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**'The Legacy of Thalidomide' - a multidisciplinary Meeting
held at the University of York, UK on September 30, 2016.**

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3 **Brief Report**
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6 **'The Legacy of Thalidomide' - a multidisciplinary Meeting held at the University of
7 York, UK on September 30, 2016.**
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60Keywords: Thalidomide, Thalidomide Survivors, Thalidomide Society, Thalidomide Trust,
Wellcome Library, Global Health History, aging with early onset disability, drug safety

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3 Abstract
45 Background
67 Between 1957-1962 thalidomide was used as a non-addictive, non-barbiturate sedative that
8 also was successful in relieving the symptoms of morning sickness in early pregnancy.
9 Infamously, thousands of babies were subsequently born with severe birth defects. The drug
10 is used again, today, to successfully treat leprosy, and tragically, there is a new generation
11 of thalidomide damaged children in Brazil. While the outward damage in babies has been
12 documented, the effects of the damage upon the survivors as they grow up, the lifestyle
13 changes and adaptations required to be made, as well as studies into ageing in survivors,
14 has received little attention and remains understudied.
1516 Methods/Results
1718 A unique multidisciplinary meeting was organised at the University of York bringing together
19 thalidomide survivors, clinicians, scientists, historians and social scientists to discuss the
20 past, the current and the future implications of thalidomide.
2122 Conclusions
2324 There is still much to learn from thalidomide, from its complex history and ongoing impact on
25 peoples' lives today, to understanding its mechanism/s to aid future drug safety, to help
26 identify new drugs retaining clinical benefit without the risk of causing embryopathy. For
27 thalidomide survivors, the original impairments caused by the drug are compounded by the
28 consequences of a lifetime of living with a rare disability, and early on-set age related health
29 problems. This has profound implications for their quality of life and need for health and
30 social care services. It is vital that these issues are addressed in research, and in clinical
31 practice if thalidomide survivors are to 'age well'.
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5 Background6
7 Landmark papers in The Lancet by Dr William McBride (McBride, 1961) and Dr Widikund
8 Lenz (Lenz, 1962) first drew the medical world's attention to Thalidomide and the extensive
9 damage the drug caused to babies when their mother took it to combat morning sickness in
10 early pregnancy. In the immediate aftermath, much was written about the health of babies
11 affected, the teratogenic effects of the drug and the scientific and legal implications of the
12 'Thalidomide disaster' (Smithells and Newman, 1992). Given the drug is now used around
13 the world again to successfully treat conditions like leprosy in Brazil, in 2014 a World Health
14 Organisation sponsored meeting of experts (World Health Organisation, 2014; www.who-umc.org/graphics/28280.pdf) reexamined the diagnostic criteria of Thalidomide embryopathy
15 and the mechanisms of causation (Vargesson, 2015). This was in response to a new
16 generation of thalidomide damaged children being seen in Brazil (Schuler-Facini et al., 2007;
17 Vianna et al., 2011; Vargesson, 2013). Yet, the effects of the damage upon the survivors as
18 they grow up, has only recently started to be studied. It is really in the past decade, as
19 Thalidomide survivors reached their 50's, there has been renewed interest in their health
20 and in particular the effects of ageing with Thalidomide embryopathy. In November 2015, a
21 symposium organised by the University of Tokyo focused on clinicians conducting research
22 into ageing and early onset age-related effects in people with Thalidomide embryopathy
23 (Honoshita, 2015).
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27 However, the issues, both practical and clinical, affecting the day-to-day life of Thalidomide
28 survivors have rarely been discussed. In addition an understanding of the long-term
29 consequences of thalidomide embryopathy in survivors remains understudied. A recent
30 meeting in September 2016 organised by Ms Elizabeth Newbronner and Prof Karl Atkin
31 (Department of Health Sciences, University of York) and held at the University of York aimed
32 to start a dialogue to begin to address these issues. The Meeting was a truly interdisciplinary
33 gathering exploring the broader legacy of Thalidomide. It brought together Thalidomide
34 survivors, historians, scientists, clinicians and social scientists to explore what lessons can
35 be learnt from the history and use of the drug, its impact and ongoing consequences today;
36 and how this knowledge can benefit Thalidomide survivors and others with rare impairments.
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40 Legacy of Thalidomide Meeting
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4243 The meeting had three sessions each highlighting different perspectives: historical,
44 contemporary and personal. Professor Karl Atkin, Head of the Department of Health
45 Sciences at the University of York, opened the day. He remarked on the importance of
46 understanding the life course when making sense of long-term conditions and in particular,
47 how ageing with a disability creates specific disadvantages which need to be addressed.
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4950 The historical perspectives session began with a joint presentation by Dr Ruth Blue,
51 (Secretary of the Thalidomide Society and Curator at the Wellcome Library) and Mr Brian
52 Payne (Trustee of the Thalidomide Society; <http://www.thalidomidesociety.org/>). In their talk -
53 *The thalidomide story: archives and voices* - they outlined the history of the Thalidomide
54 Society and gave an overview of the practical work they are doing to conserve the history
55 and advise researchers and the media. They also highlighted the wealth of Thalidomide
56 related reports, papers, photographs and films, held by the Wellcome Library
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(<http://wellcomelibrary.org/>). The archive also holds oral history recordings from Thalidomide survivors and will soon hold recordings of parents who took the drug.

Dr Julie Parle, (Honorary Associate Professor in History, School of Social Sciences, University of KwaZulu-Natal, South Africa) a UK-born Thalidomide Survivor, gave a fascinating presentation on the research she and other historians have been doing on the 'hidden histories' of thalidomide's distribution, impact and use in African countries since the 1960s (Klausen and Parle, 2015). Her talk showed that Thalidomide has many 'shadow' histories around the world, even where it has not been proven to have directly affected mothers and babies, and how some Thalidomide survivors are themselves now piecing these histories together, bit by bit. She argued that more archives need to be opened to researchers in pursuit of such histories.

The session concluded with a presentation about *Historic photographs for engagement and outreach: experiences from the Global Health Histories project* by Dr Alex Medcalf (Outreach Historian. Centre for Global Health Histories, Department of History, University of York; www.york.ac.uk/history/global-health-histories/). This project involves using visual images to tell a historical story. He highlighted some of the challenges and complexities they have faced in the project, in particular, the ethics of displaying difficult and sensitive material, and the importance of using the images to assist the argument or provoke additional questions.

The contemporary perspective session was opened by Dr Neil Vargesson, (Senior Lecturer, School of Medicine, Medical Sciences and Nutrition, University of Aberdeen). In his presentation -*Thalidomide: mechanisms of action and current challenges* – he gave an overview of current opinion on the drug's mechanisms, in embryos and in adults (Vargesson, 2015). The drugs action on blood vessel formation, its ability to induce cell death and interact with *Cereblon* are widely accepted as mechanisms of the drug's action. Indeed, he described how the drug's actions on blood vessels can result in a range of limb damage (Vargesson, 2009; Vargesson, 2015; Vargesson and Hootnick, In Press). He also described the advances his team has made in finding a 'safe' form of the drug, retaining the clinical benefits but without the side-effect of embryonic damage (Beedie et al., 2016; Beedie et al. In Press). This is extremely relevant today as sadly new generations of Thalidomide children have been born in recent decades in Brazil as the original drug is used to treat a form of Leprosy (Schuler-Faccini et al., 2007; Vargesson, 2013; Vianna et al., 2011).

The contemporary health of Thalidomide survivors in Sweden was discussed by Dr Shadi Ghassemi Jahani (Consultant Orthopaedic Surgeon, Institute of Clinical Sciences, University of Gothenburg, Sweden). Dr Ghassemi Jahani has been researching the orthopaedic problems experienced by Thalidomide survivors in Sweden as they age (Ghassami Jahani et al., 2014). She set out the findings from her work on osteoarthritis and cervical spine deterioration (Ghassami Jahani et al., 2016) and then went on to discuss her recent work on Health related quality of life. Her research showed that Thalidomide survivors have significantly lower physical health related quality of life compared with the general population.

Ms Liz Newbronner (PhD student, Department of Health Sciences, University of York) then described her research on the contemporary health of Thalidomide survivors in the UK. Despite the drug being distributed in 48 countries, little research into the health of

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3 Thalidomide survivors as they age has been undertaken and the research that has been
4 carried out is limited to just seven countries – Australia (Jankelowitz et al., 2013), Canada
5 (Vermette and Benegabi, 2013), Germany (Peters et al., 2015), Ireland (O'Carroll et al.,
6 2011), Japan (Shiga et al., 2015), Sweden (Ghassami Jahani et al., 2016) and the UK
7 (Nicotra et al., 2016). Findings from a new national health and wellbeing survey of UK
8 Thalidomide survivors (Newbronner and Baxter, 2016), undertaken for the Thalidomide Trust
9 (<http://www.thalidomidetrust.org/>) were discussed. The data shows that the health of
10 Thalidomide survivors is declining more rapidly than that of their peers in the general
11 population. Whilst this experience is similar in many ways to other people with early onset
12 disability, there are some distinctive aspects and pertinent wider lessons for health and care
13 services. In particular, the complex nature of Thalidomide damage and the implications of
14 comorbidities, both of which call for a strongly collaborative approach between clinicians and
15 Thalidomide survivors.
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19 In the final session of the day, three UK Thalidomide survivors gave their personal
20 reflections on living and ageing with Thalidomide-induced damage. They highlighted the
21 legacy of learning for Thalidomide survivors across the world, other people with rare
22 impairments (especially limb difference), and the clinicians and services that support them.
23 Geoff Adams-Spink (Deputy Chair, European Dysmelia Reference Information Centre;
24 <http://www.dysnet.org/>), discussed the power of networking between Thalidomide survivors
25 and others with limb difference. He emphasised the scope to use networking to address
26 contemporary issues such as the need for peer support, the development of 'workarounds'
27 to support everyday tasks, and improved access to specialist health services. Mr Rowland
28 Bareham (Chairman, Thalidomide Trust National Advisory Council) focused on the
29 experiences of Thalidomide survivors with hearing damage. Around a third of Thalidomide
30 survivors have total or partial hearing loss and this 'hidden' group of survivors often
31 experience higher levels of poorer mental wellbeing. The day was closed by Dr Craig
32 Millward (Member, Thalidomide Trust National Advisory Council) who spoke movingly about
33 finding out as a young adult that his disabilities had been caused by Thalidomide, and how
34 health problems in middle age had lead him into greater involvement with the Thalidomide
35 community.
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38 Conclusions

39 The meeting showed that there is still much to learn from Thalidomide, both from its complex
40 history and its impact on peoples' lives today. For Thalidomide survivors, the original
41 impairments caused by the drug are being compounded by the consequences of a lifetime of
42 living with a rare disability, and early on-set age related health problems. Their health and
43 functioning is changing, and this has profound implications for their quality of life and need
44 for health and social care services. Clinicians and healthcare services often fail to
45 understand the complex nature of Thalidomide damage, nor do they always recognise the
46 self-management knowledge Thalidomide survivors have. It is vital that both these issues
47 are addressed in research, and in clinical practice if Thalidomide survivors are to 'age well'.
48 Furthermore, the experience of Thalidomide survivors provides lessons for supporting other
49 people with rare impairments. In particular, there is a need for a flexible response which
50 recognises a person's active engagement with their condition and is sensitive to the
51 consequences of the life course. Finally, the meeting was an important reminder of the
52 continued need for research into drug safety and for pharmacovigilance.
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Conflict of Interest Statement

The authors have no conflict of interest to declare.

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For Peer Review

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