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SHARED DECISION MAKING SUPPORTED BY PATIENT DECISION AIDS FOR PROSTATE CANCER SCREENING AND TREATMENT

TOMA DE DECISIÓN COMPARTIDA APOYADA EN AYUDAS A LA DECISIÓN AL PACIENTE EN EL *SCREENING* Y TRATAMIENTO DEL CÁNCER DE PRÓSTATA

Michael J. Barry

Foundation for Informed Medical Decision Making. Harvard Medical School

Resumen

El cáncer de próstata es un problema importante para los hombres mayores en países desarrollados. Las decisiones acerca del *screening* y tratamiento del cáncer de próstata se caracterizan por múltiples opciones razonables que parecen "arriesgadas", donde las preferencias personales de los pacientes son importantes. Se va reconociendo de modo creciente la toma de decisión compartida entre el paciente y el clínico como un modelo ideal para elecciones "sensibles a las preferencias" tales como las implicadas en el *screening*, el diagnóstico, y el tratamiento. Muchos ensayos aleatorizados de ayudas a la decisión para el *screening* de cáncer de próstata han mostrado consistentemente mejorías en la calidad de la decisión, así como un mayor interés en llevar a cabo la prueba del PSA cuando los pacientes están bien informados. En contraste, es necesaria una mayor investigación sobre el efecto de las ayudas a la decisión en las decisiones sobre el tratamiento del cáncer de próstata. Sin embargo, con los datos disponibles sobre su efectividad, se hace muy necesaria la investigación sobre el modo de implantar las ayudas a la decisión en el cribado con PSA, así como en otras decisiones críticas que se dan en la práctica clínica durante el tratamiento del cáncer de próstata.

Palabras clave: Toma de decisión compartida, ayudas a la decisión, *screening* cáncer de próstata, tratamiento de cáncer de próstata, antígeno específico cáncer de próstata (PSA).

Abstract

Prostate cancer is an important problem among aging men in developed countries. Decisions about prostate cancer screening and treatment are characterized by multiple reasonable options and appear to be "close calls", where the personal preferences of patients are important. Shared decision-making between patient and clinician is increasingly recognized as an ideal model for such "preference sensitive" choices involving screening, diagnosis, and therapy. Many randomized trials of decision aids for prostate cancer screening have consistently shown improvements in decision quality as well as lower interest in and uptake of PSA testing when patients are well informed. In contrast, more research is needed on the effect of decision aids on prostate cancer treatment decisions. However, given the evidence of effectiveness available at present, research is most urgently needed on how to routinely implement patient decision aids for PSA screening, as well as other fateful decisions including prostate cancer treatment, in clinical practice.

Key words: Shared decision making, patient decision aids, prostate cancer screening, prostate cancer treatment, prostate-specific antigen.

Correspondence:

Michael J. Barry,
40 Court Street, Suite 300
Boston, MA 02108
USA
E-mail: mbarry@fimdm.org

Introduction

Prostate cancer is an important health problem among aging men in developed countries worldwide. Table 1 lists prostate cancer incidence and mortality among a selected set of developed countries. The net benefits of screening and treatment for prostate cancer remain unclear despite the recent publication of several large randomized trials[1-3] which continue to engender considerable controversy. However, decisions about prostate cancer screening and treatment are characterized by multiple reasonable options and, based on these trials, do appear to be "close calls", where the personal preferences of patients are important to making an optimal decision about how to proceed. Shared decision-making between patient and clinician is increasingly recognized as an ideal model for such "preference sensitive" choices involving screening, diagnosis, and therapy.

Shared Decision Making

In 1997, Charles et al. clarified the shared decision-making model for medical decision-making[4]. They suggested the key characteristics of shared decision-making include: the involvement of at least two participants (usually, patient and clinician); both parties sharing information (usually the clinician information about the various options and possible outcomes and the patient about their preferences); and both parties work to build consensus about the preferred management option, and ultimately reach an agreement about how to proceed. Shared decision making has received considerable attention in many countries in recently years, including as a strategy for perfecting informed consent[5], and to help reduce unwanted geographic medical practice variation[6]. This strategy might be considered an antidote to the problem of poor "decision quality;" medical decision making where

Table 1. **Prostate Cancer Incidence and Mortality in Selected Countries, (standardized for age)**[41].

Country	Incidence per 100,000	Mortality per 100,000
Ireland	126.3	14.2
France (metropolitan)	118.3	12.7
Norway	115.6	18.6
Sweden	114.2	21.4
Australia	105.0	15.4
Belgium	102.3	11.6
Canada	101.5	11.4
New Zealand	99.7	15.1
Finland	96.6	13.3
Switzerland	91.3	14.4
United States of America	83.8	9.7
Austria	83.1	12.2
Germany	82.7	11.7
The Netherlands	73.4	14.0
Denmark	72.5	19.7
United Kingdom	62.1	13.8
Italy	58.4	9.0
Spain	57.2	10.5
Portugal	50.1	15.2
Greece	17.7	9.8

patients are uninformed and uninvolved, leading to decisions inconsistent with their preferences[7].

A large, recent population-based survey of medical decision making in the United States covering decisions about cancer screening, medications for chronic conditions, and surgery suggested this type of problematic decision making is unfortunately too often the norm[8]. For example, for prostate cancer screening with the prostate-specific antigen test, about 45% of men who had faced a decision about testing had not been asked their preferences about testing, and a similar percentage could not correctly answer a single one of three basic knowledge questions relevant to the PSA screening decision[9].

Patient Decision Aids

Shared decision making may be facilitated by the use of patient decision aids. Decision aids can help clinicians efficiently transfer information about treatment options and their outcomes to patients. They can also help patients clarify their preferences regarding the possible outcome states after the treatments they may face, particularly outcome states for which they have no experience as yet.

According to the International and decision Aids Standards (IPDAS) collaboration[10], "Patient decision aids are tools designed to help people participate in decision making about health care options. They provide information on the options and help patients clarify and communicate the personal value they associate with different features of the options.

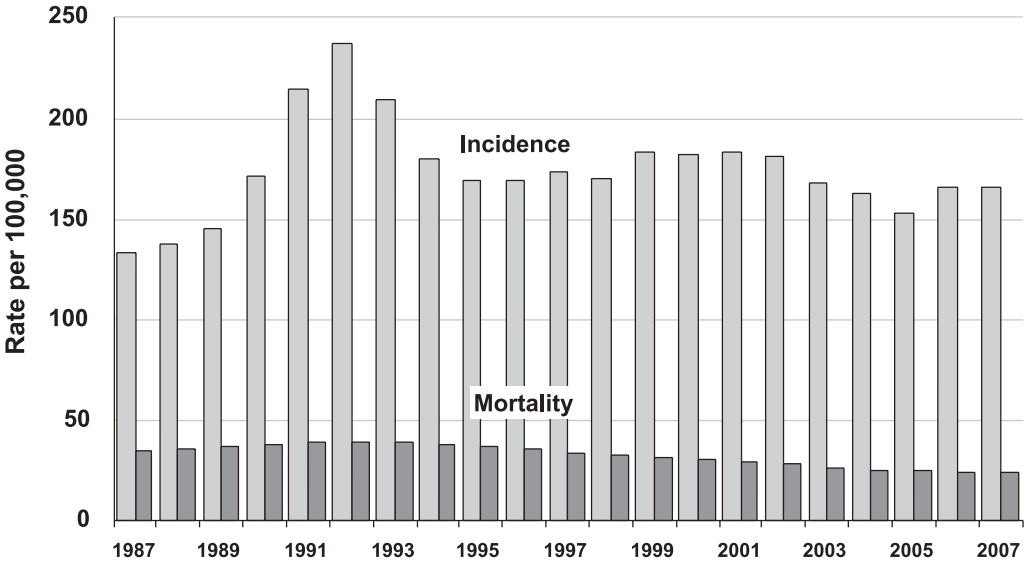
Patient decision aids do not advise people to choose one option over another, nor are they meant to replace practitioner consultation. Instead, they prepare patients to make informed, values-based decisions with their practitioner."

Numerous randomized trials of a shared decision making approach assisted by patient decision aids have been conducted for a plethora of management decisions. In a Cochrane Collaboration review of trials of patient decision aids updated in 2006, 55 randomized trials of 51 different decision aids were identified. The meta-analysis of the results of these trials documented that decision aids improved many aspects of decision quality. Subjects randomized to patient decision aids rather than usual care had greater knowledge, had lower decisional conflict relating to feeling informed and feeling unclear about personal values, were less likely to be passive in decision making, and were less likely to remain undecided about a management option. Decision aids also reduced rates of elective surgery and PSA screening by about 20%[11].

The Prostate-Specific Antigen (PSA) Screening Decision

The PSA test was introduced into clinical medicine in the United States in the late 1980's, initially as a tool for managing men with a known prostate cancer diagnosis. However, clinicians quickly began using the PSA test for early detection of prostate cancer among asymptomatic men. Because of the large reservoir of prostate cancers among older men never destined to present clinically, this strategy resulted in almost a doubling of the incidence of prostate cancer in the United States over just five years between 1987, when the PSA test was introduced, and 1992 (Figure 1). By 2005, about half of American men age 50-79 reporting having had a PSA test within the last two years[12], despite no randomized trials proving that PSA screening does more good than harm. At the individual level, widespread PSA screening in the United States has resulted in the predicted lifetime risk of a prostate

Figure 1. **Prostate Cancer Mortality and Incidence in the U.S., 1987-2007, adjusted for age**[14]



cancer diagnosis increasing from about 9% in 1985[13], before PSA screening, to about 16% based on incidence data from 2005-2007[14].

Since the incidence peak in the United States in 1992, population-based prostate cancer mortality has dropped by about 25% through 2005 (Figure 1). Screening advocates have considered this trend *prima facie* evidence that PSA screening is effective at reducing prostate cancer mortality, and is therefore worth the price in terms of the much higher risk that men will have to face a diagnosis of prostate cancer over their lifetimes, with all the attendant anxiety and treatment side effects screening engenders.

However, recent randomized trials of PSA screening have not resoundingly proved that the benefits of PSA screening so far outweigh its harms that it can be considered proven effective care, to be routinely implemented in clinical practice and public health. To some extent, this at best modest effectiveness is in part related to the poor sensitivity and specificity of the test. While a relatively high false positive rate has been appreciated for many years, an appreciable false negative rate, even for high-grade cancers, has been appreciated only recently[15]. A large trial of PSA screening in the United States randomized about 77,000 men to receive either annual PSA screening (with digital rectal exams) or "usual care"[2]. After a median follow-up of 11.5 years, the rate of a prostate cancer diagnosis was 22% higher with screening, but prostate-cancer specific mortality was not significantly reduced; in fact, the trend suggested more prostate cancer deaths with screening. Major concerns about this trial have included prescreening of a substantial proportion of the study population with PSA tests before trial entry, contamination of the control group with about half of control men receiving PSA tests, and an insufficient follow-up duration.

An even larger trial conducted in multiple European countries randomized a core group of about 162,000 men age 55-69 to more infrequent PSA screening (without digital rectal exams) than in the

US trial, usually every four years, versus usual care[3]. In the European trial, after a median follow-up of nine years, the cumulative risk of a prostate cancer diagnosis increased about 70% with screening, from 4.8% in the control group to 8.2% in the screened group. However, the death rate from prostate cancer was 20% lower, albeit with an absolute risk difference of about 7 fewer deaths per 10,000 men screened. In a subsequent analysis, the investigators estimated that with correction for contamination and dilution of the control and screening groups, respectively, the "true" benefit of consistent PSA screening might be closer to a 30% reduction in prostate cancer mortality[16].

A recent meta-analysis of these trials and several smaller ones estimated that across the trials screening resulted in a 46% higher probability of a prostate cancer diagnosis with screening, with no significant effect on prostate cancer or overall mortality, although the lower limits of the 95% confidence intervals were still consistent with a 29% and 3% reduction in these outcomes, respectively[17].

Given the quality of the evidence currently available, there is considerable uncertainty about the most effective and efficient strategy for using the PSA test for early detection of prostate cancer. Issues such as the frequency of testing, the ideal starting and stopping ages, the right threshold to consider a PSA level suspicious enough to warrant a biopsy, and whether PSA testing and digital rectal examinations should be combined, all engender heated debate. For example, one recent publication suggested an optimal strategy might be a single PSA test at age 60, with no further testing for men with low values[18].

If there were no side effects from the diagnosis and treatment of prostate cancer, there would be much less controversy about screening. However, prostate biopsies done in response to an elevated PSA level can be complicated by bleeding or infection. More importantly, men who have prostate cancer diagnosed by screening usually consider treatment with some form of surgery or radiation (see subsequent section). Surgery for prostate cancer has a small but finite risk of operative mortality, and radiation has a small risk of rectal injury resulting in gastrointestinal side effects. Both treatments carry a substantial risk of problems with continence and erectile function[19].

Because of the uncertain benefits and known risk of prostate cancer screening, national clinical practice guidelines in the United States began recommending a shared decision making approach to PSA screening as early as 1997, when the American College of Physicians' clinical guideline recommended, "Rather than screen all men for prostate cancer as a matter of routine, physicians should describe the potential benefits and known harms of screening, diagnosis, and treatment; listen to the patients' concerns; and then individual the decision to screen"[20]. Though many had hoped the US and European randomized trials would show that the benefits of PSA screening definitively outweighed the harms or vice versa, the results to date continue to suggest a close call, and considering patient preferences therefore remains critical for optimal decision making. As a result, new guidelines recently released by the American Cancer Society (ACS) after publication of the US and European screening trials emphasize shared decision making: "The ACS recommends that asymptomatic men who have at least a 10-year life expectancy have an opportunity to make an informed decision with their health care provider about screening for prostate cancer after they receive information about the uncertainties, risks, and potential benefits associated with

prostate cancer screening…Patient decision aids are helpful in preparing men to make a decision whether to be tested"[21].

Patient Decision Aids for PSA Screening

The key decision for older men reaching the age of 50, or age 40-45 if they have risk factors such as African ancestry or a first degree relative with prostate cancer, is whether to undergo periodic PSA testing for the early detection of prostate cancer. Although the evidence regarding the effectiveness of digital rectal examinations for prostate cancer screening is also problematic, this preventive maneuver has in general received less attention in medical decision-making. Interestingly, the European trial of prostate cancer screening, which arguably provides the best evidence for the effectiveness of early detection, did not include digital rectal exams.

The Ottawa Hospital Research Institute (OHRI) A to Z Inventory of Decision Aids web site lists six currently available patient decision aids on PSA screening; from the Centers for Disease Control (including a general Decision Guide and a Decision Guide for African Americans), Health Dialog, Healthwise, the Mayo Clinic, and the University of Cardiff[22]. These decision aids generally rated fairly high on the IPDAS criteria, which are also available on the OHRI web site.

Volk et al. performed a systematic review and meta-analysis of trials of PSA decisions aids, with the search for publications conducted through the end of 2006[23]. They identified 18 trials involving 6,221 participants, all using patient decision aids in the English language. Consistent with the results of the Cochrane review for decision aids in general, they found decision aids improved subjects' knowledge about PSA testing and made patients more confident about their decisions. They also found subjects exposed to decision aids as part of routine clinical care (but not subjects specifically seeking screening) were significantly less interested in PSA testing, with a relative risk of 0.88 (95% confidence interval 0.81, 0.97) in nine trials reporting that outcome. A Cochrane review conducted at about the same time focused on five trials of decision aids versus usual care, also found PSA screening interest significantly reduced with decision aids, with a relative risk of 0.80 (95% confidence interval 0.7, 1.0)[11]. Thus, it appears that well informed patients indeed become somewhat less interested in PSA screening. A paradox is that as of the time of this publication, there were no published high quality randomized trials of PSA screening, yet PSA screening was widespread, at least in the United States. And despite 18 trials showing patient decision aids improved decision quality for PSA screening, their use was, and remains, rare in clinical practice.

Several more recent randomized trials of decision aids for PSA screening deserve mention. Krist et al. randomized 496 men in a single family medical practice to a paper-based decision aid or an internet-based decision aid of their own design and compared outcomes to control subjects[24]. As in previous trials, knowledge and involvement in decision-making were increased, and PSA testing was reduced with both decision aids, with no important differences between the two decision aid formats.

Frosh et al. randomized 611 men from a Health Appraisal Clinic at Kaiser Permanate in a 2x2 factorial design to three variants of internet-based decision aids compared to referral to public web sites on prostate cancer screening maintained by the American Cancer Society and the Centers for Disease Control and Prevention[25]. The more specifically designed internet decision aids significantly improved decision quality and reduced uptake of PSA tests more

effectively than referral to the public web sites.

Another trial by Allen et al. used the novel approach of delivering a prostate cancer screening decision aid to men age 45 and older in work sites[26]. In this cluster randomized trial involving 625 subjects, decision quality was also improved, despite relatively low uptake, about 30%, among men randomized to the intervention.

Rubel et al. conducted a randomized trial of the paper-based decision aid for prostate cancer screening from the Centers for Disease Control and Prevention listed in the OHRI inventory mentioned previously[27]. Again, consistent with earlier studies, the decision aid increased knowledge and improved other aspects of decision quality.

Finally, another web-based trial of the effect of the Prosdex decision aid from the University of Cardiff, also listed in the OHRI inventory, was published by Evans et al.[28] . This trial randomized men to an internet-based or paper version of Prosdex, or a control group. Once again, men randomized to the decision aids had improved knowledge, lower decisional conflict, and no higher anxiety levels than controls. Interestingly, particularly because of the paucity of research on internet-based versus more traditional paper- and video-based decision aids, men randomized to the internet version had lower PSA testing uptake than men randomized to the paper-based decision aid group and the control group, although uptake was very low overall, probably reflecting the low level of PSA screening in Wales, where the study was conducted.

The Clinically Localized Prostate Cancer Treatment Decision

Treatment options for prostate cancer depend on the stage of disease. For prostate cancers that are judged likely to be confined to the prostate gland, attempted curative treatments include radical prostatectomy (open or laparopscopic surgery, often robotic-assisted) and radiation therapy (conformal external beam radiotherapy, intensity-modulated radiotherapy, brachytherapy, proton beam therapy, and robotic radiosurgery). Men may also pursue some form of watchful waiting (including delayed attempted curative treatment for cancer progression, also called "active surveillance")[29]. For prostate cancers with a higher risk of extracapsular disease, neoadjuvant androgen deprivation therapy may be added, particularly to radiation therapy[30]. Androgen deprivation therapy is the mainstay of treatment for metastatic prostate cancer. Another common situation where androgen deprivation is considered is a rising PSA after attempted curative treatment, evidence of residual or recurrent disease[31].

In areas where PSA screening is widespread, particularly in the U.S., the great majority of men present with clinically localized disease. Up to 25% of men who receive attempted curative therapy will have a rising PSA as some point after treatment[32]. For such men, few randomized trials are available to guide decision making[33]. In a single Scandinavian randomized trial comparing radical prostatectomy to watchful waiting for men with clinically localized cancer, surgery significantly decreased the probability of dying of prostate cancer from about 18% to 12.5% over a median of about 11 years of follow, with a similar though nonsignificant 5% absolute reduction in overall mortality[1,34]. This mortality benefit appeared confined to men younger than age 65 at diagnosis (interestingly, about one-third of men who undergo radical prostatectomy in the United states are 65 or older[35]), and does not seem to increase further after ten years of follow-

up. Moreover, few men in this study were diagnosed through PSA screening. The PIVOT trial being conducted in the United States and initiated in 1994 has a similar design but includes men largely diagnosed through PSA screening[33]. Results from PIVOT are expected in 2011.

Given the paucity of randomized trials and the plethora of treatment options, any judgments about comparative effectiveness must necessarily focus on nonexperimental studies. The Institute for Clinical and Economic Review at Massachusetts General Hospital has summarized these data in a series of reports (see http://www.icer-review.org/).

Patient Decision Aids for Prostate Cancer Treatment

Decisions about prostate cancer treatment, particularly for men with clinically localized disease, can be bewildering, given the many options, the weak evidence on comparative effectiveness, and strong financial incentives for manufacturers, clinicians and hospitals to promote particular therapies[29]. Shared decision making has been widely endorsed for prostate cancer treatment decisions[30,36].

The OHRI Inventory lists five decision aids for prostate cancer treatment, four addressing attempted curative treatment for clinically localized prostate cancer from Health Dialog, Healthwise, the Mayo Clinic, and the National Cancer Institute, and another from Health Dialog addressing the timing of androgen deprivation for a rising PSA after surgery or radiation therapy. Again, these decision aids generally perform well against the IPDAS criteria.

Lin et al. performed a systematic review of studies (not just trials) of decision aids for prostate cancer treatment with the search covering through early 2009[37]. Thirteen studies including just three randomized trials were identified. Although the evidence base is weaker for the effect of decision aids on prostate cancer treatment compared with screening decisions, the authors concluded that decision aids improve knowledge, encourage more active involvement in decision making, and decrease levels of anxiety ands stress. The effect on treatment choice was less clear, although in European studies, fewer men chose radical prostatectomy compared to historical controls.

Conclusions

In summary, randomized trials of different patient decision aids addressing prostate cancer screening in different study settings have consistently shown improvements in decision quality and, taken together, lower interest in and uptake of PSA testing when patients are well informed. In addition, use of patient decision aids for prostate cancer screening may actually reduce concerns about medical-legal liability if men do not undergo PSA screening[38]. Nevertheless, the uptake of patient decision aids themselves to help men make shared decisions about PSA screening, as recommended by many clinical practice guidelines, is low. Given the evidence of effectiveness, research is urgently needed addressing how to routinely implement decision aids for PSA screening, as well as other fateful decisions, in routine clinical practice. Legare et al. have conducted a systematic review of trials addressing interventions for improving the adoption of shared decision making by healthcare professionals[39]. Because so few trials were identified, the authors concluded, "The results of this Cochrane review do not allow us to draw firm conclusions about the most effective types of interventions for increasing healthcare professionals use of SDM."

Unlike the case for shared decision making assisted by decision aids for the PSA screening decision, more research is needed on the effect of decision aids on prostate cancer treatment decisions. This research should parallel comparative effectiveness research for prostate cancer treatments themselves, which has been listed as a top priority by a recent report from the U.S. Institute of Medicine on comparative effectiveness research[40]. However, given the strong evidence for patient decision aids in general, and the results of the research available to date, it is likely further studies will show similar salutary effects on decision quality with the use of decision aids for prostate cancer treatment.

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