BMJ open

The Scleroderma Patient-centered Intervention Network (SPIN) Cohort: protocol for a cohort multiple randomised controlled trial (cmRCT) design to support trials of psychosocial and rehabilitation interventions in a rare disease context

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To cite: Kwakkenbos L, Jewett LR, Baron M, *et al*. The Scleroderma Patient-centered Intervention Network (SPIN) Cohort: protocol for a cohort multiple randomised controlled trial (cmRCT) design to support trials of psychosocial and rehabilitation interventions in a rare disease context. *BMJ Open* 2013;**3**:e003563. doi:10.1136/bmjopen-2013-003563

▸ Prepublication history and additional material for this paper is available online. To view these files please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2013-003563).

Received 8 July 2013
Accepted 10 July 2013

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ABSTRACT

Introduction: Psychosocial and rehabilitation interventions are increasingly used to attenuate disability and improve health-related quality of life (HRQL) in chronic diseases, but are typically not available for patients with rare diseases. Conducting rigorous, adequately powered trials of these interventions for patients with rare diseases is difficult. The Scleroderma Patient-centered Intervention Network (SPIN) is an international collaboration of patient organisations, clinicians and researchers. The aim of SPIN is to develop a research infrastructure to test accessible, low-cost self-guided online interventions to reduce disability and improve HRQL for people living with the rare disease systemic sclerosis (SSc or scleroderma). Once tested, effective interventions will be made accessible through patient organisations partnering with SPIN.

Methods and analysis: SPIN will employ the cohort multiple randomised controlled trial (cmRCT) design, in which patients consent to participate in a cohort for ongoing data collection. The aim is to recruit 1500–2000 patients from centres across the world within a period of 5 years (2013–2018). Eligible participants are persons ≥18 years of age with a diagnosis of SSc. In addition to baseline medical data, participants will complete patient-reported outcome measures every 3 months. Upon enrolment in the cohort, patients will consent to be contacted in the future to participate in intervention research and to allow their data to be used for comparison purposes for interventions tested with other cohort participants. Once interventions are developed, patients from the cohort will be randomly selected and offered interventions as part of pragmatic RCTs. Outcomes from patients offered interventions will be compared with outcomes from trial-eligible patients who are not offered the interventions.

Ethics and dissemination: The use of the cmRCT design, the development of self-guided online

ARTICLE SUMMARY

Article focus

- Psychosocial and rehabilitation interventions are used to attenuate disability and improve health-related quality of life (HRQL) in many chronic diseases, but are typically not available for people with rare diseases.
- Conducting rigorous, adequately powered trials of these interventions for patients with rare diseases is difficult.
- The Scleroderma Patient-centered Intervention Network (SPIN) is an international collaboration of patient organisations, clinicians and researchers whose aim is to develop a research infrastructure to test accessible, low-cost, self-guided online interventions to reduce disability and improve HRQL for people living with scleroderma (systemic sclerosis).

ARTICLE SUMMARY

Key messages

- SPIN will employ the cohort multiple randomised controlled trial (cmRCT) design, in which patients consent to participate in a cohort for ongoing data collection.
- The cohort framework will also be used to identify patients eligible for internet-based psychosocial and rehabilitation interventions that will be developed by SPIN investigators and to conduct feasibility and, subsequently, full-scale trials of these interventions.
- Once tested, effective interventions will be made accessible through patient organisations partnering with SPIN.

Strengths and limitations of this study

- In the context of rare diseases, the advantage of the cmRCT design to conduct multiple trials that draw participants from the same patient cohort is particularly important given the difficulty of recruiting a sufficiently large patient group for any single trial.
- Unique features of SPIN, including the use of the cmRCT design, the development of self-guided online interventions delivered using a common platform, and a robust partnership with patient organisations, may serve as a model to help facilitate research in this area for other rare diseases as well.

interventions and partnerships with patient organisations will allow SPIN to develop, rigourously test and effectively disseminate psychosocial and rehabilitation interventions for people with SSc.

INTRODUCTION

Providing better patient-centred care for people living with chronic diseases is increasingly prioritised in proposals to improve healthcare.[1] Patient-centred care emphasises patient empowerment through shared decision-making, the development of care plans that take into consideration patient preferences and values, and the tailoring of care to meet the specific needs of individual patients.[2–4] Comprehensive care to attenuate disability and improve health-related quality of life (HRQL) in chronic diseases involves a combination of both pharmacological and non-pharmacological interventions.[5] People with rare diseases do not, however, typically have access to disease-specific psychosocial and rehabilitation interventions that are important components of patient-centred care.

The lack of accessible, evidence-based, disease-specific interventions is an important gap in patient care. Many people with rare diseases face unique challenges that are not addressed by generic interventions or interventions developed for other chronic diseases.[6] However, there are major obstacles to developing, evaluating and delivering psychosocial and rehabilitation interventions to meet the specific needs of people with rare diseases. An important barrier is the small number of people with a given rare disease at any single centre. Furthermore, most clinical research centres are often involved in many different trials and tend to prioritise trials of primary disease treatment over non-pharmacological intervention trials to reduce disability and improve HRQL.

Illustrating the extent of this problem, we conducted a PubMed search ('*randomized controlled trial*' (*publication type*) *NOT* '*drug therapy*' (*subheading*)) of the 6632 rare diseases listed by the US National Institutes of Health[7] and found only one randomised controlled trial (RCT) of a psychosocial or rehabilitation intervention with the sample size of at least 100 patients,[8] a relatively small number given typical sample size requirements to evaluate most psychosocial and rehabilitation interventions.[9 10] Thus, for most rare diseases, there are either no trials that have tested psychosocial and rehabilitation interventions or only very small trials that are useful to evaluate feasibility, but inadequate for assessment of treatment efficacy.[11–13]

Beyond difficulties conducting RCTs, many factors also complicate the delivery of psychosocial and rehabilitation interventions to people with rare diseases. Few centres treat enough patients with a given rare disease to sustain a disease-specific psychosocial and rehabilitation intervention programme. Additionally, many patients with rare diseases live far from major treatment centres. These individuals often receive care in local settings from healthcare providers with little or no experience treating their disease and without knowledge about the specific needs of people with the disease. Patients who live in rural areas far from specialised care are often left to cope with their illness essentially alone, may lack even relatively basic information about their disease, and, in many cases, experience substantial difficulty coping.[14 15] Thus, finding a way to develop, test and deliver psychosocial and rehabilitation interventions for patients with rare diseases in a cost-effective manner is an important, but unsolved problem.

Systemic sclerosis (SSc, also known as scleroderma) is a rare disease where patients have important unaddressed psychosocial and rehabilitation needs.[16 17] SSc is an autoimmune connective tissue disease characterised by vascular injury, immune dysfunction and an abnormal fibrotic process that can affect multiple organ systems including the skin, lungs, gastrointestinal tract and cardiovascular system.[18 19] Conditions commonly associated with SSc include Raynaud's phenomenon,[20] oesophageal disease and chronic gastrointestinal symptoms (dysphagia, dyspepsia, diarrhoea, chronic constipation and malabsorption),[21] and pulmonary disease (interstitial lung disease, pulmonary vascular disease, pulmonary arterial hypertension).[18 19] Prevalence estimates for SSc range from 7 to 489 cases per million, and approximately 80% of patients diagnosed with SSc are women.[22 23]

SSc is notable for a wide range of patient-reported problems, including limitations in physical mobility and hand function, pain, fatigue, sleep disturbance, depression, sexual dysfunction and body image distress from disfiguring changes in appearance (eg, pigment

changes, hand contractures and facial telangiectasias).[16 24–27] There are no disease-modifying treatments for SSc and its management is predicated on identifying organ-specific disease manifestations and initiating targeted therapies (eg, calcium channel blockers for Raynaud's phenomenon, proton-pump inhibitors for gastrointestinal reflux disease and ACE inhibitors for SSc renal crisis).[17] Because there is no cure, a primary goal of care is to reduce symptoms and disability, and to improve HRQL. However, as with many rare diseases, evidence-based psychosocial and rehabilitation interventions to meet the specific needs of patients with SSc are not available. The authors of recent guidelines for SSc management[17] noted the potential importance of psychosocial and rehabilitation interventions in disease management, but could not make recommendations for or against these types of interventions due to a general lack of evidence.

The Scleroderma Patient-centered Intervention Network (SPIN),[28] an international collaboration of patient organisations, clinicians and researchers was recently organised and funded by the Canadian Institutes of Health Research to address this important gap. The long-term goals of SPIN are to develop, test and disseminate accessible interventions to complement standard medical care and improve HRQL outcomes in SSc. Once tested, effective interventions will be made accessible to patients with SSc through patient organisations around the world. SPIN currently is developing a series of interventions, including (1) general SSc self-management, (2) support for better coping with emotional distress; (3) support for managing body image distress and (4) physical and occupational therapy for hands. Other interventions that address areas important to people with scleroderma (eg, fatigue and energy management, sleep problems and sexual function) may be developed subsequently, depending on need and funding availability.

An important characteristic of SPIN is that all interventions will be delivered in a self-guided online format. Across medical fields, online delivery of interventions is increasingly common, and these interventions have successfully improved HRQL.[29–31] The utilisation of web-based technology is particularly important in the case of rare diseases where patients typically have difficulty accessing specialised services. A recent study[32] found that 85% of Dutch patients with SSc had used the internet to search for information about SSc and that most of these patients (77–88%) perceived access to online information on physical, psychological and social consequences of the disease as important.

SPIN will utilise a novel research design, the cohort multiple RCT (cmRCT) design,[33] to collect longitudinal data related to problems experienced by people living with SSc and as a framework for developing, evaluating and delivering psychosocial and rehabilitation interventions. The aim of this article is to illustrate the use of the cmRCT design in a rare-disease context, which may serve as a model to help facilitate research in the area of non-pharmacological interventions for other rare diseases as well.

SPIN COHORT AIMS

The first step towards SPIN's long-term goals is the establishment of the SPIN Cohort. The specific aims of the SPIN Cohort are to:

1. Collect observational data at regular intervals on an ongoing basis in order to conduct research on problems identified by patients with SSc as important to them and to determine the best way to measure outcomes related to these problems, among other research questions that may be addressed via the cohort;
2. Use the cohort framework to identify patients eligible for internet-based psychosocial and rehabilitation interventions that will be developed by SPIN investigators and to conduct feasibility and, subsequently, full-scale trials of these interventions.

METHODS AND ANALYSIS

Design

The cmRCT design,[33] which SPIN will employ, was developed to take advantage of the benefits of cohort designs for longitudinal data collection and to address some important limitations to traditional RCT designs in the context of pragmatic RCTs. Pragmatic RCTs are intended to test the effectiveness of an intervention in everyday practice with relatively unselected participants and under flexible conditions, maximising the applicability of the trial's results to usual care settings.[34] They differ from explanatory trials in that pragmatic trials are meant to inform decisions about practice rather than explain mechanistic aspects of an intervention under ideal circumstances. In this respect, pragmatic trials are well suited to assess whether patients benefit from adding an intervention to treatment as usual, compared with treatment as usual only.

The cmRCT design involves recruitment of an observational cohort, in which patients fill out a small set of core outcomes regularly. Patients enrolled in the cohort agree to allow their longitudinal data to be used in the aggregate. They also allow their data to be used to identify them to be invited to participate in research interventions, once developed, or for comparison purposes for intervention trials that may be conducted with other patients while they are participating in the cohort. In the cmRCT design, as described to patients when they consent to participate in the cohort, only eligible patients randomly selected to be offered an intervention, but not eligible non-selected patients, are contacted and offered treatment. Eligible patients not selected are not notified about the trial. Consent for specific trials will be obtained from those eligible patients who are invited and accept the offer to participate. Postintervention outcomes among eligible patients who accept the offer to receive the intervention will be

compared with outcomes among patients from the cohort who were identified as eligible for the intervention, but were not offered the intervention and not contacted about the intervention.

In the context of rare diseases, the advantage of the cmRCT design to conduct multiple trials that draw participants from the same patient cohort is particularly important given the difficulty of recruiting a sufficiently large patient group for any single trial. No single trial will adequately address the psychosocial and rehabilitation needs of patients with a rare disease, such as SSc. The cmRCT design will enable the implementation of multiple trials over time with different inclusion and exclusion criteria, which, together, have much greater potential in this regard.

In many areas of research, interventions are tested in isolation, typically including different patient groups by different research teams. The cmRCT design allows for tests of interventions that can be compared in the same overall population with similar trial methods, thus increasing the ability to compare and contrast different trial results. Furthermore, whereas the ability to collect long-term outcomes is often limited in single RCTs, core patient measures are assessed on an ongoing basis in the cmRCT model. Thus, key outcomes can be obtained over a long period post-trial for patients who participate in trials.

The cmRCT design also offers advantages in that the patient consent process more closely replicates what occurs in actual healthcare settings compared with the consent procedures typically used in traditional RCT designs. In traditional RCTs, patients are usually told that they will be randomised to obtain the trial intervention or an alternative, which in pragmatic trials of psychosocial and rehabilitation interventions is generally usual care. In real-life healthcare situations, patients are only told of treatments that their healthcare provider can provide with certainty, and they are not told that the treatment they receive will be decided by chance. In the cmRCT design, patients are told about treatments that they will be able to access if they so choose.[33] As part of the initial consent process, patients are made aware that a number of trials may occur via the cohort, and that they will not likely be offered to participate in all of them and may not be offered to participate in any. It is explained that patients will only be notified about trials for which they will be offered the intervention, but that their data may be used for comparison purposes in the context of some interventions not offered to them.

Beyond increasing the ecological validity of the recruitment and consent process itself, it is possible that the cmRCT approach may increase the representativeness of trial participants, and thus the generalisability of results. Indeed, concerns about information and consent are the most common reasons for patients not participating at all in traditional RCTs.[35] These concerns likely play a role in the relatively low trial participation rates and may reduce the ecological validity of trials if patients who consent to participate comprise a small and qualitatively different group than the overall patient population who will receive the intervention in practice. Because the cmRCT design collects data on patients before they have accepted or refused the intervention, the cmRCT design also allows for collection of important information about the reasons that patients refuse an intervention and why certain patients were unable to complete the assigned intervention. This information is valuable both for assessing the validity of modelling assumptions and for predicting the success of the intervention in the general population.

In many pragmatic trials of psychosocial and rehabilitation interventions patients who consent to participate in a trial may do so because they would like the opportunity to receive the trial intervention rather than treatment as usual. Patients cannot usually be fully blinded regarding whether treatment has been offered. Therefore, patients randomised into the 'treatment as usual' arm, may be disappointed and some may even withdraw from the study, leading to attrition bias that might influence the results of the trial. This disappointment can also influence the perception of care and reporting of trial outcomes for patients who do not withdraw, but who are aware that they did not receive the treatment.[36] In the cmRCT design, patients will be aware when they do receive an intervention, but not when they have not been selected for an intervention trial, thus, potentially reducing the possibility of disappointment bias.

The use of the cmRCT design by SPIN to facilitate research on non-pharmacological interventions for people with SSc is feasible due to the international, multicentre nature of the network, which will facilitate the inclusion of a sufficient number of patients with SSc in the SPIN Cohort. Initially, the SPIN Cohort will be used to describe and better understand the nature of problems that have been identified by people with SSc as important[16 28] and to determine optimal outcome measures to use in SPIN intervention trials. Once SPIN interventions are developed, patients eligible for a given trial will be identified based on trial-specific criteria using core SPIN Cohort measures (see online supplementary appendix 1), and a random selection of these eligible patients will be offered the trial intervention (figure 1). In the SPIN Cohort, patients can participate in one SPIN intervention at the time, but may be offered to participate in more than one SPIN intervention sequentially. Core outcomes (25–30 min to complete) will be assessed every 6 months with brief 3-month assessments (5 min to complete) in between. For patients who are eligible for a SPIN intervention trial and are assigned to the intervention or control groups, the 3-month assessment will also include trial-specific measures. Since determination of trial eligibility will be automated using routinely collected cohort measures, all patients who are eligible for an active SPIN trial at a given point in time will automatically be administered the trial-specific measures.

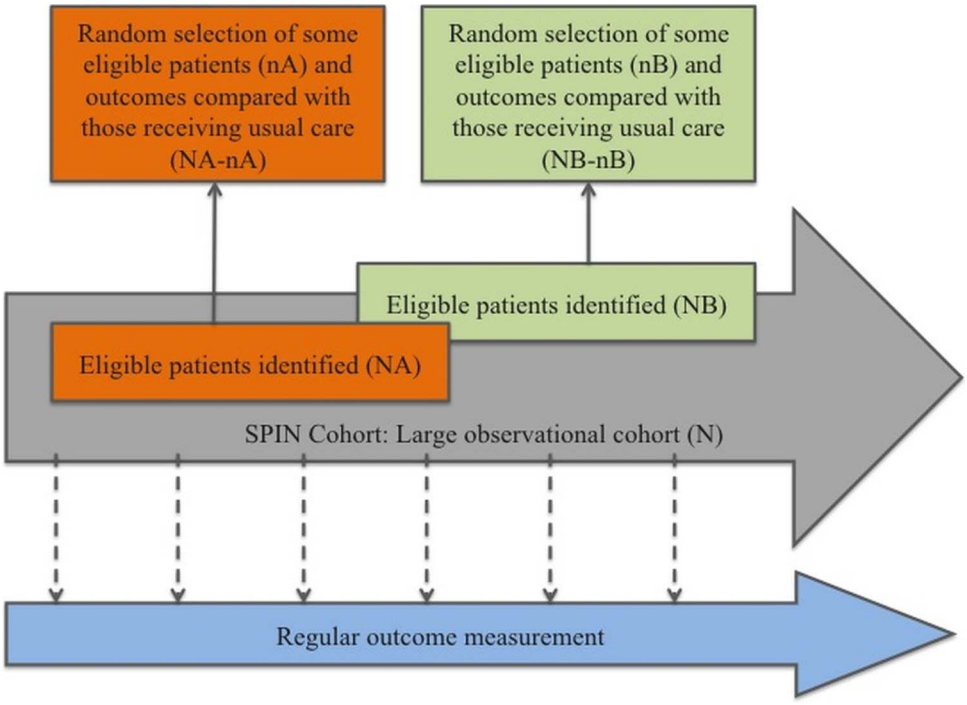

Figure 1 Outline of the cohort multiple randomised controlled trial design.

Study sample

We expect to initially recruit 1500–2000 patients for the SPIN Cohort from SPIN centres in Canada, the USA, France, the Netherlands, the United Kingdom, Spain, Mexico and Australia over a period of 5 years (2013–2018). Eligible participants will include patients ≥18 years of age who have been identified by a SPIN physician as having a diagnosis of SSc. Exclusion criteria for participation in the SPIN Cohort include having a medical disorder that compromises the ability to give informed consent, not having access to or not being able to respond to questionnaires via the internet, and not being able to respond to questionnaires in an available SPIN language (currently English, French, Spanish and Dutch).

Procedure

SSc patients treated by SPIN physicians will be recruited for the SPIN Cohort at their site, and their written informed consent will be obtained. The local participating SPIN physician, or supervised nurse coordinator, will complete a Medical Data form (see online supplementary appendix 2). This form will be submitted online to initiate patient registration in the SPIN Cohort. After completion of registration by a recruiting SPIN physician, an automated welcoming email will be sent to participants with instructions to complete the SPIN patient measures online. Two weeks prior to each 3-month follow-up, participants will receive an email reminding them to go online and complete their forms. On the date of the follow-up assessment, a second notification email will be sent to patients, reminding them to complete the questionnaires online. If 1 week after the assessment date the questionnaire has not yet been completed, an SPIN investigator will contact the patient to encourage them to go online and complete the forms. If a patient has not filled out the questionnaires within 2 weeks after the assessment date, their data will not be collected for that assessment cycle. Patients who do not complete forms at a particular SPIN Cohort assessment are eligible to continue in the SPIN Cohort and will be contacted for subsequent assessments. If patients do not complete four consecutive assessments, they will be considered to have dropped out of the SPIN Cohort.

Measures

Medical information is obtained at baseline, and SPIN Cohort participants will complete a core set of six measures online every 6 months. The core measures include measures of overall health status and functional disability, as well as measures of patient outcomes that will be targeted by the initial set of SPIN interventions that are under development (emotional distress, body image concerns, hand function, disease self-management). Additional measures will be integrated into the SPIN Cohort periodically for the purpose of conducting measurement-related substudies (with a total of 25–30 min to complete). The core measures will determine eligibility for SPIN feasibility trials and subsequent full-scale trials, once initiated. At the 3-month interval between two core measurement occasions, a brief assessment of HRQL will be completed (5 min to complete). For patients who are eligible for a SPIN intervention trial (in both the intervention and control arms), this 3-month measurement will include trial-specific measures related to the trial outcomes of interest.

Medical data

At the time of enrolment, recruiting SPIN physicians will obtain and record basic demographic and medical data from patients' medical records. Medical information will be recorded on a standardised form (see online supplementary appendix 2) and will include height, weight, date of onset Raynaud's phenomenon and first non-Raynaud's symptom, date of SSc diagnosis, disease subtype, presence of autoantibodies, skin involvement, presence of digital ulcers and pitting scars, joint involvement, organ involvement and the presence of an overlap syndrome.

Core measures

Overall health status will be assessed with the Patient Reported Outcomes Measurement Information System-29 (PROMIS-29)[37] and functional disability from SSc with the Scleroderma Health Assessment Questionnaire (SHAQ).[38] Depressive symptoms will be assessed with the Patient Health Questionnaire-8 (PHQ-8).[39–41] Body image concerns due to changes in appearance from SSc will be assessed with the Satisfaction with Appearance Scale (SWAP).[42–44] The Cochin Hand Function Scale[45] will be used to measure limitations in hand function. Self-efficacy for coping and disease self-management will be measured using the Self-Efficacy for Managing Chronic Disease Scale.[46] Further information on each measure is available in online supplementary appendix 1.

Analysis plan

Sample size

We aim to recruit 1500–2000 patients for the SPIN Cohort. This number will be sufficient to conduct longitudinal research on problems identified by patients with SSc as important to them and to determine the best way to measure outcomes related to these problems. We also expect this to be a sufficient number to identify and recruit eligible patients to participate in future SPIN trial studies, allowing us to conduct randomised controlled trials with sufficient statistical power. Sample size calculations for SPIN trials will be determined for each SPIN trial separately, and the appropriate sample size calculations will be provided in all trial protocols.

SPIN Cohort

Initially, SPIN Cohort data will be used to gain a better understanding of problems identified by patients as important to them (eg, body image, physical limitations and HRQL) via observational studies and to conduct measurement studies to determine the best way to measure outcomes related to these problems. All studies that use data from the SPIN Cohort for these purposes will be required to submit a proposal to the SPIN Data Access and Publications Committee (see below). This committee will ensure that all study designs are appropriate and that investigators adhere to a priori defined study and analysis plans.

Feasibility trials

Consistent with current best practice recommendations for intervention development and testing,[11–13] feasibility trials for all SPIN interventions will be conducted via the SPIN Cohort to ensure that trial methodology is sound, feasible and consistent with patient expectations.[11–13] Data will be collected to review the process (eg, feasibility of steps that need to take place in the full-scale study), required resources (eg, time and budget), management issues (eg, related to optimising performance of personnel and data systems) and scientific aspects (eg, recruitment rates of eligible patients, acceptability of intervention to patients and assessing performance of outcome measures). For each intervention, semistructured interviews will be conducted with 15–20 randomly selected participants to assess the acceptability, utility and practicality of intervention components, and usefulness of proposed study outcome measures. Interviews will be conducted using established methods for qualitative process evaluation of trials as developed by Donovan *et al*.[47] We will use a topic guide to ensure consistency across participants, but with a flexible format to allow participants to generate naturalistic data related to their experience and on what they consider as important and/or successful in terms of treatment outcomes. For all SPIN interventions, feasibility study results will be used to refine the methodology and analysis plans for the full-scale RCTs.

Full-scale RCTs

In traditional RCTs, the effectiveness of an intervention may be assessed using per-protocol analysis, which includes only those patients who successfully completed the treatment originally allocated, or an intention-to-treat analysis (ITT), which compares patients in the groups to which they were originally allocated after randomisation, irrespective of whether or not the patient received or completed the allocated treatment. ITT is widely recommended as the preferred analysis, since it addresses the effectiveness of the intervention for all patients who agree to attempt the treatment, rather than only for patients who successfully complete it, as with per-protocol analysis. The primary analysis for SPIN trials will be ITT, comparing the outcomes of randomly selected patients who are offered the intervention, to eligible patients who were not offered the intervention.

In the cmRCT design, however, randomisation occurs prior to offer of intervention, and some number of eligible patients who are randomly selected to be offered an intervention will not accept the offer. In addition to ITT analysis, it is of interest to assess the effect of an intervention among patients who accept the offer. Ideally, we would compare outcomes for patients who accept the offer of the intervention to patients who are not offered the intervention, but would have accepted if they had received an offer. This is because patients who agree to attempt an intervention may be different in important ways from patients who decline the offer of

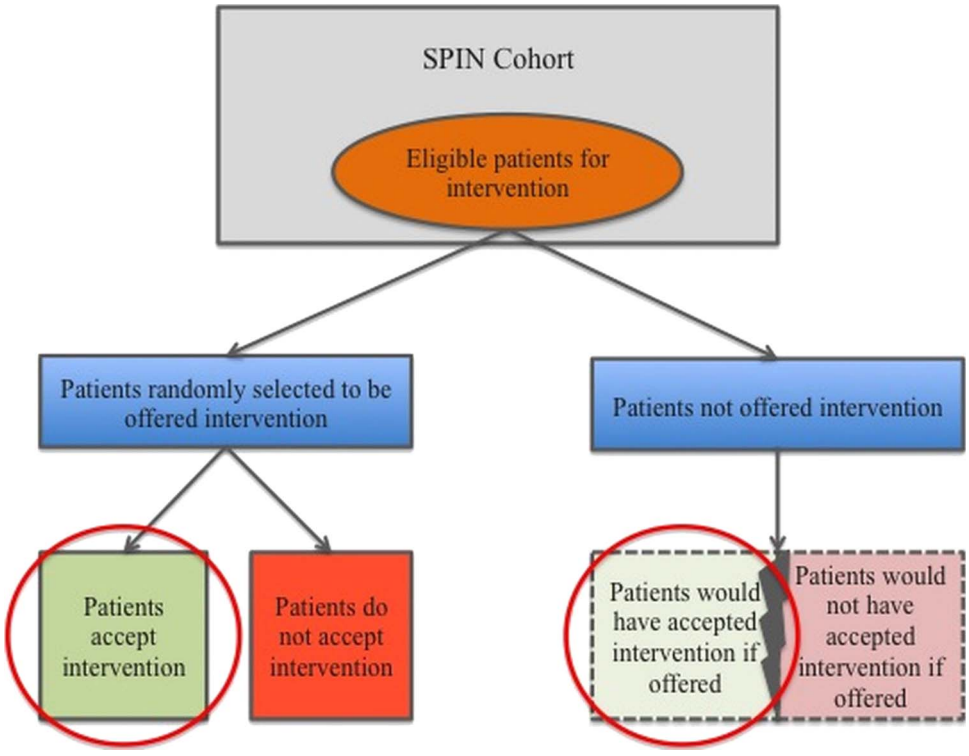

Figure 2 Outline of complier average causal effect analysis in the cohort multiple randomised controlled trial design.

an intervention. Because we cannot actually know which patients who are not offered the intervention would have accepted if offered, we will use Complier Average Causal Effect (CACE) analysis[48 49] to make this comparison, as a secondary analysis for SPIN trials. CACE assumes that the proportion of patients in the non-offer group who would have refused the offer is the same as for the group who were offered the intervention. Furthermore, CACE assumes that outcomes are the same among patients who refuse the intervention and patients who would have refused the intervention, if offered. On this basis, an intervention effect can be estimated that compares patients in the offer group who accepted the intervention offer to patients in the non-offer group who would have accepted the intervention if offered (see figure 2).

All SPIN full-scale trials will be registered[50] and will be conducted and reported in accordance with standards articulated in the Consolidated Standards of Reporting Trials (CONSORT) Extension for Non-pharmacological Trials.[51 52] A study protocol for each full-scale trial will be published, describing the study design and content of the SPIN intervention.

ETHICS AND DISSEMINATION

The study will be conducted in compliance with the principles of the Declaration of Helsinki (2008) and other major ethical guidelines of participating sites, including Canada's Tri-Council Policy Statement (2010).

In the cmRCT design, individuals consent to participate in a cohort for ongoing data collection and to allow their data to be used for comparison purposes with patients from the cohort who may be offered to participate in trials that are conducted within the SPIN Cohort. At the time of recruitment, written informed consent will be obtained. The local recruiting SPIN physician, or supervised nurse coordinator, will explain the nature and purpose of the Cohort and provide the participants with a copy of the consent and information sheet. Recruiting SPIN physicians will provide a description of SPIN and explain that agreeing to participate in the SPIN Cohort will involve (1) giving the physician or supervised nurse coordinator permission to complete the SPIN baseline Medical Data form, using information from the patient's medical record; (2) being contacted by email with instructions on how to complete SPIN patient measures via the internet at the time of enrolment and periodically going forward (every 3 months); (3) providing permission for their data to be used to select them for participation in trials or for comparison purposes for SPIN intervention trials that may be conducted while they are participating in the SPIN Cohort and (4) giving permission for SPIN investigators to contact them with an invitation to participate in SPIN interventions once developed. Patients will be informed that participation in the SPIN Cohort will not affect their usual care in any way. They will also be informed that only patients who are randomly selected to be offered an intervention will be contacted about the intervention. Finally, it is explained that patients'

current consent is only for participation in the SPIN Cohort, and that separate consent will be sought for participation in a particular SPIN intervention.

Data management and security

All data are entered into a centralised secure electronic data management system designed, managed and located at the *Data Management Unit of the Centre for Clinical Epidemiology, Lady Davis Institute for Medical Research, Jewish General Hospital, Montreal Quebec, Canada*. To protect the participants' privacy, before the recruiting SPIN physician at each centre enters the medical data, a unique patient identification number will automatically be assigned to each participant. Only de-identified data will be recorded in the database, with linking data available only to the SPIN Director. Only personnel authorised by the SPIN Director will be allowed to retrieve, enter or change data from the central database, and the database will be audited for any changes that are made. All data will be kept for 10 years after completing the cohort study for ethical and scientific reasons.

Study management

SPIN was awarded a 5-year Emerging Team Grant for Rare Diseases from the Canadian Institutes of Health Research to fund the SPIN Cohort (Funding Reference Number TR3–119192; Principal Investigator, Brett D. Thombs; 2012–2017). In addition to this funding, SPIN has received institutional contributions from the Lady Davis Institute for Medical Research of the Jewish General Hospital, Montreal, Canada, for database development and from McGill University, Montreal, Canada for student training. Previously, SPIN received funds from the Scleroderma Society of Canada, the Scleroderma Society of Ontario and Sclérodermie Québec for developmental work.

SPIN's organisational structure is depicted in figure 3. The *SPIN Steering Committee* is responsible for review of the SPIN project direction and coherence, including being informed and advising on Cohort recruitment/retention and intervention development, feasibility and full-scale testing of interventions; reviewing and approving proposals for SPIN publications; being informed of the financial well-being of the project; and helping to resolve administrative issues.

The *SPIN Advisory Board* is directed by and largely comprised of people living with SSc, supported by expert consultants. The Advisory Board will (1) review the overall SPIN project and individual SPIN intervention projects and (2) advise the Steering Committee so that SPIN maximally reflects the needs of people with SSc and ensures successful knowledge transfer within the SSc community and with the broader rare disease community.

Each *SPIN project team* has a leader, coleader(s), and a multidisciplinary group of investigators, including at least two SSc patients. Project teams, supported by the Steering Committee and SPIN Cores (see below), will design and test SPIN interventions and work with patient organisations to facilitate delivery of tested interventions.

SPIN Cores work closely with project teams to support high-quality investigative work and successful knowledge transfer. SPIN Cores provide expertise in information technology for delivering patient-centred healthcare services; data management; research methods and biostatistics; measurement of patient-oriented outcomes in SSc; health economics; knowledge transfer; and bioethics.

The *SPIN Data Access and Publication Policy* describes the procedures that will be used to ensure the scientific integrity of publications that emerge from SPIN. The policy ensures that responsibility and credit for SPIN publications as well as standard authorship requirements

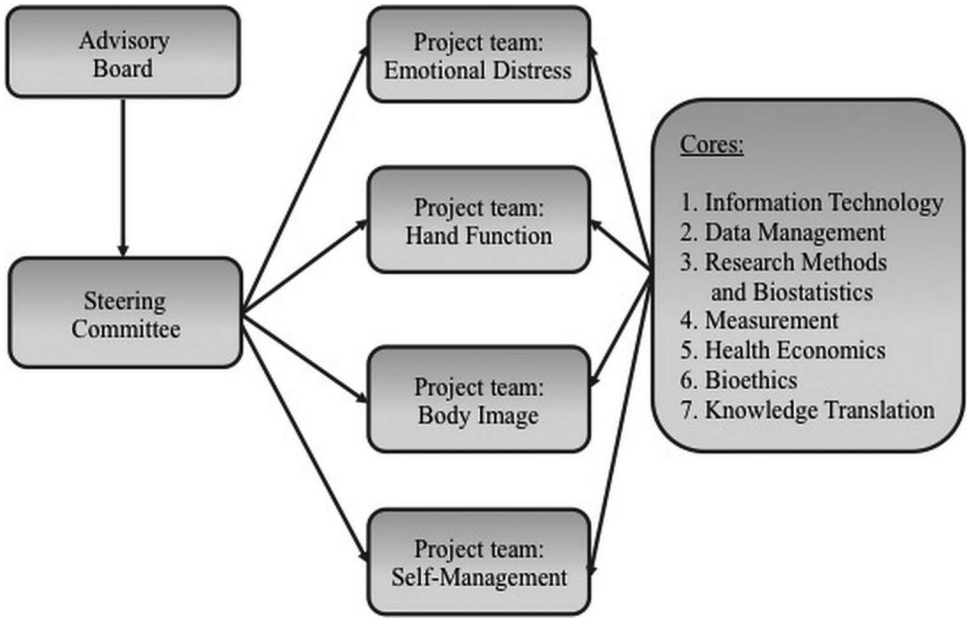

Figure 3 Scleroderma patient-centred intervention network organisational structure.

(eg, International Committee of Medical Journal Editors) are met. Proposals to conduct analyses using SPIN data must be submitted by a SPIN investigator for review to the Data Access and Publication Committee. The Committee will ensure that proposed analyses do not overlap with existing proposals and will review the proposed methods, in consultation with the SPIN Cores. It is anticipated that, at the appropriate time, access to SPIN data will be open to other investigators, consistent with the policies of the Canadian Institute of Health Research.[53] Prior to providing access to de-identified SPIN data to non-SPIN investigators, a Data Sharing Plan describing the data sharing procedures will be written and submitted for ethics approval to the Research Ethics Committee of the Jewish General Hospital in Montreal, Quebec, Canada.

DISCUSSION

Until recently, the inability to conduct rigorous, adequately powered trials of psychosocial and rehabilitation interventions in rare diseases has been a barrier to the development of evidence-based patient-centred care for people with rare diseases. The novel cmRCT design[33] that will be utilised by SPIN is a promising approach to move forward research in this area. It will allow SPIN to both collect important observational data in a longitudinal cohort and to conduct multiple pragmatic RCTs in the same cohort.

The use of the cmRCT design in SPIN is highly feasible due to its international multicentre nature. The features of the cmRCT design make it a good option for conducting research in the context of rare chronic diseases, as well as comparing psychosocial and rehabilitation interventions to treatment as usual in pragmatic trials. There may be a number of circumstances, however, in which the cmRCT design is less suitable.[33] These include, for instance, acute or short-term conditions, double-blinded trials with a placebo arm and treatments for which the uptake by patients may be low. In addition, the use of relatively easy obtainable patient-reported outcomes, as in the SPIN Cohort, facilitates research using the cmRCT design, compared to more expensive and time-intensive measures such as conducting laboratory tests, which would not be feasible in the context of the cmRCT.

The end goal of SPIN is to make psychosocial and rehabilitation interventions available through patient organisations. The collaboration of investigators with patient organisation partners has been crucial in the establishment of SPIN. Prior to launching SPIN, a series of projects were conducted in collaboration with patients from organisations across Canada (eg, Scleroderma Societies of Canada and Ontario, Sclérodermie Québec, the Scleroderma Association of British Columbia), the USA (USA Scleroderma Foundation) and Europe (Federation of European Scleroderma Associations), which has helped to better understand important problems faced by persons living with SSc and to prioritise gaps in access to psychosocial and rehabilitation services.[16 25 54] Each of the proposed SPIN interventions is grounded in this work, and integrated knowledge transfer will play a major role in developing, adapting and disseminating interventions to best address the needs of persons with SSc. Patient advocacy organisations have committed to working with SPIN on an ongoing basis to ensure that the interventions developed by SPIN will be made available to patients once developed and tested.

In summary, SPIN is a unique endeavour to develop and test psychosocial and rehabilitation care interventions in SSc and to make these interventions accessible through patient organisations around the world with a low ongoing cost. Unique features of SPIN, including the use of the cmRCT design, the development of self-guided online interventions delivered using a common platform, and a robust partnership with patient organisations, may serve as a model to help facilitate research in this area for other rare diseases as well.

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Contributors LK and LRJ participated in the design of the study and its coordination and contributed to drafting the manuscript. BDT conceived the study, participated in its design and coordination, and contributed to drafting the manuscript. MB, SJB, DF, KG, DK, VLM, MDM, LM, SP, MS, WRN, JLP, SA, IB, CE, CHME, MH, AI, AK, CL, ACM, CF, JP, RJS, MESA, SA, SCM, VCD, SG, YJ, BL, KM, SM, IR and RS participated in the design of the study and revised the manuscript critically. All authors read and approved the final version of the manuscript.

Funding SPIN is funded by a Canadian Institutes of Health Research (CIHR) Emerging Team Grant for Rare Diseases (PI, Thombs; TR3–119192). In addition to CIHR funding, SPIN has received institutional contributions from the Lady Davis Institute for Medical Research of the Jewish General Hospital, Montreal, Canada and from McGill University, Montreal, Canada. The initial organisational meeting for SPIN was funded by a CIHR Meetings, Planning, and Dissemination grant to BD Thombs (KPE-109130), Sclérodermie Québec, and the Lady Davis Institute for Medical Research of the Jewish General Hospital, Montréal, Québec. SPIN has also received operating support from the Scleroderma Society of Ontario, the Scleroderma Society of Canada and Sclérodermie Québec. SPIN's funders did not have any role in the design, collection, analysis or interpretation of data; in the writing of the manuscript; or in the decision to submit the manuscript for publication.

Competing interests DK has served as a consultant, steering committee member, or on speaker bureaus for Actelion, BMS, Bayer, DIGNA, InterMUne, Gilead, Roche and United Therapeutics. SP has served as a consultant for Pfizer, BMS and Sanofi-Aventis. BDT and MH are supported by New Investigator awards from the CIHR. MDM and SA are supported by the NIH/NIAMS Scleroderma Center of Research Translation grant no. P50-AR054144. DK is supported by a NIH/NIAMS U01 AR057936A, the National Institutes of Health through the NIH Roadmap for Medical Research Grant (AR052177). LK is supported by a Fonds de la Recherche en Santé Québec (FRSQ) postdoctoral fellowship. LJ, VD, KM and IR are supported by a CIHR Doctoral Research award. BL is supported by a FRSQ Master's Training award.

Ethics approval The SPIN Cohort has received ethical approval from the Research Ethics Committee of the Jewish General Hospital in Montreal, Quebec, Canada. Ethical approval for the SPIN Cohort will also be obtained from the local Institutional Review Boards of all participating sites prior to recruitment of patients from the sites.

Provenance and peer review Not commissioned; internally peer reviewed.

Data sharing statement It is anticipated that, at the appropriate time, access to SPIN data will be open to other investigators, consistent with the policies of the Canadian Institute of Health Research. Prior to providing access to de-identified SPIN data to non-SPIN investigators, a Data Sharing Plan describing the data sharing procedures will be written and submitted for ethics approval to the Research Ethics Committee of the Jewish General Hospital in Montreal, Quebec, Canada.

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