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Platinum Opinion

Development and Prospective Randomized Evaluation of a Decision Aid for Prostate-specific Antigen-based Early Detection of Prostate Cancer in Men Aged Between 55 and 69 Yr: The PSAInForm Trial

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The aim of early detection of prostate cancer (PCa) is to improve quality of life and decrease PCa-associated mortality. The use of prostate-specific antigen (PSA) in a population-based screening study resulted in an increased incidence of PCa, a shift toward earlier disease stages, and a reduction of metastatic disease and deaths from PCa [1]. However, this benefit is accompanied by considerable rates of overdiagnosis, which also involves potential overtreatment [2]. Published estimates of overdiagnosis range from 27% to 56% of all screen-detected cancers, depending on the screening protocol [3]. Thus, population-wide PSA screening is presently not recommended by medical guidelines; instead, most professional organizations now emphasize a personalized individual decision-making process with the aim of informing men about the potential advantages and disadvantages of PSA screening. Informed choice is said to have been taken when a man is aware of the potential risks and benefits of early detection of PCa and when his choice is consistent with his personal values [4].

Although explicitly recommended in the German PCa guidelines [5], only half of a sample of urologists from the administrative district of Muenster reported that they gave more detailed information about the advantages and disadvantages of PSA testing to men who were interested in early detection of PCa [6]. Notably, there are reasons not to engage in a complicated decision-making process, namely, concerns related to limited time resources and/or inadequate reimbursement for time-consuming explanations and discussions, patients' expectations to be screened, and misconceptions regarding the effectiveness of screening [6,7].

To shed more light on this process, the PSAInForm study investigates the influence of a decision aid (DA) and of compensating the patient's cost for PSA testing on the decisional conflict [8] in men who are between 55 and 69 yr of age.

1. Decision aid

We developed a DA to support men regarding their decision to undergo PSA-based early detection or not. The DA is to be

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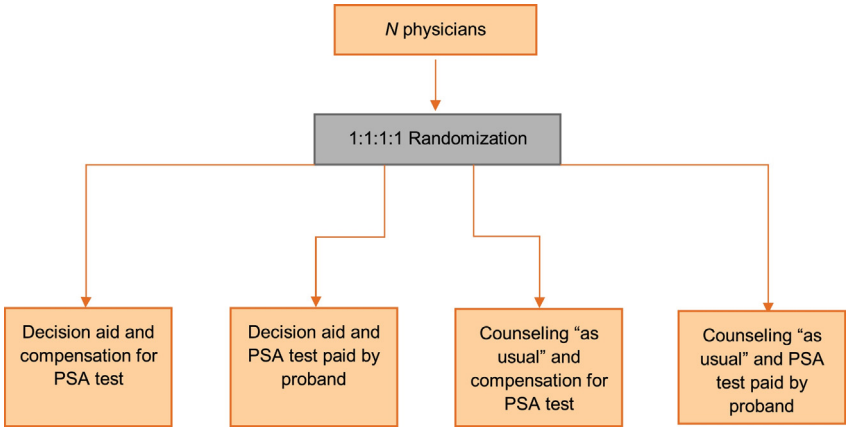

Fig. 1 – Design of the PSAInForm study, a cluster-randomized controlled trial with a 2 × 2 factorial design: physicians are randomized to one of four arms before they start to recruit participants. PSA = prostate-specific antigen.

used only during the consultation with a health professional (transactional DA). It is part of ARRIBA, a library of electronic DAs, containing modules for relevant decisions pertaining to the diagnosis, prevention, and treatment of relevant chronic diseases [9].

Within a multiple-step mixed-methods pilot study, as recommended by the International Patient Decision Aids Standards [10], this computer-based DA was designed and pre-evaluated at the Department of General Practice, Philipps-University Marburg, Germany.

The computer-based DA offers a table of contents that allows navigation to introductory material and pictograms, each based on 1000 men in the age range between 55 and 69 yr. In these pictograms, information differentiated for PSA-based early detection versus no PSA-based early detection is depicted in relation to the following risks:

1. Dying within the next 10 yr (all causes of death as compared with dying from PCa)
2. Receiving a diagnosis of PCa (potentially relevant vs nonrelevant, ie, "overdiagnosed", PCa)
3. Having false-positive or false-negative PSA test results ("unnecessary" prostate biopsies vs "false reassurance")

For the development of the DA, the results of the European Randomized Study of Screening for Prostate Cancer (ERSPC, triggering biopsy at PSA concentrations above 3 ng/ml) [1] were adapted to the recommendations for early detection of PCa in Germany (recommending biopsy at PSA concentrations above 4 ng/ml) and served as evidence for the DA to illustrate the potential benefits and harms of PSA-based early detection.

2. Trial design

We initiated a prospective, cluster-randomized trial (Fig. 1). Two treatments are compared in a 2 × 2 factorial design: DA versus counseling as usual, and compensation of costs versus no compensation of cost for PSA testing. The cluster randomization takes place at the level of the approximately 90 participating physicians (general practitioners and urologists in the administrative district of Muenster, Germany). An adaptive sequential design allows for one interim analysis and adaptation of the sample size, if necessary.

Ethical approval has been obtained from the Ethics Committee Marburg (Ref: 72/13) for the pilot study, and the Ethics Committee Muenster (Ref: 2013-367-f-S) for the main study. The trial was registered on May 6, 2015 (German Clinical Trials Register—Register Klinischer Studien; DRKS-ID: DRKS00007687).

3. Eligibility of participating physicians and probands

Before joining the study, the participating physicians should agree to the necessary additional time effort, participate in a 1-h training session introducing the DA, and have a neutral attitude toward PSA-based early detection without prejudging the proband's decision for or against PSA testing. Probands are between 55 and 69 yr of age with no history of PCa. Prior PSA testing is no exclusion criterion, but will be documented.

4. Endpoints and objectives

The primary objective is to confirm two hypotheses: (1) consultations using the DA lead to different decisional conflicts than consultations "as usual" and (2) participants who are offered a cost compensation for the PSA test have different decisional conflicts than participants who are not. Decisional conflicts are measured by the decisional conflict scale (DCS [8], primary endpoint) in telephone interviews 2 wk after the consultation in the physician's offices.

The five key secondary objectives are to compare participants with and without DA regarding the five subscales of the DCS (feeling informed, values clarity, support, uncertainty, and effective decision). Several further

secondary endpoints will be investigated, for example, the decision for or against PSA testing, shared decision making, satisfaction, and decisional regret.

5. Sample size calculation and statistical analysis

Sample size calculation is based on data from the pilot study. One interim analysis is planned after half of the participants are recruited. Sample size calculations revealed a power of >80% to confirm each primary hypothesis by a two-sample *t* test (Welch) if the total sample size in the final analysis is $n = 1614$ probands. To account for correlations due to cluster randomization, generalized estimating equations will be used for the two primary tests. A Bonferroni-based multiple testing strategy will control a global 5% level of significance and allow for confirmatory testing of the primary and key secondary hypotheses.

6. Summary

Within the scenario of a possible PSA-based early detection of PCa, the effect of a computer-based DA and/or the compensation of costs for the PSA test on the men's uncertainty regarding their decision will be evaluated in this cluster-randomized trial.

Conflicts of interest: N. Donner-Banzhoff is co-chairman of the Association for Patient-orientated Communication, a non-profit organization distributing decision-support software.

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