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Editorial

Psychosocial outcomes in the Yorkshire Kidney Screening Trial: moving the needle toward targeted screening for renal cell carcinoma

Renal cell carcinoma (RCC) has been recognised as a European healthcare issue [1].

In the context of epidemiology and public health, screening refers to the practice of investigating apparently healthy individuals to detect unrecognised disease or early disease stages, aiming to prevent or delay the onset of disease, slow its progression, and reduce (premature) death [2].

Despite screening and early detection being key priorities for clinicians and patients [3], neither population nor opportunistic screening is currently recommended for RCC [4].

Indeed, the evidence supporting the efficacy and cost-effectiveness of structured RCC screening strategies is still limited [1]. Unlike prostate cancer [5], organised efforts by international organisations, scientific associations, research foundations, and policymakers have been hardly focused on RCC during the past decades [6]. Lastly, as the goal of any screening programme is to reduce morbidity and mortality from the disease [2], whether RCC meets the WHO criteria for screening [2] is still controversial (Table 1 [7]).

As such, a thoughtful re-appraisal of the opportunities and threats of screening in this complex arena is needed to get this topic back into the game.

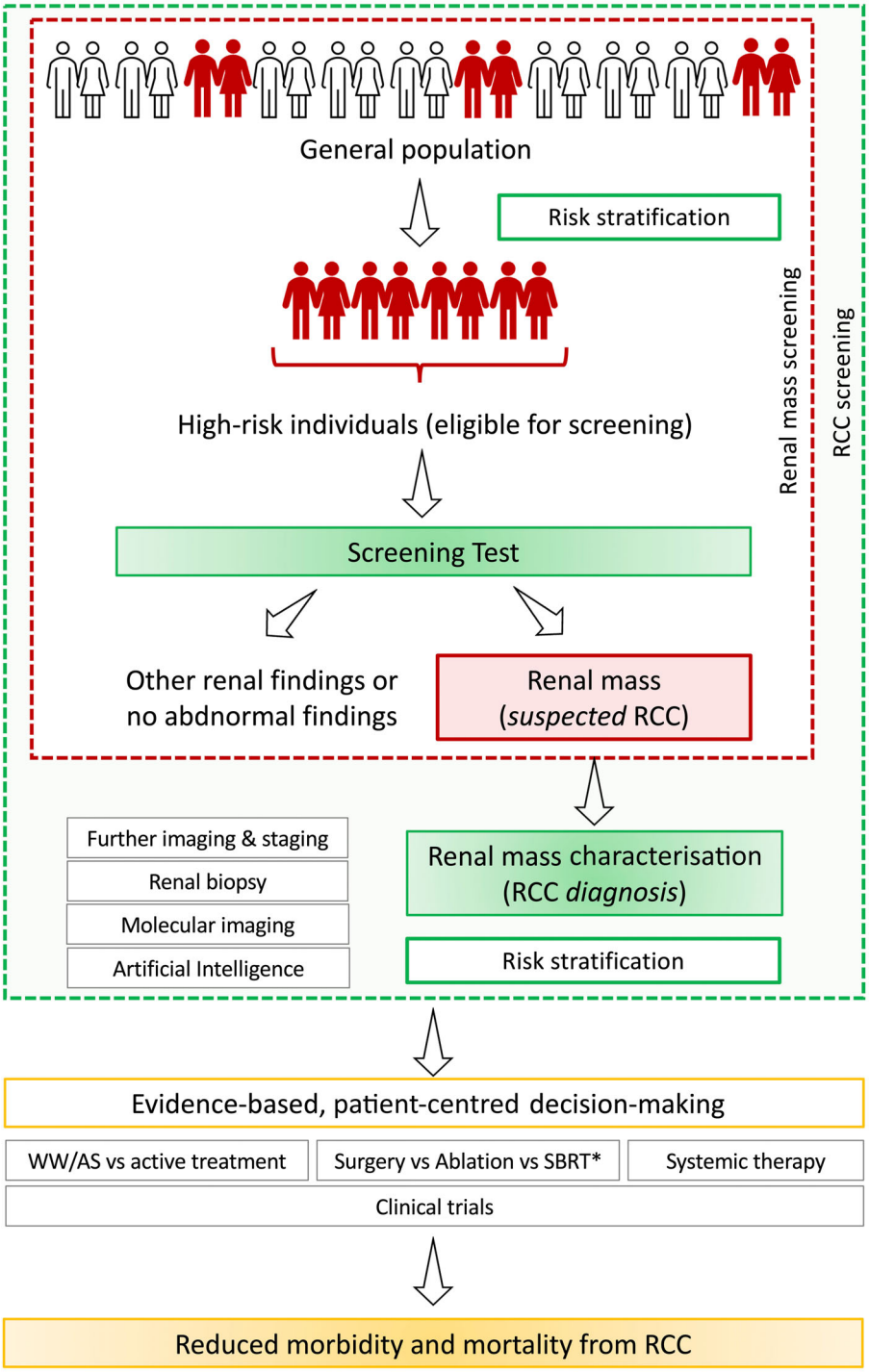
In this Issue of *BJU International*, Usher-Smith et al. [8,9] evaluated the psychological, social, and financial outcomes among individuals undergoing a non-contrast abdominal CT scan to screen for renal masses suspected of RCC and other abdominal malignancies within the Yorkshire Kidney Screening Trial (YKST), a feasibility study of adding a non-contrast abdominal CT scan to the thoracic CT for lung cancer screening. A total of 500 participants within YKST, including those with an abnormal CT scan and a random sample of one-third of those with a normal scan, were sent a questionnaire at 3- and 6-months focused on a variety of outcomes. Such measures included the Psychological Consequences Questionnaire (PCQ), the short form of the Spielberger State–Trait Anxiety Inventory (SF-STAI) and the EuroQoL five Dimensions five Levels (EQ-5D-5L) score for health-related quality of life. Moreover, five questions were designed to assess the financial consequences of having the scan. Data were analysed adjusting for participant age, sex, socioeconomic status, education, baseline quality of life, and ethnicity. Overall, 380 (76%) and 328 (66%) participants returned questionnaires at 3- and 6-months, respectively. The study showed that individuals requiring initial further investigations or referral based on the additional scan did not experience worse outcomes at 6 months as compared to participants with a normal scan. The authors concluded that

Table 1 Overview of the WHO criteria for screening, proposed by Wilson and Jungner [7] in 1968, applied to RCC.

Original screening criteria proposed by Wilson and Jungner [7]		Does RCC meet the criterion considering the current evidence?
1. The condition	a. Should be an important health problem	Yes
	b. Should have an (untreated) natural history that is adequately understood	Partially
	c. Should have a recognisable latent or early symptomatic stage	Yes
2. Treatment	a. Facilities for diagnosis and treatment should be available	Yes
	b. There should be an agreed policy on whom to treat as patients	Partially
	c. There should be an accepted treatment for patients with recognised disease	Yes
3. The test used in screening	a. Should be suitable (simple, sensitive, specific, reproducible, validated, safe, and with a known distribution and cut-off points)	Partially
	b. Should be acceptable to the population	Yes
4. Cost	The cost of case finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole	Unknown
5. The screening programme	Should be a continuing process and not a 'once and for all' project	To be defined

While some criteria (highlighted in green) are fulfilled according to the current evidence, a few of them are still controversial (highlighted in yellow). Criterion 1b: the natural history of untreated RCC is still poorly understood, especially in the long-term period. Moreover, the ideal target population for screening is unknown. Criterion 2b: the contemporary decision-making strategy regarding the management of screen-detected renal masses is still nuanced and not standardised at a clinician-, Centre- and Country-level. Criterion 3a: there is lack of evidence regarding the most suitable test for renal mass/RCC screening. Criterion 4: there is limited evidence on the cost-effectiveness of potentially available screening tests for RCC in the contemporary era. Criterion 5: the optimal strategy to make RCC screening a continuous process still needs to be addressed.

Fig. 1 Graphical overview of the key points to optimise the design of future RCC screening trials. To move from screening of renal masses (red dotted box) to early detection of clinically-significant disease (green dotted box), and ultimately to reduce morbidity and mortality from RCC, specific actions should be prioritised in clinical trial design: (i) identification of high-risk individuals for RCC from the general population; risk-stratification should be based on the available evidence on RCC modifiable and unmodifiable risk factors [1]; (ii) identification of a reliable, reproducible, and cost-effective screening test; (iii) characterisation of screen-detected renal masses, through renal tumour biopsy, novel imaging tools [10] and potentially biomarkers; risk-stratification should allow to distinguish clinically-significant RCC from benign/indolent disease entities; (iv) tailored shared decision-making in patients diagnosed with RCC (ideally by a multidisciplinary tumour board); the goal of treatment should be individualised according to patients' characteristics and disease stage/features, aiming to reach value-based care [11]. AS, active surveillance; SBRT, stereotactic body radiotherapy; WW, watchful waiting. * in the setting of a clinical trial.



such a screening strategy is unlikely to cause significant lasting psychosocial or financial harm to participants with incidental findings [9].

Usher-Smith et al. [8] should be congratulated for their pioneering efforts exploring the feasibility of a screening programme for RCC within the Yorkshire Lung Screening Trial.

The YKST is the only active prospective trial in this field and addresses a critical unmet need [1]. Of note, the results of the trial might renovate the debate over the potential value of early diagnosis for RCC. Furthermore, relying on huge clinical and logistical efforts, it might encourage the Urology Community to believe that targeted screening of RCC can be a reality.

While waiting for the analysis on the secondary outcomes of the YKST (e.g., prevalence of renal masses and RCC in appropriate age and risk group, stage distribution of RCC, prevalence of incidental renal findings, etc. [8]), this study provides preliminary insights on the participants' perspective regarding RCC screening, and its short-term psychosocial consequences.

How to leverage these results? Notably, the reported acceptability of the screening strategy proposed by Usher-Smith et al. [8], which has the potential to optimise resources by coupling screening of RCC and lung cancer in high-risk individuals, represents a first key step toward the more ambitious goal to design a full-scale randomised controlled trial (RCT) for RCC screening.

Inspired by the evolution of screening trials and ongoing endeavours in risk-based screening for prostate cancer [5], the time has come to reintroduce screening and early diagnosis of RCC in clinicians' and policymakers' agenda. While RCTs are needed to provide the scientific foundation for a paradigm change in the field of RCC, we believe that the design of such trials should be grounded into the specific biology and clinical features of this complex and heterogeneous disease [4]. To move from screening of renal masses to early detection of clinically significant disease, and ultimately to reduced morbidity and mortality from RCC, specific actions should be prioritised among screened individuals, including renal mass characterisation [10], risk-stratification of screen-detected RCC [4], and tailored shared decision-making to avoid overtreatment [11] (Fig. 1).

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Abbreviations: RCT, randomised controlled trial; YKST, Yorkshire Kidney Screening Trial.