical function (especially decline in physical function) is one of the factors highlighted as contributing to higher levels of common mental health problems amongst Thalidomide survivors [5,25,26]. Social isolation, pain, unemployment, and the need for care and personal assistance are also highlighted, although clearly these factors are likely to be linked to and influenced by physical function. Our study also found that being unable to work was associated with higher depression and anxiety scores, which appears to reinforce the association between being unable to work and symptoms of depression reported in the wider literature on TE. However, there could be several underlying and interrelated causes for this. Not working may lead to some Thalidomide survivors feeling more socially isolated, and the loss of an important social role may have psychological consequences. However, those who are unable to work may also have more severe secondary health problems, which may in turn be associated with higher levels of pain.

There are differing views about whether people with early acquired impairments have higher subjective well-being than those disabled later in life [9,27–30]. However, there is now growing evidence of the cumulative impact of disability on mental health [10,12,13]. Stress perspectives [31,32] suggest that people with disabilities are likely to experience more negative life events throughout their lives (e.g., discrimination, health problems, and financial pressures). Although, there is no evidence that people with disabilities are inherently less able to cope with these events than their peers without disabling conditions, coping occurs in a social context and is conditioned by what people have to cope with [22]. People with disabilities often experience a wider range of negative life events or stressors [33], and these stressors tend to be more complex. In addition, the stress they experience is often chronic and cumulative in nature, and may be magnified by factors related to their disabling condition, such as interpersonal discrimination, and feelings of exclusion and difference [12,13,32].

This certainly accords with the experiences of the Thalidomide survivors. As they grow older, they are being exposed to a greater range of stressors, notably increasing impairment, secondary health problems, changing social roles such as giving up paid work, and the need for more assistance [5,25,26], which can have profound implications for mental health. Healthcare practitioners need to understand these implications for all people with early acquired disability. It should not be assumed that they get used to living with disability and are in some way more able to cope with additional health problems [29]. Nor should it be assumed that depression is an inevitable consequence of disability: it can be prevented, and when it does occur, treatment should be offered.

More research is needed to understand the complex relationship between early acquired physical disability and depression. However, we also need to establish a better understanding of the mental health consequences of living a long life with disability, so that disabled people can be supported to maintain their mental well-being.

Limitations

Respondents may not be fully representative of all UK Thalidomide survivors in terms of severity of impairment and socioeconomic characteristics; slightly more women than men responded to the survey and this could have had an impact on the results; those with more vulnerable mental health may have been less likely to respond to the survey and this could have affected the results; comparisons with the general population/other groups with disabling conditions are limited.

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Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Institutional Review Board (or Ethics Committee) of the Department of Health Sciences at the University of York (LIfTS Study—approved 2 July 2018).

Informed Consent Statement: Informed consent was obtained from all subjects involved in this study.

Data Availability Statement: The survey data used to support the findings of this study may be released upon request.

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