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EDITORIAL

# Issue focusing: a new topical collection on diabetic nephropathy

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Acta Diabetologica has launched a new initiative: a series of Topical Collections starting with this one on Diabetic Nephropathy coordinated by Professor Giuseppe Pugliese and aimed at encouraging the submission of papers on this topic.

Diabetic Nephropathy, also called Diabetic Kidney Disease (DKD), is a major complication affecting approximately one-third of patients with either type 1 diabetes (T1D) or type 2 diabetes (T2D). Nowadays, it represents the leading cause of end-stage renal disease (ESRD) worldwide [1].

During the last decades, the rates of all diabetic complications, including DKD, have progressively declined [2], in parallel with a decrease in all-cause and cardiovascular mortality, to which DKD strongly contributes by increasing cardiovascular risk since its early stages. However, among diabetic complications, ESRD has shown the smallest reduction, a finding that is likely due to the reduction in competing risks, such as mortality from acute myocardial infarction and stroke, which grants more years of life for DKD progression to ESRD [2].

The natural history and clinical presentation of DKD have also changed during the last decades [1]. Though its overall prevalence has remained stable, prevalence of albuminuria has decreased, whereas that of reduced estimated glomerular filtration rate (eGFR) has increased [3]. These opposite trends have resulted in an increasing prevalence of nonalbuminuric renal impairment, which has become the prevailing DKD phenotype among T2D individuals with reduced renal function and is also frequently observed in patients with T1D [1]. Moreover, a recent report showed that mortality rates have trended downward for individuals with increased albuminuria, but have increased for those with decreased eGFR and normoalbuminuria [4].

The lower rates of complications and death probably reflect improved treatment, particularly the increased use of anti-hyperglycaemic agents, blockers of the renin–angiotensin system (RAS), and statins, which has resulted in progressively lower hemoglobin A1c, blood pressure, and LDL cholesterol levels [2, 3]. In addition, the increasingly widespread use of RAS blockers, favoring prevention and/or regression of albuminuria as well as reduction of blood pressure levels resulting, in some individuals, in decreased renal perfusion pressure and eGFR, might explain the increasing prevalence of the nonalbuminuric DKD phenotype [1, 3]. However, the rising prevalence of this phenotype and the increasing mortality associated with it indicate that changes in treatment have not impacted favorably, if anything, on eGFR reduction independent of albuminuria [4].

Altogether, these findings highlight the need for more effective treatments for DKD and, particularly, the nonalbuminuric phenotype, which has been ignored by clinical trials that have focused almost exclusively on albuminuric patients. Unfortunately, virtually, all the attempts to identify new "pathogenic" treatments for this complication have not provided encouraging results [5]. Paradoxically, the most promising results came from the cardiovascular safety trials with new anti-hyperglycaemic agents. These trials showed that SGLT2 inhibitors and GLP-1 receptor agonists, beyond their glucose-lowering action, can afford protection not only from cardiovascular disease, but also from renal disease, though renal outcomes were not primary endpoints. These data have prompted several mechanistic hypotheses to explain this protection, which are currently under investigation [5].

We hope that this initiative will be successful in collecting important new research dealing with all aspects of DKD, with a special focus on the most novel facets of this rapidly changing complication.

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## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

**Ethical approval** This article does not contain any studies with human participants performed by any of the authors.

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