Nurse geleitetes Immuntherapie-Entscheidungscoaching für Menschen mit Multipler Sklerose (decision coaching in multiple sclerosis, DECIMS) – Entwicklung und Pilotierung einer komplexen Intervention.

(Nurse-led immunotreatment decision coaching in multiple sclerosis (DECIMS) – development and piloting of a complex intervention)

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Sharing decisions with patients is not an add-on,
it is the whole meaning of the exercise.
(Richard Lehman 2016)

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I. Arbeiten der Dissertation

- **Rahn AC**, Köpke S, Kasper J, Vettorazzi E, Mühlhauser I, Heesen C (2015) Evaluator-blinded trial evaluating nurse-led immunotherapy DEcision Coaching In persons with relapsing-remitting Multiple Sclerosis (DECIMS) and accompanying process evaluation: study protocol for a cluster randomised controlled trial. *Trials,* 16: 106.

- **Rahn AC**, Backhus I, Fuest F, Riemann-Lorenz K, Köpke S, van de Roemer A, Mühlhauser I, Heesen C (2016) Comprehension of confidence intervals - development and piloting of patient information materials for people with multiple sclerosis: qualitative study and pilot randomised controlled trial. *BMC Medical Informatics and Decision Making*, 16(1): 122.

- **Rahn AC,** Köpke S, Backhus I, Kasper J, Anger K, Untiedt B, Alegiani, A, Kleiter I, Mühlhauser I, Heesen C (2017) Nurse-led immunotreatment DEcision Coaching In people with Multiple Sclerosis (DECIMS) − feasibility testing, pilot randomised controlled trial and mixed methods process evaluation. *International Journal of Nursing Studies*. doi:10.1016/j.ijnurstu.2017.08.011.

- Brand J, Köpke S, Kasper J, **Rahn A**, Backhus I, Pöttgen J, Stellmann JP, Siemonsen S, Heesen C (2014) Magnetic resonance imaging in multiple sclerosis - patients' experiences, information interests and responses to an education Programme. *PLoS One,* 9, e113252.

- Kasper J, van de Roemer A, Pöttgen J, **Rahn A,** Backhus I, Bay Y, Köpke S, Heesen C (2017) A new graphical format to communicate treatment effects to patients - A web-based randomized controlled trial. Health Expectations, 20(4): 797-804.

- **Rahn AC**, Köpke S, Schiffmann I, Stellmann JP, Mühlhauser I, Lukas C, Chard D, Heesen C (2017) Magnetic resonance imaging as a prognostic disability marker in clinically isolated syndromes: A systematic review. (eingereicht)

- **Rahn AC**, Backhus I, Riemann-Lorenz K, Köpke S, van de Roemer A, Vettorazzi E, Mühlhauser I, Heesen C (2017) Comprehension of confidence intervals in audio-visual patient information materials for people with multiple sclerosis (COCO-MS): a web-based randomised controlled, parallel group trial. (Manuskript in Vorbereitung)

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III. Abkürzungen

DECIMS	Decision coaching in multiple sclerosis
EBPI	Evidenzbasierte Patienteninformation
MRC	UK Medical Research Council
MRT	Magnetresonanztomographie
MS	Multiple Sklerose (MS)
SDM	Shared decision-making
RCT	Randomisiert kontrollierte Studie (randomised controlled trial)

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1. Zusammenfassung

Die Dissertation besteht aus drei, zur kumulativen Dissertation angenommenen Artikeln, zwei weiteren publizierten Artikeln sowie zwei weiteren Arbeiten unter der Erstautorenschaft der Autorin, deren Publikation in Vorbereitung ist.

Der Kern dieser Dissertation ist die Entwicklung und Pilotierung eines MS-Nurse[1] geleiteten Entscheidungscoachings für Menschen mit Multipler Sklerose (decision coaching in multiple sclerosis, DECIMS). Das Decision Coaching-Programm besteht aus einer Schulung von Multiple Sklerose-Nurses zum Decision Coach und der Coaching-Intervention selbst. Die komplexe Coaching-Intervention setzt sich aus mehreren Komponenten zusammen: bis zu drei Decision Coaching-Sessions pro Multiple Sklerose-Betroffenem, einer evidenzbasierten Online-Informationsplattform zur Multiplen Sklerose (DECIMS-Wiki) und einem abschließenden Arztgespräch. Ziel des Coaching-Programms ist die Förderung der gemeinsamen informierten Entscheidungsfindung bei Multipler Sklerose sowie in diesem Zusammenhang die Übernahme der entscheidungsvorbereitenden Beratung zu Immuntherapieoptionen durch weitergebildete MS-Nurses. Das Studienprotokoll (Arbeit eins) bildet den Grundstein für das wissenschaftliche Vorgehen nach den Kriterien des UK Medical Research Council zur Erstellung und Evaluation von komplexen Interventionen. Im Vordergrund des Protokolls stehen die Beschreibung des Programms und die Planung der Evaluation durch eine cluster-randomisierte kontrollierte Studie mit begleitender Prozessevaluation. Weiter wird im Protokoll die Machbarkeitstestung durch die randomisiert kontrollierte Pilotstudie adressiert. Die Pilotstudie (Arbeit drei) mit begleitender Mixed-Methods Prozessevaluation zeigt, dass die Coaching-Intervention umsetzbar ist. Insgesamt wurde die Intervention von den Nurses, MS-Betroffenen und Ärzten positiv angenommen. Allerdings lag einer von vier Nurses die Übernahme der Beratungsrolle nicht und fehlende Daten limitieren die Interpretation der Ergebnisse.

Weitere Arbeiten adressieren grafische Darstellungsmöglichkeiten von Studienergebnissen und die Entwicklung und Evaluation von Patienteninformationen, um das Verständnis dieser zu fördern. In einer randomisiert kontrollierten Studie (Arbeit fünf) wurden neu entwickelte Balkengrafiken zur Risikokommunikation evaluiert, die ein wichtiger Teil im DECIMS-Wiki sind. Zwei weitere Arbeiten (zwei und sieben) adressieren die Entwicklung und Evaluation von Patienteninformationen für Multiple Sklerose-Betroffene zum Thema Konfidenzintervalle. In einer randomisiert kontrollierten Studie konnte gezeigt werden, dass die audiovisuellen

[1] Im DECIMS Projekt umfasst der Begriff MS-Nurse Angehörige der Gesundheitsfachberufe, die tiefergehende Multiple Sklerose-Kenntnisse gewonnen haben.

Informationen verständlich sind. Die Videos können über das DECIMS-Wiki abgerufen werden.

Auf zwei Arbeiten zur Magnetresonanztomographie, dem bedeutendsten diagnostischen und prognostischen Marker bei der Multiplen Sklerose, basieren wichtige Inhalte des Coaching-Programms. Auf der Grundlage eines pilotierten Schulungsprogramms zur Magnetresonanztomographie für Multiple Sklerose-Betroffene (Arbeit vier) wurde ein Modul zur Magnetresonanztomographie für den Decision Coach-Trainingskurs entwickelt. Ein systematisches Review (Arbeit sechs) widmet sich der prognostischen Bedeutung der Magnetresonanztomographie hinsichtlich der Entwicklung einer Beeinträchtigung für Personen mit einem Verdacht auf Multiple Sklerose. Das Review zeigt, dass es einen Zusammenhang zwischen mehr als zehn Läsionen im Magnetresonanztomographie-Bild und der Zunahme der Beeinträchtigung gibt. Die Ergebnisse des Reviews wurden für das Decision Coaching aufbereitet.

Zusammenfassend wurde das Decision Coaching-Programm erfolgreich pilotiert und hat das Potenzial informierte Entscheidungen zu fördern. Allerdings zeigten sich im weiteren Evaluierungsverlauf Barrieren, die es zu adressieren gilt, um die Wirksamkeit des Ansatzes zu zeigen.

2. Abstract

The dissertation consists of the three articles accepted for the cumulative dissertation, two further published articles as well as two manuscripts under the authorship of the author, which have not yet been published.

The core of this dissertation is the development and piloting of the nurse-led immunotherapy decision coaching programme for people with multiple sclerosis (DECIMS). The decision coaching programme consists of a decision coach training course for multiple sclerosis nurses and the coaching intervention. The complex intervention has multiple components: up to three decision coaching sessions per person with multiple sclerosis by a trained nurse, an evidence-based online information platform on multiple sclerosis (DECIMS-Wiki) and a completing physician consultation. The aim of the coaching programme is to facilitate informed shared decision-making in multiple sclerosis and in this context transferring counselling on immunotreatment decision-making to trained MS-Nurses as a preparation of the decision. The study protocol (article one) outlines the research process concept according to the UK Medical Research Council guidance for the development and evaluation of complex interventions. Here, the description of the programme and the planned evaluation by a cluster randomised controlled study with accompanying process evaluation are focused. Further, the randomised controlled pilot study is addressed in the protocol in order to test the programme for feasibility. The randomised controlled pilot study (article three) with accompanying mixed methods process evaluation shows that the decision coaching intervention is feasible. Overall, the intervention was positively accepted by nurses, people with multiple sclerosis and physicians. However, one of four nurses did not like the role of counselling and results are limited by some missing data.

Further work addresses different graphical formats to present study results and the development and evaluation of patient information materials in order to facilitate comprehension of these. Newly developed bar graphs for risk communication were evaluated in a randomised controlled trial (article five), which are an essential part of the DECIMS-Wiki. Further articles (two and seven) address the development and evaluation of patient information materials on confidence intervals for people with multiple sclerosis. The evaluation by a randomised controlled trial showed that the audiovisual information versions are comprehensible. The videos can be accessed via the DECIMS Wiki.

Studies on magnetic resonance imaging, the most vital diagnostic and prognostic marker in multiple sclerosis, provide important content for the coaching programme. A module on magnetic resonance imaging was developed for the decision coach training course based on a piloted training programme on magnetic resonance imaging for people with multiple

sclerosis (article four). A systematic review on the prognostic value of magnetic resonance imaging with regard to the development of disability for people with suspected multiple sclerosis showed that there is an association between more than ten T2 lesions and future disability (article six). The results of the review were processed for the decision coaching sessions.

In conclusion, the nurse-led decision coaching programme was successfully piloted und shows the potential to facilitate informed choices. However, further evaluation revealed barriers, which have to be addressed to show the efficacy of this approach.

3. Einleitung

Multiple Sklerose (MS) ist eine chronische degenerative Erkrankung, die meist im frühen Erwachsenenalter beginnt und sehr variabel verläuft. MS geht häufig mit fortschreitender Behinderung einher und verläuft bei circa 85 Prozent der Betroffenen anfänglich in Schüben [1].

Bereits ab der Verdachtsdiagnose, dem klinisch isolierten Syndrom [2], sind MS-Betroffene erheblichen Unsicherheiten ausgeliefert, von der Diagnosestellung, über die Prognose bis zum Nutzen von Schub- und Immuntherapien. MS-Betroffene nutzen intensiv das Internet [3, 4]. Sie wünschen sich eine aktive Rolle im Entscheidungsprozess zu Immuntherapien [5] und geprüfte, online verfügbare Informationen [6]. Verschiedene Quellen mit unterschiedlichen Interessenshintergründen und zahlreiche berichtete Negativerfahrungen aus dem Versorgungsalltag verstärken hier möglicherweise Unsicherheiten.

Während der letzten zwei Dekaden wurden für die schubförmige MS zahlreiche Medikamente zugelassen [7]. Alleine für dieses Jahr werden zwei neue Zulassungen (Ocrelizumab und Cladribin) erwartet und in der Regel wird MS-Betroffenen bereits ab der Verdachtsdiagnose eine Therapie empfohlen [7]. Vor dem Hintergrund immer komplexer werdender Immuntherapiemöglichkeiten ist eine Beratung zum Nutzen und zu den Risiken der Therapieoptionen essentiell [8], aber kaum noch in einer ärztlichen Konsultation alleine zu leisten. Zusammenfassend führen die Unsicherheiten und zahlreichen Therapieoptionen zu einem erheblichen Informationsbedarf der MS-Betroffenen, der innerhalb der Standardversorgung nicht ausreichend individuell gestaltet abgedeckt werden kann.

Vorangegangene Arbeiten [9, 10] zur Immuntherapieentscheidungsfindung deuten darauf hin, dass die alleinige Bereitstellung von evidenzbasierten Patienteninformationen (EBPI) oder EBPI in Verbindung mit einer Gruppenschulung für MS-Betroffene möglicherweise nicht ausreichen, um eine informierte Entscheidung zu treffen, wenn eine solche ansteht. MS-Betroffene scheinen mehr Zeit und Unterstützung zu brauchen, um die Behandlungsmöglichkeiten zu reflektieren und zu diskutieren. Gruppenschulungen sind hier möglicherweise nicht genügend auf die individuelle Situation der Betroffenen zugeschnitten. Neben der zunehmenden Anzahl an Optionen [8] sprechen der Zeitpunkt, zu dem eine Entscheidung anliegt als auch die oft sehr unterschiedlichen Präferenzen und Werte für ein individualisiertes Coaching.

In Deutschland sollte die medizinische Entscheidungsfindung auf einem Informationsaustausch zwischen mindestens zwei Personen (Patientin bzw. Patient und Behandelnde bzw. Behandelnder) beruhen, wie im „Patientenrechtsgesetz" festgelegt [11].

Dies erfordert die Befähigung der Patienten[2] an gemeinsamen Entscheidungsprozessen teilzunehmen, wofür verständliche und evidenzbasierte Informationen unerlässlich sind [12]. Die informierte Entscheidung wurde kürzlich im Deutschen Ärzteblatt als „eigenständiger patientenrelevanter Endpunkt“ gefordert [13]. Eine individuelle Möglichkeit hierzu bietet das sogenannte Decision Coaching [14]. Im Kern des Decision Coaching-Ansatzes steht die nicht-direktive Entscheidungsbegleitung basierend auf dem Konzept der gemeinsamen Entscheidungsfindung (shared decision-making, SDM) [15] und EBPI [16]. In einer systematischen Übersichtsarbeit [14, 17] basierend auf einem Cochrane Review [18] wurde festgestellt, dass Decision Coaching in Kombination mit Entscheidungshilfen im Vergleich zu Entscheidungshilfen alleine die Beteiligung am Entscheidungsprozess erhöht, Kosten senkt und zu interventionsspezifischen positiven Ergebnissen führt. Besonders vielversprechend sind die Ergebnisse, wenn das Coaching von Nurses angeboten wurde [19–22]. Somit scheinen MS-Nurses die idealen Kandidaten zu sein, ein Decision Coaching zur Vorbereitung des Arztgespräches durchzuführen.

In Deutschland sind MS-Nurses bislang hauptsächlich für die Handhabung und Informationsbereitstellung zu Injektionstherapien etabliert [24]. Die sogenannten MS-Schwestern wurden hierzu im Zuge der Zulassung der ersten sogenannten Immuntherapien von den pharmazeutischen Unternehmen eingeführt. Hierfür haben die Unternehmen Gesundheits- und Krankenpflegende und medizinische Fachangestellte geschult [23].

[2] Zur besseren Lesbarkeit dieser Arbeit schließt der Plural die feminine und maskuline Form gleichermaßen ein.

4. Zielsetzung der Arbeit und Begriffsklärung

Mit durch MS-Nurses geleiteten Decision Coachings wird eine Umstrukturierung der Kompetenzen von Gesundheitsfachpersonal und die informierte Beteiligung von MS-Betroffenen am Entscheidungsprozess zu Immuntherapien angestrebt. Basierend auf den UK Medical Research Council (MRC) Kriterien zur Erstellung und Evaluation von komplexen Interventionen [24] sowie langjährigen Vorarbeiten [9, 25] wurde ein Decision Coaching-Programm entwickelt, pilotiert und evaluiert. In dieser Dissertation werden die Phasen *„Entwicklung“* und *„Machbarkeit und Pilotierung“* des zirkulären Evaluationsmodels adressiert. Zudem wird in der Diskussion auf die cluster-randomisiert kontrollierte Studie (RCT) zur „*Evaluation*“ der Intervention eingegangen (Abbildung 1).

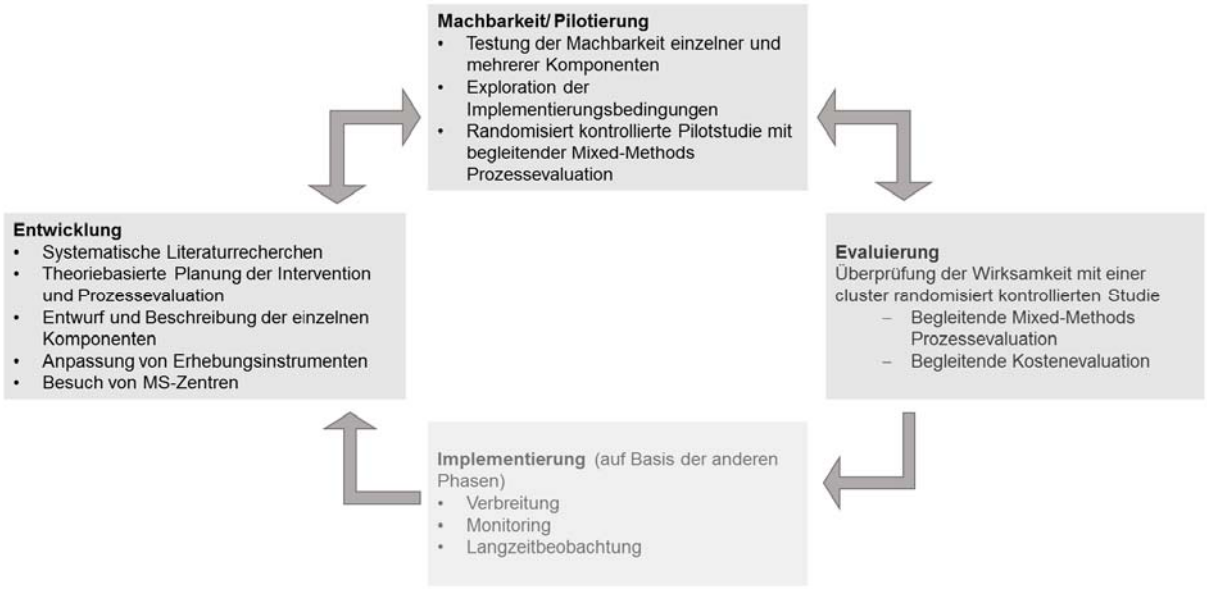

Abbildung 1: Planung des Decision Coaching-Programms nach dem MRC Framework [24]

Im DECIMS Projekt umfasst der Begriff MS-Nurse Angehörige der Gesundheitsfachberufe, wie beispielsweise medizinische Fachangestellte, Gesundheits- und Krankenpflegende und Physiotherapeuten, die durch eine Weiterbildung oder/und langjährige Erfahrung tiefergehende MS-Kenntnisse erworben haben. MS-Betroffene erhalten je nach Bedarf ein bis drei Decision Coachings mit der weitergebildeten MS-Nurse, um die Therapieentscheidung vorzubereiten. Mit der Entscheidungsvorbereitung wird in diesem Projekt ein innovativer Ansatz verfolgt, da die Aufklärung und Beratung des Patienten sowie Entscheidungen über die Therapie in Deutschland nach § 28 Abs. 1 Satz 3 SGB V nicht zu den delegierbaren Leistungen des Arztes gehören [26].

Der Begriff informierte Entscheidung [27] beschreibt eine Entscheidung von MS-Betroffenen über eine mögliche Immuntherapie, die mit adäquatem Wissen und im Einklang mit der Einstellung zur Durchführung einer Therapie getroffen wurde. Eine informierte Entscheidung ist nur auf Basis von evidenzbasierten Informationen zu allen Therapieoptionen möglich. Dazu gehört auch ausdrücklich die Kommunikation der Option, keine Immuntherapie zu beginnen bzw. abzuwarten (Ersttherapie) oder eine bestehende Therapie abzubrechen (Therapiewechsel).

5. Synopsis

Die Dissertation besteht aus fünf publizierten Artikeln sowie zwei weiteren Arbeiten deren Publikation in Vorbereitung ist.

Das Studienprotokoll zur Evaluation der Begleitung von Entscheidungen zur Immuntherapie von Personen mit Multipler Sklerose durch MS-Nurses (Decision-Coaches) ist die erste Arbeit [28]. Im Vordergrund stehen die Beschreibung des Programms und die Planung der Evaluation durch eine Cluster-RCT. Besonderen Raum nimmt hier die Darstellung der begleitend geplanten Mixed-Methods[3] Prozessevaluation zur Evaluation von fördernden Faktoren und Barrieren hinsichtlich des Coaching-Programms ein. Weiter wird auch die Machbarkeitstestung durch die Pilot-RCT beschrieben. Das Studienprotokoll wurde nach der SPIRIT-Checkliste (Standard Protocol Items: Recommendations for Interventional Trials) [29] zur Erstellung von Studienprotokollen verfasst und bildet den Grundstein für das wissenschaftliche Vorgehen nach den MRC Kriterien zur Erstellung und Evaluation von komplexen Interventionen [30].

Da das Verständnis von statistischen Informationen eine Schlüsselfunktion in der Beratung zu Therapieoptionen einnimmt, wurde mit der Erstellung und Evaluation von kurzen Informationsmaterialien zu den wichtigsten statistischen Begriffen begonnen. In der zweiten Arbeit wird daher die Entwicklung und Pilotierung von Patienteninformationen in Form von PowerPoint Präsentationen für MS-Betroffene zum Thema Konfidenzintervalle (Vertrauensbereiche) adressiert [31]. Zudem wurde ein Fragebogen zu Konfidenzintervallen entwickelt und getestet. Betroffenenexperten und MS-Nurses waren am Entwicklungsprozess und der Testung der Machtbarkeit beteiligt. Es wurden drei verschiedene Patienteninformationen entwickelt. In der Kurzversion werden Konfidenzintervalle ohne Beispiel beschrieben, während in den beiden anderen Versionen das illustrative Beispiel eines Apfelfarmers verwendet wurde (Abbildung 2). Der Farmer will in der einen Version („Durchschnittsgewichte“) das durchschnittliche Gewicht seiner Äpfel und in der anderen Version („Apfelbehandlung“) die Wirksamkeit einer Behandlung herausfinden, um den Wurmbefall seiner Apfelbäume zu verhindern. Die qualitative Pilotierung mit 12 MS-Betroffenen zeigt vielversprechende Ergebnisse hinsichtlich der Akzeptanz und Machbarkeit.

[3] Forschungsansatz beim dem qualitative und quantitative Methoden verzahnt werden.

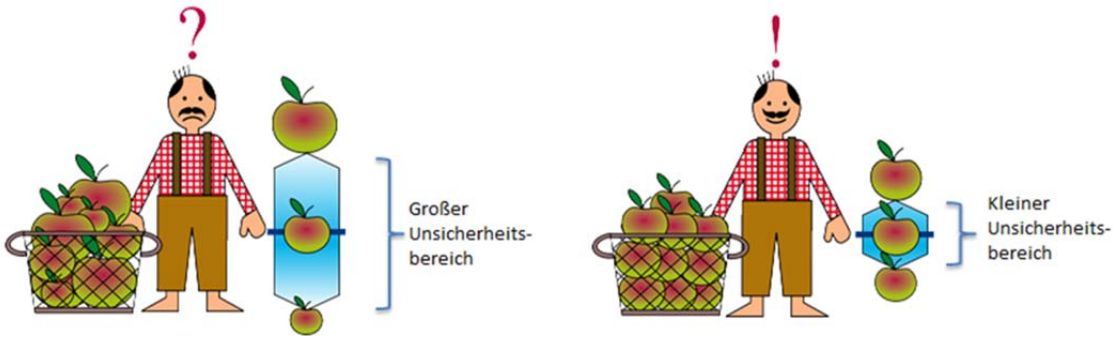

Abbildung 2: Abbildung aus der Version „Durchschnittsgewichte“ [32]

Die Ergebnisse der randomisiert kontrollierten Pilotstudie mit n=64 Teilnehmern weisen, mit durchschnittlich 4,8 von 6 richtig beantworteten Fragen darauf hin, dass die Patienteninformation gut verstanden wird und dass das Wissen zu Konfidenzintervallen mit 6 Fragen erhoben werden kann.

Die dritte Arbeit ist der Kern der Dissertation [33]. Hier werden die Ergebnisse der randomisierten kontrollierten Pilotstudie mit begleitender Mixed-Methods Prozessevaluation dargestellt. Nurses, MS-Betroffene und Betroffenenexperten waren am Entwicklungs- und Evaluationsprozess des Decision Coaching-Programms beteiligt. Das Programm beinhaltet:

- Eine 16-stündige Schulung für MS-Nurses (siehe [33])
- Die Coaching-Intervention: bis zu drei Coaching-Sessions mit der Nurse pro MS-Betroffenen, Moderationskarten zur Unterstützung, Patienten-Arbeitsbücher zur Frühtherapie und zum Therapiewechsel, Zugang zur evidenzbasierten Informationsplattform (DECIMS-Wiki) und ein abschließendes Arztgespräch (Abbildung 3).

Das Coaching beinhaltet alle wichtigen Themen rund um die Therapieentscheidung: Diagnose, Prognose, Therapieoptionen, Präferenzen, Werte, Ängste und Sorgen sowie die Umsetzung der Entscheidung entsprechend den sechs Schritten zum SDM [34]. Durch die individuelle Entscheidungsbegleitung haben MS-Betroffene Zeit, die Optionen zu überdenken, diese zu besprechen, zu reflektieren und persönliche entscheidungsrelevante Punkte einzubringen. Dabei wird die evidenzbasierte Online-Informationsplattform (DECIMS-Wiki) nicht nur während des Coachings genutzt, sondern MS-Betroffene haben auch von zu Hause aus die Möglichkeit, auf die Plattform zuzugreifen. Nach der Pilotierung der Schulung und der Materialien erfolgte eine Evaluation durch eine Pilot-RCT mit begleitender Prozessevaluation in zwei Zentren mit vier MS-Nurses. Die Pilotstudie [33] konnte bei n=73 Betroffenen mit Verdacht auf oder schubförmiger MS deskriptiv eine Überlegenheit des Coachings bezogen auf den primären Endpunkt informierte Entscheidung (Wissen,

Einstellung und Therapiebeginn) zeigen. Daten von 51 MS-Betroffenen standen für die Berechnung des primären Endpunkts zur Verfügung. 15 von 31 (48%) MS-Betroffenen in der Interventionsgruppe trafen eine informierte Entscheidung, verglichen mit 6 von 20 (30%) in der Kontrollgruppe. Die Analyse von n=18 Coaching-Videos zeigte eine gute Einbindung der MS-Betroffenen in den SDM-Prozess (Erfassung mit MAPPIN'SDM [35]).

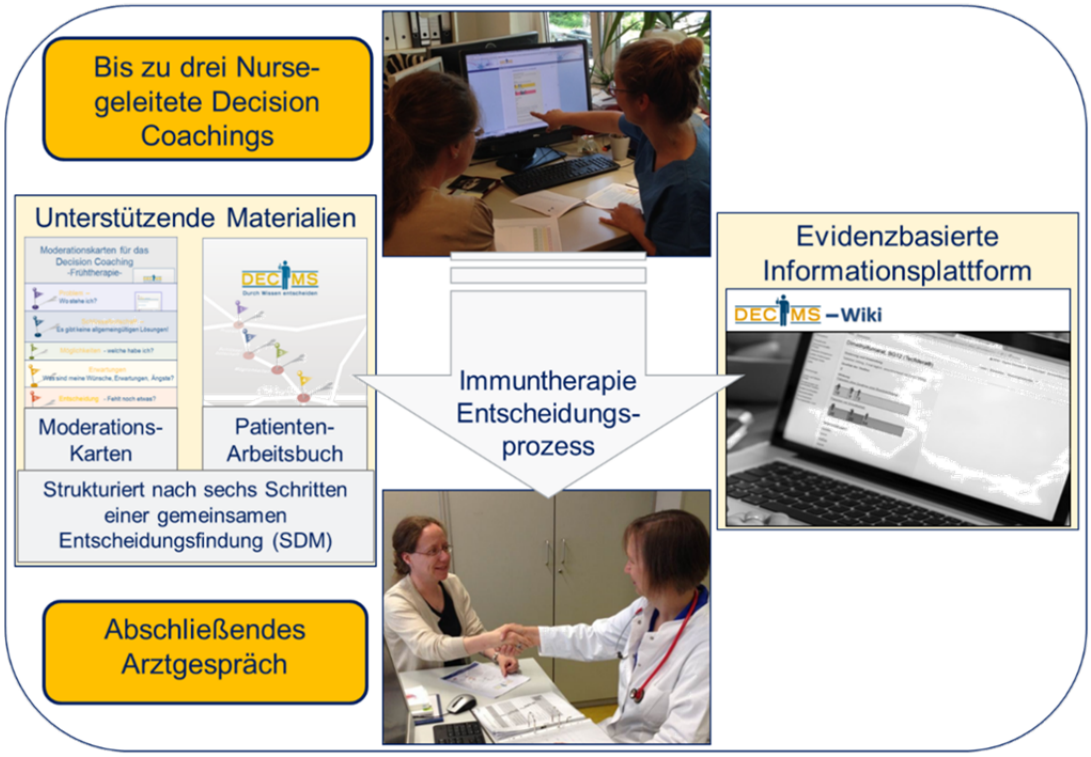

Abbildung 3: Decision Coaching-Intervention

Die Prozessevaluation zeigte positive Reaktionen von MS-Betroffenen, Nurses und Ärzten auf die Intervention. Die Arbeit belegte, dass die Decision Coaching-Intervention machbar ist und insgesamt von den Nurses, MS-Betroffenen und Ärzten positiv angenommen wurde. Allerdings stellen fehlende Daten, insbesondere in der Kontrollgruppe, eine Limitierung dar.

In der vierten Arbeit wird die Entwicklung und Pilotierung eines Schulungsprogramms zur Magnetresonanztomographie (MRT) für MS-Betroffene dargestellt [36]. Die Ergebnisse unterstützen die Weiterentwicklung eines evidenzbasierten Schulungsprogramms zur MRT, um die Teilnahme von MS-Betroffenen an Therapieentscheidungen oder zum Erkrankungsmanagement zu fördern. Ein Modul zur MRT für den Decision Coach-Trainingskurs wurde auf Basis der Schulung entwickelt.

Die fünfte Arbeit adressiert die Ergebnisse einer vierarmigen RCT mit 682 Teilnehmern [37]. Hier wurden neu entwickelte Balkengrafiken zur Kommunikation absoluter Risiken evaluiert. Diese Grafiken sind der zentrale Baustein im DECIMS-Wiki zur Darstellung und

Kommunikation des Nutzens der Immunmedikamente. Die Studie zeigt, dass sich die beiden Grafiken (100er Piktogramm und Balkengrafik) weder in einer statischen noch in einer animierten Darstellung hinsichtlich des korrekten Verständnisses der absoluten Risikoreduktion unterschieden, jedoch die statischen Grafiken besser verstanden werden. Insgesamt ist das Verständnis mit knapp 50 Prozent richtig beantworteter Fragen jedoch niedrig.

In der sechsten Arbeit [38] werden die Ergebnisse eines systematischen Reviews zur prognostischen Bedeutung der MRT hinsichtlich der Entwicklung der Beeinträchtigung für Personen, die mit einem klinisch isolierten Syndrom eine MS Verdachtsdiagnose erhalten haben, berichtet. In das Review wurden insgesamt 13 Studien eingeschlossen. Das Hauptergebnis des Reviews, dass es einen Zusammenhang zwischen mehr als zehn T2 Läsionen im MRT-Bild und der Zunahme der Beeinträchtigung gibt, findet sich in den DECIMS-Materialien wieder und wird im Coaching im Zusammenhang mit der Prognose besprochen. Diese Arbeit ist zur Publikation eingereicht und wird deshalb als deutschsprachige Kurzfassung dargestellt.

Die letzte Arbeit [40] beinhaltet die Weiterentwicklung der oben genannten PowerPoint Präsentationen zu Konfidenzintervallen in Form von audiovisuellen Informationen als Videos sowie die Evaluation mittels einer vierarmigen RCT. Die Ergebnisse der webbasierten Studie, an welcher 734 MS-Betroffene teilgenommen haben, zeigen, dass Informationen zu Konfidenzintervallen verständlich sind und die ausführlichen audiovisuellen Informationen besser verstanden werden. Die Videos können mittlerweile über das DECIMS-Wiki und YouTube [39] abgerufen werden und sind somit für MS-Betroffene und die Decision-Coaches nutzbar, um das Verständnis der Grafiken mit Konfidenzintervallen im DECIMS-Wiki zu fördern. Die Publikation zu dieser Arbeit ist in Vorbereitung. Hier wird eine deutschsprachige Kurzfassung der Studie berichtet.

6. Kumulativer Teil der Dissertation

6.1. Rahn AC, Köpke S, Kasper J, Vettorazzi E, Mühlhauser I, Heesen C (2015) Evaluator-blinded trial evaluating nurse-led immunotherapy DEcision Coaching In persons with relapsing-remitting Multiple Sclerosis (DECIMS) and accompanying process evaluation: study protocol for a cluster randomised controlled trial. *Trials*, 16: 106.

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TRIALS

STUDY PROTOCOL Open Access

Evaluator-blinded trial evaluating nurse-led immunotherapy DEcision Coaching In persons with relapsing-remitting Multiple Sclerosis (DECIMS) and accompanying process evaluation: study protocol for a cluster randomised controlled trial

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Abstract

Background: Multiple sclerosis is a chronic neurological condition usually starting in early adulthood and regularly leading to severe disability. Immunotherapy options are growing in number and complexity, while costs of treatments are high and adherence rates remain low. Therefore, treatment decision-making has become more complex for patients. Structured decision coaching, based on the principles of evidence-based patient information and shared decision-making, has the potential to facilitate participation of individuals in the decision-making process.
This cluster randomised controlled trial follows the assumption that decision coaching by trained nurses, using evidence-based patient information and preference elicitation, will facilitate informed choices and induce higher decision quality, as well as better decisional adherence.

Methods/Design: The decision coaching programme will be evaluated through an evaluator-blinded superiority cluster randomised controlled trial, including 300 patients with suspected or definite relapsing-remitting multiple sclerosis, facing an immunotherapy decision. The clusters are 12 multiple sclerosis outpatient clinics in Germany. Further, the trial will be accompanied by a mixed-methods process evaluation and a cost-effectiveness study.
Nurses in the intervention group will be trained in shared decision-making, coaching, and evidence-based patient information principles. Patients who meet the inclusion criteria will receive decision coaching (intervention group) with up to three face-to-face coaching sessions with a trained nurse (decision coach) or counselling as usual (control group). Patients in both groups will be given access to an evidence-based online information tool.
The primary outcome is 'informed choice' after six months, assessed with the multi-dimensional measure of informed choice including the sub-dimensions risk knowledge (questionnaire), attitude concerning immunotherapy (questionnaire), and immunotherapy uptake (telephone survey). Secondary outcomes include decisional conflict, adherence to immunotherapy decisions, autonomy preference, planned behaviour, coping self-efficacy, and perceived involvement in coaching and decisional encounters. Safety outcomes are comprised of anxiety and depression and disease-specific quality of life.
(Continued on next page)

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Discussion: This trial will assess the effectiveness of a new model of patient decision support concerning MS-immunotherapy options. The delegation of treatment information provision from physicians to trained nurses bears the potential to change current doctor-focused practice in Germany.

Trial registration: Current Controlled Trials (identifier: ISRCTN37929939), May 27, 2014.

Keywords: Multiple sclerosis, Coaching, Shared decision-making, Cluster randomised controlled trial, Patient information, Nurses, Self-management, Evidence-based medicine

Background

Multiple sclerosis (MS) is a chronic, inflammatory, autoimmune disorder, which is characterised by destruction of myelin in the central nervous system. The disease affects mainly young adults, with an average age of onset of around 30 years [1,2].

Around 2,000,000 people worldwide are affected with MS and at least 120,000 people in Germany have MS [3]. Further, recent insurance company based numbers have estimated there to be around 180,000 affected people in Germany [4]. There are between 3,000 to 5,000 new cases every year in Germany (four to six per 100,000).

Due to the long course of this disease and resulting severe disabilities, MS is of major health economic relevance [5]. Annual costs per patient in Europe are estimated at €18,000 for mild MS (Expanded Disability Status Scale (EDSS) <4.0), €36,500 for moderate MS (EDSS 4.0 to 6.5) and €62,000 for severe MS (EDSS >7.0) [6]. Total societal costs in Germany have been estimated at around €4,000,000,000 in 2001 [3].

Due to many uncertainties such as the possibility of a benign variant of MS [7,8], and unclear long-term benefits of treatments, some of them with life-threatening risks [9], immunotherapy decisions are not straightforward. In addition, recent studies have shown non-adherence rates of up to 50% within the first two years of treatment [10]. Thus, immunotherapy decision-making and decisional adherence are of high personal and societal relevance.

A shared decision-making (SDM) approach is currently regarded as the ideal approach in medical decision-making, based on the ethical principle of patient autonomy and on patient preferences [11]. A prerequisite of SDM is the availability of balanced and understandable information emphasising the crucial position of evidence-based patient information (EBPI) in this process [11]. A second aspect of SDM is self-reflection on values and preferences, which might substantially differ between patients and physicians [12]. This ideal concept of informed SDM is confronted with the current situation of medical care in Germany and other European countries, characterised by an increased burden of work for increasingly fewer physicians [13].

During recent years, so-called MS specialist nurses have been established, partially with the support of pharmaceutical companies for coaching patients on injectable treatments [14]. Although in some countries nurses already have active roles [15], there has been no widespread, systematic integration of MS nurses into immunotherapy decision-making processes based on EBPI. Coaching, provided in a structured manner and according to the principles of EBPI, can facilitate participation of individuals in the decision-making process. In this trial the following coaching definition of Stacey *et al*. [16] is applied: 'Coaching is defined as the provision of support by a trained individual (either in person or remotely - for example by telephone or internet), who is supportive but non-directive, for a patient or family facing a decision' [16]. Further, decision coaching is determined by the inclusion of SDM and EBPI components, as for example the assessment of patients' decision-making needs, provision of information on benefits and harms of each option, and the facilitation and monitoring of the decision-making progress [16].

In a recent systematic review [17], decision coaching provided along patient decision aids has been summarised based on trials reviewed in a Cochrane review [18]. The systematic review could not show a benefit regarding knowledge improvement compared to provision of patient decision aids only. For other outcomes, the trials produced diverse results, yet no negative effects have been demonstrated. Due to these findings and the limited number of trials, the authors concluded that further research in this area is needed [17]. However, in those trials where coaching has been provided by nurses, results are in general more promising [19-21].

We assume that beyond thoroughly developed decision support technologies and advanced communication concepts, structural change in clinical decision-making is essential for successful implementation of patient involvement into clinical practice. Therefore, this trial aims at clarifying the possible gains of, and also barriers to, giving MS nurses a crucial role in immunotherapy decision-making processes. The nurse decision coach model has been developed to redistribute health professionals' tasks in supporting patients' decision-making processes [22]. Here, the physician encounter is supplemented by the provision of an evidence-based online patient information tool (DECIMS-Wiki) and up to three decision coaching sessions with specialist MS nurses (decision

coaches) supporting patients to process the information, to clarify patients' own values, and to identify personal barriers in the decision-making process before a decision is made. By this stepwise structured and individualised process, we expect patients to be able to deeper elaborate their own decisions and to more actively participate in decision processes. Clarification of patients' own values, identification of barriers, evidence-based information, and participation in decision processes are prerequisites for patients in order to make informed choices and to achieve high decision quality.

This protocol has been developed and structured following the recommendations of the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) 2013 statement for clinical trial protocols [23]. Please see Additional file 1 for the complete SPIRIT checklist. Further, the Consolidated Standards of Reporting Trials (CONSORT) extensions for cluster randomised trials and for randomised controlled trials of non-pharmacologic treatments have been considered and will be used for reporting study results [24,25].

A recent Cochrane review showed that decision aids [26] in health treatment enhance accurate expectations and increase patient involvement. Also patient-physician communication is positively influenced if values are explicitly clarified. However, effects on decisional adherence and health outcomes remain inconsistent. In another Cochrane review [27] on interventions for health professionals to enhance SDM, all three trials out of 39 trials using a nurse-based educative intervention showed changes in consultations [28] and on patient relevant outcomes [29,30], stressing the relevance of this approach. In addition, our own Cochrane review on information provision interventions in MS identified 10 randomised controlled trials with heterogeneous approaches and inconsistent results [31].

Since 2001, we have studied EBPI and SDM in MS and conducted four controlled trials [32]. All interventions were based on the concept that more patient involvement through carefully developed information leads to a greater sense of control and empowers patients for disease-specific self-management especially regarding treatment decision making. While epidemiological studies in MS have consistently shown that objective and perceived stress is a relevant relapse risk factor [33], altered psychological factors might even impact on the overall disease process [34]. Our first randomised controlled trial clearly showed altered health behaviour in MS relapse management after a four-hour educational intervention in a cohort of 150 MS patients followed up on for two years [35]. Interestingly, trained patients had less relapses. On the other hand, a printed EBPI on immunotherapy alone was not sufficient to alter decision-making processes in another trial [36].

Other groups have engaged in the evaluation of patients' attitudes and risk behaviours as well as in the effects of information provision (for review see Giovannoni and Rhoades [37]). However, decision-making about, and adherence to, immunotherapy with the aim of an individualised treatment in MS remains a highly complex topic.

Recently, we finished a multicentre study with 192 patients with early MS comparing group education to a stress management intervention [38]. The intervention significantly improved relevant risk knowledge and informed choice. The same applies to another recently terminated study addressing MS patients in rehabilitation clinics offering an immunotherapy group education programme [39]. In both trials, informed choices significantly increased in the intervention group (IG), but no effects on therapy decision-making or health outcomes were found.

In summary, results for EBPI and decision support indicate that it might not be sufficient to solely provide information and/or decision aids. Apparently, patients need time and support to reflect on the information and discuss options. In case of more complex decisions, for example on immunotherapy, the formerly applied approaches seem to not be sufficient, and individual decision support might be helpful in supplementing physician consultations in order to achieve successful informed SDM. In addition, group interventions are not tailored to the individual treatment decision setting and can therefore not account for differences in decision-making priorities or individual information processing.

Here, specialist MS nurses seem the ideal candidates to act as decision coaches, a concept successfully administered in other diseases [17]. Up to now only one controlled study addressed the impact of MS nurse counselling, showing beneficial effects in sexual quality of life [40].

Aims and objectives

We hypothesise that structural changes in immunotherapy decision-making, including redistribution of tasks between specialist nurses (decision coaches) and physicians, will enhance elaborated decisions and improve healthcare management in MS. First, the intervention will empower patients to make more informed choices, tailored to their preferences and values. Second, decisional conflict will be lower compared to controls, and decisional adherence will be maintained. Third, decisional encounters will demonstrate more SDM. Finally, self-efficacy and coping competences will be enhanced.

Methods/Design

The DEcision Coaching In persons with relapsing-remitting Multiple Sclerosis (DECIMS) trial will be carried out as a superiority cluster randomised controlled trial.

Due to the nature of the intervention and the cluster design, only outcome assessment can be blinded.

A cluster design is adequate as the intervention is delivered to centres, specifically the nurses; therefore centres have to be the unit of allocation. Thus, contamination between nurses and patients of differently treated groups based on a randomisation within the centre is avoided. Moreover, it is possible to induce and observe possible structural changes in the participating MS-outpatient clinics.

Following the Medical Research Council guidance for the development and evaluation of complex interventions [41], the intervention was pre-tested with regard to feasibility and is currently piloted in two centres (St Josef-Hospital Bochum and University Medical Center Hamburg-Eppendorf). Furthermore, the main study will be accompanied by a process evaluation and an economic evaluation.

Study setting

The study will be conducted in different neurological outpatient clinics throughout Germany. At present, 14 centres participate in the DECIMS trial (see Additional file 2 for details). The two study sites participating in the feasibility and pilot trial (St Josef-Hospital Bochum and University Medical Center Hamburg-Eppendorf) will not participate in the main study.

Eligibility criteria

Neurological outpatient clinics in German hospitals which have a specialisation in MS are eligible to participate. Nurses are eligible if they specialise in the field of MS and are currently employed at the participating centres. Specialisation is defined as special qualifications and/or long-standing professional experience in patients with MS.

Patient inclusion criteria

Patients older than 18 years with possible MS, defined by a typical clinical syndrome and at least one MRI lesion and/or positive oligoclonal bands [42]; and patients with relapsing-remitting MS (RRMS), according to the McDonald criteria [43], will be included. To achieve a homogeneous sample, only patients deciding on starting, stopping, or changing first-line MS immunotherapy therapy (glatiramer acetate, interferon-beta preparations, dimethyl fumarate or teriflunomide) will be included. This will lead to inclusion of recently diagnosed MS patients as well as patients under treatment, considering switching from an injectable to an oral drug. Although patients with very early or established RRMS under treatment might differ considerably with respect to attitudes, disease experience, and disability, as well as availability of therapeutic options, these factors can be controlled for and any effect of disease stage can be investigated. Likewise, these two scenarios are highly representative for daily routine and practice.

The study will use the internet for information provision and data collection; therefore only patients with access to the internet will be included.

Patient exclusion criteria

Patients with secondary-progressive MS, primary-progressive MS, or any suspected central nervous system disease other than MS will be excluded. Furthermore, patients who are considered non-responders to a first-line treatment and who are facing a decision on escalation immunotherapy therapy (such as natalizumab, fingolimod, or alemtuzumab) or symptomatic therapy will be excluded. Also, severe cognitive deficit or major psychiatric illness affecting information uptake are exclusion criteria. In addition, patients who are related to medical personnel from the participating study centres will be excluded from the study.

Interventions

Intervention group

The 'decision coach programme' has been developed according to the Medical Research Council's framework for developing and evaluating complex interventions [41]. Considering the SDM communication concept [44], nurses specialising in MS will take part in a training course to acquire relevant skills to perform immunotherapy decision coaching. Afterwards, they will conduct the study intervention, which consists of up to three decision coaching sessions per patient. As part of the intervention, a web-based information tool, the DECIMS-Wiki, moderation cards, and a patient workbook have been developed to provide information and to give guidance throughout the decision-making process (see Figure 1).

The DECIMS-Wiki has been developed based on literature searches and an update of available brochure-based information materials from previous studies [45]. The tool was drafted by the research group at the study centre in Hamburg and will be continuously revised in cooperation with all participating study centres. In addition, each patient will be provided with a patient workbook, which is targeted to the specific kind of decision to be made (first treatment or switchers). The decision nurses are instructed to organise the coaching process considering six subsequent topics to be discussed in a decision-making process [46]. The six steps of an SDM-process are:

1. to review the problem requiring a decision-making process;
2. key message: decisions cannot be made based on evidence alone. It is the patient who needs to decide;
3. information about pros and cons of each option (including no immunotherapy);

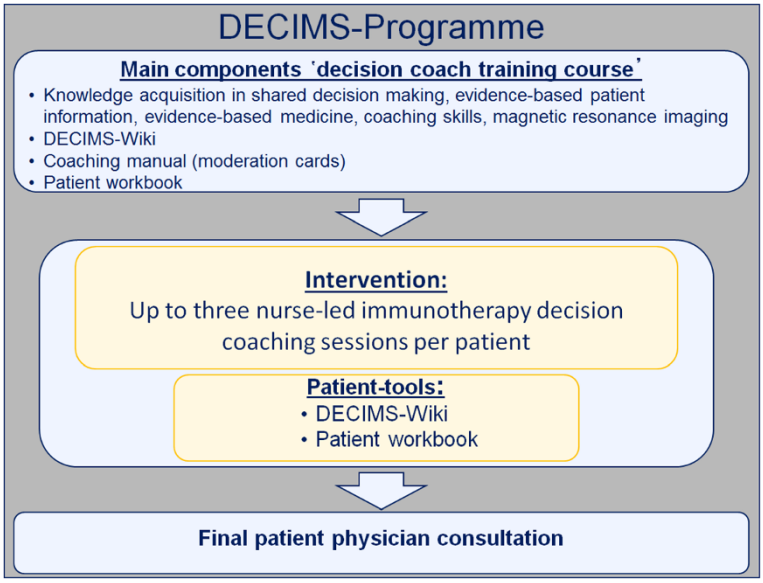

Figure 1 The DEcision Coaching In persons with relapsing-remitting Multiple Sclerosis (DECIMS) trial programme.

4. expectations of the patient;
5. decision (progress in decision-making, deferment is a possible decision); and
6. arrangements.

The moderation cards and the patient workbook are structured according to the above described six SDM steps. Further, the moderation cards guide the inclusion and connection of the DECIMS-Wiki and the patient workbook into the coaching process.

The curriculum of the training programme is based on previous expertise in the training of consumer representatives [47]. Moreover, train-the-trainer expertise from a previous programme was used [48]. The training focuses basic skills in SDM, including EBPI and coaching, using methods established in physician communication trainings [49,50]. The training includes further guidance on using the DECIMS-Wiki and insight into the use, interpretation, and impact of findings on magnetic resonance imaging (MRI) scans.

After randomisation, nurses in the intervention clusters will receive special training. All nurses will receive the same training provided by the same research team. The training consists of provision of preparatory materials and tasks, a training course (three days, 16 hours in total), and a structured feedback (via telephone) concerning coaching performance in practice after the training course. Knowledge gain of the nurses will be evaluated through questionnaires (before and after training). Up to six coaching sessions per decision coach will be video-recorded shortly after the training to give structured feedback on coaching performance. The videos will be evaluated independently by two researchers who will use standardised forms to assess the quality of the coaching session (in terms of SDM, EBPI, and coaching competencies). When nurses, do not implement important aspects which ensure a standardised delivery of the intervention despite receiving this feedback, they will be excluded from the study. Those aspects are:

1. no coaching according to the SDM criteria,
2. no use of the DECIMS-Wiki during the coaching,
3. not able to explain the bar charts on treatment effects to participants,
4. no appropriate use of the moderation cards or their contents during the coaching.

However, before a nurse will be excluded from the study, efforts will be taken to communicate that information (for example through extra training).

Eligible patients will receive their first coaching session with the decision coach within two weeks after inclusion with up to three coaching sessions per patient. Periods between sessions should not exceed two weeks. A single coaching session will last up to one and a half hour. Patients and decision coaches (nurses) will evaluate the coaching sessions via web-based questionnaires. Additionally, decision coaches will keep a logbook to document each coaching session.

Patients will be given access to the DECIMS-Wiki to prepare for coaching sessions, to gain further relevant knowledge, and to be able to reflect upon options between coaching sessions. After the final coaching session, patients will see a physician within two weeks to

decide upon immunotherapy. It is possible that in individual patients more than one medical encounter will be necessary in order to make a decision. A total of 40 physician-patient encounters will be audiotaped in four centres in order to measure possible changes in the physician-patient communication (for detailed information see process evaluation).

In addition, physicians in both groups will receive an information package on SDM. The package consists of the following information:

1. A letter, including information about the study, the SDM concept, and the request to follow the SDM concept during the study.
2. A link to a video (password protected), which shows a physician-patient conversation according to the SDM concept.
3. An article, which provides information about SDM in the field of neurology [51].

This information will be handed out to all participating physicians in the IG as well as in the control group (CG), since it is intended to assess the effects of the decision coaching intervention using trained nurses alone.

Control group

The CG will be given access to the evidence-based online patient information-tool (DECIMS-Wiki), which will also be used in the IG, including an information sheet on how to use it, and otherwise receive care as usual.

Offering both groups access to evidence-based information will allow for a better estimate whether possible differences between groups can be attributed to nurse-led decision coaching. For the same reason, physicians in the CG also receive the SDM package.

Criteria for discontinuation

Adverse events

Our previous work has shown that even complex information about MS treatment evidence is appreciated by patients [32]. Handing over information provision from physicians to nurses might induce concerns among MS patients. However, the framing of the intervention is as 'preparation for a medical encounter', therefore, we do not believe that patients perceive the intervention as a reduction of physician attention. The process is individualised to the decision pace of individual patients, allowing for individual decision-making processes. To account for possible adverse events, we will continuously monitor satisfaction with the process, which will be also communicated to the Data and Safety Monitoring Board (DSMB). We do not foresee any other harm of the intervention.

Patient withdrawal

Patients in both groups can quit the study at any time point. Patients who withdraw from the study are asked whether they agree to continue to fill in a limited set of questionnaires related to the primary study outcome.

Physician encounters

It is aimed that patients do not see a neurologist during the coaching stage. However, there are situations where patients have to or want to see a neurologist (for example, for relapse management). In these cases, neurologists in the participating outpatient clinics and practises are asked whenever possible not to discuss immunotherapy options. Still, this might not always be appropriate and some patients might also consult a practice-based neurologist. Any physician encounter will be documented.

Strategies to improve adherence

Decision coaches

All decision coaches will receive a study coach folder including all relevant documents of the training, the patient workbooks, moderation cards, and further material on communication and coaching.

Coaching fidelity will be secured through different measures: first, an interactive three-day training course in Hamburg; and second, video feedback of two coaching patients per nurse in the respective centre. Also, they will be contacted regularly (monthly during the first three months and every two to three months afterwards) to ensure quality standards of coaching sessions and support the decision coaches. Calls will consist of open and closed questions and decision coaches will have the opportunity to come up with their own aspects (as for example questions concerning coaching procedures or the DECIMS-Wiki). Furthermore, we aim to hold three to four telephone conferences per year with participating nurses from the IG. This will provide an opportunity for the nurses to connect and share experiences, for example to discuss difficult coaching situations.

Logbook

Decision coaches are further asked to use an online logbook for each participant to support a standardised delivery of the intervention.

Coaching sessions

Moderation cards will be provided to decision coaches to ensure that the key components of the intervention are delivered to the patients. This adds to the patient workbook, which also provides guidance through the SDM steps. Coaches might prepare sessions by looking into the coaching cards. In each coaching session it is aimed that the DECIMS-Wiki, the moderation cards,

and the patient workbook are used. Moreover, the workbook and the moderation cards do serve as structuring aids for the encounters.

Strategies to facilitate the utilisation of the DECIMS-Wiki

Decision coaches will be informed about the DECIMS-Wiki and use the tool during the training course, and the DECIMS-Wiki will be addressed during telephone calls and in the logbook. Beyond that, decision coaches will be informed when the platform has been updated.

Patients

If patients miss an appointment, they will be contacted by the decision coach to arrange a new appointment. Patients will be contacted by email by a member of the coordinating centre in Hamburg when it is time to fill in a form, and will be asked to complete the questionnaires within a specified time period. Patients who miss the completion will again be reminded by email and telephone. When appropriate, patients will be asked to fill in a questionnaire in the outpatient clinic directly after an encounter.

Decision coaches will inform patients about the DECIMS-Wiki and use the tool during the first coaching sessions reminding patients to use it between sessions. All patients will receive a personal password for the DECIMS-Wiki and an information leaflet about the tool.

Relevant concomitant care

Relapse management

In case of deterioration, for example a relapse during the coaching stage, the participant is free to consult a specialist and receive appropriate treatment.

Outcomes

For a list of the major endpoints of the DECIMS trial, see Table 1.

Primary outcome

We have previously applied the multi-dimensional measure of informed choice in two controlled trials [52]. Here,

Table 1 Major endpoints CRCT

Instrument	Measurement time points						
	Enrolment	Allocation	Post-allocation				
	$-t_1$	t_0	t_1	t_2	t_3	t_4	t_5
Eligibility screen	X						
Informed consent	X						
Allocation							
Sociodemographic data	X	X					
EDSS		X					
SDMT		X					
MS-related data and resource use		X				X	X
MMIC:							
Risk knowledge		X			X	X	X
Attitude			X	X	X		
Immunotherapy status		X			X	X	X
Dyadic DCS			X (nurse)	X (physician and patient)			
Dyadic MAPPIN'SDM			X (nurse and patient)	X (physician and patient)			
HCR trust scale (Physician/Nurse trust)			X	X			
PBMS		X			X		X
CPS		X			X		X
Decision autonomy					X	X	X
CSES		X			X		X
HAQUAMS		X			X		X
HADS		X			X		X

t_1 = after last decision coaching; t_2 = directly after final physician decision encounter; t_3 = two weeks after final physician encounter; t_4 = three months after final physician encounter; t_5 = six months after final physician encounter. CPS: Control Preference Scale; CSES: Coping self-efficacy scale; DCS: Decisional Conflict Scale; EDSS: Expanded Disability Status Scale; HADS: Hospital Anxiety and Depression Scale; HAQUAMS: Hamburg Quality of Life in MS Scale; HCR trust scale: Health care relationship trust scale; MAPPIN'SDM: Multifocal Approach to Sharing in Shared Decision Making; MMIC: Multi-dimensional measure of informed choice; MS: Multiple Sclerosis; PBMS: Planned Behaviour in MS Scale; SDMT: Symbol Digital Modalities Test.

informed choice is defined as a compound measure combining three dichotomous measures: risk knowledge, attitude, and therapy uptake. Informed choice encompasses adequate risk knowledge, with either uptake or non-uptake of immunotherapy, and a corresponding (congruent) positive or negative attitude. Attitude will be assessed using a single question directly after the final physician encounter. Uptake will be evaluated from the patient after six months. Risk knowledge will be measured using a previously developed and adapted questionnaire 14 days, and three and six months after the last physician encounter [53]. As applied in a previous trial, the cut off for adequate risk knowledge will be defined *a priori* as the value that 30% of all patients with highest scores reach at baseline. In addition, risk knowledge will be analysed as a continuous variable to enable comparability with other studies. Earlier trials have shown that patients who meet the primary endpoint more often realise their preferences [38,39].

Secondary outcomes

The Decisional Conflict Scale ((DCS) [54]) has been used in numerous decision support interventions and is regarded as a tool to monitor comfort with the decision process. Here, a dyadic DCS [55] (patient - decision coach and patient - physician) will be applied as key secondary endpoint after the last coaching session (IG) and after the final physician encounter (for both the IG and CG).

Further tools will be used to monitor decisional processes assessing autonomy preferences (Control Preference Scale (CPS) [56]), behavioural beliefs, and self-efficacy (Planned Behaviour in MS Scale (PBMS) [57]). Coping and self-efficacy will be assessed by application of the recently validated Coping Self-efficacy Scale (unpublished data Pöttgen J, Mohr DM, Ziegler K, Gold SM, Heesen C) based on Chesney *et al.* [58]). Perceived involvement in coaching and decisional encounters from patients' as well as physicians' and nurses' perspectives will be evaluated with the Multifocal Approach to Sharing in Shared Decision Making (MAPPIN'SDM) evaluation [59]; applying a newly developed short version. We will assess participants' trust in nurses and physicians [60].

Decisional adherence (including the decision against immunotherapy) and acceptance of the intervention will be assessed from patients using a standardised questionnaire at three and six months after the last physician encounter (for both the IG and CG). Finally, duration of decision coaching and physician encounters will be documented.

Tertiary outcomes (control and safety parameters)

As control parameters we will use measures for anxiety and depression using the Hospital Anxiety and Depression Scale ((HADS) [61]), and disease-specific quality of life using the Hamburg Quality of Life in MS Scale ((HAQUAMS) [62]). Moreover, standard disease-monitoring parameters will be obtained; relapses and disability as measured by Expanded Disability Status Scale ((EDSS) [63]) and the Symbol Digital Modalities Test ((SDMT) [64]) for cognition. Occurrence of relapses will be evaluated at baseline, 14 days, and three and six months after the last physician encounter (for both the IG and CG) using a standardised questionnaire.

Health economic outcomes

Data to perform health economic analyses will be assessed with an adapted tool used in a previous trial [35]. Patients will be asked to consent for collection of health insurance data for the study period.

Focus will be the rate of patients initiating MS immunotherapy as well as relapse treatment prescription (including route of administration). Further, number of MS-related visits to neurologists and general physicians, number of MRI scans, missed days at work, and hospital stays will be evaluated.

Participant timeline

For a description of the flow of the DECIMS trial see Figure 2.

CRCT: cluster randomised controlled trial; DCS: Decisional Conflict Scale; MAPPIN'SDM: Multifocal Approach to Sharing in Shared Decision Making; MMIC: Multi-dimensional measure of informed choice RRMS: relapsing-remitting multiple sclerosis

Screening visit

As it is not possible to coach all suitable patients in every participating centre, not all potentially eligible patients will be included. To avoid selection bias, possible recruitment days will be randomly determined by a statistician for those centres, and an independent person will call the study sites weekly to inform them about the recruitment day(s).

Nurses (for both the IG and CG) will create a list on all recruitment days, recording all MS patients who attend the outpatient clinic that day. Potentially eligible patients will be identified using a screening form (form one) during an appointment. Screening form one has to be filled in for every patient. Therefore, reasons why patients are not suitable will be documented as well. When patients seem to be suitable for the study, they will receive information about the study from the physician or from a nurse. For diagnostic cases in which an early treatment will be discussed, physicians will invite patients after having communicated diagnostic test findings. In the case of treatment switchers, the encounter is stopped before counselling about the possible immunotherapy options will take place. Physicians have to fill in a second screening form, including the study inclusion criteria, for all patients who seem to be suitable

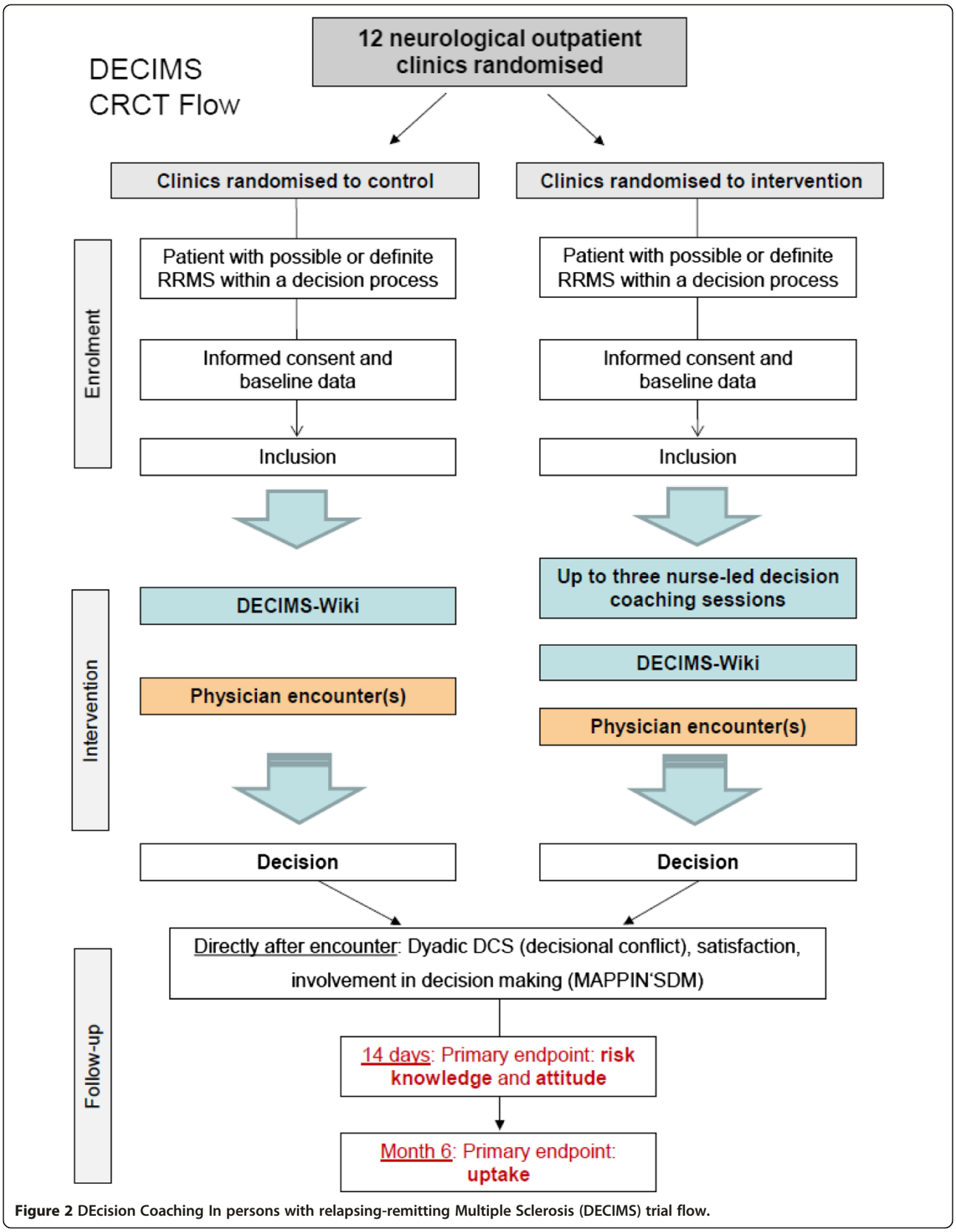

Figure 2 DEcision Coaching In persons with relapsing-remitting Multiple Sclerosis (DECIMS) trial flow.

for the study. Informed consent will be obtained from patients fulfilling the inclusion criteria after they have had enough time to read the study information sheet and ask questions. The encounter will be stopped when informed consent is given, and patients will be invited to fill-in baseline data via an online questionnaire database and will receive an access code to the DECIMS-Wiki after the completion of baseline questionnaires. Depending on the cluster's group allocation, patients will receive a new appointment with the physician or an appointment with the decision coach. Suitable patients, who are not willing to participate in the study, will be asked for the reason (screening form two).

Baseline data and allocation

After information about group allocation, patients in the CG will receive an information sheet about the DECIMS-Wiki from a nurse, will receive usual care, and a decisional encounter with the physician will be scheduled. In the IG, apart from information about access to the DECIMS-Wiki, an appointment for a first encounter with the decision coach will be scheduled within 14 days. After inclusion and the completion of baseline questionnaires, patients will receive an electronic access code to the DECIMS-Wiki, which is linked to the information technology platform of the *Krankheitsbezogenes Kompetenznetz Multiple Sklerose* ((KKNMS) Competence Network Multiple Sclerosis). Further appointments will be planned at the end of each encounter, which could be up to two more with the decision coach and up to two with a physician.

Encounters and web-based visits

After the last encounter with the decision coach, prompt feedback from patients will be collected at the centre by web-based questionnaires. After up to three meetings with the decision coach (visits one to three), up to two decisional encounters with a physician will take place within four weeks. Decision coach encounters will be videotaped and sent to the Hamburg study centre for analysis by the research group.

Patients will be followed up on using web-based questionnaires within 14 days, after the final encounter with the physician (web-based visit), after three months (web-based visit), and after six months (web-based visit and standardised telephone interview).

Additional visits

At least three randomly selected patients from each intervention cluster will be contacted after the follow-up period and asked to take part in an additional interview, which will be conducted in the context of the accompanying process evaluation (for details see process evaluation). Furthermore, when additional funding is provided, patients will be contacted via telephone by the study centre to assess their current treatment status after 12 and 24 months.

Sample size

The primary endpoint of the DECIMS trial is informed choice, that is, a fitting of good knowledge, a given attitude, and the corresponding uptake. Each of these three dimensions will get a dichotomous rating of 'yes' or 'no'. Based on data from prior studies [35,36], we assume that after the intervention, 60% of patients in the IG will show 'adequate' knowledge compared to 40% in the CG. Adequate knowledge is defined as the number of questions correctly answered by 30% of patients at baseline, which was also applied in previous work. We assume that in the IG group about 80% of attitudes and decisions are congruent, compared to 70% in the CG. Therefore, we expect 48% of IG patients to make informed decisions compared to 28% of patients in the CG. In order to detect this difference with a power of 90% and a significance level of alpha = 0.05, 12 clusters with 23 patients per cluster will be needed, assuming an intra-cluster correlation coefficient of 0.0045, which is a conservative estimate based on data from our previous trial [38].

Assuming a dropout rate of 10%, 25 participants per centre will be needed, accounting for a total of 300 participants in 12 clusters. In all our previous trials on EBPI, loss to follow-up was less than 10%. Therefore, 10% seems a realistic and conservative assumption.

Recruitment

Contact persons of different MS clinics in German hospitals were contacted by the project leader (CH) and informed about the study. All outpatient clinics which were willing to participate have been included in the study. Recruitment strategies will be individualised to ensure that centres' specific requirements are addressed (please see screening visit). The feasibility of recruitment is currently being tested in the pilot study.

Allocation

Clusters will be stratified by type of hospital (university hospital or community based hospitals). Allocations will be computer generated and will be performed by a statistician not involved in the conduct of the trial. Prior to randomisation of the centres, contextual factors of the participating centres will be assessed in a baseline survey.

Centres will be aware of their allocation status. To minimise selection bias, patients will not receive explicit information about their allocation group, but will only be informed that they will be assigned to one of two methods of information provision about MS immunotherapy (information provision only or information provision plus information by a nurse).

Blinding

Blinding of patients in patient information trials is difficult as the intervention can be easily detected. Therefore, due to the nature of the intervention it is not possible that clusters and patients are blinded. Nevertheless, contamination is avoided by the cluster design and patients will only be informed that two different ways of decision support regarding immunotherapy, information provision only or information provision plus information by a nurse, will be assessed. Assessment of the endpoints will be evaluator blinded as persons concerned with outcome assessment (by telephone interviews) will not be informed about patient and centre allocation.

Data collection methods

Data will be collected at seven time points using web-based questionnaires (see Table 1). Use of the web platform will be explained via information sheets and through personal information within the study centres. Additionally, some data will be collected by telephone using trained and blinded interviewers after six months and, depending on funding, after 12 and 24 months (see Additional file 1).

Statistical methods

For the primary outcome measure, the proportion of informed decisions within a treatment group, a generalised linear mixed model, reflecting the hierarchical structure of the data will be used [65]. Due to the relatively small numbers of clusters, imbalances in baseline characteristics on cluster and individual level may occur which are not fully covered by randomisation. Therefore the model will be adjusted for baseline variables. The treatment effect will be analysed at cluster level, whereas covariates will be analysed individually by the model. For the secondary outcome measures linear mixed models or generalised linear mixed methods will be used adjusting for clusters by random effects. These models also allow analyses of subgroups. All analyses will be performed on the intention-to-treat population.

It is planned to perform subgroup analysis of the two groups of patients included in the trial: first, those with a recent diagnosis, facing an initial decision on immunotherapy and second, those considering changing to an oral treatment. Apart from demographic baseline data, all analyses will be cluster-adjusted. We will report causes for study withdrawal for each patient to clarify whether there are any differences between the intervention and control clusters.

In addition, a sensitivity analysis will be performed to evaluate the robustness of study results and to explore different imputation techniques. Altman [66] addressed that there is no ideal method to address missing data. Therefore, different common imputation techniques [67] will be applied and reported with as well as without imputation techniques as suggested by Altman [66]. Last observation carried forward, as well as best and worst case scenario for dichotomous outcomes and multiple imputation techniques, will be conducted in the sensitivity analysis [68].

Harms

As relevant adverse events are unlikely, no interim analyses are planned and no stopping rules will be applied. Nevertheless, safety measures are applied as tertiary endpoints to control for anxiety, depression, and disease-specific quality of life. Furthermore, standard disease monitoring parameters will be collected (such as relapse rate, disability status, and functional status).

Research ethics approval

Ethical approval has been obtained from the ethical committee of Hamburg Chamber of Physicians (approval number: PV4576), and has been obtained from local committees at each centre location. Please see Additional file 2 for details.

Feasibility study and pilot trial

The intervention and the study procedures including outcome assessment were pre-tested through a feasibility study and are currently being tested in a subsequent pilot randomised controlled trial in the study centres in Hamburg and Bochum. The pilot study aims at first testing the randomisation procedure and second to gather data on feasibility of conducting the main trial.

For the feasibility study, four nurses specializing in MS from the centres in Hamburg and Bochum have received training in Hamburg. The feasibility study has been conducted over six months and 12 patients were included. Each decision coach has coached three patients, chosen by either the decision coach or the physician. The feasibility study aimed to evaluate the training course, access the acceptability of the programme (decision coaches, patients, and study sites), and to detect barriers and facilitators. Therefore, telephone interviews with included patients were conducted and analysed.

Currently, a pilot randomised controlled trial is being performed in the two centres in Hamburg and Bochum. Here, we aim to recruit 30 patients per centre, following the main study procedure with the following adaptation: both intervention and control intervention will be tested in each study centre. Therefore, both centres will receive randomised days to recruit either for the IG or CG.

Both the feasibility and pilot study follow the main hypothesis that the concept is feasible for decision coaches and patients. In detail, it is tested whether:

1. patients agree on initially consulting a nurse (decision coach),
2. the patient workbook is acceptable for patients and decision coaches,
3. the DECIMS-Wiki is helpful in the decision process,
4. the patient workbook and information platform can be used together during encounters,
5. study recruitment is feasible, and
6. outcome measurements are acceptable.

Data from the feasibility study have been used to adapt the train-the-trainer course to nurses needs in the encounters and we developed moderation cards (instead of an information sheet) for the decision coaches. Further, as a result of the pilot study, it has been decided to videotape all coaching sessions.

In addition, different possibilities to present data of risk communication (for example graph or pictogram) will be evaluated in terms of knowledge and understanding via web-based surveys in cooperation with the German MS Self-help Society (DMSG). For example, an education tool to support the comprehension of confidence intervals will be tested.

Process evaluation

Process evaluations should generally be accompanying complex intervention studies in order to measure programme fidelity and explore reasons for an effective or ineffective intervention [69]. Following the guidance of the Medical Research Council, the cluster randomised controlled trial will be accomplished by a process evaluation in order to assess study processes concerning patients, decision coaches, and the setting and context of the study. A process evaluation is of great use to understand the results of a study, and to later translate a successful intervention into practice [41,70].

Recently, Grant *et al*. [70] have published guidance for the development of process evaluations specifically addressing process evaluations for cluster randomised controlled trials of complex interventions. This framework will be used to guide the process evaluation of this study.

Ferlie and Shortell [71] suggest four levels of change which have to be considered in order to reach quality improvements in health care systems: individual level, group or team level, overall organisation level, and larger system level or environment in which individual organisations are embedded. Thus, teams build an important basis for changes. Depending on the level(s) and the intervention targets, different theories are relevant [71]. The intervention in this project targets people with MS, who face a decision) concerning immunotherapy (begin, start or change of immunotherapy). Therefore, MS nurses who work in an outpatient clinic will be trained as decision coaches. The study intervention affects all persons who are involved in the decision-making process; patients, physicians, and nurses. Presumably, a successful intervention depends on the support and attitude of the whole MS outpatient team towards the planned decision coaching intervention. However, it is hypothesised that a successful implementation of the intervention relies decisively on the motivation and attitude of the trained MS nurses.

The knowledge, which will be imparted during the nurse training course, is based on the principles of evidence-based medicine [72], and the knowledge transfer reflects established educational theories and concepts [73,74]. Further, the theory of planned behaviour [75] has been applied concerning contents of the training and the transfer of knowledge into practise (decision coaching performance).

Overall, the project is guided and determined by the principles of evidence-based medicine [72] and EBPI [76]. Further guidelines and concepts are considered: the MRC guidance for developing and evaluating complex interventions [41] for the design of the study and the SDM concept [46] to design and conduct the decision coaching intervention.

As mentioned above, the process evaluation is a mixed-methods study [77]. Qualitative and quantitative methods will be applied in combination and will be analysed together in order to illustrate and explore changes related to the decision coaching intervention on the cluster level (as for example change of structure in the outpatient's clinics), as well as the individual level (as for example attitudes of the nurses). Partly, the quantitative results of the trial will be used to determine questions of the qualitative interviews to be conducted after the study. Therefore, quantitative and qualitative methods are used intentionally to acquire a comprehensive impression of study processes and mechanisms.

In this process evaluation, a variation of the embedded design of mixed-methods studies is applied [78]. Besides, qualitative methods have been used within the feasibility study before the start of the trial to investigate study materials (the DECIMS-Wiki and patient workbook) with regard to user-friendliness and comprehensibility (see also trial protocol).

The framework proposed by Grant *et al*. [70] consists of 10 domains (Figure 3). Three domains are comprised of processes in which clusters are involved: recruitment of clusters, delivery to clusters, and response of clusters. Three domains address the processes within the target

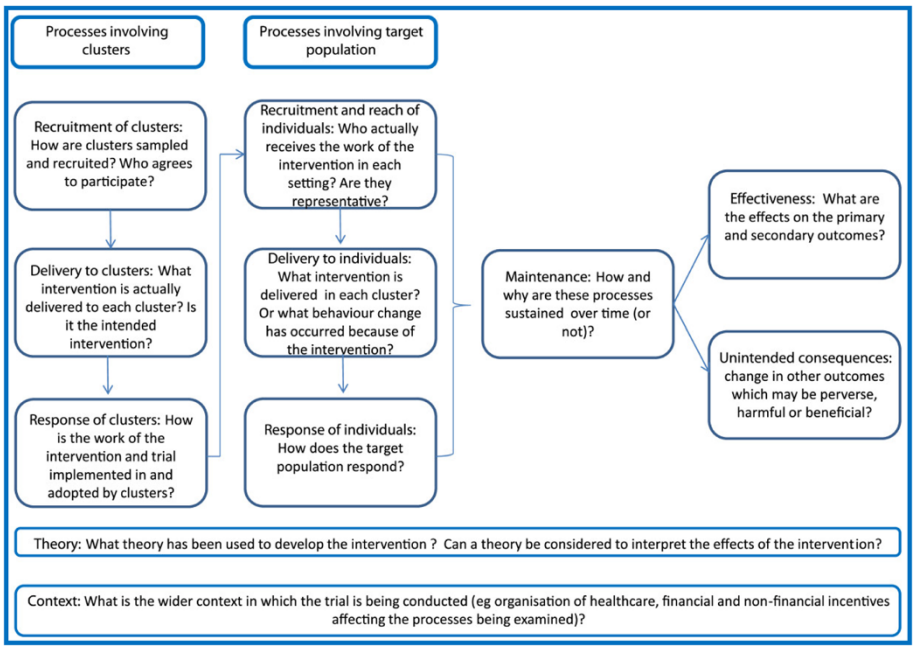

Figure 3 Overview of the process evaluation steps (from Grant *et al.* [70]).

population: recruitment and reach in individuals, delivery to individuals, and response of individuals. Further chapters cover theory, context, maintenance, and unintended consequences (see Figure 3).

As shown in Figure 3, effectiveness is displayed additionally to the 10 process evaluation steps. This concerns the results of the trial, which for instance determine the research questions of the qualitative interviews with patients after the trial is finished.

The primary aim of this theory based process evaluation is to explore underlying mechanisms and to determine effect modifying factors. Following the framework, the objectives are to:

1. explore the reaction of the clusters (such as the delivery of the intervention, response to the training course, and maintenance);
2. identify barriers and facilitators concerning the delivery of the intervention (coaching) to the patients;
3. assess cluster-specific differences (such as cluster reach and organisational differences);
4. measure the reaction of individuals with respect to responsiveness towards study recruitment and the intervention;
5. identify barriers and facilitators of study participation and of study retention;
6. ascertain structural problems;
7. analyse which study components work or do not, and for which reason; and
8. look for unintended consequences of the intervention (decision coaches, patients, and clusters).

Additional file 3 shows the application of the framework to this study. In the following, the planned components of the single domains are described in more detail. Questionnaires, which will be used for this process evaluation, have been developed by the research team and were tailored to the intervention. The questionnaires have been tested for usability. Nonetheless, published work in this field has provided useful guidance for the development of the questionnaires for nurses [79]. Most of the described content of this process evaluation refers to the IG. Content which also refers to the CG is marked (CG).

Context

Relevant factors of the German health system will be described and their relevance for this project will be discussed. A total of 14 different MS outpatient clinics are involved in the study, nine related to university hospitals and five to community based hospitals. Depending on the location, there is significant variation between the outpatient clinics, and due to factors such as size, practice hours, and clinical focus of the clinics, the number of potential study participants vary considerably. In the planning phase of the study, participating centres were visited in order to gain important information about structure and processes within the outpatient

clinics. Based on the evaluation of this information, the conduct of the study and process evaluation content was adapted.

Patient populations of the different outpatients clinics consist of patients who:

1. recently received a diagnosis and require information about therapy options,
2. visit the outpatient clinic regularly and now face a treatment decision (start, stop, or change of immunotherapy),
3. seek a second opinion, and/or
4. other (for example acute relapse).

Accordingly, the staffing (doctors, study nurses, MS nurses, and receptionists) and the roles of outpatient clinics in the respective neurological department are organised differently. Similarly, the clinics differ in terms of everyday processes, the functions assumed (by doctors and nurses) in patient care, and patient populations. Many of these differences have been noticed during the visits. As a result, the analyses of these different contextual conditions will provide important information concerning transferability of the concept to MS outpatient clinics in Germany, and to other countries and medical fields.

Prior to randomisation of the centres, study contextual factors will be assessed in a baseline survey (self-developed questionnaire (for both the IG and CG)). In addition, certain aspects of possible centre-specific effects (promoting factors and barriers) will be explored in more detail after completion of the study through qualitative interviews. For example, the possible advantages and disadvantages of the team structure (such as number and qualification of employees) for the work of decision coaches will be studied by qualitative interviews.

Recruitment of clusters

Clusters consist of participating MS outpatient clinics (see above). Within the collection of baseline data, it is planned to ask the physicians and nurses within the centres why they are participating in the study. Centres that withdraw participation will be asked for the reason.

Delivery to clusters

The decision coach training, which one or two MS nurses from all intervention clusters will receive, has been developed and will be performed by the study working group in Hamburg. In order to better understand and interpret modes of action of the complex intervention, a feasibility study, followed by an ongoing pilot study, was performed. Based on the results of these studies, both the training of nurses and the intervention (coaching sessions and supplementary materials) have been revised.

The intervention leads to changes in common practice within intervention clusters. On the one hand, MS nurses get involved in a new or expanded field of activity and acquire the relevant skills for this through the decision coach training. In addition, the local structure in MS outpatient clinics is changed due to the implementation of the coaching concept.

As part of the process evaluation it is determined to which extent clusters have received the intervention. The focus of the observation is to evaluate whether the intervention has been conveyed to all clusters in the same way. For this purpose, it is documented whether all participating nurses attend all training lectures, including subsequent training activities. Important aspects related to the training are assessed at the end of the training using questionnaires covering, for example, satisfaction and understanding. A knowledge assessment on relevant training content is performed before and after the training.

Further, it will be measured whether the course of the study (for example recruitment) has been communicated to all outpatient clinics (intervention and control clusters). Moreover, it will be captured whether physicians have received the SDM information, and if at least all principal investigators participated in the web-based meeting where the initiation of the DECIMS trial at the centre was performed (for both the IG and CG).

Response of cluster

An important part of the process evaluation is the attitudes of stakeholders (doctors and nurses) about the intervention and related structural changes. Quantitative surveys will be conducted at two time points (outpatient clinic teams in the intervention and control clusters) and at five time points (decision coaches: baseline, after training, after six weeks, six months, and after study completion) to determine changes in the course of the study (see Additional file 4).

In addition, physicians and nurses in the intervention clusters are interviewed after study completion to determine whether attitudes have changed during the course of the study and, if so, what factors have led to these change. Interviews will be semi-structured [80] and are subsequently evaluated by content analysis [81].

Further, it will be evaluated whether there are any changes in the professional relationship between nurses and physicians due to the intervention. Besides possible changes in the professional relationship between physicians and nurses, changes in the physician-patient communication will be addressed. Therefore, in four centres 10 physician-patient encounters will be audiotaped and analysed concerning SDM content (MAPPIN'SDM).

An important aspect is the implementation of the intervention in different centres and to determine characteristics

of centres that determine successful implementation (barriers and facilitators). For example, the number of patients within centres or the qualification of the MS-nurse might be important factors here.

Apart from interviews with decision coaches, facilitators and barriers of standardised implementation of the decision coaching will be assessed through a nurse logbook for each patient. In this web-based logbook, nurses record important information about patients and coaching appointments, such as duration or discussed SDM steps.

Following the training, the decision coaches perform training coaching sessions with two patients, recorded on video. As mentioned above, these first coaching sessions are evaluated and nurses receive telephone feedback after every patient by AR, together with a psychologist.

Willingness of nurses to work and further train in the new action field, use of the distributed materials (moderation cards and patient workbook), use of the DECIMS-Wiki, and gathering information beyond the provided information are also an important part of the process evaluation and will be assessed through logbooks, questionnaires, and qualitative interviews after study completion.

Some evaluation questions are based on the theory of planned behaviour [75] and aim to determine factors for a good immunotherapy coaching. Good immunotherapy coaching, as defined in the study, is provided when all six SDM steps have been addressed. Therefore, all coaching sessions will be videotaped and we aim to analyse the videos of at least 50 randomly chosen patients (dyadic MAPPIN'SDM evaluation [59]). Upon completion of the study, questions which arise from the video analysis and quantitative evaluation are addressed through qualitative interviews. In addition, it will be assessed by questionnaires whether and to what extent the intervention has had an impact on nurses in the intervention clusters who did not receive the training. In the following, a selection of aspects that will be covered is listed for the physicians of the IG:

1. attitude towards the intervention,
2. distress through additional organisational effort,
3. reduction of workload due to nurses' counselling,
4. handing over responsibility to nurses,
5. change in patient communication, and
6. change in communication with nurses.

A selection of aspects that will be covered is listed for the decision coaches of the IG:

1. attitude towards the intervention and personal interest,
2. higher workload versus work routine,
3. changes in the inter-professional relationship to the physicians and others, and
4. facilitating factors and barriers.

Recruitment and reach in individuals

To ensure a standardised recruitment, the recruitment procedure was determined after most of the participating centres had been visited by members of the research team. A non-responder analysis will be conducted in all centres. On the one hand it should be ascertained whether there are fundamental differences between control and intervention centres. On the other hand it should be determined if there are considerable variations in the reasons for or against study participation in individuals. Therefore, patients will be briefly asked for their reason/s not to take part in the study (screening form two). Moreover, reasons for taking part in the trial will be surveyed.

Delivery to individuals (dose delivered)

As aforementioned, all coaching sessions will be videotaped and analysed. The analysis focuses the assessment of coaching quality on respective SDM content Here, patient information about benefits and harms of therapy options, using the DECIMS-Wiki, are of particular relevance. In addition, nurses document in the logbooks which SDM steps have been discussed during the coaching session, how many coaching sessions have been performed, and duration of sessions. Patients are asked to fill in a short questionnaire directly after the last physician encounter. The questionnaire assesses, among other things, the use of and satisfaction with the DECIMS-Wiki, especially focussing on nurses as a possible influencing factor. For instance, the attitude of the nurse towards the intervention could have an impact on coaching performance.

After study completion, three patients per IG centre (purposeful sampling) will be questioned, using semi-standardised interviews, in order to determine which aspects of the intervention were helpful for the patient in the decision-making process, and where any action or change was needed. The interview guide will be created based on the analysis of the questionnaires. Depending on resources, use of the DECIMS-Wiki will be evaluated in the CG.

Response of individuals (dose received)

Apart from monitoring the transmission of the intervention, patients' responses will be investigated, focussing on:

1. changes in risk knowledge (using the risk knowledge questionnaire [53], for both the IG and CG);
2. satisfaction with the intervention (for both the IG and CG);
3. changes in patients' attitudes (for example concerning immunotherapy; for both the IG and CG);
4. structural barriers or barriers with regard to content, which hinder patients to actively participate in decision-making;

5. promoting factors; and
6. influence of coaching on patient-physician communication.

Questionnaires (with some open questions; for both the IG and CG), videos of consultations (IG), and interviews (for both the IG and CG) and/or focus groups (for both the IG and CG) will be used for the evaluation. Some aspects are already covered by primary and secondary endpoint questionnaires. Subgroup analyses are intended to determine whether coaching of patients seeking a change of immunotherapy has a greater or smaller effect compared to treatment-naïve patients.

Maintenance

The collection of possible behavioural changes in decision coaches can provide important information to explore which factors serve to maintain the implementation of the intervention or have a limiting influence. The following aspects will be covered for decision coaches:

1. DECIMS-Wiki-use as a potential factor,
2. change of DECIMS-Wiki use in the course of the study,
3. self-assessed changes in knowledge and skills (for example coaching skills) during the study,
4. use of the materials (moderation cards and patient workbook),
5. willingness to work and train in the new field of activity,
6. self-assessed change in attitude of nurses in the course of the study (for example, in terms of coaching and about immunotherapies (see also nurses and response of cluster)).

The following aspects will be covered for patients:

1. factors that lead to reconsidering the decision for or against immunotherapy (for both the IG and CG),
2. DECIMS-Wiki use as a potential factor (for both the IG and CG), and
3. contact with the decision coach after the coaching session(s) (IG).

Unintended consequences

Patients

Potentially, negative as well as positive effects may be caused by the intervention. Therefore, security parameters (HADS [61] and HAQUAMS [62]) are applied to assess positive and negative changes in patients. In addition, other possible effects of the intervention will be identified on the basis of interviews and questionnaires.

Decision coaches

It will be assessed (by questionnaires and interviews) whether the training or coaching evokes unintended consequences such as anxiety, burden within the situation, and/or a conflict between their beliefs or current practice in the outpatient clinics and the content of the intervention, in trained nurses.

Physicians (intervention group)

Possible effects of the intervention on the relationship between physicians and patients and physicians and trained nurses will be evaluated via questionnaires and interviews.

Theory

The Theory of Planned Behaviour (TPB) is based on the assumption that behaviour is largely the result of setting, beliefs, and expectations regarding future events. When weighing different alternatives, an individual will choose the action that most likely causes a positive result. According to the theory of planned behaviour, the domains 'attitude', 'subjective norm', and 'perceived behavioural control' determine the behaviour of a person. In a previous project, a questionnaire based on the theory has been developed in order to elaborate the intended behaviour respective to a decision of patients with MS on immunotherapy [57]. This is one of the questionnaires used in the trial.

Beyond that, the development of the training programme for nurses was guided by the theory of planned behaviour, and the theory will be considered and used in the development of the process evaluation questionnaires to identify barriers and supporting factors. Beyond the TPB as on underlying framework of this project, the concepts of SDM, evidence-based medicine, and EBPI have contributed significantly to the development and the contents of the intervention [46,75].

Data analysis (process evaluation)

As described by Creswell and Plano Clark [78], the main steps for the data analysis in the embedded mixed-methods design are:

1. analysis of the primary data set (trial data, see Table 1),
2. analysis of the secondary data (process data),
3. specification of dimensions by which the results should be compared,
4. specification of what information from dimensions should be compared,
5. comparison of data sources, and
6. data interpretation according to the research questions (in which way do secondary data sets contradict, augment, or support trial results?).

First, the process evaluation and trial data will be analysed separately. After that, the data will be connected and the results will determine the interview questions. Finally, all data sets will be merged (joint display).

The trial endpoint data analysis will be performed according to the protocol. Quantitative process evaluation data (surveys and evaluation forms) will be analysed descriptively using SPSS (International Business Machines Corporation (IBM), Armonk, United States of America) or R (R Development Core Team) software. Some subgroup analyses will be performed (for example, regarding the start or change of immunotherapy and decision type) in order to explore the impact of the intervention on different groups. Interviews will be analysed by content analysis [81] and coded thematically with a specific software programme (QCAmap (P. Mayring and T. Fenzl), Klagenfurt, Germany)

Qualitative data analysis will be guided by the TPB.

Summary process evaluation

The framework of Grant *et al.* [70] facilitates systematically retrieving, appraising, and analysing important aspects of the complex intervention of decision coaching. The planned questionnaires allow for an elaborate interpretation of study results. In addition, the qualitative interviews enable further exploration of facilitators and barriers concerning the implementation of the intervention in different centres with different structures and processes, as well as different groups of people. The process evaluation offers the opportunity to capture the way in which the complex intervention causes effects, and to determine factors that have a supporting or hindering influence. Intentionally, besides some open questions in the evaluation forms, no qualitative data is collected during the trial, so as not to interfere with the processes of the complex intervention. However, important potential problems can be detected by regular telephone calls with the nurses of all centres. Through qualitative interviews and possibly focus groups after the trial, it is possible to further elaborate on the results of the quantitative questionnaires. Due to the interpretation of the data, new questions may be raised that can be addressed in the interviews. All quantitative questionnaires of the process evaluation were specified and created before the beginning of the trial. The qualitative interview guides are created after the completion of the study, in order to respond with flexibility, for example to unexpected events.

Discussion

The proposed cluster randomised controlled trial aims to assess the effectiveness of a new model of patient decision support concerning MS immunotherapy options in Germany. As this intervention is associated with substantial structural changes, as for example nurses in Germany seldom explain treatment options, the trial is accompanied by a thoroughly developed mixed-methods research process evaluation in order to explore the underlying processes.

This is the first cluster randomised controlled trial where a nurse-led immunotherapy decision coaching intervention in persons with RRMS is evaluated. This study responds to Stacey *et al.*'s [16] call for more research to evaluate the value of decision coaching beyond patient decision aids.

In conclusion, this trial will investigate whether patients with MS who are facing an immunotherapy treatment decision will benefit from decision coaching delivered by trained nurses.

Trial status

Patient recruitment for the trial started in autumn 2014.

Additional files

Additional file 1: DECIMS SPIRIT 2013 Checklist [82-90].

Additional file 2: Lead investigators in participating centres and ethical committees.

Additional file 3: Overview process evaluation. CRCT: Cluster randomised controlled trial; EBM: Evidence-based medicine, EBPI: Evidence based patient information, SDM: Shared decision making.

Additional file 4: Instruments DECIMS process evaluation. EF: evaluation form; IG: intervention group; CG: control group.

Abbreviations

CG: Control group; CPS: Control Preference Scale; CSES: Coping self-efficacy scale; DCS: Decisional Conflict Scale; DGN: *Deutsche Gesellschaft für Neurologie* (German Society of Neurology); DSMB: Data and Safety Monitoring Board; DMSG: *Deutsche Multiple Sklerose Gesellschaft* (German MS Self-help Society); EBPI: Evidence-based patient information; EDSS: Expanded Disability Status Scale; HADS: Hospital Anxiety and Depression Scale; HAQUAMS: Hamburg Quality of Life in MS Scale; HCR trust scale: Health care relationship trust scale; IG: Intervention group; KKNMS: *Krankheitsbezogenes Kompetenznetz Multiple Sklerose* (Competence Network Multiple Sclerosis); MAPPIN'SDM: Multifocal Approach to Sharing in Shared Decision Making; MMIC: Multi-dimensional measure of informed choice; MMR: Mixed methods research; MS: Multiple sclerosis; MRC: Medical Research Council, MRI, Magnetic resonance imaging; PBMS: Planned Behaviour in MS Scale; RIMS: Rehabilitation in Multiple Sclerosis; RRMS: Relapsing-remitting multiple sclerosis; SDM: Shared decision-making; SDMT: Symbol Digital Modalities Test.

Competing interests

AR, SK, JK, EV and IM have nothing to declare. CH has received research grants, congress travel compensations, and salaries for talks from BiogenIdec, Genzyme, Sanofi-Aventis, Bayer Healthcare, Merck Serono, Teva Pharma, and Novartis.

Authors' contributions

CH is the principal investigator of the study. IM supervises the research process and has contributed to study planning. The study was conceived by CH, SK, and JK. AR contributed to detailed study planning. AR and SK developed the accomplishing process evaluation. CH, IM, and JK added to the specification of the process evaluation. CH, SK, JK, and AR created the nursing training. AR and JK are grant holders from the German Ministry of Education and Research. EV has planned and will be conducting the statistical analysis. All authors read and approved the final manuscript.

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Additional file 1: DECIMS - SPIRIT 2013 Checklist

Section	Item Number	Included in publication (Y (yes) or described below
Administrative Information		
Title	1	Y
Trial registration	2a	Y
	2b	Y
Protocol version	3	13.02.2015, Version 8a
Funding	4	Y
Roles and responsibilities	5a	Y Christoph Heesen and the research team will be responsible for the following points: - design of DECIMS - conduct of DECIMS - preparation of study protocol and revisions - preparation of case report files (CRFs) - organising steering committee meetings - analysis of study results - publication of study results. Data collection and completion of CRFs as well as follow up of study patients will be monitored by AR.
	5b	**Bundesministerium für Bildung und Forschung [Federal Ministry of Education and Research]** Projektträger im Deutschen Zentrum für Luft- und Raumfahrt e.V. Gesundheitsforschung Dr. Svenja Diekhoff Heinrich-Konen-Str. 1 D-53227 Bonn **Krankheitsbezogenes Kompetenznetz Multiple Sklerose [Competence Network Multiple Sclerosis]** Klinikum rechts der Isar Prof. Dr. B. Hemmer TU München Neurologische Klinik und Poliklinik Ismaninger Straße 22 D-81675 München
	5c	Y
	5d	**Steering committee:** F. Paul (Berlin), R. Diem (Heidelberg), I. Kleiter (Bochum), CH and SK. All steering committee members have to agree to the final protocol. Further responsibilities: Reviewing progress of study and if necessary agreeing changes to the protocol to facilitate the conduction of the study. **Data Manager** G. Antony G. Antony is responsible for the maintenance of the trial IT system and data verification.

		Data and safety monitoring board (DSMB): A. Solari (Milano), G. Giovannoni (London), D. Stacey (Ottawa), H. Leino-Kilpi (Helsinki) Principal Investigator (CH) and research team (AR, SK, JK, EV)
Introduction		
Background and rationale	6a 6b	Y Y
Objectives	7	Y
Trial design	8	Y
Methods Participants, interventions, and outcomes		
Study setting	9	Y
Eligibility criteria	10	Y
Interventions*	11a 11b 11c 11d	Y Y Y Y
Outcomes	12	Y
Participant timeline	13	Y
Sample size	14	Y
Recruitment	15	Y
Assignment of interventions Allocation		
Sequence generation	16a	Y
Allocation concealment mechanism	16b	Y
Implementation	16c	Y
Blinding (masking)	17a 17b	Y Y
Data collection, Management and analysis		
Data collection methods	18a	**Primary endpoint** Informed choice (MMIC [82]) including the sub-dimensions risk knowledge, attitude and uptake is the primary endpoint. A modified version of the questionnaire has been tested ahead of the main trial through a web-based survey in order to evaluate acceptability and design changes. The questionnaire has shown robust results in a cohort of n=705 MS patients with a mean of 9,58 correct items out of 19 items (SD 3.28), showing normal distribution and good internal consistency (Cronbach's alpha, 0,8). **Secondary endpoints** (1) Decisional Conflict Scale (DCS): Decisional Conflict [54] is the key secondary endpoint. The English language scale version was evaluated in 909 individuals and had a test-retest reliability coefficient of 0.81 [83]. The German translation has been conducted by Buchholz and colleagues [84]. However, we

will apply the dyadic version of the scale [54] which has been recently validated in a large MS cohort within the PERCEPT study [85] measuring patients' and nurses' as well physicians' perspective.

(2) Control Preference Scale (CPS): Autonomy preference will be assessed using a web-based card set (CPS [56]), which has recently been validated, showing satisfactory results concerning reliability [86].

(3) Planned Behaviour in MS (PBMS): Decision making processes concerning immunotherapy will be assessed using the PBMS, which has been developed by our research group in German language [57]. The questionnaire showed sensitivity to change in a recent RCT [38].

(4) The Coping-Self-Efficacy-Scale has been developed in the context of HIV behavioural interventions [58]. It integrates a coping instrument and a self-efficacy measure asking patients for their confidence in applying the right coping strategy depending on a given challenge. The German version has been applied in a cross-sectional study [87] and has been used in pilot work on a behavioural intervention in MS showing validity of the tool (unpublished data). The longer questionnaire CSES version has been also applied in MS patients [88].

(5) MAPPIN'SDM as an additional measure of SDM based on fitting of physicians' and nurses' perceptions with patients views [59]. All coaching sessions will be videotaped and at least a randomised cohort of eight coaching's from each centre will be rated independently by two researches with the observer-based instrument.

(6) The HCR trust scale has been developed by Bova et al [89] and has been translated from English to German for the current study. The English version produced acceptable reliability by illness status and gender as well as in multiple age groups [89].

Assessment of safety

(1) Emotional distress will be measured using the Hospital Anxiety and Depression Scale (HADS), which has been used in different MS studies [38, 39].

(2) Disease specific quality of life will be

		evaluated using the Hamburg Questionnaire on Quality of Life in MS, which has shown validity and reliability (HAQUAMS [62] updated in [90]). (3) Disability: Expanded-Disability-Status-Scale (EDSS [63]) and perceived progression (HAQUAMS). (4) Cognition: Symbol-Digit-Modalities-Test (SDMT) measuring information processing as a widely accepted screening tool for cognitive dysfunction in MS [64]. Together, these two measurements (EDDS and SDMT) are suitable to describe and compare the baseline characteristics of patients concerning MS disease status. Data collection forms in German language are available on request.
	18b	**Retention** As successfully performed in previous studies, we aim to promote retention of study patients using email and telephone reminders. Patients will be asked to complete questionnaires within a pre-specified time period. Study participants who miss the proposed completion period will be reminded per email (after 7 and 14 days). Individuals, who still have not filled in the questionnaires after three weeks, will be contacted by telephone. Information about expected time to fill in the questionnaires will be provided by reminder emails (see also strategies to improve adherence).
Data management	19	All electronic data will be captured and processed through the IT platform of the KKNMS supervised by G. Antony who will be unaware of patients' allocation. Patients will receive an email with the username as well as a second email with a database link and need to generate a password to gain access to the questionnaires. Therefore, data entry by the research team will only be necessary on special occasions, e.g. when patients feel unable to complete the web-based questionnaires. In those cases, data will be entered by blinded members of the coordinating centre in Hamburg. All data will be entered by one team member. Nevertheless, to ensure data accuracy, entered data will be controlled by two blinded members of the research team in Hamburg at the end of the study. Data will be pseudonymised with clusters coded using numbers and patients using a mixed code with letters and numbers, the latter will be automatically generated by the database. Electronic and paper based data will be stored for 10 years at a save place at the University of Hamburg.

Statistical methods	20a	Y
	20b	Y
	20c	Y
Monitoring		
Data monitoring	21a	A data and safety monitoring Board (DSMB) will be established with international experts who are not involved in the current study. The DSMB will receive annually reports concerning adherence to the study protocol and standards of good clinical practice.
	21b	As relevant adverse events are unlikely, no interim analyses are planned, no stopping rules applied. However, the DSMB can demand the conduction of an interim analysis and subsequently give advice whether to continue, modify, or stop the trial, and provide the funding organisation with information and advice. The DSMB will be independent from the study sponsor.
Harms	22	Y
Auditing	23	There are no planned audits. However, regulatory authorities might choose to audit the study.
Ethics and dissemination		
Research ethics approval	24	Y
Protocol amendments	25	The DSMB will need to approve major changes of the study protocol e.g. concerning outcome measures. Also an amendment of the study protocol would be submitted to the ethical committees. Minor changes to the protocol, which will not affect the conduction of the study, will be communicated to the DSMB. Information about changes will be added to the study registration.
Consent or assent	26a	Informed consent will be obtained by a person in the participating centres involved in the study i.e. a physician or a (study) nurse.
	26b	Not applicable
Confidentiality	27	All personal information will be entered into the database by participants or nurses (at baseline and logbook) and in exceptional cases by study managers. Data will be pseudonymised and there will be no possibility to link data to persons without access to the code list. Through the personal access of patients to the DECIMS-Wiki based on a personal account (sent via email), it will be possible to individually track the use of the DECIMS-Wiki (e.g. frequency, use of different parts), which will be used to analyse the DECIMS-Wiki use as well as the value of different parts of the DECIMS-Wiki. This will be performed with ExtraWatch, an encapsulated plugin to the Joomla platform. Therefore, the DECIMS-Wiki users IP address will be stored by the system but shielded to anyone but the system administration by G. Antony, C. Heesen and A. Rahn. However, data analyses of DECIMS-Wiki use will be based on

		pseudonyms.
Declaration of interests	28	Y
Access to data	29	The study centre will coordinate the intra-study data sharing process. All principal investigators will be given access to the cleaned data sets.
Ancillary and post-trial care	30	Not applicable.
Dissemination policy	31a	Results will be published in major journals and presented at scientific conferences as e.g. European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS), Rehabilitation in Multiple Sclerosis (RIMS), International Shared Decision Making Conference (ISDM), European Association for Communication in Healthcare (EACH). Furthermore, it is planned to publish main results on relevant patient websites. All patients will receive structured feedback and copies of major publications. If the trial is successful, an implementation study will be applied for to transfer the findings into care.
	31b	Authorship will be shared between persons involved in the study following the current guidelines of the International Committee of Medical Journal Editors (ICMJE). No professional writers will be employed and no persons not directly involved in the study will be granted authorship.
	31c	Y It is not planned to make the data set and statistical code publicly accessible, but on request from researchers, individual data will be provided.
Appendices		
Informed consent materials	32	Available on request in German language
Biological specimens	33	Not applicable

Additional file 2: Lead investigators in participating centres and ethical committees

Lead investigators in participating centres	Ethical committee
Orhan Aktas, Prof. Dr. Neurologische Klinik Heinrich-Heine-Universität Düsseldorf	Ethikkommission der Medizinischen Fakultät der Heinrich-Heine-Universität Düsseldorf (reference no.: 4681)
Martin Berghoff, Dr. Klinik und Poliklinik für Neurologie Universitätsklinikum Gießen	Ethik-Kommission am Fachbereich Medizin (Justus-Liebig Universität Giessen) (reference no.:82/14)
Ricarda Diem, Prof. Dr. Neurologische Klinik Universität Heidelberg	Ethikkommission der Med. Fakultät Heidelberg (reference no.: S-264/2014)
Jürgen H. Faiss, Prof. Dr. Klinik für Neurologie und Neurophysiologie Asklepios Fachklinikum Teupitz	Ethik-Kommission der Landesärztekammer Brandenburg (reference no.: AS 92(bB)/2014)
Christoph Heesen (CH), Prof. Dr. Institut für Neuroimmunologie und klinische Multiple Sklerose Forschung (inims) Universitätsklinikum Hamburg-Eppendorf	Ethik-Kommission der Ärztekammer Hamburg (reference no.: PV4576)
Frank A. Hoffmann, Dr. Klinik für Neurologie Krankenhaus Martha-Maria Halle-Dölau	Ethical committee: Ethikkommission der Ärztekammer Sachsen-Anhalt (reference no.: 42/14)
Ingo Kleiter, Prof. Dr. Neurologische Klinik St. Josef-Hospital Bochum	Ethik-Kommission der Med. Fakultät der Ruhr Universität Bochum (reference no.: 4846-13)
Luisa Klotz, Dr. Klinik für Neurologie Universitätsklinikum-Münster	Ethik-Kommission der Ärztekammer Westfalen-Lippe und der Medizinischen Fakultät der Westfälischen Wilhelms-Universität (reference no.: 2014-235-b-S)
Wolfgang Köhler, Dr. Klinik für Neurologie und neurologische Intensivmedizin Fachkrankenhaus Hubertusburg, Wermsdorf	Ethikkommission bei der Sächsischen Landesärztekammer (reference no.: EK-BR-80/14-1)
Mathias Mäurer, Prof. Dr. Klinik für Neurologie Caritas Krankenhaus Bad Mergentheim	Ethik-Kommission der Friedrich-Alexander Universität Erlangen Nürnberg (reference no.: 191_14 Bc)
Friedemann Paul, Prof. Dr. NeuroCure Clinical Research Center Charité – Universitätsmedizin Berlin, Campus Mitte	Ethikausschuss 1 am Campus Charité - Mitte (reference no.: EA1/151/14)
Alexander Simonow Neurologische Klinik Sorpesee	Ethik-Kommission der Ärztekammer Westfalen-Lippe und der Medizinischen Fakultät der Westfälischen Wilhelms-Universität (reference no.: 2014-235-b-S)
Susanne Windhagen, Dr. MVZ Multiple Sklerose Klinikum Osnabrück	Ethikkommission der Ärztekammer Niedersachsen (reference no.: Grae/109/2014)
Uwe Zettl, Prof. Dr. Klinik und Poliklinik für Neurologie Universitätsmedizin Rostock	Ethikkommission an der Medizinischen Fakultät der Universität Rostock (reference no.: A 2014-0073)

Additional file 3: Overview process evaluation

Overview process evaluation DECIMS			
Domain	**Objects of investigation**	**Ascertainment**	**Time point**
Context	Context factors in Germany (health system)	Description	Pre-intervention
	Barriers and promoting factors in the participating outpatient clinics	Visits in the participating centres, survey	Pre-intervention
Recruitment of clusters	Cluster recruitment Reason for study participation Cluster-specific differences	Documentation of cluster recruitment Survey (physicians and nurses) Interviews, surveys	Pre-, during and post-intervention
Delivery to clusters **Staff level**	Development of the intervention	Visits in the participating centres, piloting of study materials (e.g. think aloud), feasibility and pilot study	Pre-intervention
	Delivery of the intervention to nurses (participation, reach, attitude)	Evaluation forms, documentation, knowledge questionnaire	Pre-intervention
	Delivery of the recruitment strategy to all centres	Documentation of participation in web-conferences	Pre-intervention
Response of clusters	Stakeholders (intervention and control group): attitude in participating centres (lead investigator, physicians, nurses) respective the intervention	Evaluation forms, interviews	Pre- and post-intervention
	Decision coaches (trained nurses): coaching performance (delivered as intended) E.g.: acquired routine, barriers attitude and willingness to work and further train in the new action field	Evaluation form, video recording (coaching), logbook, interviews	Pre-, during and post-intervention
	Physicians (intervention and control group): change in routine through the intervention	Evaluation form, interviews	Pre- and post-intervention
	Nurses (control group): change in routine through the control intervention	Evaluation form, interviews	Pre- and post-intervention

Recruitment & reach in individuals	Non-responder analysis	Checklist	During the intervention
	Recruitment procedure	Web-based call, documentation of study, recruitment (screening lists)	Pre- and during intervention
Delivery to individuals (Dose delivered)	Intervention group: delivery of the intervention to individuals (decision coaching and DECIMS-Wiki)	Video recording (coaching), evaluation form, interviews	During and post-intervention
	Control group: delivery of the control intervention to individuals (DECIMS-Wiki)	Evaluation form, interviews	Post-intervention
Response of individuals (Dose received)	E.g.: Satisfaction with the intervention, knowledge, attitude, barriers and facilitators	Questionnaires (primary and secondary endpoints CRCT), evaluation form, interviews	Post-intervention
Maintenance	Decision coaches: Knowledge and attitude, acquired routine, coaching performance DECIMS-Wiki use	Questionnaire, evaluation form, video recording (coaching), interviews	Pre- during and post-intervention
	Patients: further needs (coaching, DECIMS-Wiki), autonomy preferences, knowledge	Evaluation form, questionnaires (primary and secondary endpoints CRCT), interviews	During and post-intervention
Unintended consequences	Decision coaches: Stress, professional relationship to physicians and patients, barriers Patients: anxiety, barriers, physician contact, negative impact on quality of life	Evaluation form, video recording (coaching), interviews Evaluation form, questionnaires (security parameters CRCT), Interviews	During and post-intervention During and post-intervention
	Physicians: professional relationship to nurses and patients, barriers	Evaluation form, interviews	During and post-intervention
Theory	TPB, SDM, EBPI, EBM	Application during study planning and the development of study materials, used in evaluation forms, during video analysis	Pre- during and post-intervention

Additional file 4: Instruments DECIMS process evaluation

Evaluation MS-outpatient clinics (nurses, physicians and decision coaches)						
Instrument/group	**Pre centres randomisation**	**Pre-training**	**Post-training**	**Begin of study recruitment**	**6 months after study recruitment**	**12 months after study recruitment**
Survey outpatient clinics (lead investigators)	**x**					
EF (IG): Decision-Coaches		**x**	**x**	**x**	**x**	**x**
EF (IG): physicians				**x**		**x**
EF (IG): untrained nurses				**x**		**x**
EB (CG): nurses				**x**		**x**
EF (CG): physicians				**x**		**x**
EB (CG): untrained nurses				**x**		**x**
Video records (decision coaches)			**2 patients (run-in)**			
Structured telephone calls IG: decision coach	**Monthly during the first three months and every two to three months afterwards during study recruitment**					
Structured telephone calls CG: nurse	**Monthly during the first three months and every two to three months afterwards during study recruitment**					
Interviews IG: decision coaches	**After the study is finished**					

Interviews IG and CG: some nurses and physicians	**After the study is finished**			
Evaluation patients (IG and CG)				
Instrument/group	**Baseline**	**Directly after final physician decision encounter**	**3 months after final physician encounter**	**6 months after final physician encounter**
EF patients IG	**x**	**x**	**x**	**x**
EF patients CG	**x**	**x**	**x**	**x**
Video records decision coaching	**All coaching sessions (every patient)**			
Logbook IG (filled in by decision coaches)	**Baseline after every coaching and until the final physician decision encounter**			
Logbook CG (filled in by nurses)	**Baseline and until the final physician decision encounter**			
Screening forms (filled in by physicians)	**Has to filled in by physicians for every patient**			
Interviews patients (IG and CG)	**Purposeful sampling after the study is finished**			

6.2. Rahn AC, Backhus I, Fuest F, Riemann-Lorenz K, Köpke S, van de Roemer A, Mühlhauser I, Heesen C (2016) Comprehension of confidence intervals - development and piloting of patient information materials for people with multiple sclerosis: qualitative study and pilot randomised controlled trial. *BMC Medical Informatics and Decision Making*, 16(1): 122.

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RESEARCH ARTICLE Open Access

Comprehension of confidence intervals - development and piloting of patient information materials for people with multiple sclerosis: qualitative study and pilot randomised controlled trial

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Abstract

Background: Presentation of confidence intervals alongside information about treatment effects can support informed treatment choices in people with multiple sclerosis.
We aimed to develop and pilot-test different written patient information materials explaining confidence intervals in people with relapsing-remitting multiple sclerosis. Further, a questionnaire on comprehension of confidence intervals was developed and piloted.

Methods: We developed different patient information versions aiming to explain confidence intervals. We used an illustrative example to test three different approaches: (1) short version, (2) "average weight" version and (3) "worm prophylaxis" version. Interviews were conducted using think-aloud and teach-back approaches to test feasibility and analysed using qualitative content analysis. To assess comprehension of confidence intervals, a six-item multiple choice questionnaire was developed and tested in a pilot randomised controlled trial using the online survey software UNIPARK. Here, the average weight version (intervention group) was tested against a standard patient information version on confidence intervals (control group). People with multiple sclerosis were invited to take part using existing mailing-lists of people with multiple sclerosis in Germany and were randomised using the UNIPARK algorithm. Participants were blinded towards group allocation. Primary endpoint was comprehension of confidence intervals, assessed with the six-item multiple choice questionnaire with six points representing perfect knowledge.

Results: Feasibility of the patient information versions was tested with 16 people with multiple sclerosis. For the pilot randomised controlled trial, 64 people with multiple sclerosis were randomised (intervention group: $n = 36$; control group: $n = 28$). More questions were answered correctly in the intervention group compared to the control group (mean 4.8 vs 3.8, mean difference 1.1 (95 % CI 0.42–1.69), $p = 0.002$). The questionnaire's internal consistency was moderate (Cronbach's alpha = 0.56).
(Continued on next page)

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(Continued from previous page)

Conclusions: The pilot-phase shows promising results concerning acceptability and feasibility. Pilot randomised controlled trial results indicate that the patient information is well understood and that knowledge gain on confidence intervals can be assessed with a set of six questions.

Trial registration: German Clinical Trials Register: DRKS00008561. Registered 8th of June 2015.

Keywords: Patient information, Multiple sclerosis, Confidence interval, Interview, Pilot randomised controlled trial

Background

Without knowledge and correct interpretation of numerical information, informed decision-making is impeded. The way statistical information is presented and explained has a high impact on understanding and interpretation [1]. In addition to information on absolute and relative risk reduction, thoughtfully developed information on confidence intervals (CI) for comparing treatment effects of immunotherapy options may be useful for communicating with people with multiple sclerosis (PwMS).

To correctly interpret study results, patients need to understand that study findings are effect estimates generated in a limited sample, which is assumed to represent the total population [2]. CI provide information about how accurate estimates are and thus add important information about the uncertainty of point estimates [3]. Understanding the relevance of CI in addition to basic event rates and absolute risk reductions may support patients and clinicians when evaluating study results and making informed choices [3]. The current Cochrane Handbook recommends to communicate both relative and absolute measures of risk and CI, which should be displayed in a 'Summary of findings' table [4]. However, approaches to explain CI to patients and consumers are rare [5] and no systematic evaluation exists.

For PwMS informed decision-making on disease-modifying drugs is highly relevant for self-managing their lives with this chronic progressive disease. PwMS are confronted with different choices concerning disease-modifying drugs, which are only partially effective but also bear relevant risks [6]. Adherence rates to disease-modifying drugs are as low as 30 % [7] indicating deficits also in the decision-making process. Communicating uncertainties may be an important step towards a better patient-medical-professional communication to achieve informed choices to which patients adhere to. Recent work has shown that addressing uncertainties does not induce anxiety and fear, but increases involvement and even adherence to disease-modifying drugs in MS [8]. In order to make informed medical decisions, PwMS not only need information about treatment effects in numbers, such as absolute risk reductions, but also information on the certainty of these estimates from clinical studies.

Therefore, this study aims to develop and pilot-test patient information (PI) materials to explain CI to PwMS. As currently no validated questionnaire assessing knowledge on CI is available, we aimed to develop and pilot-test a multiple-choice questionnaire to assess comprehension of CI.

Methods

Study design

Different PI materials were developed and pilot-tested according to the Medical Research Council's framework for developing and evaluating complex interventions [9].

Development

A systematic literature search was performed to identify studies evaluating approaches to explain CI. In total three different versions of PI materials were developed to explain CI to PwMS. The recommendations concerning the construction of evidence-based PI were considered [10, 11]. Different approaches were applied to explain CI; using the illustrative example of an apple farmer in two PI versions.

Feasibility/piloting

Assessment of feasibility included testing acceptability of PI materials and exploring to what extent the PI was judged suitable and attractive [12]. Practicability of the PI was tested by assessing the time needed to process the information, composition of text and graphic illustration as well as understandability. Feasibility of PI was tested in two consecutive stages. In a **pre-test phase,** three different PI versions were tested with non-academic staff members from the MS day hospital in Hamburg and a consumer representative from a self-help initiative. In a subsequent **pilot-test phase**, the three PI versions were piloted with a sample of PwMS. The multiple-choice questionnaire was tested with pilot-test phase participants [12]. Finally, in a **pilot-RCT,** one PI (average weight version, see below for details) was piloted together with the questionnaire in 64 PwMS (see Fig. 1).

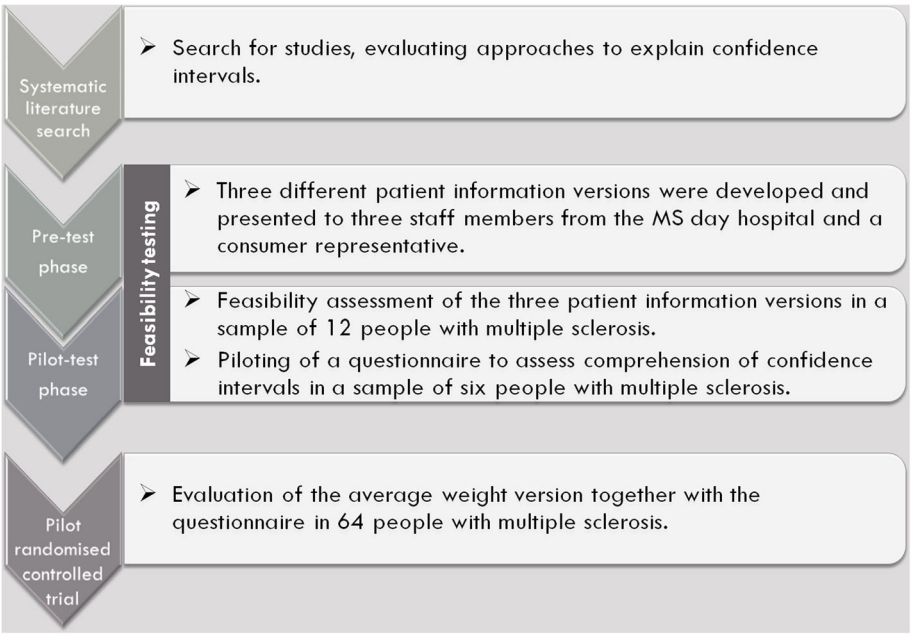

Fig. 1 Study Flow

Participants

Pre-test and pilot-test phase

A convenience sample was used in the pre-test phase. In total three female staff members of the MS day clinic and one female consumer representative participated in the study.

In the pilot-test phase, a purposeful sampling strategy was applied to cover different distinct characteristics. In total 21 PwMS aged 18 years or older were selected from the MS day hospital, of whom eight declined to take part in the study due to timing issues. In total six of 13 PwMS received ≥ 12 years of education and thereof access to higher education Germany. Disease durations varied from 1 month to 19 years. Seven participants (54 %) were female. One patient dropped out at the beginning of the interview, because she expected a different input. Therefore, the final sample consisted of 12 PwMS.

Pilot RCT

Participants were recruited using mailing-lists of the MS day hospital, the local MS self-help society and other self-help initiatives [13–16].

After assessing the web-survey platform, participants were informed about the study and asked to provide demographic and disease specific data [17] and answer five questions on numeracy [18]. Participants were excluded with a notification by the system in case they filled in to be less than 18 years old or that they are not diagnosed with MS. After that, they were randomly allocated, using the UNIPARK randomisation sequence, to receive either the newly developed information or standard information. Directly after the intervention, they were asked to fill in the multiple-choice questionnaire.

Setting and procedure

A think-aloud approach combined with semi-structured interviews was used to evaluate the PI and the questionnaire [19]. Participants (4 (staff members/consumer representative) and 12 (PwMS)) were asked to read the PI via a computer screen and verbalise their thoughts afterwards [19]. The teach-back method was employed to allow further improvement and clarification of the PI [20, 21].

All interviews, except one pre-test interview (telephone-interview), were held face-to-face and were audio-recorded at the MS day hospital by FF. There was no professional relationship between interviewer and participants. Interviews were not interrupted and recordings were of very good audio quality. Interviews ranged from 30 to 70 min.

The multiple-choice questionnaire with closed questions was developed following the recommendations by Haladyna et al. [22] and evaluated in the pilot-test phase and in the pilot-RCT. The average weight version on CI was tested against standard information on CI based on a formerly developed decision aid for PwMS [23] using the online survey software UNIPARK [24]. The average weight version, where a farmer wants to estimate the average weight of his apples, was chosen because this version was preferred by PwMS and contains all information considered to be important to understand confidence intervals (see 3.2.3 for details). The minimum sample size was set to 60 people, assuming that this

would allow gaining sufficient information for the planned evaluation of the questionnaire and the PI in a larger sample. It was not aimed to reach a statistical significant difference between the two groups, yet to use the results after successfully piloting for the sample size calculation of a future RCT to evaluate the PI in a larger sample.

Data analysis

Feasibility and pilot-phase

Interview recordings were transcribed using consistent rules [25] and transcripts were content analysed using Burnard's approach [26]. The coding tree (Additional file 1) was developed along the gathered data and the structure of the interview guides. All transcripts were analysed using MAXQDA (version 11) and reviewed by a second person (AR).

Pilot-RCT

Data analysis was performed using the SPSS (version 21). Demographic data were analysed using descriptive statistics. An item analysis considering difficulty, distribution and discriminatory power was performed on the 6-items on CI comprehension [27]. Cronbach's alpha (Kuder-Richardson) was calculated to determine internal consistency. Discriminant validity was assessed comparing the results to the abbreviated numeracy scale [18].

The questionnaire was complemented by four questions (Likert scale from 1–10) to evaluate an overall subjective rating of the understandability of the PI, the relevance of the topic, subjective knowledge and estimated subjective benefit of the PI.

Results

Systematic literature search

No study that explained CI to laypeople was identified (see Additional file 2 for detailed information).

Feasibility and pilot-phase (written information)

Written patient information versions

A figure to display CI (Fig. 2) had been developed for an information platform on MS as part of the DECIMS (Decision Coaching in MS) project [28]. In the figure both the absolute risk reduction and CI are presented.

We decided to explain CI using a non-medical example followed by an MS specific example and developed three different PI on CI:

1) the average weight version
2) the worm prophylaxis version and
3) the short version.

Each version consists of an introduction, a main and a final part, with only the main part differing between versions. The introduction starts with a question from a virtual patient and is supposed to give participants an idea in which context and why CI are used. For the main part three versions were developed to cover different levels of complexity and different approaches to explain CI. The final part aims to transfer the gathered knowledge about CI to MS specific medications. While in the short version, CI are explained as briefly as possible without using an example, in the average weight and worm prophylaxis versions the story of an apple farmer is used to explain CI. In the average weight version, the farmer wants to estimate the average weight of his apples and CI are illustrated using small and large random samples of apples to estimate the average weight. In contrast, in the worm prophylaxis version, the farmer wants to test whether an anti-worm treatment is effective to prevent his apples from worm infestation. At first he tries to treat a small sample of apples, then a larger one, while he compares the results to untreated apples.

Pre-Test phase written patient information

During the pre-test the PI versions were revised before they were shown to the next participant. Significant changes were made in order to clarify contents. The narrative line was optimised and sentences were shortened. A statistician was introduced as a second virtual character, apart from the farmer, to better structure the information.

Pilot-test phase written patient information

For the pilot-test interviews, participants were first shown the average weight version, followed by the short and the worm prophylaxis version. We chose to present the short version between the other two versions to allow participants to rest between the two longer and more complex versions. In general, participants' reactions ranged from positively interested on the one end, to being overwhelmed on the other (interview no. 8 and 11). In total four PwMS (interview no. 3, 5, 8 and 12) did comment on the need of explaining CI to patients. It was considered as important and PwMS wanted to read more about it, but there were also contrary voices (interview no. 5). Please see Additional file 3 for example quotes.

Understandability

In total five PwMS (interview no. 1, 3, 6, 8, and 10) stated that the information on CI was easy to understand and one person that it was well described (interview no. 9). Other points, raised by one PwMS respectively, were: too many pages with same content making it difficult to stay attentive (interview no. 9); the information was partly confusing, a lot at once and some parts had to be read more than once (interview no. 11); and that some sections need shorter sentences to be better understood (interview no.10). No PwMS expressed that the content was not understandable.

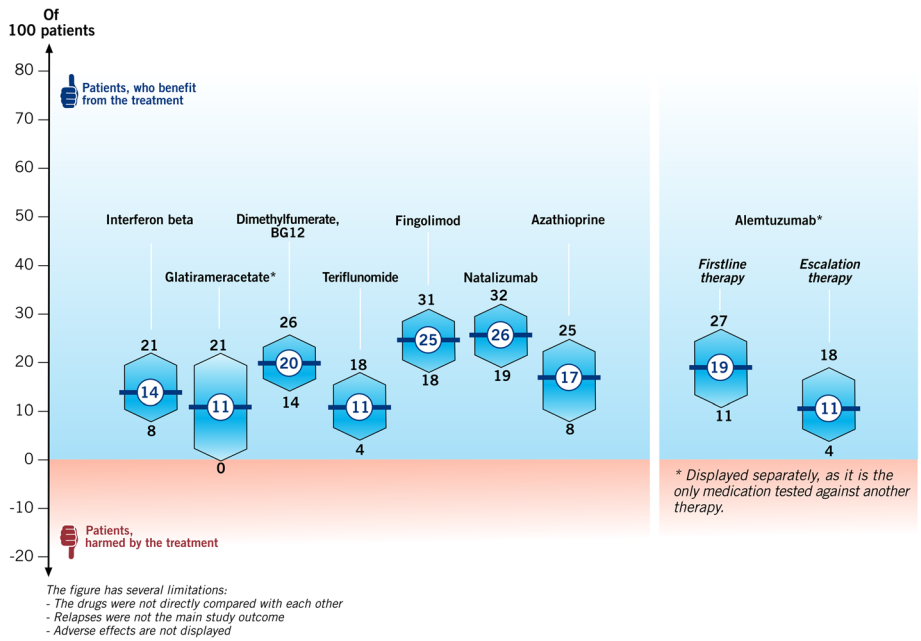

Fig. 2 Confidence intervals (drug therapy effects in relapsing-remitting MS), Number of patients without relapses for 2 years due to drug therapy. References [30, 31, 35–39, 40–43]

In general, the presentation of numbers was described as a burden by four PwMS (interview no. 4, 5, 9 and 10). One PwMS reported that he found it difficult to tell whether numbers were derived from calculations of real figures or were made up as an example (interview no. 8). Two PwMS also stated that their numerical skills and their competencies in mathematics were weak (interview no. 4 and 8). On the contrary, another PwMS pointed out to remember the content visually presented, but later stressed to have problems with numbers (interview no. 9).

Different versions and comparison of the different versions

In total six PwMS were positive about the apple farmer approach (interview no. 1, 3, 6, 8, 10 and 12). While five PwMS clearly expressed that they preferred the average weight version; three PwMS liked the worm prophylaxis version better and one PwMS liked the short version most. Another PwMS stated that he could not choose one, because every version yielded different information and only all three versions combined gave a complete picture of CI. Information about the favourite version was missing for two PwMS.

Confidence intervals and multiple sclerosis specific medications

PwMS did not comment much on the final part of the PI. Two PwMS were pleased about the transfer to MS and MS medications (interview no. 4 and 8). Despite the dense and relatively difficult text, negative comments were rare (two persons, interview no. 5 and 6).

Comprehension of confidence intervals

The comprehension of CI was mostly assessed by the teach-back phase and the multiple choice questionnaire. Questionnaire results are presented in section 3.3.

Teach back

All PwMS of the pilot-test phase were asked to teach back the following aspects: definition of CI, benefits of using CI, width of CI, statistical significance and the apple farmer's approach to answer his question (e.g. to estimate the average weight of his apples).

Overall, it was difficult for the PwMS to teach-back the content. However, some PwMS were able to teach-back the content quite well, whereas others could not teach-back the content predominantly correct. Some PwMS were able to teach-back the content of some parts while they had problems with other parts (see Additional file 4: Table S1).

Development and pilot-testing of the multiple choice questionnaire

The developed questionnaire initially consisted of eight multiple choice questions, of which four were visually illustrated. The questions addressed:

– the definition of CI

– the interpretation of CI and of point estimates based on an example
– the meaning of the width of CI and of the zero-line
– the interpretation of CI as well as influencing factors.

The questionnaire was pilot-tested with six of the 12 PwMS. Five of eight questions were answered correctly by five or more PwMS (see Additional file 4: Table S2).

Further development of the multiple choice questionnaire

According to the feed-back of the PwMS, the questionnaire was further adapted. Two questions were deleted, as they addressed for the same content as other questions and wording of some questions was changed. The revised questionnaire was assessed again by four PwMS (see Additional file 5). No further need for revision was revealed.

Pilot randomised controlled trial

About 1000 persons were invited to take part via the mailing-lists. Participating PwMS were randomised to receive either the average weight version (IG) or standard information (CG). The survey was started by 115 PwMS, with 64 finishing the survey (36 IG/ 28 CG) (see Fig. 3).

Baseline demographics and disease specific data information are presented in Table 1. There were significantly more female PwMS in the CG. Otherwise there were no statistically significant differences in demographic parameters.

PwMS in the IG answered 4.8 (mean, SD 1.3) of six questions correctly, while PwMS in the CG answered 3.8 (SD 1.2) questions correctly (mean difference 1.1 (95 % CI 0.42–1.69), $p = 0.002$, two-tailed t-test).

Table 1 Baseline data

Baseline data	IG $N = 36$	CG $N = 28$
Age (mean)	47.3	43.8
Females	19 (53 %)	22 (79 %)*
Education (highest degree)		
Secondary school	15 (41.7 %)	16 (57.1 %)
Academic degree	21 (58.3 %)	12 (42.9 %)
Disease course**		
CIS	0	2 (7.4 %)
RRMS	22 (61.1 %)	20 (71.4)
SPMS	9 (25 %)	4 (14.3 %)
PPMS	0	2 (7.1 %)
Other	3 (8.3 %)	0
Disease duration (mean)	9.1 years	9.5 years
Currently on Immunotherapy	18 (50 %)	11 (39.3 %)
PDDS (mean)	2.86	2.04

IG intervention group, *CG* control group, *CIS* clinically isolated syndrome, *RRMS* relapsing remitting multiple sclerosis, *SPMS* secondary progressive multiple sclerosis, *PPMS* primary progressive multiple sclerosis, *PDDS* patient determined disease steps *Statistical significant difference ($p = 0{,}039$), **Missing data for two participants in the IG

The questionnaire was developed to assess knowledge on CI in the context of study results on treatment options. As there was no comparative instrument available,

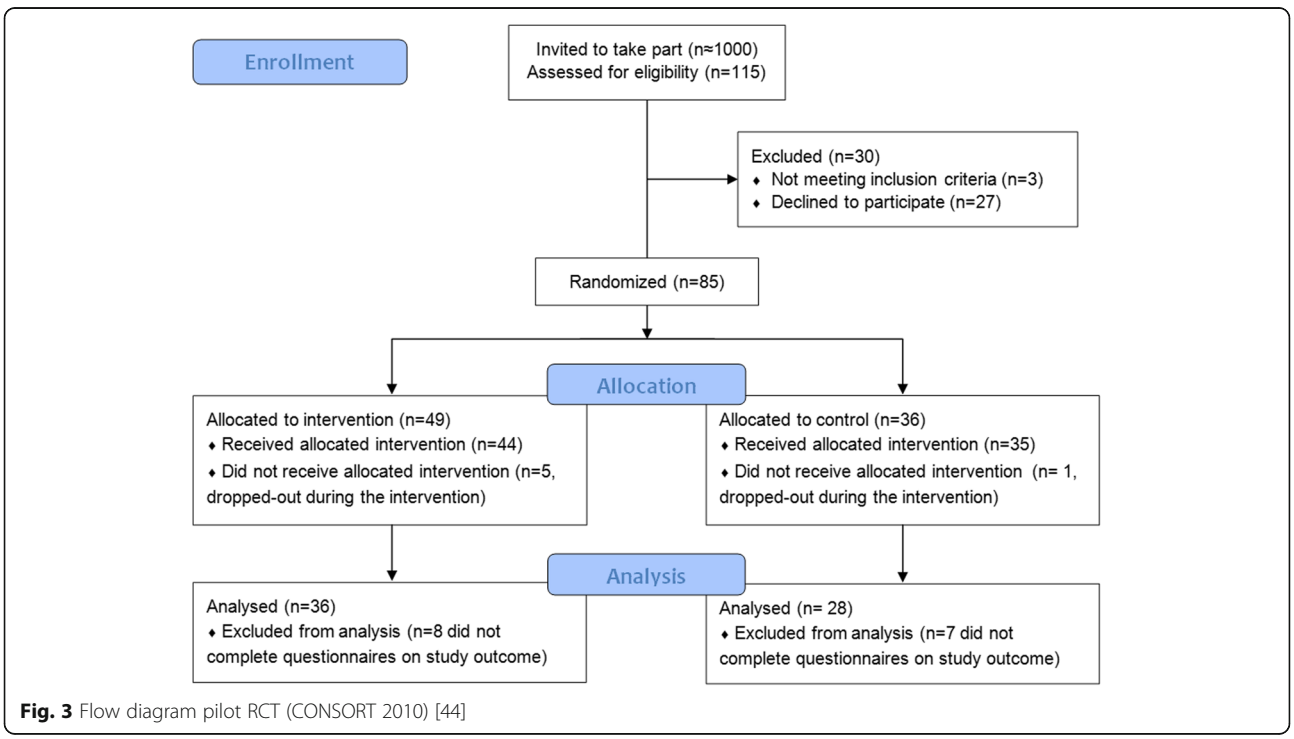

Fig. 3 Flow diagram pilot RCT (CONSORT 2010) [44]

the two groups were analysed separately concerning difficulty, internal consistency and discriminatory power [27].

The difficulty of the six items ranged between 0.43 and 0.94 in the IG and between 0.36 and 0.86 in the CG (Table 2).

Cronbach's alpha was 0.57 in the IG and 0.21 in the CG. Discriminatory power ranged between 0.17 and 0.45 in the IG and between 0.15 and 0.28 in the CG.

Due to a software error, only two of five questions on numeracy could be analysed. There was no significant correlation between numeracy and questionnaire results for the whole sample (0.161, $p = 0.21$). Numeracy in the CG correlated (Pearson's r) positively (0.473, $p = 0.01$) with the mean sum score of the questionnaire, but not in the IG (-0.06, $p = 0.7$).

Concerning the general evaluation questions, the average weight version received better results. Results concerning understandability, subjective knowledge and benefits of the PI significantly favoured the IG ($p = 0.01$) (Table 3).

Table 3 Evaluation questions

Item	IG $N = 36$	CG $N = 36$
Understandability	6.5	4.5
Relevance	7.6	6.6
Subjective knowledge	6.6	4.8
Benefit of the PI	7.8	6.0

Understandability of the PI (1 = not understandable at all – 10 = very good to understand), Relevance of the topic CI (1 = not relevant at all – 10 = very relevant), Subjective knowledge on CI (1 = not understood at all – 10 = fully understood), Benefit of a PI on CI (1 = not helpful at all – 10 = very helpful)

Discussion and conclusion

Discussion

To our knowledge this is the first study to explain CI to patients. We developed and pre-tested three different PI versions on CI and piloted them successfully following the Medical Research Council's guidance for developing and evaluating complex interventions [9]. Our pilot data indicate that CI can be made understandable through adequate PI interventions. PwMS contributed valuably to improve readability as well as understandability and enhanced comprehension. The majority of PwMS preferred either the average weight version or the worm prophylaxis version. The worm prophylaxis version was more difficult, but mirrored the setting of clinical trials very well, because of the treatment example. Therefore, this example could ease the transfer to immunotherapy decision making, as emphasised by some PwMS.

Statistical illiteracy by physicians and patients can result in misunderstanding study results, especially of numbers and verbal frequency statements [10, 29]. CI are beneficial for judging on the clinical relevance of statistical reporting and to reduce the chance of results being misinterpreted [3], because point estimates are complemented. Therefore, our graphical PI on CI, displaying both absolute risk reduction and significance of results, may be a step forward in patient education. The communication of CI could help to judge on the validity of the estimate by giving additional information to simply reporting point estimates. For example, the CI for the absolute risk reduction of glatiramer acetate (Copaxone®) concerning disability over 2 years ranges from zero to 21 and can be compared to other treatment options [30, 31]. However, not every patient needs to process and understand point estimates and CI as roles within decision making process have to be clarified [32] and thus might lead to a physician-led decision. Nonetheless, comprehensive information has to be made accessible in order to allow patients to get involved as much as they want based on the bioethical principle of autonomy [33]. Therefore, medical management should always strive for the highest possible degree of patient autonomy. This study is embedded in an ongoing project, in which a nurse-led decision-coaching intervention is evaluated to enable PwMS to make informed treatment choices [28]. The patient information will be made accessible on the online information platform after its evaluation in an RCT [34].

Limitations of this study

There are some shortcomings of this study. PwMS of this pilot-study had the advantage of comparing all three versions with each other. The teach-back of the content indicated that some PwMS benefited from going through more than one version as they could teach back more

Table 2 Item difficulty and discriminatory power

	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6
Mean item difficulty (SD)						
IG ($N = 36$)	0.94 (0.23)	0.80 (0.40)	0.75 (0.44)	0.43 (0.51)	0.86 (0.35)	0.92 (0.28)
CG ($N = 36$)	0.68 (0.48)	0.86 (0.36)	0.54 (0.51)	0.36 (0.49)	0.5 (0.51)	0.82 (0.39)
Discriminatory power						
IG ($N = 36$)	0.17	0.33	0.41	0.45	0.27	0.23
CG ($N = 36$)	- 0.15	- 0.04	0.28	0.23	0.10	0.14

IG intervention group, *CG* control group

information correctly after they had read the average weight and worm prophylaxis version. However, as the average weight version was always seen first by PwMS, the results might differ to another possible order. To account for this in a future RCT to evaluate all PI versions in larger sample [34], PwMS can watch a second video after having answered the questions. Due to the length and dense of information and drop-out rates it is not scheduled that PwMS see more than one PI material.

Caused by the small sample, the percentage of females in our pilot trial was imbalanced between the groups. However, we do not believe that this effected study results. Nevertheless, we will investigate on the impact of sex on the outcomes in the larger study.

Internal consistency and discriminatory power of the questionnaire were lower than aimed. For a high internal consistency, Cronbach's alpha should have been over 0.70 and discriminatory power should have ranged between 0.40 and 0.70 [27], which was not reached for any question in the CG, whereas it was reached in two out of six questions in the IG. However, because the questionnaire consists of six questions only aiming to evaluate disease specific knowledge and comprehension on confidence intervals in general, high internal consistency would have been difficult to reach. Higher Cronbach's alpha level in the IG indicates that gained knowledge leads to more consistent replies. The lack of a correlation of correct answers with numeracy in the IG might be due to the fact that a high score in numeracy is not necessarily helpful to understand the topic. However, this needs further evaluation.

With a mean difference of one question between groups clinical and practical relevance is an open question. Nevertheless, with more than two thirds of the questionnaire answered correctly by the IG it could be assumed that this kind of information on treatment options is understandable for PwMS. However, results need to be confirmed in a larger sample. Further, other presentation formats as for example videos might be a more attractive format for the user to receive information on CI than written information.

Finally, recruitment for the pilot-RCT was conducted via mailing-lists of the MS day hospital and self-help initiatives. Therefore, only PwMS, who are potentially interested in being updated by those institutions, were reached. Being aware that not all people read the newsletter, to us the response rate with 64 replies out of 115 who did login into the survey seemed sufficient for a pilot study and our recruitment target of 60 PwMS was fulfilled. However, a large study with a less biased sample is needed to evaluate the PI on CI.

Conclusion

The pilot-phase shows promising results concerning acceptability and feasibility of different information materials on CI. PwMS may benefit from understanding CI, because they will be able to better compare different therapy options.

Understanding CI and other numerical data is of high importance for an informed treatment decision making process. Therefore, further research should focus on possibilities to explain numerical data of different formats in different patient groups.

Additional files

Additional file 1: Coding tree. (DOC 30 kb)

Additional file 2: Systematic literature search. (DOC 37 kb)

Additional file 3: Example quotes patient information versions (pilot-phase). (DOC 33 kb)

Additional file 4: Table S1. Teach-back results. **Table S2.** Results pilot-test questionnaire. (DOC 32 kb)

Additional file 5: Multiple choice questionnaire "Comprehension of CI". (DOC 192 kb)

Abbreviations

CG: Control group; CI: Confidence interval; DECIMS: Decision coaching in multiple sclerosis; IG: Intervention group; MS: Multiple sclerosis; PI: Patient information; PwMS: People with multiple sclerosis; RCT: Randomised controlled trial

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Availability of data and materials

The dataset supporting the conclusions of this article is available from the authors on request.

Authors' contributions

CH is the principal investigator of the study. IM supervised the research process and contributed to study planning. The study was conceived by CH, AR, FF, SK, IB and KRL. The figures were developed by VDR. All authors read and approved the final manuscript.

Competing interests

AR, IB, KRL, SK, FF, VDR and IM have nothing to declare. CH has received research grants, congress travel compensations, and salaries for talks from BiogenIdec, Genzyme, Sanofi-Aventis, Bayer Healthcare, Merck Serono, Teva Pharma, and Novartis.

Consent for publication

Not applicable.
All patient/ personal identifiers have been removed or disguised so the patient/ person(s) described are not identifiable and cannot be identified through the details of the story.

Ethical approval and consent to participate

The ethics committee of the Hamburg chamber of physicians (PV4576, amendment) approved the study.
We obtained written informed consent from all interview participants (pre-test and pilot-test phase). Participants of the web-based pilot RCT were informed that the study runs anonymously and they were free to end participation at any stage. We informed potential participants that proceeding with the study was considered as given consent to participate in the study.

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Additional file 1: Coding tree

1. **Feasibility**
    - Acceptability
    - Introduction
    - Narrative line
    - Practicality
    - Graphic illustration
        - Introduction
        - Average weight
        - Anti-worm treatment
        - Short version
        - MS specific ending
        - MS questionnaire
    - Understandability/ Clarity
        - Introduction
        - Average weight
        - Worm prophylaxis
        - Short version
        - MS specific ending
        - MC questionnaire
        - Other
2. **Comprehension**
    - Definition of confidence intervals
    - Application of using confidence intervals
    - Width of confidence intervals
    - Statistical significance and confidence intervals
    - True value
    - Sampling and estimation
3. **Methodology**
    - Think-aloud method
    - Teach-back method

Additional file 2: Systematic literature search

In order to describe the current state of literature, a research question using the PICO-principle was formulated to perform a search [1]. A systematic literature search was performed via OVID in MEDLINE, EMBASE and PsycInfo to identify studies in which interventions aiming to explain CI were applied. Further searches were conducted in DART Europe, Open Thesis, OPUS, ProQuest, ERIC, ESS, and Web of Science.

Here the term “confidence interval” and variations were combined with “comprehension” and related terms using the Boolean operator AND. The search resulted in 1293 hits (table B1). All titles were screened by one researcher (FF). Title screening was performed over inclusive to identify relevant literature. After this scan, 35 results remained and abstracts were scanned. The full-text of the remaining 10 publications was assessed by two researchers (FF and AR), using a pre-defined screening checklist. The checklist allowed structured screening by the inclusion criteria (explanation of CI or statistics to patients, explanation of CI to medical professionals, evaluation of comprehension of CI).

No studies were identified that explained CI to laypeople.

Table: Results of the literature searches

Databases	Results
MEDLINE, EMBASE, PsycInfo via OVID:	1272
Web of Science:	15
All other databases:	6

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Additional file 3: Example quotes patient information versions (pilot-phase)

	Participant quotes
General impression	*"I really like it. It's cheerfully designed, I find it very agreeable."* (interview no. 8) *"Oh ok, it's a bit confusing. Maybe that's because of me, but that is just so much information at once."* (interview no. 11)
Understandability	[Question of the interviewer: "How would you assess the understandability overall?"]. *"It was good." (interview no. 1)* *That is clear so far, but is again so that I have problems in concentrating […] These are already three pages describing the same […] As a patient, I can't pay attention this long anymore." (interview no. 9)* *"The font size was well chosen. I usually have difficulties reading, I skip a line very often, but here it was fine […] This kind of wording was beneficial. I didn't have to read it twice." (interview no.6)* *"I didn't pay attention. I have other things to worry about, which are more important to me." (interview no. 5)* *"This is where it'd be handy to be mathematician, maybe my kids would understand. But the majority of people, including me, don't.(interview no. 4)*
Different versions	*"Very illustrative and well presented. The transfer to MS could be easily followed." (interview no. 6)* *"If somebody tried to explain this to me using fruits and apples, I would be very confused. I don't see the relevance in it. You can't compare it with diseases […] It's silly! […] I found the apple example strange. Anti-worm treatment was very good." (interview no. 4)*
MS specific medications	*"Ah, ok. Here we go. Now things become clear. This is also a question* [headline of the ending is: "How can this knowledge be transferred to MS drugs?"] *I've been asking myself."(interview no. 8)* *"This is much more meaningful than the things before. I simply understand it. There are 100 patients; one drug works better than the other. That's a clear statement." (interview no. 4)*

Additional file 4: Additional tables

Table S1: Teach-back results

	Good teach-back results	Mixed teach-back results	Not able to teach-back
Number of PwMS	3 (interview no. 1, 6 and 10)	6 (interview no. 3, 4, 5, 8, 9 and 11).	3 (interview no. 2, 7 and 12)

PwMS = People with multiple sclerosis

Table S2: Results pilot-test questionnaire

	Question 1	Question 2	Question 3	Question 4	Question 5	Question 6	Question 7	Question 8
Number of correct answers	5	5	4	5	3	3	5	6

Number of correct answers according to questions from n=6 people with multiple sclerosis in the qualitative study

Additional file 5: Multiple choice questionnaire "Comprehension of confidence intervals"

Question 1

What is meant by the term „confidence intervals"?

(Only one answer is correct)

o	They help to judge the certainty or uncertainty of study results.
o	They show the effectiveness of a drug.
o	They show in how many patients a treatment is effective and in how many it is harmful.
o	They are statistical aids, which have to be calculated by the reader at first.

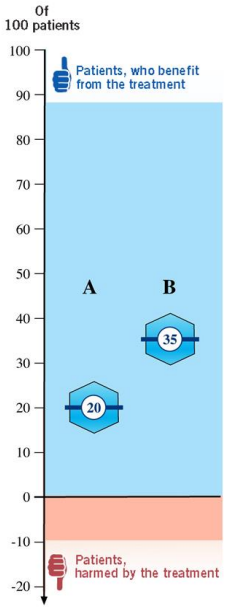
Question 2

Here, treatment effects of two medications are graphically displayed.

Which medication is more effective?

(Only one answer is correct)

o	Medication A
o	Medication B
o	There is no difference between the medications

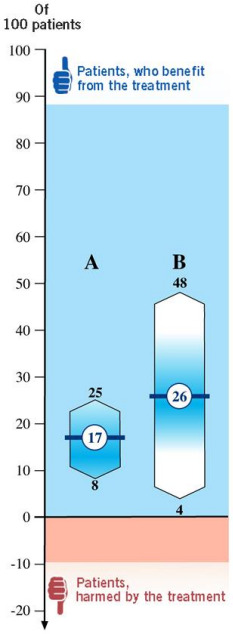


Question 3

Here, treatment effects of two medications are graphically displayed. For which of the medications the benefit is demonstrated with more certainty?

(Only one answer is correct)

o	Medicament A
o	Medicament B
o	There is no difference between the medications



Question 4

What does it mean, when the confidence interval crosses the zero line, thus includes positive and negative numbers?

(Only one answer is correct)

o	It has no special meaning
o	Confidence intervals cannot reach into a negative area
o	The benefit of the investigated medication is not sure
o	In case of negative numbers, the medication causes additional side effects.

Question 5

What is the meaning of the size of confidence intervals?

(Only one answer is correct)

o	The size of the confidence interval does not say anything about the certainty of the results
o	A wider confidence indicates a <u>few</u> participants
o	Study results with wide confidence intervals stand for great trustworthiness
o	A wide confidence interval indicates <u>many</u> participants

Question 6

Which statement about confidence intervals is correct?

A narrow confidence interval …

(Only one answer is correct)

o	… suggests that the benefit of a medication has been determined with considerable certainty
o	… is usually based on chance
o	… is worse than a wide confidence interval
o	… suggests that the benefit of a medication is uncertain

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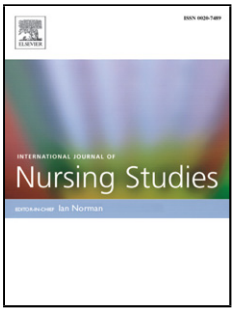

Title: Nurse-led immunotreatment DEcision Coaching In people with Multiple Sclerosis (DECIMS) – feasibility testing, pilot randomised controlled trial and mixed methods process evaluation

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Nurse-led immunotreatment DEcision Coaching In people with Multiple Sclerosis (DECIMS) – feasibility testing, pilot randomised controlled trial and mixed methods process evaluation

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Highlights

What is already known about the topic?

- People with multiple sclerosis prefer an informed shared decision-making approach.
- In general, MS nurses in Germany as in many other countries do not provide counselling on treatment options.
- No systematic approach exists to involve MS nurses in the counselling on immunotreatment options based on a shared decision-making approach.

What this paper adds

- The decision coaching approach is feasible and well accepted by people with multiple sclerosis, nurses and physicians.
- Nurses can successfully provide evidence-based decision coaching on immunotreatment options.

Abstract

Background: Treatment decision-making is complex for people with multiple sclerosis. Profound information on available options is virtually not possible in regular neurologist encounters. The “nurse decision coach model” was developed to redistribute health professionals’ tasks in supporting immunotreatment decision-making following the principles of informed shared decision-making.

Objectives: To test the feasibility of a decision coaching programme and recruitment strategies to inform the main trial.

Design: Feasibility testing and parallel pilot randomised controlled trial, accompanied by a mixed methods process evaluation.

Setting: Two German multiple sclerosis university centres.

Participants pilot trial: People with suspected or relapsing-remitting multiple sclerosis facing immunotreatment decisions on first line drugs were recruited. Randomisation to the intervention (n = 38) or control group (n = 35) was performed on a daily basis. Quantitative and qualitative process data were collected from people with multiple sclerosis, nurses and physicians.

Methods: We report on the development and piloting of the decision coaching programme. It comprises a training course for multiple sclerosis nurses and the coaching intervention. The intervention consists of up to three structured nurse-led decision coaching sessions, access

to an evidence-based online information platform (DECIMS-Wiki) and a final physician consultation. After feasibility testing, a pilot randomised controlled trial was performed. People with multiple sclerosis were randomised to the intervention or control group. The latter had also access to the DECIMS-Wiki, but received otherwise care as usual. Nurses were not blinded to group assignment, while people with multiple sclerosis and physicians were. The primary outcome was 'informed choice' after six months including the sub-dimensions' risk knowledge (after 14 days), attitude concerning immunotreatment (after physician consultation), and treatment uptake (after six months). Quantitative process evaluation data were collected via questionnaires. Qualitative interviews were performed with all nurses and a convenient sample of nine people with multiple sclerosis.
Results: 116 people with multiple sclerosis fulfilled the inclusion criteria and 73 (63%) were included. Groups were comparable at baseline. Data of 51 people with multiple sclerosis (70%) were available for the primary endpoint. In the intervention group 15 of 31 (48%) people with multiple sclerosis achieved an informed choice after six months and 6 of 20 (30%) in the control group. Process evaluation data illustrated a positive response towards the coaching programme as well as good acceptance.
Conclusions: The pilot-phase showed promising results concerning acceptability and feasibility of the intervention, which was well perceived by people with multiple sclerosis, most nurses and physicians. Delegating parts of the immunotreatment decision-making process to trained nurses has the potential to increase informed choice and participation as well as effectiveness of patient-physician consultations.
The study was funded by the German Ministry of Education and Research and the main trial was registered in "Current Controlled Trials" (ISRCTN37929939).

Keywords: decision coaching, mixed methods, multiple sclerosis, nurses, patient information, pilot randomized controlled trial, process evaluation, shared decision making

1. Background

Multiple sclerosis is an inflammatory degenerative disease of the central nervous system. About 2,300,000 people worldwide and 200,000 in Germany are affected by multiple sclerosis, with a disease onset around the age of 30 (Browne et al., 2014; Petersen, 2013; WHO, 2008). In approximately 85% of people with multiple sclerosis, the disease is characterised by a relapsing-remitting course (McKay et al., 2015). Due to the chronic nature

of the disease as well as ongoing approvals of new high price so called disease modifying drugs, multiple sclerosis is of high health economic relevance (Wingerchuk and Weinshenker, 2016). Moreover, non-adherence to disease modifying treatment in up to 70% of people with multiple sclerosis has been reported (Bruce and Lynch, 2011; Hansen et al., 2015). People with multiple sclerosis in Germany wish an active role in treatment decision-making (Heesen et al., 2004; Solari et al., 2013). According to the German patients' right act, patients have to be informed about treatment options including possible benefits and risks (Gesetz zur Verbesserung der Rechte von Patientinnen und Patienten, 2013). Many uncertainties as e.g. the unclear long-term benefit of treatments (Boggild et al., 2009), a possible benign multiple sclerosis variant (Amato and Portaccio, 2012; Hawkins, 2012) as well as the number of treatment options (Wingerchuk and Weinshenker, 2016) underline the necessity for counselling of patients on treatment options. As 15 different immunotreatments will be available in 2017, profound information on benefits and risks through physician encounters is becoming increasingly difficult.

Studies on evidence-based patient information and decision support in multiple sclerosis (Köpke et al., 2016; Köpke et al., 2014) indicate that provision of information and/ or decision-making tools alone may not be sufficient to achieve informed immunotreatment decision-making. People with multiple sclerosis seem to need more time and support to process and discuss the treatment options whereas group training alone might not be tailored enough to the individual situation of people with multiple sclerosis (Rahn et al., 2015). There is strong evidence for the effectiveness of efforts to include patients and consumers in decision-making on health issues (shared decision-making, SDM) (Stacey et al., 2017). Consequently, an individual approach accompanying physician consultations appears as a possibly essential strategy to promote informed decision-making (Rahn et al., 2015). A sub-analysis (Stacey et al., 2013) of a systematic review of patient decision aids (Legare et al., 2014) found that decision coaching, combined with decision aids compared to decision aids alone, increases the participation in the decision-making process, lowers costs and leads to intervention-specific positive results. Here, especially decision coaching interventions led by nurses showed promising results (Stacey et al., 2013). In Germany, multiple sclerosis specialist nurses have been established merely for the handling and information provision on injectable treatments (Hartung et al., 2011), but have no systematic role in disease modifying treatment decision-making. For people with multiple sclerosis, decision coaching (Stacey et al., 2012; Stacey et al., 2013), performed by trained multiple sclerosis nurses, offers the opportunity to individually discuss treatment options by allowing individual timing, knowledge and support needs in the decision-making process. Health professionals' tasks are redistributed by giving nurses a central role in supporting treatment decision-making based on evidence-based patient information materials (Bunge et al., 2010)

and a shared decision-making approach (Charles et al., 1997). Therefore, we assumed that our novel non-directive nurse-led decision coaching intervention allows for more active participation of people with multiple sclerosis in decision processes and more efficient physician consultations.

We report on the development and piloting of a decision coaching programme in multiple sclerosis, which is the first evaluation on the delegation of immunotreatment information provision to trained nurses in Germany. After feasibility testing, a pilot randomised controlled trial (RCT) was performed. It was aimed to test the recruitment procedure for the main cluster RCT and to gain data on feasibility of the intervention, accomplished by a mixed methods process evaluation in two pilot multiple sclerosis centres in Germany (Rahn et al., 2015).

2. Methods

We developed and piloted our multicomponent decision coaching in multiple sclerosis (DECIMS) programme following the British Medical Research Council's framework for developing and evaluating complex interventions (Craig et al., 2008). Figure 1 illustrates the steps of the decision coaching project. After the development of the programme, data on the feasibility of the nurse training course and the decision coaching intervention were gathered. Afterwards, a pilot RCT was conducted. A mixed methods process evaluation (Creswell JW, Plano Clark VL, 2011; Rahn et al., 2015) was performed alongside the pilot RCT following the recommendations of Craig et al. (Craig et al., 2008) to conduct process evaluations alongside complex interventions (Moore et al., 2015).

2.1 Development of the decision coaching programme

The concept of the decision coaching programme is described in the study protocol (Rahn et al., 2015). The programme comprises a training course for multiple sclerosis nurses and the coaching intervention.

2.1.1 Training course

A three day training course curriculum (16 hours) for decision coaches following the train-the-trainer principle based on the teaching approach of Roth (Roth, 1971) was developed. It intended to convey understanding and knowledge gain on the principles of evidence-based patient information, evidence based medicine and shared decision-making. The use of an online information platform on multiple sclerosis (DECIMS-Wiki, see below) to provide treatment information was trained. Role plays with case examples and simulated patients were performed to practice decision coaching by including supporting materials (Rahn et al., 2015). The training course (see suppl. material 1) was tested for feasibility with four nurses.

2.1.2 Decision coaching intervention

The intervention consists of up to three coaching sessions, access to the DECIMS-Wiki and up to two physician consultations (figure S1 suppl. material 5).

Decision coaching sessions

The decision coaching sessions are structured following the six steps of shared decision-making: (1) reviewing the problem, (2) key message, (3) information about pros and cons of each option, (4) expectations of the patient, (5) decision, and (6) arrangements (Elwyn et al., 2001). Patient workbooks, one on first line treatment and one for people with multiple sclerosis considering a treatment change as well as a coaching guide were developed to support and guide the decision coaching. Both workbooks and the coaching guide were pre-tested for feasibility (see suppl. material 2 for the workbook on first line treatment).

DECIMS-Wiki

The DECIMS-Wiki aims to provide information on several relevant topics on multiple sclerosis, but mainly focusses on treatment options. The content was built on former developed evidence-based patient information brochures and literature searches (Rahn et al., 2015). Information on benefits and side effects on all available drugs are provided. Therefore, bar charts on disability progression and relapses were developed to display the absolute risk reduction for each immunotreatment option. The comprehension of the bar charts was evaluated in a randomised controlled trial (Kasper et al., 2016).
For feasibility testing, feedback on the DECIMS-Wiki was obtained from two consumer representatives from a self-help initiative, nurses and people with multiple sclerosis. One consumer representative worked over a year regularly on the development of the DECIMS-Wiki and discussed the content with the researchers.
People with multiple sclerosis received login details and a user guide after they filled in the baseline questionnaires. The DECIMS-Wiki was also used during coaching sessions (see above).

Physician consultation

The coaching process finishes with up to two physician consultations, where the final decision is made (Rahn et al., 2015). All physicians received an information package on SDM (information sheet, paper and video on SDM) at the beginning of the study. Otherwise, consultations were conducted as usual.

2.2 Feasibility testing

Feasibility testing was conducted with a convenient sample of four nurses and 12 people with multiple sclerosis between July and December 2013. Four multiple sclerosis specialised nurses (two from each centre) received the training course in Hamburg and filled in questionnaires (knowledge and training course feedback) before and after training. A feedback round after the training course was audio recorded. One of the nurses (Bochum) dropped out directly after the study and one nurse with experience in the provision of evidence-based patient information from Hamburg was additionally trained. Each decision coach was coaching three people with multiple sclerosis. All people with multiple sclerosis gave structured feedback (questionnaire with open questions) on the coaching, the DECIMS-Wiki, the physician consultation and materials. Five people with multiple sclerosis were additionally called or asked in person for feedback. Materials to support the decision-making process were further tested and improved during this phase.

2.3 Pilot randomised-controlled trial

The pilot RCT was performed between March 2014 and March 2016 (first person with multiple sclerosis in, last person with multiple sclerosis out). The pilot RCT followed the main assumption that the concept is feasible for decision coaches and people with multiple sclerosis. It aimed to gather information on whether the decision coach intervention is accepted by people with multiple sclerosis, the materials are acceptable as well as helpful for people with multiple sclerosis and nurses, recruitment procedures are feasible, and outcome assessment is acceptable for people with multiple sclerosis (Rahn et al., 2015).
A convenient sample of 73 people with multiple sclerosis with suspected or relapsing-remitting multiple sclerosis facing an immunotreatment decision was recruited in the two study centres for the parallel group trial by physicians or nurses. It was assumed that around 60 people with multiple sclerosis would be sufficient for piloting the coaching programme. The leading ethical approval was obtained from the Ethics Committee of the Hamburg Chamber of Physicians. People with multiple sclerosis in the intervention group received the decision coaching intervention (see above and suppl. material figure S1). The control gained access to the DECIMS-Wiki. Both groups had final physician consultations. People with multiple sclerosis were allocated to the intervention (intervention group) or control group (control group) by randomised recruitment days. This recruitment procedure by days was chosen to test the feasibility of the procedure for the cluster RCT. Lists with randomised recruitment days were generated by an external statistician (EV) for both centres and one of two researchers (IB or AR) informed the nurses in the afternoon before recruitment days. Therefore, allocation concealment of the nurses was assured. On recruitment days, all people with multiple sclerosis were to be screened using standardised forms by the decision coaches and physicians. Decision coaches were not blinded to group assignment, while

people with multiple sclerosis and physicians were.
People with multiple sclerosis were eligible to participate when they were 18 years or older, had suspected (Miller et al., 2012) or relapsing-remitting multiple sclerosis (Polman et al., 2011), were facing a decision on starting or switching a first line treatment and had internet access. Exclusion criteria were: secondary-progressive or primary-progressive multiple sclerosis as well as any other suspected central nervous system disease, facing a decision on escalation immunotreatment or on symptomatic treatment, and severe cognitive deficit or major psychiatric illness affecting information uptake.

2.3.1 Outcome measures

Primary outcome was “informed choice”, using the “multi-dimensional measure of informed choice” (MMIC) (Marteau et al., 2001; Rahn et al., 2015) including the sub-dimensions risk knowledge measured by the “risk knowledge in relapsing multiple sclerosis” (RIKNO) questionnaire ((Heesen et al., 2015) assessed after 14 days), attitude concerning immunotreatment (one question assessed after physician consultation), and immunotreatment uptake (survey after six months). Based on previous studies (Kasper et al., 2008; Köpke et al., 2016; Köpke et al., 2014), informed choice is defined as adequate risk knowledge and congruency between attitude towards immunotreatment and therapy uptake (Rahn et al., 2015). Secondary outcomes included application of the “decisional conflict scale” (Buchholz, A, Hölzel L, Kriston L, Simon D, Härter M, 2011) supplemented by a version for health professionals to achieve dyadic measurement and analyses of videotaped coaching sessions assessing SDM as well as people with multiple sclerosis’, physicians’ and coaches’ evaluation of SDM by the standardised MAPPIN’SDM questionnaire (Kasper et al., 2012). The videos were analysed for all six SDM steps. The “control preference scale” (CPS, (Degner et al., 1997)) was used to monitor decisional processes and autonomy preferences. Further “coping self-efficacy” (Chesney et al., 2006) as well as trust in physicians and decision coaches were assessed (Bova et al., 2012). We did not analyse “planned behaviour in multiple sclerosis” (PBMS, (Kasper et al., 2012b)) as a new scaling format was applied. Therefore, results will be analysed separately.
Control parameters comprised anxiety and depression using the “hospital anxiety and depression scale” (HADS, (Zigmond and Snaith, 1983)), and disease-specific quality of life using the “Hamburg quality of life in multiple sclerosis scale” (HAQUAMS, (Gold et al., 2001)). Disability was measured by the “expanded disability status scale” (EDSS, (Kurtzke, 1983)) and assessed at baseline.
Data were collected at baseline, after the final coaching session, after the physician consultation as well as two weeks, three and six months after the physician consultation. We have chosen a six month frame as applied previously (Köpke et al., 2014) to allow some time

for people with multiple sclerosis to arrange all the organisational issues of disease management as e.g. baseline lab tests or receiving drug prescriptions from neurologists. All data were managed with the secuTrial® database of the German Competence Network Multiple Sclerosis (KKNMS). Nurses, people with multiple sclerosis and physicians filled in questionnaires online. After six months, some data were collected by phone via a standardised questionnaire (see suppl. material 3).

2.4 Process evaluation

The pilot RCT was accompanied by an embedded mixed methods (Creswell JW, Plano Clark VL, 2011) process evaluation to gain information on the feasibility and the acceptability of the programme (Grant et al., 2013). There is a growing body of literature to guide the conduction of process evaluations alongside randomised controlled trials (Grant et al., 2013; Moore et al., 2015). In our process evaluation, the framework proposed by Grant et al. for cluster RCTs was used (Grant et al., 2013; Rahn et al., 2015). Feasibility was defined as test of practicality (e.g. use of the questionnaire platform, use of materials during coaching sessions) and acceptance of the intervention (Bowen et al., 2009) using qualitative as well as quantitative methods. Moreover, it was explored whether process evaluation data support the pilot RCT findings in general.

The pilot RCT was accompanied by questionnaires for nurses (baseline, after six and 18 months) during the course of the study, people with multiple sclerosis (baseline, after two weeks, three and six months) and physicians (baseline or when they started in the centre and after 18 month) consisting of closed and open questions. Because baseline measurements were taken at the beginning of the pilot study, the coaches had already gained some coaching experience during the feasibility phase. Questionnaires aimed to assess the feasibility and the practicality of the intervention and to identify possible barriers and facilitators (see suppl. material 3 and 4). More details on the process evaluation are provided in the protocol (Rahn et al., 2015). All data were managed with the secuTrial® database.

Qualitative data were collected by semi-structured interviews with all nurses and a convenient sample of people with multiple sclerosis (n = 9, 5 intervention group and 4 control group) after the study was finished. The last interviews were conducted in January 2016. The interview-guides (decision coaches and people with multiple sclerosis) were developed by taking the results of the quantitative process evaluation into account. The guide for nurses consists of questions concerning the general impression of the study, intervention aspects (e.g. DECIMS-Wiki, coaching, moderation cards), and the decision coach role (e.g. change of work routine, attitude). The guide for people with multiple sclerosis in the intervention

group consists of questions concerning the general impression of the study, intervention aspects (e.g. DECIMS-Wiki, coaching, patient workbook), immunotreatment decision-making, attitude, the physician consultation and organisational aspects (e.g. questionnaires). All people with multiple sclerosis were interviewed via phone by a trained single interviewer, who was not involved in study planning and provision of the intervention. Interviews with the coaches were performed face-to face (three interviews) or by phone (one interview) by a single interviewer (KA), who was not involved in study planning and the nurse training. All interviews (coaches and people with multiple sclerosis) were audio recorded.

2.5 Analyses

Data were analysed using SPSS version 21 (International Business Machines Corporation (IBM), Armonk, United States of America).

Due to the pilot character of the study we refrained from statistical testing (for further information see suppl. material 5, additional information S1: Statistical analyses). For the primary outcome measure, the proportion of informed choices (good risk knowledge and congruence between attitude and uptake) within a treatment group was assessed. Because it is a compound measure, only people with multiple sclerosis who provided data on all three measures (risk knowledge, attitude and uptake) were included in the analysis.

Quantitative data (questionnaires and evaluation forms) were analysed descriptively.

Interviews were analysed deductively with openness to new arriving themes by content analysis (Mayring, 2014) using the software programme QCAmap (P. Mayring and T. Fenzl, Klagenfurt, Germany). Two researches (AR and KA) independently analysed all interviews using a pretested coding guide. Non-agreement was resolved by discussion. A good coder agreement was reached in all three analyses (people with multiple sclerosis intervention group, people with multiple sclerosis control group and decision coaches).

3. Results

3.1 Training course

Four nurses, three females and one male, took part in the decision coach training course in July 2013 in Hamburg. Decision coaches' knowledge improved on average from 28% to 42% (mean) correct answers. Overall, decision coaches were satisfied with the training, found it informative and felt well prepared for the decision coaching, but the nurses suggested reducing the length of the training.

3.2 Feasibility testing

Feasibility was tested after the training course in the two study centres with three nurses in

Hamburg and one in Bochum. During the feasibility phase, feedback on the materials was gathered leading to the following changes for the pilot RCT: (1) It was decided to video record all coaching sessions to assess shared decision-making. (2) Moderation cards were developed as the initial coaching guide was not perceived to give sufficient structure and support. One set of moderation cards was developed for decisions on first line treatments and one for switchers following the six decision steps by giving information to every step as well as guidance to make use of the resources (DECIMS-Wiki, patient workbook). (3) Minor changes in the workbook.
People with multiple sclerosis expressed to be satisfied with the coaching and the materials. No person with multiple sclerosis found it problematic to receive information on treatment options from a nurse instead of a physician.

3.3 Pilot randomised controlled trial

In total, 785 people with multiple sclerosis were screened with 107 (14%) fulfilling the inclusion criteria. Of those 64 (60%) were included in the study. Most people with multiple sclerosis declined to participate because it was too much effort to have further appointments (8 times) or they refused to participate in studies in general (7 times). Only once, participation was declined because the person with multiple sclerosis did not want to speak with a nurse or/ and wanted to speak with a physician immediately. In total five people with multiple sclerosis (13%) dropped-out in the intervention group and ten (29%) in the control group (figure 2). In addition, several people with multiple sclerosis did not fill in the questionnaires at different measurement points. Together that led to a considerable amount of missing data:

- Intervention group: baseline: 8%, after coaching: 11%, after physician consultation: 8%, after 14 days: 16%, after three months: 24%, after six months: 13%
- Control group: baseline: 17%, after physician consultation: 26%, after 14 days: 40%, after three months: 40%, after six months: 34%.

3.3.1 Informed choice (primary endpoint)

Data of 51 people with multiple sclerosis (70%) were available for the primary endpoint calculation.

In the intervention group 15 of 31 (48%) people with multiple sclerosis and in the control group 6 of 20 (30%) people with multiple sclerosis achieved informed choices.

3.3.2 Further outcomes

The “risk knowledge in relapsing multiple sclerosis” questionnaire consists of 19 questions. Descriptive data on mean-scores indicated improvement in both groups over time: baseline (intervention group (n = 35): 8.3 (SD 3.4)/ control group (n = 29): 8.1 (SD 3.1)), after two weeks (intervention group (n = 30): 9.7 (SD 3.7)/ control group (n = 21): 9.1 (SD 3.8)), after three months (intervention group (n = 29): 10.2 (SD 3.2)/ control group (n = 21): 9.6 (SD 3.2)) and after six months (intervention group (n = 30): 10.1 (SD 4.1)/ control group (n = 20): 10.3 (SD 3.4)).

MAPPIN’SDM assessment by questionnaires (people with multiple sclerosis, physicians and decision coaches (intervention group only)) showed high levels of involvement in both groups (table 2). Objective video-based ratings were less positive. However, due to a technical problem, only videos from the centre in Hamburg were available. Here, the nurses recorded coaching sessions of 18 people with multiple sclerosis.

Decisional conflict was low in both groups (scale from 0-4 with higher scores indicating lower decisional conflict). Mean scores were 3.4 (SD 0.4) in the intervention group (n = 33) and 3.1 (SD 0.6) in the control group (n = 26) after the physician consultation rated by people with multiple sclerosis. Physicians rated decisional conflict 3.4 (SD 0.4) for the intervention group (n = 30) and 3.0 (SD 0.7) for the control group (n = 25). Directly after the last coaching session, coaches rated decisional conflict low (3.4 (SD 0.6)) for people with multiple sclerosis in the intervention group (n = 35).

The descriptive analyses of the control preference scale indicated that people with multiple sclerosis preferred an informed choice decision-making approach in both groups.

Values respective trust in physicians were 38.4 (SD 12) in the intervention group (n = 30) and 40 (SD 9.2) in the control group (n = 24) assessed after the last physician consultation. The score ranges from 0-52 and higher values indicate more trust. In the intervention group (n = 27), trust in decision coaches with a mean score of 47.8 (SD 5.4) was high, assessed after the last coaching session.

Descriptive results of the “coping self-efficacy” scale are displayed in the suppl. material 5. While the depression score was inconspicuous at any time point in both groups, anxiety scores showed borderline values at baseline in the intervention group. During follow-up, all anxiety score measurements were inconspicuous.
Health related quality of life was high and stable during the study.

3.4 Process evaluation

Please see suppl. material 4 for a summary of barriers and facilitators according to individual domains and suppl. material 5 for additional information on the process evaluation.

Nurses (decision coaches)

The study was well accepted by decision coaches, who experienced and valued positive feedback from people with multiple sclerosis. Most coaches rated that they enjoyed conducting the coaching. The interviews highlighted that most coaches made positive experiences in their new role. *"So, I have only had positive experiences, both, feedback from the patients and for myself, so, I felt very comfortable in the role" (Interview I).* Two nurses stated that being videotaped during the coaching sessions was burdening.
Decision coaches were confident about their coaching competence during the study, gained coaching routine and had no worries that they could not appear competent. They stated having enough knowledge to perform the coaching. Some coaches felt at least partly distressed during the coaching sessions. Reasons to feel stressed were: difficulties to motivate people with multiple sclerosis to fill in the patient workbook, complex questions on specific disease modifying drugs, interruptions, depending on the individual people with multiple sclerosis, and being videotaped.
While coaches rated that there was no change in their professional relationship to physicians, another aspect mentioned in the interviews was that contact with physicians was more professional and that they thought that physicians appreciated them more. *"(...) but I believe, the physicians now have a different appreciation towards us. (...) So in the eyes of the assistant physicians here, I believe, we have risen in esteem (Interview II).*
Decision coaches rated the DECIMS-Wiki to be helpful during the coaching sessions and very helpful to look something up. This positive response was further mirrored in the interviews: “*There were no technical difficulties, and I got along well with it. It is easy, understandable and it helped me a lot” (Interview III).*

The coaches evaluated the moderation cards as helpful to structure the coaching sessions alongside the SDM steps and to receive guidance in coaching: *"Yes, that is just a good guideline, which could be used right at the beginning quite well"* (Interview IV). During follow up, some nurses stated not to use moderation cards anymore, because they had gained enough routine.
The decision coaches rated the patient workbook as helpful to accompany the coaching, but there were also difficulties raised such as the complex diagnosis part.
Overall, there were no indications that programme changes were necessary.

Physicians

At baseline seven and at the end of the study six physicians filled in the questionnaire. However, only one physician recruited people with multiple sclerosis in Bochum and filled in the questionnaires. Three neurologists (one senior) and four assistant physicians answered the questionnaires.
Most physicians were positive that the study was conducted in their centres. On study recruitment days, the working routine changed or changed somewhat. At the end of the study physicians gave the following reasons why their working routine changed: Interruption of conversations (three times), no provision of information on immunotherapies (two times), time exposure to present the study (one time), and more efficient procedure (one time). The organisational workload was burdening for some physicians. Most physicians reported that it was not difficult to interrupt the conversation to inform the people with multiple sclerosis about the study. All physicians stated that their workload was reduced when a person with multiple sclerosis received coaching. They rated the coaching as helpful for people with multiple sclerosis as well as beneficial for the consultations. Most physicians stated that there was no change in the working relationship with trained nurses.
Most physicians did not agree that every person with relapsing-remitting multiple sclerosis should start immunotreatment. They thought that they could counsel people with multiple sclerosis generally on immunotreatment options without giving an explicit advice. All physicians rated that people with multiple sclerosis participated more actively on immunotreatment decisions through the coaching. They stated that they could accept the decision of well-informed people with multiple sclerosis even when they would advise otherwise.

People with multiple sclerosis

DECIMS Wiki (both groups)
The DECIMS-Wiki was rated as usable and the information as understandable. Please see supplementary material 5 for self-reported use of the DECIMS-Wiki and usability ratings.

Further, the use of the DECIMS-Wiki was tracked. Data were available for 18 people with multiple sclerosis in the intervention group and 19 in the control group. There was a mean login of 3 (SD 1.6) times in the intervention group and of 2 (SD 1.4) times in the control group.

Intervention group (Decision coaching)

The expectations of people with multiple sclerosis on the decision coaching are summarised in the suppl. material 5. Most people with multiple sclerosis had two decision coaching sessions and found the number just right. People with multiple sclerosis rated that they felt very well informed through the decision coaching (VAS 9 (SD 1.1) out of 10) and very well prepared for the physician consultation (VAS 9 (SD 1.8) out of 10). The coaching and the DECIMS-Wiki were rated as most helpful for decision-making.

The interviews with all five people with multiple sclerosis illustrate the high acceptance of the decision coaching: *“I would recommend this to every multiple sclerosis patient when he has to decide about a drug” (interview I intervention group)*. It was elaborated by people with multiple sclerosis that it was very positive that the decision had to be made by oneself and that the nurse and the physician did not try to influence, but were rather informative by giving advice and assistance. Another people with multiple sclerosis described why the coaching was so essential: “*So nice it is this Wiki that you go for yourself, but you simply need someone who has an idea from the subject and at times when I am at home and read through, there always arise questions. And so, it was just nice in the face to face conversations that I could ask directly what that concerned and that you got a qualified answer from someone who knows and that I found very important” (interview III intervention group).*

Some people with multiple sclerosis emphasized their trust in the nurse as one positive aspect: *“At the physician one always has the feeling, okay; maybe he rather prescribes the medicine (...) I had more trust, I think, in the nurse than to the physician, from the point of view that she just has a completely neutral approach”* (Interview III intervention group). Most people with multiple sclerosis told that the coaching was helpful or assuring in immunotreatment decision-making. They rated that they did not receive a recommendation from the decision coach (table 3).

The DECIMS-Wiki was described as helpful by people with multiple sclerosis, especially the information on drugs (see supplementary material 5).

Four people with multiple sclerosis commented that they never used the patient workbook at home and one person with multiple sclerosis that it was only used twice for a brief look at home. *"So, then I either did not take it, or immediately filed it in my documents, I have never used it"* (interview I intervention group). Some people with multiple sclerosis commented that

they found the workbook useful during the coaching. The self-reported use of the patient workbook is summarised in the suppl. material 5.
In general, people with multiple sclerosis commented positively on the final physician consultation to discuss the decision: *"What I also found very well is that I then also had a conversation with the physician, where finally my decision again has been touched upon, why and why now this drug and no other" (interview I intervention group).* Three and six months after the final physician consultation, most people with multiple sclerosis said that they were still fine with the number of coaching sessions they had.

Physician consultation (both groups)
Most people with multiple sclerosis in both groups had one physician consultation after the intervention and most of them rated the number of consultations as just right. The results of self-reported assessment of the length of the first consultation (in minutes) are summarised in the suppl. material 5. Results on whether people with multiple sclerosis felt that they received a clear recommendation in favour of or against immunotreatment from a physician are displayed in table 3.

4. Discussion and conclusion

4.1 Discussion

The results of this pilot RCT on a novel immunotreatment decision coaching programme show that the programme is feasible and well accepted by people with multiple sclerosis, nurses, and physicians. Overall, outcomes are in line with our pre-defined assumptions. The results of the process evaluation are of particular relevance for this complex intervention. Quantitative and qualitative results collected from different perspectives support the RCT data and illustrate that the intervention is practicable and well accepted. Further, the study showed feasibility of the recruitment procedure and data entry through the secuTrial® database by nurses, people with multiple sclerosis and physicians.
The targeted endpoint was informed choice and descriptive results indicate more informed choices in the intervention group. Also, risk knowledge, the prerequisite for informed decision-making, improved in both groups over the study course with highest values three and six month after the intervention. Nonetheless, improvement in risk knowledge was small, which is mainly explained by the fact that the “risk knowledge in relapsing multiple sclerosis” questionnaire addresses risk knowledge in multiple sclerosis in general and is not specifically tailored to the intervention.
Our pilot study adds to the rare knowledge on nurse-led decision coaching. Similar to our

descriptive pilot study results, a review on decision coaching interventions showed no additional improvement in knowledge when decision coaching was compared to decision aids (Stacey et al., 2013). Nonetheless, trials where nurses provided the coaching intervention showed in general favorable results (Stacey et al., 2013). Hamann et al. (Hamann et al., 2006) for example showed that going through a decision aid with a nurse is feasible and more patients participated in psychoeducation and socio-therapeutic interventions afterwards. In another study (Lerman et al., 1997) counselling on BRCA1 gene testing was mostly provided by trained nurses. While the intervention increased the perceived importance on risks and limitations of the screening and also decreased the perceived benefits of the testing, the intentions of having BRCA1 testing did not change. Comparable to these results, there was no difference in immunotherapy uptake shown descriptively in our pilot RCT and quantitative as well as qualitative process data illustrated no change in attitude but rather confirmation of people with multiple sclerosis' attitudes by the coaching. Here, the main trial will produce stronger evidence whether there is a change in immunotreatment uptake and adherence as result of the coaching intervention.

Shared decision-making was evaluated by the MAPPIN'SDM approach. Here, the questionnaire results showed only slight differences between groups. Therefore, including video analyses in the main trial seems indispensable. As we only videotaped coaching sessions, no data are available from this pilot trial to further explore shared decision-making in the control group. A limitation is caused by the circumstance that coaching sessions were only videotaped in Hamburg. As physician consultations were not videotaped, we were unable to analyse the full SDM process.

Interestingly, people with multiple sclerosis in the intervention group tended to express higher trust in decision coaches than in physicians. There was no difference shown in trust in physicians and nurses in a study by Bova et al. (Bova et al., 2012) applying the questionnaire to a random sample of adult primary care patients who, on the other hand, trusted attending physicians more than medical residents. Reasons may be that people with multiple sclerosis felt more confident and experienced fewer barriers to ask questions and demanded the time needed. In a pilot trial (Dobke et al., 2008), where information was provided in a telemedicine approach before a face-to-face consultation with a surgical specialist, it was suggested that patients may benefit from a different discussion atmosphere, which might be reflected by our results on trust in physicians and nurses. These interesting finding needs further investigation and will be explored in the ongoing RCT.

The process evaluation showed that people with multiple sclerosis felt very well informed through the coaching and it can be concluded, supported by further process evaluation results that the coaching intervention was well accepted by people with multiple sclerosis. Only in two instances, people with multiple sclerosis stated that they did not want to

participate in the study because they did not want to speak with a nurse or/ and wanted to speak with a physician immediately. While the people with multiple sclerosis rated the patient workbook as helpful, qualitative data from people with multiple sclerosis and decision coaches indicate that not all patients may use it outside coaching sessions. The DECIMS-Wiki was well accepted by people with multiple sclerosis. As people with multiple sclerosis are particularly internet-minded (Colombo et al., 2014; Marrie et al., 2013) and respond well to internet programmes (Fischer et al., 2015; Pöttgen et al., 2015), the DECIMS-Wiki fulfils the growing demand for reliable online information. However, while only few people with multiple sclerosis stated that they had never used the DECIMS-Wiki, we cannot reliably estimate the amount of time spent for using the DECIMS-Wiki. We assume that some people with multiple sclerosis did not use this resource.

Most decision coaches reflected positively on their new role. The video analysis showed that coaches are able to give accurate information on treatment options using a SDM approach. Nurses also rated to have gained routine during the course of the study. Limited time to conduct the coaching was seen as a barrier. Here, the process evaluation shows that the coaching was rated to be better if it was integrated into the daily routine. Also, being videotaped was a permanent barrier for at least one coach, while most coaches felt not disturbed. Comments on the patient workbook were mixed. Therefore, the usability of the workbook has to be further explored. Data from larger samples of trained nurses from more centres are required to get a more complete picture on coaching competencies and factors influencing coaching performance.

The intervention was well accepted by physicians, who did not indicate important barriers to integration of trained nurses in the process of immunotreatment decision-making. Therefore, it seems that the concept of informed SDM, which might be related to an increased work burden for increasingly fewer physicians in Germany (Blum and Löffert, 2010; Korzilius, 2012), could be successfully supported by trained nurses.

Limitations of this study

The study is limited by the small sample. However, as this is a pilot study, it was not aimed to test for statistical significance (for further information see suppl. material 5). The power calculation of the larger cluster randomised trial to assess effectiveness of the approach is based on the results of an earlier RCT on evidence based patient information (Köpke et al., 2014) as outlined in the study protocol (Rahn et al., 2015). The objectives to test the recruitment procedures and feasibility were reached.

There was a considerable amount of missing data despite e-mail reminders, telephone calls and the option to receive the questionnaire via postal mail. There were more missing data in the control group. Maybe this is caused by the fact that in the control group, people with

multiple sclerosis received less attention from nurses compared to the intervention group. Here, most data were missing after 14 days and three months, when there were no longer appointments with coaches. After six months, people with multiple sclerosis received a standard phone call (standardised questionnaire), which might explain better response rates at this time point.

Further, the study could have been biased by the fact the physicians could easily find out or might have been told in the consultation, which people with multiple sclerosis received the intervention and might have behaved differently in the final physician consultation.

Another limitation is caused by the circumstance that in Hamburg nearly ideal prerequisites for the coaching intervention were given as previous work on evidence based patient information has been performed in this centre. Support was provided in particular through the head of the centre and principal investigator of the study (CH). As most people with multiple sclerosis were included in Hamburg, data from other centres are important to show the feasibility of the coaching intervention outside research centres or practices with a particular and high motivation.

4.2 Conclusion

This pilot-study showed promising results concerning acceptability and feasibility of transferring parts of the immunotreatment decision-making process to nurses. The intervention was valued and well perceived by people with multiple sclerosis, most nurses and physicians. Further, it was shown that nurses are able to perform evidence-based decision coaching on immunotreatment options. The innovative approach of delegating treatment information provision to trained nurses using evidence-based patient information has the potential to facilitate informed choice in multiple sclerosis and support physicians in Germany.

4.3 Practice Implications

Patient engagement is of high priority in multiple sclerosis and by giving nurses a crucial role in the treatment decision-making process; resources are redistributed considering limited physician resources and growing treatment options. The ongoing cluster RCT will further elaborate whether it is possible to engage people with multiple sclerosis as well as healthcare professionals and institutions in immunotreatment decision-making in Germany. Meanwhile, the programme is implemented in Hamburg, but further research needs to clarify the value of decision coaching by trained nurses in multiple sclerosis as well as in other settings (Berger-Höger et al., 2015). More elaborate nurse education and integration of new roles in the health system has a substantial potential to increase patient involvement. Policy makers in Germany and other countries should address structural prerequisites including

financial concepts.

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Authors' contributions: CH is the principal investigator of the study and AR conducted the study. IM and SK supervised the research process and contributed to study planning. The study was conceived by CH, SK, and JK. AR contributed to detailed study planning. AR and SK developed the accomplishing process evaluation. CH, IM, IB and JK added to the specification of the process evaluation. CH, SK, JK, and AR created the nursing training. CH, SK, JK, IB and AR conducted the nurse training. IB and AR planned the statistical analysis and IB conducted the analysis. AR and KA performed the qualitative analysis. BU performed the video analysis. AR wrote the manuscript. CH and IK obtained ethical approval and supervised the study at the respective study centres. CH, IM, IK, AA, IK and SK commented on and edited the manuscript. All authors read and approved the final manuscript.
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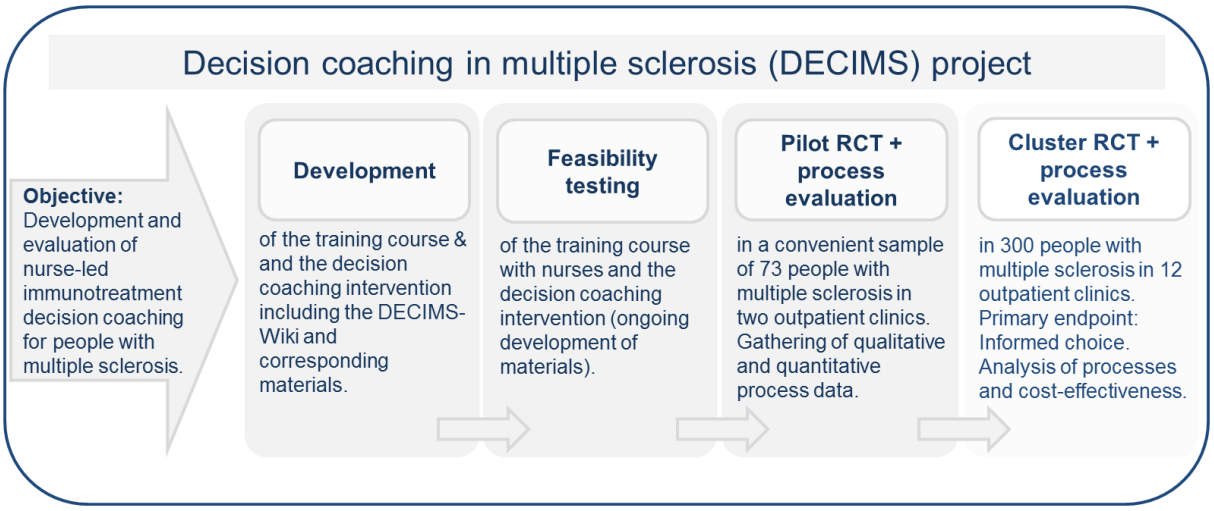
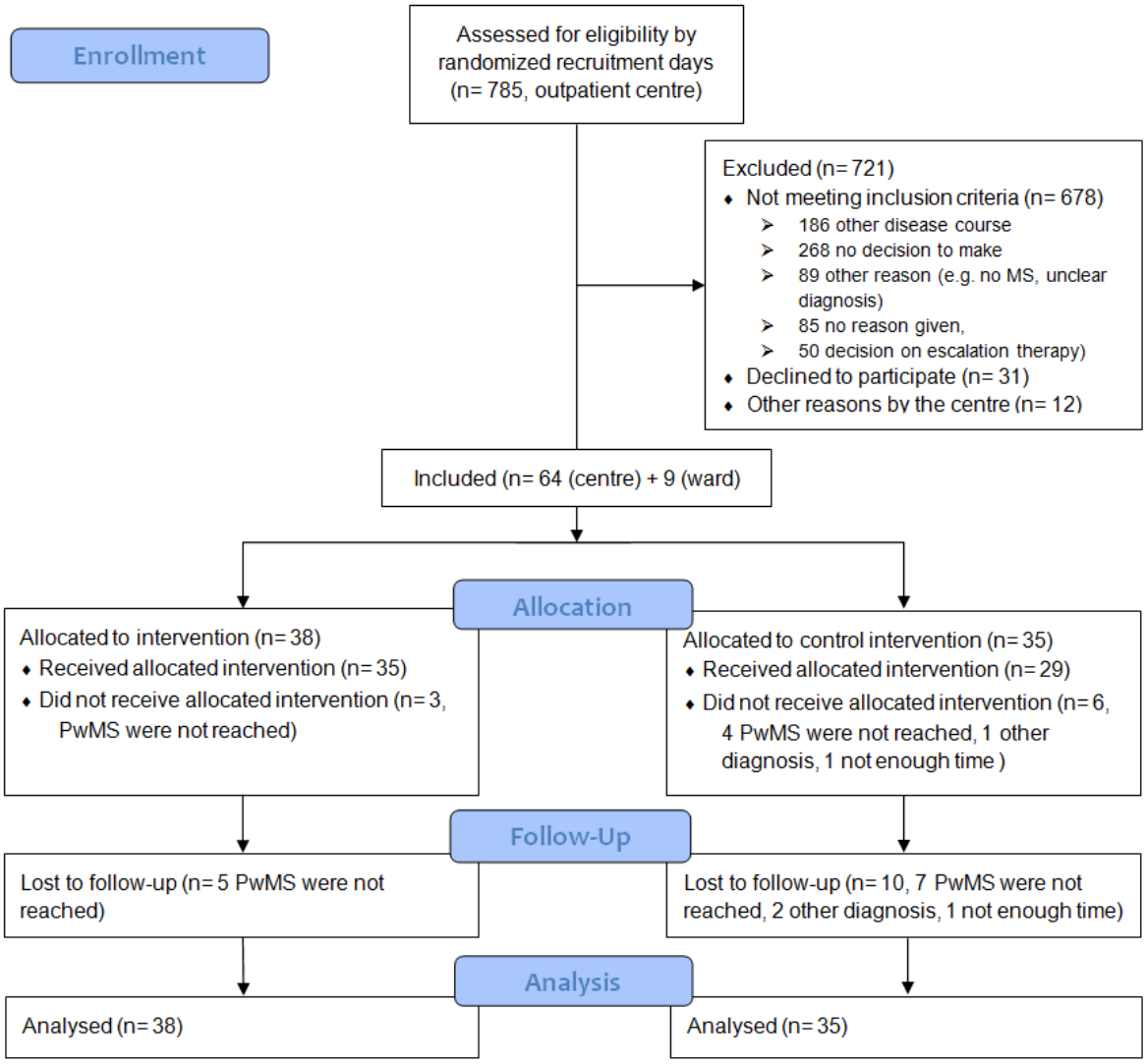


Figure 1: Decision coaching in multiple sclerosis (DECIMS) project

Legend: The results of the feasibility testing and the pilot RCT are reported in this paper. The cluster RCT is ongoing.

Figure 2: Pilot randomised controlled trial flow (Eldridge et al., 2016)



In total, 73 people with multiple sclerosis were included in the pilot RCT, 38 in the intervention group and 35 in the control group (figure 2). Groups were comparable at baseline (table 1).

Table 1: Baseline data

Baseline data	**Intervention group (n = 38)**		**Control group (n = 35)**	
	n	%	n	%
Female	26	68	28	80
Decision type First line treatment (%) Treatment change (%) Unclear (%)	 22 15 1	 58 40 3	 22 12 1	 63 34 3
Higher education	18*	51.1*	20**	69**
At least part-time employment	26	74.3	24	88.9
	mean	SD	mean	SD
Age (years)	38.3	9	36.2	11
Disease duration (months)	41.4	56,5	56.5	79.5
EDSS	1.9	1.2	1.7	1
Relapse rate (last 12 months)	0.8	0.7	1.1	0.9

*Missing data for three people with multiple sclerosis, **missing data for six people with multiple sclerosis, EDSS = Expanded disability status scale, SD = standard deviation

Table 2: Shared decision-making

Shared decision-making (physician consultation)											
People with multiple sclerosis (Questionnaire)				**Physicians (Questionnaire)**				**Observer (Video analysis)**			
Intervention group (n = 33)		**Control group (n = 26)**		**Intervention group (n = 30)**		**Control group (n = 25)**					
mean	SD	mean	SD	mean	SD	mean	SD				
3.5	0.6	3.2	0.4	3.5	0.4	3.2	0.5				
Shared decision-making (decision coaching)											
People with multiple sclerosis (Questionnaire)				**Nurses (Questionnaire)**				**Observer (Video analysis)**			
Intervention group (n = 32)		**Control group**		**Intervention group (n = 35)**		**Control group**		**Intervention group (n = 18)**		**Control group**	
mean	SD			mean	SD			mean	SD		

3.6	0.5			3.5	0.5			2.4	0.6		

The scale ranges from 0-4 with 4 indicating the highest levels of shared decision-making, SD = standard deviation

Table 3: Perceived immunotreatment recommendation

By the physician	**Intervention group (n = 38)**		**Control group (n = 35)**	
	n	%	n	%
No	19	50	6	17
Yes, a little	7	18	9	26
Yes, very much	7	18	11	31
Missing	5	13	9	26
By the decision coach (nurse)	**Intervention group (n = 38)**		**Control group**	
No	21	55		
Yes, a little	9	24		
Yes, very much	3	8		
Missing	5	13		

In both groups, people with multiple sclerosis rated that their expectations towards the study were met after the final physician consultation.

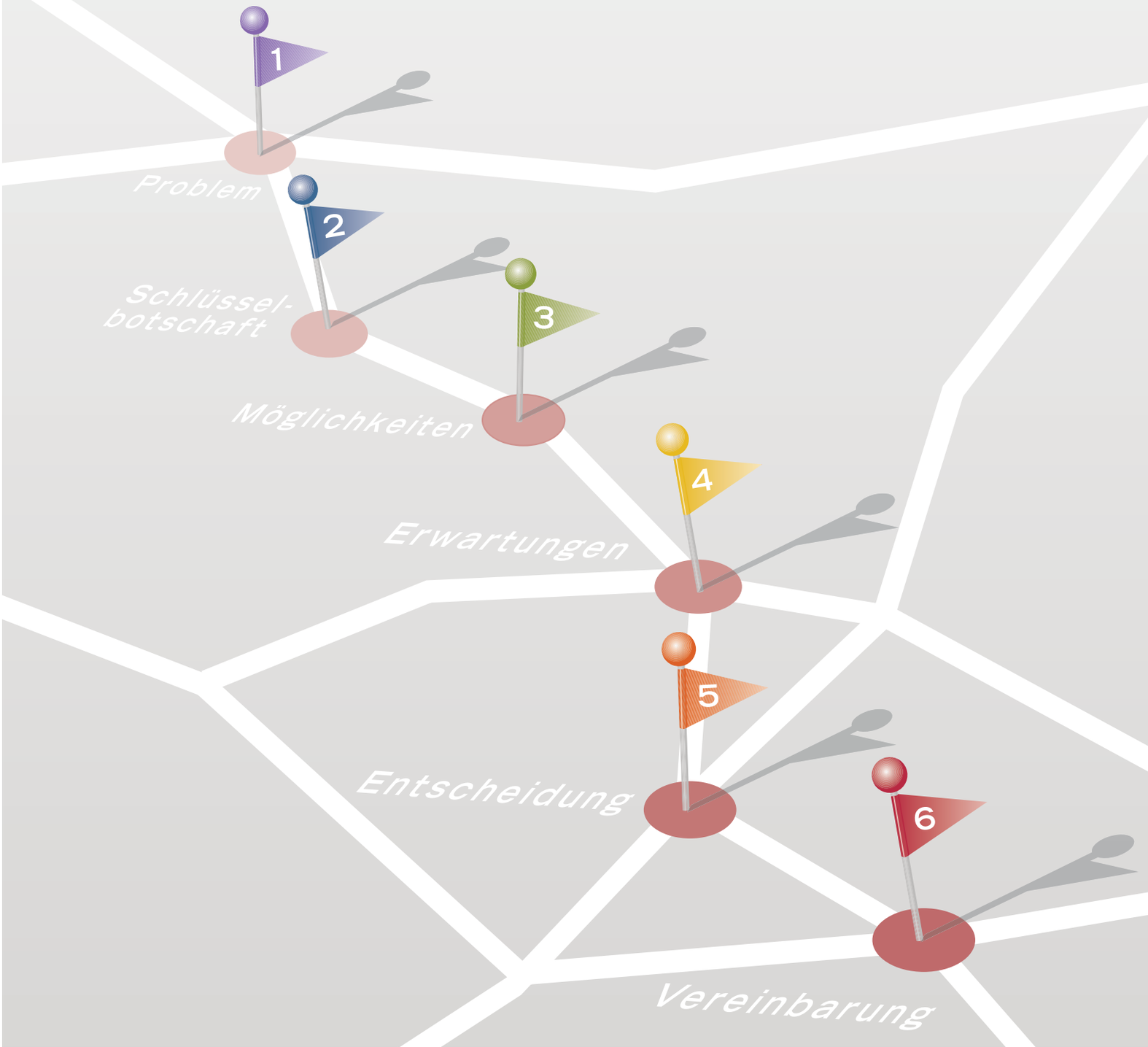
Supplemental material 1: Nurse training course DECIMS

1. Training day (from 3 am – 7 pm)			
Time	**Steps**	**Training plan**	**Resources**
3:00 pm	**Introduction**	Welcome and introduction (participants and training course programme)	Flip-chart
3:20		Questionnaires	
3:50	**Motivation**	Gaining interest and awareness through the example about a MS patient in a decision making process	Video
4:00	**Overcoming difficulties (1)**	Information on disease modifying treatment is conflicting! Information on different study results (absolute and relative risk reduction) by an example	Power point presentation
Break (ten minutes)			
4:45	**Overcoming difficulties (2)**	Discussion: - What is new? - How does the experienced fit my current knowledge/ information stand? - What does this to me?	
5:15	**Finding solutions (1)**	Evidence based information	Power point presentation
Break (Fifteen minutes)			
6:15	**Finding solutions (2)**	Introduction of the DECIMS-study	Power point presentation
6:45	**Finding solutions (3)**	Video on decision coaching with the six shared decision making steps	Video
Dinner			
2. Training day 9 am – 5:30 pm			
9:00 am		DECIMS-Wiki (introduction, work assignment)	DECIMS-Wiki (website) and worksheet
Break (fifteen minutes)			
10:45		Shared decision making steps, introduction of the materials	Materials
11:05	**Acting and performing**	Familiarisation with the DECIMS-Wiki and decision coaching (SDM step 3)	Role-playing (case example)
11:55	**Acting and performing**	Discussion of the practice	

Break (five minutes)			
12:30 pm	**Acting and performing**	Practice of step 3	Role-playing (case example)
Break (45 minutes)			
2:00		MRI-module	Power point presentation
3:00	**Acting and performing**	Further information on the six SDM steps	Power point presentation
3:15	**Practising and recalling**	Practice of the SDM steps 1-3 Two cases: coaching on first presentation and therapy change	Role-playing with case examples and simulated patients
Break (ten minutes)			
4:15	**Practising and recalling**	Practice of the SDM steps 4-6	Role-playing with case examples and simulated patients
5:00	**Practising and recalling**	Discussion of the practice	
5:20		Collecting of open questions for the next day	Sheet
Dinner			
3. Training day (9 am – 1 pm)			
9:00 am		Discussion of open questions	
9:30	**Practising and recalling**	Further information on decision coaching using the theory of planned behaviour (barriers, when to take a break because the patient is not ready for decision making...)	Power point presentation
10:00	**Practising and recalling**	Discussion of the implementation of the coaching (dealing with conflicting in formation)	Power point presentation
10:30	**Transfer and integration**	Analysis of video sequences	Video
Break (fifteen minutes)			
11:15		Organisational information (choosing the first patients, camera function…)	Materials
11:45		Feedback and questionnaires	
In the outpatient clinic			
	Transfer and integration	Feasibility phase	

DECIDE MS

Durch Wissen entscheiden



Frühtherapie

Arbeitsbuch für Patienten

Vorbemerkung

Das DECIMS-Arbeitsbuch für Patienten ist als Strukturierungs- und Dokumentationshilfe für eine Immuntherapieberatung entwickelt worden.

Das Arbeitsbuch stellt keine Patienteninformation dar, sondern soll den Patienten bei der Entscheidungsfindung bezüglich einer Immuntherapie (Beginn, Abbruch oder Wechsel) begleiten.

Es folgt in seinem Aufbau den wesentlichen Elementen des so genannten »Shared-decision-making«, der gemeinsamen geteilten Entscheidungsfindung. Grundsätzlich soll es während des Coachings mit einer trainierten MS-Nurse genutzt werden und anschließend mit nach Hause und später in das Arztgespräch genommen werden.

Alle Themen und Begriffe werden im DECIMS-Wiki (Informationsplattform) erläutert und können dort nachgelesen werden.

Sechs Etappen zur guten Entscheidung: Frühtherapie

1. Problem

Wo stehe ich? 4 - 9

Habe ich eine MS?

Wenn ja - welche Verlaufsform, welche Aktivität?

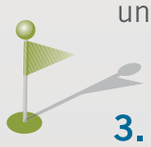
Was bringt mir die Zukunft?

Warum und worüber muss jetzt eine Entscheidung getroffen werden?

2. Schlüsselbotschaft 10

Es gibt keine allgemeingültigen Lösungen

Es gibt verschiedene Möglichkeiten des Umgangs mit der Erkrankung mit und ohne Medikamente. Die Entscheidung liegt bei mir.



3. Möglichkeiten 11-13

Welche Möglichkeiten habe ich?

Welche Therapien haben welche Wirkungen und Nebenwirkungen?

Was passiert, wenn ich warte?

4. Erwartungen 14

Was sind meine Wünsche, Erwartungen, Ängste?

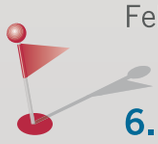
Was würde eine/keine Therapie für mich bedeuten?

Was ist mein Therapieziel für das nächste Jahr, für die nächsten 5 Jahre?

5. Entscheidung 15

Wie weit bin ich mit der Entscheidung?

Fehlt noch etwas?

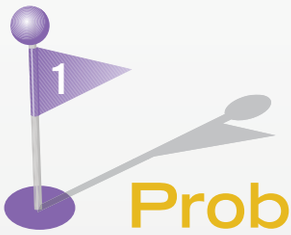


6. Vereinbarung 16

Wie setze ich die Entscheidung um und überprüfe sie?

Wie erfolgt die Medikamenteneinnahme?

Wann überprüfe ich womit den Nutzen und Schaden?



Problem - Wo stehe ich?

Nach der Diagnose: Wie geht es mir?

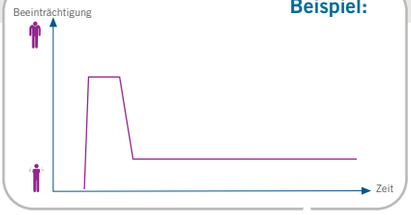
Wie gehe ich mit der Situation um?

Beeinträchtigung

hoch

Zeichnen Sie bitte die Entwicklung Ihrer MS als Kurvenverlauf ein.

Beispiel:



gering

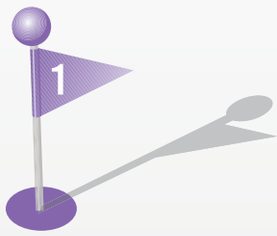
Zeit

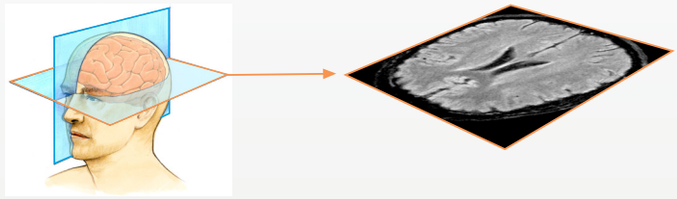
Beginn:

Heute:

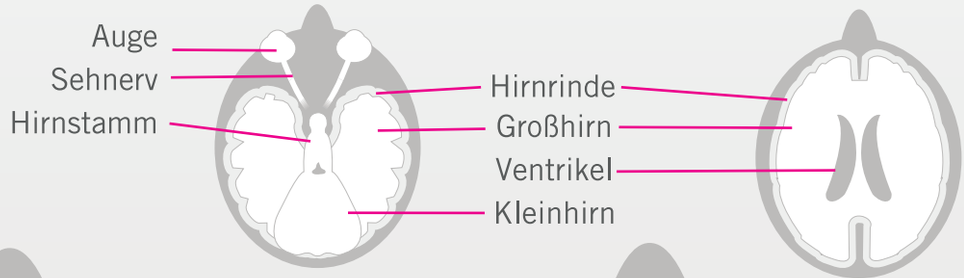
Welche Untersuchungen wurden gemacht?

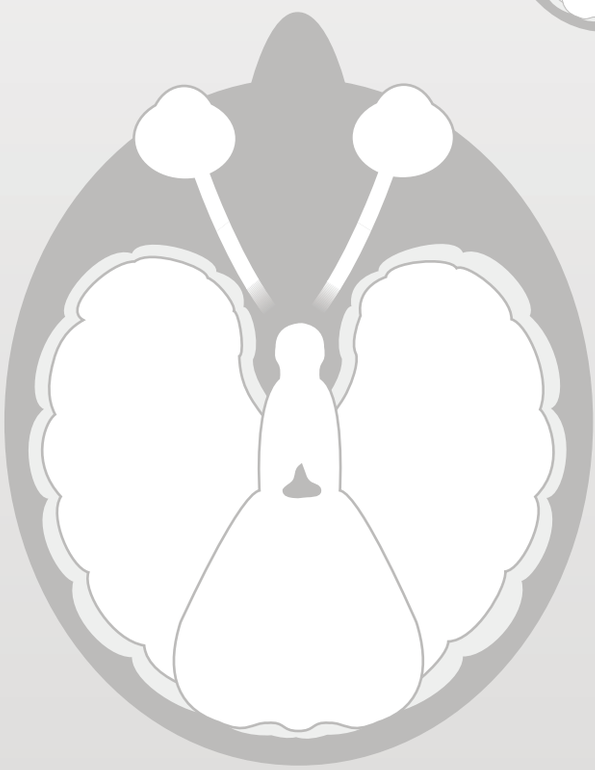
- ○ Kernspin vom Kopf? Datum:
- ○ Kernspin von der Wirbelsäule? Datum:
- ○ Untersuchung des Nervenwassers? Datum:



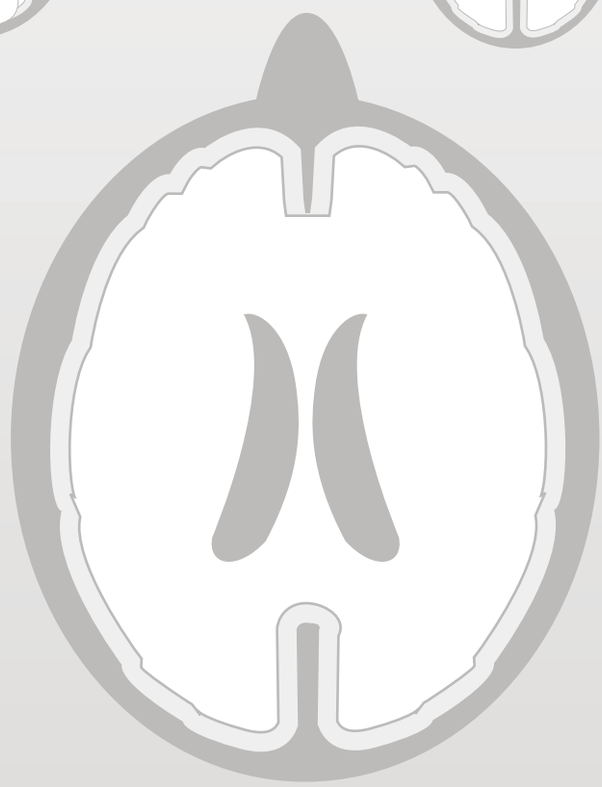


Was zeigt das Kernspin?





Schnitt Groß- und Kleinhirn

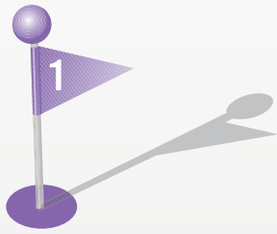


Schnitt Großhirn mit Ventrikel

Kontrastmittelanreicherungen (Anzahl)

Herde:

- ○ Periventrikulär (am Rande der Ventrikel (Nervenwasser gefüllte Hohlräume))
- ○ Juxtakortikal (nahe an der Hirnrinde gelegen)
- ○ Infratentoriell (im Kleinhirn gelegen)
- ○ Spinal (im Rückenmark gelegen)
- ○ Andere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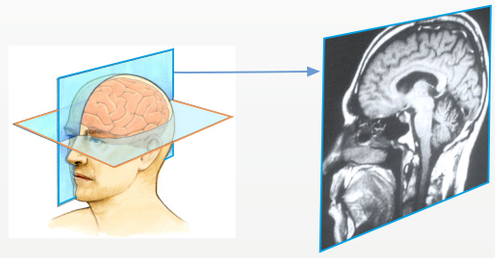
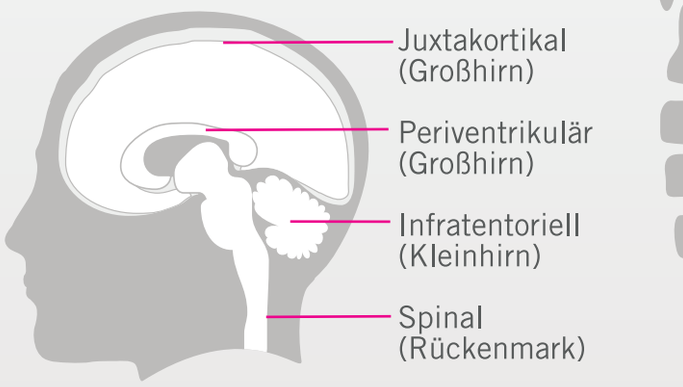
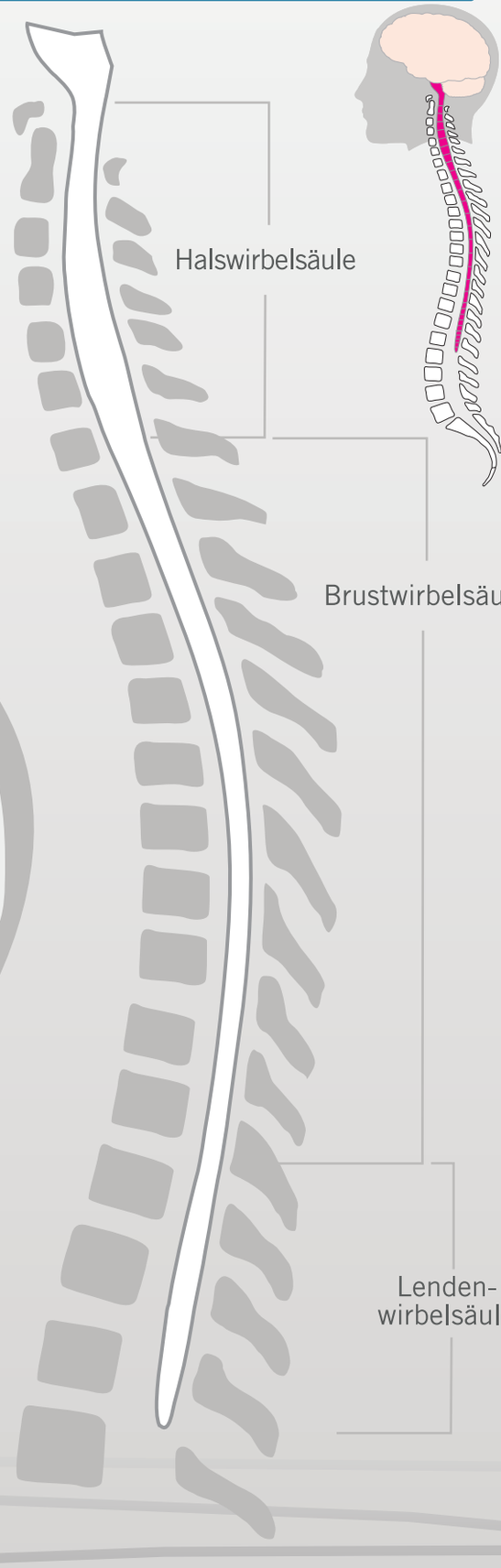
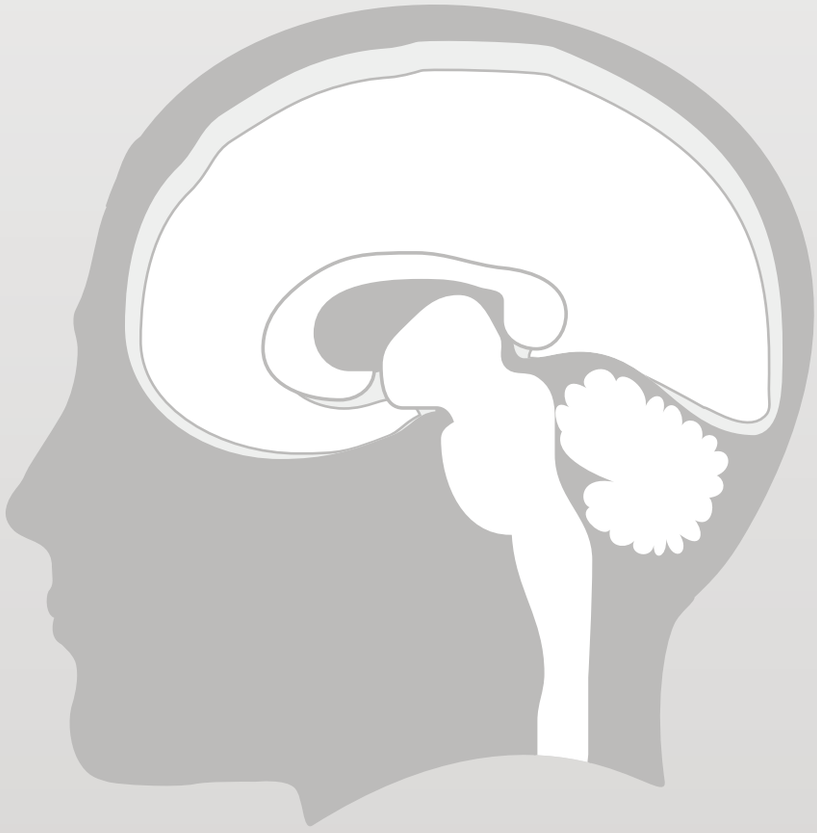
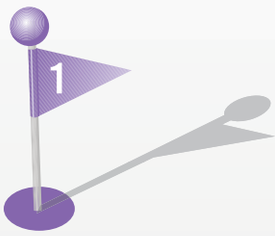



Juxtakortikal
(Großhirn)
Periventrikulär
(Großhirn)
Infratentoriell
(Kleinhirn)
Spinal
(Rückenmark)


Halswirbelsäule
Brustwirbelsäule
Lenden-
wirbelsäule





Besteht eine klinisch-sichere MS-Diagnose (Poser-Kriterien)?

○ Ja ○ Nein

Besteht eine Dissemination (Streuung) im Raum?

Swanton-Kriterien = mindestens je 1 aus 2 Regionen:

- ○ Periventrikuläre Herde
- ○ Juxtakortikale Herde
- ○ Infratentorielle Herde
- ○ Spinale Herde

Besteht eine Dissemination (Streuung) in der Zeit?

Kontrastmittelanreicherung, die keine Beschwerde macht ○ Ja ○ Nein

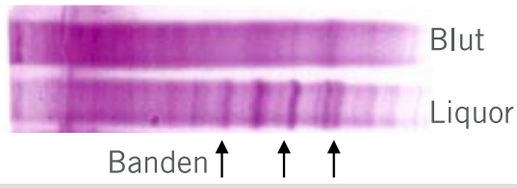
Mindestens 1 neuer Herd ○ Ja ○ Nein

Was zeigt der Liquor?

/3

Zellzahl:

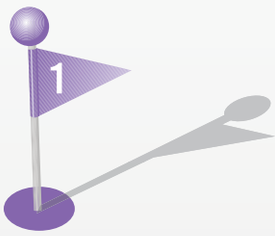
Antikörperbildung im Nervensystem / oligoklonale Banden: ○ Ja ○ Nein



Habe ich eine MS?

○ Sicher ○ Möglich ○ Unklar

Was spricht dafür?

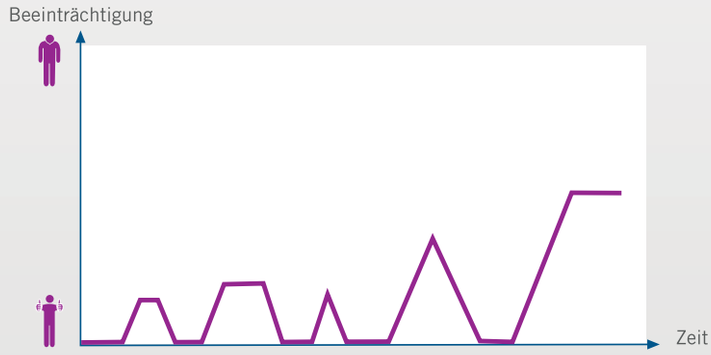


Was lässt sich zur Prognose sagen?

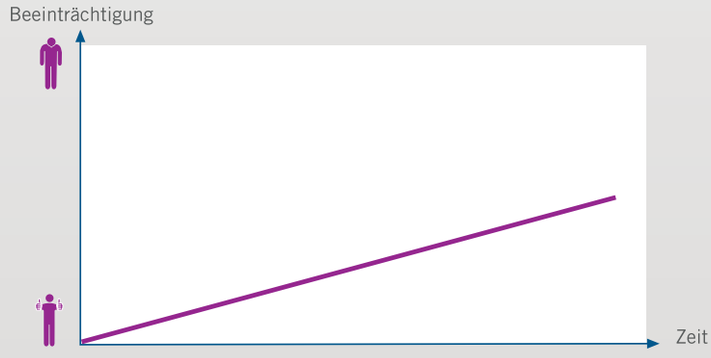
Wie ist der Verlauf bisher? (siehe Figur Seite 4)

Welche Verlaufsform?

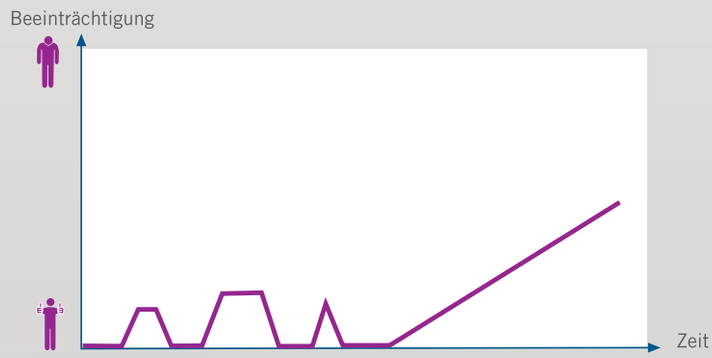
○ Noch unklar



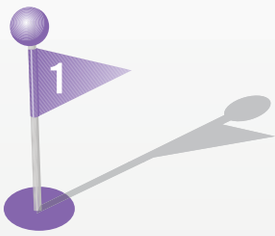
○ Schubförmig



○ Primär chronisch



○ Sekundär chronisch



Wie wird der Verlauf sein?

Zu den Faktoren, welche die Prognose (vermutlicher Krankheitsverlauf) bestimmen, liegen zum Teil widersprüchliche Daten aus populationsbasierten Prognosestudien vor (siehe DECIMS-Wiki, „Was erwartet mich bei Multipler Sklerose ohne Therapie?"). Lediglich das Alter und bestimmte Verlaufsformen der MS sind gesicherte negative Faktoren für den weiteren Krankheitsverlauf. Für positive Faktoren ist die Datenlage noch unsicherer. Grundsätzlich werden in den Untersuchungen Prognosedaten über die Zunahme der Beeinträchtigung nach 10-20 Jahren herangezogen. Die Effekte aller untersuchten Faktoren sind dabei insgesamt mäßig.

In der folgenden Tabelle ist aufgeführt, welche Bedeutung verschiedene Faktoren auf den Verlauf der Krankheit haben können:
++ = bewiesen bedeutsam, + = möglicherweise bedeutsam, +/0 = eher keine Bedeutung, 0 = keine Bedeutung.

Sie können die für Sie zutreffenden Faktoren ankreuzen.

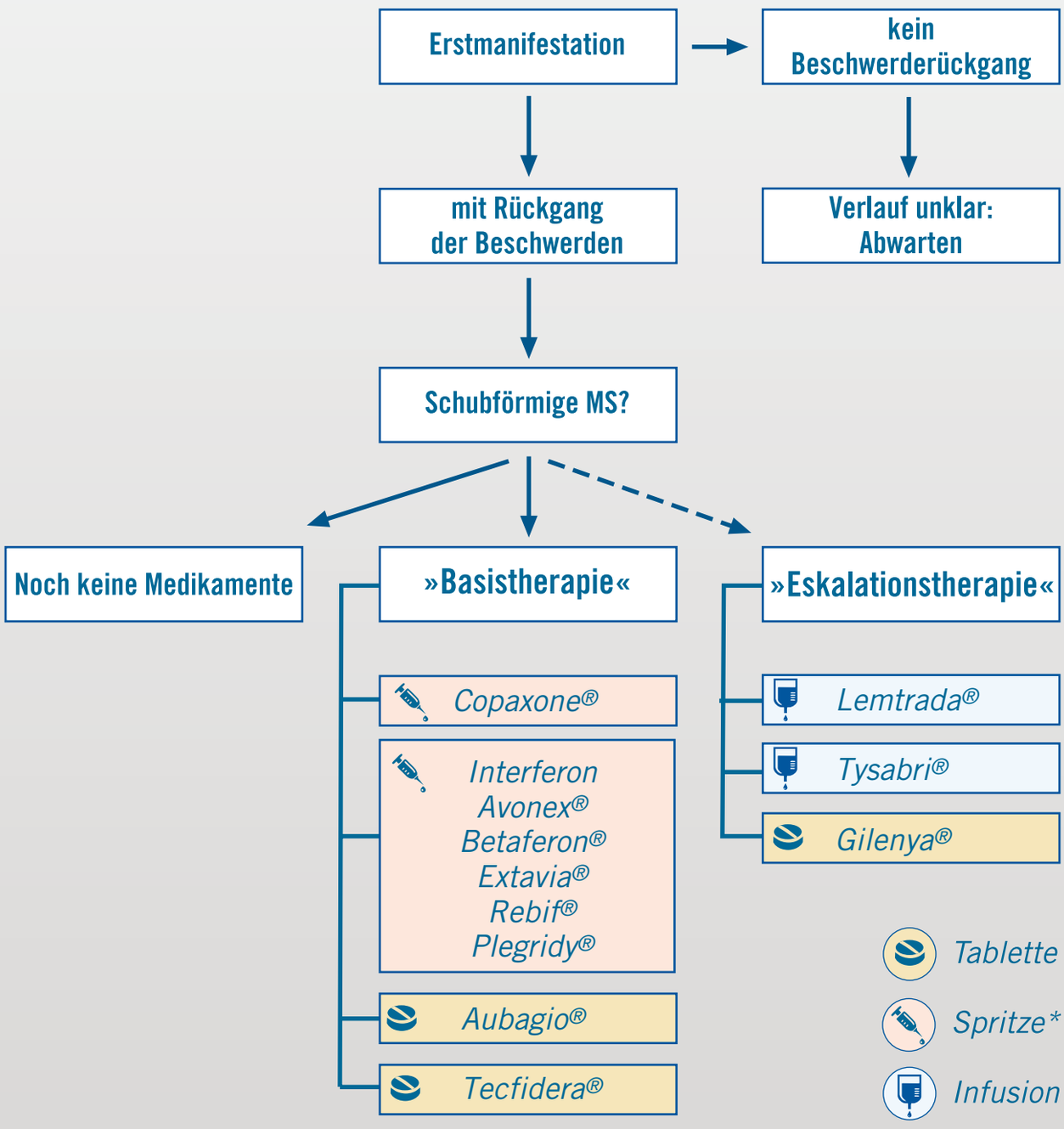
Prognostisch ungünstige Faktoren	Bedeutung	Bei mir vorliegend
Höheres Lebensalter bei Beginn	++	◯
Primär chronischer Verlauf	++	◯
Unvollständige Rückbildung der Erstbeschwerden	+	◯
Mehr als 3 Schübe in den ersten 2 Jahren	+	◯
Zunahme der bleibenden Beeinträchtigung in den ersten 5 Jahren	+	◯
Mehr als 10 Herde im ersten Kernspin	+	◯
Deutliche Zunahme der Herde (in den ersten 5 Jahren)	+/0	◯
Stark beeinträchtigende Erstbeschwerde	+/0	◯
Bestimmte Funktionsstörungen, z.B. in der Koordination	+/0	◯
Männliches Geschlecht	+/0	◯
Unterschiedliche Funktionsstörungen bei Beginn	0	◯
Prognostisch günstige Faktoren		
Wenige Herde im ersten Kernspin	+	◯
Negativer Liquorbefund	+	◯
Großer zeitlicher Abstand zwischen den ersten beiden Schüben	+	◯

Schlüsselbotschaft:
Es gibt keine allgemeingültigen Lösungen

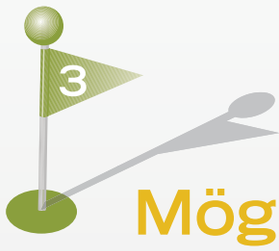
**Es gibt verschiedene Möglichkeiten des Umgangs mit der Erkrankung mit und ohne Medikamente.
Die Entscheidung liegt bei mir.**

Bemerkungen:

Möglichkeiten - Welche habe ich?



** Diese Therapien sind ausdrücklich im Fall einer Erstmanifestation bei MS-Verdacht ohne gesicherte Diagnose zugelassen.*



Möglichkeiten - Welche habe ich?

Therapie (Medikamente)	Nutzen/Schaden (x von 100 mit Nutzen/Schaden)
Keine Medikamente	

Mögliche Alternativen: Bitte tragen Sie die für Sie möglichen Alternativen ein (z. B.: Ernährung, Stressmanagement, Sport, etc.). Weitere Informationen finden Sie auf der DECIMS-Wiki Website.

Für alle diese Ansätze gibt es bisher noch keine medizinisch anerkannten Studien, welche belegen, dass diese den Krankheitsprozess beeinflussen. Andererseits konnte auch nicht gezeigt werden, dass diese Alternativen keinen Effekt auf das Krankheitsgeschehen haben.

Vorteile	Nachteile	Gesamtbewertung			
		++	+	n+/-	-
		☺	☺	😐	☹
		☺	☺	😐	☹
		☺	☺	😐	☹
		☺	☺	😐	☹
		☺	☺	😐	☹
		☺	☺	😐	☹
		☺	☺	😐	☹

13

Erwartungen

Was sind meine Wünsche, Erwartungen, Ängste?

Meine Erkrankung macht mir Angst

trifft nicht zu ○ ○ ○ ○ ○ trifft voll zu

1 5

Ich bin in der Lage, mich aktiv an der Entscheidungsfindung zu beteiligen

trifft nicht zu ○ ○ ○ ○ ○ trifft voll zu

Ich bin vom Nutzen der Therapie für mich überzeugt

trifft nicht zu ○ ○ ○ ○ ○ trifft voll zu

Ich habe Angst, ohne Therapie etwas zu verpassen

trifft nicht zu ○ ○ ○ ○ ○ trifft voll zu

Eine Therapie durchzuführen, würde mich im Alltag sehr belasten (Durchführung, Nebenwirkungen)?

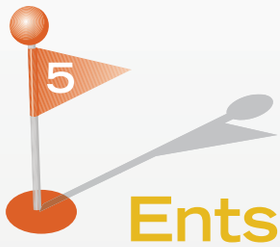
trifft nicht zu ○ ○ ○ ○ ○ trifft voll zu

Ich kann meine Entscheidung problemlos umsetzen

trifft nicht zu ○ ○ ○ ○ ○ trifft voll zu

Was würde mir eine Immuntherapie bringen?

… für 1 Jahr
… für 5 Jahre



Entscheidung - Fehlt noch etwas?

Wie weit bin ich mit meiner Entscheidung?

ganz unentschieden — 1 — 2 — 3 — 4 — 5 — ganz entschieden

Möchte ich die Entscheidung lieber aufschieben?

○ Ja ○ Nein

Was fehlt mir, um entscheiden zu können?

Wer hilft bei der Entscheidungsfindung?

Was sagen Freunde, Familie?

Was sind Themen für Folgegespräche?

Vereinbarung

Wie setze ich die Entscheidung um?

Wann und womit überprüfe ich die Entscheidung?

Was muss überwacht werden?

Wann bekomme ich das Rezept?

Wie läuft die Einstellung auf das Medikament?

Meine Fragen für das nächste Gespräch:

Notizen

DECIMS

Durch Wissen entscheiden

Was ist DECIMS?

DECIMS ist ein multizentrisches Forschungsprojekt mit dem Ziel, Patienten darin zu unterstützen, informierte Entscheidungen zu treffen. Eine zentrale Rolle im Projekt haben sogenannte Decision-Nurses.
Diese qualifizieren sich in einem eigens dafür entwickelten Training für die evidenzbasierte Beratung zu Therapieentscheidungen.

Das DECIMS Projekt geht vom Institut für Neuroimmunologie und Klinische MS Forschung im Universitätsklinikum Hamburg Eppendorf aus und wird von Prof. Christoph Heesen geleitet.

Gefördert wird das Projekt vom Bundesministerium für Bildung und Forschung im Rahmen des Kompetenznetzes Multipe Sklerose.
Didaktische Beratung: Dr. A. van de Roemer, Institut für Didaktik in der Medizin.

Kompetenznetz Multiple Sklerose

Bundesministerium für Bildung und Forschung

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Supplemental material 3: Measurements DECIMS

Instrument		Measurement time points pilot randomised controlled trial						
		Enrolment	Allocation	Post-allocation				
		$-t_1$	t_0	t_1	t_2	t_3	t_4	t_5
Eligibility screen		X						
Informed consent		X						
Allocation								
Socio-demographic data		X	X					
EDSS			X					
MS related data & resource use			X				X	X
MMIC	Risk knowledge		X			X	X	X
	Attitude		X	X	X	X		
	Immunotherapy status		X			X	X	X
Dyadic DCS				X (nurse)	X (physician & patient)			
Dyadic MAPPIN'SDM				X (nurse & patient)	X (physician & patient)			
HCR trust scale (Physician/ Nurse trust)				X	X			
PBMS			X			X		X
CPS			X			X		X
Decision autonomy						X	X	X
CSES			X			X		X
HAQUAMS			X			X		X
HADS			X			X		X

Instrument	Measurement time points process evaluation: PwMS						
	Enrolment	Allocation	Post-allocation				
	$-t_1$	t_0	t_1	t_2	t_3	t_4	t_5
Evaluation form		X		X		X	X
Video records decision coaching	All coaching sessions (every patient)						
Logbook (filled in by decision coaches)	Baseline, (after every coaching) and until the final physician decision encounter						
Interviews	After the study is finished						

Instrument	Measurement time points process evaluation: nurses & physicians				
	Pre-training	Post-training	Begin of study recruitment	6 months after study recruitment	End of recruitment
Evaluation form decision coaches	X	X	X	X	X
Evaluation form physicians			X		X
Video records decision coaching	All coaching sessions (every patient)				
Structured telephone calls or visits	Monthly during the first three months and every two to three months afterwards during study recruitment				
Interviews decision coaches	After the study is finished				

Abbreviations: t_1 = after last decision coaching; t_2 = directly after final physician decision encounter; t_3 = two weeks after final physician encounter; t_4 = three months after final physician encounter; t_5 = six months after final physician encounter; CPS: Control Preference Scale; CSES: Coping self-efficacy scale; DCS: Decisional Conflict Scale; EDSS: Expanded-Disability-Status-Scale; HADS: Hospital anxiety and depression Scale; HAQUAMS: Hamburg Quality of Life in MS Scale; HCR trust scale: Health care relationship trust scale; MAPPIN'SDM: Multifocal Approach to Sharing in Shared Decision Making; MMIC: Multi-dimensional measure of informed choice; PBMS: Planned Behaviour in MS Scale; PwMS: people with multiple sclerosis

Supplemental material 4: Overview of process evaluation

Domain	Research focus	Main facilitators and barriers
Context	Context factors in participating outpatient clinics	Facilitators: Motivation from both centres to take part in the study, principle investigator is head of the centre in Hamburg, two decision coaches (one in Bochum and one in Hamburg) highly motivated Barriers: The decision coach in Bochum not working in the outpatient centre but on the neurological ward
Recruitment of centres	Centre recruitment Centre-specific differences	Facilitators: Easy access centres, especially Hamburg Barriers: None
Delivery to centres **Staff level**	Development of the intervention	Facilitators: Experiences from earlier trials on evidence based patient information, decision coaches easy to reach Barriers: Implementation of the coaching directly after the study (summer time), one nurse changed the working place after the training (Bochum)
	Delivery of the intervention to nurses	
	Delivery of the recruitment strategy to all centres	
Response of centres	Attitude, delivered as intended (decision coaches), change in routine	Facilitators: Positive attitude of the investigators, nurses and recruiting physicians towards the intervention Barriers: Recruitment more difficult in Bochum, no videos from Bochum
Recruitment & reach in people with multiple sclerosis	Recruitment procedure	Facilitators: 64 of 107 (60%) screened people with multiple sclerosis, who fulfilled the inclusion criteria, were willing to participate, disease demographic parameters indicate a typical relapsing-remitting multiple sclerosis cohort Barriers: 8 of 32 people with multiple sclerosis were not willing to participate because it was too much effort to have further appointments
	Non-responders	

Delivery to people with multiple sclerosis	Intervention group: decision coaching and DECIMS-Wiki Control group: DECIMS-Wiki	Facilitators: Nearly all people with multiple sclerosis in the intervention group received the coaching intervention, people with multiple sclerosis in Hamburg were highly interested to take part in the study Barriers: Not all people with multiple sclerosis used the DECIMS-Wiki
Response of people with multiple sclerosis	Satisfaction with the intervention, knowledge, attitude, barriers and facilitators	Facilitators: People with multiple sclerosis in both groups were satisfied with the intervention, risk knowledge improved in both groups, there was a tendency of more informed choices in the intervention group Barriers: Missing data in both groups, possibly due to large number of questionnaires
Maintenance	Decision coaches: Knowledge and attitude, acquired routine, coaching performance, DECIMS-Wiki use	Facilitators: Decision coaches gained routine in integrating and conducting the coaching, positive attitude, most decision coaches liked the new role, intervention was performed as intended at least in Hamburg (confirmed by video analyses) Barriers: Being videotaped, limited time in daily routine, not working in the outpatient centre
	People with multiple sclerosis: further needs (coaching, DECIMS-Wiki), autonomy preferences, knowledge	Facilitators: Satisfaction with the intervention Barriers: Limited time to take part in the study (new appointment in the centre needed and distance too large)
Unintended consequences	Decision coaches: Stress, professional relationship to physicians and people with multiple sclerosis, barriers	One decision coach did not like being videotaped, one decision coach did not like to counsel patient on treatment options
	Patients: anxiety, barriers, physician contact, negative impact on quality of life	None observed unintended consequences measured
	Physicians: professional relationship to nurses and patients, barriers	None observed unintended consequences measured

Supplementary material 5: Tables and additional information

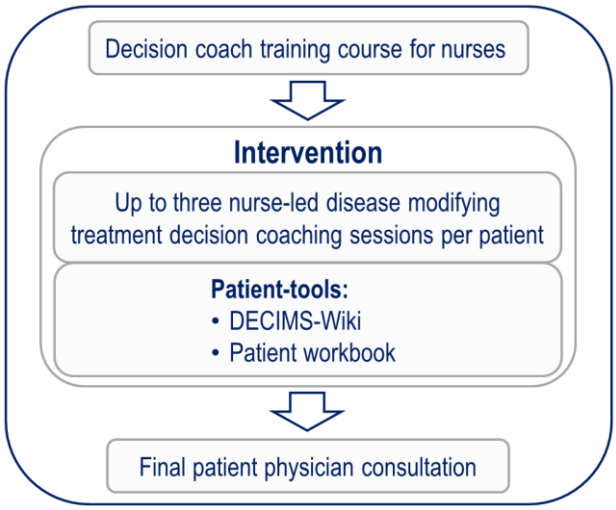

Figure S1: Immunotreatment decision coaching programme

Additional information S1: Statistical analyses

The question of whether performing statistical analyses in pilot studies has been discussed controversially (Lancaster et al., 2004; Leon et al., 2011). For this study, we found it appropriate to follow recommendations to focus on descriptive results and refrain from inferential statistics as it was not planned to test effectiveness in our pilot RCT (Torgerson and Torgerson, 2008). The power calculation of the larger cluster RCT to assess effectiveness of the approach was based on the results of an earlier RCT as mentioned in the discussion.

We performed a retrospective power analysis to explore how many people would have been needed to show a statistically significant difference on the primary outcome (informed choice). Based on the results of our pilot RCT a sample of n=250 would be needed considering a p-value of 0.05 and a power of 80% in order to detect a patient relevant difference of 18% between groups (IG 15 of 31 (48%), CG 6 of 20 (30%)).

Additional information S2: Further outcomes

Table S1: Coping self-efficacy

	Baseline		**14 days after final physician consultation**		**Six months after final physician consultation**	
	IG (n=34)	***CG (n=29)***	***IG (n=28)***	***CG (n=21)***	***IG (n=23)***	***CG (n=17)***
Coping self-efficacy	73 (22)	85 (25)	81 (28)	87(27)	84 (30)	86 (23)

Values are means (standard deviation, SD), the scale ranges from 0-130 with higher values indicating higher self-efficacy, CG = control group, IG = intervention group

Additional information S3: Process evaluation

Context and delivery to centres

The decision to pilot-test the programme in Hamburg and Bochum had been made for reasons of convenience. Both are university hospitals with a multiple sclerosis centre. However, the organisational structures and accounting differ slightly as the clinic in Hamburg is running as a day hospital. In Bochum, around 1000 and in Hamburg around 1500 people with multiple sclerosis are seen every year. With 12 neurologists in Bochum there were more neurologists than with 4-5 in Hamburg seeing people with multiple sclerosis. However, most neurologists in Bochum attend the clinic only for two hours per week. The four multiple sclerosis nurses in Bochum worked on average five hours per week, while one multiple sclerosis nurse in Hamburg worked 35 hours per week in the outpatient clinic. Regarding study nurses and offered services, clinics were comparable. Prior to the study, the centre in Bochum was visited by two members of the research team to get an impression of the centre and to discuss study feasibility. Two nurses from Bochum were willing to participate in the decision coach training programme. In total, three nurses from the clinic in Hamburg participated in the programme. After the feasibility study, the pilot RCT was initiated locally in Hamburg and via a web conference in Bochum. All nurses participated in the meetings as well as the study investigators and physicians. Both centres received the same information.

Nurses

Integration in daily routine

Coaches felt supported by colleagues to be able to conduct the coaching sessions. Most coaches stated that there were no difficulties to conduct the coaching, while one coach commented it as difficult because of difficulties to find a quiet place and due to a lack of time. While the additional work of the study was rated as difficult to be integrated into daily routine at baseline it was rated as easy to integrate at the follow-up measurements.

In concordance with the questionnaire, interviews showed that having a free room and lack of time are the major hurdles to integrate the coaching session into the daily routine: *"(…) only too little time, thus time management so to speak, bit difficult, thus in daily routine" (interview 1).*

Attitude

The opinion of the coaches concerning immunotreatment did not change at any measurement time point during the study. Decision coaches rated decision coaching as helpful for people with multiple sclerosis in immunotreatment decision-making and evaluated that they believed that physicians liked it that the nurses conducted the coaching.

Further, coaches thought that people with multiple sclerosis participated more actively in the decision-making process through the coaching and that patient physician consultations benefit from the coaching. Concerning the question whether people with RRMS should start immunotreatment in general most nurses did not think so.
The interviews too showed no change in attitude: "(*…) I have the attitude regarding counselling on therapy, it has always been so that I have respected absolutely for which the patient decides or even if he decides for nothing" (Interview IV).*

Control group

People with multiple sclerosis believed at baseline that the DECIMS-Wiki would help them to better weigh their possibilities. After the final physician consultation people with multiple sclerosis were a little disturbed (n=13) or not disturbed (n=12) through the use of the DECIMS-Wiki. The DECIMS-Wiki was rated as helpful for decision-making. Further, patients wrote most often that among others the opinion of the physician was important.
The interviews with four people with multiple sclerosis illustrate that in general they accepted the study: *"So it was all clearer to me, I had a better understanding by the study what that all is, at all. Better than on the Internet, so in general, these public sites. Yes, a very good study"* (Interview I control group).
The DECIMS-Wiki was well accepted by people with multiple sclerosis: *"I felt that it was positive for me to have this information, still in any case"* (interview II control group).
The people with multiple sclerosis commented that the DECIMS-Wiki was easy to use: "From the user guide I found it good I would say yes. So, you just have to get familiar, but I found it easy to use "(interview II control group).

Table S2: DECIMS-Wiki

	After final physician consultation		Three months after final physician consultation		Six months after final physician consultation	
	CG (n = 35)	***IG (n=38)***	***CG (n = 35)***	***IG (n = 38)***	***CG (n = 35)***	***IG (n = 38)***
DECIMS-Wiki use since the last survey						
Never	2 (6%)	1 (3%)	9 (26%)	7 (18%)	12 (34%)	17 (45%)
1 - 4 times	18 (51%)	23 (61%)	11 (31%)	20 (53%)	8 (23%)	13 (34%)
5 - 10 times	5 (14%)	5 (13%)	0	2 (5%)	0	0
> 10 times	1 (3%)	3 (8%)	0	0	0	0
Missing	9 (26%)	6 (16%)	15 (43%)	9 (24%)	15 (43%)	8 (21%)
Easy to get along*	7 (1.7)	7 (2.4)	7 (2.2)	7 (2.4)	7 (2.6)	7 (2.3)
Information understandable*	8 (1.8)	8 (1.7)	8 (1.4)	7 (2.1)	7 (2.4)	8 (2)

*Likert Scale from 0-10 with higher values indicating more positive ratings, CG = control group, IG = intervention group

Table S3: Expectations on decision coaching

Expectations on decision coaching	**IG (Baseline)**
Explore which information is needed in immunotherapy decision-making.	8 (2.5)
Review the situation with an experienced nurse.	8 (1.9)
Review the situation with an impartial nurse.	8 (2.6)
No expectations.	3 (3.1)
Easier to talk openly and find an own position with a nurse than a physician.	5 (2.9)
Overwhelmed by the diagnosis and want to clarify open questions and insecurities.	6 (2.8)
More effective conversation on therapy options with the physician afterwards.	9 (1.2)
Coaching & DECIMS-Wiki will help to weight opportunities.	8 (1.8)

Likert Scale from 0-10 with higher values indicating higher expectations, IG = intervention group

TableS4: Patient workbook use

	After final physician consultation	Three months after final physician consultation	Six months after final physician consultation
	IG (n=38)	*IG (n=38)*	*IG (n=38)*
Number of times workbook used			
Never	5 (13%)	14 (37%)	12 (32%)
1-4 times	23 (61%)	14 (37%)	15 (40%)
5-10 times	3 (8%)	1 (3%)	3 (8%)
More than 10 times	0	0	0
Missing	7 (18%)	9 (24%)	8 (21%)
Kind of workbook use (multiple answers possible)			
During coaching	21 (55%)		
During consultation (multiple sclerosis centre)	2 (5%)	9 (24%)	7 (18%)
During consultation (practitioner)		1 (3%)	3 (8%)
Conversation with relatives, friends	8 (21%)	5 (13%)	8 (21%)
To resume options	22 (58%)	11 (29%)	12 (32%)
Other	3 (8%)	2 (5%)	1 (3%)

CG = control group, IG = intervention group

Table S5: Self-reported duration first physician consultation

Duration physician consultation	CG (n=35)	IG (n=38)
≈ 5 min	1 (3%)	4 (11%)
≈ 15 min	12 (34%)	18 (47%)
≈ 30 min	8 (23%)	10 (26%)
≈ 45 min	5 (14%)	1 (3%)
≈ 60 min	0	0
Missing	9 (26%)	5 (13%)

CG = control group, IG = intervention group

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7. Weitere Arbeiten

7.1. Brand J, Köpke S, Kasper J, Rahn A, Backhus I, Pöttgen J, Stellmann JP, Siemonsen S, Heesen C (2014) Magnetic resonance imaging in multiple sclerosis - patients' experiences, information interests and responses to an education programme. *PLoS One*, 9, e113252.

PLOS ONE

RESEARCH ARTICLE

Magnetic Resonance Imaging in Multiple Sclerosis – Patients' Experiences, Information Interests and Responses to an Education Programme

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Competing Interests: The authors have declared that no competing interests exist.

Abstract

Background: Magnetic resonance imaging (MRI) is a key diagnostic and monitoring tool in multiple sclerosis (MS) management. However, many scientific uncertainties, especially concerning correlates to impairment and prognosis remain. Little is known about MS patients' experiences, knowledge, attitudes, and unmet information needs concerning MRI.

Methods: We performed qualitative interviews (n=5) and a survey (n=104) with MS patients regarding MRI patient information, and basic MRI knowledge. Based on these findings an interactive training program of 2 hours was developed and piloted in n=26 patients.

Results: Interview analyses showed that patients often feel lost in the MRI scanner and left alone with MRI results and images while 90% of patients in the survey expressed a high interest in MRI education. Knowledge on MRI issues was fair with some important knowledge gaps. Major information interests were relevance of lesions as well as the prognostic and diagnostic value of MRI results. The education program was highly appreciated and resulted in a substantial knowledge increase. Patients reported that, based on the program, they felt more competent to engage in encounters with their physicians.

Conclusion: This work strongly supports the further development of an evidence-based MRI education program for MS patients to enhance participation in health-care.

Introduction

People with multiple sclerosis (MS) give information about magnetic resonance imaging (MRI) and about its relevance for diagnosis and prognosis highest priority [1]. Currently, MRI is the most important para-clinical tool in the diagnosis and management of MS, especially in monitoring treatment effects.

However, there are substantial scientific uncertainties in the application of MRI which need to be communicated to patients. Based on MRI, MS can be diagnosed now after a single clinical event [2] which means a very early confrontation of patients with a non curable possibly sub-clinical chronic disease. Using these more sensitive criteria, conversion rates to clinical definite MS might be lower than based on older criteria [3]. Diagnostic accuracy, i.e. sensitivity and specificity of MRI, however remains unsatisfactory [4]. A radiological isolated syndrome (RIS) has been defined as a pre-stage of MS without clinical signs solely based on MRI even more eliciting the question of conversion rates and treatment needs [5]. The number of lesions at first presentation as well as the increase in lesion load during the first 5 years of MS has shown some prognostic value, however these findings are based on a single cohort with 107 patients [6]. Short-term epidemiological studies and findings from MS treatment trials are inconclusive. Metaanalytic work from n=223 patients in 31 placebo cohorts of MS treatment trials has for example shown that T2 lesion load and Gadolineum enhancement has no independent prognostic value for disability [7]. In another review from epidemiological and treatment studies (n=302 patients) Gadolinium enhancement was not predictive of disability progression [8]. On the other hand recent review work of interferon-beta treatment trials postulate a predictive value of new T2 lesions and Gadolineum enhancement for relapse activity and disability progression when occurring on treatment [9]. Although persistent MRI activity during disease modifying drug (DMD) treatment is considered a criterion of non-response, no consensus has been obtained to judge responsiveness solely on an MRI base [10]. In the future, newer MRI techniques might improve the so far limited clinical correlates and prognostic value [11].

In clinical practice, the scientific uncertainties concerning MRI are not mirrored in patients' knowledge. Based on clinical experience, physicians tend to overemphasize the predictive value of MRI. Clinical experience indicates important divergence in usage of MRI. However, to our knowledge systematic care-oriented research data on how MRI is applied in daily life are missing. Consensus criteria on relevant MRI sequences in clinical management have been suggested [12], but monitoring frequency criteria only exist on a center basis [13]. In addition MRI is a costly medical procedure.

In Germany, patients tend to take home MRI images on CD as well as a radiological report, but no standards on disclosure of findings exist among radiologists, neuroradiologists, or neurologists. While on the one hand patients have access to their own images, on the other hand they report fear and lack of knowledge on how to interpret MRI images and reports. This is in contrast to numerous studies showing that MS patients aim for active roles in the

management of their disease [14, 15]. In order to enable such a role, patients demand and need evidence-based information on the complex issue of MRI.

We performed a systematic literature search in PubMed on the topics MS, MRI, and patient education and patient information to clarify the current stage of research, which yielded 312 hits with no relevant studies identified after title and abstract screening (see suppl. data).

Therefore, we studied patients' experiences, knowledge and interest concerning MRI using qualitative and quantitative survey methodology. We hypothesized a substantial perceived threat concerning the investigation and important knowledge gaps. As a result an evidence-based patient education program on MRI in MS was developed and piloted as a group training. We assumed that carefully developed information not only increases knowledge but also motivates patients to engage more in medical decision making.

Methods

This work is part of a larger study on patient information and coaching on immunotherapy decisions. The study on the development of a MRI education program has been specifically approved by the Ethics Committee of the Hamburg Chamber of physicians (number PV4576). For the survey, written informed consent was obtained from all participants. All participants of the pilot education program enrolled voluntarily.

Qualitative Research

In a first step, five patients from the MS Outpatient Clinic of the University Medical Center (UMC) Hamburg Eppendorf, Germany, were recruited for semi-standardized interviews consisting of nine open questions regarding their experiences with MRI and their areas of interests as well as preferences for contents and structure of an MRI education program. The interviews were audio-recorded and analyzed and content analysis was guided by the thematic framework analysis of Ritchie and Spencer [16]. The aim of these interviews was to assess patients' perceptions and preferences concerning a questionnaire to be used in a representative survey.

Survey

A 32-item questionnaire was developed on MRI issues and sent via email to 200 randomly selected MS patients from the database of the MS outpatient registry of the UMC Hamburg Eppendorf, who had presented between 11/2010 and 11/2012 (n=1374). The sample size was based on previous survey results [1]. We included patients with either long-term disease duration (time since diagnosis $\geqslant$10 years) or short-term disease duration (time since diagnosis $\leq$5 years) following the hypothesis that patients with longer disease duration have more MRI experience and higher MRI knowledge scores than patients with a more recent diagnosis.

Most patients of the outpatient clinic present once or twice a year especially when the disease is already established for some time.

Eight letters were returned undeliverable due to a change of address and contact details. The overall response rate of the questionnaire was 58% (112 out of 192). Out of 112 returned mails, 73% (n=82) were filled-in, while the remaining 27% (n=30) patients gave a feedback of not being interested (20 female and 10 male), of which 47% (14) gave 'No interest in educational program' as a reason. Other reasons were: 'no time', 'no interest in MS' and 'no MS diagnosis'. 22 further consecutive patients from the MS Outpatient Clinic of the UMC Hamburg Eppendorf fulfilling the inclusion criteria were asked in November 2012 to complete the survey adding to 104 analyzable questionnaires.

MRI questionnaire

The questionnaire contained four parts with a total of 32 items, 26 of which were newly developed within the research team. Four items were taken from an own MS risk knowledge questionnaire (RIKNO) [17], two derived from the Hamburg Quality of Life in MS questionnaire (HAQUAMS) [18]. The questionnaire covered the following topics:

Part 1 (6 items): MS demographic data and disease associated anxiety and depressive mood. On an ordinal scale patients indicated perceived distress during an MRI investigation.

Part 2 (9 items): Patients' experiences with MRI regarding frequency and communication about findings with their physician.

Part 3 (5 items): Patients' interests, ideas and preferences for a patient education program concerning length, group size, and MRI topics. In order to specify the fields of interest within an MRI education module, different topics were presented (1 item). Other items addressed the preferred format of the education program (4 items).

Part 4 (12 items): MRI knowledge assessment (see appendix) comprised 11 multiple-choice questions that were summarized to an MRI knowledge score of 17 possible points (see appendix). Questionnaire items addressed neuro-anatomy (1 item, 7 points), practical issues of MRI conduct (3 items, 3 points), basic knowledge on brain lesions (2 items, 2 points) and the value of the MRI for diagnosis and prognosis as well as DMD treatment effects (5 items, 5 points). Subjective MRI knowledge was assessed using a visual analogue scale from 'no knowledge' to 'highest knowledge' as applied earlier [1]. The scale was divided into 10 sections with 10 representing highest knowledge (1 item).

Development and evaluation of the education program

Based on the results of the qualitative study and the survey, a power point-based education program was developed, covering the most relevant information on MRI for MS patients. The initial draft was discussed and revised several times in our work group (JB, CH, JK, SK, SS). Corresponding to the concept of evidence-

based patient information [19], contents were based on literature researches and two systematic reviews, one concerning 'MRI and diagnosis' [20] and another concerning 'MRI and prognosis' (manuscript under preparation).

The electronic patient newsletter of the MS Day Hospital was used to recruit participants for a pilot training session. The program was presented by JB, an MS educated medical student to 26 MS patients who responded to the newsletter in two pilot groups of 13 patients each. After the 90-minute presentation, an open question and answer round was conducted. Participants' comments were audio-recorded and analyzed using content analysis [16].

Patients' knowledge on MRI was tested using a questionnaire with 15 knowledge questions based on the survey. It was administered directly before and directly after the education program. The quality of the program was assessed using 4-point Likert scales, where patients marked the level of agreement to given statements. Three domains of quality were evaluated: satisfaction with the education program (9 items), anticipated effects of the increased MRI knowledge (7 items), and the assumed impact on patient-physician communication (6 items). Mean item scores of the three domains were summarized to three sub-scores.

Ethical issues

This work is part of a larger study on patient information and coaching on immunotherapy decisions and has been agreed upon by the Ethics Committee of the Hamburg Chamber of physicians (number PV4576). Informed consent was obtained from all participants.

Statistical analysis

Most data were analyzed descriptively using SPSS 21.0 for Windows. We performed t-tests for independent samples to analyze MRI knowledge score differences between the two patient groups in the first survey. Correlation between subjective and objective knowledge in the survey was analyzed using Fisher's-Z-test in order to generate Pearson correlation coefficients. T-tests for paired samples in the evaluation of the program were conducted to assess before-after comparisons of subjective and objective knowledge.

Results

Qualitative study (Table 1)

The patient group consisted of five female patients with relapsing-remitting MS (RRMS) aged between 22 and 48 years with an average disease duration of four years.

All five interviewees showed considerable interest in MRI, mostly reporting a substantial lack of knowledge and considerable fear, not only concerning the results, but also concerning the procedure itself. For the stage of the diagnostic

Table 1. Interview and focus group findings.

MRI experience		
Major category	subcategory	Patient statement
To be at the mercy of the investigation	Noisiness and narrowness	''It was pretty loud and narrow. The narrowness is a problem.''
	Relaxation strategies	''Other patients recommended MRI practices where I might pick my favorite music.''
To be at the mercy of the results	Incomprehension	''The doctor reviewed the images with me, but I did not understand what he was saying.''
	Information timing	''Only the diagnosis M'' was of importance for me. I did not care about images. I felt like being in a movie, everything just passed by.''
	Non-disclosure of findings	''Images were neither shown nor explained to me, just handed out in an envelope.''
	Disgust	''Seeing the inner body feels a bit disgusting, especially the eyes.''
Expectations towards MRI education		
Self-management of MRI images	Understanding images	''I felt better once I had received the diagnosis. I want to know where the wind blows.''
	Understanding reports	''Being able to read and understand the doctor's report would be great.''
	Own comparisons	''Being able to compare the images myself and understand what the doctors really talk about.''
	Being independent from physician	''To know about my own body and not having to rely on the doctor all the time.''
	Empowerment within physician encounters	''I would like to be prepared better for medical consultations.''
Ambivalence of a deeper understanding	Interest in neuro-anatomy	''I would like to know more about different areas of the brain function.''
	Clinical correlate of images	''I can see a white spot. That means there was a relapse.''
	Excitement towards results	''I find it fascinating even though I fear my results.''
	Fear of unfavorable prognostic information	''My only concern would be the MRI showing me the future of my disease. The other question is, if this is really possible?''

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process participants reported ambivalence towards having a deeper insight into MRI issues. In contrast, all interviewees stressed the need for more insight into MRI issues during the further course of the disease. In general, MRI was perceived as a procedure where patients felt substantially uncomfortable, not only during the procedure itself but also while receiving information on the results. A putative deeper insight through an education program was associated with ambivalence as some interviewees feared the disclosure of a potentially unfavorable prognosis.

Asking patients to assess a T1 weighted coronal planed image on the level of the eyes led to excitement and interest in four patients and disgust in one patient.

Table 2. Demographic data of survey on MRI experiences.

Time since diagnosis	0–5 years	>10 years	all
n (%)	43 (41.3)	61 (58.7)	104 (100)
Disease duration, years (mean ±SD)	1.23 (1.65)	19.80 (8.59)	11.3 (11.9)
RRMS	27 (62.8)	9 (14.8)	36 (34.6)
PPMS	1 (2.3)	6 (9.8)	7 (6.7)
SPMS	4 (9.3)	38 (62.3)	42 (40.4)
Disease course unclear	11 (25.6)	8 (13.1)	19 (18.3)
Ongoing immunotherapy	13 (30.2)	19 (31.1)	32 (30.8)
High level of education*	25 (58.1)	40 (65.6)	65 (62.5)
Subjective MRI knowledge** (mean, SD)	4.27 (2.17)	4.49 (2.33)	4.42 (2.27)
MRI knowledge*** (mean, SD)	10.51 (3.18)	9.57 (3.39)	9.96 (3.32)

Values are numbers (%) if not indicated differently.
* 12 or more years of school,
** Range 0–10 with higher values indicating good knowledge.
*** Objective MRI knowledge (range 0–17 with higher values indicating good knowledge).

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Survey

104 questionnaires were analyzed. Participants had an average age of 48 years (range: 19–69). 43 had short disease durations of ≤5 years, while 61 had disease durations of ⩾10 years. As expected, there were more participants with progressive disease courses in the patient group with longer disease durations (table 2).

MRI usage

While 43.3% (n=45) indicated irregular MRI scans, 17.3% (n=18) reported a frequency of one MRI per year, followed by 10.6% (n=11) with two MRI per year. Only 2 out of 104 patients had more than 2 MRI per year. Of patients with longstanding MS, 56.7% tended to have irregular MRI opposed to 20.6% of patients with a more recent diagnosis. 26.5% only had one MRI during the last 2 years. 76.5% reported to have repeated images performed at the same scanner. Reasons for changing locations were named as relocation of or dissatisfaction with the first location.

Burden related to MRI

40% (n=42) of patients rated the MRI investigation as 'not stressful at all' while 3.9% (n=4) ticked the highest level of stress. Top three stressors were noise (31.7%, n=32), lying without movement (30.8%, n=31) and narrowness (26.9%, n=27). Fear of the scan-results was reported by 11.5%.

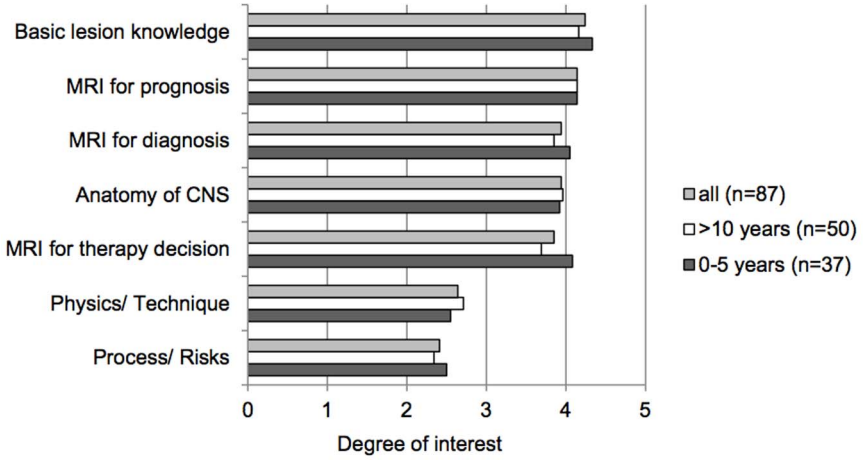

Figure 1. Degree of interest in MRI. Degree of interest is displayed with ratings from 0 (=no interest) to 5(=high interest). Values are means. CNS= Central nervous system.

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Communication of MRI results

Out of 99 patients, 9% (n=9) indicated that, to their knowledge, MRI images were compared to former scans. Both radiologists (51.5%, n=51) and neurologists (44.4%, n=44) performed these comparisons. 68% (n=68) of the participants assessed the quality of physicians' delivery of MRI results as 'elaborate', 33% (n=34) as 'short' and 2% (n=2) had received no results at all. Nearly a quarter of the survey patients (23.7%, n=23) at least once sought a second opinion on MRI results.

Patient recommendations for an MRI education program

Concerning overall interest in an MRI education program, 61.5% (n=64) marked 'interesting' and 28.8% (n=30) even 'extremely exciting'. Only 7.7% (n=8) ticked 'rather uninteresting' while 'not interesting' was not mentioned.

For the possible content of a program, highest ratings were given for knowledge on different lesion types and their meaning (mean 4.24, SD 0.63 out of 5) and the value of MRI for the prognosis of MS (mean 4.14, SD 0.48 out of 5). Differences in interests between groups were minor, with the highest difference of 0.61 points in the area of treatment decisions based on MRI, which was considered more relevant in early patients (see figure 1).

When asked for a favorite presentation format, small group education programs not exceeding eight participants received the highest priority (58.6%), followed by brochures or leaflets (16.2%), individual trainings (14.1%), and online programs (8.1%). The majority of patients (51.5%) opted for a two to three hour training program, followed by a group session for one hour (20%). Only three patients voted for more than one session. Patients' goals for an MRI education program are given in table 3.

Table 3. Personal goals concerning MRI education (n=99) (multiple answers possible).

	n	%
To achieve situational awareness	64	64.6
Better understanding of physicians	56	56.6
To develop own ideas	41	41.4
Shared decision making	38	38.4
Personal responsibility	34	34.3
To reduce anxiety about MRI investigation	7	7.1
To reduce anxiety about MRI results	7	7.1

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Patients expressed hope for better understanding of their disease status through MRI knowledge. More than half of the participants thought that an MRI education can help them during communication with their physician, with one third hoping for more participation in decision making. In contrast, only few patients believed in a reduction of anxiety towards MRI results through MRI knowledge (6.7%, n=7).

MRI knowledge

MRI knowledge was fair and did not differ significantly between groups with a mean difference of 0.94 out of 17 points (early MS 10.51 points (SD 3.18), late MS 9.57 points (SD 3.39), p=0.15, see table S2 in File S1). Subjective knowledge values (ranging from 0 to 10) were also comparable between groups: Patients with early MS estimated their MRI knowledge slightly lower with a mean of 4.27 points (SD 2.17) than patients with MS⩾10 years with a mean of 4.49 points (SD 2.33). Objective MRI knowledge scores and subjective knowledge correlated significantly, but weakly with a Pearson correlation of 0.386 ($p<0.05$).

Basic anatomy questions to detect nose, cerebrum and spinal cord on MRI images were mostly answered correctly. Half of the participants (52.9%, n=55) could name the lateral ventricles and 58.7% (n=61) knew that computer tomography (CT) has a higher radiation exposure than the MRI. Only 25% (n=26) were able to name the correct contrast agent used for MS patients (Gadolinium). 50% (n=52) were aware of the limited information of a contrast-enhancing MRI shortly after a steroid pulse therapy. (For more details please see table S2 in File S1).

Pilot MRI education program

The 90 minute power point based education program contains illustrative material, especially MRI images aiming to encourage participant involvement (for contents see table 4).

The program starts with a round of introductions, where all participants can state expectations and reasons for participating, and ends with a feedback round.

Table 4. Content of the MRI education program.

Principle of MRI technique
Risks and contraindications of MRI imaging.
The clinicoradiological paradox [20]
Rationale of gadolinium
Typical MS lesions and their evolution
Differentiation between new lesions and relapses
Typical locations of lesions and recent diagnostic MRI criteria
Anatomy of the CNS
MRI to measure treatment response [8]
Prognostic value for disability [5]

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Pilot evaluation study

The cohort consisted of 16 female and 10 male patients with a mean age of 46 years (SD 10 years). Most participants (69%, n=72) had RRMS, with a mean disease duration of 6 years (SD 5 years). 16 (62%) participants had a higher education level and all had experienced at least one MRI with a mean number of MRI since disease onset of 8 (SD 6).

On a scale from 0 to 10, subjective knowledge increased from a mean of 3.71 (SD 2.01) before to a mean of 7.75 (SD 1.07) after the education program ($p<0.001$). Objective knowledge increased from 10.4 (SD 4.65) to a mean of 17.64 (SD 3.49) out of 24 possible points ($p<0.001$).

All patients emphasized the empowering effect of the program and overall agreement with the program's content was 3.22 out of a maximum of 4. The majority (92.3%, n=24) was satisfied with program length and difficulty. 80.8% of participants (n=21) completely agreed that the program should be recommended to other MS patients. 76.9% (n=20) completely agreed that their knowledge on MRI has increased substantially and the remaining patients rather agreed. 92.3% (n=24) of the participants felt capable of assessing the images at home after the training and felt that this knowledge would help them to cope with their disease.

All patients completely or rather agreed that the program would empower them to discuss their MRI results with their physicians. Patients did not express a need for more frequent MRI investigations, but 69.2% (n=18) rather agreed to be able to co-decide on the usefulness of a future MRI investigation. A considerable number (38.5%, n=10) would not trust to leave the diagnosing of their MRI images to their physician alone in the future. (For more details see table S3 in File S1).

Discussion

MRI is of crucial relevance in diagnosing and managing MS. Although patients claim substantial MRI information needs [1], no study has yet addressed

patients' attitudes, knowledge and detailed information needs concerning MRI in any detail. This study shows the vulnerable emotional situation especially of patients having their first MRI scan performed. They often feel they are at the mercy of a machine and the findings from the procedure. Although the process of giving information on MRI findings may differ between health care settings and countries, in most cases there will be a time lag between MRI performance and interpretation of the results, prolonging a phase of uncertainty, while patients might even have a report and/or a CD containing MRI scans at hand. Interviews indicated that this process requires better structuring. While interviewees explained substantial fear towards MRI results, survey results show that most patients were aware that lesions neither strongly correlate to disability nor to prognosis. This disagreement might be explained by the gap between somehow obtained general information about MRI and concrete findings in an individual case. One might assume that broad information could help to alleviate the stress elicited by MRI findings. However, interviews show that the timing for such information should not be too close to the diagnostic disclosure.

Interestingly, most patients thought that better MRI knowledge would help them to more actively participate within physicians' encounters. Knowing that more than 2/3 of patients claim active roles in encounters [14], MRI education might therefore enable more shared decision making. Even after an intervention as short as 90 min, 69% of the participants claimed that from now they would aim to assess their own images.

Answering an average of 10 out of 17 knowledge questions correctly, patients do possess a basic knowledge on MRI that can be built upon in an education program. Interestingly, knowledge on some basic aspects, such as radiation exposure and applicability of contrast agents, could only be answered by a minority of patients. Here, education might help to avoid unnecessary imaging soon after steroid treatment.

Beyond the expected knowledge increase directly after the short educational intervention, the substantial subjective knowledge increase together with the increased trust of patients to engage in physician encounters indicate the patient empowerment potential of the intervention. Complementary to the concept of shared-decision making [21], empowerment stresses more autonomy [22]. Interestingly, after the training, about one third does not want to leave the interpretation of MRI images to their physician. Eventually, participants tend to be skeptical towards results and interpretations of physicians, potentially causing distrust. This may indicate the need for further discussions about the challenging aspects of 'expert patients' [21].

As a limitation the response rate was low and based on a university outpatient cohort. Therefore findings might be biased towards higher educated, more interested patients. This means that knowledge might be even worse in less active patients, which emphasizes our findings. However, we

cannot rule out that a substantial group of MS patients might not be interested in MRI education. Further work should look at consecutive patients in different treatment settings to overcome these limitations. As we did not obtain education level data, we cannot conclude on the actual impact on knowledge. We did not study possibly different views on MRI of females and males which also needs to be investigated in further work together with correlating individual MRI burden and perception of MRI.

In conclusion, this pilot work strongly supports further development of an evidence-based patient education program on MRI for patients with MS. However, our data already indicate that physicians should tailor their MRI communication strategies more to patient's preferences. These may substantially differ from the early diagnostic workup image to a follow-up scan during immunotherapy. Physicians need to be aware that a relevant amount of patients would even be happy to be able to read their own images to some extent. A controlled trial should be performed to show the added value to standard care as well as also possible side-effects. As patients' needs might substantially differ within the diagnostic process and the later disease course, these differences need to be studied in further work. Such a program should be developed and evaluated following the MRC's framework for the development and evaluation of complex interventions [23]. This pilot work offers an important preparatory basis for such a trial. Our data indicate that such an intervention might not only lead to more participation and empowerment, but also to a more rational use of health-care resources. This adds to previous studies, which have shown less demand of physicians and steroid treatments after relapse education [24] and a trend for increased adherence after thorough information on diagnosis, prognosis and early treatment effects for patients with early MS [25].

Supporting Information

File S1. Table S1, Systematic search in Pubmed (date of search Jan 5th, 2014). Table S2, Results of MRI knowledge questionnaire. Given are mean numbers of correct answers and percentages in brackets. **Table S3, Evaluation of the education program: Statements and degree of consent.** *Level of agreement: 1= lowest level of agreement…4=highest level of agreement. **Converted scores. **Survey S1, Qualitative Research: Item and questions of semi-structured interviews. Survey S2, MRI knowledge questionnaire.**
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Author Contributions

Conceived and designed the experiments: JB SK JK AR IB JP JPS SS CH. Performed the experiments: JB CH. Analyzed the data: JB CH JP. Contributed reagents/materials/analysis tools: JB CH. Wrote the paper: JB SK JK SS CH.

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Supplemental File S1

Table S1
Systematic search in Pubmed (date of search Jan 5th, 2014)

	Search terms	hits (n)
#4	#1 AND #2 AND #3	**312**
#3	"Magnetic Resonance Imaging"[Mesh] OR magnetic resonance imaging OR mri	404470
#2	"Multiple Sclerosis"[Mesh] OR "Myelitis, Transverse"[Mesh] OR "Demyelinating Diseases"[Mesh] OR "Encephalomyelitis, Acute Disseminated"[Mesh] OR (("multiple sclerosis" OR "transverse myelitis" OR "optic neuritis" OR “adem” OR "neuromyelitis")	87635
#1	education OR "patient education" OR "education* method*" OR "education* material*" OR "education* program*" OR (information AND coping) OR "patient information*" OR "health information*" OR "information* method*" OR leaflet* OR lecture* OR "communications media" OR "information sheet*" OR "patient guidance" OR brochure* OR pamphlet* OR counselling OR "patient counselling" OR "telephone call*" OR "web site*" OR website* OR (teaching AND computer*) OR (audiovisual AND information) OR "decision making" OR "shared decision making" OR "informed choice" OR "decision support" OR advice OR "Health Education" OR "Consumer Health Information" OR "Decision Making" OR "Decision Support Techniques" OR "Informed Consent" OR "Communication" OR "Patient Participation" OR "Self Care" OR "Health Status Indicator*" OR "Drug Information Services" OR "Information Dissemination" OR "Access to Information"	1431925

Survey S1
Qualitative Research: Item and questions of semi-structured interviews

Gender:

Age:

Diagnosis of MS (year):

Disease Course:

Treatment:

MRI experience (first and most recent, frequency):

What do you feel when looking at the image (transversal scan with eyes cut) below?

How was your first time in the MRI scanner? Can you describe it?

Do you remember the first time looking at your own MR images? How did it take place?

Are you interested in participating in an MRI education program? Why?
How much time would you be able or willing to spend?
In which manner would you like to have the information presented?

Please rank the following topics. How much are you interested in them if 0 means no interest and 5 means highest interest?

- Basics of the MRI (contrast agent, physics)
- The process of an MRI scan
- Neuroanatomy and MS symptoms
- Lesions and their meaning
- MRI used to diagnose MS
- MRI used to make a prognosis of the disease course
- MRI to measure the effectiveness of a treatment

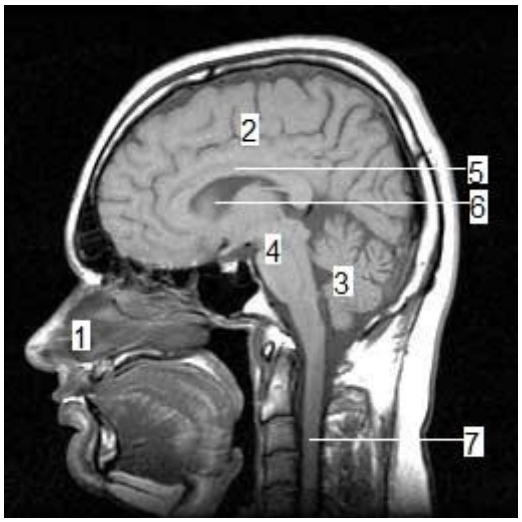
Do you feel frightened or do you have any concerns towards an MRI education program?

How much do you already know about MRI?

Can you show me the MS lesions on the image (example T2 scan)?

Survey S2
MRI knowledge questionnaire

1) Please relate the numbers in the image to the correct anatomical structures.



1) Nose
2) Cerebrum
3) Cerebellum
4) Brain stem
5) Corpus callosum
6) Ventricle
7) Spinal cord

2) How much is the radiation exposure of magnetic resonance imaging (MRI) compared to the radiation exposure of computer tomography (CT)?

- Same radiation exposure in CT and MRI.
- No radiation exposure in CT and high radiation exposure in MRI.
- ✓ No radiation exposure in MRI and high radiation exposure in CT.
- Both investigations do not cause any radiation.

3) Which contrast agent is often used for multiple sclerosis patients?

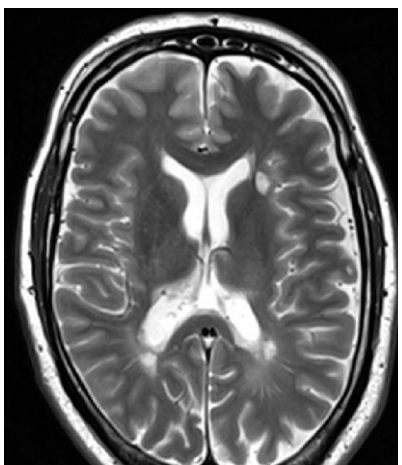
- Barium sulfate
- ✓ Gadolinium
- Iodine-containing contrast agent
- Carbon dioxide

4) In which sequence is the contrast agent visible?

- ✓ In T1.
- In T2.

5) How many lesions can you find in the image on the right?

- One
- Two
- ✓ Three
- More than five.



6) What does ‚black hole' mean?

- An abscess-like accumulation of fluid.
- ✓ An area, where neuronal tissue is irreparably destroyed.
- A sign of reconstruction of the myelin sheath.
- An active lesion, where the immune system is attacking nerve cells.

7) Is it possible to estimate the course of MS reliably from the number of lesions on an MR image?

- Yes.
- ✓ No.

8) Is it possible to estimate the degree of disability from an MR image?

- Yes.
- ✓ No.

9) Does a large number of contrast enhancing lesions on the image anticipates a relapse?

- Yes.
- ✓ No.

10) Is it reasonable to do an MRI investigation with contrast agent shortly after a cortisone pulse therapy?

- Yes.
- ✓ No.

11) Which of the following statements is <u>not</u> correct?

- MRI is useful in the early stage of the disease.
- ✓ As a principle, multiple sclerosis patients should have MRI once a year.
- Regular MRI investigations are helpful during immunotherapy.
- Besides diagnosis MRI is especially useful to monitor treatment effects.

<u>Results</u>:
Early MS (0-5 years disease duration): 10.51 out of 17 points (SD 3.18)
Late MS (>10 years disease duration): 9.57 out of 17 points (SD 3.39)
All: 9.96 out of 17 points (SD 3.32)

Table S2: Results of MRI Quiz

Topic See survey S2 for details	Group 1 (0-5 years) (n=43)	Group 2 (>10 years) (n=61)	all (n=104)
1. Anatomy-nose	41 (95.3)	57 (93.4)	98 (94.2)
2. Anatomy-cerebrum	40 (93.0)	51 (83.6)	91 (87.5)
3. Anatomy-cerebellum	32 (74.4)	36 (59.0)	68 (65.4)
4. Anatomy-spinal cord	41 (95.3)	47 (77.0)	88 (84.6)
5. Anatomy-brain stem	28 (65.1)	27 (44.3)	55 (52.9)
6. Anatomy-corpus callosum	20 (46.5)	21 (34.4)	41 (39.4)
7. Anatomy-ventricle	25 (58.1)	30 (49.2)	55 (52.9)
8. Radiation exposure	24 (55.8)	37 (60.7)	61 (58.7)
9. Contrast agent	12 (27.9)	14 (23.0)	26 (25.0)
10. Sequences T1, T2	8 (18.6)	10 (16.4)	18 (17.3)
11. Lesion count	29 (67.4)	39 (63.9)	68 (65.4)
12. Black hole	19 (44.1)	27 (44.3)	46 (44.2)
13. Value of MRI-disease course	38 (88.4)	51 (83.6)	89 (85.6)

14. Value of MRI-disability	30 (69.7)	36 (59.0)	66 (63.5)
15. Value of MRI-relapse predict	27 (62.8)	44 (72.1)	71 (68.3)
16. MRI and steroid therapy	21 (48.8)	31 (50.8)	52 (50.0)
17. Frequency of investigations	17 (39.5)	26 (42.6)	43 (41.3)

Given are mean numbers of correct answers and percentages in brackets.

Table S3: Evaluation of the education program: Statements and degree of consent

Evaluation of the education program	Level of agreement*
Part 1: Satisfaction with the program	Sub-score**: 3.22
1.1 Altogether, I am satisfied with the education program.	3.96
1.2 I was interested in the contents.	3.62
1.3 The program was too extensive/ long.	1.62**
1.4 There was a good balance between training and breaks.	3.36
1.5 The program was too difficult.	1.52**
1.6 To many technical terms were used.	1.96**
1.7 I was able to clarify my questions and issues.	3.54
1.8 There was sufficient participation of the group.	3.73
1.9 I would recommend the program to MS-patients.	3.85
Part 2: Perceived effects	Sub-score**: 3.22
2.1 My knowledge on MRI has increased significantly.	3.77
2.2 I learned how to rate my MRI results.	3.46
2.3 I can now understand the significance of my MRI results for the overall assessment of my disease.	3.58
2.4 I have more control about my disease now.	2.65
2.5 I lost fear of the MRI investigation.	2.87
2.6 I lost fear of the MRI results.	2.92

2.7 The imparted knowledge helps me to cope with my disease.	3.31
Part 3: Conversion into action	Sub-score**: 3.59
3.1 Now, I can discuss MRI results with my physician.	3.36
3.2 In the next medical consultation I would like to talk more about the MRI.	3.48
3.2 Now, I feel more competent in an encounter with my physician.	3.32
3.3 I am now able to co-decide whether an MRI would be useful.	3.23
3.4 I would like to have more frequent investigations now.	1.83**
3.5 I am now able to take a look at my MRI images at home.	3.23
3.6 Despite of my new knowledge, I leave the diagnosing to the doctors.	2.73

* Level of agreement: 1=lowest level of agreement…4=highest level of agreement

** converted scores.

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ORIGINAL RESEARCH PAPER

WILEY

A new graphical format to communicate treatment effects to patients—A web-based randomized controlled trial

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Abstract

Objective: Patients making treatment decisions require understandable evidence-based information. However, evidence on graphical presentation of benefits and side-effects of medical treatments is not conclusive. The study evaluated a new space-saving format, CLARIFIG (clarifying risk figures), aiming to facilitate accuracy of comprehension.

Methods: CLARIFIG displays groups of patients with and without treatment benefits as coloured sectors of a proportional bar graph representing in total 100 patients. Supplementary icons indicate the corresponding group's actual condition. The study used an application showing effects of immunotherapy intended to slow disease progression in multiple sclerosis (MS). In a four-arm web-based randomized controlled trial, CLARIFIG was compared to the reference standard, multifigure pictographs (MFP), regarding comprehension (primary outcome) and processing time. Both formats were presented as static and animated versions. People with MS were recruited through the website of the German MS society.

Results: Six hundred and eighty-two patients were randomized and analysed for the primary end point. There were no differences in comprehension rates (MFP_{static}=46%, $CLARIFIG_{static}$=44%; P=.59; $MFP_{animated}$=23%, $CLARIFIG_{animated}$=30%; P=.134). Processing time for CLARIFIG was shorter only in the animated version (MFP_{static}=162 seconds, $CLARIFIG_{static}$=155 seconds; P=.653; $MFP_{animated}$=286 seconds, $CLARIFIG_{animated}$=189 seconds; P≤.001). However, both animated versions caused more wrong answers and longer processing time than static presentation (MFP_{static} vs $_{animated}$: P≤.001/.001, $CLARIFIG_{static}$ vs $_{animated}$: P=.027/.017).

Conclusion: Comprehension of the new format is comparable to MFP. CLARIFIG has the potential to simplify presentation in more complex contexts such as comparison of several treatment options in patient decision aids, but further studies are needed.

KEYWORDS

evidence based medicine, medical decision making, multiple sclerosis, patient education, patient preference

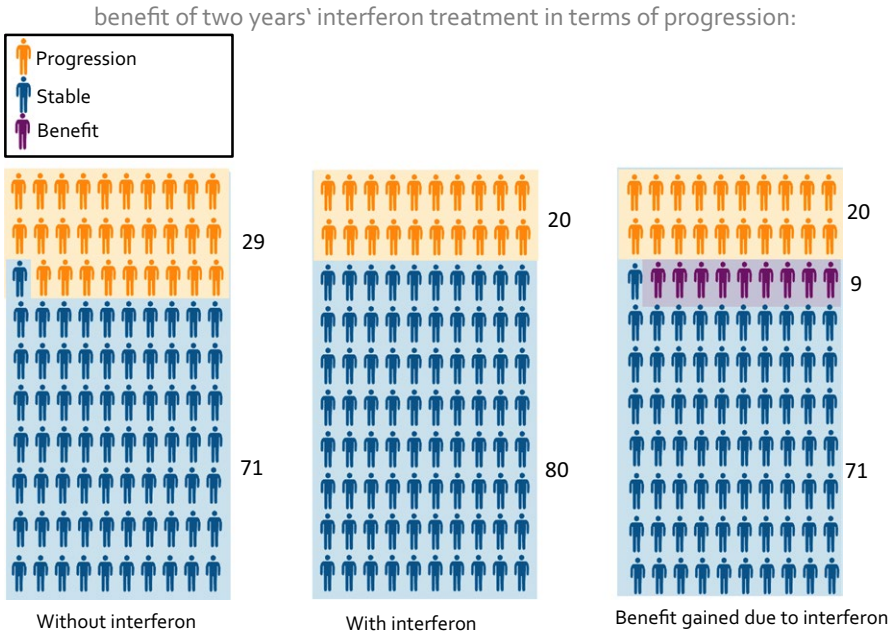

FIGURE 1 Multiple-Figure Pictogram: study example [Colour figure can be viewed at wileyonlinelibrary.com]

1 | BACKGROUND

Patient involvement is particularly indicated in medical decisions comprising more than one option usually including the option of watchful waiting.[1] Medical reasoning might be capable of comparing treatment efficacy with regard to a defined outcome parameter. The patient's opinion is needed to weigh up the values of different outcomes with potential side-effects. This applies even more for complexly structured decisions and/or for decisions associated with pronounced scientific uncertainty such as in the case of multiple sclerosis treatments.

Multiple sclerosis (MS) is a chronic inflammatory and degenerative disease starting predominantly in young adults. Apart from symptomatic therapies, the range of treatments comprises an increasing variety of immunotherapeutic options. Making decisions amongst them is challenging with regard to putative risks and uncertain benefit.[2,3] Comparison of drugs is a complex endeavour as few comparative studies exist and even less evaluating treatment escalation series or long-term effects of immunotherapies.

To be able to make informed choices about immunotherapies, MS patients need information prepared in line with the criteria of evidence-based patient information.[4,5] These criteria require communication of benefits and harm for each option presented as changes of absolute risk together with an estimation of the information's trustworthiness. Furthermore, the criteria include presenting event rates by the additional use of graphical frequency formats. Previous studies have shown that different graphical formats visualizing probabilistic information using bar graphs, survival curves and pie charts[4,6] improve patients' understanding[7] and even the quality of physician patient communication[8,9] when compared to text-only risk information. Frequently, multiple-figure pictographs (MFP) (also called icon arrays) are used in evidence-based patient information as, for example, in decision aids (DA).[4,10] MFPs show proportions of patients with effects and no effects of a medical intervention using a given reference number of stick figures or smileys (N=100 or N=1000) (Figure 1). MFPs have been proven effective in establishing sustainable comprehension of the difference between relative and absolute risk reduction in MS patients.[11] Compared to bar graphs, MFPs lead to equal comprehension of the proportions shown. Qualitative evidence suggests that MFPs are better suited to conveying the message of uncertainty about whether or not an individual will belong to the benefit group.[12] There are, however, practical drawbacks associated with using MFPs, particularly in multiple-option decisions like those addressed in our previous studies.[13-15] As the number of three consecutive MFPs needed to present the benefit of a single option (Figure 1) multiplies with the number of outcomes reported for benefit and harm and the number of available options, information materials easily become long and difficult to comprehend.[16] Also, elements of MFPs, that is stick figures or smileys, do not indicate the nature of clinical outcomes (eg in the MS example "disease progression" or "relapses") and therefore need additional explanations in the graphic's legend. Based on the elaborate qualitative design methodology,[17] we recently introduced CLARIFIG (clarifying risk figures) combining advantages of both proportional bar graphs and stick figure icons in a new space-saving format.

This article reports on an investigation aiming to evaluate the new presentation format's efficacy with regard to communicating study effects comprehensibly. Comprehension was defined in terms of accuracy of understanding the given quantities and time needed to process and complete the task. The first research question was: Does CLARIFIG lead to better comprehension and faster processing compared to MFP as the gold standard? Considering the increasing importance of making patient information tools feasible for web-based presentation, we also aimed at elucidating possible advantages of a stepwise animation. Our second research question was: Does animated presentation lead to better comprehension and faster processing than static presentation?

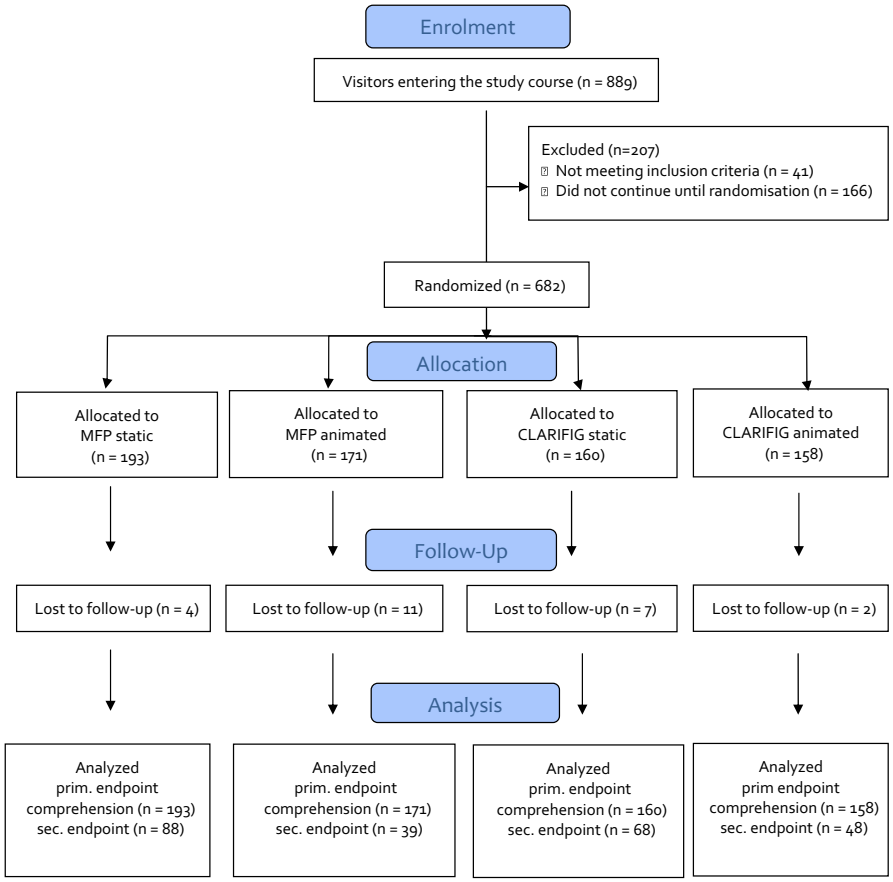

FIGURE 2 Flowchart [Colour figure can be viewed at wileyonlinelibrary.com]

2 | METHODS

2.1 | Design

The study used a web-based four arm randomized controlled trial (Figure 2) using a basic information example considering the effect of interferon-beta treatment in slowing disease progression in MS.[18] The previously tested basic example of CLARIFIG (Figure 3) was compared with a corresponding application of the MFP reference standard (Figure 1) and with animated versions of the two graphs, respectively.

The study was part of a research project within the German Multiple Sclerosis Competence network on decision coaching on immunotherapies in MS, which was approved by the Ethics Committee of the Hamburg Chamber of Physicians (PV4576).

2.2 | Intervention

CLARIFIG presents a sequence of three didactic steps condensed into one proportional bar graph with additional stick figure icons indicating the particular condition of the group represented by each segment of the bar graph (Figure 3). To explain possible results of a treatment option, the following three relevant groups are shown: (i) patients experiencing benefit, (ii) patients who worsen in spite of treatment and (iii) patients who do not benefit because the intended result would have occurred naturally. Applied to the study information example, CLARIFIG shows dichotomous outcome (benefit vs no benefit) indicated by the colour of the bar graph segment and three different types of results as described above: (i) patients remaining stable as a result of immunotherapy treatment, (ii) patients with progression in spite of treatment and (iii) patients who would have remained stable anyway. The patients' actual clinical condition is additionally indicated by three icons, one with the hands behind the back (indicating stability), one with a thumb up (indicating stability due to treatment) and one with a walking stick (indicating disease progression).

The information displayed in Figure 3 can be summarized by saying that nine of 100 patients benefit (blue bar segment/thumb up) and another 91 do not benefit (yellow segment) but present in two conditions, stable (hands behind the back) and progressed (icon with stick). The study tested the identical application of the CLARIFIG graph previously used during its development.

2.3 | Sample

To allow for a representative sample of people with MS, we used only two self-reported inclusion criteria: age ≥18 and a confirmed diagnosis of MS. The sample size was calculated based on the results of the pre-test. Accordingly, N=143 participants were needed in each group to detect a difference between 10% and 25% of the participants meeting the primary end point. The calculation was based on two-sided testing with a 5% alpha error and a 90% power. Compensating a 20% dropout rate, this calculation resulted in a proposed sample size of N=686 participants.

benefit of two years' interferon treatment in terms of progression:

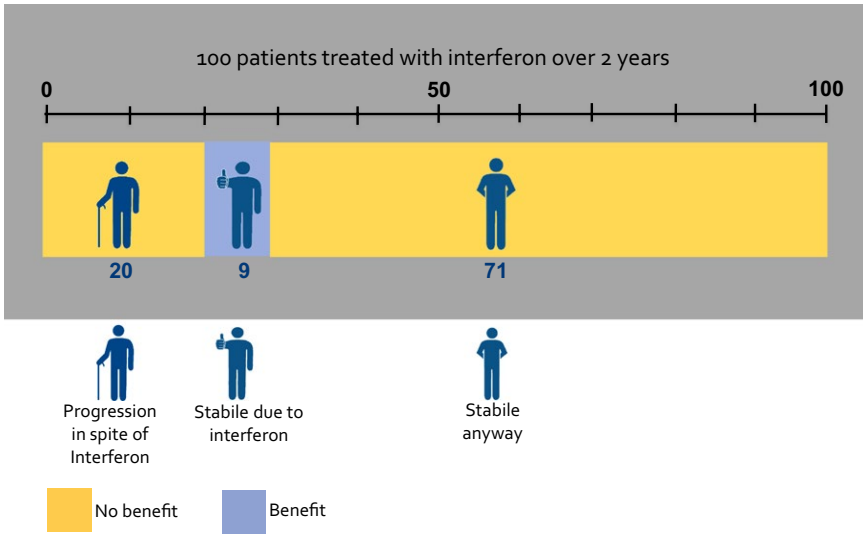

FIGURE 3 New CLARIFIG graph: study example [Colour figure can be viewed at wileyonlinelibrary.com]

2.4 | Procedure

Web presentation of the study was programmed using Unipark software[19] and accessed from the starting page of the German MS Self-help Society website (DMSG). It included the following components: invitation teaser, study instructions, the actual intervention consisting of a common introduction and four different presentations of the same information example and common questionnaires. Visitors to the teaser on the DMSG website were invited to participate in a research study about communication of frequencies in patient information materials. Complete anonymity was assured. The explanations about the study aim emphasized usability and comprehensibility of the presentation formats rather than the participants' performance. Although aware of the existence of various study arms, participants were blinded towards their own allocation. Randomization was conducted individually and documented automatically by a random algorithm within the Unipark software. A second participation via the same IP address was not possible. Participants were free to decide on how much time they wanted to spend on each chart. However, returning to a previous chard was not possible. After entering the study, patients were asked to provide demographic- and disease-related personal data. Briefing the participants for the coming information example, a short presentation (three charts) was then provided. Depending on group allocation, graphical presentations about the benefit of interferon treatment to delay disease progression varied slightly with regard to length (one to three charts) and presentation mode (static vs animated). The primary end point, comprehension, was assessed immediately after display of graphical presentations (Figure 4). To prevent memory effects, display of the respective graph was continued until all questions had been answered. After the completion of

Please answer the following questions referring to the graphic:		
1	How many of 100 patients benefit from the treatment?	☐
2	How many of 100 patients do not have a benefit?	☐
3	How many of 100 patients remain stable without Interferon?	☐
4	Identify the correct explanation for the following fact: Although stable during interferon treatment, patients might not benefit, because …	
	☐	… it is uncertain, whether those patients' extent of disability will increase in the future.
	☐	… those patients are not cured though.
	☐	… their condition did not improve.
	☐	… they would have been stable during that time even without treatment.

FIGURE 4 Primary end point

the questionnaire, the system registered a participant as a finisher. However, before the procedure was officially finished, participants were additionally asked to fill in a numeracy questionnaire.

2.5 | Measurements

The primary end point was previously developed and tested as a measure of accurate comprehension of the given quantitative information.[17] The score was dichotomized, defining four correct answers to the given set of four questions as correct and any other combination as false including missing answers. Beyond the recall of the pure quantity of benefit, the measure requires full comprehension of the complementary frequencies of patients without benefit. Mostly challenging (lowest estimate of item difficulty) was item 4, a multiple-choice question assessing understanding of the possibility of "no benefit" even though patients remained stable (Figure 4). Our previous qualitative research found the idea that the actual medical result cannot necessarily be equated with benefit to be counterintuitive at first glance and therefore difficult to understand. The secondary end point, processing time, was measured from the start of the study presentation and until completion of the primary end point questionnaire. Systematic variation of the time needed to complete the task was caused only by the presentation format, as all other parts of the study were identical. Differences in processing time were considered important, although the type of hardware used as well as connection speed might have led to individual differences, but no differences between groups were expected due to randomization. Disability was assessed with an eight-step ordinal measure based on the CAMBS scale.[20] To assess subjectively perceived cognitive impairment, four ordinally scaled items of the HAQUAMS instrument were applied.[21] In addition, the questionnaire assessed age, education, disease course, disease duration, medication status and previous participation in related studies. Numeracy was assessed using five of nine dichotomous test items from the Berlin Numeracy scale.[22]

2.6 | Analyses

Descriptive statistics were used to characterize the sample and the four study groups (Table 1) with regard to demography, disease-related data and numeracy. In the data matrix used by the statisticians analysing the trial, the nature of the four conditions was disguised. Participants were included in the analyses of the primary end point if they at least reached the place where the four-item comprehension test was provided. Missing values were counted as "not correct." Analyses of primary and secondary end points were conducted pairwise within the relevant factor steps. Fisher's exact tests were applied to test for the effects of the frequency format on comprehension separately for the two presentation types. *T* tests for unpaired samples were applied to test for effects of the frequency format on processing time. However, only finishers with correct results were included in this analysis. The impact of the presentation type (static vs animated) was tested separately for the two formats using Fisher's exact tests for comprehension and unpaired *t* tests for processing time.

The influence of numeracy and cognitive impairment was tested using unpaired *t* tests between subgroups of participants meeting and not meeting the primary end point and divided by median split of processing time, respectively.

Moderation of the rate of primary end point achievement by education or disease progression was tested using Fisher's exact tests, moderation of the secondary end point using ANOVA.

All statistical analyses were conducted using IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.

3 | RESULTS

Of 889 interested visitors, 682 completed the demographic questionnaire, fulfilled the inclusion criteria and were randomized. About 658

TABLE 1 Descriptive data from RCT

	MFP static	MFP animated	CLARIFIG static	CLARIFIG animated	Total
n	193	171	160	158	682
Age	39.6 (10.7)	38.0 (10.9)	41.4 (10.9)	41.4 (11.0)	40.1 (10.9)
Disease course					
Early	13 (7%)	15 (9%)	6 (4%)	7 (4%)	41 (6%)
Relapsing remitting	131 (68%)	101 (59%)	103 (64%)	99 (63%)	434 (63.6%)
Secondary chronic	20 (10%)	28 (16%)	25 (16%)	24 (15%)	97 (14.2%)
Primary chronic	14 (7%)	6 (4%)	10 (6%)	9 (6%)	39 (5.7%)
Unclear	15 (8%)	21 (12%)	16 (10%)	19 (12%)	71 (10.4%)
Female	143 (74%)	116 (67.8%)	113 (70.6%)	113 (71.5)	485 (71%)
University-level education	61 (31.6)	56 (32.7%)	47 (29.4%)	47 (29.4%)	47 (29.7%)
Wheelchair-dependent	9 (4.7%)	14 (8.2%)	15 (9.4%)	10 (6.3%)	48 (7%)
Cognitive impairment	2.5 (0.9)	2.3 (1.0)	2.3 (1.0)	2.5 (1.0)	2.4 (1.0)
Numeracy	2.14 (1.06)	2.22 (.95)	1.91 (1.1)	1.87 (1.1)	2.04 (1.1)

completed the study (for demographic data see Table 1) by at least finishing the primary end point task. The rate of dropout was generally low (n=24, 2.7%), but differed slightly between study conditions [MFP_{static} 4 (2.1%), $MFP_{animated}$ 11 (6.4%), $CLARIFIG_{static}$ 7 (4.4%), $CLARIFIG_{animated}$ 2 (1.3%)]. Characteristics of participants were comparable between study groups.

3.1 | Primary end point

The two formats did not differ with regard to frequencies of comprehension, neither in the static nor in the animated presentation (MFP_{static}=46%, $CLARIFIG_{static}$=44%; *P*=.59; animated $MFP_{animated}$=23%, $CLARIFIG_{animated}$=30%; *P*=.134) (Table 2). Single correct answers within the four-item comprehension questionnaire were more frequent; 85% of the participants identified the correct number of patients benefiting from treatment (Table 2).

For the static presentation, the animated formats led to significantly less comprehension and longer processing time (MFP: *P*≤.001).

3.2 | Secondary end point

CLARIFIG showed advantages regarding processing time only in the animated version (MFP_{static}=162 seconds. (SD 100), $CLARIFIG_{static}$=156 seconds. (SD 76); *P*=.653; $MFP_{animated}$=286 seconds (SD 172), $CLARIFIG_{animated}$=188 seconds. (SD 62); *P*≤.001). However, compared to the static presentation, the animated formats led to significantly less comprehension and longer processing time (MFP: *p* <= .001 / .001, CALRIFIG: *p* = .027/.017) (Table 3).

Comprehension was unrelated to processing time in all study groups (static: *P*=.138; animated: *P*=.776). Numeracy was positively related to comprehension (*P*=.016), but had no impact on processing time (static: *P*=.404; animated: *P*=.18). No moderator effects on primary or secondary end points were seen for either cognitive impairment or education level.

TABLE 2 Descriptive results primary end point

Results in the four-item comprehension test				
Format	**MFP**		**CLARIFIG**	
Presentation	**Static**	**Animated**	**Static**	**Animated**
Sample size	193	171	160	158
Question 1	86%	80%	86%	89%
Question 2	64%	71%	67%	43%
Question 3	86%	39%	91%	90%
Question 4	77%	75%	76%	82%
Total score	88 (46%)	39 (23%)	68 (44%)	48 (30%)

TABLE 3 Results for secondary end point: processing time needed

	Processing time			
	MFP	**CLARIFIG**		***P***
Static presentation				
Time to complete the survey	87 162.49 (SD: 99.7)	67 155.89 (SD: 75.89)	154	.653
Animated presentation				
Time to complete the survey	39 285.74 (SD: 172.11)	47 188.45 (SD: 62.16)	86	.001

4 | DISCUSSION

This paper describes the testing of a new format for communication of treatment effects to patients composed of a simple proportional bar graph including stick figure icons. Frequency graphs are only one element in a cocktail of essential ingredients of comprehensible patient information. Following the criteria of evidence-based patient information,[4] this cocktail also includes, for example, the definitions of possible treatment goals and patient-relevant outcomes. Other essential elements are a balanced presentation of possible benefits between various medical options and presentation of potential harm alongside presentation of benefits. The complex nature of medical decisions justifies a new format for their presentation. The results of this study clearly show that using the new and condensed format, the quantitative information can be presented as understandably as using the well-established MFPs.[10,12,23-26]

However, there was a gap between recognizing and fully understanding the crucial information about the chance of benefiting from treatment. About 85% of participants (irrespective of group affiliation) correctly identified the proportion benefiting (9%), while <50% of participants in all conditions fully understood this figure was clearly below 50% in all conditions. We are not aware of other studies using the latter instead of the former parameter to assess understanding of numerical risk information. However, our choice of the more rigorous parameter as the primary end point reflects our claim to enable patients to make informed choices. As this requires knowledge about both the absolute rate of benefit and the natural course, our end point was meant to assess complete understanding of the graph. This implied, for example, that patients who have not deteriorated do not necessarily belong in the benefit group. We feel that a patient armed with this knowledge would have a good grasp of the options and would even be capable of unmasking a misleading explanation by their physician, for example communicating relative risk reductions only. The knowledge that positive medical results (such as absence of disease progression) can occur naturally, without treatment, is usually not part of standard information. Misleading information on benefit provided by health professionals and the pharmaceutical industry might therefore have contributed to unrealistic expectations regarding treatment effects and to the primary end point's low-item difficulty (low frequency of correct solutions).[27] Nevertheless, this rate is still substantially low in the light of a sound development process. Limits in understanding frequency formats could be caused not only by a lack of conclusiveness of the format itself, but also by a lack

of fundamental numerical skills in a high percentage of the public.[28] Besides numeracy, patients' understanding of graphical risk communication is moderated by other competencies, by pre-existing knowledge and beliefs.[29] Participants in our pilot testing reported internal resistance to accepting the information because of the low rate of benefit indicated. Therefore, they tended to interpret the numbers based on their previous beliefs rather than on the figures provided in the graph. This means, in turn, that graphics are only partially capable of compensating for absent skills.[30]

Due to confounding of various moderators potentially impacting on processing time, the secondary end point should be discussed cautiously. Time in this experiment cannot conclusively be attributed to the extent of cognitive burden. As participants were not aware of a time criterion, variance due to individual working styles might have clouded the meaning of the parameter. More rigorous standardization of the end point would on the other hand have been difficult to apply without putting pressure on participants. With regard to the comparison conducted in this study, consideration of processing time as a compound parameter with practical importance seemed to us nevertheless appropriate.

Contrasting the MFP approach, CLARIFIG manages to explain the frequencies without mentioning a placebo condition, which we initially considered essential. However, by following the patients' reasoning in our qualitative work, we arrived at a much simpler graphical solution than we had assumed would be necessary. A maximum of simplification of the single frequency formats is required to allow for composing clear presentation of comprehensive information. With regard to its concise format, we expect CLARIFIG to improve comprehension accuracy in comprehensive and more complex contexts. As CLARIFIG meets the needs of patients with multiple sclerosis who often have to consider a broad variety of options, we are currently applying the new method to comparative communication of risks and benefits in decisions with up to seven options.[31] Due to its handy format and intuitive completeness, CLARIFIG is also used for explaining frequencies of benefit and side-effects in decision aids on the Norwegian platform "Mine Behandlingsvalg."[32]

The stepwise ("animated") appearance of the graphic elements used in two of the study conditions obviously confused participants rather than providing meaningful structure. Participants in the animated conditions performed much less well on both comprehension and processing speed than those seeing a stable diagram. Although contradicting our hypotheses, this finding is in line with studies from other authors.[24,33] Zikmund-Fischer et al. showed disadvantages of eight animated frequency formats compared with two static presentations. Unanimity of the latter results including ours is important with regard to the increasing availability of web-based evidence-based patient information.

The study is strong with regard to large sample size and the low dropout rate, but might be challenged with regard to the representativeness of the study population. Because of the web-based approach, only patients with a special interest or competence might have accessed the study. Most of the patients in our sample probably were not currently involved in making decisions about immunotherapy, which might have limited the motivation to process the information and might have led to underestimation of the total comprehension rate.

By only looking at two end points (comprehension and processing time), the present study failed to investigate the new graph's possible impact on a number of reasonable end points, such as perception of uncertainty, motivation to take an active role in the decision-making process, memorability of the information and transfer competence. Most importantly, however, its impact on the decision-making process in terms of facilitating shared decision making, informed choices and realistic expectation should be focused in further studies.

Effects of frequency formats on risk perception are not yet fully understood,[12,33] and the optimal format has not yet been found.[6] Moreover, as the context of the information, the target group and even the numerator size itself moderate the formats' suitability, current evidence is far from being able to inform systematic recommendations for developers and users of frequency formats.[6] In this respect, our study responds to a persistent lack of comparative studies and systematic developments in the field of communication and understanding of frequency formats.[6]

In summary, the new format is promising because it has undergone a sound development process involving patients and a rigorous evaluation within a randomized controlled trial. As is immediately evident, CLARIFIG complies with the criteria of evidence-based patient information,[4] but also shows practical advantages with regard to multiple-format arrangements in limited space.

5 | CONCLUSION

Comprehension and processing speed of the new format, CLARIFIG, is comparable to commonly used multifigure pictographs (MFPs). The new format is advantageous with regard to space requirements and will facilitate the comparison of different treatment options in comprehensive patient information. This trial is considered exploratory as it compared the methods in a limited application using information from just one isolated study. Having found low comprehension rates irrespective of the experimental condition, the study demonstrates the gap between recognizing and fully understanding the information on the rate of benefit. This result implies that further research is needed on strategies to establish realistic expectations regarding the disease's natural course. Moreover, further studies are needed to prove the format's advantages in more complex contexts such as patient decision aids presenting information on various treatment options in parallel and in other medical domains.

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AUTHORS' CONTRIBUTIONS

JK (principal investigator) together with CH, SK and AvdR designed the study and protocol. JK led the development of the graph. The development was conducted together with JP, YB, IB and AvdR, who is responsible for the graphical solutions. JK analysed data, interpreted results and wrote the article with important contributions from CH and SK. All authors contributed to the interpretation of study results and writing of the article.

CONFLICT OF INTERESTS

JK, AvdR, JP, AR, IB and SK have no conflict of interests. CH has received grants from Biogen, Genzyme Sanofi Aventis, Novartis, Merck-Serono.

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Rahn AC, Köpke S, Schiffmann I, Stellmann JP, Mühlhauser I, Lukas C, Chard D, Heesen C (2017) Magnetic resonance imaging as a prognostic disability marker in clinically isolated syndromes: A systematic review.

Kurzfassung

Einleitung

In circa 85 Prozent der Fälle manifestiert sich die Multiple Sklerose (MS) in Form eines klinisch isolierten Syndroms (KIS). Der Begriff KIS charakterisiert eine erste klinische Episode mit Symptomen, die auf Multiple Sklerose hindeuten und oftmals die Sehnerven, das Rückenmark, das Kleinhirn oder den Hirnstamm betreffen [1].
Die Magnetresonanztomographie (MRT) ist der wichtigste diagnostische und prognostische Marker beim KIS [2, 3], wobei der variable Krankheitsverlauf eine prognostische Aussage erschwert. Personen mit einem KIS erhalten immer häufiger eine Immuntherapie mit dem Ziel, die Konversion zu einer klinisch gesicherten MS zu verhindern bzw. zu verzögern und das Risiko einer zukünftigen Beeinträchtigung zu reduzieren.
Es gibt Hinweise, dass durch frühe MRT Untersuchungen zumindest teilweise eine kurz- (< 2 - 3 Jahre) und längerfristige (≥ 5 Jahre) Zunahme der Beeinträchtigung vorhergesagt werden kann [3, 4].
Es gibt Reviews zur MRT und dem Risiko der Entwicklung einer MS nach einem KIS [5, 6], die aber nicht den Kriterien an systematische Reviews entsprechen [7, 8]. Bislang gibt es kein systematisches Review zum prognostisches Wert der MRT hinsichtlich einer Zunahme der Beeinträchtigung. Das vorliegende systematische Review zielt darauf ab, diese Lücke zu schließen.

Methoden

Prospektive und retrospektive Längsschnittstudien wurden berücksichtigt, wenn diese mindestens 50 Personen mit einem KIS eingeschlossen haben, ein Follow-up von 5 Jahren oder mehr hatten und mindestens eine strukturelle MRT-Messung (T1-Läsionen, T2-Läsionen, T1-kontrastmittelverstärkende Läsionen oder Hirnatrophie) berichten. Placebogruppen von randomisiert kontrollierten Studien (RCT) zu Immuntherapien wurden nicht berücksichtigt, da diese Gruppen in der Regel nach zwei Jahren ebenfalls das getestete Medikament erhalten.
Primärer Endpunkt war die Beeinträchtigungszunahme, erhoben mit der „Expanded Disability Status Scale“ (EDSS) [9] im Zusammenhang mit dem prognostischen Faktor (MRT).
Wir haben eine systematische Literaturrecherche nach Studien in MEDLINE (bis Juni 2015) und EMBASE (bis Mai 2013) via Ovid unter Berücksichtigung von Prognosefiltern durchgeführt [10, 11] (Siehe Anhang b für die Suchstrategie in MEDLINE). Ergänzend wurden die Referenzen der eingeschlossenen Studien geprüft, um weitere Studien zu identifizieren. Die Volltexte mussten in deutscher oder englischer Sprache vorliegen. Die Suchen wurden zu allen MS Verlaufsformen durchgeführt, da es auch gemischte Kohortenstudien gibt. In diesem Review werden die Ergebnisse zum KIS dargestellt.
Alle Schritte der Literaturrecherche (Titel und Abstractscreening, Volltextscreening, Qualitätsbeurteilung) und die Datenextrahierung erfolgten standardisiert und immer

unabhängig durch zwei Personen. Das "Quality In Prognosis Studies" (QUIPS) Tool wurde zur Erfassung des Risikos für Bias [12, 13] angewendet und die Vollständigkeit der MRT-Berichterstattung wurde auf Basis eines zuvor angewendete Instruments bewertet [14].

Ergebnisse

Insgesamt wurden 3498 Abstracts gescreent (Abbildung 1) und 56 Studien im Volltext beurteilt. Insgesamt 13 Studien [4, 15–26] erfüllten die Einschlusskriterien.

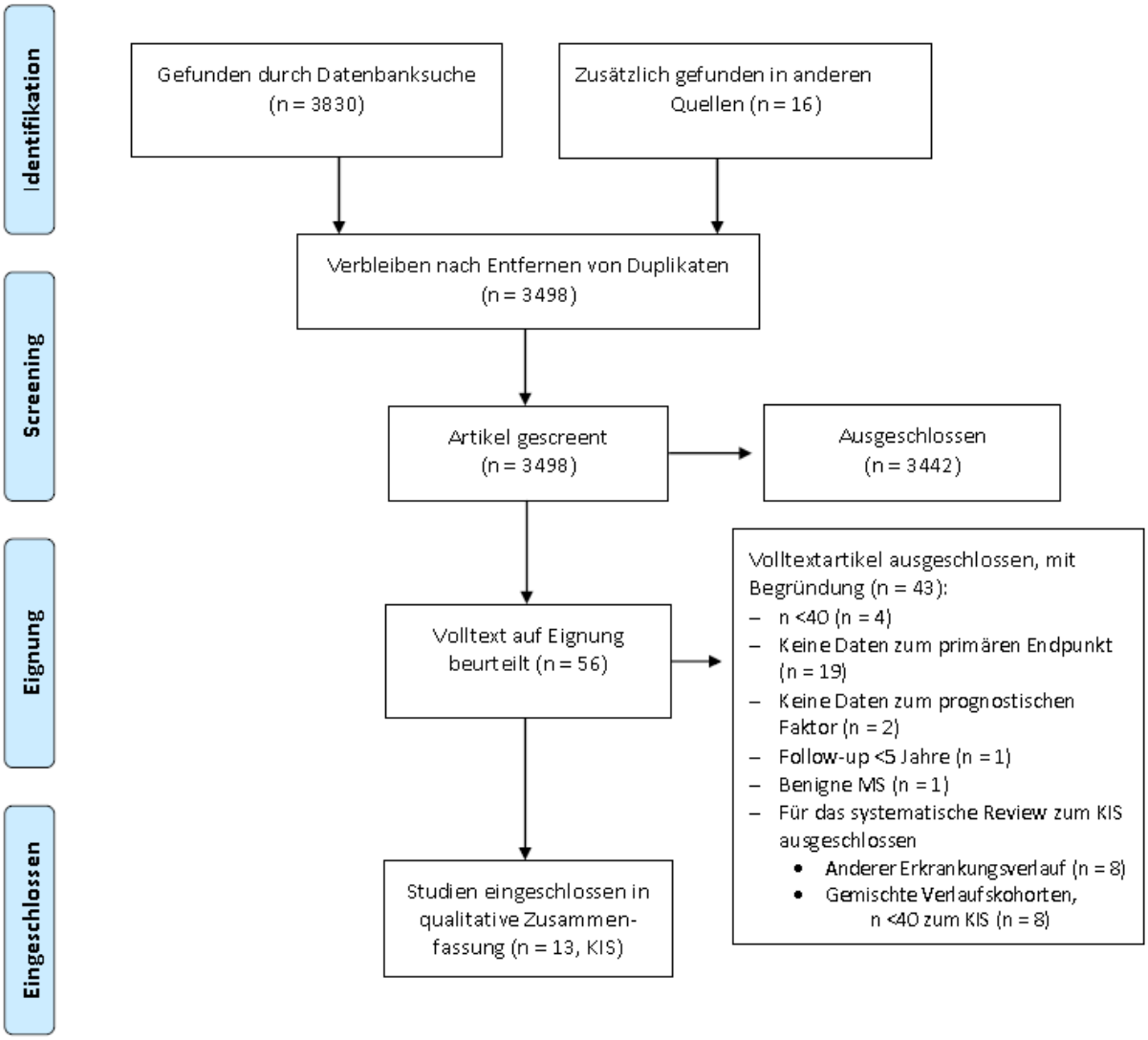

Abbildung 1: PRISMA Flussdiagramm

Publikationen zu Kohortenstudien aus London (zwei Kohorten, sieben Publikationen) und Barcelona (eine Kohorte, drei Publikationen) sowie drei Publikationen zum Langzeit Follow-up einer RCT zur Behandlung der Optikusneuritis (ONTT) wurden eingeschlossen. Die 13

Studien sind mit einer Studiendauer von 5 bis 20 Jahren und hinsichtlich der MRT Untersuchung (siehe Anhang b), des Einschlussbeginns, der Einschlusskriterien sowie der Studiendesigns heterogen.

Die Qualitätsbewertung hinsichtlich potenzieller Bias zeigte gemischte Ergebnisse. Speziell für die Dimensionen “prognostic factor” (MRT), “outcome measurement” (z.B. EDSS Erhebung) und “confounding measurement and account” (z. B. Immuntherapie) fehlten in den meisten Studien detaillierte Informationen, während zur “analysis” in der Regel ausreichend Angaben vorlagen (Abbildung 2).

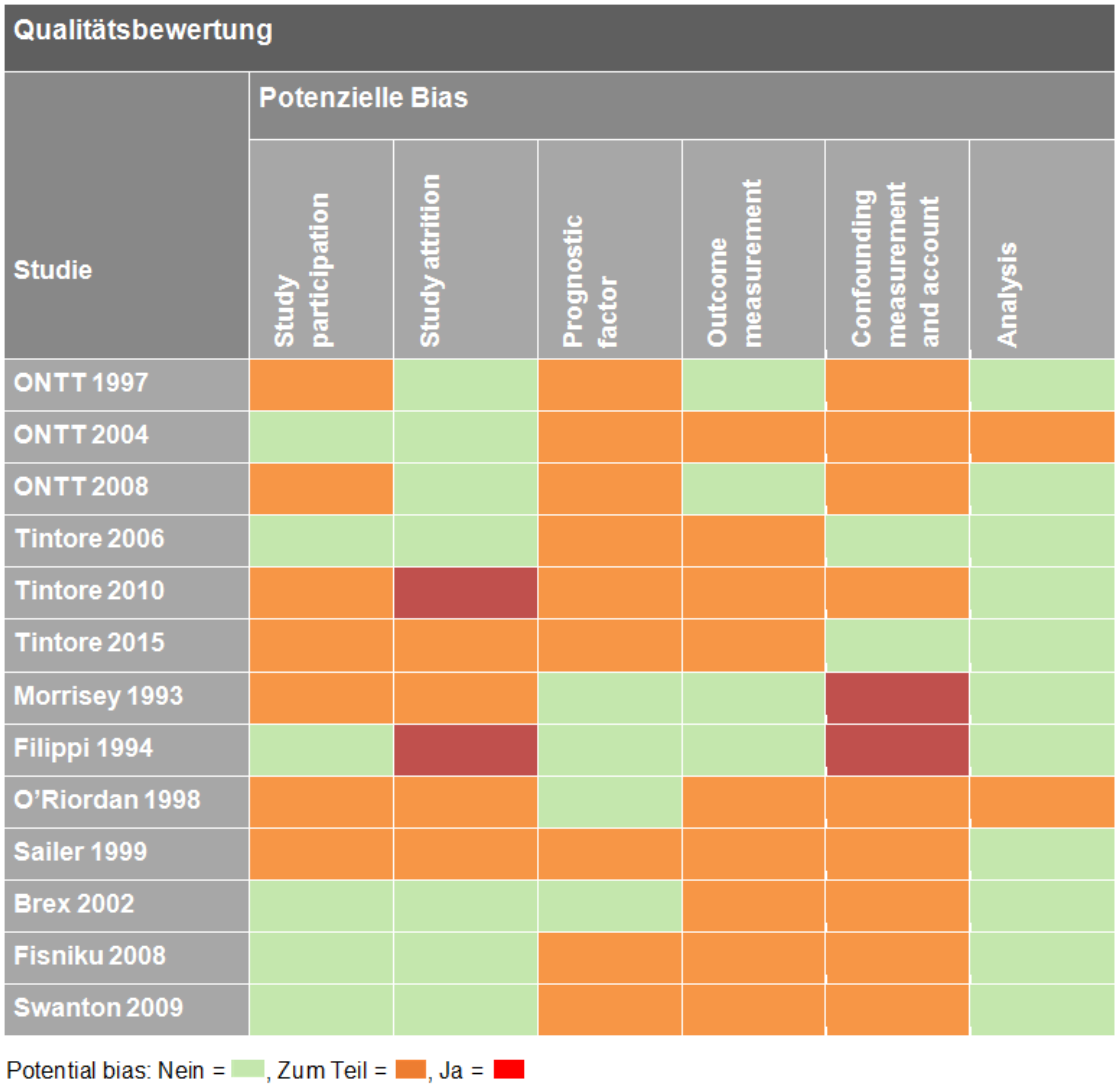

Abbildung 2: Qualitätsbewertung

Schlussfolgerung

Insgesamt liegen Daten aus wenigen Kohorten vor. Die Ergebnisse zeigen, dass wenige Studien die prognostische Bedeutung der MRT in Bezug auf die Entwicklung der

Beeinträchtigung über einen Zeitraum von mehr als fünf Jahren untersucht haben. Insgesamt zeigt die Evidenz, dass eine frühe hohe T2-Läsionslast ein moderater prognostischer Marker für eine höhere Beeinträchtigung nach fünf bis sieben Jahren beim KIS ist. Weiterhin scheinen infratentorielle Läsionen bei der Prognose der Beeinträchtigung von besonderer Bedeutung zu sein (Tabelle 1). Allerdings ist die Vorhersagekraft auf individueller Ebene begrenzt. Die MRT Ergebnisse sollten daher als ein Faktor für die Therapieentscheidungsfindung bei Personen mit einem frühen Verdacht auf MS (KIS) sein.

Tabelle 1: Evidenz für eine Assoziation zwischen MRT Messungen und Beeinträchtigungszunahme

KIS Kohorten	**5 – 7 Jahre**	**8 – 14 Jahre**	**15 – 20 Jahre**
T2 Läsionszahl	+	+/-	n.b.
T2 Läsionsvolumen	+/-	+/-	+/-
10 oder mehr T2 Läsionen	+/-		n.b.
Veränderung der Läsionsanzahl	+/-*	+/-	n.b.
Veränderung des Läsionsvolumens	+/-	+/-	+/-
Infratentorielle Läsionszahl	n.b.	+/-	n.b.
Infratentorielles Läsionsvolumen	+/-	n.b.	n.b.
Optikusneuritis Kohorten	**5 – 7 Jahre**	**8 – 14 Jahre**	**15 Jahre**
T2 Läsionszahl	+/-	--	--
T2 Läsionsvolumen	n.b.	n.b.	n.b.
10 oder mehr T2 Läsionen	n.b.	n.b.	n.b.
Veränderung des Läsionsvolumens	n.b.	n.b.	n.b.
Infratentorielle Läsionszahl	+/-	n.b.	n.b.
Infratentorielles Läsionsvolumen	n.b.	n.b.	n.b.

+ = moderate evidence of effect, +/- = limited evidence of effect, -- = no evidence[30], n.b. = nicht berichtet (Daten wurden nur berücksichtigt, wenn p-Werte oder Konfidenzintervalle angegeben wurden); *die Anzahl neuer Läsionen innerhalb der letzten fünf Jahre korrelierte mit der Veränderung der Beeinträchtigung während des Zeitraums.

Ergänzende Informationen

Das Bundesministerium für Bildung und Forschung hat das Projekt im Rahmen einer Förderung des Krankheitsbezogenen Kompetenznetz Multiple Sklerose (KKNMS) finanziert.

CH, AR und JB haben die Suchstrategie entwickelt und AR und JB führten die Suche durch. JB, SK, AR und CH haben die Artikel gescreent. AR, CH und AMK beurteilten die eingeschlossenen Studien und extrahierten die Daten. AR hat das eingereichte englische Manuskript und die Kurzfassung geschrieben.

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7.4. Rahn AC, Backhus I, Riemann-Lorenz K, Köpke S, van de Roemer A, Vettorazzi E, Mühlhauser I, Heesen C (2017) Comprehension of confidence intervals in audio-visual patient information materials for people with multiple sclerosis (COCO-MS): a web-based randomised controlled, parallel group trial. (Manuskript in Vorbereitung)

Rahn AC, Backhus I, Riemann-Lorenz K, Köpke S, van de Roemer A, Vettorazzi E, Mühlhauser I, Heesen C (2017) Comprehension of confidence intervals in audio-visual patient information materials for people with multiple sclerosis (COCO-MS): a web-based randomised controlled, parallel group trial.

Kurzfassung

Einleitung

Immer mehr verfügbare Immuntherapieoptionen führen zu einem komplexen Entscheidungsprozess für Betroffene mit schubförmig verlaufender Multipler Sklerose (MS). Evidenzbasierte Informationsmaterialien über den Nutzen und Schaden von Medikamenten sind essentiell für informierte Therapieentscheidungen. In der Literatur zur MS gewinnt die Kommunikation von Risiken zunehmend an Bedeutung [1, 2]. Neben Informationen zum Behandlungseffekt kann die Kommunikation von Konfidenzintervallen (Abb. 1) hilfreich sein, um die Reliabilität der Schätzungen aus klinischen Studien zu bewerten [3, 4].

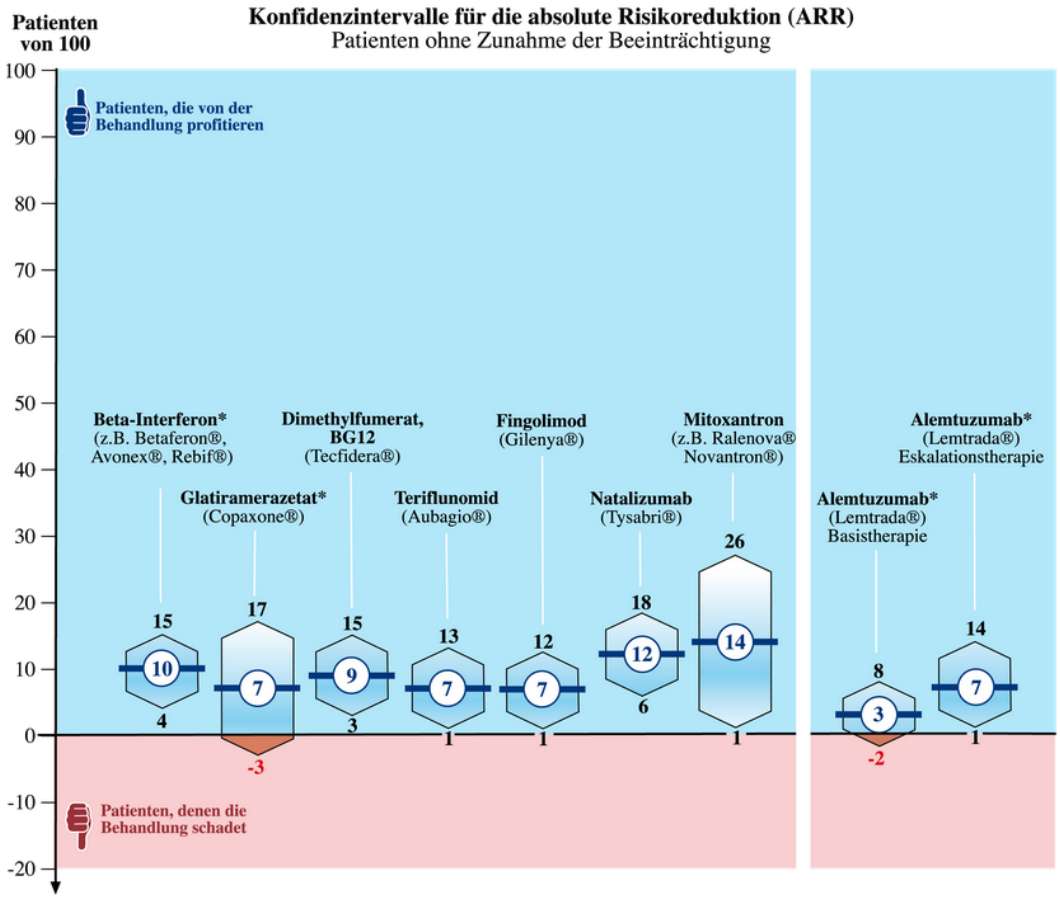

Abbildung 1: Wirkungsvergleich der zugelassenen Immunmedikamente zur Therapie der schubförmigen Multiplen Sklerose mit Konfidenzintervallen [5]

Das Ziel der Studie war die Evaluation von drei verschiedenen audiovisuellen Patienteninformationen zu Konfidenzintervallen mittels einer vierarmigen, webbasierten, randomisiert kontrollierten Studie (RCT).

Methoden

Wir folgten den MRC Kriterien zur Entwicklung und Evaluation komplexer Interventionen [6], um die Patienteninformationsmaterialien zu Konfidenzintervallen zu entwickeln, zu pilotieren und zu evaluieren.
Eine systematische Literatursuche identifizierte keine relevanten Studien, in der audiovisuelle Informationen zu statistischen Informationen evaluiert wurden. Aufbauend auf den vielversprechenden Ergebnissen der Pilot-RCT entwickelten wir drei audiovisuelle Patienteninformationsversionen zu Konfidenzintervallen [3].
Für die audiovisuellen Patienteninformationen wurden detaillierte Informationssätze durch mündliche Erklärungen ausgetauscht und wichtige Aussagen unterstützend als Kernaussagen visuell gezeigt. Insgesamt gibt es drei Sprecher (Erzähler, Statistiker und MS-Betroffene).
Die audiovisuelle Version „Durchschnittsgewichte“ wurde in qualitativen Interviews mit vier MS-Betroffenen hinsichtlich der Akzeptanz und Nutzbarkeit [7] getestet, wobei „think aloud"-[8] und „teach back"-Techniken [9] angewandt wurden. Die qualitative Inhaltsanalyse [10] zeigte keinen weiteren Revisionsbedarf, weshalb die beiden anderen audiovisuellen Patienteninformationen nicht pilotiert wurden.
Studienteilnehmer (≥ 18 Jahre) mit schubförmiger MS wurden für die RCT über die Webseiten der österreichischen und deutschen Multiple Sklerose Gesellschaften rekrutiert und zur Online-Befragungsplattform (UNIPARK) weitergeleitet. Die randomisierte Zuteilung auf eine der drei Interventionsarme (audiovisuelle Information) oder den Kontrollarm (Standardinformation) erfolgte über die UNIPARK Software:
Arm I: Audiovisuelle Patienteninformation zu KI am Beispiel „Durchschnittsgewichte“
Arm II: Audiovisuelle Patienteninformation zu KI am Beispiel „Apfelbehandlung“
Arm II: Audiovisuelle Patienteninformation „Kurzversion“ zu KI
Arm IV: Standardinformation zu KI.
Der primäre Endpunkt, Verständnis von Konfidenzintervallen, wurde mittels eines Multiple-Choice Fragebogens mit sechs Fragen erhoben [3]. Der Fragebogen wurde in einem Pilot-RCT (n=64) getestet und die Berechnung der Stichprobe (572 Teilnehmer, $\alpha \leq .05$, $1-\beta \geq .9$) erfolgte auf Basis der Ergebnisse [3]. Als sekundärer Endpunkt wurde eine Version des Multiple Choice-Fragebogens mit sieben Fragen angewendet und hinsichtlich der Validität geprüft. Zudem wurden demographische Daten (Alter, Geschlecht, Bildung), krankheitsspezifische Daten (Krankheitsverlauf und Dauer, Diagnose sowie Schweregrad der Krankheit [11]) und Risikokompetenz [26] erhoben.
Darüber hinaus wurden vier Evaluationsfragen zur Bewertung von Relevanz, Verständlichkeit und Nützlichkeit der Informationen für zukünftige Behandlungsentscheidungen angewendet (Likert-Skala von 1-10).
Die Teilnehmer wurden entsprechend der Zuteilung analysiert. Für den primären Endpunkt wurden die Mittelwerte der korrekt beantworteten Fragen in jedem der drei Interventionsarme mit den Ergebnissen des Arms IV (schriftliche Standardinformation) verglichen (ANOVA). Korrelationen zwischen dem Verständnis von Konfidenzintervallen und der Risikokompetenz

sowie der Bildung wurden nach Pearson oder Spearman geschätzt. Eine Regressionsanalyse wurde durchgeführt, um den Einfluss von Risikokompetenz und Bildung auf das Verständnis von Konfidenzintervallen zu untersuchen. In das Modell sind zudem Alter, Geschlecht, Krankheitsdauer, Immuntherapiestatus und Beeinträchtigung der Betroffenen eingeflossen. Alle Analysen wurden mit SPSS Version 21 bzw. 22 durchgeführt. Weitere Ergebnisse wurden deskriptiv dargestellt.

Ergebnisse

Die webbasierte RCT startete im Juni 2015 und die Rekrutierung wurde im Januar 2016 abgeschlossen. 1068 Personen wurden auf die 4 Studienarme randomisiert. Es wurden Daten von allen Teilnehmern (n = 734) ausgewertet, die mindestens 4 von 6 Fragen zum Verständnis von Konfidenzintervallen direkt nach der Intervention beantwortet haben.
Im Arm I haben 217 (76%), im Arm II 172 (63%), im Arm III 186 (76%) und im Arm IV 159 (60%) Teilnehmer die Befragung abgeschlossen (Abbildung 2). Die Gruppen waren hinsichtlich soziodemographischer und krankheitsbezogener Charakteristika vergleichbar. Es gibt Unterschiede in der Verteilung des Bildungsstands zwischen Teilnehmern die vorzeitig abgebrochen haben und Teilnehmern, die die Befragung beendet haben. Dieser Unterschied ist für Arm III (p=0,002) und IV (p=0,001) signifikant. Hier haben mehr Teilnehmer mit einem niedrigen Bildungsstand die Studie abgebrochen.

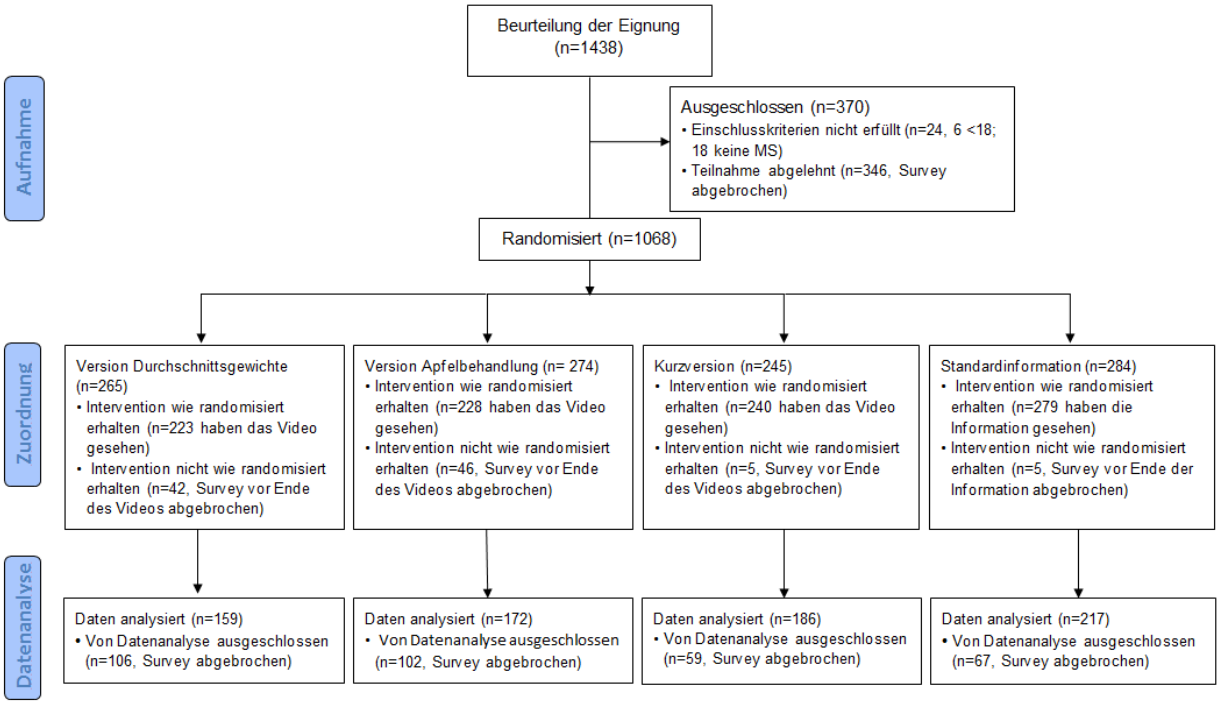

Abbildung 2: Flussdiagramm

Im Arm I beantworteten die Teilnehmer im Mittel 4,6 (Standardabweichung (SD) 1,5) von 6 Fragen zu den Konfidenzintervallen richtig, im Arm 2 II 4,5 (SD 1,4), in Arm III 3,8 (SD 1,2) und in Arm IV 4,2 (SD 1,2, Abb. 5). Teilnehmer der Arme I und II haben im Mittel signifikant

mehr Fragen richtig beantwortet als Teilnehmer des Arms IV (Fisher‘s LSD, p= 0,005 bzw. 0,007). Teilnehmer des Arms III haben signifikant weniger Fragen richtig beantwortet im Vergleich zum Arm IV (Fisher‘s LSD, p=<0,001, Abbildung 3).
Bezüglich der Risikokompetenz gab es keinen signifikanten Unterschied; die Teilnehmer erreichten im Mittel 3 von 5 Punkten. Alle Ergebnisse zum Verständnis von Konfidenzintervallen korrelierten in allen Armen positiv mit der Risikokompetenz (Arm I: 0,38, Arm II: 0,38, Arm III: 0,39, Arm 4: 0,35; Spearman-Rho: p=<0,001).

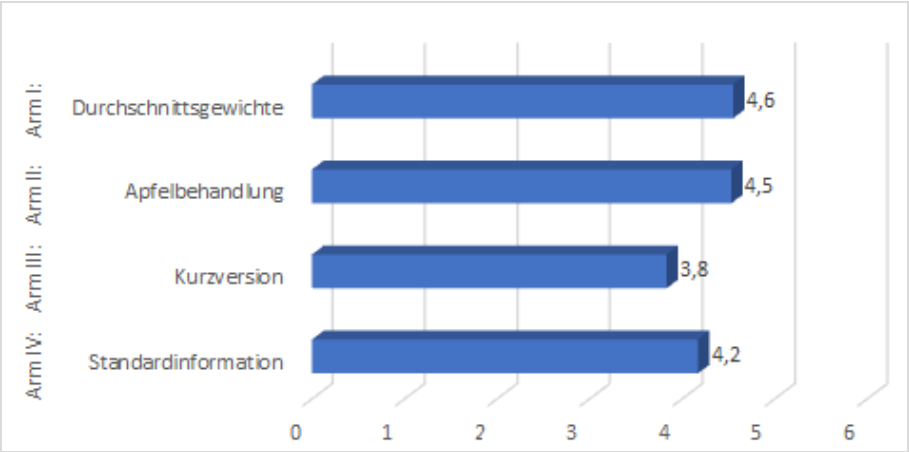

Abbildung 3: Verständnis on Konfidenzintervallen

Teilnehmer der Arme I, II und III bewerteten die jeweilige Präsentation hinsichtlich Verständlichkeit, Relevanz, Nützlichkeit und subjektivem Wissen auf einer 10-stufigen Likert Skala im Mittel um einen Punkt höher als Teilnehmer des Arms IV (Abbildung 4). Als häufigste Hindernisse ihr Wissen zu Konfidenzintervallen nutzen zu können, wurden genannt: mangelnder Zugang (30,1%), fehlende Informationen (21,4%) und die Befürchtung, dass der behandelnde Arzt nicht über Unsicherheiten bei Therapieentscheidungen diskutieren möchte (16,8%).

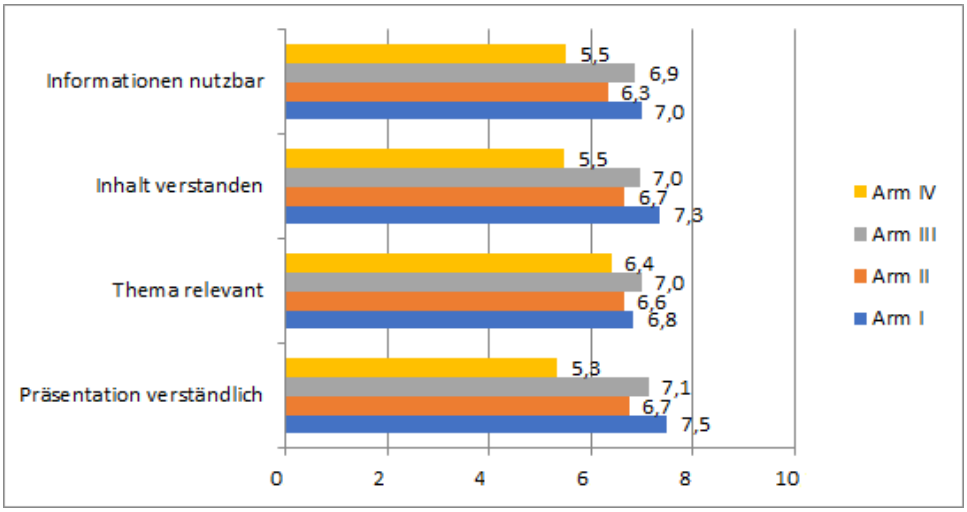

Abbildung 4: Evaluationsfragen

Die lineare Regressionsanalyse zeigte, dass nur Bildung und Risikokompetenz das Verständnis von Konfidenzintervallen beeinflusst haben, wobei die Risikokompetenz einen höheren Einfluss hatte.

Schlussfolgerung

Die Studie zeigt, dass Informationen zu Konfidenzintervallen verständlich sind. Die ausführlichen audiovisuellen Informationen werden besser verstanden, allerdings haben bei der Version „Apfelbehandlung“ mehr Teilnehmer die Studie vorzeitig abgebrochen. Eine gute Risikokompetenz ist anscheinend hilfreich zum Verständnis der Informationen. Das Wissen zu Konfidenzintervallen kann Patienten helfen die Effekte verschiedener Behandlungsmöglichkeiten zu vergleichen und informierte Entscheidungen im Einklang mit persönlichen Werten und Präferenzen zu treffen.

Ergänzende Informationen

Die RCT wurde prospektiv registriert (German Clinical Trials Register DRKS00008561) und das Studienprotokoll ebenfalls mit Registrierung veröffentlicht [12].
Das Bundesministerium für Bildung und Forschung hat das Projekt im Rahmen einer Förderung des Krankheitsbezogenen Kompetenznetz Multiple Sklerose (KKNMS) finanziert.
Die Studie wurde von CH, AR, SK, IB und KRL konzipiert. IM betreute den Forschungsprozess und trug zur Studienplanung bei. AR und KRL entwickelten das Studienprotokoll. AR, IB und KRL entwickelten die audiovisuellen Patienteninformationsversionen. Die Grafiken wurden von VDR entwickelt. Der Analyseplan wurde von EV, IB und AR entwickelt und die statistische Analyse wurde von EV, AR und IB durchgeführt. AR schreibt das Manuskript und hat die Kurfassung erstellt.

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8. Diskussion und Ausblick

Die hier aufgeführten Arbeiten schließen an vorangegangene Projekte zur informierten Entscheidungsfindung von MS-Betroffenen an [9, 10, 25]. In dieser Diskussion wird das Decision Coaching-Programm als Kernstück der Dissertation fokussiert. Mit dem DECIMS Projekt wurde erstmals ein individuelles Programm zur Begleitung von Immuntherapieentscheidungen entwickelt und pilotiert. Durch das Coaching zu Immuntherapien von MS-Nurses wird auch die Übernahme neuer Rollen durch Gesundheitsfachberufe erprobt. Hierbei wurde nach den MRC Kriterien zur Entwicklung und Evaluation komplexer Interventionen vorgegangen [24]. Einen besonderen Raum hat die Entwicklung und Durchführung einer begleitenden Mixed-Methods Prozessevaluation eingenommen [41–43].

Die sorgfältige theoriebasierte Entwicklung des Coaching-Programms in der ersten Phase (Abbildung 1) stellt eine der Stärken der Arbeit dar. In dieser Phase wurden unter anderem interessierte MS-Zentren besucht, um die Intervention praxisnah zu planen. Des Weiteren wurde das MAPPIN'SDM-Fragebogen-Inventar um die Perspektive der Nurses erweitert [28, 33].

Nach der Testung der Machbarkeit in der zweiten Phase wurde eine Pilot-RCT mit begleitender Prozessevaluation durchgeführt. Diese zeigt grundsätzlich die Machbarkeit und Akzeptanz der Intervention und deutet an, dass das Decision Coaching informierte Entscheidungen fördern kann.

Das Wissen zur Wirksamkeit von Decision Coaching-Interventionen durch trainierte Nurses ist begrenzt [14]. Ähnlich wie unsere deskriptiven Pilotstudienergebnisse, zeigte auch das Review von Stacey et al. [14] keine zusätzliche Verbesserung des Wissens durch Decision Coaching-Interventionen in Kombination mit Entscheidungshilfen gegenüber Entscheidungshilfen alleine. Der von uns eingesetzte Fragebogen zum Risikowissen [44] ist jedoch nicht auf die individuelle Situation der MS-Betroffenen zugeschnitten, sondern adressiert beispielsweise auch Therapieoptionen für einen hochaktiven Verlauf der MS. Eine Wissensverbesserung ist damit nicht einfach zu erreichen und wird durch die Komplexität des Fragebogens weiter erschwert. Allerdings wurde mit der informierten Entscheidung ein primärer Endpunkt gewählt, für den mit dem Fragebogen ein evaluiertes Messinstrument zur Verfügung stand [73].

Die Pilot-RCT zeigte deskriptiv keinen Unterschied hinsichtlich des Beginns einer Immuntherapie. Die quantitativen sowie qualitativen Prozessdaten zeigten keine Änderung in der Haltung, sondern deuten eine Bestätigung der Einstellung durch das Coaching an. Eine Limitation der Pilotstudie stellt jedoch die hohe Anzahl fehlender Daten, insbesondere in der

Kontrollgruppe, dar. Diese fallen bei dem mehrdimensionalen Endpunkt „Informierte Entscheidung“ besonders ins Gewicht [33]. In einer anderen Studie zum Decision Coaching [20] wurde die Beratung zum BRCA1-Gen-Test meist von Pflegenden angeboten. Während die Intervention die Wahrnehmung hinsichtlich der Risiken und Einschränkungen des Screenings erhöhte und hinsichtlich des Nutzens verringerte, gab es auch hier keine Veränderungen in der Absicht, am Screening teilzunehmen.
Die Messung von SDM mittels Fragebögen zeigt sich schwierig, da sich andeutet, dass die Instrumente möglicherweise nicht sensitiv auf Veränderungen reagieren [45]. Die Pilot-RCT zeigt deskriptiv hohe SDM-Werte in beiden Gruppen. SDM lässt sich somit gegenwärtig möglicherweise nur durch die Aufzeichnung des gesamten SDM-Prozesses und anschließenden Ratings angemessen bewerten [35]. Dieses komplexe Vorgehen wurde für das Decision Coaching durch Nurses erstmals in einer aktuellen Studie als primärer Endpunkt gewählt [46]. In unserem Projekt haben wir nicht den gesamten SDM-Prozess durch Videoaufnahmen erfasst. Die Arztgespräche wurden nicht aufgezeichnet. Die Analyse der Nurse Coachings anhand des Beobachtungsinventars MAPPIN‘SDM [47] zeigt jedoch, dass Nurses eine Beratung nach dem Ansatz der gemeinsamen Entscheidungsfindung zu den komplexen Immuntherapien durchführen können.

Das Follow-up der Cluster-RCT (Phase drei der MRC Kriterien) läuft noch und die qualitativen Interviews der Prozessevaluation befinden sich in Planung. Die Durchführung gelang jedoch lediglich an drei von acht Interventionsclustern. Verschiedene Barrieren, wie die Fluktuation von MS-Nurses sowie andere Prioritäten der zumeist universitären Zentren und Praxen, führten dazu, dass die geplante Fallzahl in der Studie nicht erreicht werden konnte. Es scheint sinnvoll den Arzt zukünftig noch mehr in den SDM-Prozess zu integrieren, um eine optimale Struktur für die Betroffenen zu gewährleisten. Bisher haben teilnehmende Ärzte lediglich eine Kurzinformation erhalten. Vorarbeiten haben gezeigt, dass ein kurzes Feedback nach Analyse von Videos mit Arzt-Patient-Gesprächen von Ärzten wertgeschätzt wird [75]. Die Entwicklung und Pilotierung eines Ärztemoduls ist Gegenstand eines aktuellen Antrags. Zudem ist eine Decision Coaching-Intervention (telefonisches oder Online-Coaching) zum Thema Schwangerschaft und MS geplant. Somit werden nach den MRC Kriterien zur Entwicklung und Evaluation komplexer Interventionen im DECIMS Projekt, mit neuen Modulen und möglichen Änderungen nach der der Auswertung der Cluster-RCT, zunächst wieder die Phasen eins und zwei adressiert. Darauf aufbauend sollte eine Studie zur Evaluation der Wirksamkeit der Intervention geplant werden, welche die zeitlichen Ressourcen der MS-Nurses durch eine direkte Finanzierung sicherstellt und mehr Unterstützung, zum Beispiel durch die Deutsche Multiple Sklerose Gesellschaft, erhält.

Grundsätzlich reicht es aber nicht nur auf der Mikroebene, den MS-Zentren, die Weichen für die Implementierung des Decision Coaching-Konzepts zu stellen. Dieses muss auch auf der Meso- (z.B. Änderung der Curricula) und Makroebene (z.B. Vergütung, Zertifizierung) erfolgen. So sollte es eine grundsätzlich evidenzbasierte Ausbildung der Gesundheitsfachberufe geben [48], um die Implementierung von und Forderung nach evidenzbasierten Interventionen in der Praxis als eine Selbstverständlichkeit zu fördern. Während insbesondere die Akademisierung von Pflegenden langsam voranschreitet, sind deren Rollen in der Versorgung noch weitgehend unbestimmt [48]. „Advanced Nursing Practice“ [49] wäre in der Neurologie mit verschiedenen Spezialisierungen der Pflegenden (z.B. MS, M. Parkinson, Schlaganfall und Kopfschmerz) sicher vielversprechend, um die Weiterentwicklung des Decision Coaching-Konzepts zu fördern. Hierfür müsste der mögliche Nutzen aber zunächst durch RCTs belegt werden. Anschließend müsste zumindest der Delegation der Beratung zu Therapieentscheidungen als Vorbereitung auf ein Arztgespräch beispielsweise im Rahmen eines Modellprojekts zugestimmt werden. Die Schwierigkeiten zeigt die aktuelle Entwicklung zum „Physician Assistant“ auf. Das Studium richtet sich zur Weiterbildung an Gesundheitsfachberufe mit einer dreijährigen Ausbildung. Allerdings gehören auch hier, unter anderem, die Beratung des Patienten sowie die Entscheidung über die Therapie weiterhin nicht zu den delegierbaren Tätigkeiten [50]. Dies steht im Kontrast zu den international längst etablierten Versorgungsstrukturen mit erweiterten Rollen für Pflegefachpersonen. Der Deutsche Berufsverband für Pflegeberufe kritisiert die erneute Ablehnung der Substitution ärztlicher Leistungen und Aufgaben durch nichtärztliche Gesundheitsberufe scharf. Generell lehnt der Verband den „Physician Assistant“ als Arztentlastungsmodell ab und weist auf „Advanced Nursing Practice“ für speziell qualifizierte Pflegefachpersonen hin [51]. So ist das Decision Coaching-Konzept ein aussichtsreicher Ansatz, um die Entwicklung neuer Rollen für die Gesundheitsberufe voranzutreiben, da hier bei teilweise reduzierter Facharztdichte [52] und zunehmender Komplexität der Entscheidungen [33] neue Konzepte gefragt sind, um die informierte Beteiligung von Patienten zu realisieren.

Zusammenfassend zeigt das Konzept der intensiven, hochindividuellen sowie zeitlich adäquaten Entscheidungsbegleitung durch MS-Nurses das Potential, die Beteiligung der Betroffenen an Immuntherapieentscheidungen zu erhöhen. Somit könnte hier eine Versorgungslücke geschlossen werden, wobei dafür noch einige Hürden zu überwinden sind. Weitere Forschung sollte den Wert des Entscheidungscoachings für Akteure im Gesundheitswesen, die Erfassung des SDM-Prozesses, andere Entscheidungsfelder und die Schaffung der strukturellen Voraussetzungen adressieren.

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10. Anhang

a. Auflistung der verwendeten Gefahrenstoffe nach GHS

Es wurden keine Gefahrenstoffe nach GHS verwendet.

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Anne Rahn Hamburg, 30.08.2017

b. Unterstützende Informationen

I. Suchstrategie MEDLINE (via OVID)

1.	Multiple Sclerosis.mp. or Multiple Sclerosis/
2.	Myelitis, Transverse/
3.	Encephalomyelitis, Acute Disseminated/
4.	"clinically isolated syndrome".mp.
5.	Multiple Sclerosis, Chronic Progressive/
6.	Multiple Sclerosis, Relapsing-Remitting/
7.	Demyelinating Diseases/
8.	chronic progressive multiple sclerosis.mp.
9.	progressive relapsing multiple sclerosis.mp.
10.	secondary progressive multiple sclerosis.mp.
11.	relapsing remitting multiple sclerosis.mp.
12.	primary progressive multiple sclerosis.mp.
13.	remitting-relapsing multiple sclerosis.mp.
14.	acute relapsing multiple sclerosis.mp.
15.	"devic disease".mp.
16.	demyelinating disease.mp.
17.	adem.mp.
18.	demyelinating disorder.mp.
19.	transverse myelitis.mp.
20.	acute disseminated encephalomyelitis.mp.
21.	encephalomyelitis.mp.
22.	neuromyelitis.mp.
23.	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22
24.	Magnetic Resonance Imaging/ or MRI.mp.
25.	MRT.mp.
26.	MR.mp.
27.	T2.mp.
28.	T1.mp.
29.	lesion load.mp.
30.	Magnetic Resonance Imaging.mp.
31.	Magnetic Resonance Tomography.mp.
32.	24 or 25 or 26 or 27 or 28 or 29 or 30 or 31

33.	23 and 32
34.	prognosis.sh.
35.	diagnosed.tw.
36.	cohort:.mp.
37.	predictor:.tw.
38.	death.tw.
39.	exp models, statistical/
40.	34 or 35 or 36 or 37 or 38 or 39
41.	33 and 40
42.	limit 41 to yr="1991 -Current"

II. Baseline reported magnetic resonance imaging acquisition and processing information in clinically isolated syndrome cohorts

Study	T2 lesion sequence	T2/pd	T1	Tesla	Raters blinded to clinical details	Number of raters	Gadolinium dosage	Reported Information per study[1]
ONTT 1997	n.r.	n.r.	n.r.	n.r.	n.r.	n.r.	n.r.	0
ONTT 2004	T2	5 mm Axial: 2.5 mm	n.r.	1.5	n.r.	n.r.	n.r.	3
ONTT 2008	n.r.	5mm (2.5 mm gap)	n.r.	1.5 primarily	n.r.	n.r.	n.r.	2
Tintore 2006	T2, pd	n.r.	n.r.	1 or 1.5	yes	2 (not sure if independently)	n.r.	4
Tintore 2010	T2, pd	5 mm (1.5 gap)	5 mm (1.5 gap), T1 spin echo	1 and 1.5	yes	2 (not sure if independently)	0.1mmol/kg	5
Tintore 2015	T2, pd, flair	3-5 mm	3-5 mm	1.5 or 3.0	n.r.	n.r.	0.1–2.0mmol/kg	3
Morrissey 1993	n.r.	5 mm, 10 mm (some scans 1984/85)	uncertain	0.5	yes	2	n.r.	4
Filippi 1994	n.r.	10 mm (20 scans), 5mm	n.r.	0.5	n.r.	1	n.r.	3
O'Riordan 1998	n.r.	5 mm, 10 mm (some scans 1984/85)	uncertain	0.5	yes	2 (not sure if independently)	n.r.	4
Sailer 1999	T2	5 mm half BL or 10 (23 BL)	n.r.	0.5	n.r.	1	n.r.	4
Brex. 2002	T2	10 mm: 38 scans, 5 mm: 33 scans	n.r.	0.5	n.r.	n.r.	n.r.	3
Fisniku 2008	T2	10 mm (early), 5 mm	n.r.	0.5	yes	1	n.r.	5
Swanton 2009	T2	3 mm	3 mm, partly 5 mm	1.5	n.r.	1	n.r.	4
Reported (%)[1]	**8 (62)**	**11 (85)**	**[1]Excluded**	**12 (92)**	**5 (39)**	**8 (62)**	**[1]Excluded**	

[1]The items "T1" and "Gadolinium dosage" were excluded from the analysis, n.r. = not reported. pd = proton density. BL=Baseline

c. Formalia

Curriculum vitae

Anne Christin Rahn (*1981), MSc Health Sciences

a) Wissenschaftlicher und beruflicher Werdegang

Seit 2016	Wissenschaftliche Mitarbeiterin am Institut für Neuroimmunologie und Multiple Sklerose, Hamburg
2016	Abschlussstipendium der Universität Hamburg, Hamburg
2013 - 2015	Wissenschaftliche Mitarbeiterin in den Gesundheitswissenschaften, Universität Hamburg und am Institut für Neuroimmunologie und Multiple Sklerose, Hamburg
2010 - 2011	Studium der Gesundheitswissenschaften, University of York, York (MSc Health Sciences)
2007 - 2012	Studium: Lehramt Oberstufe - Berufliche Schulen, Gesundheit (Fachrichtung), Geschichte (Unterrichtsfach), Universität Hamburg, Hamburg (1.Staatsexamen)
2005 - 2006	Anstellung als Gesundheits- und Krankenpflegerin am Universitätsklinikum Schleswig-Holstein, Campus Kiel, Klinik für Allgemeine Innere Medizin, Kiel
2004 - 2005	Beschäftigung als Gesundheits- und Krankenpflegerin beim Mobilen Pflegeservice Kiel, Kiel
2001 - 2004	Ausbildung zur Gesundheits- und Krankenpflegerin, DRK-Anschar-Schwesternschaft e.V., Kiel

b) Lehrtätigkeiten

Seit 2016	MSH Medical School Hamburg (Einführung Forschungsmethoden)
2013 – 2015	Gesundheitswissenschaften, Universität Hamburg (Systematische Literaturrecherche, Projektseminar, Pflegetheorien, Pflegeforschung)

c) Stipendien, Auszeichnungen und Mitgliedschaften in wissenschaftlichen Gesellschaften

	Netzwerk Evidenzbasierte Medizin (DNEbM)
	The European Academy of Nursing Science (EANS)
	European network for best practice and research in multiple sclerosis rehabilitation (RIMS)
	Deutsche Gesellschaft für Pflegewissenschaft e.V. (DGP)
2017	„UKE Auszeichnung 2016 zur Patientenorientierung und Patientensicherheit“ für das Projekt „Nurse geleitetes Immuntherapie-Entscheidungscoaching für Menschen mit Multipler Sklerose“ (Teamauszeichnung)
2016	Abschlussförderung (Gleichstellungsfond der Universität Hamburg)
2013 - 2015	Doctoral student (summer school), the European Academy of Nursing Science (EANS)

Publikationen und Vorträge

Publikationen

Veröffentlichungen in begutachteten Fachzeitschriften

Rahn AC, Köpke S, Backhus I, Kasper J, Anger K, Untiedt B, Alegiani, A, Kleiter I, Mühlhauser I, Heesen C (2017) Nurse-led immunotreatment DEcision Coaching In people with Multiple Sclerosis (DECIMS) − feasibility testing, pilot randomised controlled trial and mixed methods process evaluation. *International Journal of Nursing Studies*. doi:10.1016/j.ijnurstu.2017.08.01.

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Rahn AC, Backhus I, Fuest F, Riemann-Lorenz K, Köpke S, van de Roemer A, Mühlhauser I, Heesen C (2016) Comprehension of confidence intervals - development and piloting of patient information materials for people with multiple sclerosis: qualitative study and pilot randomised controlled trial. *BMC Medical Informatics and Decision Making*, 16(1): 122.

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Buhse S, **Rahn AC**, Bock M, Mühlhauser I (2017) Causal interpretation of correlational studies - analysis of medical news on the website of the official journal for German physicians. (In Revision, *PLoS One)*

Alegiani AC, Köpke S, **Rahn AC**, Steckelberg A, Joice S, Hedegaard U, Thomalla G, Heesen C (2017) Quality of stroke patient information applied in randomized controlled trials. (Unter Begutachtung, *Patient Education and Counseling*)

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Beiträge in Fachzeitschriften ohne Begutachtungsverfahren

Kasper J, Eiring Ø, **Rahn AC**, Heesen C, Kienlin S (2016) Samvalgsveiledning gitt av sykepleiere for å involvere pasienter med multippel sklerose i beslutninger om immunterapi. Om BestPractice, November 18.

Buchbeiträge

Heesen C, **Rahn A,** Schiffmann I (201): Arzt-Patienten Beziehung in der Neurologie. In: U. K. Zettl und J. P. Sieb (Hg.): Diagnostik und Therapie neurologischer Erkrankungen – State of the Art. Publikation in Vorbereitung. 1. Aufl. München: Elsevier. (Im Druck)

Wissenschaftliche Vorträge und Posterpräsentationen

Vorträge

Untiedt B, Pust GE (presenter), Liethmann K, Rholoff T, Köpke S, **Rahn A**, Heesen C (2017) Adherence in multiple sclerosis: A qualitative study comparing firstline and secondline immunotherapies. 22nd Annual RIMS Conference – Shaping the Future if MS Rehabilitation, 04-06.05.2017, Barcelona. *Multiple Sclerosis Journal*, 23(6): 878–916.

Köpke S, Meyer G, **Rahn A**, Steckelberg A, Möhler R (2017) Implementierung von innovativen Rollen für Pflegende im evidenzbasierten interprofessionellen

Gesundheitssystem der Zukunft: Barrieren und Chancen. 18. Jahrestagung des Deutschen Netzwerks Evidenzbasierte Medizin; Klasse statt Masse - wider die wertlose Wissenschaft; Deutsches Netzwerk Evidenzbasierte Medizin e.V., 09.-11.03.2017, Hamburg. *German Medical Science GMS Publishing House,* DOC17ebmS1 /20170223/.

Rahn AC, Buhl A, Köpke S (2017) Umsetzung der Leitlinie zur Vermeidung freiheitseinschränkender Maßnahmen in den Diensten und Einrichtungen der AWO Pflege Schleswig-Holstein. 18. Jahrestagung des Deutschen Netzwerks Evidenzbasierte Medizin; Klasse statt Masse - wider die wertlose Wissenschaft; Deutsches Netzwerk Evidenzbasierte Medizin e.V., 09.-11.03.2017, Hamburg. *German Medical Science GMS Publishing House,* DOC17ebmV52 /20170223/.

Buhse S, **Rahn AC**, Bock M, Mühlhauser I (2107) "Einsamkeit ist schlecht für Herz und Kreislauf" - Kausale Interpretation von Assoziationsstudien in Medizin-News des Deutschen Ärzteblatts. 18. Jahrestagung des Deutschen Netzwerks Evidenzbasierte Medizin; Klasse statt Masse - wider die wertlose Wissenschaft; Deutsches Netzwerk Evidenzbasierte Medizin e.V., 09.-11.03.2017, Hamburg. *German Medical Science GMS Publishing House,* DOC17ebmV16 /20170223/.

Rahn AC, Behncke A, Buhl A, Köpke S (2017) Implementation of a guideline-based programme on physical restraint reduction in home care and nursing homes in northern Germany – multi-centre before-after study. European Academy of Nursing Science and the Swedish Society of Nursing Summer Conference 04.-05.07.2017, Malmö. *BMC Nursing*, 16(Suppl 1): S5.

Rahn A, Köpke S, Backhus I, Kasper J, Krützelmann A, Kleiter I, Mühlhauser I, Heesen C (2016) DEcision Coaching In Multiple Sclerosis (DECIMS) – pilot randomised controlled trial and process evaluation. EANS Summer Conference 13.-14.07.2016, Halle. *BMC Nursing,* 15(Suppl 1): 67.

Krützelmann AC, Köpke S, **Rahn A**, Thomalla G, Heesen C (2016) Erfüllen Informationsmaterialien für Schlaganfallpatienten Kriterien evidenzbasierter Patienteninformation? 17. Jahrestagung des Deutschen Netzwerks Evidenzbasierte Medizin; Gemeinsam informiert entscheiden; Deutsches Netzwerk Evidenzbasierte Medizin e.V., 03.-05.03.2016, Köln. *German Medical Science GMS Publishing House*, DOC16ebmC1b /20160223/.

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Brand J, Köpke S, Kasper J, **Rahn AC**, Backhus I, Pöttgen J, Stellmann J-P, Siemonsen S (2014) Magnetic resonance imaging in MS - patients experiences, information interests and responses to an education programme. 19th Annual RIMS Conference - Supporting behaviour change: linking science to clinical practice, 06.-07.06.2014, Brighton. *Multiple Sclerosis Journal*, 20(7): 967–975.

Poster

Rahn AC, Buhl A, Behncke A, Köpke S (2017) Physical restraint reduction in long-term care: implementation of a guideline-based program. 21st International Association of Gerontology and Geriatrics (IAGG) World Congress. 23.-27.07.2017, San Francisco, *Innovation in Aging*, 1(Issue suppl_1, 1): 1–1452.

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Engels K, Schiffmann I, Duit T, Anger K, **Rahn A,** Backhus A, Lukas C, Chard D, Heesen C (2017) Understanding MRI imaging in MS (UMIMS) – development of a web–based education tool. 22nd Annual RIMS Conference – Shaping the Future if MS Rehabilitation, 04-06.05.2017, Barcelona. *Multiple Sclerosis Journal*, 23(6): 878–916.

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Riemann-Lorenz K, Eilers M, Schulz K.-H, von Geldern G, **Rahn A,** Köpke S, Heesen C (2016) Multiple sclerosis and diet: systematic review, internetbased survey and pilot-testing of an evidence based patient education programme. 32nd Congress of the European Committee for Treatment and Research in Multiple Sclerosis 14.-17.09.2016, London. *Multiple Sclerosis Journal*, 22(S3): 88–399.

Aschenbrenner A, **Rahn A**, Köpke S (2016) Einstellung und Belastung von Pflegenden zu freiheitseinschränkenden Maßnahmen in der ambulanten und stationären Altenpflege - Querschnittliche Befragung. 17. Jahrestagung des Deutschen Netzwerks Evidenzbasierte Medizin; Gemeinsam informiert entscheiden; Deutsches Netzwerk Evidenzbasierte Medizin e.V., 03.-05.03. 2016, Köln. *German Medical Science GMS Publishing House,* DOC16ebmP26 /20160223/.

Rahn AC, Riemann-Lorenz K, Backhus I, Köpke S, Fuest F, van de Roemer A, Heesen C Comprehension of confidence intervals through audio-visual patient information materials for people with multiple sclerosis (COCO-MS): a web-based randomised controlled trial (DRKS-ID: DRKS00008561). 17. Jahrestagung des Deutschen Netzwerks Evidenzbasierte Medizin; Gemeinsam informiert entscheiden; Deutsches Netzwerk Evidenzbasierte Medizin e.V., 03.-05.03. 2016, Köln. *German Medical Science GMS Publishing House,* DOC16ebmP10 /20160223/.

Rahn AC, Riemann-Lorenz K, Backhus I, Köpke S, Fuest F, van de Roemer A, Mühlhauser I, Heesen C (2015) Comprehension of confidence intervals in audiovisual patient information materials for people with multiple sclerosis (COCO-MS): a web-based randomised controlled trial. 31st Congress of the European Committee for Treatment and Research in Multiple Sclerosis 07.-10.10.2015, Barcelona. *Multiple Sclerosis Journal* 2015; 21(S11): 76–653.

Rahn A, Fuest F, Köpke S, Backhus I, van de Roemer A, Mühlhauser I, Heesen C (2015) Comprehension of confidence intervals in patient information materials: development and evaluation of patient information for people with multiple sclerosis. 20th Annual RIMS Conference - Translational Research and Patient-Centered Outcomes, 09.-11.04.2015, Milan. *Multiple Sclerosis Journal* 2015; 21(4): 492–534.

Rahn AC, Köpke S, Kasper J, Backhus I, Mühlhauser I, Heesen C (2014) Nurse-led immunotherapy DEcision Coaching In Multiple Sclerosis (DECIMS) - design and feasibility study for a clusterrandomised controlled trial. 19th Annual RIMS Conference - Supporting behaviour change: linking science to clinical practice, 06.-07.06.2014, Brighton. *Multiple Sclerosis Journal* 2014; 20(7): 976–1010.

Brand J, Köpke S, Kasper J, **Rahn AC**, Stellmann JP, Siemonsen S, Heesen C Magnetresonanztomographie (MRT) bei Multipler Sklerose (MS): Erfahrungen und Präferenzen von Patienten sowie Evaluation eines Schulungsprogramms. 15. Jahrestagung des Deutschen Netzwerks Evidenzbasierte Medizin; Prävention zwischen Evidenz und Eminenz; Deutsches Netzwerk Evidenzbasierte Medizin e.V., 13.-15.03. 2014, Halle. *German Medical Science GMS Publishing House*, DOC14ebmP11c /20140310/. (Gewinner des ersten Posterpreises dotiert mit 500€)

Rahn AC, Köpke S, Kasper J, Backhus I, Mühlhauser I, Heesen C Nurse geleitetes Immuntherapie-Entscheidungscoaching für Menschen mit Multipler Sklerose (DECIMS) - Vorstellung einer cluster-randomisiert-kontrollierten Studie (cRCT). 15. Jahrestagung des Deutschen Netzwerks Evidenzbasierte Medizin; Prävention zwischen Evidenz und Eminenz; Deutsches Netzwerk Evidenzbasierte Medizin e.V., 13.-15.03. 2014, Halle. *German Medical Science GMS Publishing House*, DOC14ebmP4c /20140310/.

Wissenschaftliche Gutachtertätigkeiten

- Journal of European Academy of Dermatology Venerology (2017)
- Oxford University Press: book proposal review (2016)
- Journal of Geriatric Medicine and Gerontology (2016)
- PloS One (2015)

Lehrtätigkeiten

Universität Hamburg

- Sommersemester 2014 bis Sommersemester 2015: Projektseminar I - III
- Sommersemester 2014: Grundlagen der Pflegewissenschaft
- Wintersemester 2013/2014 und Wintersemester 2014/2015: Literaturrecherche
- Wintersemester 2013/2014 und Wintersemester 2014/2015: Ausgewählte Themen der Pflegewissenschaften

MSH Medical School Hamburg

Seit 2016: Einführung Forschungsmethoden

Versicherung und Erklärung des eigenständig geleisteten Anteils an den zur Dissertation eingereichten Publikationen

Rahn AC, Köpke S, Kasper J, Vettorazzi E, Mühlhauser I, Heesen C (2015) Evaluator-blinded trial evaluating nurse-led immunotherapy DEcision Coaching In persons with relapsing-remitting Multiple Sclerosis (DECIMS) and accompanying process evaluation: study protocol for a cluster randomised controlled trial. *Trials,* 16, 106.

Bei dieser Arbeit handelt es sich um das Studienprotokoll zur Evaluation der Begleitung von Entscheidungen zur Immuntherapie von Personen mit Multipler Sklerose durch MS-Nurses (Decision-Coaches). Vorwiegend geht es in dem Protokoll um die Planung der Evaluation durch eine cluster-randomisierte kontrollierte Studie mit begleitender Prozessevaluation. Weiter wird auch die Machbarkeitstestung durch eine randomisiert kontrollierte Pilotstudie adressiert. Das Decision-Coaching Programm besteht aus einer Schulung von MS-Nurses zum Decision-Coach und der Intervention. Die Intervention fußt auf dem Prinzip der gemeinsamen Entscheidungsfindung (shared decision making) und setzt sich aus mehreren Komponenten zusammen: bis zu drei Decision-Coaching Sessions pro Multiple Sklerose-Betroffenem durch eine trainierte MS-Nurse, einer evidenzbasierten online Informationsplattform zum Thema Multipler Sklerose, einem begleitenden Arbeitsbuch und einem abschließenden Arztgespräch. Das Programm stellt den Kern dieser Dissertation dar. Die Studie wurde vom Bundesministerium für Bildung und Forschung im Rahmen einer Förderung des Kompetenznetzes Multiple Sklerose gefördert. Herr. Prof. Dr. med. Christoph Heesen hat das Projekt geleitet. Zudem fand eine Supervision durch Frau Prof. Dr. med. Ingrid Mühlhauser und eine enge Betreuung durch Herrn Prof. Dr. phil. Sascha Köpke statt. Die Studienidee stammt von Christoph Heesen und Sascha Köpke. Anne Rahn hat unter Betreuung die detaillierte Studienplanung übernommen und das Studienprotokoll eigenständig nach der SPIRIT-Checkliste (Standard Protocol Items: Recommendations for Interventional Trials) zur Erstellung von Studienprotokollen erstellt. Zudem hat Anne Rahn unter der maßgeblichen Betreuung von Sascha Köpke die begleitende Prozessevaluation entwickelt und das Vorgehen ebenfalls in der Publikation niedergelegt. Zu der detaillierten Entwicklung der Prozessevaluation haben weiter Christoph Heesen, Ingrid Mühlhauser und Prof. Dr. phil. Jürgen Kasper beigetragen. Anne Rahn, Sascha Köpke, Christoph Heesen und Jürgen Kasper haben den Trainingskurs zum Decision Coach entwickelt. Anne Rahn hat zudem die randomisiert kontrollierte Pilotstudie unter der Betreuung von Ingrid Mühlhauser und Christoph Heesen geplant und das Vorgehen im Studienprotokoll beschrieben. Eik Vettorazzi hat als Biometriker maßgeblich die Planung der statistischen Analyse der cluster-

randomisiert kontrollierten Studie übernommen. Das Manuskript wurde von Anne Rahn eigenständig verfasst. Alle Autoren haben das Manuskript gelesen, ggf. kritisch kommentiert und der Einreichung zugestimmt.

Rahn AC, Backhus I, Fuest F, Riemann-Lorenz K, Köpke S, van de Roemer A, Mühlhauser I, Heesen C (2016) Comprehension of confidence intervals - development and piloting of patient information materials for people with multiple sclerosis: qualitative study and pilot randomised controlled trial. BMC Medical Informatics and Decision Making. 16, 122.

Hierbei handelt es sich um die Publikation zur Entwicklung und Pilotierung von Patienteninformationen in Form von Power Point Präsentationen für Multipler Sklerose-Betroffene zum Thema Konfidenzintervalle (Vertrauensbereiche). Das Verständnis von statistischen Informationen nimmt eine Schlüsselfunktion in der Beratung zu Therapieoptionen ein. Deshalb haben wir begonnen kurze Informationsmaterialien zu den wichtigsten statistischen Begriffen zu erstellen. Diese Power Point Präsentationen wurden in einem nächsten Schritt zu audiovisuellen Informationen in Form von Videos weiterentwickelt und erfolgreich mittels einer randomisiert kontrollierten Studie (Rahn et al, Publikation in Vorbereitung) evaluiert. Diese Videos können inzwischen über das oben genannte DECIMS-Wiki abgerufen werden. Das DECIMS-Wiki wird während des Coachings und darüber hinaus von den Multiple Sklerose-Betroffenen und den Decision-Coaches genutzt. Somit stellen diese Informationsmaterialien eine wichtige Wissensquelle für die Decision-Coaches und Multiple Sklerose-Betroffenen dar.
Die Planung und Durchführung der Studie fand maßgeblich durch Christoph Heesen und Anne Rahn statt. Franz Fuest hat im Rahmen einer Masterarbeit an der Uni Hamburg (Fuest (2014) Comprehension of confidence intervals: development and piloting of a patient information. Universität Hamburg. Masterarbeit) die Patienteninformationen entwickelt und pilotiert. Die Betreuung der Masterarbeit erfolgte durch Anne Rahn und Christoph Heesen. Anne Rahn hat alle Entwicklungsschritte mit geplant und begleitet (Erstellung eines Studienprotokolls, systematische Literaturrecherche, Entwicklung der Patienteninformationen, Testung der Machbarkeit und Pilotierung, Entwicklung eines Fragebogens zum Verständnis von Konfidenzintervallen, Planung der Auswertung). Anschließend wurde eine randomisierte kontrollierte Pilotstudie durchgeführt in welcher auch die Validität des entwickelten Fragebogens getestet wurde. Anne Rahn und Christoph Heesen haben die Studie hauptverantwortlich geplant. Die Durchführung erfolgte durch die Study Nurse, Imke Backhus, unter der maßgeblichen Anleitung und Betreuung von Anne Rahn und unter der Supervision von Christoph Heesen. Ingrid Mühlhauser und Sascha

Köpke haben die Studie ebenfalls begleitet. Die Auswertung hat Imke Backhus unter Anleitung und Betreuung von Anne Rahn und Christoph Heesen durchgeführt. Anne Rahn hatte die Verantwortung für die Qualitätskontrolle (z.B. Daten, Dokumentation). Das Manuskript zur Publikation wurde von Anne Rahn auf Basis der Daten eigenständig verfasst. Hierfür hat Anne Rahn auch alle Transkripte zu den Interviews gelesen und die qualitative Analyse der Interviews von Franz Fuest weitergeführt. Alle Autoren haben das Manuskript gelesen, ggf. kritisch kommentiert und der Einreichung zugestimmt.

Rahn AC, Köpke S, Backhus I, Kasper J, Anger K, Untiedt B, Alegiani A, Kleiter I, Mühlhauser I, Heesen C (2017) Nurse-led immunotreatment DEcision Coaching In people with Multiple Sclerosis (DECIMS) – feasibility testing, pilot randomised controlled trial and mixed methods process evaluation. International Journal of Nursing Studies. (zur Publikation angenommen)

In dieser Publikation werden die Ergebnisse der randomisierten kontrollierten Pilotstudie mit begleitender Prozessevaluation dargestellt.
Anne Rahn hat die Studie unter der Leitung von Christoph Heesen durchgeführt. Zudem haben Ingrid Mühlhauser und Sascha Köpke den Forschungsprozess betreut. Christoph Heesen, Sascha Köpke, Jürgen Kasper, Imke Backhus und Anne Rahn haben den Decision Coaching Training Kurs durchgeführt. Das Monitoring haben Imke Backhus und Katrin Anger als Study Nurses unter der Betreuung von Anne Rahn durchgeführt. Anne Rahn hat die Decision Coaches nach der Schulung während der Studie betreut. Anne Rahn und Imke Backhus haben die deskriptive quantitative Analyse geplant, eine Beratung durch einen Biometriker erhalten (Eik Vettorazzi) und Imke Backhus führte die Analyse unter der Betreuung von Anne Rahn durch. Anne Rahn hatte die Verantwortung für die Qualitätskontrolle (z.B. Daten, Dokumentation). Anne Rahn und Katrin Anger haben die qualitativen Analysen durchgeführt, die maßgeblich von Anne Rahn geplant wurden. Die zusammenfassende qualitative Analyse hat Anne Rahn durchgeführt. Benthe Untiedt und Jan Keppler führten die Analysen der Coachingvideos durch. Das Manuskript zur Publikation wurde von Anne Rahn auf Basis der Daten eigenständig verfasst. Alle Autoren haben das Manuskript gelesen, ggf. kritisch kommentiert und der Einreichung zugestimmt.

„Hiermit versichere ich an Eides statt, die vorliegende Dissertation selbst verfasst und keine anderen als die angegebenen Hilfsmittel benutzt zu haben. Die eingereichte schriftliche Fassung entspricht der auf dem elektronischen Speichermedium. Ich versichere, dass diese Dissertation nicht in einem früheren Promotionsverfahren eingereicht wurde.“

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Anne Rahn Hamburg, 30.08.2017