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Understanding magnetic resonance imaging in multiple sclerosis (UMIMS) and accompanying process evaluation: study protocol for a double-blind, randomized controlled trial using an evidence-based patient information website

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Study protocol

Keywords: Multiple sclerosis, evidence-based patient information, magnetic resonance imaging, risk-knowledge, disease-specific knowledge, autonomy preferences, shared decision making, randomized controlled trial, process evaluation

Posted Date: February 21st, 2020

DOI: https://doi.org/10.21203/rs.2.24184/v1

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Version of Record: A version of this preprint was published on December 9th, 2020. See the published version at https://doi.org/10.1186/s13063-020-04855-5.

Understanding magnetic resonance imaging in multiple sclerosis (UMIMS) and accompanying process evaluation: study protocol for a double-blind, randomized controlled trial using an evidence-based patient information website

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Abstract:

Background: While Magnetic Resonance Imaging (MRI) plays a major role in the lives of people with multiple sclerosis (pwMS), studies have shown that MRI-specific knowledge in pwMS is limited. Moreover, poor knowledge was associated with negative feelings towards MRI (e.g. anxiety concerning MRI scan). Because information sources about MRI in MS for pwMS are not available, we designed and evaluated an evidence-based online educational platform about MRI in MS called "Understanding MRI in MS" (UMIMS). Based on a pilot study in 104 subjects, an educational intervention was found to be feasible and effective. We hypothesize, that MRI-specific knowledge can be increased by using UMIMS and that, subsequently, negative feelings towards MRI will be reduced and shared decision making competences increased.

Methods: This randomized, controlled, double-blinded trial will recruit n=120 pwMS. The intervention group will receive access to UMIMS. The control group will get access to a specifically developed control website, which visually imitates UMIMS, and contains the standard information available by several MS self-help organisations. The change in MRI-specific knowledge assessed via the MRI-risk knowledge questionnaire (MRI-RIKNO) after the intervention is the primary endpoint at 2 weeks. Several secondary endpoints will be assessed at different timepoints throughout the study, e.g. emotions towards MRI, autonomy preferences, threat by MS and shared decision-making competences. The study includes a process evaluation.

Discussion: The aim of this randomized, controlled, double-blind trial recruiting n=120 pwMS is to assess the effect of the evidence-based online educational tool "UMIMS" on MRI-specific knowledge. Additonally, secondary endpoints (e.g. emotions towards MRI) will be assessed and a process evaluation will be included.

Trial registration: Clinicaltrials.gov, NCT03872583, registration date: 13th March 2019

Key words: Multiple sclerosis, evidence-based patient information, magnetic resonance imaging, risk-knowledge, disease-specific knowledge, autonomy preferences, shared decision making, randomized controlled trial, process evaluation

Background:

Multiple sclerosis is a chronic demyelinating disease mainly affecting young adults. In Germany more than 200.000 people are afflicted by the disease. (1) Magnetic resonance imaging (MRI) plays a major role in the diagnosis (2) and is frequently used to predict the prognosis (3) as well as controlling treatment effectiveness during the course of the disease. (4) Especially at the beginning of the disease, pwMS may have several MRIs within 12 months. Even in the absence of clinical disease activity, annual MRI monitoring has been suggested (Magnetic Resonance Imaging in MS (MAGNIMS)-Network). (5) While the number and location of MS lesions in the MRI after the first clinical event has a limited predictive value for the progression in the following 7 or 20 years (6), lesion load during the course of the disease is virtually unrelated to clinical appearance of a patient. This discrepancy is called the „clinico-radiological paradox“. (7) There is no international consensus about handling the occurrence of new MS lesions when assessing treatment efficacy. For example, while there is evidence that the appearance of more than 3 new T2-lesions predicts treatment failure in pwMS treated with interferon, (4) other researchers follow the NEDA-concept (no evidence of disease activity) and may change treatment even after the appearance of a single new T2-lesion. (8)

Oftentimes, when MRI results are discussed in the context of initiation or change of a disease-modifying drug (DMD), there is no clear medically superior option. These so-called preference-sensitive decisions are predestined for a shared decision making (SDM) approach, in which physician and patient discuss options together. A prerequisite for SDM is a sufficient disease-specific knowledge. In pwMS, however, this knowledge has proven to be only moderate with around 60 percent of correctly answered questions in MS-specific (9, 10) and MRI-specific knowledge questionnaires (11). Apart from being a necessity for medical decision making, a high

disease-specific knowledge can also influence patients' emotions: While there are no studies investigating this interaction in MS yet, a low disease-specific knowledge was associated with greater levels of fear in patients with chronic obstructive pulmonary disease. (12) Also, patient education has been shown to decrease anxiety before medical procedures, e.g. in the perioperative setting. (13) Therefore, increasing MRI knowledge might not only lead to a better understanding of one's own disease and increase shared decision making, it may also decrease anxiety concerning MRI.
To our knowledge, evidence based and patient-friendly information on MRI in MS is currently not available, hindering patient participation. We have therefore developed an online patient education tool on MRI in MS called „Understanding MRI in MS" (UMIMS). This randomized controlled trial (RCT) aims to assess the effect of this online education tool on knowledge about and emotions towards MRI in n=120 pwMS.

Aims and objective:

We hypothesize that access to an online education tool about MRI in MS will lead to an increase in MRI-specific knowledge in pwMS. Increased knowledge will be accompanied by a decrease of fear of MRI and increased feelings of competence during the patient-physician encounter. The intervention will enhance patient empowerment and increase patients' desire for participation in MRI-related decisions. Finally it will increase SDM when considering MRI-activity based treatment changes or decisions about subsequent MRIs during clinical interactions. At large, this study is guided by the principles of evidence-based medicine (EBM) (Sackett 1996) and EBPI (Bunge et al., 2010) and the Medical Research Council (MRC) framework for developing and evaluating complex interventions (Craig et al., 2008).

Methods

Design:

The UMIMS trial will be carried out as a double-blind, superiority randomised controlled trial. Following the MRC guidelines for the development and evaluation of complex interventions (14). The questionnaires used in the RCT were developed and validated in an online-survey with n=457 pwMS. (15) The website including the outcome instruments used in the RCT were pre-tested in a feasibility study with n=120 participants recruited via the website of the German MS society. In detail, the feasability study tested if patients had technical issues accessing or using the website, asked how much time patients spent on it and if patients found the content understandable, interesting and relevant. Furthermore, the main study will be accompanied by a process evaluation. (14)

Study setting:

The study will be conducted in five German clinics specialized in MS care (2 university clinics, 1 out-patient clinic and 2 private practices) throughout Germany.

Eligibility criteria

PwMS are eligible to participate if they are older than 18 years old and have been diagnosed with a relapsing-remitting MS (RRMS) according to the McDonald criteria (2) within the previous 10 years and had an active disease course (i.e. treatment change or new T2 lesion within the previous year) or a clinically isolated syndrome (CIS) with at least one MS-typical T2 lesion.

In order to realistically assess, whether the education tool changes the attitude towards MRI, patients can only be included, if they are scheduled to receive an MRI within 2 weeks to 6 months following randomization.
Because the study will use the internet for information provision and data collection, 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. Additionally, severe cognitive deficit or major psychiatric illness affecting information uptake are reasons for exclusion.

Interventions

Intervention group

After answering the baseline questionnaires and randomization, patients in the intervention group will receive access to the newly developed, evidence-based, online education tool „Understanding MRI in MS“ (UMIMS). The tool was developed based on previous research (Brand et al., 2014) and the input of pwMS, MRI experts and expert patients. It consists of 3 sections:

1. „About MRI“ (MRI education)
2. „Learning to read“ (interactive MRI training with real MRI images)
3. Training (MRI quiz)

“About MRI“ covers topics, which emerged during the interviews with pwMS and/or were deamed relevant by the expert patients, MRI experts or the research team. Expert patients are defined as people affected by an illness, that, among other characterictis, have both personal and experimental experiences with the disease,

are knowledgeable in symptoms and treatment of it and that have active roles or even hold responsibillties in self-help organisations (e.g. as board members). (16) It includes evidence-based information on the importance of MRI for prognosis, diagnosis and treatment control in MS, the MRI procedure, contrast-enhancing agents, basic neuroanatomy, lesion knowledge and MRI sequences. Easy-to-understand figures, videos and explanations of technical terms simplify the learning process. All evidence sources are cited. In „Learning to read“ users are presented with 3 different doctor’s letters, which are translated into layman’s terms and 7 original MRI images with a step-by-step explanation for interpretation of the results. In the „Training“-section, patients can test their acquired knowledge in a quiz.

Control group

After answering the baseline questionnaires and randomization, patients in the control group will receive access to a newly created website providing standard information on MRI in the same design as the UMIMS website. The standard information consists of the content, that was freely available on the websites of several European as well as major English-speaking MS self-help organizations (Germany, France, Belgium, Netherlands, Great Britain, Canada, Australia, USA; time of access September 2018). All topics that were permanently hosted on the websites were included; single articles, which were only available via a separate search were not included. The topics are: Importance of MRI for diagnosis and treatment control in MS, MRI procedure and contract enhancing agents.

Outcomes

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

Table 1: Major endpoints

Instrument	Measurement time point				
	Enrolment	Allocation	Post-allocation		
	t_{-1}	t_0	t_1	t_2	t_3
Eligibility screen	x				
Informed consent	x				
Allocation	x				
Sociodemographic data	x	x			
PDDS		x			
MS-related data and ressource use		x			
MRI-RIKNO		x*	x		
Subjective knowledge		x	x		
MRI-EMA		x	x	x	
CPS		x	x	x	
Numeracy		x			
Threat by MS		x	x		
HADS		x	x		
Process evaluation			x	x (patient and physician)	x
MAPPIN 'SDM				x (patient and physician)	
MAPPIN'SDM audio (n=5 CG/IG)				x (external rater)	
Treatment/MRI decision				x	x

t_1= 2 weeks after allocation and access to the intervention/control website; t_2 = immediately after patient physician encounter; t_3 = 6 months after patient-physican encounter;
CPS = Control preference scale; HADS = Hospital anxiety and depression scale; MAPPIN'SDM = Multifocal Approach to Sharing in Shared Decision Making; MRI-EMA = emotions and attitude towards MRI; MRI-RIKNO = magnetic resonance imaging risk knowledge questionnaire; PDDS = patient determined disease steps, * = primary endpoint

Primary endpoint

The primary enpoint is MRI-risk knowledge measured by the MRI-risk knowledge questionnaire 2.0 (MRI-RIKNO) (11). It comprises n=14 items (maximum score of n=22) concerning basic neuroanatomy and lesion knowledge, the MRI procedure and the meaning of MRI for diagnosis, prognosis and treatment control. MRI-risk knowledge will be assessed twice during the trial: t_0 (allocation) and t_1 (after a 2-week-access to the intervention or control website). The primary endpoint is change of MRI-RIKNO score from baseline to t_1. The study is powered to detect a 10% difference in the proportion of correct answers.

Secondary endpoints

Emotions and attitude towards MRI will be assessed using the validated questionnaire “MRI emotions and attitude” (MRI-EMA) at t_0, t_1 and t_2 (15). Autonomy preference will be assessed using the Control Preference Scale (CPS) (17) (moderate internal consistency and good convergent validity (18)) before and after the (control) intervention (at t_0 and t_1) as well as after the patient-physician encounter (realized autonomy preferences) (t_2). Perceived involvement in decisional encounters concerning MRI results and their consequences will be evaluated with the Multifocal Approach to Sharing in Shared Decision Making (MAPPIN’SDM; inter-rater-reliabilities in the observer scales and internal consistencies high to excellent) evaluation (19); applying a newly developed short version. For a subgroup of n=5 participants of each group, who have specifically consented to it, the encounter will be audiotaped and the degree of SDM will be assessed via an external rater using the MAPPIN’SDM. Decisions on future MRIs and treatment changes as well as acceptance of the intervention will be assessed from patients using a standardised questionnaire immediately (t_2) and six months after the patient-physician encounter

(t_3) (for both the IG and CG). Quality of life (QoL) will be assessed using the subscales of the HAmburg QUAlity of life questionnaire in MS (HAQUAMS) (20) (internal consistency and retest coefficients high) (only subscales relevant to the study content were chosen to minimized work burden for patients: Fatigue, cognition, visual impairment, communication, mood).

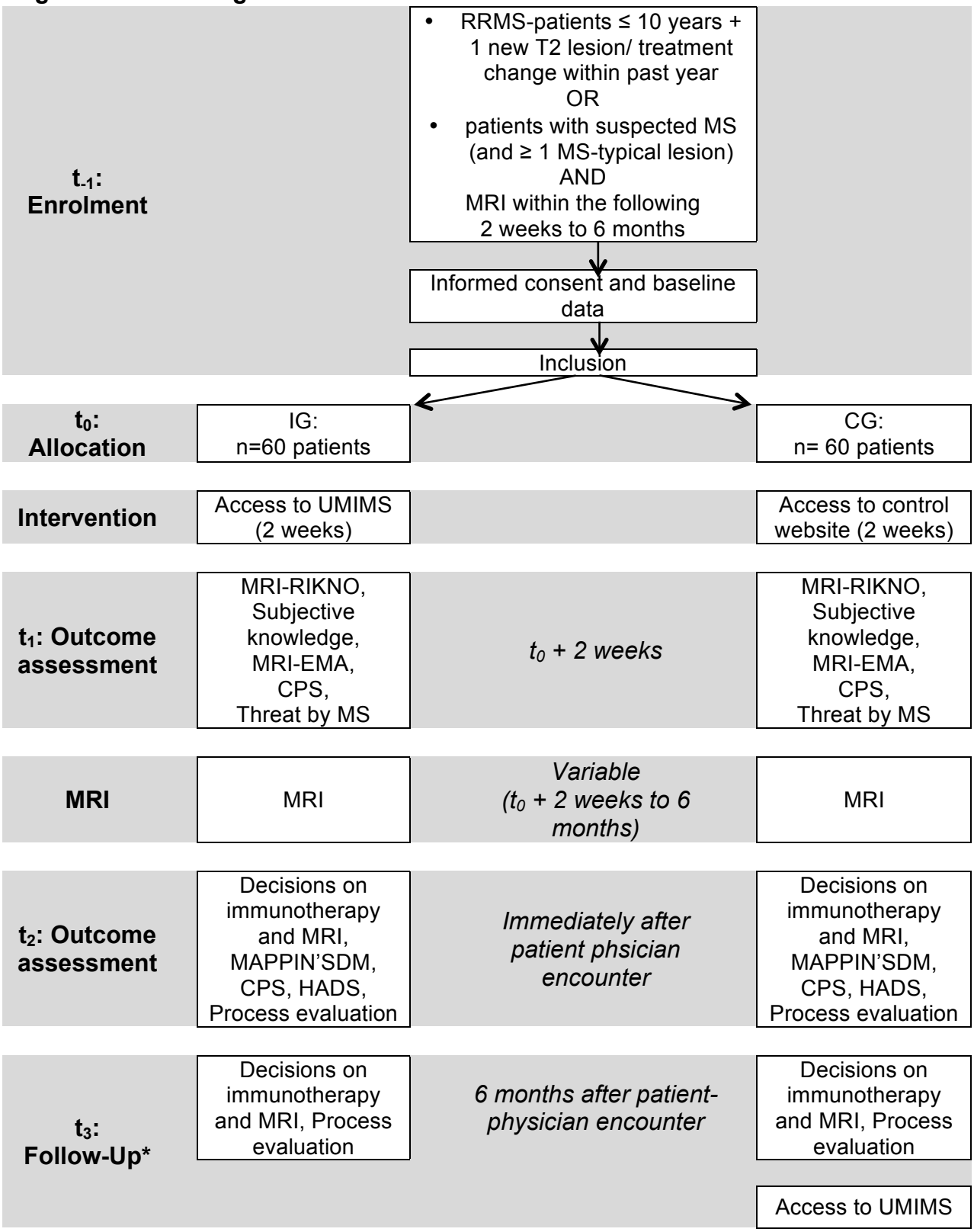
Tertiary outcomes (control and safety parameters)

Anxiety and depression using the Hospital Anxiety and Depression Scale (HADS) (21) will be assessed as a control parameter. Occurrence of relapses will be evaluated at baseline (t_0), after patient-physician encounter (t_2) and at the 6-months-follow up (t_3) (for both the IG and CG) using a standardised questionnaire.

Participant timeline

For a presentation of the flow of the UMIMS trial see Figure 1.

Figure 1: RCT-Design



* facultative

CG = control group, CPS = Control preference scale; HADS = Hospital anxiety and depression scale; IG = intervention group, MAPPIN'SDM = Multifocal Approach to Sharing in Shared Decision Making; MRI = magnetic resonance imaging; MRI-EMA= emotions and attitude towards MRI; MRI-RIKNO = magnetic resonance imaging risk knowledge questionnaire; UMIMS = Understanding MRI in MS

Baseline data

After inclusion and random allocation to either the IG or CG, all patients will answer baseline questionnaires, that assess demographic and clinical data, MRI knowledge (using the MRI-RIKNO), emotions and attitude towards MRI (using the MRI-EMA), autonomy preferences (using the CPS), numeracy and general internet use. Patients in the IG will receive an access code to the education tool UMIMS, and patients in the CG will receive a similar access code to the control website. The study nurse or other medical personal will schedule the MRI appointment and the patient-physician encounter at the end of the visit.

Post-MRI patient-physician encounter

Next, patients receive a 2-week-access to either UMIMS or the control website, at the end of this period, the primary and several secondary endpoints are assessed. The MRI then takes place in 2-week- to 6-month-window after randomization. Participants then return to the study center to discuss their MRI results. SDM concerning decisions based on MRI findings will be assessed via the MAPPIN'SDM-questionnaire (19) and the actual decisions will be noted. All participants will be asked, whether they agree to be audiotaped during the patient-physician encounter. The aim is to externally evaluate the SDM process in a subgroup of at least n=5 patients from both groups. Both, physicians and patients, will answer questions for the process evaluation.

Follow-up

Six months after the patient-physician encounter, participants will be called to assess, if the MRI-based decisions have lead to any behavioural action, i.e. new MRI, treatment change. Patients will be asked for their assumed group allocation.

Unblinding might occur, if participants suspect to be in the control group due to the limited amount of information on the control website.

Sample size

The primary endpoint of the UMIMS trial is difference of change in MRI-specific risk knowledge between baseline and t_1 between intervention and control group. The sample size calculation is based on data from prior studies comparing n=120 pwMS with and n=497 pwMS without access to the educational program (15). PwMS with access to the educational program answered 75% of thh MRI-RIKNO questionnaire correctly (16.3 out of 22 possible points, SD +/- 3.0), while participants without access answered 65% of questions correctly (14.5 of 22 possible points, SD +/- 3.0). In order to detect this difference with a power of 90% and a significance level of alpha = 0.05, n=49 patients in each group will be needed. Assuming a dropout rate of 20%, n=11 additional participants will be needed, accounting for a total of n=120 participants. In most of our previous trials on evidence-based patient information (EBPI), loss to follow-up was less than 10%. Therefore, 20% seems a realistic and conservative assumption.

Recruitment, screening, allocation and blinding

Recruitment

Consecutive patients will be recruited in 5 participating multiple sclerosis centers (2 private practices, 1 outpatient clinic, 2 university medical centres).

Screening

To minimize selection bias during the enrollment period, physicians are asked to consider every patient they see in a patient-physician encounter for the study.

Eligible patients will be invited to participate and receive information about the study. Informed consent will be obtained from patients fulfilling the inclusion criteria after they have had enough time to read the study information and ask questions; participants then receive a pseudonym. Suitable patients, who are not willing to participate in the study, will be asked for the reason.

Allocation

Permuted-block randomization will be computer generated and performed by a statistician not involved in the conduct of the study. In a previous study, analysis of covariance did not reveal an influence of sociodemographic variables on MRI knowledge, therefore no stratification will take place except for study site. Study materials, including the randomly assigned logins to the intervention or control website, will be provided by a member of the research team that is not involved in any outcome assessment or the analysis of the study.

Blinding

In the consent form, patients will be informed, that 2 different types of information will be tested. Blinding is achieved by providing a control group website featuring standard information on MRI in MS but following the same graphical format as the active intervention. Physicians and study nurses at the recruting centers as well as 2 external raters for the shared decision making during the patient-physician encounter will be blinded. An employee not involved in the analysis or any outcome assessment will provide logins as well as technical support for the participants.

Relevant concomitant care

Physician encounters

Patients are free to consult a physician and receive treatment for e.g. relapses at any point of the study. Any physician encounter will be documented.

Technical support

An employee that is not involved in the analysis of the study will answer any e-mail from participants reporting e.g. technical problems concerning the website. During this contact, content of the website (e.g. if a participant does not understand a certain figure and asks for an explanation) will not be discussed.

Criteria for discontinuation

Adverse events

The intervention website contains complex medical information, which has the potential to overwhelm participants. Additionally, it provides information on the prognostic value of MRI and participants may learn, that they fulfill negative prognostic criteria. However, our previous work has shown, that pwMS understand complex medical information and are able to cope with negative information. (22) We do not foresee any other harm of the intervention. As relevant adverse events are unlikely, a data monitoring committte does not exist, no interim analyses are planned and no stopping rules will be applied. Nevertheless, safety measures are applied as tertiary endpoints to control for anxiety and depression.

Patient withdrawal and non-adherence

At any point, patients in both groups can quit the study. Patients who withdrew from the study will be asked whether they agree to continue to fill in a limited set of

questionnaires related to the primary study outcome. The data of non-adherent participants (e.g. with missing questionnaires) will be included in the intention-to-treat analysis.

Strategies to improve adherence

If appropriate, patients will be be asked to fill in a questionnaire in the outpatient clinic directly after an encounter. When questionnaires have to be answered independently of an appointment, patients will be contacted by e-mail by a member of the coordinating centre in Hamburg and asked to complete the questionnaires within a specified time period. Patients that miss the completion will again be reminded by e-mail and telephone. If patients miss the physician appointment to discuss their MRI results, they will be contacted by the study nurse to arrange a new appointment.
To ensure the use of the education website, a study nurse will call the participants in the control and intervention group shortly after inclusion and encourage them to use the education tool. Addtionally, participants will receive biweekly e-mail reminders concerning the tool.

Data collection methods

Data will be collected at 4 time points using paper-pencil questionnaires (see Table 1). Follow-Up data will be collected by telephone using trained and blinded interviewers after six months.

Statistical methods

Continuous data will be described using means and standard deviations (SDs) and compared using Student’s t-test. Categorical data will be presented using

contingency tables and raw percentages and will be compared using Fisher's exact test.

The primary endpoint, change in MRI-RIKNO from t_0 to t_1, will be analysed using an ANCOVA model with adjustment for baseline. Secondary endpoints will be analysed accordingly dependending on the scale of measurement either by ANCOVA models for continuous endpoints or (ordinal) lofgistic regression models for dichotomous or ordinal endpoints.

It is planned to perform subgroup analysis of the 2 groups of patients included in the trial: first, those with an RRMS-diagnosis of less than 10 years and active disease and second, those with suspected MS. We will report causes for study withdrawal for each patient to clarify whether there are any differences between the intervention and control group.

All data will be analyzed on an intention-to-treat as well as per-protocol basis. In addition, sensitivity analyses will be performed to evaluate the robustness of study results and to explore different imputation techniques. Altman (23) addressed that there is no ideal method to address missing data. Therefore, different common imputation techniques (24) will be applied and reported with as well as without imputation techniques as suggested by Altman (23). Best and worst case scenario for dichotomous outcomes and multiple imputation techniques, will be conducted in the sensitivity analysis (25).

Process evaluation

This randomized controlled trial will be accompanied by a process evaluation to measure the intervention's fidelity and determine reasons for an (in)effective study outcome, following the guidelines of the Medical Research Council (14, 26). The process evaluation will be used to investigate study processes related to participants, physicians and the context and setting of the study. The framework of the process evaluation is based on a previous study including a process evaluation (27) as well as guidelines by Moore et al. (28).

In this process evaluation, quantitative elements will be used to explore expected and unexpected events arising from the intervention. The overall aim is to uncover barriers and facilitators for reaching study goals and to explore mechanisms that lead to explanations for failure or success of the intervention.

In detail, the objectives are to:

1. Explore the reaction of individuals (such as user-friendlyness of, hours spent on and feelings evoked by the website)
2. Detect barriers and facilitators for the interventions delivery (such as technical problems with the website) and for the dose received by participants (such as disease-related or internet-related problems participants may experience)
3. Find barriers and facilitators of study termination, participation and retention
4. Analyze reasons why study elements work or do not work out as planned
5. Reveal contamination of the intervention and control group (such as the use of other information materials other than those provided during the trial)
6. Identify unintended consequences of the study (such as depression and anxiety)

All questionnaires have been constructed by the research team and were tailored specially to the study. The content of this process evaluation refers to both IG and CG. There will be one separate questionnaire for the IG evaluating the different chapters of the intervention website in detail in order to collect data for the website's improvement.

Domains covered by the process evaluation

Following the MRC Framework (29), the following domains will be covered by the process evaluation:

1) Implementation: Fidelity, Dose, Reach; (as no adaptations will be made to the study throughout the trial, the domain "Adaptations" is not covered)

2) Mechanisms of impact

3) Context.

Implementation: Fidelity

Measuring to which extent the intervention is actually delivered as planned is difficult. There is still ongoing research on how to best collect data on fidelity (26). Considering that the intervention is an online resource, the quality of the intervention will remain stable, therefore mostly the received dose will vary. Fidelity could however be breached, if physicians talk about the meaning of the participant's MRI throughout the study. Whether this is the case, is assessed after the patient-physician encounter. Additionally, it is recorded if participants of the IG and CG really visited the respective website. Additionally, we will ask participants in the follow-up questionnaire (t_3) and physicians after the patient-physician-encounter (t_2) if they have been unblinded during the study.

Implementation: Dose

The dose of an intervention can be subcategorized into:

- dose *delivered*, i.e. the amount or number of intended units of each intervention or component delivered or provided by interventionists, and
- dose *received*, i.e. the extent to which participants actively engage with, interact with, are receptive to, and/or use materials or recommended resourcesm this can include “initial use” and “continued use”. The collection of data on the initial and continued use of the study materials, and information on what barriers and facilitators hinder or serve to maintain the implementation, can be used to interpret study outcomes.

In this trial, the dose *delivered* is the same for all participants, because the intervention is a website and therefore available at all times.

Concerning the dose *received*, the following aspects will be captured:

1. The use of the website (number of logins, duration of use, visited chapters)
2. Reasons for amount/lack of usage
3. Expenditure of the study.

Implementation: Reach

The reach describes the proportion of the intended audience that participates in the intervention, it can be measured by attendance and includes documentation of barriers to participation. Demographic data is collected for all participants to properly describe the study population. In participants, reasons for participation as well as early exit will be registered (t_0). PwMS who qualify for the study, but do not want to participate will be asked for the main reason why (t_{-1}).

Mechanism of impact

The domain *Mechnism of impact* covers the participants' responses to, and interactions with, the intervention, mediators as well as unanticipated consequences. Overall, it examines, how the intervention triggers change. For the evaluation, questionnaires with Likert-scales, multiple choice and open questions will be used in IG and CG.

First, the satisfaction with the educational-tool as well as relevance, importance of topics, understandability and handling of the website will be assessed. Participants of the IG will additionally answer a short questionnaire concerning the content of the intervention website. Secondly, barriers and promoting factors for the usage of the website (e.g. age, internet access and skills, amount of free time) will be assessed. Thirdly, several of the primary and secondary outcomes (e.g. change in MRI-risk knowledge (subjective and objective) and attitude towards MRI) of the trial will be analyzed to estimate, how participants interacted with the website.

To monitor unintended consequences, threat by MS, change in quality of life, depression and anxiety or patient-physician-relationship/communication will be measured.

Context

Overall, 5 different MS centres are participating study centres; 2 of them are university hospitals, one a community-based hospital and 2 private-practices. Depending on size and location, there is a variation in terms of the number of potential participants, practice hours, clinical focus of each clinic and access to an MRI. Therefore there might be a difference in e.g. the number in prescribed MRIs or length of the waiting periods for patients.

As the access to the internet may also vary in urban versus rural areas, internet availiability and skills are assessed. Further, participants might also find information on MRI in MS on other platforms e.g. websites, blogs, magazines, books (…). Participants will therefore be asked, if they searched for additional information and what they found. Questions concerning contextual factors will be in the form of multiple choice and open questions (t_0, t_1, t_2).

Data analysis (process evaluation)

Data analysis of the process evaluation will follow descriptively (see above) and SPSS (International Business Machines Corporation (IBM), Armonk, United States of America) or R (R Development Core Team) will be used. Furtrher, relevant trial outcomes will used as decribed and the process evaluation results will be inpreteted considering all study results. In case of a failed trial or inconclusive findings, it will be considered to use the quantitative data to determine questions for qualitative interviews.

Summary process evaluation

The applied framework of Moore et al. (28) facilitates systematically appraising, analysing and retrieving relevant aspects of this complex intervention. The questionnaires are designed to permit an elaborate and more precise interpretation of the study results.

Discussion

PwMS, while being constantly confronted with MRI results, possess a poor knowledge on the meaning of MRI in MS. They often do not feel competent to discuss their MRI results with their physician and receiving results may cause a relevant amount of fear (15). At the same time, pwMS consider MRI to be very important and desire for MRI education. The UMIMS trial is the first RCT to assess the effect of an MRI education in pwMS. It aims to prove that access to an education tool on MRI in MS will increase pwMS' knowledge on this complex topic, facilitate communication with their physician and enhance SDM when discussing decisions involving MRI results. If the trial proves to be effective, the website is an easily accessible tool, which can be maintained and made available nationwide at a low cost.

Trial status

The RCT is registered at clinicaltrials.gov (identifier NCT0387258). Recruitment has started in 15th March 2019 and is ongoing (estimated recruitment end 31st March 2021). Protocol version 1.1, date: 12th December 2019.

List of abbreviations

CIS: Clinically isolated syndrome

CPS: Control Preference Scale

CR: Control group

DMD: Disease-modifying drug

EBPI: Evidence-based patient information

HADS: Hospital Anxiety Depression Score

HAQUAMS: HAmburg QUAlity of life questionnaire in MS

IR: Intervention group

MAGNIMS: Magnetic Resonance Imaging in MS

MAPPIN'SDM: Multifocal Approach to Sharing in Shared Decision Making

MRC: Medical Research Council

MRI: Magnetic Resonance Imaging

MRI-EMA: MRI-emotions and attitude questionnaire

MRI-RIKNO: MRI-risk knowledge questionnaire

MS: Multiple sclerosis

NEDA: No evidence of disease activity

PDDS = patient determined disease steps

PwMS: People with multiple sclerosis

QoL: Quality of life

RCT: Randomized controlled trial

RRMS: Relapsing remitting MS

SDM: Shared Decision Making

Declarations

Ethics approval and consent to participate:

Ethical approval has been obtained from the ethical committee of Hamburg Chamber of Physicians (approval number: PV5722) as well as local committees at each centre location. Written informed consent will be obtained from all study participants.

Consent for publication

Not applicable.

Availability of data and material

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

Insa Schiffmann has received travel grants from Sanofi-Genzyme.

Magalie Freund has nothing to declare.

Eik Vettorazzi has nothing to declare.

Anne Rahn was supported by a research grant from the National MS Society, USA (grant no. G-1508-06034).

Jan-Patrick Stellmann received research funding from Deutsche Forschungsgemeinschaft and reports grants from Biogen and Genzyme.

Susanne Heyer-Borchelt has nothing to declare.

Marie D'Hooge has nothing to declare for this study.

Vivien Häußler has nothing to declare.

Christoph Heesen received speaker honoraries and grants from Biogen, Genyzme, Merck, Novartis, Roche.

Funding

The study is funded by Sanofi-Genzyme. The sponsor did not and will not have any influence on the study design, collection, management, analysis or interpretation of data, writing of the report; and the decision to submit the report for publication.

Authors' contributions

Each author is expected to have made substantial contributions to a) the conception OR b) design of the work; OR c) the acquisition, d) analysis, OR e) interpretation of data; OR f) the creation of new software used in the work; OR g) have drafted the work or h) substantively revised it.

Insa Schiffmann: A, B, C, D, E, G, H

Magalie Freund: B, C, E, G

Eik Vettorazzi: D, H

Jan-Patrick Stellmann A, B, E, H

Susanne Heyer-Borchelt B, C, H

Marie D'Hooge A, B, H

Vivien Häußler C

Anne Rahn A, B, E, H

Christoph Heesen A, B, C, D, E, G, H

Acknowledgements:

We would like to acknowledge the contributions of Katharina Engels, Dr. Jutta Scheiderbauer, Prof. Dr. Carsten Lukas and Prof. Dr. Declan Chard to the work leading to this trial.

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Figures

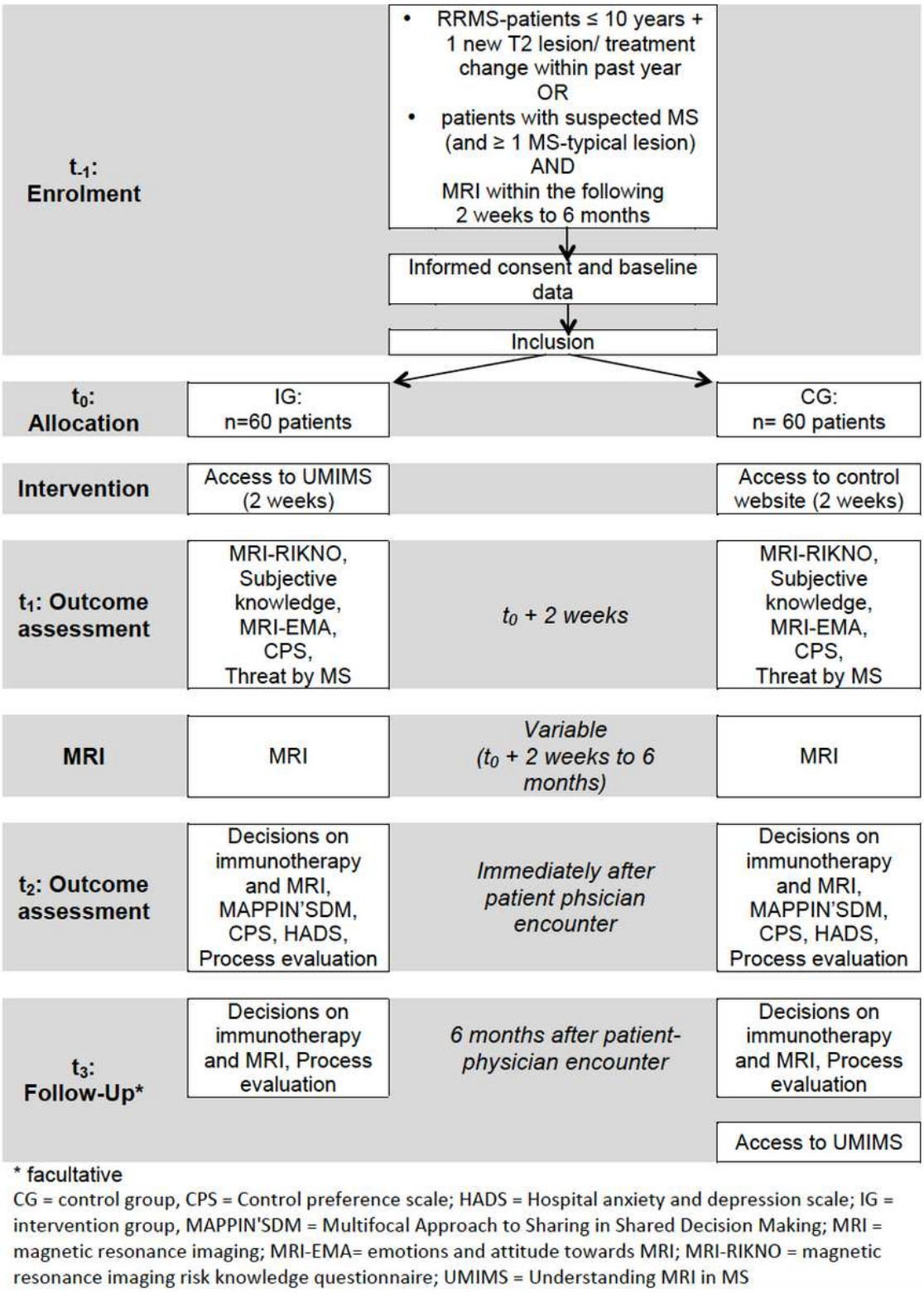

Figure 1

RCT-Design

Supplementary Files

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