

1 **Supplementary Material 1: Trial protocol and statistical analysis plan**

2

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8

9 **Original Protocol**

10

11 **PRINCIPAL/OVERALL INVESTIGATOR**

12 Ishani Ganguli MD MPH

13

14 **PROTOCOL TITLE**

15 CASCADES Trial: A consumer-focused approach to initiate shared decision-
16 making on care cascades after common medical tests

17

18 **FUNDING**

19 Robert Wood Johnson Foundation

20

21 **VERSION DATE**

22 3/24/2021

23

24 **SPECIFIC AIMS**

25

Concisely state the objectives of the study and the hypothesis being tested.

26 **Aims:**

- 27 1. Develop a simple, scalable intervention to prompt conversations about
28 the downstream consequences of potentially discretionary medical tests
29 in the primary care setting.
30 2. Implement this text-based intervention in the primary care setting.
31 3. Rigorously evaluate the impact of this intervention using a randomized
32 controlled trial study of 200 patients by their primary care physician.
33

34 **Hypotheses:**

- 35 1. The intervention is feasible to implement in primary care practices with
36 no major recruitment barriers as defined by recruiting 20 physicians from
37 clinics affiliated with one academic medical center, and 200 patients of all
38 sexes and a range of ages, ethnicities, income levels (as correlated with
39 zip code), and education levels.
40 2. Intervention arm patients are more likely to have higher quality
41 conversations about medical testing decisions (primary outcome).
42

43 **BACKGROUND AND SIGNIFICANCE**

44 Provide a brief paragraph summarizing prior experience important for understanding the
45 proposed study and procedures.

46 Medical tests can have sizable downstream consequences including further
47 tests, treatments, office visits, and even hospitalizations. Known as *care*
48 *cascades*, these downstream services have significant direct and indirect
49 cost implications for patients. In some cases, downstream services are
50 medically appropriate, such as when an initial test is medically indicated and
51 has a high degree of accuracy. However, many tests are performed even
52 when they are not medically indicated (e.g., at a patient’s request), and may
53 have high rates of false positives or of incidental findings (i.e., unrelated to
54 the purpose of the test). Notably, the following tests are commonly ordered,
55 may be overused, and have a high risk of false positives and incidental
56 findings (and therefore care cascades): imaging tests, electrocardiograms,
57 and blood tests including blood count, electrolyte, kidney function, and liver
58 function tests. Some estimates suggest that up to 52% of radiology and
59 laboratory tests produce incidental findings, and that rate may increase with
60 advances in technology.

61
62 Studies of specific cascades using national administrative claims data also
63 suggest that these cascades can be costly – in one example by Ganguli et al,
64 cascades following pre-operative electrocardiograms for cataract surgery
65 cost ten times the initial electrocardiograms (ECGs). A recent national study
66 of US internists conducted by Ganguli et al. also found that almost all
67 responding physicians had experienced cascades after incidental findings
68 that did not lead to clinically meaningful outcomes yet caused physical,
69 psychological, or other harms to patients or the physicians themselves.
70 Although some of these cascades may eventually reveal clinically important
71 findings, more often they find nothing significant. This is especially true
72 when the initial test is discretionary or even known to be of low-value, as in
73 the example of pre-operative ECGs for cataract surgery. It is likely that few
74 patients are aware of the potential for cascades or risk of false positives
75 when making the decision with their clinicians to proceed with medical
76 tests.

77
78 Despite the prevalence and burden of care cascades, little effort has been
79 devoted to addressing them. Consideration of care cascades have not been
80 incorporated into best practices for shared decision-making and we are not

81 aware of any interventions that have been developed or evaluated to
82 educate patients or clinicians on the financial or psychological risk of
83 care cascades.

84

85 **RESEARCH DESIGN AND METHODS**

86 Briefly describe study design and anticipated enrollment, i.e., number of subjects to be enrolled
87 by researchers study-wide and by Partners researchers. Provide a brief summary of the
88 eligibility criteria (for example, age range, gender, medical condition). Include any local site
89 restrictions, for example, “Enrollment at Partners will be limited to adults although the
90 sponsor’s protocol is open to both children and adults.”

91 **Design:** During Phase I, we will implement a user-centered design process
92 to develop the educational content and implementation strategy for the
93 intervention. Specifically, we will conduct focus groups with patients and
94 clinicians in which we iteratively solicit feedback on the language and
95 dissemination of text/email-based messages and interactive content for
96 patients, on the tip sheet for physicians, and on survey items for both.

97

98 In Phase II, we will randomize 20 primary care physicians to intervention
99 and control arms, recruit 10 patients per physician with upcoming wellness
100 visits, and implement our intervention. We will collect pre- and post-
101 intervention surveys of patients and physicians, as well as post-study
102 interviews of patients and physicians. In Phase III, we will use mixed
103 methods analysis to study the data collected in Phase II.

104

105 **Enrollment:** For Phase I, we will recruit up to 20 patients for the patient
106 advisory committee and interviews and up to 20 practicing BWH primary
107 care physicians for interviews.

108

109 For phase II, we will recruit 20 BWH primary care physicians who actively
110 see patients and meet our inclusion criteria (based on patient-deidentified
111 EDW data on test ordering rates during annual physicals). We will then
112 recruit 10 patients for each of these PCPs. All patients of the selected PCPs
113 who are at least 18 years old, speak English, and have access to Email are
114 eligible to participate.

115 Briefly describe study procedures. Include any local site restrictions, for example, "Subjects
116 enrolled at Partners will not participate in the pharmacokinetic portion of the study." Describe
117 study endpoints.

118 In phase I, we will develop educational content for patients and a tip sheet
119 for providers. To this end, we will work with the BWH Center for Patients and
120 Families to select and convene a 5-10 member patient advisory council. We
121 will host two focus groups with this council, aided by discussion guides, to
122 first identify key issues and then to suggest refinements to our intervention.

123

124 We will also recruit both patients and physicians for in-depth interviews. We
125 will recruit up to 20 primary care physicians through the Patient-Based
126 Research Network (PBRN) and suggestions from clinic medical directors. We
127 will recruit up to 20 patients through the above Patient Advisory Council and
128 the Rally platform. We will conduct up to 20 in-depth interviews each with
129 these physicians and patients to understand their experiences with cascades
130 and to cognitively test survey items.

131

132 Finally, we will review patient educational materials and the clinician tip
133 sheet with clinic medical directors for their approval.

134

135 In phase II, we will work with clinic leads in the BWH PBRN to recruit 20
136 physicians who have not previously been involved. We will select these
137 physicians from among those who fall in the top 50th percentile of test
138 ordering rates during annual physicals. We will use matched pair
139 randomization to randomize these PCPs to the control or intervention arms.
140 For each physician, we will identify 10 of their patients who are scheduled
141 for a physical in the next 6 months and meet our inclusion criteria (based on
142 key demographics from the electronic health record (EHR)). We will recruit
143 them using use mailed letters and patient portal messages.

144

145 Intervention arm: We will send emails to physicians with feedback on how
146 they compare to their peers in aggregate on test ordering during annual
147 physicals, along with links to the physician-facing materials. We will not
148 share identifiable data with a given physician on their peer physicians. One
149 to two days before their visit, we will send patients educational materials via
150 text, email, or both depending on their preference.

151

152 Control arm: One to two days before their visit, we will send patients general
153 information on visit preparation.

154

155 **NOTE:** We acknowledge that during the covid19 pandemic, clinical
156 operations have changed drastically to protect both patients and health care
157 workers. For instance, routine wellness visits have been cancelled or
158 converted to virtual. Given our commitment to protect the safety and
159 welfare of our study subjects and staff, and to avoid disrupting clinic
160 operations during this challenging time, we plan to conduct phase I of our
161 study virtually and to begin the intervention phase only once it is deemed
162 safe and feasible to do so.

163

164

165 For studies involving treatment or diagnosis, provide information about standard of care at
166 Partners (e.g., BWH, MGH) and indicate how the study procedures differ from standard care.
167 Provide information on available alternative treatments, procedures, or methods of diagnosis.

168

169 Treatment and diagnosis are not part of this protocol.

170

171 Describe how risks to subjects are minimized, for example, by using procedures which are
172 consistent with sound research design and which do not unnecessarily expose subjects to risk
173 or by using procedures already being performed on the subject for diagnostic or treatment
174 purposes.

175

176 There are no known risks to participating in this study. Patient and clinician
177 subjects may voluntarily participate and withdraw at any time.

178

179 There is a theoretical risk of breach of data confidentiality and that PHI could
180 become known to unauthorized persons, but we will take all steps necessary
181 to protect PHI (see below). To mitigate this risk, we will follow all compliance
182 and data confidentiality procedures for research at Partners. Specifically, we
183 will use procedures consistent with sound research design and which do not
184 expose subjects to unnecessary risk. Data monitoring will be conducted
185 regularly (see below). All data analyzed will be de-identified and reported in
186 aggregate.

187

188 Describe explicitly the methods for ensuring the safety of subjects. Provide objective criteria
189 for removing a subject from the study, for example, objective criteria for worsening
190 disease/lack of improvement and/or unacceptable adverse events. The inclusion of objective
191 drop criteria is especially important in studies designed with placebo control groups.

192

193 **This is a minimal risk study.** There is no known physical or medical safety
194 threat to patient or clinician subjects who participate. Furthermore,
195 participation is voluntary and all subjects will be informed that they may opt-
196 out any time (see below). Given the minimal risk to subjects, our data safety
197 and monitoring procedures, and the relatively small sample size, we do not
198 plan on having drop criteria.

199

200 **FORESEEABLE RISKS AND DISCOMFORTS**

201 Provide a brief description of any foreseeable risks and discomforts to subjects. Include those
202 related to drugs/devices/procedures being studied and/or administered/performed solely for
203 research purposes. In addition, include psychosocial risks, and risks related to privacy and
204 confidentiality. When applicable, describe risks to a developing fetus or nursing infant.

205

206 **For patient and clinician subjects, there are no known risks to**
207 **participating in our data collection activities.** There is a potential risk of
208 physicians feeling psychological discomfort in knowing their test ordering
209 rates. We will mitigate this by offering an option if they have concerns to
210 speak with clinic leaders about these concerns. The main risks are breach of
211 confidentiality and privacy of information shared. Every effort will be made
212 to maintain confidentiality and privacy of information shared and collected
213 and subsequent data analysis (see below), and efforts will be made to
214 minimize the duration of data collection activities.

215

216 **EXPECTED BENEFITS**

217 Describe both the expected benefits to individual subjects participating in the research and the
218 importance of the knowledge that may reasonably be expected to result from the study. Provide
219 a brief, realistic summary of potential benefits to subjects, for example, "It is hoped that the
220 treatment will result in a partial reduction in tumor size in at least 25% of the enrolled subjects."
221 Indicate how the results of the study will benefit future patients with the disease/condition being
222 studied and/or society, e.g., through increased knowledge of human physiology or behavior,
223 improved safety, or technological advances.

224
225 Individual subjects may benefit by learning about (and, if appropriate,
226 avoiding) possible downstream consequences of medical testing, and having
227 their physicians become more informed about these consequences and how
228 to discuss them. Future patients will benefit through improved knowledge of
229 a possible intervention to facilitate patient-clinician conversations about
230 cascades that may in turn help to reduce their negative effects.

231
232 **EQUITABLE SELECTION OF SUBJECTS**

233 The risks and benefits of the research must be fairly distributed among the populations that
234 stand to benefit from it. No group of persons, for example, men, women, pregnant women,
235 children, and minorities, should be categorically excluded from the research without a good
236 scientific or ethical reason to do so. Please provide the basis for concluding that the study
237 population is representative of the population that stands to potentially benefit from this
238 research.

239
240 Our goal will be to enroll eligible patients whose characteristics are
241 representative of the entire population of eligible patients. We will
242 specifically target patients of all sexes and a range of ages, ethnicities,
243 income levels and education levels.

244
245 When people who do not speak English are excluded from participation in the research, provide
246 the scientific rationale for doing so. Individuals who do not speak English should not be denied
247 participation in research simply because it is inconvenient to translate the consent form in
248 different languages and to have an interpreter present.

249
250 We will approach English-speaking patients only. The scientific rationale for
251 this limitation is because the text-based intervention will be available in
252 English in this early stage of development. All clinician subjects caring for
253 patients at BWH speak English.

254
255 For guidance, refer to the following Partners policy:
256 Obtaining and Documenting Informed Consent of Subjects who do not Speak English
257 [https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Non-](https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Non-English_Speaking_Subjects.1.10.pdf)
258 [English_Speaking_Subjects.1.10.pdf](https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Non-English_Speaking_Subjects.1.10.pdf)

259
260
261
262 **RECRUITMENT PROCEDURES**

263 Explain in detail the specific methodology that will be used to recruit subjects. Specifically
264 address how, when, where and by whom subjects will be identified and approached about

265 participation. Include any specific recruitment methods used to enhance recruitment of
266 women and minorities.

267
268 For phase I, we will recruit the PAC and physician focus groups as described
269 above.

270
271 For phase II, we will work with clinic leads in the BWH PBRN to recruit 20
272 physicians who have not previously been involved with our study. We will
273 select these physicians from among those who fall in the top 50th percentile
274 of test ordering rates during annual physicals, starting from PCPs with the
275 highest test ordering rates and proceeding in descending order. Once we
276 have recruited 20 physicians, we will use matched pair randomization to
277 randomize these PCPs to the control or intervention arms.

278
279 Eligible patient participants will then be identified by research assistants
280 trained in the protection of human subjects based on upcoming appointment
281 and demographics including age, race, sex, and zip code (to link to area-
282 level census data on income and education) using “minimum necessary”
283 information in the EHR. Once identified, the research assistant will send the
284 patient both a letter through the patient portal and a mailed letter inviting
285 them to participate on behalf of the BWH PI. In the letter we will include an
286 email address and phone number that allows the patient to opt out. The
287 letter will also include a link to REDCAP which will include an electronic
288 consent form with information sheet, invitation to enroll, preference for
289 communication (phone versus email), and the baseline survey.

290

291 Provide details of remuneration, when applicable. Even when subjects may derive medical
292 benefit from participation, it is often the case that extra hospital visits, meals at the hospital,
293 parking fees or other inconveniences will result in additional out-of-pocket expenses related to
294 study participation. Investigators may wish to consider providing reimbursement for such
295 expenses when funding is available

296
297 Patient subjects in both arms will be compensated \$10 at the completion of
298 the study. Physician subjects will be compensated \$50 for the whole study.

299

300 For guidance, refer to the following Partners policies:

301 Recruitment of Research Subjects

302 [https://partnershealthcare-](https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Recruitment_Of_Research_Subjects.pdf)
303 [public.sharepoint.com/ClinicalResearch/Recruitment_Of_Research_Subjects.pdf](https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Recruitment_Of_Research_Subjects.pdf)

304

305 Guidelines for Advertisements for Recruiting Subjects

306 [https://partnershealthcare-](https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Guidelines_For_Advertisements.1.11.pdf)
307 [public.sharepoint.com/ClinicalResearch/Guidelines_For_Advertisements.1.11.pdf](https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Guidelines_For_Advertisements.1.11.pdf)

308
309 Remuneration for Research Subjects

310 [https://partnershealthcare-](https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Remuneration_for_Research_Subjects.pdf)
311 [public.sharepoint.com/ClinicalResearch/Remuneration_for_Research_Subjects.pdf](https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Remuneration_for_Research_Subjects.pdf)

312

313

314 **CONSENT PROCEDURES**

315 Explain in detail how, when, where, and by whom consent is obtained, and the timing of
316 consent (i.e., how long subjects will be given to consider participation). For most studies
317 involving more than minimal risk and all studies involving investigational drugs/devices, a
318 licensed physician investigator must obtain informed consent. When subjects are to be
319 enrolled from among the investigators' own patients, describe how the potential for coercion
320 will be avoided.

321

322 In phase I, eligible physician subjects will be informed about our research
323 initiative via email and patients via RALLY. Prior to participation in
324 interviews, we will confirm verbal consent. Specifically, these subjects will be
325 informed that: 1) participation is voluntary—they may stop the interview at
326 any time, and 2) data collected will be analyzed and reported in aggregate.

327
328 In phase II, potential patient subjects will be informed as part of the letter
329 or patient portal message, and the REDCAP link that it will contain. This
330 information will contain the purpose of the study, risks/benefits, methods of
331 ensuring confidentiality, and voluntary nature of participation. Specifically,
332 patient subjects will be informed that: 1) participation is voluntary—they may
333 withdraw at any time; 2) a decision to not participate will in no way affect
334 their care at BWH/BWFH; 3) information shared will remain confidential and
335 used only for research purposes; and 4) data collected will be analyzed and
336 reported in aggregate. We will not request verbal consent as this will be
337 prohibitively burdensome for this minimal risk study and because this study
338 does not share any personal health information with the patients.

339

340 **NOTE:** When subjects are unable to give consent due to age (minors) or impaired decision-
341 making capacity, complete the forms for Research Involving Children as Subjects of Research

342 and/or Research Involving Individuals with Impaired Decision-making Capacity, available on the
343 New Submissions page on the PHRC website:

344 <https://partnershealthcare.sharepoint.com/sites/phrmApply/aieipa/irb>

345

346 For guidance, refer to the following Partners policy:

347 Informed Consent of Research Subjects:

348 <https://partnershealthcare->

349 [public.sharepoint.com/ClinicalResearch/Informed_Consent_of_Research_Subjects.pdf](https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Informed_Consent_of_Research_Subjects.pdf)

350

351

352

353 **DATA AND SAFETY MONITORING**

354 Describe the plan for monitoring the data to ensure the safety of subjects. The plan should
355 include a brief description of (1) the safety and/or efficacy data that will be reviewed; (2) the
356 planned frequency of review; and (3) who will be responsible for this review and for
357 determining whether the research should be altered or stopped. Include a brief description of
358 any stopping rules for the study, when appropriate. Depending upon the risk, size and
359 complexity of the study, the investigator, an expert group, an independent Data and Safety
360 Monitoring Board (DSMB) or others might be assigned primary responsibility for this monitoring
361 activity.

362

363 NOTE: Regardless of data and safety monitoring plans by the sponsor or others, the principal
364 investigator is ultimately responsible for protecting the rights, safety, and welfare of subjects
365 under his/her care.

366

367 The principal investigator and research assistant/project coordinator will
368 monitor data collection activities, maintain data integrity and quality control,
369 protect the rights, safety, and welfare of study subjects, and adhere to
370 standards set by the Partners IRB. All data will be stripped of PHI and
371 electronic data will be kept on a secured shared file area (SFA) behind the
372 Partners firewall with anti-virus software or Partners Research Computing
373 approved cloud storage services. Data about consented patients will also be
374 stored behind the RAND Corporation firewall in accordance with the terms of
375 the consent. Any paper forms and/or audio recordings will be destroyed after
376 being transcribed into electronic format. Monitoring will be performed on a
377 monthly basis during the study period and will include a review of
378 enrollment, data analysis, and breaches of confidentiality, and any adverse
379 events that may occur. Any adverse events will be graded as to their

380 attribution to the intervention and reported according to IRB guidelines. The
381 principal investigator will review any complaints reported from patient and
382 physician subjects. These will be reported to the Partners IRB annually or
383 immediately if the complaint is serious. Given the minimal risk of the study,
384 we are not planning to use automatic stopping rules or a DSMB. We
385 emphasize that this study does not involve any invasive procedures.

386

387 Describe the plan to be followed by the Principal Investigator/study staff for review of adverse
388 events experienced by subjects under his/her care, and when applicable, for review of sponsor
389 safety reports and DSMB reports. Describe the plan for reporting adverse events to the sponsor
390 and the Partners' IRB and, when applicable, for submitting sponsor safety reports and DSMB
391 reports to the Partners' IRBs. When the investigator is also the sponsor of the IND/IDE, include
392 the plan for reporting of adverse events to the FDA and, when applicable, to investigators at
393 other sites.

394

395 NOTE: In addition to the adverse event reporting requirements of the sponsor, the principal
396 investigator must follow the Partners Human Research Committee guidelines for Adverse Event
397 Reporting

398

399 Voluntary participation in data collection activities are not expected to cause
400 adverse events to patient or physician subjects. However, if an adverse
401 event occurs, the principal investigator will follow PHS HRC guidelines for
402 adverse event reporting.

403

404 **MONITORING AND QUALITY ASSURANCE**

405 Describe the plan to be followed by the principal investigator/study staff to monitor and assure
406 the validity and integrity of the data and adherence to the IRB-approved protocol. Specify who
407 will be responsible for monitoring, and the planned frequency of monitoring. For example,
408 specify who will review the accuracy and completeness of case report form entries, source
409 documents, and informed consent.

410

411 NOTE: Regardless of monitoring plans by the sponsor or others, the principal investigator is
412 ultimately responsible for ensuring that the study is conducted at his/her investigative site in
413 accordance with the IRB-approved protocol, and applicable regulations and requirements of the
414 IRB.

415

416 The principal investigator and research assistant/project coordinator will
417 monitor and assure the validity and integrity of the data collection and
418 adherence to the procedures outlined in this protocol. They will review the

419 study database on a monthly basis, ensuring data integrity, accuracy, and
420 completeness. The principal investigator will supervise the research
421 assistant/project coordinator in all data collection activities over the course
422 of the study.
423

424 For guidance, refer to the following Partners policies:

425 Data and Safety Monitoring Plans and Quality Assurance

426 [https://partnershealthcare-](https://partnershealthcare-public.sharepoint.com/ClinicalResearch/DSMP%20in%20Human%20Subjects%20Research.pdf)
427 [public.sharepoint.com/ClinicalResearch/DSMP in Human Subjects Research.pdf](https://partnershealthcare-public.sharepoint.com/ClinicalResearch/DSMP in Human Subjects Research.pdf)

428
429 Reporting Unanticipated Problems (including Adverse Events)

430 [https://partnershealthcare-](https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Reporting%20Unanticipated%20Problems%20including%20Adverse%20Events.pdf)
431 [public.sharepoint.com/ClinicalResearch/Reporting Unanticipated Problems including Adverse Even](https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Reporting Unanticipated Problems including Adverse Events.pdf)
432 [ts.pdf](https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Reporting Unanticipated Problems including Adverse Events.pdf)

433 434 435 436 **PRIVACY AND CONFIDENTIALITY**

437 Describe methods used to protect the privacy of subjects and maintain confidentiality of data
438 collected. This typically includes such practices as substituting codes for names and/or medical
439 record numbers; removing face sheets or other identifiers from completed
440 surveys/questionnaires; proper disposal of printed computer data; limited access to study data;
441 use of password-protected computer databases; training for research staff on the importance of
442 confidentiality of data, and storing research records in a secure location.
443

444 NOTE: Additional measures, such as obtaining a Certificate of Confidentiality, should be
445 considered and are strongly encouraged when the research involves the collection of sensitive
446 data, such as sexual, criminal or illegal behaviors.

447 All information from individuals or entities in the course of this study that
448 identifies an individual or entity will be treated as confidential in accordance
449 with section 903c of the Public Health Service Act (42 U.S.C.299a-1). This
450 will be done by keeping all personal identifiers in a separate location from
451 the data, and only approved research personnel and study investigators
452 trained in the protection of human subjects will have access to the linked
453 data. All research staff will be properly trained in the importance of
454 confidentiality of data.
455

456 All electronic data and files will be stored on a password-protected database
457 in a shared file area (SFA) on a Partners password-protected computer
458 behind the Partners firewall with anti-virus software or on Partners Research
459 Computing approved cloud storage services. Data about consented patients
460 will also be stored behind the RAND Corporation firewall in accordance with
461 the terms of the consent. Patients' identifiers and other data collected on
462 paper will be kept in locked filing cabinets. Data collection instruments used
463 during the project and stored on laptop or desktop computers will also be
464 password protected. Printed computer data with PHI will be shredded and
465 disposed of upon completion of the study and any record-keeping
466 requirements. Any identifiers will be removed prior to any analysis and all
467 results will be presented in aggregate. The principal investigator will be
468 responsible for the confidentiality and security of all study databases. These
469 measures should be effective in preventing breaches of confidentiality.
470

471 **SENDING SPECIMENS/DATA TO RESEARCH COLLABORATORS OUTSIDE**
472 **PARTNERS**

473 Specimens or data collected by Partners investigators will be sent to research collaborators
474 outside Partners, indicate to whom specimens/data will be sent, what information will be sent,
475 and whether the specimens/data will contain identifiers that could be used by the outside
476 collaborators to link the specimens/data to individual subjects.

477

478 No specimens or data will be sent to anyone outside of BWH.

479 Specifically address whether specimens/data will be stored at collaborating sites outside
480 Partners for future use not described in the protocol. Include whether subjects can withdraw
481 their specimens/data, and how they would do so. When appropriate, submit documentation of
482 IRB approval from the recipient institution.

483

484 Not applicable.

485 **RECEIVING SPECIMENS/DATA FROM RESEARCH COLLABORATORS OUTSIDE**
486 **PARTNERS**

487 When specimens or data collected by research collaborators outside Partners will be sent to
488 Partners investigators, indicate from where the specimens/data will be obtained and whether
489 the specimens/data will contain identifiers that could be used by Partners investigators to link
490 the specimens/data to individual subjects. When appropriate, submit documentation of IRB
491 approval and a copy of the IRB-approved consent form from the institution where the
492 specimens/data were collected.

493

494 No specimens or data will be received from anyone outside of BWH.

495

496 **Final Protocol**

497

498 **PRINCIPAL/OVERALL INVESTIGATOR**

499 Ishani Ganguli MD MPH

500

501 **PROTOCOL TITLE**

502 A Multi-pronged Intervention to Initiate Shared Decision-making on Medical
503 Tests and Care Cascades in the Primary Care Setting

504

505 **FUNDING**

506 Robert Wood Johnson Foundation

507

508 **VERSION DATE**

509 10/27/2022

510

511 **SPECIFIC AIMS**

512 Concisely state the objectives of the study and the hypothesis being tested.

513 **Aims:**

- 514 4. Develop a simple, scalable intervention to prompt conversations about
515 the downstream consequences of potentially discretionary medical tests
516 in the primary care setting.
- 517 5. Implement this email and text-based intervention in the primary care
518 setting.
- 519 6. Rigorously evaluate the impact of this intervention using a randomized
520 controlled trial study of 20 primary care physicians and at least 200
521 patients.

522

523 **Hypotheses:**

- 524 3. The intervention is feasible to implement in primary care practices with
525 no major recruitment barriers as defined by recruiting 20 physicians from
526 clinics affiliated with one academic medical center, and at least 200
527 patients of all genders and a range of ages, race/ethnicities, and
528 education levels.
- 529 4. Intervention arm patients are more likely to have higher quality
530 conversations about medical testing decisions (primary outcome).

531

532 **BACKGROUND AND SIGNIFICANCE**

533 Provide a brief paragraph summarizing prior experience important for understanding the
534 proposed study and procedures.

535

536 Medical tests can have sizable downstream consequences including further
537 tests, treatments, office visits, and even hospitalizations. Known as *care*
538 *cascades*, these downstream services have significant direct and indirect
539 cost implications for patients. In some cases, downstream services are
540 medically appropriate, such as when an initial test is medically indicated and
541 has a high degree of accuracy. However, many tests are performed even
542 when they are not medically indicated (e.g., at a patient’s request), and may
543 have high rates of false positives or of incidental findings (i.e., unrelated to
544 the purpose of the test). Notably, the following tests are commonly ordered,
545 may be overused, and have a high risk of false positives and incidental
546 findings (and therefore care cascades): imaging tests, electrocardiograms,
547 and blood tests including blood count, electrolyte, kidney function, and liver
548 function tests. Some estimates suggest that up to 52% of radiology and
549 laboratory tests produce incidental findings, and that rate may increase with
550 advances in technology.

551

552 Studies of specific cascades using national administrative claims data also
553 suggest that these cascades can be costly – in one example by Ganguli et al,
554 cascades following pre-operative electrocardiograms for cataract surgery
555 cost ten times the initial electrocardiograms (ECGs). A recent national study
556 of US internists conducted by Ganguli et al. also found that almost all
557 responding physicians had experienced cascades after incidental findings
558 that did not lead to clinically meaningful outcomes yet caused physical,
559 psychological, or other harms to patients or the physicians themselves.
560 Although some of these cascades may eventually reveal clinically important
561 findings, more often they find nothing significant. This is especially true
562 when the initial test is discretionary or even known to be of low-value, as in
563 the example of pre-operative ECGs for cataract surgery. It is likely that few
564 patients are aware of the potential for cascades or risk of false positives
565 when making the decision with their clinicians to proceed with medical
566 tests.

567

568 Despite the prevalence and burden of care cascades, little effort has been
569 devoted to addressing them. Consideration of care cascades have not been
570 incorporated into best practices for shared decision-making and we are not

571 aware of any interventions that have been developed or evaluated to
572 educate patients or clinicians on the financial or psychological risk of
573 care cascades.

574

575 **RESEARCH DESIGN AND METHODS**

576 Briefly describe study design and anticipated enrollment, i.e., number of subjects to be enrolled
577 by researchers study-wide and by Partners researchers. Provide a brief summary of the
578 eligibility criteria (for example, age range, gender, medical condition). Include any local site
579 restrictions, for example, "Enrollment at Partners will be limited to adults although the
580 sponsor's protocol is open to both children and adults."

581

582 **Design:** During Phase I, we will implement a user-centered design process
583 to develop the educational content and implementation strategy for the
584 intervention. Specifically, we will conduct focus groups with patients and
585 clinicians in which we iteratively solicit feedback on the language and
586 dissemination of text/email-based messages and interactive content for
587 patients, on references and peer comparison emails for physicians, and on
588 survey items for both.

589

590 In Phase II, we will randomize 20 primary care physicians to intervention
591 and control arms, recruit at least 10 and up to 20 patients per physician with
592 upcoming wellness visits, and implement our intervention. We will collect
593 pre- and post-intervention surveys of patients and physicians, as well as
594 post-study interviews of patients and physicians. In phase III, we will use
595 mixed methods analysis to study the data collected in Phase II.

596

597 **Enrollment:** For Phase I, we will recruit up to 27 patients for the patient
598 advisory committee and interviews and up to 20 practicing BWH primary
599 care physicians for interviews.

600

601 For phase II, we will recruit 20 BWH primary care physicians who actively
602 see patients and meet our inclusion criteria (based on patient-deidentified
603 electronic health record data on test ordering rates during annual physicals).
604 We will then recruit at least 10 patients for each of these PCPs. We will allow
605 up to 20 patients per physician in the enrollment phase to ensure adequate
606 sampling in case of loss to follow-up. All patients of the selected PCPs who
607 are at least 18 years old, speak English, have access to email, and have not

608 opted-out of receiving research invitations from Mass General Brigham are
609 eligible to participate.

610

611 Briefly describe study procedures. Include any local site restrictions, for example, “Subjects
612 enrolled at Partners will not participate in the pharmacokinetic portion of the study.” Describe
613 study endpoints.

614

615 In phase I, we will develop a multi-pronged intervention for patients and
616 clinicians. To this end, we will work with the BWH Center for Patients and
617 Families to select and convene a 5-15 member patient advisory council. We
618 will host two focus groups with this council, aided by discussion guides, to
619 first identify key issues and then to suggest refinements to our intervention.

620

621 We will also recruit both patients and physicians for in-depth interviews. We
622 will recruit up to 20 primary care physicians through the Patient-Based
623 Research Network (PBRN) and suggestions from clinic medical directors. We
624 will recruit up to 20 patients through the above Patient Advisory Council and
625 the Rally platform. We will conduct up to 20 in-depth interviews each with
626 these physicians and patients to understand their experiences with cascades
627 and to cognitively test survey items.

628

629 Finally, we will review patient educational materials, clinician references, and
630 clinician peer comparison emails with clinic leaders for their approval.

631

632 In phase II, we will work with clinic leaders in the BWH PBRN to recruit 20
633 physicians who have not previously been involved. We will select these
634 physicians from among those who fall above the 25th percentile of test
635 ordering rates during annual physicals. We will use matched pair
636 randomization by testing rate and gender to randomize these PCPs to the
637 control or intervention arms. For each physician, we will identify at least 10
638 of their patients who are scheduled for a physical in the next 6 months and
639 meet our inclusion criteria. We will recruit them using patient portal
640 messages.

641

642 Intervention arm: We will send emails to physicians with feedback on how
643 they compare to their peers in aggregate on test ordering during annual

644 physicals, along with links to the physician-facing materials. We will not
645 share identifiable data with a given physician on their peer physicians. One
646 to two days before their visit, we will send patients educational materials via
647 text and email.

648

649 Control arm: One to two days before their visit, we will send patients general
650 information on visit preparation.

651

652 We will perform an exploratory chart review analysis of visits in the
653 intervention and control arms to assess any documentation of discussion
654 about medical testing and ordering of medical tests. Specifically, we will
655 record physical visit note details on medical test conversations and medical
656 tests ordered. This will help us understand if the intervention may have
657 influenced ordering practices.

658

659 **NOTE:** We acknowledge that during the COVID-19 pandemic, clinical
660 operations have changed drastically to protect both patients and health care
661 workers. For instance, routine wellness visits have been cancelled or
662 converted to virtual. Given our commitment to protect the safety and
663 welfare of our study subjects and staff, and to avoid disrupting clinic
664 operations during this challenging time, we plan to conduct phase I of our
665 study virtually and to begin the intervention phase only once it is deemed
666 safe and feasible to do so.

667

668

669 For studies involving treatment or diagnosis, provide information about standard of care at
670 Partners (e.g., BWH, MGH) and indicate how the study procedures differ from standard care.
671 Provide information on available alternative treatments, procedures, or methods of diagnosis.

672

673 Treatment and diagnosis are not part of this protocol.

674

675 Describe how risks to subjects are minimized, for example, by using procedures which are
676 consistent with sound research design and which do not unnecessarily expose subjects to risk
677 or by using procedures already being performed on the subject for diagnostic or treatment
678 purposes.

679

680 There are no known risks to participating in this study. Patient and clinician
681 subjects may voluntarily participate and withdraw at any time.

682

683 There is a theoretical risk of breach of data confidentiality and that PHI could
684 become known to unauthorized persons, but we will take all steps necessary
685 to protect PHI (see below). To mitigate this risk, we will follow all compliance
686 and data confidentiality procedures for research at Partners. Specifically, we
687 will use procedures consistent with sound research design and which do not
688 expose subjects to unnecessary risk. Data monitoring will be conducted
689 regularly (see below). All data analyzed will be de-identified and reported in
690 aggregate.

691

692 Describe explicitly the methods for ensuring the safety of subjects. Provide objective criteria
693 for removing a subject from the study, for example, objective criteria for worsening
694 disease/lack of improvement and/or unacceptable adverse events. The inclusion of objective
695 drop criteria is especially important in studies designed with placebo control groups.

696

697 **This is a minimal risk study.** There is no known physical or medical safety
698 threat to patient or clinician subjects who participate. Furthermore,
699 participation is voluntary and all subjects will be informed that they may opt-
700 out any time (see below). Given the minimal risk to subjects, our data safety
701 and monitoring procedures, and the relatively small sample size, we do not
702 plan on having drop criteria.

703

704 **FORESEEABLE RISKS AND DISCOMFORTS**

705 Provide a brief description of any foreseeable risks and discomforts to subjects. Include those
706 related to drugs/devices/procedures being studied and/or administered/performed solely for
707 research purposes. In addition, include psychosocial risks, and risks related to privacy and
708 confidentiality. When applicable, describe risks to a developing fetus or nursing infant.

709

710 **For patient and clinician subjects, there are no known risks to**
711 **participating in our data collection activities.** There is a potential risk of
712 physicians feeling psychological discomfort in knowing their test ordering
713 rates. We will mitigate this by offering an option if they have concerns to
714 speak with clinic leaders about these concerns. The main risks are breach of

715 confidentiality and privacy of information shared. Every effort will be made
716 to maintain confidentiality and privacy of information shared and collected
717 and subsequent data analysis (see below), and efforts will be made to
718 minimize the duration of data collection activities.

719

720 **EXPECTED BENEFITS**

721 Describe both the expected benefits to individual subjects participating in the research and the
722 importance of the knowledge that may reasonably be expected to result from the study. Provide
723 a brief, realistic summary of potential benefits to subjects, for example, “It is hoped that the
724 treatment will result in a partial reduction in tumor size in at least 25% of the enrolled subjects.”
725 Indicate how the results of the study will benefit future patients with the disease/condition being
726 studied and/or society, e.g., through increased knowledge of human physiology or behavior,
727 improved safety, or technological advances.

728

729 Individual subjects may benefit by learning about (and, if appropriate,
730 avoiding) possible downstream consequences of medical testing, and having
731 their physicians become more informed about these consequences and how
732 to discuss them. Future patients will benefit through improved knowledge of
733 a possible intervention to facilitate patient-clinician conversations about
734 cascades that may in turn help to reduce their negative effects.

735

736 **EQUITABLE SELECTION OF SUBJECTS**

737 The risks and benefits of the research must be fairly distributed among the populations that
738 stand to benefit from it. No group of persons, for example, men, women, pregnant women,
739 children, and minorities, should be categorically excluded from the research without a good
740 scientific or ethical reason to do so. Please provide the basis for concluding that the study
741 population is representative of the population that stands to potentially benefit from this
742 research.

743

744 Our goal will be to enroll eligible patients whose characteristics are
745 representative of the entire population of eligible patients. We will
746 specifically target patients of all genders and a range of ages,
747 race/ethnicities, and education levels.

748

749 When people who do not speak English are excluded from participation in the research, provide
750 the scientific rationale for doing so. Individuals who do not speak English should not be denied
751 participation in research simply because it is inconvenient to translate the consent form in
752 different languages and to have an interpreter present.

753

754 We will approach English-speaking patients only. The scientific rationale for
755 this limitation is because the intervention will be available in English in this

756 early stage of development. All clinician subjects caring for patients at BWH
757 speak English.

758

759 For guidance, refer to the following Partners policy:
760 Obtaining and Documenting Informed Consent of Subjects who do not Speak English
761 [https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Non-](https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Non-English_Speaking_Subjects.1.10.pdf)
762 [English_Speaking_Subjects.1.10.pdf](https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Non-English_Speaking_Subjects.1.10.pdf)

763

764

765

766 **RECRUITMENT PROCEDURES**

767 Explain in detail the specific methodology that will be used to recruit subjects. Specifically
768 address how, when, where and by whom subjects will be identified and approached about
769 participation. Include any specific recruitment methods used to enhance recruitment of
770 women and minorities.

771

772 For phase I, we will recruit the PAC and physician focus groups as described
773 above.

774

775 For phase II, we will recruit physicians as described above. Eligible patient
776 subjects will then be identified by research assistants trained in the
777 protection of human subjects based on upcoming appointment using
778 “minimum necessary” information in the EHR. To meet recruitment criteria,
779 patients must not have opted out of receiving Mass General Brigham (MGB)
780 research invitations. The research assistant will send the patient recruitment
781 list and a letter created using the template provided by the MGB IRB to the
782 DHeCare Research Team to create a letter project. Following project
783 creation, the research assistant will send patients a letter through the
784 patient portal. The letter includes an email address and phone number that
785 allows patients to opt out. The letter also includes a link to REDCAP which
786 will include an electronic consent form with information sheet, invitation to
787 enroll, and the baseline survey.

788

789 Provide details of remuneration, when applicable. Even when subjects may derive medical
790 benefit from participation, it is often the case that extra hospital visits, meals at the hospital,
791 parking fees or other inconveniences will result in additional out-of-pocket expenses related to
792 study participation. Investigators may wish to consider providing reimbursement for such
793 expenses when funding is available

794

795 Patient subjects in both arms will be compensated \$10 at the completion of
796 the study. Physician subjects will be compensated \$50 for the whole study.

797

798 For guidance, refer to the following Partners policies:

799 Recruitment of Research Subjects

800 [https://partnershealthcare-](https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Recruitment_Of_Research_Subjects.pdf)
801 [public.sharepoint.com/ClinicalResearch/Recruitment_Of_Research_Subjects.pdf](https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Recruitment_Of_Research_Subjects.pdf)

802
803 Guidelines for Advertisements for Recruiting Subjects

804 [https://partnershealthcare-](https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Guidelines_For_Advertisements.1.11.pdf)
805 [public.sharepoint.com/ClinicalResearch/Guidelines_For_Advertisements.1.11.pdf](https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Guidelines_For_Advertisements.1.11.pdf)

806
807 Remuneration for Research Subjects

808 [https://partnershealthcare-](https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Remuneration_for_Research_Subjects.pdf)
809 [public.sharepoint.com/ClinicalResearch/Remuneration_for_Research_Subjects.pdf](https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Remuneration_for_Research_Subjects.pdf)

810

811

812 **CONSENT PROCEDURES**

813 Explain in detail how, when, where, and by whom consent is obtained, and the timing of
814 consent (i.e., how long subjects will be given to consider participation). For most studies
815 involving more than minimal risk and all studies involving investigational drugs/devices, a
816 licensed physician investigator must obtain informed consent. When subjects are to be
817 enrolled from among the investigators' own patients, describe how the potential for coercion
818 will be avoided.

819

820 In phase I, eligible physician subjects will be informed about our research
821 initiative via email and patients via RALLY. Prior to participation in
822 interviews, we will confirm verbal consent. Specifically, these subjects will be
823 informed that: 1) participation is voluntary—they may stop the interview at
824 any time, and 2) data collected will be analyzed and reported in aggregate.

825

826 In phase II, potential patient subjects will be informed as part of the patient
827 portal message and the REDCAP link that it will contain. This information will
828 contain the purpose of the study, risks/benefits, methods of ensuring
829 confidentiality, and voluntary nature of participation. Specifically, patient
830 subjects will be informed that: 1) participation is voluntary—they may
831 withdraw at any time; 2) a decision to not participate will in no way affect
832 their care at BWH; 3) information shared will remain confidential and used
833 only for research purposes; and 4) data collected will be analyzed and
834 reported in aggregate. We will not request verbal consent as this will be

835 prohibitively burdensome for this minimal risk study and because this study
836 does not share any personal health information with the patients.
837
838

839 NOTE: When subjects are unable to give consent due to age (minors) or impaired decision-
840 making capacity, complete the forms for Research Involving Children as Subjects of Research
841 and/or Research Involving Individuals with Impaired Decision-making Capacity, available on the
842 New Submissions page on the PHRC website:

843 <https://partnershealthcare.sharepoint.com/sites/phrmApply/aieipa/irb>
844

845 For guidance, refer to the following Partners policy:

846 Informed Consent of Research Subjects:

847 [https://partnershealthcare-](https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Informed_Consent_of_Research_Subjects.pdf)
848 [public.sharepoint.com/ClinicalResearch/Informed_Consent_of_Research_Subjects.pdf](https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Informed_Consent_of_Research_Subjects.pdf)

849

850

851

852 **DATA AND SAFETY MONITORING**

853 Describe the plan for monitoring the data to ensure the safety of subjects. The plan should
854 include a brief description of (1) the safety and/or efficacy data that will be reviewed; (2) the
855 planned frequency of review; and (3) who will be responsible for this review and for
856 determining whether the research should be altered or stopped. Include a brief description of
857 any stopping rules for the study, when appropriate. Depending upon the risk, size and
858 complexity of the study, the investigator, an expert group, an independent Data and Safety
859 Monitoring Board (DSMB) or others might be assigned primary responsibility for this monitoring
860 activity.

861

862 NOTE: Regardless of data and safety monitoring plans by the sponsor or others, the principal
863 investigator is ultimately responsible for protecting the rights, safety, and welfare of subjects
864 under his/her care.

865

866 The principal investigator and research assistant/project coordinator will
867 monitor data collection activities, maintain data integrity and quality control,
868 protect the rights, safety, and welfare of study subjects, and adhere to
869 standards set by the Partners IRB. All data will be stripped of PHI and
870 electronic data will be kept on a secured shared file area (SFA) behind the
871 Partners firewall with anti-virus software or Partners Research Computing
872 approved cloud storage services. Data about consented patients will also be

873 stored behind the RAND Corporation firewall in accordance with the terms of
874 the consent. Any paper forms and/or audio recordings will be destroyed after
875 being transcribed into electronic format. Monitoring will be performed on a
876 monthly basis during the study period and will include a review of
877 enrollment, data analysis, and breaches of confidentiality, and any adverse
878 events that may occur. Any adverse events will be graded as to their
879 attribution to the intervention and reported according to IRB guidelines. The
880 principal investigator will review any complaints reported from patient and
881 physician subjects. These will be reported to the Partners IRB annually or
882 immediately if the complaint is serious. Given the minimal risk of the study,
883 we are not planning to use automatic stopping rules or a DSMB. We
884 emphasize that this study does not involve any invasive procedures.

885

886 Describe the plan to be followed by the Principal Investigator/study staff for review of adverse
887 events experienced by subjects under his/her care, and when applicable, for review of sponsor
888 safety reports and DSMB reports. Describe the plan for reporting adverse events to the sponsor
889 and the Partners' IRB and, when applicable, for submitting sponsor safety reports and DSMB
890 reports to the Partners' IRBs. When the investigator is also the sponsor of the IND/IDE, include
891 the plan for reporting of adverse events to the FDA and, when applicable, to investigators at
892 other sites.

893

894 NOTE: In addition to the adverse event reporting requirements of the sponsor, the principal
895 investigator must follow the Partners Human Research Committee guidelines for Adverse Event
896 Reporting

897

898 Voluntary participation in data collection activities are not expected to cause
899 adverse events to patient or physician subjects. However, if an adverse
900 event occurs, the principal investigator will follow PHS HRC guidelines for
901 adverse event reporting.

902

903 **MONITORING AND QUALITY ASSURANCE**

904 Describe the plan to be followed by the principal investigator/study staff to monitor and assure
905 the validity and integrity of the data and adherence to the IRB-approved protocol. Specify who
906 will be responsible for monitoring, and the planned frequency of monitoring. For example,
907 specify who will review the accuracy and completeness of case report form entries, source
908 documents, and informed consent.

909

910 NOTE: Regardless of monitoring plans by the sponsor or others, the principal investigator is
911 ultimately responsible for ensuring that the study is conducted at his/her investigative site in

912 accordance with the IRB-approved protocol, and applicable regulations and requirements of the
913 IRB.

914

915 The principal investigator and research assistant/project coordinator will
916 monitor and assure the validity and integrity of the data collection and
917 adherence to the procedures outlined in this protocol. They will review the
918 study database on a monthly basis, ensuring data integrity, accuracy, and
919 completeness. The principal investigator will supervise the research
920 assistant/project coordinator in all data collection activities over the course
921 of the study.
922

923 For guidance, refer to the following Partners policies:

924 Data and Safety Monitoring Plans and Quality Assurance
925 [https://partnershealthcare-](https://partnershealthcare-public.sharepoint.com/ClinicalResearch/DSMP_in_Human_Subjects_Research.pdf)
926 [public.sharepoint.com/ClinicalResearch/DSMP in Human Subjects Research.pdf](https://partnershealthcare-public.sharepoint.com/ClinicalResearch/DSMP_in_Human_Subjects_Research.pdf)

927

928 Reporting Unanticipated Problems (including Adverse Events)

929 [https://partnershealthcare-](https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Reporting_Unanticipated_Problems_including_Adverse_Events.pdf)
930 [public.sharepoint.com/ClinicalResearch/Reporting Unanticipated Problems including Adverse Even](https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Reporting_Unanticipated_Problems_including_Adverse_Events.pdf)
931 [ts.pdf](https://partnershealthcare-public.sharepoint.com/ClinicalResearch/Reporting_Unanticipated_Problems_including_Adverse_Events.pdf)

932

933

934

935 **PRIVACY AND CONFIDENTIALITY**

936 Describe methods used to protect the privacy of subjects and maintain confidentiality of data
937 collected. This typically includes such practices as substituting codes for names and/or medical
938 record numbers; removing face sheets or other identifiers from completed
939 surveys/questionnaires; proper disposal of printed computer data; limited access to study data;
940 use of password-protected computer databases; training for research staff on the importance of
941 confidentiality of data, and storing research records in a secure location.
942

943 NOTE: Additional measures, such as obtaining a Certificate of Confidentiality, should be
944 considered and are strongly encouraged when the research involves the collection of sensitive
945 data, such as sexual, criminal or illegal behaviors.

946

947 All information from individuals or entities in the course of this study that
948 identifies an individual or entity will be treated as confidential in accordance
949 with section 903c of the Public Health Service Act (42 U.S.C.299a-1). This
950 will be done by keeping all personal identifiers in a separate location from
951 the data, and only approved research personnel and study investigators
952 trained in the protection of human subjects will have access to the linked
953 data. All research staff will be properly trained in the importance of
954 confidentiality of data.

955
956 All electronic data and files will be stored on a password-protected database
957 in a shared file area (SFA) on a Partners password-protected computer
958 behind the Partners firewall with anti-virus software or on Partners Research
959 Computing approved cloud storage services. Data about consented patients
960 will also be stored behind the RAND Corporation firewall in accordance with
961 the terms of the consent. Patients' identifiers and other data collected on
962 paper will be kept in locked filing cabinets. Data collection instruments used
963 during the project and stored on laptop or desktop computers will also be
964 password protected. Printed computer data with PHI will be shredded and
965 disposed of upon completion of the study and any record-keeping
966 requirements. Any identifiers will be removed prior to any analysis and all
967 results will be presented in aggregate. The principal investigator will be
968 responsible for the confidentiality and security of all study databases. These
969 measures should be effective in preventing breaches of confidentiality.
970

971 **SENDING SPECIMENS/DATA TO RESEARCH COLLABORATORS OUTSIDE**
972 **PARTNERS**

973 Specimens or data collected by Partners investigators will be sent to research collaborators
974 outside Partners, indicate to whom specimens/data will be sent, what information will be sent,
975 and whether the specimens/data will contain identifiers that could be used by the outside
976 collaborators to link the specimens/data to individual subjects.

977

978 No specimens or data will be sent to anyone outside of BWH.

979

980 Specifically address whether specimens/data will be stored at collaborating sites outside
981 Partners for future use not described in the protocol. Include whether subjects can withdraw
982 their specimens/data, and how they would do so. When appropriate, submit documentation of
983 IRB approval from the recipient institution.

984

985 Not applicable.

986

987 **RECEIVING SPECIMENS/DATA FROM RESEARCH COLLABORATORS OUTSIDE**
988 **PARTNERS**

989 When specimens or data collected by research collaborators outside Partners will be sent to
990 Partners investigators, indicate from where the specimens/data will be obtained and whether
991 the specimens/data will contain identifiers that could be used by Partners investigators to link
992 the specimens/data to individual subjects. When appropriate, submit documentation of IRB
993 approval and a copy of the IRB-approved consent form from the institution where the
994 specimens/data were collected.

995

996 No specimens or data will be received from anyone outside of BWH.

997

998

999 **Statistical Analysis Plan**

1000

1001 **Measures**

1002 **Outcomes:** The primary outcome will be the Shared Decision-Making Process survey
1003 (SDMP_4 score), a 4 item measure that is validated as a patient-reported outcome performance
1004 measure. Each response will be scored as binary and added for a range of 0-4. Patient-level
1005 secondary outcomes will be presence of a testing discussion, satisfaction with the testing
1006 discussion, presence of a discussion of next steps, whether the doctor explained tests in a way
1007 that was easy to understand, and patient knowledge (a score of 0-4 based on correct responses
1008 to each of 4 knowledge survey items). Patient-level exploratory outcomes will include patients'
1009 survey responses about which tests were discussed, who raised the idea of tests, and the
1010 importance of various factors in testing decisions. Physician-level exploratory outcomes will
1011 include the importance of various factors in testing decisions, consideration of patient out-of-
1012 pocket costs in clinical decisions, self-reported discussion with patients about false positives,
1013 incidental findings, and cascades, and barriers to cascade conversations.

1014

1015 Among intervention group patients, we will use server log data to count how many viewed the
1016 website. This will produce a lower-bound estimate as some participants may copy-paste the link
1017 without the code to view the website, preventing us from tracking those views.

1018

1019 **Physician characteristics:** Time since residency, gender, race, ethnicity, time in outpatient
1020 practice, and prior experience with cascades (all from pre-study survey).

1021

1022 **Patient characteristics:** Age, gender, race, ethnicity, education (from pre-study survey),
1023 primary insurance (from electronic health record), time with PCP (from post-study survey),
1024 approach to medical action, decision-making preferences, and health literacy (from pre-study
1025 survey).

1026

1027 **Quantitative Analysis**

1028 Our primary analysis will be Intention to Treat with multiple imputation of missing outcomes. We
1029 will summarize all data using simple descriptive statistics (means with standard deviations for
1030 continuous variables and frequencies with percentages for categorical variables) overall and in
1031 each arm. We will compare baseline characteristics between physicians in each group using t-
1032 tests and chi-square tests as appropriate and accounting for clustering by matched pair and by
1033 physician nested within matched pair. We will then summarize and compare baseline
1034 characteristics among 1) all enrolled patients in each group, 2) enrolled patients in each group
1035 with missing post-study surveys, and 3) enrolled patients in each group who completed post-
1036 study surveys (final sample), using t-tests and chi square tests as appropriate and clustering
1037 standard errors by matched pair and by physician nested within matched pair.

1038

1039 To estimate differences between intervention and control groups in our primary and secondary
1040 outcomes, we will use linear regression models (generalized estimating equations (GEE))
1041 adjusted for patient age, gender, race/ethnicity, and education (because these covariates may
1042 be associated with the primary outcome) and any additional baseline covariates in the model
1043 that exhibit significant differences ($p < 0.05$) between groups. We will also include standard errors
1044 clustered by matched pair and by physician nested within matched pair. Linear regression using

1045 GEE to compare mean scores between treatment and control groups is robust to non-normality
1046 of the outcomes.

1047
1048 We estimate that we will have >80% power to detect a 0.5 standard deviation difference in the
1049 SDMP_4 measure between the intervention and control arms based on an expected sample of
1050 200 patient-visits and a 2-sided type I error rate of 5% and assuming intra-cluster correlation
1051 coefficient (ICC) for patients from the same physician of 0.05.

1052
1053 *Exploratory analysis of the primary outcome:* To explore how the effect of the intervention on the
1054 primary and secondary outcomes varies within relevant population strata, we will repeat these
1055 analyses after stratifying patients by physician gender (male vs female), time with PCP
1056 (dichotomized), and health care preferences (wait and see vs taking action, make decisions vs
1057 defer decisions).

1058
1059 *Analysis of patient-level exploratory outcomes* – We will build GEE linear models with
1060 adjustment as described above.

1061
1062 *Analysis of physician-level exploratory outcomes* – We will use paired t-tests to compare
1063 intervention and control group physicians on pre-post differences in their responses to survey
1064 items on factors in testing decisions, consideration of patient out-of-pocket costs; self-reported
1065 discussion with patients about false positives, incidental findings, and cascades; and barriers to
1066 cascade conversations.

1067
1068 We will use R statistical software for data analysis and consider 2-sided P values to be
1069 significant at <0.05.

1070 1071 **Qualitative Analysis**

1072 We will transcribe patient and physician interviews and will use an inductive thematic approach
1073 to analyze these qualitative data. Specifically, study authors will develop a code book, code the
1074 data using deductive (based on the interview guides) and inductive (based on categories that
1075 emerge during analysis) methods, resolve coding differences by consensus, and identify key
1076 categories and themes.

1077
1078
1079