

Hinoshita : OK, everybody. Now it's time 2:40 PM. Then let's start the next session of this symposium.

©**Dr. Dee Morrison and Ms. Elizabeth Newbronner**

“**The Thalidomide Trust activities and its research in thalidomiders in UK**”

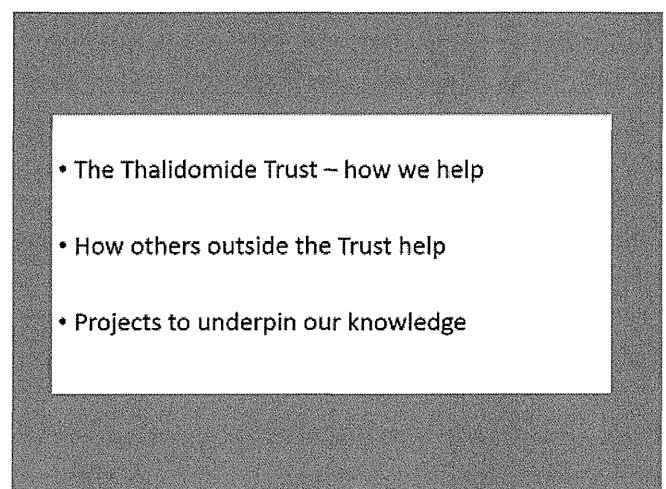
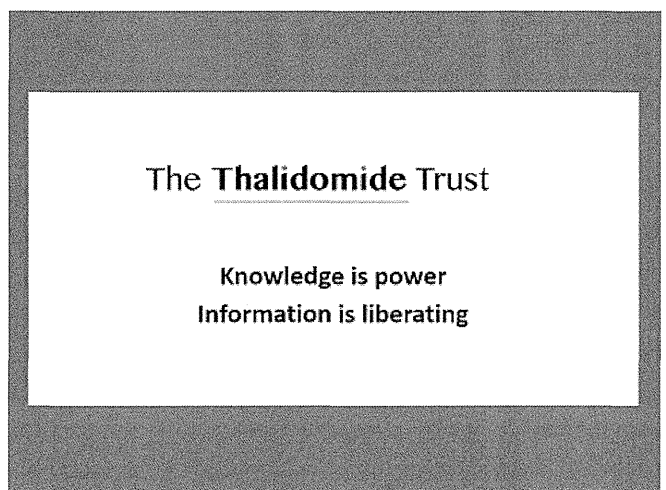
Hinoshita : As for the next presentation, here are two guest presenters. One of them is Dr. Dee Morrison over there. I should introduce her to you. She graduated from Liverpool University of medical school in 1986. Basically she has been working as partner in general practice at Walnut Tree health center in Milton Keynes for about 20 years. She began a medical adviser to the thalidomide trust since 2012. Since then she has vigorously been working as a medical adviser, tapering her work volume in general practice. I saw her at the Thalidomide Trust in last October. She accepted us warmly and gave us a ride on the way to and from the station in a new gorgeous car, BMW. I still imagine that she and her family might have greatly been attracted by German products, maybe just like thalidomide. Then, Dr. Morrison, please.

Morrison : Thank you. Knowledge is power. Information is liberating. Thank you, Dr. Hinoshita for the introduction. As you have said I am a General practitioner having been a partner in a busy training practice for over 20 years. I also have 6 years experience of helping managers understand the clinical aspects of or our work to help change the way referrals to specialists are managed. But for the last 3.5 years I have been working part time as Medical Adviser to the Thalidomide Trust for 3 days a week and now have just a small GP commitment. I am being helped today in my talk by Liz Newbronner from Firefly research and we have split the talk in two sections with myself talking for the first 30 minutes explaining;

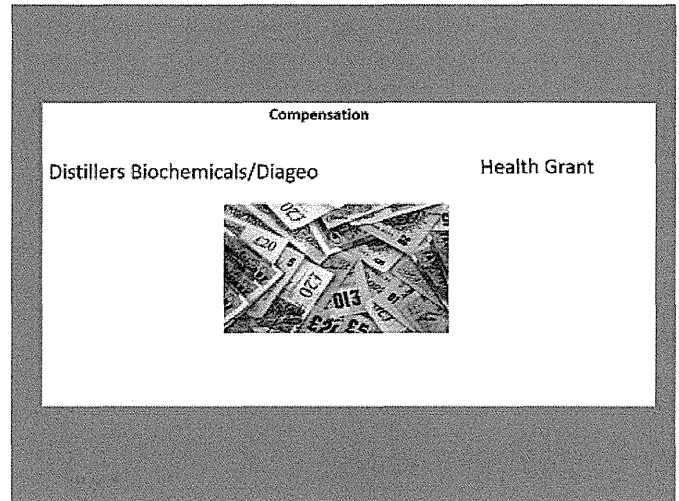
- The Thalidomide trust , what it is and how we help beneficiaries;
- How others outside the Trust help our beneficiaries and 2 case examples;
- 2 large research projects which have helped underpin our knowledge.

Then I am going to hand you over to Liz for the last 15 minutes to look at one further research project in more detail. I suggest we take Q&A at the end.

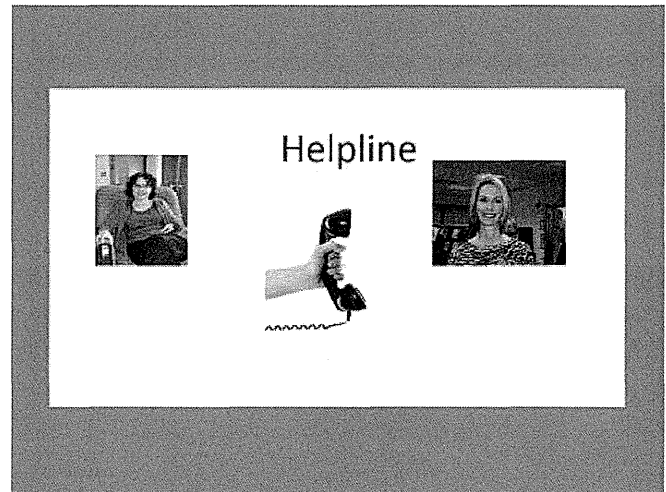
However, please let me know if you have any translation issues as I go along.



If I turn first to the Trust, I wanted to explain what we are here for, what we can help with and who else can help. The Thalidomide Trust's main role is to look after and distribute the compensation fund set up for those affected with thalidomide embryopathy arising from thalidomide manufactured and distributed in the UK by Distillers now Diageo. Depending on their level of damage every individual receives an award. Since 2010, they have also been awarded an individual amount from the UK government called the Health Grant. This is guaranteed for the next seven years. I mention money because it is important. It has a direct correlation with the individual's lifestyle and in turn their health. Also the Trust has had to undertake research to help lobby for increments in the award, the initial amount and its' continuance, as well as the obvious need to research to develop our knowledge of the medical issues. So to summarize, the Trust's main role is the investment and annual distribution of the compensation fund.



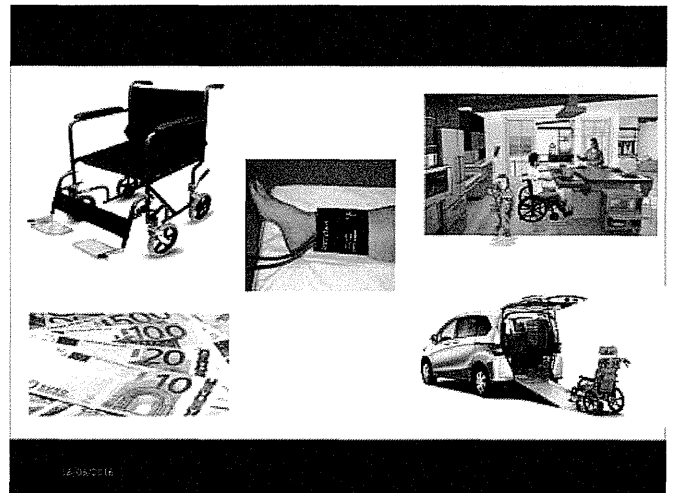
So how do we help individuals? Well, for past 10 years, the Trust has operated a telephone helpline to support beneficiaries, more recently this has included email exchange. This is mainly answered by Ann Horten, who has an occupational therapist background but is also affected by thalidomide herself. She has upper limb damage. For the last three and half years I've helped as a GP. We have recently appointed a social worker as we perceive an increasing need for state benefits as individuals lose their independence as they age and need more help with state benefits. Alongside the helpline we are also able to visit and assess individuals in their



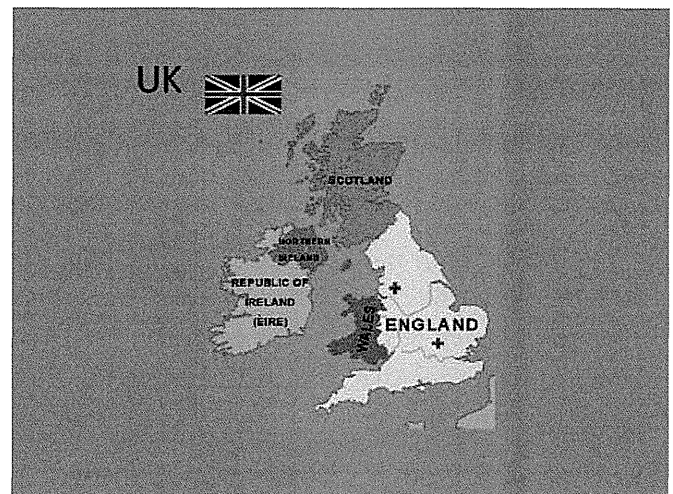

own home. The wider team within the Trust helps with this particularly the overall Trust director and also the finance director. We have a pool of beneficiaries who provide much needed peer to peer support for individuals. We have an active NAC made up from beneficiaries who have been elected for a fixed term to help. We have annual meeting for the deaf community who also have a private Facebook page. We hold talks annually at the NAC meeting. This year, for example, we had a psychologist affected by thalidomide himself from Australia speaking about managing chronic pain. Last year we had a talk on cereblon and causation, a talk about the Blood pressure project and also Dr. Cowan, a neuro-orthopedic doctor talking. So we do regularly try to keep everyone u p dated about the issues we can help with. We also send out a newsletter. This is how we help.

So what issues do we help with? We can help with wheelchair purchase, gadgets and gizmos - I think some might call this aides, dressing sticks etc. Kitchen adaptations and home adaptations. Anne might visit the individual, or take them to see the home of another beneficiary who has had their home adapted.

So it's very hands on. She is also fully knowledgeable about cars. She has visited the garages where they do the adaptations, and she will help with individual car enquiries. We also can help with car tax though we are stopping this. As many are claiming state benefits, we can also help with the claims for this. It is a very important area. Emily, who is a social worker and new to the Trust, will be helping more with this side. We also help with finding people to help care for them and personal assistants.



We have undertaken leaflets to help with the measurement of blood pressure for those who need to take it in the leg and for those who cannot have a blood pressure taken at all. We emphasize making sure that the right size of cuff is used and that the limb with the cuff is at the same level as the heart. We are open to any suggestions to improve them. We have given the leaflets to EDRIC who have adapted them for their website and we have had enquiries from Australia and Canada and shared them with them as well. We have also a telephone counsellor, again affected by thalidomide herself, who provides private counselling by phone. This service this has been independently assessed and found to be a worthwhile service to offer.

Thalidomide damage is not unique
 International reputation
 Expert congenital deformity – custom make joint
 Complex surgery specialists
 Good bedside manners
 Seen others affected by thalidomide

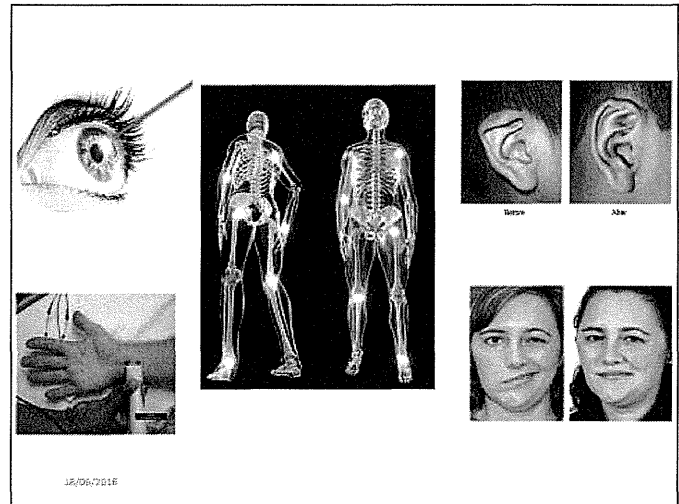
Role of the Thalidomide Trust

“A quick expert opinion and treatment options from a specialist familiar with thalidomide damage”

Before I move on to other medical issues we help, I wanted to mention very quickly the style of help within the Trust. Individuals can be fiercely independent, they can resist help and up to now some have not even considered themselves to be disabled despite severe limb reduction. Some have a fear of medical professionals due to difficult childhood experiences from having blood taken etc. and some do not wish to take medication because of how their damage arose. They often value advice from others affected by thalidomide and peer to peer support is very important to them. Anne, our OT, over time has developed

a way of working with them. If you remember she is affected by thalidomide herself, so is our telephone counsellor and so are our volunteer visitors. If you wish to learn more about this we have written articles for Pain News.

So we move now to my role and how I help. I get involved when an individual wishes to understand more about the cause of their symptoms and in particular is needing help with investigations or an opinion from a specialist. This involves liaising with the individual and their GP, to find the best opinion possible. It's



very much dependent on how far the individual will travel. Our beneficiaries are spread throughout the UK and some now live across the world. We do not rely on a single center and have many hospitals which help. However we mainly liaise with the Royal National Orthopaedic Hospital (RNOH) just north of London but it has no hand specialists. So we also work with Wrightington Hospital in the Northwest of England which has all orthopedic specialties apart from spinal surgery.

When we are choosing specialists we take into consideration;

- no thalidomide damage is unique – there are other groups with similar damage
- we usually choose experts with an international reputation in their field i.e they receive referrals from across the world.
- Particularly for limb damage they are often experts in congenital deformity with the ability to custom make a joint replacement. They are able to put a replacement joint in and out and this is called a revision specialist because of the relative young age we are dealing with.
- They are complex surgery specialists.
- They all have good bedside manners - we take the feedback from beneficiaries. This is very important because of peer to peer support.
- They have seen others affected by thalidomide and can discuss lifestyle management and the pros and cons of surgery. This is very important for individuals who are using their bodies to compensate for a short reach.

Hence, the Trusts role is to facilitate a quick expert opinion with options for treatment from a specialist familiar with thalidomide damage.

We also have a neuro orthopedic doctor working with us -Dr. Cowan from the RNOH- I mentioned before North of London. He is looking at non-surgical issues. He specializes in complex rehabilitation. He looks after other groups with conditions such as post-polio patients and joint hypermobility and other complex conditions.

So how do these experts help?

Many of our individuals have physiotherapy, massage, acupuncture locally to where they live and use their own Health Grant to pay for regular sessions. Currently Dr. Cowan at the RNOH helps individuals via their GP find therapists. However, if they need inpatient rehabilitation he can also arrange this at the RNOH.

We have helped a few individuals with laser eye surgery because they cannot manage with short arms

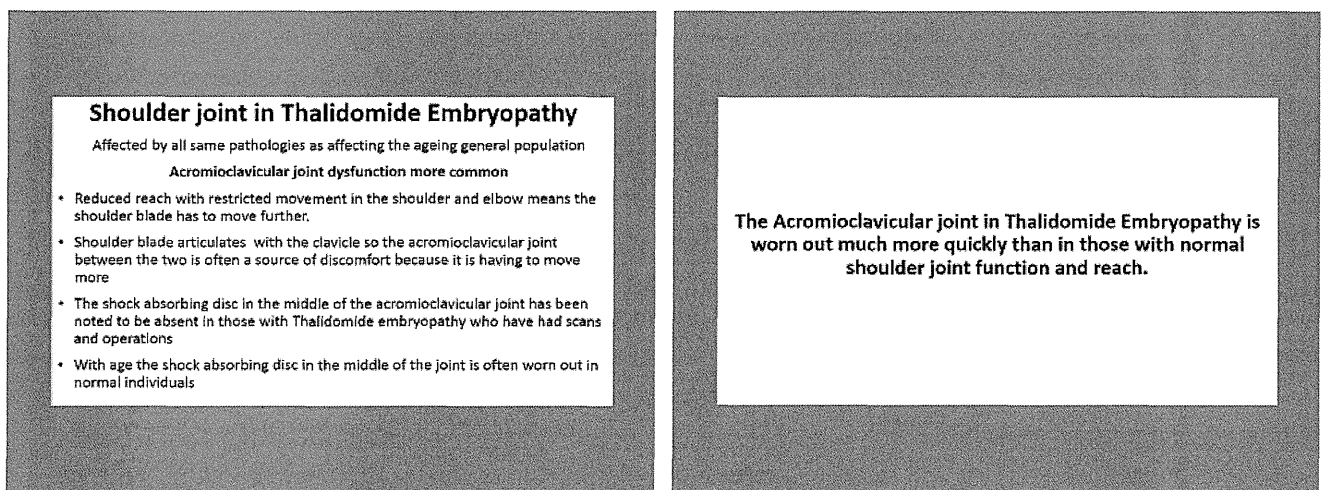
to put glasses on and off. We have had a few enquiries about ear reconstruction. Many of them had failed ear reconstruction as children. But now there are new techniques around. We have had one or two enquiries about facial reanimation surgery where they graft new muscle and nerve onto the face. I'm not quite sure how much we should be advertising these cosmetic techniques.

If I move now onto orthopedic issues, for hand issues we refer to Professional Trail at Wrightington Hospital. He is a wrist replacement specialist and an upper limb surgeon. He is able to help diagnose the hand pain. We also have a hand specialist in London. Regarding elbows we refer again to Professor Trail working at Wrightington but more so to Mr Lambert at the Royal National Orthopedic Hospital (RNOH). These are the two hospitals I mentioned before for orthopaedic surgery.

For shoulders we used to refer to Prof Wallace in Nottingham, but he has now retired having undertaken several shoulder replacements for individuals. We now refer to Mr. Lambert at the RNOH, more later. For the spine, we use Mr. Casey who is a complex spinal surgery specialist at the Royal orthopedic hospital. He holds joint appointments across 2 hospitals working also in one of the London neurology hospitals. For hip surgery we use Mr Skinner again at the RNOH. For nerve conduction studies, which I will mention more about a little later with the neuropathy study, we use Charing Cross hospital in London.

I wanted to briefly show you 2 case examples- these are from the individual perspectives -to demonstrate where we refer to and how much they have to travel around to get the best opinion. But before I do that I first show you some information about Mr. Lambert, the shoulder consultant, gave me to share with you.

Those with shoulder deformity due to thalidomide are affected by all the same pathologies which affect the aging general population. However, acromioclavicular joint dysfunction is more common because they have reduced reach and their restricted movement in the shoulder and elbow means the shoulder blade has to move further. The shoulder blade articulates with the clavicle so the acromioclavicular joint



between the two is often a source of discomfort because it is having to move more. The shock absorbing disc in the middle of the acromioclavicular joint has been noted to be absent in those with thalidomide embryopathy who have had scans and operations. With age this shock absorbing disc in the middle of the joint is often worn out in normal individuals. Hence it's no surprise in those with thalidomide

embryopathy, that this AC joint is worn out much quicker than those with normal shoulder joint function and reach. If we go to the shoulder joint itself, deformity causes the humeral head- the ball of the ball and socket joint - to be more ovoid (rather than round) with a smaller under-developed glenoid- the socket. This makes the shoulder joint rock rather than move with a rotational roll of a normal shoulder joint. The range of movement is restricted and hence at the extreme range the joint actually hinges so increasing the pressure on the margin of the joint which then becomes arthritic. This accelerated arthritis occurs in all causes of deformity of the shoulder joint- not just thalidomide embryopathy. If we note also the muscles may be small and weak but still present due to the underdevelopment of the bones of the joint.

So in summary, the muscular components are still in general present in TE. So whilst the bones between the joints are short and deformed lengthening and torsional deformities can be somewhat compensated through joint replacement arthroplasty for osteoarthritis to help pain and limitation of movement of the shoulder joint.

As said I have 2 case examples to show you how the referrals work.

The first case is a nurse who has upper limb damage, short forearms, radial club hands and bilaterally dislocating shoulders. She was experiencing debilitating shoulder pain and increasing restriction in movement. We can see the black circle, that's where she lived. She had been to physio and had seen a local consultant a few years before she contacted us. It had been suggested she consider a shoulder replacement when she couldn't stand the pain any more. We involved her in a small project with Prof Trail at Wrightington looking at arm pain and how the Trust could help. He agreed with the diagnosis of shoulder arthritis and injected both shoulders with steroid; this didn't help and he advised her to consider shoulder replacement when she couldn't put up with the pain any longer. She returned home and several months later she returned again to see a local consultant who again suggested shoulder replacement. So she talked to the Trust after he suggested she needed to see someone more experienced than himself. She told us Professor Trail was

Shoulder Joint in Thalidomide Embryopathy

- Deformity causes the humeral head to be more ovoid with a smaller, under developed glenoid
- This makes the shoulder joint rock rather than the normal rotational roll
- The range of movement is restricted and hence at the extreme range the joint actually hinges, so increasing the pressure on the margin of the joint which then becomes arthritic
- Accelerated arthritis occurs in all causes of deformity of the shoulder joint- not just Thalidomide embryopathy.
- Muscles maybe small and weak due to underdevelopment of the bones of the joint.

Hence, the muscular components are still in general present in Thalidomide Embryopathy.

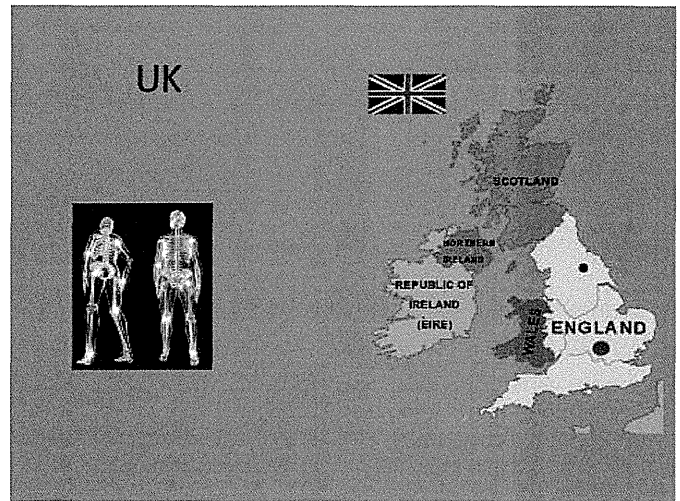
So, whilst the bones between the joints are short and deformed, joint replacement arthroplasty can somewhat compensate for lengthening and torsional deformities and help pain and limitation of movement from early arthritis in the shoulder joint.

UK

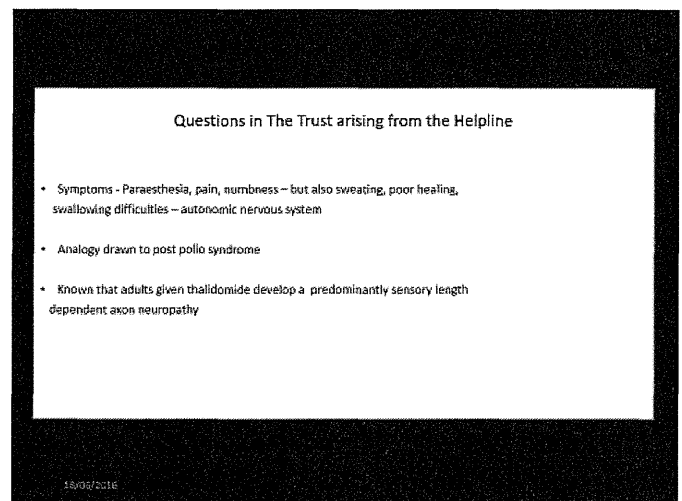



too far away from where she lived and she also wanted to see someone who had actually operated on others within the group for this issue. So we suggested Mr. Lambert at the RNOH. He did CT and MRI scans. She remembers him telling her repeatedly she was too young for such surgery. But she wanted to go ahead. So she had a left hemiarthroplasty – in simple terms the ball was replaced. This X-ray is not hers as unfortunately the XRs did not arrive in time for this presentation. She reports that she now has more movement in her shoulder than she has had for years and her pain levels are much reduced. She is hoping physiotherapy will further improve her movement. And now four months later, she is on the waiting list for her other shoulder. She is very happy.

Second case example - again similar upper limb damage. The Individual phoned the Trust describing pain all over. It was difficult on the phone to decide what was the most important issue and he had been referred already by his local GP to a hip consultant. I suggested referral to Dr. Cowan at the RNOH for an overall assessment. There he was found to have good hip movement and it was felt the sacro-iliac joint was a problem. So he was referred back to physio near where he lived to help with this. Dr. Cowan also suggested he had hand pain and with the paraesthesia needed to see Professor Trail at Wrightington Hospital. There he was found to have weakness of flexion and abduction of the fingers particular on the ulnar side of the hand. He referred him for nerve conduction studies at Charing Cross Hospital in London where our neuropathy study took place. But as he was also complaining of shoulder pain Prof Trail also injected the shoulder joint and AC joint. In the meantime he continued to have hand therapy and physiotherapy for his sacro-iliac joint. On review the shoulder joint injections hadn't worked. So he reinjected the joints again this time from a different approach. The nerve conduction studies came back negative, and the unit in London suggested an MRI scan of his neck. The MRI scan showed some nerve compression in the neck so he has now been referred to the spinal surgeon, Mr Casey, back at the RNOH. In the meantime he is feeling a lot better, with the pain in his hands and back and following the second set of shoulder injections his shoulder pain has improved.



So I've explained what the Trust is, how we help and how others can help. I want to now explain about 2 of our projects. The first project, a peripheral neuropathy study came about because of questions within the Trust. Individuals were complaining about paresthesia, pain, numbness, but also they were describing sweating, swallowing difficulties bladder and bowel problems. An analogy was drawn with post-polio syndrome. We were also aware that adults given thalidomide develop a predominantly sensory, length dependent, axonal neuropathy. So the study was set up with Charing Cross Hospital in






Peripheral nerve dysfunction in middle-aged subjects born with Thalidomide Embryopathy

Hypothesis – early exposure to thalidomide could damage the nerves, heal, but with age be more sensitive to the aging process and cause problems later in life

17 individuals – upper limb damage and symptoms paraesthesia, pain numbness relatively normal lower limbs that were generally asymptomatic

- Large nerve fibres – weakness, pins and needles, O/E abnormal reflexes
- Nerve conduction studies
- Small nerve fibres- pain and temp
- Thermal thresholds of both hands and feet
- Autonomic nerve fibres – HR, pulse, sweating, sexual function, bladder and bowel
- Sympathetic skin responses

18/05/2016



Peripheral nerve dysfunction in middle-aged subjects born with Thalidomide Embryopathy


A large proportion of the 17 individuals showed had results suggestive of nerve compression – mainly wrist, nerve roots lower back, in spinal cord of the neck

Due to the complex anatomy and difficulty interpreting the clinical and neurophysiological findings together with deciding on diagnosis and treatment options they should be referred to specialists familiar with the issues.

Hence Neurologist/ neurophysiologist and surgeon should work together

18/06/2016

London with their neurology team. The hypothesis was that early exposure to thalidomide can damage the nerves, the nerves can heal but knowing that the function of nerves declines with age they wondered if the nerves exposed to thalidomide would be more sensitive to the aging process and result in problems in later life. So we took 17 individuals with upper limb damage and neurological symptoms with normally formed lower limbs and had controls. The paper is awaiting publication with PLOS ONE so the results etc are not reported here. However,



Peripheral nerve dysfunction in middle-aged subjects born with Thalidomide Embryopathy


Results consistent with hypothesis but other causes and issues:

- one moment in time, may have been born this way
- difficult to test the upper limbs
- not known if lower limbs nerves were in the correct anatomical place or had right connections
- other causes - alcohol, vitamin deficiencies, diabetes
- sometimes only one leg showed abnormal test results

Technical problems

- Sympathetic skin response – autonomic nerve fibres – affected by carpal tunnel
- Statistics for ANS were different in the hands and feet
- Thermal thresholds- better test would be skin biopsy

18/05/2016




Peripheral nerve dysfunction in middle-aged subjects born with Thalidomide Embryopathy


Post polio analogy – concern about this analogy

- Polio – infection, clinically apparent neurological dysfunction, recovers, long period stability, further deterioration with age
- Only affects motor nerves
- Re-innervation cause giant motor units – inherently unstable and deteriorate with time

However the suggestion of deterioration with age is possible



18/05/2016



Peripheral nerve dysfunction in middle-aged subjects born with Thalidomide Embryopathy

Letter

- compression of nerves common
- Such symptoms should be properly investigated by specialists
- other causes looked for e.g. diabetes, alcohol, vitamin deficiencies

When asked to help – Trust refers to centres of expertise

Autonomic neuropathy – great caution against attributing any symptoms without firm diagnostic consideration or firm evidence;

- Swallowing difficulties - number causes, not necessarily neurological and maybe treatable; not an early symptom of autonomic dysfunction
- Bladders/bowel dysfunction – prompt investigation for spinal and cauda equina causes; must be no assumption of any autonomic neuropathy

Referral on for pain management

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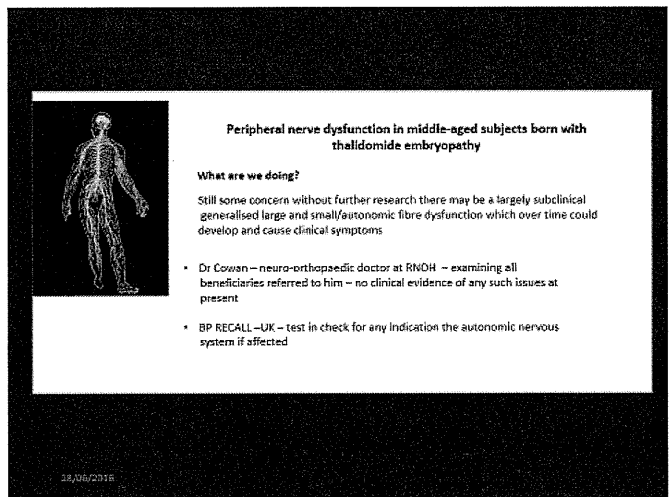
clinically it is important as compressive neuropathies were found to be more common. Due to the complex anatomy, and difficulty in interpreting the clinical and neurophysiology findings together with deciding on diagnosis and treatment options it was concluded that such individuals should be referred to specialists familiar with the issues. Hence, the neurologist, neurophysiologist and surgeon should work together. This is why we often refer to experts in different hospitals depending on the issues and why I showed you the case studies.

Following the study the Trust sent a letter out to beneficiaries as it was taking a long time for the paper to be accepted for publication, with a letter from the neurologist encouraging referral for such symptoms as they were potentially reversible and needed investigation. Also other causes should be excluded such as diabetes, alcohol, vitamin deficiency etc.

The second project is a Blood pressure project called BP RECALL UK . It is a research project with Professor Williams, a cardiologist and an expert in Blood Pressure and his team in London.

The project has national credibility being included in the National Institute Health Research portfolio with particular value for patient outcomes.

As you are aware many of our individuals have difficulty having a blood pressure taken in the upper limb. Though, as I have mentioned, we have written leaflets on how to take a blood pressure in the leg etc. They are not endorsed by experts due to lack of research. Also the leg is increasingly unreliable as individuals age due to peripheral artery disease.



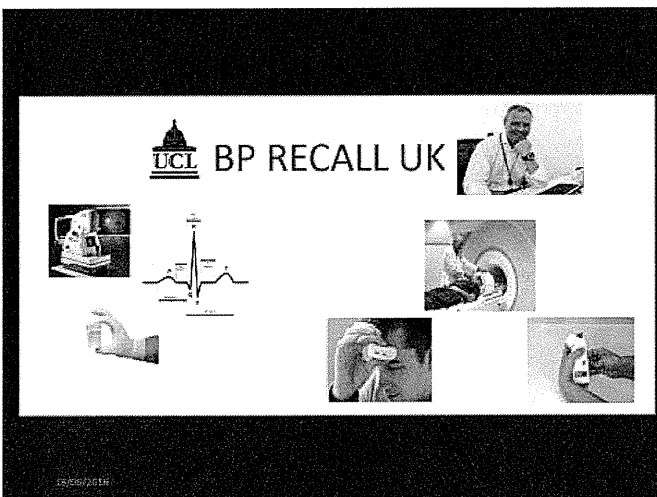
Peripheral nerve dysfunction in middle-aged subjects born with thalidomide embryopathy

What are we doing?

Still some concern without further research there may be a largely subclinical generalised large and small/autonomic fibre dysfunction which over time could develop and cause clinical symptoms

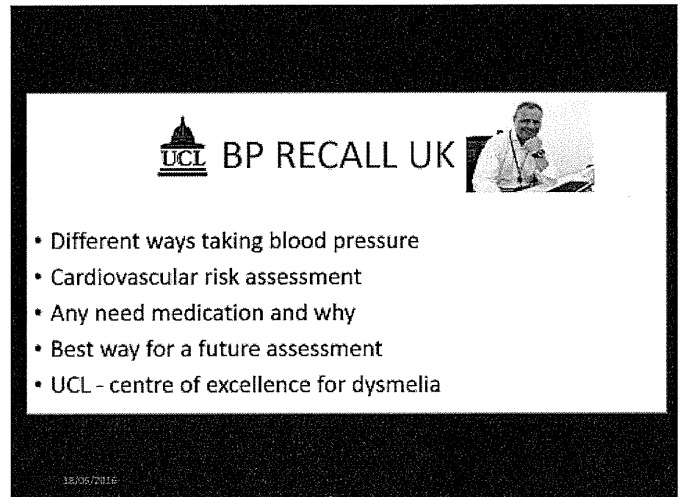
- Dr Cowan – neuro-orthopaedic doctor at RNDH – examining all beneficiaries referred to him – no clinical evidence of any such issues at present
- BP RECALL –UK – test in check for any indication the autonomic nervous system if affected

18/06/2016



UCL BP RECALL UK

18/06/2016



UCL BP RECALL UK

- Different ways taking blood pressure
- Cardiovascular risk assessment
- Any need medication and why
- Best way for a future assessment
- UCL - centre of excellence for dysmelia

18/06/2016

The study is aiming to take 50 individuals and look at existing ways of doing a cardiovascular risk assessment eg. retinal photography, ECG, and 24 hour urine etc. However, it will look at other ways of taking a Blood Pressure in the upper limb, fingers and head rather than the usual way in the upper arm. It will use a specialized new MRI scanner. This will look in detail at the heart, the kidneys, the brain, body fat etc. It will match, therefore, any BP taken with damage from blood pressure in the body, e.g. forehead and finger. We have also included a test for the autonomic nerves system.

Very simply the outcomes are:

- The individual will receive their own risk of heart attack or stroke-cardiovascular risk assessment and advice as to whether they need to take medication to reduce the risk.
- It will also suggest the best way they should be followed up in the future such as different ways the blood pressure may be taken or repeat MRI scan. Due to their current age it is envisaged that if there is no end organ damage currently present then it is unlikely the individual will have to worry about their blood pressure in the future.
- It will help individuals reluctant to take medication feel more secure as to the need to take

it.

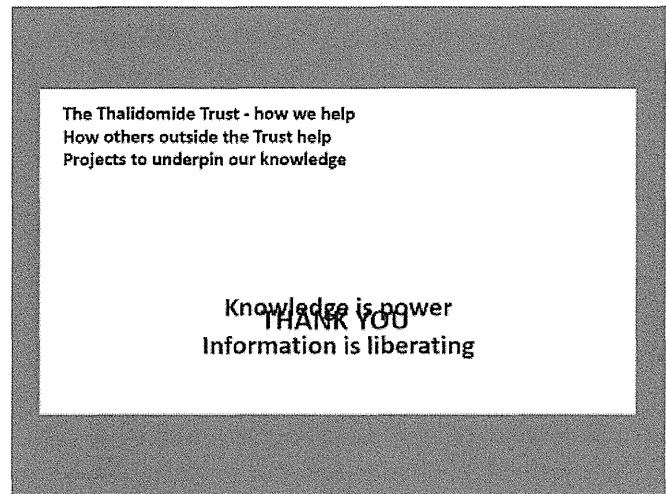
- We hope it will lead to UCL being a centre of excellence for all those with dysmelia and provide advice to centres abroad.

It would take a lot more time to outline the full depth of the intended research. However, if you wish to read more you can have a copy of the full proposal.

In summary I have explained to you, The Thalidomide Trust, what it helps with and how others help and also explained about 2 of our major research projects which help to develop our knowledge.

Slide- Knowledge is power - information is liberating.

We feel it is very important to share our knowledge and to learn what others are doing so our limited resources can be used wisely. Hence we are grateful to our hosts and Dr. Hinoshita for holding this conference.



I will now pass you over to Liz Newbronner for our last very important area of research within the Trust.

Hinoshita : Thank you very much, Dr. Morrison. Dr. Morrison, may we have a few questions now or later? Later, OK.

Next I should introduce Ms. Elizabeth Newbronner. She is a co-speaker with Dr. Morrison. She, Ms. Newbronner, graduated from University of Cambridge majoring in geography 1982. She got MBA (Health and Social Services) at University of Leeds at 1995. Now she is studying Ph.D. course of University of York. She has owned researching company named Firefly Research which worked for universities, government, national charities and foundations. Her main research interests are in the fears of the disability, long term conditions, self-management, old people, and family care. Then, Ms. Newbronner, please.

Newbronner : Thank you. I'd like to thank Dr. Hinoshita for inviting me here to speak. It's a great honor and I'm extremely pleased be here. So thank you very much.

I just want to try briefly today and give you some initial result from survey of all UK thalidomide survivors we conducted the end of the summer and early autumn. The survey built on results from previous qualitative work we've been conducting for last five or six years, and the monitoring of the Health Grant to thalidomide survivors in the UK. Briefly just say the aims of the survey were – The survey was conducted for the Thalidomide Trust and it was to get a much clear the picture of the living circumstances, work situations of UK thalidomiders. To better understand the physical



health problems they were experiencing and also to assess well-being and health related quality of life. So there were three main aims, and the intention is the Trust will use that information to help develop the Trusts services, as Dr. Morrison has described. Hopefully to secure the continuation of the Health Grant when the current Grant ends seven year time and also to support negotiations with the Diageo about the compensation funding for UK thalidomide survivors. So in conducting the survey we send the survey through the Thalidomide Trust to all 467 UK born thalidomide survivors. And people could respond by post or online or they could complete the survey on the telephone with support from myself. 351 people completed the survey which gave us a response rate 75 percent which we were extremely pleased with. Thirteen percent of the people chose to complete survey anonymously, but because the majority gave us the names, we were able to draw data from the Thalidomide Trust about the compensation points and to get some indication of the level of impairment they've experienced originally. 169 respondents were female and obviously rest were the male. But 11 for some reason didn't give us a gender but anyway, that breakdown of the genders is very much mirror of the population, thalidomide population in the UK. And because we have information about people's original compensation points and we can see impairment levels in our survey group more most exactly mirror the whole population in the UK. And I can show you brief slide about that shortly.

So in terms of the survey content, we had 10 sections gathering information about the personal circumstances, work and pensions, self-reported information about their original thalidomide impairment and the health problems and also information about mobility and equipment and use help services, social care. We use two standard questionnaires to explore health related quality of life. So we used SF12 and particularly we chose that because we have used it before and we're also aware of studies using it in Germany and in Sweden. So we were quite keen to have the possibility of international comparison. And we also used mental well-being scale which was developed in the UK, and we chose that because it were able us to make comparison with the general population in the UK very easily because it's used by a national government to monitor mental well-being. The survey closed in October,

Aims of the survey

Main aims were to:

- Get a picture of peoples' current living circumstances and work situations
- Better understand of the physical health problems people are experiencing
- Assess mental wellbeing and health related quality of life

This information will be used to:

- Help the Trust develop its services
- Secure the continuation of the Health Grant
- Support negotiations with Diageo about future funding

The Thalidomide Trust

Firefly
ILLUMINATING RESEARCH

Conducting the Survey

- Sent by the Thalidomide Trust to all 467 UK born Thalidomide survivors
- People could respond by post, on-line or complete it on the telephone with support
- 351 people completed the survey – a response rate of just over 75%
- 13% chose to complete the survey anonymously
- 169 of the respondents were female; 171 were male; and 11 did not give their gender
- The impairment levels of the survey respondents closely matched those of all UK Thalidomide survivors

The Thalidomide Trust

Firefly
ILLUMINATING RESEARCH

Survey Content & Analysis

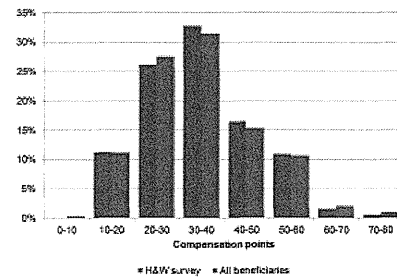
- Survey had ten sections - About You; Family and Housing; Work and Pensions; Original Thalidomide Impairments; Mobility and Equipment; Health Problems; Use of health Services; Social Care Support; Mental Wellbeing; Health Related Quality of Life
- Included two standard questionnaires:
 - SF12 Health Related Quality of Life
 - Warwick Edinburgh Mental Well Being Scale
- Currently analysing the data
- Initial results are presented here with a focus on health

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so we're currently analyzing the data, so I feel a bit nervous because these are very initial results. So I'm just going to present a few things here with particular focus on health but we'll show a little bit about peoples living circumstances, and work situations. So as I said, the spread of the people on the survey very much mirror the whole UK population of thalidomiders. And I just show this slide because I think it also shows the distribution of compensation points it's very similar to the German situation. So I think that just help to think about international comparison. And for the purpose of this analysis we're going to split the group within our survey into a number of impairment groups so that we can sort of look at things in a little bit more detail. We may focus down further but for the moment we are thinking we'll have two arm group. So the first group would be people with arm shorter than their elbow and second group would be people with arms longer than their elbow. Then we also had a group for damage to legs only and people were affected both in their arms and legs. So we were sort of looking at those splits for the analysis, and then here, just showing a little bit more information about all the problems people reported including hearing impairment, deafness. So there is sort of brief breakdown there for you. In terms of people's living circumstances, we found that 64 percent of our group live with partner, or their partner and children or another family member which again I think mirrors Peter's findings in Germany. 11 percent live with another family member which could be like a parent or sibling. And 22 percent live alone and I think these are the groups that we have some concerns about. Just 10 of our sample live with paid care worker or in residential care. Interestingly 85 percent owned their own home and so have a reasonable level of security in terms of their home. The work situation for UK thalidomiders I think it's a little bit different from other European countries. We only have 16 percent of our group who are able to work fulltime or who are working fulltime. And almost two-thirds are not working at all. So I think that's very different to the German situation. We also asked people about changes in the working lives. As Cristina said, a number of people said their work situation changed since 2000, and I think this might partially due to the physical changes that people experiencing deterioration in the health but also in the UK people gave received much financial compensation since 2000 both their main compensation and the Health Grant,

Thalidomide Compensation Points



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Thalidomide Impairments

| Impairment | Number | % |
|---------------------------------|--------|-----|
| Dysmelia – arms (major) | 92 | 26% |
| Dysmelia – arms (moderate) | 111 | 32% |
| Dysmelia - legs | 40 | 11% |
| Dysmelia – arms and legs | 65 | 19% |
| Scoliosis | 77 | 22% |
| Deaf or hearing impairment | 123 | 35% |
| Blind or partially sighted | 40 | 11% |
| Damage to face and/or outer ear | 65 | 19% |
| Damage to internal organs | 110 | 31% |

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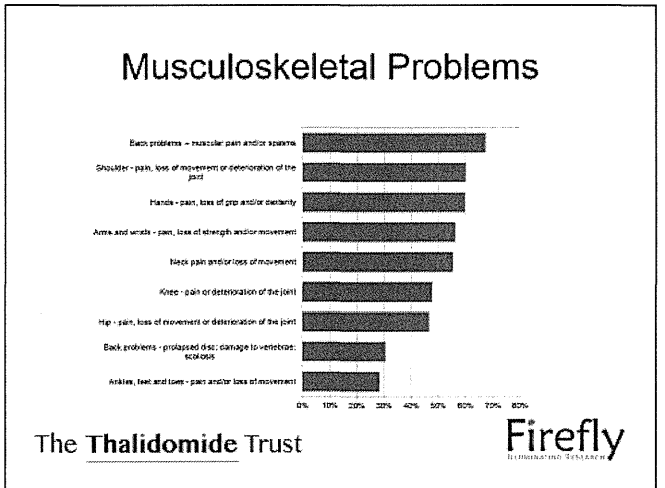
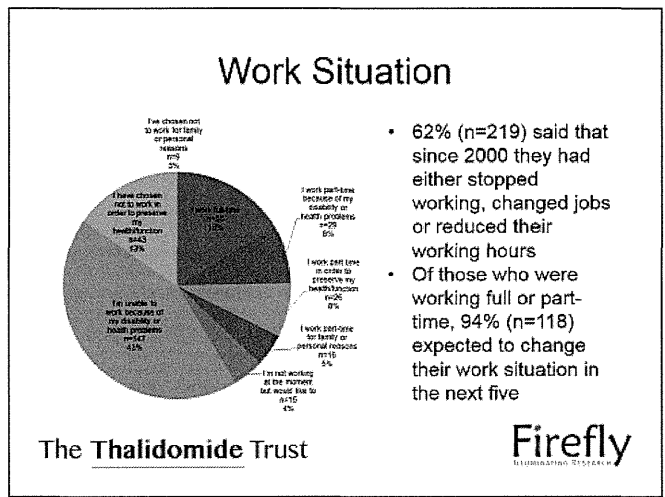
Living Circumstances

- 64% live with their partner or their partner and their children/other family member
- 11% live with another family member/s (e.g. parents or sibling)
- 22% live alone
- Ten people live at home with paid carers or live in residential care
- The majority (85%) own their own home

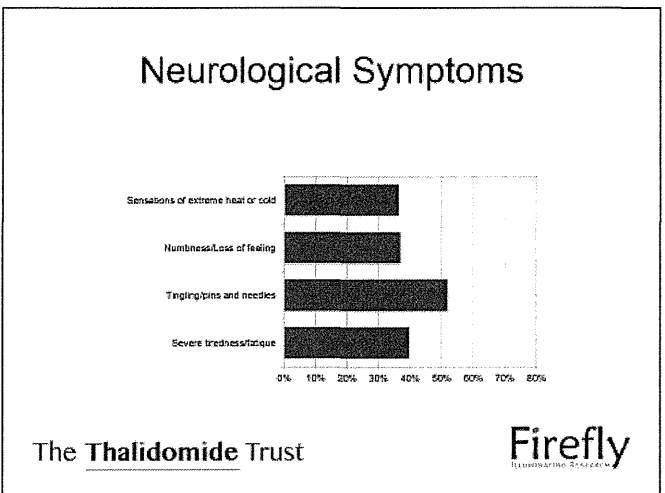
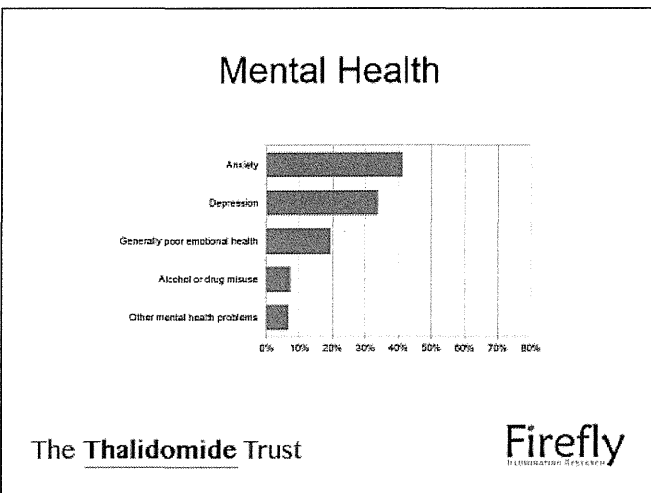
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and also being exempt from taxation. So I think the financial position has changed for people. We asked people about how the things might change in the future and a great many said they would have to make further changes to their work situation - either reduce their working hours, change their job or give up working. So I think this is a major concern for people. I'd like to touch briefly on the self-reported health problems. These are self-reported issues as we don't have clinical examinations, but 93 percent of group were experiencing a pain or loss of movement in one or more joint. So that was the overwhelming issue



that they were reporting. But almost half reported generalized pain and again half reported they had one or more mental health problem, currently or recently in the last you know, few months. And nearly three quarter were experiencing neurological problems. And as Dr. Morrison says we know there maybe

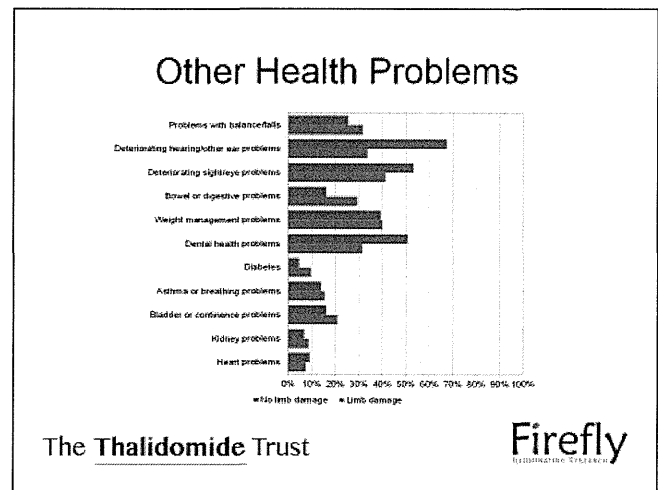


a variety of causes around for people but nevertheless it is major concern for thalidomiders in the UK. And this just gives a very brief breakdown for the musculoskeletal problems and again I think this Swedish study the back problems were major concern for people. Again there maybe a variety of reasons but self-reporting is significant. In terms of mental health, quite number of people reported more than one mental health problem but the key issue I think is a lot of people with anxiety closely followed by

depression. I think this is where the Trust would like to explore further the experiences people are having and look at the relationship between mental health and people's living circumstances, their work situations, and their impairment or the decline in their functional abilities. Another area is neurological symptoms although they may be a variety of causes, it is certainly a major cause of concern and I think the recent nerve study will hopefully shed more light on that.

Interestingly one of the, anecdotally problems reported among thalidomiders in the UK are problems with balance and falls and that did come out of survey in the self-reported health problems. And again I think that is something to investigate further because it's not quite clear and there could be multitude of causes for that. But the consequences as a whole and fractures and so on are quite serious for a lot of thalidomiders. So something to explore further. I think the other thing that quite important in the UK particularly in terms of lifestyle prevention of further problems like management issues and one of the things that trust is supporting is fitness project which has learn from Swedish, thalidomiders fitness project. So there is a lot of interesting in helping thalidomide survivors self-manage, to improve the diet and hopefully prevent future problems.

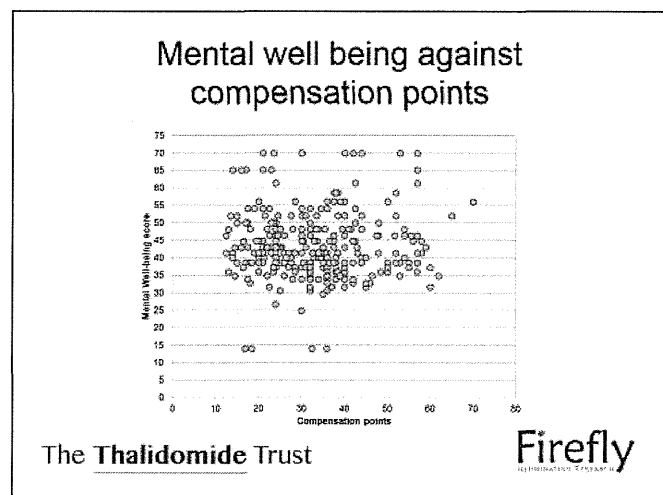
So just maybe quickly I'm conscious at the time, so I just move quickly on the work we did about mental well-being and health related quality of life. So using the standard instrument, the Warwick Edinburgh Mental Wellbeing Scale (WEMWBS) we found the mean score for UK thalidomide survivors was 43.6



Mental Well Being Scores

- Mean score for UK Thalidomide-survivors = 43.6
- Mean score for general population aged 45-54 = 50
- Lower well being scores (bottom 40%) appear to be associate with living alone and still working full time
- No obvious relationship between mental well being sore and level of impairment

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where as the UK mean score for the general population is 50. And so the early result suggest that the lower scores - the bottom 40 percent are most strong associated with living alone and not actually related to level of impairment those are the social factor seem to be very important. Another slide - this is just simple scatter plot, We need to do more work but the level of compensation points and the person's mental well-being score seems very random, but we need to do more analysis about.

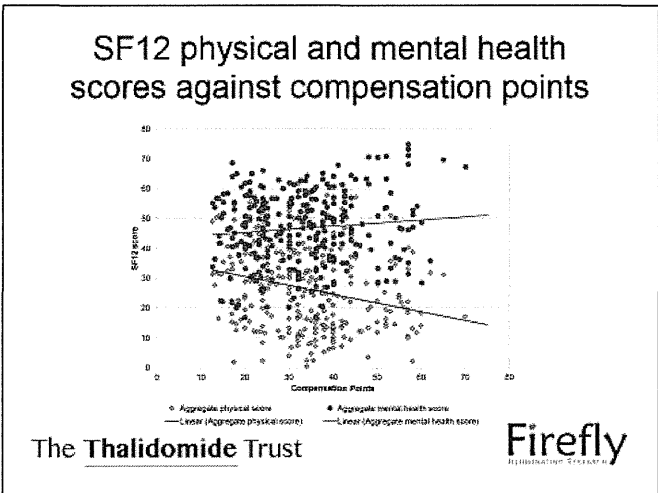
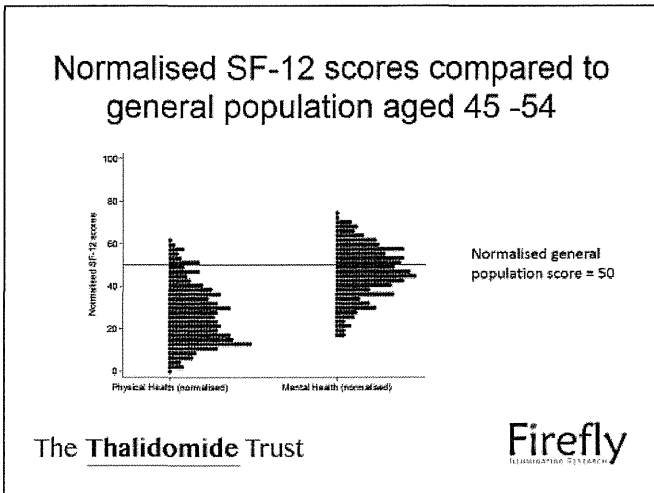
So and then just moving on to the SF12 results. Here are just wanted to show the scales and subscales

because as I say I know the colleagues I using this measurement. What we found in the UK consistently - this is the third time we use this method - is that the physical score is substantially lower than normalised score of 50 for the general population of similar age. Interestingly mental health score is not that different from normalised score for the general population. But there are number of people, if I just move on, you see from this graph. There are a number of people who have very low scores and I think again that something that we want to try and explore further to understand why certain groups have that very,

Normalised Responses for SF12v2 - aggregate scores and subscales

| Component | UK Mean | Min | Max |
|----------------------------------|-------------|-------------|-------------|
| Aggregate Physical Health | 26.7 | 0.5 | 61.7 |
| Physical Functioning (PF) | 20.9 | 1.7 | 57.6 |
| Role Limitation Physical (RP) | 36.4 | 21.9 | 55 |
| Pain (BP) | 33.6 | 14.2 | 59.2 |
| General Health (GH) | 33.7 | 13.7 | 63.7 |
| Aggregate Mental Health | 46.5 | 16.8 | 74.9 |
| Vitality (VT) | 40.4 | 21.3 | 68.2 |
| Role Limitation Emotional (RE) | 43.5 | 23.7 | 55.3 |
| Social Functioning (SF) | 34.6 | 2.0 | 55.5 |
| Mental Health (MH) | 40.7 | 7.4 | 64.5 |

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very low scores. And again, a very simple scatter plot just gives indication, but as you can see maybe not surprisingly the blue line that goes down is suggest there is a relationship between level of impairment and the score for physical health related quality of life. but curiously he red line suggest that there might also be a relationship between people who have lower levels of physical impairment but have poorer levels of mental health related quality of life. So again something we very much want to explore further. And I've just got two more slide, I should just round off by saying that I think my perception from doing

- ### Discussion
- Many Thalidomide survivors with mild to moderate levels of impairment are now reporting a rapid loss of function
 - Most are self-managing their pain and loss of function through lifestyle changes, non-prescription pain medication and complementary therapies
 - Despite having lifelong impairments some Thalidomide survivors feel 'newly disabled' and this has important implication for their mental well being
 - The majority of survey respondents had experienced one or more problems with quality or access to health services, especially lack of knowledge/understanding of Thalidomide damage amongst health professionals
 - Further analysis will use multiple regression to explore the relationship between key variables
- The **Thalidomide** Trust **Firefly**
HEALTHCARE STRATEGISTS

qualitative work with the thalidomiders in the UK, is that many thalidomide survivors who have mild moderate levels of impairment are now reporting rapid loss of function. Many people in the UK because the financial resources in the last few years, are self-managing, taking steps to self-manage the pain and loss of function through lifestyle changes, non-prescription medication, complimentary therapy. But as Dr. Morrison says that may not be enough for some people they may need more medical intervention or at least much better understanding of the problems they are experiencing. I think there is also an issue, although thalidomiders have been living with lifelong impairments. I think many people have not

seen themselves really as disabled. And for those who are now losing some function, they have become newly disabled and that has important implications for people sense of mental well-being. And I think coupled with that people experiencing quite lots of problems accessing health services, particularly the local routine health services, often don't understand the problems they're experiencing, hence all the trust work to develop the network of specialist across the UK. And lastly can I just say that this is very much first impressions of the data that we have. But we hope to do much more statistical analysis and get more solid result.

So the next few month hopefully colleagues and another countries to make some comparisons. So I just wanted to say thank you again for inviting me and giving me the time to speak today.



Hinoshita : Thank you. Do you have any questions? Two presentations given by Dr. Morrison and Ms. Newbronner. So may I ask you, Dr. Morrison? I am thinking of chronic pain and serious joint problems. It seems you are more active for the surgical treatment, operations, in your country. How do you think of it? In this respect, we are not so active to proceed the operational treatments in Japan. How do you think of it?

Morrison : I think the consultants carefully assess whether they can help the condition. As I mentioned with the nurse and the partial shoulder replacement, with her nurse training background she knew what the risks were for shoulder surgery and she was counselled that she was very young many times for this particular surgery. I think the surgeons are happy to operate when they have the knowledge to do so but it is a last resort. They're not quite so happy with a hip necessarily if the arms are short. They may be using the hip instead of their arms to eat etc. If the operation goes wrong, they are going to lose a major part of their ability to function or the hip replacement would not allow them to be so flexible with the leg. And again with spinal fusion for pain they would carefully assess the issues as to what benefit the individual will have because they don't want to lose flexibility to compensate for other areas of the body. But certainly shoulder replacement seems to be helping – there have only been a few but so far the outcomes have been good.

Hinoshita : I see. So you have ever found the successful cases with the operation?

Morrison : Yes. Yeah.

Hinoshita : OK. Next.

Peters : But the number of surge groups here is going up in Germany as well. But the patients have already done surgery and several ones on the waiting list will do that next month. I think because also developing osteoarthritis in hips, knees, also in shoulders.

Hinoshita : OK. In your case, there are some patients waiting for the surgeries? Hip joints, shoulder and so on. OK. All right.

Morrison : As children many had operations which didn't work so they are afraid of operations. So it's a difficult situation we have.

Hinoshita : It seems this program may be controversial. OK, doctor.

McCredie : Just to admit that we have one of a bilateral upper limb defects who has had seven hip replacements and one shoulder replacement and all failed.

Hinoshita : Right, Dr. Kayamori.

Kayamori : I am against about operation for shoulder. Just in the morning I showed the slide that means the skeletal musculatures were really hypoplastic. They tried to make the muscles stronger but in vain. So I don't think surgical treatment for shoulder joint replacement is indicated. It must be not successful. That's my opinion. Thank you.

Morrison : This is why I brought the information from Mr Lambert on shoulder surgery and went through how they can help and why. I have two pages he actually wrote for me and which I can share with you. He is an expert in operating with congenital deformity. They see the complex cases at the RNOH which is the national center and they are specialist surgeons.

Kayamori : As long as I did a lot of patients examined with nerve conduction study, but I couldn't find evidence showing polyneuropathy except for compression neuropathy.

Morrison : Did you look at the small nerve fibers and the autonomic nervous system?

Kayamori : No, no, I didn't do that too.

Morrison : Yes.

Kayamori : Sympathetic nerve, I didn't do that. But sensory motor nerve, only I did. Thank you.

Hinoshita : It seems that Dr. Lambert has been good at the shoulder joint surgery. So if you have any patient suffering from shoulder joint pain or motion problems, how about introducing him or her to Dr. Lambert in UK? Anyway let's wait for more scientific results. Is there any other comment or opinion from German doctors about this problem? OK? Let's get back to this program later at the joint discussion or meeting.

⑦Dr. Rudolf Beyer

“Pain control in people with thalidomide embryopathy”

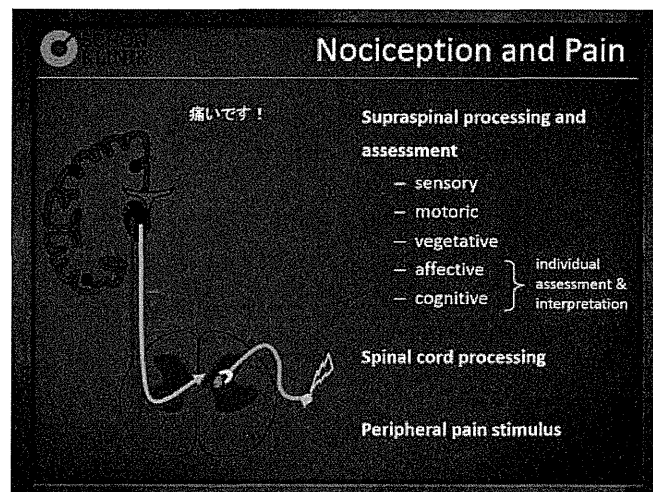
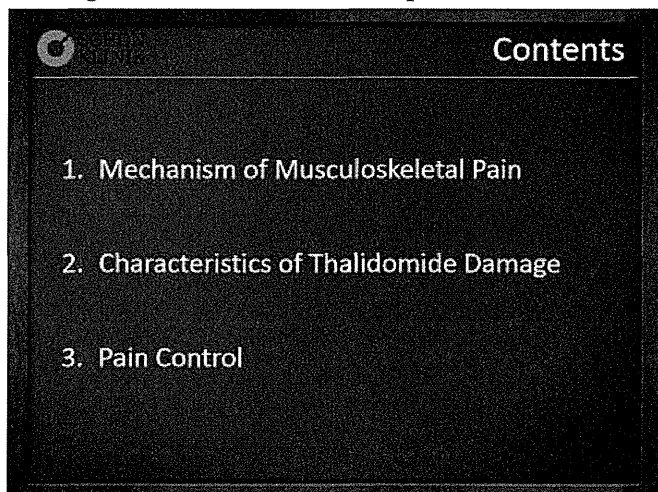
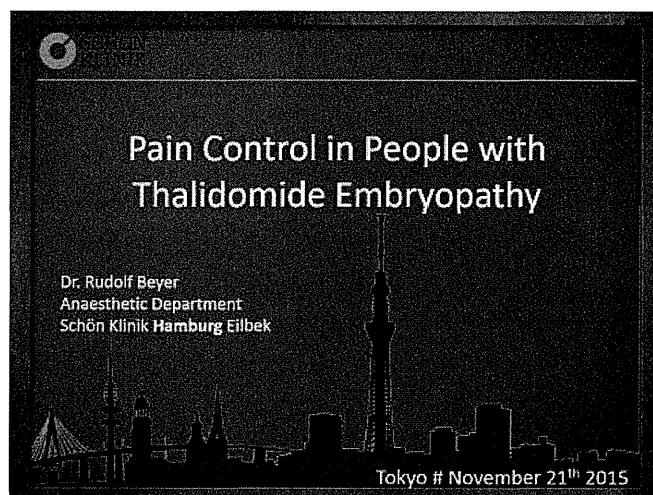
Hinoshita : Then go ahead to the next presentation. The next oral presentation will be given by Dr. Rudolf Beyer. His title is “Pain control in people with thalidomide embryopathy.” I will introduce him to you. He graduated from University of Hamburg in 1987. He has been always specializing anesthesiology

and pain control. He had been working as consultant anesthetist, Schön Klinik Eilbek, Hamburg. He had been working at Department of Anesthesiology and Pain Medicine from 2007 through 2012. Now he is senior physician, Schön Klinik Eilbek, Hamburg since 2014. Then Dr. Beyer, please.

Beyer : Thank you, Dr. Hinoshita, for the kind invitation for the possibility to be here, this nice meeting.

Hinoshita : You're welcome.

Beyer : I would like to talk about pain and pain control in people with thalidomide embryopathy. Pain is a complex output of sensory organ, and I'm convinced that we need to receive best knowledge all to develop good strategy for the treatment of pain. Therefore I will say some words on the subject of pain mechanisms before I focus on the various options of treating pain. Now go back to the university. A pain stimulate as caused a mechanical, thermal or chemical agent in the periphery, and this transferred to the spinal cord wire the peripheral nerves. Within the spinal cord, the signal is via the tractus spinothalamicus. At

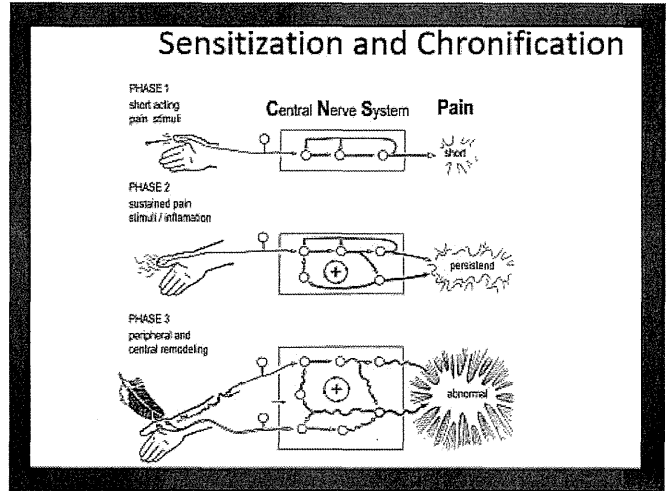


this time enhancing and inhibiting influences modulate the signal significantly. Within the brain a more complex process takes place that leads to the ultimate tangible sensational pain. Furthermore, what we consider to be pain could be divided into different components. The sensory alert notification, namely the location and the dimensional damage, the direct motoric answer to get out of the danger zone, vegetative answer to prepare the body for fight or flight. The affective emotional component, and at the end, analyzing of the incident comparing with past experience. Especially the affective component has a major influence of how we feel the pain and therefore how we present or express our pain to other people. This whole slide shows the normal way of normal pain processing.

Over the last 20 years more mechanisms of pain chronification has been discovered. So researchers determined to make 2 major steps. In the first step, a long acting pain stimulus leads to sensitization of the nerve system. And in the second step, remodeling of the nerve system leads to chronification. For

better understanding I would like to explain how this is working. Even today, you will find doctors who believe that pain processing is a matter of wiring and nerves work like electrified cable system. But I would say it's more like a well network computer system.

A sustained pain stimulus leads to a local inflammatory process which presents as pronounced tenderness and pain at motion. After a while, structural changes of the nerve system leads to the development of new functional pathways for pain. This is basically done by changing the properties of the ion channels. And by “waking up” hibernating synapses.



Sensitization and Chronification

Sustained Pain Stimuli

- Release of neuropeptides from the nerve ending
- Increased permeability of the blood vessels leads to local edema
- Sensitivity increased by inflammatory mediators

➤ Pronounced tenderness and pain at motion

Sensitization and Chronification

1. Structural changes of ion channels

- Increased permeability of Sodium and Calcium (uncontrolled neuronal „fire“)
- Activation of normally “sleeping” synapses

➤ Development of new functional pathways for pain processing

By altered gene encoding within the neuron, so the cell properties change permanently, that means the neuron reacts more easily and more strongly to stimuli even if they are subthreshold, and the end point of chronification consists of structural remodeling of the peripheral and central nerve system that leads to new pathways for not nociceptive information and long-term pain.

Sensitization and Chronification

2. Altered gene encoding

- Synthesis of modified ion channels and receptors
- Increased number and more docking sites for nociceptive stimuli

➤ Permanent alteration of the neuron

Sensitization and Chronification

The endpoint of chronification consists of structural remodeling of the peripheral and central nerve system that leads to new pathways for nociceptive information and long term pain

So every one of us has most likely experience nociceptive pain. As I mentioned before, this is a normal way of pain processing. In case of neuropathic pain the damage is in the nerve system itself, and a treatment approach is common pain killers usually fails. For example, phantom pain does not really respond to opioids and non-steroidal inflammatory drugs.

Types of Pain

Acute Pain

- is an important warning that protect us from hazards
- duration is related to tissue healing

Chronic Pain

- has lost the function of protecting
- last longer than 6 month
- affects biological, psychological and social wellbeing

Types of Pain

Nociceptive Pain
Tissue damage affects free nerve endings (Nociceptors)

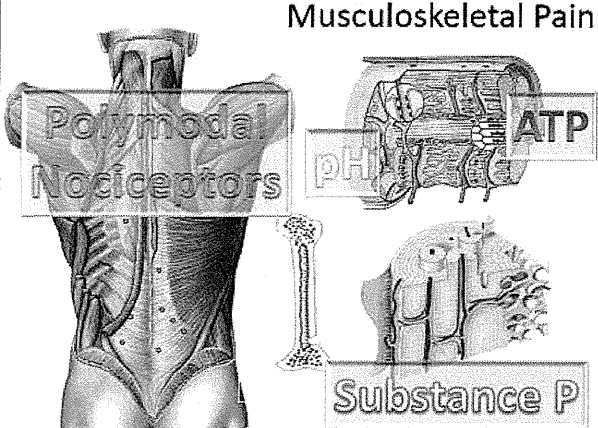
- Bone
- Muscles
- Fasciae

Neuropathic Pain
Damage of nerve tissue (mechanic, toxic, ishaemic)

- peripheral
- spinal
- central

The fare most pain has its origin in the locomotor system and they were also lots of anatomical research on this in the last decade. They found pain processing receptors nearly everywhere. It has shown that there is wide appearance of mechanical receptors with polymodal properties in the connective tissue that envelopes the muscles, namely the polymodal nociceptors.

Musculoskeletal Pain



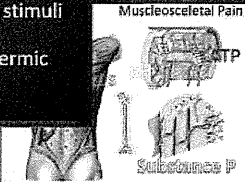
Musculoskeletal Pain

Fasciae:

Widespread appearance of sensible nerve endings, especially in the region of muscle insertion

Most nociceptors are polymodal, they simultaneously respond to different stimuli

Nociception due to mechanically, thermic and chemical stimuli



In the muscle itself there are large number of free nerve endings which respond to the products of muscle metabolism like adenosine triphosphate or a low tissue pH, and also in the bone marrow free nerve endings and substance P are found. At the end of the day, all these anatomic findings show us that the locomotor system is a perfect sensory organ for sensation of pain.

Besides biological aspect, we also have to consider physiological and social aspect of pain. A chronic pain will influence our mood in a bad way and to turn it round a manifest depression, and fear will affect our