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Evaluation of a Multi-modal, Direct-to-Patient Educational Intervention Targeting Barriers to Osteoporosis Care: A Randomized Clinical Trial

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Abstract

Osteoporosis treatment rates are declining, even among those with past fractures. Novel, low-cost approaches are needed to improve osteoporosis care. We conducted a parallel group, controlled, randomized clinical trial evaluating a behavioral intervention for improving osteoporosis medication use. A total of 2,684 women with self-reported fracture history after age 45 not using osteoporosis therapy from U.S. Global Longitudinal study of Osteoporosis in Women (GLOW) sites were randomized 1:1 to receive a multi-modal, tailored, direct-to-patient, video intervention vs. usual care. The primary study outcome was self-report of osteoporosis medication use at 6-months. Other outcomes included calcium and vitamin D supplementation, bone mineral density

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(BMD) testing, readiness for behavioral change, and barriers to treatment. In intent-to-treat analyses there were no significant differences between groups (intervention vs control) in osteoporosis medication use (11.7% vs 11.4%, p=0.8), calcium supplementation (31.8% vs 32.6%, p=0.7), vitamin D intake (41.3% vs. 41.9%, p=0.8) or BMD testing (61.8% vs 57.1%, p=0.2). In the intervention group, fewer women were in the pre-contemplative stage of behavior change, more women reported seeing their primary care provider, had concerns regarding osteonecrosis of the jaw, and difficulty in taking/remembering to take osteoporosis medications. We found differences in BMD testing among the subgroup of women with no prior osteoporosis treatment, those who provided contact information, and those with no past BMD testing. In per protocol analyses, women with appreciable exposure to the online intervention (N=257) were more likely to start non-bisphosphonates (OR=2.70 [1.26, 5.79]) compared to usual care group. While our intervention did not increase the use of osteoporosis therapy at 6-months, it increased non-bisphosphonate medication use and BMD testing in select subgroups, shifted participant's readiness for behavior change, and altered perceptions of barriers to osteoporosis treatment. Achieving changes in osteoporosis care using patient activation approaches alone is challenging.

Trial Registration—clinicaltrials.gov identifier: NCT01907269

Despite medications that lower fracture risk at some sites by more than 50% [1–4] and guidelines endorsing the need for treatment following a fracture,[5] many fragility fracture patients fail to receive osteoporosis treatment,[2, 6] and do not associate their fracture with osteoporosis.[7] Some women consider osteoporosis as benign, do not associate fractures with osteoporosis and view osteoporosis as a natural process of aging. [8] As a result, there is a growing "osteoporosis care gap".[9, 10] Perceived barriers to osteoporosis treatment include concerns about medication side effects, polypharmacy, and limited drug efficacy.[11–16] Addressing patient barriers through interventions designed to overcome and modify patient perceptions may improve osteoporosis care.[16]

Multifaceted interventions may increase the diagnosis and treatment of osteoporosis.[17–20] Many studies have attempted to improve osteoporosis care through physician-targeted interventions with limited success.[21–28] Those that have evaluated direct-to-patient interventions[29–37] include post-fracture care coordination[36, 37] and patient activation promoting better participation in osteoporosis care.[29–35] The latter have shown somewhat favorable results for osteoporosis outcomes including patient knowledge,[33–35] calcium intake,[30] physical activity,[31] and bone mineral density (BMD) testing.[29] However, most of the low-cost, effective, and generalizable direct-to-patient interventions aimed at improving care have largely been limited to other chronic conditions, such as hypertension[38] or HIV medication adherence.[39]

In an attempt to improve rates of osteoporosis treatment among a high-risk population who previously reported a fracture but currently were not using osteoporosis therapies, we designed a multi-modal, patient-centered, tailored, video-based behavioral intervention, to encourage patients to seek osteoporosis diagnosis and treatment.[16] Our intervention was implemented and evaluated in the Activating Patients at Risk for OsteoPorOsiS (APROPOS) study, targeting participants within the Global Longitudinal study of Osteoporosis in Women (GLOW) cohort.[16]

Methods

Study Design and Participants

The APROPOS study was a parallel, controlled, randomized clinical trial, in which participants received either usual care alone (control group), or in combination with a multi-modal, patient-tailored, behavioral intervention (intervention group).[16] APROPOS was nested within the GLOW cohort,[40] an international, prospective, observational study of women 55+ years of age. The participants in APROPOS were enrolled from 7 U.S. GLOW sites (Birmingham, AL; Los Angeles, CA; Worcester, MA; New York, NY; Cincinnati, OH; Pittsburgh, PA; Seattle, WA). Human subject protocols and consent procedures were reviewed and approved by each site's Institutional Review Board.

GLOW participants were preliminarily eligible for APROPOS if on one of the five GLOW surveys they self-reported a fracture after age 45. In September 2013, we mailed baseline questionnaires to 4,928 preliminarily eligible GLOW participants; 3,226 (64%) completed baseline surveys, of which 2,684 women, who did not report currently using osteoporosis medication (the second eligibility criteria) besides estrogen, formed the APROPOS study population, and were randomized.

Randomization

We performed stratified randomization by site, self-reported history of osteoporosis treatment, whether contact information was supplied, and whether barriers to osteoporosis treatment were disclosed on the APROPOS baseline survey.[16] In each stratum, patients were randomly assigned to control and intervention groups in a 1:1 ratio using computer-generated lists of random numbers. The allocation of patients was made by a statistician (DTR) without knowledge of the participants' details. Study investigators were not blinded to the intervention assignment.

Intervention

Development of the behavioral intervention employed in APROPOS has been previously described.[16] Our personalized, direct-to-patient intervention included video vignettes was grounded in the principles of narrative communication ("storytelling"),[41, 42] and guided by the constructs of the Information, Motivation and Behavioral skills model.[43] These vignettes contained stories developed from actual osteoporosis patients' experiences portrayed by actresses of patient-identified race/ethnicity. The videos were tailored according to participant's reported race/ethnicity and perceived barriers ranked by participants (e.g., general fears of medications, preference for alternative therapies, concerns about long-term adverse events),[12] or readiness for behavior change, or osteoporosis treatment history. The videos utilized in APROPOS are available at: https://www.youtube.com/channel/UCH3RCRlNvr5B7iuw9tOqQBg/playlists?view_as=public.

The intervention materials were emailed as a hyperlink to a personalized webpage and also mailed in a DVD format. The intervention included three components: (1) an introduction video explaining the reason for receiving the materials, (2) personalized videos addressing barriers to osteoporosis therapy or presenting general osteoporosis information (for those

who did not rank barriers to treatment), and (3) a video on "How to communicate with your doctor about bone health" to encourage discussions between participants and their health care provider.[44] The duration of the video intervention program ranged between approximately 5 and 15 minutes. The intervention also included follow-up telephone calls and interactive voice response system (IVR) reminders to view the videos for participants that had not logged on to the intervention online. In the subgroup who viewed the intervention online, we defined appreciable exposure to the intervention as a participant logging on and viewing at least 20 seconds (e.g., the duration of 2 testimonials in the introductory video duration) of their personalized intervention.

Baseline Data Collection

A baseline questionnaire[40, 45] evaluated use of osteoporosis prescription medication and dietary supplements, fracture and general health history, perceived ability to communicate with health care providers about bone health,[46] health literacy,[47] and items from the Patients' Views about Osteoporosis and Use of Therapy scale.[12] Respondents ranked up to three of the nine potentially modifiable barriers to osteoporosis treatment, which were defined using qualitative methods involving nominal groups and expert opinion.[16] We also assessed participants' readiness for behavior change using a modified form of the Weinstein Precaution Adoption Process Model (PAPM).[48] We defined pre-contemplative participants as those that had no intent of initiating osteoporosis treatment and self-classified in the unaware and unengaged stages of PAPM.[16] Contemplative participants, defined by the undecided, decided not to act, and decided to act stages of PAPM, were those individuals considering their decision about starting treatment for osteoporosis.[49]

Outcomes and Follow-up

The primary study outcome was self-report of current osteoporosis medication use including: a) bisphosphonate (risedronate, alendronate, ibandronate, zoledronic acid), and b) non-bisphosphonate (raloxifene, teriparatide, calcitonin, denosumab) medications at 6-months. Secondary outcomes were self-reported initiation of calcium and/or vitamin D supplementation, and receipt of BMD testing at 6-months. The follow-up surveys also collected data on exploratory outcomes: barriers to osteoporosis treatment, discussion with health care provider regarding bone health, engagement with intervention components, comorbid medical conditions, fracture history, items from the Patients' Views about Osteoporosis and Use of Therapy scale.[12] In addition, for participants who accessed the intervention online, we objectively assessed their intervention viewing duration. We also examined osteoporosis care (osteoporosis medication use, BMD testing) at 18-months to account for possible delay in healthcare access.

Statistical Analyses

Assuming that 10% of participants in the control arm would start osteoporosis medication during the study period, we determined that a sample size of 1,342 per group would provide greater than 80% power to detect a 4% absolute difference between the randomized groups in the proportion of new osteoporosis medication use, using a two-sided test at alpha 0.05. We imputed missing data based on available baseline APROPOS and previous GLOW surveys, assuming data missing at random. In intent-to-treat analyses we compared primary,

secondary, and exploratory outcomes between the randomized groups at 6- and 18-months. In per protocol analyses we compared participants who had appreciable intervention exposure online to the control group for the following outcomes: self-report of osteoporosis treatment, BMD testing, stage of behavioral change and barriers to treatment. We examined the data for the heterogeneity of treatment effects by an aggregate of likely fragility fractures (any fracture except skull, hands, feet, fingers, toes), sites for major osteoporotic fractures (hip, spine, wrist, humerus), perceived fracture risk, treatment barriers, prior osteoporosis medication use, supplied phone number or email address, and readiness for behavior change.

We used means and standard deviations (SD) to describe continuous variables and proportions for categorical variables. Chi square tests and multivariable logistic regression were used to compare outcomes between the control and intervention, or appreciable exposure to the intervention groups, respectively. We report odds ratios (OR) and adjusted OR (aOR) as results of these analyses. In multivariable logistic regression models we included as covariates those baseline variables, which were found at $p<0.10$ to be associated with both appreciable intervention exposure and the outcomes considered in the analyses. These covariates included the following characteristics: age, race, education, health literacy, email/phone number being provided, self-rated risk of fracture, prior osteoporosis treatment, BMD testing, and general health. The criterion for statistical significance was $p<0.05$. No multiple comparison adjustment was performed. All analyses were conducted in SAS (v9.3, Enterprise Guide v4.3, Cary, NC).

Results

Characteristics of the Participants at Study Baseline

As seen in the CONSORT (Consolidated Standards of Reporting Trials) diagram for the study (Figure 1), we randomized the 2,684 women recruited (September 2013) in the APROPOS study and performed survey follow-up at 6 (May-June 2015) and 18 (June 2016) months following our intervention deployment. Socio-demographic, clinical and osteoporosis-related characteristics of the participants by group assignment, including those who had appreciable intervention online exposure (N=257 [19.2%]) are presented in Table 1. Overall, the study participants were predominately Caucasian, had mean ages in mid-seventies, were college educated (76.7%), in good or excellent health (84.6%), and were using vitamin D or calcium supplementation. Fewer than 10% of women had sustained a fracture in the 12 months prior to randomization. There were no significant differences in socio-demographic characteristics between intervention or control group (Table 1).

Compared with women assigned to the control group, those who had appreciable exposure to the intervention materials were more likely to be Caucasian, supply contact information, report good or excellent general health, have adequate health literacy, and have previously used osteoporosis medications (Table 1).

Intent-to-treat Analysis of the Outcomes

A total of 1,123 (83.7%) women in the intervention group and 1,079 (80.4%) in the control group reported seeing their primary health care provider in the 6-months following

intervention deployment (OR=1.25, 95% CI [1.21, 1.30]) (Table 2), and 583 (43.4%) vs. 573 (42.7%) women reported talking with a health care provider about bone health in the intervention vs. control group, respectively (p=0.74).

For the primary outcome, 157 (11.7%) and 153 (11.4%) women self-reported use of osteoporosis prescription medication in the intervention and control groups, respectively (p=0.83) (Table 2). Similarly, we observed no significant differences by study group in the secondary outcomes (starting calcium; starting vitamin D; and BMD testing). Osteoporosis care rates were not different between the intervention and the control groups at 18 months: 131 (11.5%) women in the intervention group and 136 (10.5%) women in the control group started osteoporosis medications (p=0.47); and 530 (82.4%) women in the intervention group and 522 (78.7%) reported having DXA scan one year after the 6-months survey (p=0.09).

For exploratory outcomes, we found that our behavioral intervention influenced participants' readiness for behavior change at 6-months, with a significantly lower proportion of participants in the pre-contemplative stage in the intervention compared to control group (860 [64.1%] vs. 923 [68.8%], OR=0.90 [0.82, 0.99]) (Table 2). In addition, compared with the control group, at 6-months participants in the intervention group were slightly more likely to report being concerned about treatment barriers that included osteonecrosis of the jaw (387 [28.9%] vs 331 [24.6%], OR=1.11 [1.01, 1.23]) and difficulty in taking/remembering to take osteoporosis medications (295 [22.0%] vs 242 [18.1%], OR=1.13 [1.01, 1.26]).

Analyses of Heterogeneity of Treatment Effects (Subgroups)

We found significant differences in self-reported BMD testing among the subgroup of women with no prior osteoporosis treatment (OR=1.30 [1.01, 1.66]), among those who provided contact information (OR=1.33 [1.01, 1.74]), and among those who did not report past BMD testing (OR=1.53 [1.40, 1.68]) (Figure 2A). There were no significant intervention effects for primary and secondary outcomes among the subgroup of women with past fragility fractures or major osteoporotic fractures. Additionally, there were no significant intervention effects for self-reported receipt of osteoporosis medication, initiation of calcium or vitamin D, or for BMD testing in subgroups of women with self-reported barriers to osteoporosis treatment or history of past osteoporosis treatment. Subgroups defined by general health rating, perceived fracture risk, readiness to behavior change, visit with primary care provider, discussion with physician about bone health, and contact information availability did not exhibit differential intervention effects.

Per Protocol Analyses

Follow-up surveys at 6-months were completed by 2,006 (74.7%) women. Compared to the control group, at 6-months a significantly greater proportion of women in the intervention group failed to complete the follow-up survey (29.0% vs 21.5%, p= 0.0001).

Figure 1S in the Supplemental Materials presents the distribution of the duration of interaction with the intervention materials. Among those who watched for at least 20 seconds the mean (SD) duration of exposure to the educational materials was 389 (374)

seconds, with a median viewing time of 346 seconds. The proportion of self-reported osteoporosis treatment was similar between those with appreciable exposure to the online intervention compared with the control group (aOR=1.22 [0.73, 2.04]) at 6-months (Figure 2B). However, women with appreciable exposure to the intervention were more likely than those in the control group to report starting non-bisphosphonate osteoporosis medications (11 [4.5%] vs 23 [1.8%], OR=2.70[1.26, 5.79]) (Table 3), which remained significant at 18-months (12 [6.5%] vs 24 [2.7%], OR=2.54 [1.22, 5.29]). Of note, nine of the women who took non-bisphosphonate drugs at 18-months in the intervention group were also taking them at 6-months suggesting persistence on osteoporosis therapy. Compared to the control group, those with appreciable exposure to intervention materials were more likely to report being concerned about osteonecrosis of the jaw and to be in the contemplative stage of behavioral change (Table 3). Those who watched longer than the median viewing time (see Figure S1) had similar outcomes as those who we defined earlier as having appreciable exposure to the intervention.

Discussion

The APROPOS study tested the effectiveness of a multi-modal tailored, patient-directed, behavioral intervention to improve the rates of osteoporosis treatment in women at high risk for future fracture. Among more than 2,500 participants, there were no significant differences in rates of self-reported initiation of osteoporosis treatment, or BMD testing between groups at 6- and 18-months. However, among women who had appreciable exposure to the intervention, we found an increase in non-bisphosphonate medication use. Women with no prior osteoporosis treatment, as well as those who supplied an email address and phone number, were more likely to report BMD testing at 6-months. Taken together our findings in specific subgroups and per protocol analyses indicate that our intervention approach may have potential to improve osteoporosis care and that further refinement of our strategy is needed. We observed that the rate of osteoporosis treatment initiation was ~11% in APROPOS, similar to low rates of osteoporosis pharmacotherapy initiation in high-risk women nationally.[50, 51] This low rate of treatment initiation emphasizes the sizable challenges in encouraging women who have already experienced a fracture to initiate osteoporosis treatment. Using self-reported fracture history to ascertain past fractures may be subject to recall bias and may misclassify future fracture risk, which potentially represents a limitation to our study. However, self-reported fracture history is a relatively well-accepted and validated approach to fracture ascertainment, which has been used in past large epidemiological studies. [52–54] In addition, for some women that participated in our study, osteoporosis medications might not have been indicated because they lacked sufficient prior history of a fragility fracture.

Influencing a person’s behavior to initiate treatment through a behavioral intervention is a multi-stage process. The behavioral intervention we employed in APROPOS addressed the early steps of this pathway from lack of awareness to action, steps that encompass the construct of readiness for behavior change.[55, 56] We observed that women in the intervention group were less likely to be pre-contemplative compared to those in the control group, a finding suggesting that they had transitioned to a decision making-stage and were considering whether to pursue osteoporosis treatment and/or testing. Despite the significant

effect of the APROPOS intervention on participants' readiness for behavioral change, a large proportion of women in the intervention group remained pre-contemplative. A potential explanation may be the belief held by some APROPOS women about their low risk for future fracture, as previously noted in the GLOW cohort[57, 58] and by others.[59, 60] The perception of a low personal susceptibility to future fracture, even among women who have previously fractured, is concordant with reluctance to acknowledge personal susceptibility to health problems[61] (e.g. osteoporosis). This may have acted as a barrier to engaging in osteoporosis management within APROPOS. A possible explanation for the low rate of osteoporosis medication initiation in our study may stem from participants having difficulty trusting the content of the video vignettes included in the intervention, since these educational materials were not endorsed by a source familiar to the patient (e.g. their treating physician).

Timing of the intervention with regard to a previous fracture may influence the relevance of adopting osteoporosis treatment. Consonant with the concept of a "teachable moment," persons may be more receptive to adopting behavior change[62] when engaged by an intervention shortly after a fracture rather than months/years later. In APROPOS, a very low proportion of participants reported a fracture in the 12-months prior to the intervention deployment; thus, the intervention may have reached the participants at a suboptimal time. In another study, patients who received advice to discuss osteoporosis with their physician immediately after hip fracture repair were more likely to receive appropriate therapeutic intervention.[63] In addition, a meta-analysis of osteoporosis interventions demonstrated that more intensive interventions involving care coordination for secondary fracture prevention can impact both BMD testing and treatment initiation.[64] However, these more intensive and costly approaches may work within select settings such as managed health care [36, 37] or in countries offering socialized medicine, but have limited generalizability to all care environments.

We developed our highly personalized intervention taking into account each participant's own health. Interestingly, the intervention paradoxically increased participants' knowledge/concerns of barriers to osteoporosis treatment, with more women in the intervention group reporting fears of osteonecrosis of the jaw and/or difficulty in taking/remembering to take osteoporosis medications. Osteonecrosis of the jaw concern was an important barrier to treatment reported in GLOW and other studies, leading us to develop educational content to overcome potential concerns about this very rare event. Our findings suggest that materials addressing treatment barriers could inadvertently increase anxiety (i.e., nocebo effect) and lead to less treatment initiation. This finding is similar to the observation that media attention to high-consequence, low-probability adverse effects may raise the patient's knowledge, risk perceptions, and reporting, and thus result in non-adherence.[65–69]

The success of a behavioral intervention is influenced by the participants' engagement. Despite efforts to encourage its uptake, just under 30 percent of participants accessed the intervention online,[16] and the proportion of participants who interacted appreciably with the intervention was even lower. Considering that the participants were required to self-initiate the personalized video program, engagement with the online intervention in APROPOS was relatively high compared to other studies.[70, 71] However, implementing an

online intervention in a population with an average age of 74 years might have contributed to its relatively low uptake, because older age groups are generally thought to be less technology inclined. We partially mitigated this issue by also mailing DVD players and DVDs containing the intervention materials.

For our approach to be successful, once individuals decide to take action they need to effectively communicate their preferences to health care providers. Initiating such communication may be a difficult conversation and intervention group participants could not directly control whether their physician prescribed osteoporosis treatment or testing. Our results are concordant with others showing that patient activation interventions alone, without offering direct engagement in care,[29, 72] may not improve the rates of osteoporosis testing or treatment initiation.[73–75] Therefore, despite the limited success[21–28] in improving osteoporosis care through physician-targeted interventions, combining tailored, patient-directed interventions with physician-targeted interventions could prove to be a fruitful strategy in advancing osteoporosis care.

In APROPOS, we tried to create a highly tailored intervention by identifying modifiable barriers to osteoporosis treatment, but some participants failed to list any treatment barriers or ranked several barriers equally.[16] This demonstrates the difficulty of consistently capturing treatment barrier information, which is essential to developing an intervention individually tailored, as we intended. Because ~ 65% of the patients received previous osteoporosis treatments, it is possible that prior treatment may have influenced the patient perception of need to take future osteoporosis medications In addition, many salient characteristics of optimal tailoring for osteoporosis behavior change may be unknown.

In conclusion, achieving changes in osteoporosis care using patient activation approaches is challenging. While our personalized, multi-modal behavioral intervention did not increase the use of osteoporosis therapy at 6-months, it increased non-bisphosphonate medication use and BMD testing in select subgroups, shifted participant's readiness for behavior change, and altered perceptions of common barriers to osteoporosis treatment within exploratory analyses, suggesting future research with similarly designed interventions may merit study when applied to select populations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

BMD	bone mineral density
GI	gastrointestinal
GLOW	Global Longitudinal Study of Osteoporosis in Women
IMB	information, motivation, behavioral skills model
IVR	interactive voice-response
NG	nominal group
NHANES	National Health and Nutrition Examination Study
PAPM	Precaution Adoption Process Model
ONJ	osteonecrosis of the jaw

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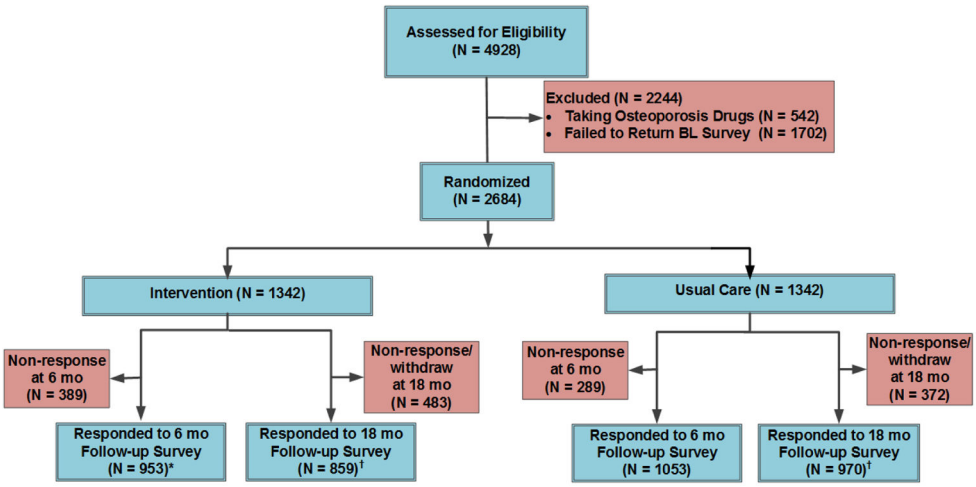

Figure 1.

APROPOS Study Design CONSORT. *Chi-square $p < 0.05$ for the comparison between response rates in the intervention vs control group at 6-months. †Chi-square $p < 0.01$ for the comparison between response rates in the intervention vs control group at 18-months. BL, baseline; OP, osteoporosis; Rx, prescription.

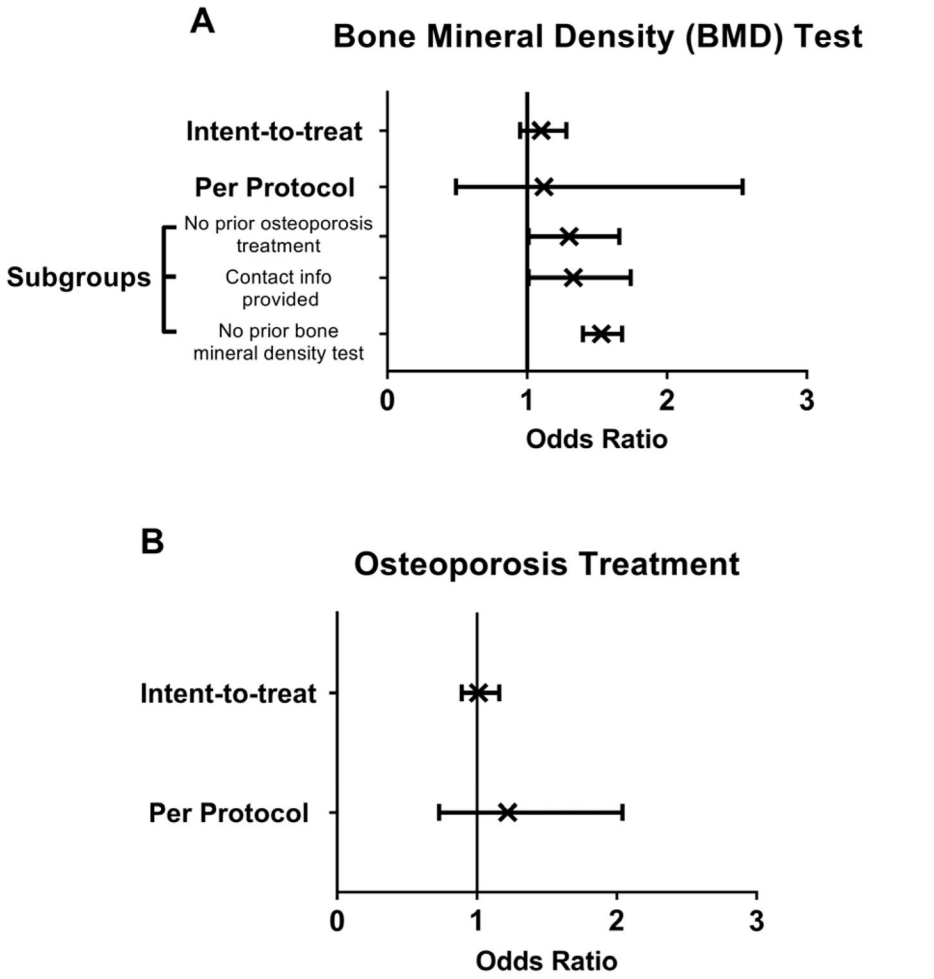

Figure 2.

Odds Ratio (x) and 95% CI (bands) of Uptake of Osteoporosis Diagnosis Testing by Bone Mineral Density Test (A) and Osteoporosis Treatment (B) Based on Type of Analysis (Intent-to-treat vs Per protocol) at 6-Months. Intent-to-treat was defined as comparison of treatment groups including all patients as originally randomized. Per protocol was defined as comparison of appreciable exposure to the intervention group with the control group.

Table 1

APROPOS Participant Baseline Characteristics by Treatment Group and Subgroup of Treatment Groups with Appreciable Intervention Online Exposure[†]

Characteristic	Control N = 1342	Intervention N = 1342	Appreciable Exposure N = 257
Age, years, mean (SD) ***	74.9 (7.9)	74.9 (8)	73.2 (6.9)
Race/Ethnicity *			
Non-Hispanic Caucasian	1239 (92.3%)	1247 (92.9%)	246 (95.7%)
Black	52 (3.9%)	46 (3.4%)	1 (0.4%)
Hispanic	21 (1.6%)	25 (1.9%)	3 (1.2%)
Asian	13 (1.0%)	13 (1.0%)	4 (1.6%)
Other/Not specified	10 (0.8%)	3 (0.2%)	3 (1.2%)
Education ***			
Some high school or less	53 (4.0%)	40 (3.0%)	2 (0.8%)
High school graduate	271 (20.3%)	255 (19.2%)	23 (9.1%)
Some college or more	1007 (75.7%)	1030 (77.8%)	228 (90.1%)
Fracture history			
Wrist	384 (28.6%)	382 (28.4%)	78 (30.4%)
Vertebral	106 (7.9%)	105 (7.8%)	15 (5.8%)
Hip	84 (6.3%)	79 (5.9%)	15 (5.8%)
Fracture history within the previous 12 months			
Yes	123 (9.4%)	96 (7.3%)	24 (9.5%)
General health			
Excellent, very good, or good *	1107 (84.2%)	1113 (85.0%)	229 (89.8%)
Comorbidities			
Depression	276 (21.3%)	272 (21.2%)	52 (21.2%)
Dementia	20 (1.6%)	14 (1.1%)	3 (1.2%)
Risk of fracture			
Lower than average	504 (38.3%)	542 (41.8%)	115 (46.0%)
Average	524 (39.8%)	501 (38.6%)	83 (33.2%)
Higher than average	288 (21.9%)	255 (19.7%)	52 (20.8%)
Osteoporosis prescription treatment			
Prior treatment (including estrogen) **	815 (64.0%)	826 (64.8%)	182 (72.8%)
Other medications, current			
Vitamin D	1062 (82.8%)	1080 (84.1%)	216 (86.1%)
Calcium supplement	867 (68.7%)	863 (68.6%)	178 (71.2%)
Phone and email provided			
Phone **	892 (66.5%)	899 (67.0%)	194 (75.5%)
Email ***	657 (49.0%)	641 (57.5%)	207 (80.5%)

Characteristic	Control N = 1342	Intervention N = 1342	Appreciable Exposure N = 257
Readiness for osteoporosis behavior change			
Pre-contemplative	806 (72.0%)	822 (72.2%)	169 (72.8%)
Contemplative	270 (24.1%)	274 (24.1%)	53 (22.8%)
Health literacy			
Adequate ***	1119 (86.1%)	1144 (87.5%)	238 (93.7%)
Bone mineral density testing *			
No	204 (15.6%)	186 (14.3%)	24 (9.6%)
Yes in the last 12 months	284 (21.8%)	277 (21.3%)	60 (24.0%)
Yes, more than 12 months ago	818 (62.6%)	835 (64.3%)	166 (66.4%)

† Appreciable exposure to the intervention online (defined as at least 20 seconds of viewing time); All comparisons examine appreciable exposure versus control:

* $p<0.05$,

** $p<0.01$,

*** $p<0.0001$.

Table 2

Rates and Odds Ratios (95% CI) of Receipt of New Osteoporosis Treatments, Testing, Barriers to Treatment, and Stage of Behavioral Change at 6-Month Post Intervention (Intent-to-treat).

Outcomes	Control N=1342	Intervention N=1342	Odds Ratio (95% CI)
Primary Outcomes			
Any osteoporosis treatment	153 (11.4%)	157 (11.7%)	1.01 (0.89, 1.16)
Bisphosphonate	132 (10.0%)	129 (9.8%)	0.99 (0.86, 1.15)
Non-bisphosphonate	32 (2.6%)	36 (2.9%)	1.06 (0.83, 1.37)
Secondary Outcomes			
Vitamin D supplements	562 (41.9%)	554 (41.3%)	0.99 (0.90, 1.08)
Calcium supplements	437 (32.6%)	427 (31.8%)	0.98 (0.90, 1.08)
Bone mineral density testing	268 (57.1%)	290 (61.8%)	1.10 (0.95, 1.28)
Self-reported barriers to osteoporosis treatment			
Medication interactions	310 (23.1%)	331 (24.6%)	1.04 (0.94, 1.16)
Gastrointestinal problems	328 (24.4%)	377 (28.1%)	1.10 (0.99, 1.22)
Osteonecrosis of the jaw *	331 (24.6%)	387 (28.9%)	1.11 (1.01, 1.23)
Atypical fractures	329 (24.5%)	355 (26.5%)	1.05 (0.95, 1.16)
Preference for natural remedies	339 (25.2%)	371 (27.6%)	1.06 (0.96, 1.18)
Medication inefficacy	281 (20.9%)	297 (22.1%)	1.04 (0.93, 1.15)
Bone density not improving or had fracture	150 (11.2%)	153 (11.4%)	1.01 (0.90, 1.15)
Difficulty taking or remembering *	242 (18.1%)	295 (22.0%)	1.13 (1.01, 1.26)
Dentist recommendation	278 (20.7%)	299 (22.3%)	1.05 (0.94, 1.17)
Readiness for osteoporosis treatment behavior change			
Pre-contemplative *	923 (68.8%)	860 (64.1%)	0.90 (0.82, 0.99)
Contemplative *	329 (24.5%)	389 (29.0%)	1.12 (1.01, 1.24)
Discussion with health care provider about bone health	573 (42.7%)	583 (43.4%)	1.03 (1.00, 1.06)
Visit with primary care provider ***	1079 (80.4%)	1123 (83.7%)	1.25 (1.21, 1.30)

* $p < 0.05$,

*** $p<0.001$

Table 3

Rates, Odds Ratios (95% CI) and Adjusted Odds Ratios (95% CI) for New Osteoporosis Treatment, Testing, Stage of Behavioral Change, and Barriers Among the Subgroup with Appreciable Intervention Online Exposure (N=257) Referent to All Control Women (N=1,342) at 6-Months.

Outcomes	Control (N=1342)	Appreciable Exposure (N=257)	Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)
Treatment				
Any osteoporosis medication	91 (6.8%)	21 (8.2%)	1.22 (0.75, 2.01)	1.22 (0.73, 2.04)†
Bisphosphonate	71 (5.4%)	11 (4.5%)	0.82 (0.43, 1.57)	0.80 (0.41, 1.54) ‡
Non-bisphosphonate **	23 (1.8%)	11 (4.5%)	2.54 (1.23, 5.27)	2.70 (1.26, 5.79)§
Bone mineral density testing	141 (46.5%)	31 (62.0%)	1.87 (1.01, 3.46)	1.12 (0.49, 2.54) ‖
Discussion with health care provider about bone health	706 (53.9%)	141 (56.4%)	1.11 (0.84, 1.46)	1.01 (0.74, 1.39)¶
Readiness for osteoporosis treatment behavior change				
Contemplative *	175 (13.0%)	49 (19.1%)	1.57 (1.11, 2.23)	1.48 (1.01, 2.15)††
Self-reported barriers to osteoporosis treatment				
Any barriers	369 (27.5%)	90 (35.0%)	1.42 (1.07, 1.89)	1.27 (0.94,1.72)‡‡
Osteonecrosis of the jaw as a barrier *	217 (16.2%)	60 (23.4%)	1.58 (1.14, 2.18)	1.52 (1.08, 2.13)§§

* $p < 0.05$,

** $p < 0.01$ for adjusted models

† Adjusted by baseline characteristics: general health, self-rated risk of fracture, prior osteoporosis treatment, and bone mineral density (BMD) testing

‡ Adjusted by baseline characteristics: self-rated risk of fracture, prior osteoporosis treatment, and BMD testing

§ Adjusted by baseline characteristics: self-rated risk of fracture, prior osteoporosis treatment, and BMD testing

‖ Adjusted by baseline characteristics: age, race, education, self-rated risk of fracture, prior osteoporosis treatment, email being provided, health literacy, and BMD testing

¶ Adjusted by baseline characteristics: age, self-rated risk of fracture, prior osteoporosis treatment, phone provided, and BMD testing

†† Adjusted by baseline characteristics: education, self-rated risk of fracture, prior osteoporosis treatment, and BMD testing

‡‡ Adjusted by baseline characteristics: education, self-rated risk of fracture, prior osteoporosis treatment, health literacy, and BMD testing

§§ Adjusted by age, education, self-rated risk of fracture, prior osteoporosis treatment, health literacy and BMD testing