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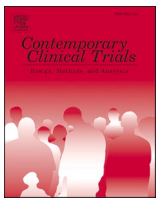

Medical Imaging Decision And Support (MIDAS): Study protocol for a multi-centre cluster randomized trial evaluating the ESR iGuide

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ABSTRACT

Objectives: Medical imaging plays an essential role in healthcare. As a diagnostic test, imaging is prone to substantial overuse and potential overdiagnosis, with dire consequences to patient outcomes and health care costs. Clinical decision support systems (CDSSs) were developed to guide referring physicians in making appropriate imaging decisions. This study will evaluate the effect of implementing a CDSS (ESR iGuide) with versus without active decision support in a physician order entry on the appropriate use of imaging tests and ordering behaviour.

Methods: A protocol for a multi-center cluster-randomized trial with departments acting as clusters, combined with a before-after-revert design. Four university hospitals with eight participating departments each for a total of thirty-two clusters will be included in the study.

All departments start in control condition with structured data entry of the clinical indication and tracking of the imaging exams requested. Initially, the CDSS is implemented and all physicians remain blinded to appropriateness scores based on the ESR imaging referral guidelines. After randomization, half of the clusters switch to the active intervention of decision support. Physicians in the active condition are made aware of the categorization of their requests as appropriate, under certain conditions appropriate, or inappropriate, and appropriate exams are suggested. Physicians may change their requests in response to feedback. In the revert condition, active decision support is removed to study the educational effect.

Results/conclusions: The main outcome is the proportion of inappropriate diagnostic imaging exams requested per cluster. Secondary outcomes are the absolute number of imaging exams, radiation from diagnostic imaging, and medical costs.

Trial registration number: Approval from the Medical Ethics Review Committee was obtained under protocol numbers 20–069 (Augsburg), B 238/21 (Kiel), 20–318 (Lübeck) and 2020–15,125 (Mainz). The trial is registered in the ClinicalTrials.gov register under registration number *NCT05490290*

Abbreviations: ACR, American College of Radiology; CDSS, Clinical Decision Support System; CPOE, Computerized Physician Order Entry; CPT ®, Current Procedural Terminology; DSMB, Data Safety Monitoring Board; ESR, European Society of Radiology; GDPR, General Data Protection Regulation; ICC, Intracluster Correlation Coefficient; MREC, Medical Research Ethics Committee; MIDAS, Medical Imaging Decision And Support; RCT, Randomized Controlled Trial; ρ_c, Cluster autocorrelation; ρ_s, Individual autocorrelation.

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1. Introduction

Contemporary medicine relies heavily on diagnostic imaging, which guides patient management decisions on a daily basis. Early diagnosis may open the door to early treatment and has been considered a holy grail in medicine. However, long-term risks are not always weighed against the immediate short-term potential diagnostic benefit [1]. Striving for early diagnosis may also lead to practicing defensive medicine, which results in a substantial overuse of diagnostic tests, overdiagnosis [2–7], unnecessary diagnostic workup and overtreatment. Subsequent false positive and incidental findings can have dire consequences [2,8,9]. Potential patient consequences of overdiagnosis include radiation exposure, allergies to contrast agents, delayed or unnecessary treatment, and the experienced burden associated with undergoing procedures [1,8,9]. For society at large, overdiagnosis and treatment mean that scarce healthcare resources are not allocated to the people who need them the most [6,7].

Costs of diagnostic imaging represent approximately 10% of total healthcare costs [10,11]. Utilization is driven by advanced technologies; expanding indications for imaging including prevention; physician self–referral; patient demand; and defensive medicine [7,12,13]. The development of effective strategies to optimize diagnostic test ordering has become a major area of interest [14,15]. A key concept to value-based radiology, aimed to enhance the quality of care and lower imaging costs, is the appropriateness of imaging requests. [16–18] The developed Appropriate Use Criteria are statements that describe when it is appropriate to perform a medical procedure or service, where expected benefits exceed the expected risks. They serve as evidence-based criteria that assist ordering clinicians when ordering diagnostic imaging for specific clinical conditions.

Imaging is listed prominently as an overused service, with an estimated 20–50% of imaging procedures being estimated as unnecessary [13]. A survey by the European Society of Radiology (ESR) indicated that referral guidelines are insufficiently known by health professionals [19]. In many countries, actions have been undertaken to change this situation, including campaigns, financial measures and educational messages, but all with limited effects [14,20–22]. This limited effect indicates that awareness alone is insufficient to change clinician ordering behaviour.

To address these challenges, clinicians can be supported by Clinical Decision Support Systems (CDSSs) [18]. CDSSs embedded in a computerized physician order entry (CPOE) environment enable point-of-care advice and feedback on ordering behaviour. In radiology they consist of imaging referral guidelines and inform clinicians on the appropriateness of imaging exams and the associated evidence [23]. The developed software for these systems is commonly based on the Appropriate Use Criteria set by various medical societies, including the American College of Radiology (ACR) and the ESR.

Although numerous studies suggest that CDSS interventions are effective in changing practice, many studies are small, not or poorly controlled, or were retrospective audits [14,24–26]. Several quality improvement initiatives that incorporated CDSSs showed reductions in the use of advanced imaging, but such results have not been consistently replicated [27].

A systematic review on CDSSs for imaging referrals showed that in 8 out of 14 pre−/post-intervention studies the system had the intended effect [28]. Nevertheless, the high-profile Medicare Imaging Demonstration project showed only a small effect [29–31]. As the CDSS was not deemed comprehensive enough and only insufficiently addressed individual patient health problems it did not achieve buy-in from ordering physicians. The results of the first randomized controlled trial (RCT) on CDSS for imaging referrals demonstrated a small reduction in targeted imaging orders, but no statistically significant change in the total number of high-cost scans ordered [32]. Another stepped-wedge randomized study showed that CDSSs were associated with a small but statistically significant improvement in appropriateness scores, but found no change in actual imaging utilization [33].

These studies provide insight into the possible benefits of a CDSS on medical imaging referrals, but the available evidence remains limited [27]. At the same time, CDSSs are increasingly implemented, and in some cases have become mandatory [18]. The MIDAS study is designed to investigate key outcomes related to the use of a CDSS for image ordering using a controlled and randomized approach. The overall objective of this project is to promote the appropriate, meaningful, value-based, and personalized use of medical imaging. Specific objectives of the MIDAS study are to:

- Determine the trends over time of the implementation of an imaging referral CDSS in key outcomes related to the appropriate use of diagnostic imaging tests [16].
- Compare these trends between departments randomized to the implementation of the active intervention (with decision-support) and the control condition (no decision-support).

2. Materials and methods

2.1. Study design

The study will be performed as a multi-center cluster randomized trial with departments acting as clusters, combined with a before-after-revert design (Table 1, Table 2) Four hospitals with each 8 participating departments for a total of 32 clusters will be included in the study. All departments will start in the control condition. Subsequently, stratified per surgical or non-surgical specialty, two of the four departments – chosen at random – will switch to the active intervention while the other two remain in the control condition (Table 1, Table 2).

The rationale for evaluating the intervention at the department cluster level is that the intervention is implemented in the electronic health records, and thus the intervention affects all referring physicians. Since referring physicians within one department consult each other, have meetings to discuss patients and protocols, and have shared educational events, they are likely to influence each other's ordering behaviour in such a way that this would expose the control arm to the intervention. Randomization at the physician or patient level would therefore likely lead to "contamination" [34]. Possible contamination between physicians requires an aggregated level of evaluation of the CDSS rather than at the physician level. Furthermore, the CDSS can be implemented at the departmental level and the number of imaging referrals at the departmental level in a 3-month period is large enough to make meaningful inferences. Aggregating at an even higher level, namely the hospital, would require a large number of hospitals to participate and introduces bias due to differences across hospitals. Thus, the departmental level was deemed to be the optimal cluster level.

2.2. Interventions

Our study uses the CDSS *ESR iGuide*, which is based on the ACR Appropriateness Criteria. The iGuide contains over 1000 individual imaging Current Procedural Terminology (CPT ®) codes and over 15,000 individual Appropriate Use Criteria covering all medical imaging modalities.The guidelines aim to cover around 80% of requests in daily practice by reviewing clinical scenario's, indications and recommendations for the topic groups Breast, Cardiac, Gastrointestinal, Musculoskeletal, Neurologic, Paediatric, Thoracic, Urologic, Vascular and Women's imaging. As not all conditions are covered by the ESR iGuide, conditions with numerous imaging requests, namely oncological, were mapped to receive additional appropriateness scores to support workflow and tested by the medical and technological study teams and in the clinical setting prior to randomization. Additionally, conditions that were unanimously regarded as pre-defined, such as pre-interventional orders or post-operative follow-up imaging do not receive a score through the CDSS.

Table 1
Study design and data collection.

	Period			
	Month 1–3	Month 4–6	Month 7–9	Month 10–12
	Before implementation	Early implementation	Established implementation	Revert situation
Group: Active A	No decision support Baseline measurement A0	Decision support A1	Decision support A2	No decision support Educational effect A3
Group: Control C	No decision support Baseline measurement C0	No decision support Comparator for A1 C1	No decision support Comparator for A2 C2	No decision support Comparator for A3 C3

Table 2
Example of a possible cluster randomization scheme.

Department	Hospital			
	Hospital B	Hospital X	Hospital P	Hospital L
Internal Medicine	Control	Active	Control	Active
Neurology	Active	Control	Active	Control
Gastroenterology	Active	Active	Control	Control
Oncology	Control	Active	Control	Active
Neurosurgery	Control	Control	Active	Active
Trauma surgery	Active	Control	Control	Active
Urology	Control	Active	Active	Control
Gynaecology	Active	Control	Active	Control

The before-implementation situation will consist of computerized order entry with structured data entry of the clinical indication and tracking of the imaging exams requested. That is, the CDSS is implemented in the background whilst requested exams and their indications are tracked, but no decision support is provided. Physicians are blinded to the appropriateness scores. Their ordering behaviour is documented, and their imaging requests are categorized as appropriate (green), under certain conditions appropriate (orange), and inappropriate (red) without feedback to them. The departments randomized to the control condition will continue to use the system without decision support.

The during- and after-implementation situation will consist of computerized order entry with structured data entry of the clinical indication and decision support. That is, the CDSS is implemented with decision support in the active intervention group. Physicians are made aware of the appropriateness scores and appropriate exams are suggested. Their imaging requests are categorized as appropriate (green), under certain conditions appropriate (orange), and inappropriate (red), and feedback is provided. The rankings display the suggested exams and their appropriateness. The physician can follow an additional link for more information on the relevant evidence and guideline. Physicians can change their requests in response to feedback. Ordering behaviour and changes in requested exams are documented. In the revert condition, decision support is removed to study the sustainable educational effect. This effect would be demonstrated by a retained reduction in inappropriate exam requests after decision support is removed.

As all ordering is done through the CPOE, physicians are aware that their ordering behaviour is being recorded. Blinding departments to which group they are randomized in this situation is neither feasible nor desirable, as the intervention consists of active decision support provided by the CDSS.

2.3. Study population

Departments in the 4 participating hospitals that could integrate the ESR iGuide system into the ordering system and submitted sufficient imaging requests over a 3-month period in accordance to the sample size calculation were eligible to participate. All diagnostic imaging procedures of all patients requested through a computerized order entry system in the eligible participating departments and that are indexed by the ESR iGuide system in participating hospitals are included.

2.4. Sample size calculation

Four hospitals will participate in the study. In each hospital, we aim to include at least 8 large departments (examples listed in Table 2) for a total of $4 \times 8 = 32$ departments, 16 in the active intervention group and 16 in the control group. We consider those deparments that are expected to generate at least the number of observations per condition per department as per the sample size calculation as large enough to participate.

An estimated 20% of exams are assumed inappropriate across all hospitals and departments [13,35]. We aim to demonstrate a reduction to 10% inappropriate exams or lower. To demonstrate a difference of 10% vs 20% at the department level comparing active versus control conditions (Table 1. A2 vs C2) with a power of 0.90 and an alpha value of 0.01, with 16 clusters per condition, an intracluster correlation coefficient (ICC) of 0.03, an individual autocorrelation coefficient (ρ_s) of 0.75 and a cluster autoccorrelation(ρ_c) of 0.75 would require 22 observations per department-condition cluster (active intervention or control) per 3-month observation period (calculated with the function cpa.did.binary from R package clusterPower, v. 0.7.0, available on Repository CRAN) [36].

The most uncertain parameters of the sample size calculation are the ICC, ρ_s and ρ_c . ICCs for this type of situation are typically on the order of 0.03 [36]. ρ_s is expected be high in cohort designs when the identity of individuals (in this case physicians) remain the same across time, however, it is not expected to be as high as 1 since most variables are not perfectly reproducible between occasions [37]. ρ_c represents the correlation between population means from the same cluster at two time-periods (over-time correlation at the group-level), which we also estimate as high due to the enduring influence of department-level characteristics, practices, and policies [37]. We performed a sensitivity analysis for ICC = 0–0.04: the sample size per cluster ranged from 13 to 27. Assuming ICC = 0.03 and for values ranging from ρ_s 0.4–0.9 and ρ_c 0.4–0.9 the cluster sample size ranges from 6 to 744. We have not specified a maximum number of observations. Even if the number of observations is large leading to statistical significance, but the difference in the proportion of inappropriate exams is small, we will still conclude that the intervention is not clinically relevant.

2.5. Randomization and consent

Randomization will be done through stratified block randomization. Stratification will be done by hospital and by surgical- vs nonsurgical specialty. Due to the differences in departments across hospitals and differences in participating departments and their scopes it was not possible to randomize per subspecialty, however, we anticipated that surgical and non-surgical departments were more likely to exhibit similar patterns in ordering behaviour. Block size for hospitals will be the number of departments per hospital (=8) such that 4 departments from each hospital are randomized to the active intervention and 4 to the control condition (Table 2). Block size for specialty will be the

number of participating hospitals (=4) such that 2 departments from each specialty type are randomized to the active intervention and 2 to the control condition (Table 2). Since this is a cluster RCT and the intervention is unblinded, the fact that the block size is small and known is irrelevant. Randomization will be performed using statistical software R and R package blockrand [38,39].

As the interventions are aimed at professionals, they are likely to affect all patients within a department as a professional-cluster [40]. Individuals are neither recruited nor randomized. Consent for a cluster to participate in the MIDAS study will be obtained through a guardian who possesses the legitimate authority to make decisions on the cluster or organizations' behalf [41,42]. Guardians of the clusters are the chairs of each participating department or delegated persons. Individuals are not able to withdraw, as the intervention is implemented in the imaging referral system. Physicians may however at all times choose not to follow the recommendations provided by the CDSS. The study does not collect any identifiable information from patients or physicians, therefore no additional individual consent for data collection will be sought.

2.6. Outcomes

The CDSS distinguishes appropriate (green), under certain conditions appropriate (orange), and inappropriate requests (red). The primary outcome of the MIDAS study is the proportion of inappropriate (red) diagnostic imaging exams requested per cluster (department). This proportion will be calculated by dividing the number of inappropriate exams ordered by the total number of exams ordered. Inappropriateness is determined by the CDSS based on the ESR imaging referral guidelines and scores of common (mainly oncological) indications that were not covered by the ESR iGuide which were mapped by the MIDAS consortium.

The secondary study parameters include:

- **The absolute number of imaging exams ordered,** total and by exam type.
- **Medical radiation from diagnostic imaging**. For all types of exams performed the average radiation dose will be determined and multiplied by the number of those types of exams performed. Summing the products provides the estimated total medical radiation.
- **Medical costs for diagnostic imaging** from the healthcare perspective.

  For all types of exams performed the average costs (German costs, healthcare perspective) will be determined and multiplied by the number of those types of exams performed. Summing the products this provides the estimated total costs for diagnostic imaging.

2.7. Data analysis

The main analysis is the comparison of the primary outcome (reduction in the proportion of inappropriate exam requests) aggregated at the department level and aggregated for 3-month periods, comparing the 16 active and 16 control groups (Table 1 A2-A0 vs C2-C0). This analysis will take into account the clustered design and intracluster correlation [43]. First, we will calculate the reduction in the proportion of inappropriate exam requests per cluster. Then we will calculate the mean of this proportion reduction for the active and control groups respectively, weighing each cluster by the inverse of the variance to account for the intracluster correlation and varying cluster size. The means in the active and control clusters will be compared using an independent samples *t*-test and the confidence intervals will be calculated based on the distribution. The width of this distribution will reflect the variation in reduction between clusters. Significance and confidence intervals will be determined using an alpha value of 0.01.

We will perform additional analyses to evaluate the change of outcome measures over time using segmented regression analysis incorporated in mixed models [44–47]. We will evaluate changes over time taking into account the date that the decision support is switched on and off. With time windows of 1 month, we will have 3 data points before implementation (A0), 3 early after implementation (A1), 3 during established implementation (A2), and 3 reverting to the control condition (A3). We will produce graphs for the active intervention groups and the control groups for visual comparison. The mixed model will account for the clustered design and the intracluster correlations. We will account for the clustered nature of the data by evaluating the fixed effects of decision support (active versus control group) and time period, and the random effects of the department, specialty type, and hospital. These analyses are listed in Table 3.

All requests go through the electronic ordering system and the system forces clinicians to enter the exam type and indication. Thus, we anticipate no missing data in this regard. Physicians may however start a request without completing it. This may be at random (being called away) or related to the outcome (stopping a request entirely as the CDSS stated the request was inappropriate, or restarting a request based on CDSS feedback to immediately select the appropriate request) resulting in underestimation of effectiveness. We will investigate differences in the proportion of incomplete requests between the control and intervention group and report the results of sensitivity analyses where all incomplete requests are set to be inappropriate and appropriate sequentially to investigate how the results of our main outcome change.

All analyses will be performed with the open-source statistical software R [38] under the guidance of a biostatistician.

3. Discussion

This study protocol outlines the methodology for the MIDAS study, a multi-centre cluster randomized trial with departments acting as clusters combined with a before-after-revert design. The study aims to promote the appropriate, meaningful, value-based and personalized use of medical imaging. The intervention provides a referral decision support system for physicians and is consistent with competent practice in radiology [41].

3.1. Strengths

The benefits of the CDSS intervention stem from improved decision making in ordering radiological imaging procedures. It provides access to an integrated educational tool for physicians that could help prevent the overuse of diagnostic tests, and reduce radiation exposure and imaging costs.

Although CDSSs are designed to improve quality of care and reduce costs through the reduction of inappropriate imaging, robust evidence that this goal will be achieved is still lacking [27]. This study will build

Table 3
Planned analyses and data exploration.

Question of interest	Analysis or exploration method
The proportion of inappropriate requested exams	Mixed effects logistic regression
The absolute number of imaging exams ordered	Poisson or Negative Binomial mixed model
Medical radiation from diagnostic imaging	Linear mixed model.
Medical costs for diagnostic imaging	Linear mixed model
Changes in the proportion of inappropriate requests over time without decision support, comparing C0, C1, C2, C3	Descriptive statistics and graphical visualization
Changes in the proportion of inappropriate requests due to the short-term learning effect comparing A0, A1*, A2* where * indicates the initial requests before feedback from the system	Descriptive statistics and graphical visualization
The sustainability and educational effect of changes after removal of decision support, A3 vs A2	Descriptive statistics and graphical visualization
Changes in the proportion of inappropriate requests over time by exam type and common indications	Descriptive statistics and graphical visualization

on previous findings and will provide rigorous data on the impact of these interventions on healthcare systems and patients.

An important strength of the study design lies in the methodological features of cluster-randomized trials, including increased administrative efficiency, lessened risk of experimental contamination, and likely enhancement of subject compliance [48]. The MIDAS study is multicentred, which allows for the inclusion of a larger number of imaging requests, different geographic locations, the ability to compare results among specialty types, and broader populations, all of which increase the generalizability of the study [49].

The implementation of the CDSS in the regular workflow makes it more likely that the reported results reflect its value in routine clinical care. The revert design makes it possible to demonstrate a sustainable educational effect.

3.2. Limitations

The study design is however also subject to several limitations, which are minimized where possible.

An often-discussed potential limitation inherent to cluster randomized trials relates to ethical considerations involving the need to obtain informed consent [42,48,50]. As the intervention is offered at the professional-cluster level and the data-analysis performed at this level, it is unnecessarily complicated to obtain individual consent and collect data from patients or physicians. Risks associated with data collection procedures are minimized and stand in reasonable relation to the knowledge to be gained. No identifiable data will be collected during the study. This choice in collected data however also limits our ability to review the role of physician-specific characteristics, such as experience, or individual willingness to change ordering behaviour, and does not allow for adjustment specifically for correlation of appropriateness scores within physicians. Also, our analysis does not account for differing numbers of physicians across departments. However, we consider this to be an appropriate choice for our data analysis, given the high level of interconnectivity between members of a department in decisions on imaging requests, and adjustment for intra-physician correlation was considered sufficiently covered through adjustment performed with the intra-cluster correlation.

We use a cluster design with departments as clusters to minimize possible contamination between the intervention and the control groups. While our design accounts for contamination due to within-department joint educational sessions, protocols, and collaborative decision making, our design does not address potential contamination between departments.

As the interventions are aimed at physicians requesting imaging and affect all patients undergoing imaging within a department, the intervention's nature dictates its application at the cluster level [48]. A guardian is therefore appointed for each cluster to represent participants' and patients' interests. Random assignment of the clusters is justified due to the uncertainty as to whether CDSSs improve practice [27]. The control condition follows usual practice. The study does not allow for participants to be blinded to their participation in the trial or the interventions. However, as our study concerns an educational intervention, blinding is neither possible nor desirable. By choosing an objective outcome measure (the number of inappropriate exams requested) reduce our study's susceptability to observer bias.

Methodological challenges underlying cluster randomized trials are that, compared to individually randomized trials, they are more complex to design, require more participants to obtain equivalent statistical power, and require more complex analyses [51]. A potential limitation in the effectiveness of implementing a CDSS that has been previously reported is the development of an Alert Fatigue among physicians, who may ignore feedback provided by the CDSS or experience it as a burdensome regulation rather than a tool to improve the appropriateness of their requests [52]. Additionally, there may be an increased administrative burden experienced by departments in the control conditions, who follow an adjusted workflow through the CDSS, but do not receive the benefit of feedback. This may complicate buy-in from departments at the recruitment stage of the study. We mapped common (mainly oncological) indications that were not covered by the ESR iGuide and translated guidelines and keywords into German to limit the added burden on physicians, however these adjustments may alter the generalizability of findings to those from the original ESR iGuide. We however believe that these alterations are justified to support workflow, and will share all alterations alongside the manuscript. It is our expectation that the ESR iGuide itself will continue to develop over time to include these alterations and based on user feedback.

It is possible that physicians start an imaging request but do not finalize the request. Potential reasons for doing so may be unrelated to the requests, for example being called away to another patient. However, if the physician starts a request, and stops halfway through, they may have received feedback which they may use in a new request – which then would be scored as appropriate. In order to track and make inferences about prematurely terminated imaging requests, we will track the number of terminated requests in all groups and perform sensitivity analyses with varying assumptions on the missing observations. To prevent "gaming the system" [53], physicians in participating departments are educated in the purpose of the study and the importance of complete and honest information when filling out request forms. Additionally, there may still be residual contamination between departments due to consultations or multidisciplinary discussions. However, we believe that this will be limited as the ordering physician will still make the final imaging request through their department-linked account and whether they receive CDSS support will depend on the department's randomization status.

Lastly, a potential risk is that the CDSS may also advise imaging procedures with higher radiation exposure or cost than the physician had planned to order. In each scenario, the physician may still choose to ignore the guidance provided by the CDSS. The requirement, that ionizing radiation for diagnostic imaging needs to be ordered by a physician certified according to German law ensures that in both scenarios the ordered imaging exam follows good clinical practice [54].

4. Conclusion

The results of this study will provide critical evidence for clinicians and policy makers to promote the appropriate, meaningful, value-based and personalized use of medical imaging.

Funding

The MIDAS study is funded by the German Innovation Committee at the Federal Joint Committee (reference: Förderkennzeichen 01VSF18008). The funder played no role and/or will play no role in the study design; collection, management, analysis and interpretation of data; writing of the report; and the decision to submit the report for publication.

Informed consent

Randomization and intervention in the MIDAS study will be executed at a departmental level. Individuals are neither recruited nor randomized. Consent for a cluster to participate in the MIDAS study will be obtained through a guardian who possesses the legitimate authority to make decisions on the cluster or organizations' behalf. Guardians of the clusters in the MIDAS study are the chairs of each participating department or delegated persons. Individual subjects are not able to withdraw, as the intervention is implemented in the radiological imaging referral system. Physicians may however at all times choose not to follow the recommendations provided by the CDSS.

Protocol version

Approval from the Medical Research Ethics Committee (MREC) was obtained under protocol numbers 20–069 (Augsburg), B 238/21 (Kiel), 20–318 (Lübeck) and 2020–15125 (Mainz). The trial is registered in the Clinical Trials Register (http://www.ClinicalTrials.gov) under trial number NCT05490290. This manuscript details the latest version of the protocol as per October 2023. The original sample size calculation was amended on clinicaltrials.gov in 2023 based on this newer and more appropriate function of the clusterPower package. The study will be conducted according to the principles of the WMA Declaration of Helsinki [55]. All changes to the study protocol will be shared with the MREC that gave a favourable opinion to the study, and all significant changes will be noted in the public trial registry. The current manuscript follows the recommendations by the SPIRIT guidance [56]. The SPIRIT figure is presented in the main manuscript as Table 1.

Study participant consent

Interventions and randomization in the MIDAS study will be executed at a professional-cluster level. As the interventions are aimed at professionals, they are likely to affect all patients within a department [40].

Consent for a cluster to participate in the MIDAS study will be obtained through a guardian who possesses the legitimate authority to make decisions on the cluster or organizations' behalf [42]. Guardians in the MIDAS study are the chairs of each participating department or delegated persons.

Outcomes are measured using routine data at the cluster level, namely the radiology information system. The study does not collect any identifiable information from patients or physicians, therefore no additional individual consent for data collection will be sought.

Data handling and storage

Data will be handled confidentially. The data collected does not fall into the category of "personal data" as defined by the General Data Protection Regulation (GDPR) which defines personal data as "any information which are related to an identified or identifiable natural person" [57]. Since we will not be following patients over time there is no need to collect personal information and all collected data will be anonymized. The primary outcome will come directly from the CDSS. All secondary outcomes are aggregated data derived from hospital and/or radiology information systems. Collected data will be available to the research team.

Monitoring

The intervention in the MIDAS study is implemented at the department level and directed at guiding physicians in ordering diagnostic imaging. No adverse events to participants can be expected related to providing this guidance. The CDSS intervention remains a recommendation to the physician, and the referring physician can at all times decide not to follow its recommendations. The responsibility for the imaging referral is that of the ordering physician, and the responsibility of performing the exam remains with the radiologist [54].

A Data Safety Monitoring Board (DSMB) will be formed comprising at least 3 independent researchers. The DSMB will be consulted should any safety issues arise or if protocol changes are deemed necessary for safety reasons.

Trial registration number

Approval from the Medical Ethics Review Committee was obtained under protocol numbers 20–069 (Augsburg), B 238/21 (Kiel), 20–318 (Lübeck) and 2020–15125 (Mainz). The trial is registered in the ClinicalTrials.gov register under registration number NCT05490290.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Dr. Dijk receives research funding from the Gordon and Betty Moore Foundation

Dr. Kröncke receives (or received within the past 36 months) research funding outside the submitted work from The Bavarian Centre for Cancer Research, the national Network University Medicine (NUM) and Siemens Healthineers, has received honoraria for educational symposia from SIRTEX Medical, Boston Scientific and Abbott Medical GmbH and re-imbursements of expenses related to his work in the executive committee and congressional events of the Cardiovascular and Interventional Radiological Society of Europe.

Dr. Claudia Wollny has no conflicts of interest to report.

Dr. Halfmann has no conflicts of interest to report

Dr. Jansen receives (or received within the past 36 months) research funding outside the submitted work from DFG (German scientific society), has received speaker fee from Philips Medical, Rapid AI, mRAY, Boehringer and Bayer and has received consultant honoraria from TÜV Süd, Radiologie Holding and Stryker.

Dr. Hunink receives (or received in the past 36 months) Royalties from Cambridge University Press for a textbook on Medical Decision Making, reimbursement of expenses from the European Society of Radiology (ESR) for work on the ESR guidelines for imaging referrals, reimbursement of expenses from the European Institute for Biomedical Imaging Research (EIBIR) for membership of the Scientific Advisory Board, and research funding from the American Diabetes Association, the Netherlands Organization for Health Research and Development, Netherlands Educational Grant ("Studievoorschotmiddelen"), and the Gordon and Betty Moore Foundation.

Data availability

No data was used for the research described in the article.

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