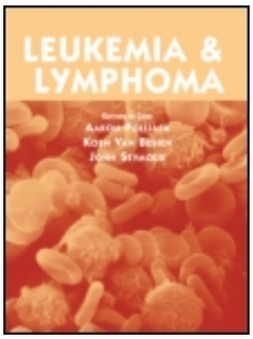

Leukemia & Lymphoma

ISSN: 1042-8194 (Print) 1029-2403 (Online) Journal homepage: informahealthcare.com/journals/ilal20

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To cite this article: Stefano Luminari (2013) Bridging the gap between epidemiology and clinical research in lymphoma, Leukemia & Lymphoma, 54:9, 1855-1856, DOI: 10.3109/10428194.2013.777838

To link to this article: https://doi.org/10.3109/10428194.2013.777838

Leukemia & Lymphoma, September 2013; 54(9): 1855–1856

ISSN: 1042-8194 print / 1029-2403 online
DOI: 10.3109/10428194.2013.777838

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COMMENTARY

Bridging the gap between epidemiology and clinical research in lymphoma

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Epidemiology and clinical research have represented in recent years two sides of research in oncology and hematology, and are seen by most as different and non-communicating approaches to the study of tumors.

Epidemiologists work to provide the most accurate data on incidence and mortality, analyzing risk factors for all cancer subtypes including malignant lymphomas. From a methodological point of view they describe what happened in the past, using retrospective studies that, due to the population-based approach, have very few or negligible selection biases. In other words, epidemiologists have the unique opportunity to describe how a given disease actually was in the "real world," also including less common conditions (e.g. rare histotypes, patients with comorbidities, elderly subjects, etc).

In contrast, clinical oncologists and hematologists are more focused on the search for novel and more effective treatment strategies and prognostic factors. Prospective clinical trials are one of the most important tools used by clinicians as they attain the highest levels of detail on the effectiveness of a therapy. The main problems with this approach are the low representativeness of the studied population, the reproducibility of results, and costs. Although patients included in clinical trials are very well investigated, they represent a selected minority of the real world. Most of the atypical or rare histotypes are usually excluded from trials. Data from clinical trials are then highly suitable to answer clinical questions addressed by the study, but always need validation before they can be confirmed as a step forward in the approach to the disease.

Both clinical and epidemiological research should then represent two alternative but complementary approaches to the study of cancer, focused on either exploration (clinical trials) or validation (population-based studies). A prerequisite to render communication between epidemiologists and clinicians successful is that the definition of the studied clinical condition does not change with time. Actually, if a disease is deeply and rapidly modified in the diagnostic or therapeutic approach, the informative and methodological gap between the two sides of research may become unbridgeable. In this case the clinical relevance of retrospective epidemiological studies may become very limited, and much work is required for epidemiologists to update their coding systems and to start accumulating new data before they can provide data of clinical relevance.

In the case of malignant lymphoma, the approach to this disease was greatly modified in the mid-1990s with the publication of the Revised European-American Lymphoma Classification (REAL), and with subsequent updates of the World Health Organization (WHO) classification of hematopoietic disorders. From then, lymphomas were no longer seen as a single disease with heterogeneous clinical features, but as a group of distinct clinical entities, each with the dignity of a different disease. As a result, today more than 60 different lymphomas are defined, and more are likely to be defined with the recent advances in genomic medicine [1–3]. Pathologists and onco-hematologists were the first to translate the new diagnostic approach into new diagnostic/staging protocols, different prognostic indexes and different therapies. For epidemiologists, the new diagnostic approach first represented a matter of reorganization and validation of coding systems and of population-based archives. Subsequently, most population-based studies continued to speak an old language, and it took approximately 10 years for the most organized and advanced cancer registries to provide the first modern epidemiological description of lymphoma [4]. To date, few other reports have been published describing the epidemiology of the different lymphoma entities as defined by the REAL/WHO classifications and revealing new unexpected features.

In this issue, Kuper-Hommel *et al*. [5] provide another good example of how a modern approach to the epidemiological study of lymphomas can provide results that are relevant to onco-hematologists, reducing the gap between oncologists and epidemiologists. In their study the authors describe the incidence, therapy and outcome of a large series of 1714 patients with localized marginal zone lymphoma (MZL) diagnosed in The Netherlands from 1994 to 2010. The most important finding of this population-based study was a drop in the incidence of gastric MZL in recent years

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This commentary accompanies an article to be published in *Leukemia & Lymphoma*. Please refer to the table of contents of the print issue in which this commentary appears.

that is consistent with similar recent studies, and that can be explained by a reduction in the prevalence of *Helicobacter pylori* (HP) infection [6]. As suggested by the same authors, clinicians should be aware that patients with MZL who are seen today are different from those seen in the past. The suggested higher prevalence of HP-negative gastric MZL would represent a new challenge for clinicians, as HP-negative patients are less likely to respond to standard therapies, and the outcome of recently diagnosed patients with gastrointestinal mucosa-associated lymphoid tissue (MALT) lymphoma is worse than in other cases of MZL. This epidemiological study has relevant clinical implications, as it describes how a disease has changed and, at least for MZL, that a different kind of patient will be expected in the future. Most important, the results provided by Kuper-Hommel *et al*. would have never been described by a clinical trial but only by a well-organized and modern cancer registry. This, as well as other similar reports, confirms that epidemiologists and clinicians must have a strong connection in serving one another. As oncology is moving rapidly into the era of genomic medicine, the definition of the disease and the availability of new therapies is likely to change substantially in future years for all types of cancer. The eye of the epidemiologist should then be kept wide open to catch all relevant new findings and to timely provide an updated and clinically useful picture of the "real world" of cancer.

Potential conflict of interest: A disclosure form provided by the author is available with the full text of this article at www.informahealthcare.com/lal.

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