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## Review – Statistics in Urology

# Global Burden of Urologic Cancers, 1990–2013

Geolani W. Dy<sup>a,b</sup>, John L. Gore<sup>a</sup>, Mohammad H. Forouzanfar<sup>b</sup>, Mohsen Naghavi<sup>b</sup>,  
Christina Fitzmaurice<sup>b,c,\*</sup>

<sup>a</sup> Department of Urology, University of Washington, Seattle, WA, USA; <sup>b</sup> Institute for Health Metrics and Evaluation, University of Washington, Seattle, WA, USA; <sup>c</sup> Division of Hematology, Department of Medicine, University of Washington, Seattle, WA, USA

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### Abstract

**Context:** Kidney, prostate, and bladder cancers increase with age and are influenced partly by modifiable risk factors. Urological cancer rates may increase substantially amid a growing, aging population.

**Objective:** To describe kidney, bladder, and prostate cancer incidence, mortality, and risk factor-attributable bladder and kidney cancer deaths between 1990 and 2013, by age, sex, and development status.

**Evidence acquisition:** Cancer mortality data were derived from global vital registries. Incidence data from cancer registries were transformed to mortality estimates using separately estimated mortality incidence ratios. These sources served as input data for an ensemble modeling approach to estimate bladder, prostate, and kidney cancer mortality. Cause-specific mortality estimates were transformed into incidence estimates using mortality incidence ratios.

**Evidence synthesis:** In 2013, 2.1 million kidney, bladder, and prostate cancers cases occurred worldwide, increasing 2.5-fold since 1990. Mortality increased 1.6-fold between 1990 and 2013. Eight-two percent of new cases in 2013 occurred in individuals aged 60 yr and older. Men from developed countries had the highest age-standardized death rates among all three cancers. Smoking-attributable kidney cancer deaths decreased while obesity-related deaths rose, most prominently in women from developing countries. Smoking-related bladder cancer deaths increased among women from developed countries and decreased among men.

**Conclusions:** Urologic cancer burden has increased globally amid population growth and aging. High income countries face the highest incidence and death rates; however, obesity-attributed kidney cancer deaths are increasing in developing countries. Efforts to expand the global oncologic workforce and reduce preventable factors may lessen cancer disparities in developing countries.

**Patient summary:** We describe the impact of population growth, aging, and lifestyle factors such as smoking and obesity, on kidney, bladder, and prostate cancer rates worldwide. More new cancer cases and deaths occur in developed countries compared with developing countries. In addition to preventive efforts, healthcare systems must emphasize training of a urologic oncology workforce.

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\* Corresponding author. Department of Medicine, Division of Hematology, Institute for Health Metrics and Evaluation, 2301 5th Avenue, Suite 600, Seattle, WA 98121, USA.  
Tel. +1-206-897-3701; Fax: +1-206-897-2899.  
E-mail address: [Cf11@uw.edu](mailto:Cf11@uw.edu) (C. Fitzmaurice).

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## 1. Introduction

Amid an expanding and aging global population, cancer-related deaths have grown substantially, as have treatment and prevention efforts targeting certain cancers [1,2]. Urologic cancers, including bladder, prostate, and kidney cancer, are more likely to affect older individuals and men [2], and are variably impacted by modifiable behavioral, metabolic, and environmental risk factors.

Previous epidemiological studies describing urologic cancers reported international variations in cancer incidence and mortality [3–7]. However, in addition to the effectiveness of the healthcare system, the differential biological influence of sex, tobacco use, and obesity substantially affect the incidence and outcomes of urologic malignancies and have not been characterized on a global scale.

This study aims to describe trends in the global burden of urologic cancers from 1990 to 2013 by age, sex, and development status in the form of incidence and mortality rates, and to describe the contribution of risk factors to bladder and kidney cancer deaths. Understanding the evolving burden of disease in a maturing population, the differential outcomes in resource-limited settings, and the changing risks of modifiable behaviors and exposures allows for a targeted health policy and research priority settings for these prevalent cancers.

## 2. Evidence acquisition

The methods for the Global Burden of Disease (GBD) Study 2013 have been previously published [1,8–10]. In this study we report the GBD results for incidence, mortality, and risk factors for bladder, prostate, and kidney cancer for the years 1990 through 2013.

### 2.1. Mortality and incidence estimation

Supplementary Figure 1 displays our analytic strategy. Prostate, kidney, and bladder cancer mortality and incidence data were extracted from global cancer registries. The most recent data available for any source through 2012 were incorporated. International Classification of Diseases, Ninth and Tenth Revision, diagnosis codes for bladder, prostate, and kidney cancer cases are described in the Global Burden of Cancer Study [1]. Mortality incidence (MI) ratios (ie, cancer deaths divided by incident cancer cases) were estimated for the three cancer sites by country, age category, sex, and year. MI ratios were applied to cancer incidence data to obtain mortality estimates. These mortality estimates were added to prostate, kidney, and bladder mortality data from vital registration system data. The cancer-specific mortality data were used as inputs for a Cause of Death Ensemble Model to generate estimates of prostate, kidney, and bladder cancer mortality for each country over time by sex [11]. An explanation of the covariates used in analysis of each urologic cancer can be found in the online Supplementary data.

Diseases in the GBD study are estimated at the individual cause level. Since the sum of all diseases often exceeds the

separately determined all-cause mortality, an algorithm is then used to scale the single cause estimates to the all-cause mortality. Prostate, kidney, and bladder cancer incidence is estimated by applying the MI ratio estimates to the final mortality estimates.

In order to determine the isolated effect of population growth on cancer incidence, two scenarios were estimated. Firstly, the population size of 2013 was applied onto the rate, sex, and age structure of 1990. The difference between the observed 1990 estimates and the simulated estimates generated using 2013 data can be attributed to population growth. Secondly, we estimated 2013 incidence using 1990 age-specific rates but the actual population structure and size from 2013. The difference between the two models is due to population aging.

### 2.2. Risk factor estimation

Risk factor analysis follows the GBD comparative risk assessment methodology described previously [8]. Mortality and incidence data are associated with various risk factors and evidence-based assumptions on the burden associated with minimal risk exposure, estimating how much of the observed burden is risk-factor attributable.

The population attributable fraction (PAF) was estimated by comparing observed health outcomes with those that would have been observed if the counterfactual level of exposure had instead occurred. The goal is to quantify how much disease burden could be averted by shifting the distribution of a risk to the level that would lead to the greatest improvement in population health, a theoretical minimum risk exposure.

Risk factors selected included smoking and obesity. The World Health Organization International Agency for Research on Cancer (IARC) classified tobacco smoking as a Group 1 carcinogen, with sufficient evidence that it causes cancers of the urinary bladder and kidney [12]. Excess body mass index (BMI; defined as 25 kg/m<sup>2</sup> or greater) is also considered to have strong evidence of association with kidney cancer by the World Cancer Research Fund International [13] and IARC. Thus, we analyzed smoking as a risk factor for both bladder and kidney cancer, and elevated BMI as a risk factor for kidney cancer.

To estimate the burden attributable to tobacco, we calculated the smoking impact ratio. The smoking impact ratio was developed to reflect past exposure, duration, and intensity of smoking in a population [8,14]. Tobacco smoking exposure was estimated based on lung cancer mortality data derived from cancer registries, vital registration, as well as household and national health surveys. The metabolic risk factor of high BMI was estimated using systematic review of the literature, including examination of surveys and epidemiological studies [8]. The risk factor burden of diets high in sugar sweetened beverages was analyzed for kidney cancer and mediated through elevated BMI.

Outcomes of interest include: total incident cases and age-standardized incidence rates (ASIRs) of kidney, bladder, and prostate cancer, deaths and age-standardized death rates (ASDRs) for each cancer by sex, development status

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