Burden of Cardiovascular, Renal and Metabolic (CVRM) Diseases

Cardiovascular disease (CVD)

Approx. 523M people globally have a form of CVD.[1]

CVD accounts for 32% of all global deaths.[5]

Up to 20% of heart attack patients in Sweden will have another attack, stroke or death within the first three years.[10]

Raised LDL cholesterol is a major risk factor for CVD and is estimated to cause 2.6M deaths globally each year.[14]

Heart failure (HF)

64M people are living with HF worldwide.[2]

Approx. half of all HF patients die within five years of diagnosis, and more than 50% of those with severe HF die within one year.[7,8]

HF is a leading cause of hospitalisations for those aged 65+.[12]

Chronic kidney disease (CKD)

Approx. 850M people are affected globally.[3]

In advanced countries, 2-4% of the annual healthcare budget is spent on end-stage kidney disease (ESKD) treatment.[9]

CKD is expected to become the world's 5th leading cause of death by 2040.[13]

Metabolic disease

537M adults live with diabetes worldwide.[4]

650M+ adults live with obesity globally.[6]

3-5% of the global population is estimated to be affected by NASH, an advanced form of non-alcoholic fatty liver disease (NAFLD).[11]

Diagnosed NASH patients worldwide are expected to increase by 63% by 2030.[15]

Interconnections of CVRM diseases

Established commonality

- CVRM diseases remain underdiagnosed, undertreated, and their interconnections under recognised.[16]
- Science has advanced our understanding of how CVRM diseases are often interlinked, sharing underlying mechanisms of action and demographics of people affected. For example, SGLT2is, a class of drug originally developed for type 2 diabetes (T2D), has now been indicated for both CKD and HF.[17,18]
- Different CVRM diseases will often impact each other to speed up disease progression, which can affect patients' quality of life and prognosis.[19]

Proof points

- Globally, 80% of end-stage renal disease cases are caused by diabetes, hypertension, or both.[20]
- CVD accounts for up to 30% of CKD deaths.[21]
- Around 55% of patients with HF also have CKD.[22]
- More than 93% of people with T2D have at least one other CVRM disease in the US.[23]
- The estimated global prevalence of NASH among patients with T2D is 37.3%.[24]

Comprehensive Approach to Addressing CVRM Diseases

Uncovering the underlying mechanisms that link CVRM diseases together can fundamentally transform care for the millions of people who are living with these complex diseases. Understanding how CVRM diseases are connected can enable earlier intervention to protect vital organs and advanced science to slow or stop disease progression, and one day even cure these debilitating, degenerative and life-threatening conditions.

Continued research into CVRM diseases collectively rather than in silos can help better address the interconnections between diseases. Innovations across the entire research and clinical development continuum from preclinical research, clinical development and clinical trials, to collaborations with academic, biotech, governmental and policy organisations to develop innovative screening and detection methods, are critical to help diagnose patients earlier and improve access to CVRM care.

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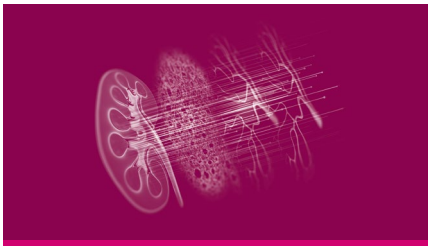
AstraZeneca Cardiovascular, Renal and Metabolism (CVRM)

Innovating at every stage of clinical development



Next gen therapeutics

- Addressing multiple risk factors across CVRM diseases to improve health outcomes through:
  - Novel small molecules
  - Drug combinations
  - Nucleotide-based therapeutics
  - Cell therapies
  - Advanced biologics
- Leveraging a **precision medicine approach** to target the underlying drivers of disease and identify novel drug targets and biomarkers
- Working to slow or stop disease progression and regenerate organs through the discovery of cutting-edge **cell and gene therapies**

Early-stage R&D advances

- Using **AI and machine-learning tools** to identify new targets across CVRM indications
  - Collaborating with BenevolentAI to produce the first AI-generated targets for CKD to enter the pipeline
- Applying the following models to **better understand the complexities of CVRM diseases** and bridge the gap between animal models and clinical trials:
  - Kidney 'organ-on-a-chip'
  - 'Heart-in-a-jar'
  - Liver organoids
- Accelerating **innovative scientific and R&D processes** to more effectively discover and predict the clinical effectiveness of candidate drug molecules

Clinical trial modernisation

- Deploying a **patient-centric and site-centric approach** to improve and simplify the recruitment process, delivering benefits to physicians and patients
- **Improving diversity in clinical trials** to better reflect the patient population and ensure a robust and reliable body of evidence
- Applying AI and data science to **optimise clinical trials at different stages** to accelerate progress and reduce inefficiencies overall
- **Linking a network of genetic pre-screening sites to a collection of interventional trials** to rapidly assess patient eligibility (one time only) for NASH and other related trials

Generating a diverse pipeline for CVRM

AstraZeneca is uniquely positioned to improve the outcomes of patients living with CVRM diseases today and tomorrow through its strong and expanding portfolio and one of the broadest, deepest, most innovative pipelines in the industry.

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Over 25 novel targets and molecules being investigated across CVRM diseases.[1]

- Type 2 diabetes
- NASH fibrosis
- Dyslipidaemia
- Nephropathy
- CVD
- HF
- Obesity with related co-morbidities
- CKD
- Hereditary or wild-type transthyretin-mediated amyloid cardiomyopathy (ATTR CM)
- Hereditary transthyretin-mediated amyloid polyneuropathy (hATTR-PN)

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19 CVRM medications approved in various markets across the globe.[2]

- Type 2 diabetes
- HF
- CVD
- Acute major bleeding
- CKD
- Hyperkalaemia

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