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Introduction to the Special Issue on the US Million Person Study of health effects from low-level exposure to radiation

The epidemiologic study of one million US radiation workers and veterans on health effects following low-level radiation exposure (Boice et al. 2019a), or the million person study (MPS¹), has been underway in some form for more than a quarter of a century. The MPS was designed to examine health effects after chronic exposure to low dose-rates of radiation, in contrast to the brief exposure at a high dose-rate experienced by the Japanese atomic bomb survivors. The study will provide important scientific evidence needed for sound radiation protection policy and recommendations (NCRP 2018a; Boice et al. 2019b). This special issue consists of 26 articles, including this introduction and an editorial (Wakeford 2021). The aim for this special issue is to present a comprehensive overview of the MPS with regard to: its conceptual development and historical perspectives, methodological approaches for both epidemiology and dosimetry, the first publications of quantitative results to date, as well as a summary of the first international virtual symposium with key stakeholders and researchers on the MPS that also casts a vision for the future.

Articles grouped as ‘Reviews’ specifically address the importance of the MPS and its history (Boice et al. 2019a), including the relevance to space exploration and Mars (Boice 2019). In addition, one article discusses the historical perspective of the U.S. Department of Energy (DOE) mortality studies with an emphasis on collection and storage of individual worker data (Ellis et al. 2018) while another provides a 5-decade overview of the Nuclear Regulatory Commission’s (NRC) Radiation Exposure Information and Reporting System (REIRS) database

¹ also known as the Million U.S. Workers and Veterans Study (MWS), and earlier as the Atomic and Nuclear Energy Worker (ANEW) Study (Boice 2012) [<http://anewstudy.org/>].

focusing on the importance of this “registry” of radiation workers to the MPS (Hagemeyer et al 2018). The Comprehensive Epidemiologic Data Resource (CEDR) was created in 1990 to allow researchers to access data from the U.S. DOE epidemiological studies program (US DOE 2020). CEDR became a major source of data used to extend the follow up of U.S. DOE worker cohorts for the MPS. All MPS studies are planned to be uploaded to CEDR once they are completed and published, and not just the U.S. DOE worker cohorts. Currently, the studies of Mound, Rocketdyne and Mallinckrodt workers are available on CEDR, the atomic veteran and the Los Alamos National Laboratory studies shortly, and most of the others published in this special issue within a year.

Articles within the ‘Methods’ section identify certain key epidemiologic methods utilized for the MPS, including the evaluation of statistical modeling approaches for such studies of low-level radiation health effects (Golden et al. 2018), the essential methods of obtaining vital status and cause of death on a million persons (Mumma et al. 2018b), and the validation of census data on education as a measure of socioeconomic status (Cohen et al. 2018). A fourth article in this section provides a profile for a pilot sub-cohort of a multicenter medical radiation worker component of the MPS, including early worker data prior to the 1960s (Dauer et al. 2019).

Exquisite dosimetry is the key to quality epidemiology and several articles are grouped within the ‘Dosimetry’ section. The first summarizes the dosimetry methods recommended by the National Council on Radiation Protection and Measurements (NCRP) in Report No. 178 (NCRP 2018b) emphasizing the dosimetry and uncertainty approaches for the MPS (Dauer et al. 2018). An article delineating the specific dosimetry associated with individual veterans who participated in nuclear weapons testing emphasizes the importance of an in-depth understanding of exposure scenarios (Till et al. 2014; Beck et al. 2017; Till et al. 2018a), while another addresses approaches associated with dose reconstruction for internal emitters (Leggett et al. 2018a). Dosimetry for medical radiation workers also is particularly unique and was given

specific development attention with a focus on absorbed doses to the lung, brain, heart, colon and red bone marrow (Yoder et al. 2018). Largely based on this work and additional development, the NCRP published general guidance in NCRP Commentary 30 (NCRP 2020; Yoder et al. 2021) specifically directed toward the MPS for using personal monitoring records to derive organ doses for medical radiation workers. The final article in this section identifies potential improvements in brain dose estimates for internal emitters as relevant to possible cognitive impairment following high-LET exposures (Leggett et al. 2018b). The concepts discussed in this paper helped form the basis of a forthcoming NCRP Commentary on the development of kinetic and anatomical models for brain dosimetry for internally deposited radionuclides, developed by NCRP Scientific Committee SC 6-12 (NCRP 2021).

Perhaps the pièce de résistance of this special issue are 10 articles, grouped within the ‘Original Articles’ section, that provide the first quantitative publication of results from epidemiologic analyses of specific and wide-ranging MPS cohorts. Six articles provide results on mortality (including leukemia, cancer, heart disease, Parkinson’s disease, and other diseases) among large cohorts of the MPS, including: U.S. nuclear power plant workers (Boice et al. 2021c), medical radiation workers (Boice et al. 2021a), U.S military participants (atomic veterans) at eight aboveground nuclear weapons test series (Boice et al. 2020), Mallinckrodt uranium processing workers (Golden et al. 2018), Los Alamos National Laboratory workers (Boice et al. 2021b), and Tennessee Eastman Corporation uranium processing workers (Boice et al. 2021d) including both male and female employees. The MPS has re-opened the epidemiologic study of the extremely important and influential study of the radium dial workers (Martinez et al. 2021), complemented with a new NCRP Scientific Committee 6-13 on *Methods and Models for Estimating Organ Doses from Intakes of Radium*. Quantitative information on female and male lung cancer risks is provided among workers in the MPS and TB-fluoroscopy cohorts (Boice et al. 2019c). In addition to radiation, the MPS

evaluated asbestos exposure and mesothelioma and asbestosis mortality among radiation-monitored occupational cohorts including the atomic veterans (Till et al. 2018b; Boice et al. 2020), industrial radiographers and nuclear power plant workers (Mumma et al 2018a; Boice et al. 2021c).

The 'Meeting Report' section represents the finale of the special issue. A comprehensive paper (Boice et al. 2021e) summarizes the first international virtual MPS symposium wherein key stakeholders and researchers discussed the importance of the MPS, its relevance for radiation protection, what has been done, current emerging results, plans for the future, as well as a vigorous question and answer dialogue with the over 300 participants. It is anticipated that a powerful evaluation of radiation effects at low doses and low dose rates will be achieved when all MPS cohorts are completed and pooled, i.e., combined to provide substantial statistical power to evaluate health effects following low-level exposures. A continued follow-up of the 34 individual cohorts comprising the MPS is planned for the next several decades. Incidence data on the occurrence of disease, in addition to mortality data, are forthcoming as is a comprehensive approach to obtain individual information on tobacco use via linkages with the Centers for Medicare and Medicaid Services (CMS) nationwide databases (Boice et al. 2021e). A National Center for Radiation Epidemiology and Biology is envisioned.

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