Abstract: Cardiovascular disease (CVD) leads to one-third of all deaths in Argentina. To implement patient-centric strategies for reducing CVD burden, available data on hypertension and hypercholesterolemia patients at different stages of their journey: awareness, screening, diagnosis, treatment, adherence, and control were analysed. A semi-systematic review in peer-reviewed databases (EMBASE and MEDLINE) and unstructured sources such as Google Scholar, Argentine Ministry of Health, and World Health Organization websites was conducted till 06.07.2021 for hypertension and dyslipidemia. English articles published in 2010–2021, depicting patient journey data for hypertension or hypercholesterolemia of the nationally representative adult population of Argentina were included. Thesis abstracts, letters to the editor, editorials, and case studies were excluded. No limits were used for unstructured sources. Weighted or simple means were estimated for patient journey stages. Out of 296 and 1257 articles retrieved for hypertension and hypercholesterolemia, respectively, five articles were retained for each of the conditions. The estimates for hypertension and hypercholesterolemia, respectively, were 46.6% and 30.7% for prevalence, 61.6% and 37.3% for awareness, 97.5% and 28.9% for screening, 64.1% and 29.0% for diagnosis, and 49.7% and 36.6% for treatment, and 19.9% and 20% for overall control. Adherence data were not available for hypercholesterolemia, while the same for hypertension was 50.4%. Various determinants are responsible for low adherence such as patient-level barriers, physician-related barriers, and health system-related issues. The review reveals that hypertension and hypercholesterolemia are poorly controlled in Argentina. Although further studies with more accurate data are needed to confirm these results, they should alert the medical community and the public health institutions to take urgent corrective actions.

Keywords: adherence, CVD, hypercholesterolemia, hypertension, prevalence

Introduction
Cardiovascular disease (CVD) is the leading cause of disability and death across the globe.1 In 2010, the estimated global cost of treatment of CVD was USD 863 billion, which is expected to increase to USD 1044 billion by the year 2030.2 CVD includes a wide range of vascular conditions like ischemic heart disease, and cardiac arrest, heart failure, and peripheral arterial disease.3 Hypertension and dyslipidemia are major contributors to cardiovascular morbidity and mortality.4 Globally, the overall prevalence of hypertension in adults is 30% to 45%.5 Raised cholesterol is estimated to cause 2.6 million deaths (4.5% of total) and accounts for 29.7 million adjusted disability-adjusted life years (DALYs), or 2% of total DALYs.6 In Argentina, all over 34% of CVDs-related to deaths.7 Prevalence of hypertension and dyslipidemia is reported highest in Argentina across Latin America and the prevalence of CVD is increasing in Argentina.8

In lower- and middle-income countries (LMICs),9 CVD along with diabetes, cancer, chronic respiratory diseases, and mental health disorders10–12 constitute the major non-communicable diseases (NCDs). The rising burden of NCDs in LMICs is due to the increasing prevalence of risk factors such as smoking, excessive alcohol use, unhealthy diet, and physical inactivity.13–15 Eighty percent of all deaths and three-quarters of premature deaths in LMICs occur due to NCDs, most of which are due to CVDs.14,15

Healthcare provision in Argentina has been impacted by the increased healthcare expenditure burden due to the exponential growth and aging of the population.7,16 Rural areas lack an effective health system and access to peripheral
hospitals, making it difficult for inhabitants to come repeatedly for getting screening screened and seek lifelong medications. Moreover, although the cost of treatment for chronic conditions is covered by the government, comprehensive public sector insurance providing healthcare coverage is still lacking. The health-care infrastructural issues are coupled with inadequate manpower in the peripheral hospitals. Resources to train health-care providers are also lacking.

Effective control of hypertension and dyslipidemia by transiting patients through various stages of NCD care is essential to ensure optimal cardiovascular health of the population. Patients with NCDs are prescribed lifelong medicines for both hypertension and dyslipidemia and are advised to modify their lifestyle with respect to diet, exercise, and reduction of harmful habits, like alcohol consumption and smoking. They generally have a lifelong and fragmented journey through the health system unlike those with communicable diseases. The stages of the continuum of care need motivation for repeated contact and interactions with the patient and health behaviour to sustain the progress. These stages are classified as awareness of the disease, screening, diagnosis, treatment, adherence to the prescription, and control of the disease. Quantifying stages of the patient journey in particular geography reflects the overall status of care for the disease and the outcome of the overall healthcare provision in a given country, while different factors play their role by influencing the corollary. This also helps to focus on locally relevant issues, prevalent practices, and socio-economic and educational factors. The Global Action Plan on the prevention and control of NCDs 2013–2020 has emphasized the need to enhance the national capacity for high-quality research on the prevention and control of NCDs. Similarly, the United Nations Sustainable Development Goals (SDGs) reiterate the need for research on NCDs that encroach upon the health of people living in LMICs. These stress the need to obtain a dipstick of the nationally-representative population data. The information regarding the quantification of stages of the patient journey is generally lacking in LMICs.

The current study was undertaken to elucidate the data related to stages of patient journey for hypertension and hypercholesterolemia in Argentina and to further explore practices in CVD management and provide recommendations for improved CVD care for patients. The quantification methodology adopted in this study was broadly based on the “Mapping the Patient Journey Towards Actionable Beyond the Pill Solutions (MAPS)” initiative. MAPS follows a semi-systematic review approach to generate evidence on NCD patient journey from multiple sources, ie, peer-reviewed databases, grey, and local expert opinions to suggest locally relevant and effective solutions for gaps in the patient journey. Previously, researchers have highlighted five touchpoints of the patient journey for NCDs in LMICs, while the methodology in MAPS considers an additional stage of “control” in the patient journey.

Materials and Methods

Search Strategy

Methods of conducting the review and eligibility criteria were documented in advance. Data collection was performed by an independent reviewer following a structured and unstructured search strategy using an established approach of doing a semi-systematic review. Articles related to the prevalence and patient journey stages (awareness, screening, diagnosis, treatment, adherence, and control) in Argentina in the context of hypertension and dyslipidemia were primarily sought using keywords through a structured systematic search on Embase and MEDLINE databases using OVID access, as these databases ensured comprehensive coverage of biomedical databases, journals, and article types. Refer to Appendix 1 for keywords used. The unstructured search was conducted on Google Scholar, and among the articles from the websites of Incidence and Prevalence Database (IPD), World Health Organization (WHO), and the Argentina Ministry of Health. The last search was run on 06.07.2021.

The most commonly followed criteria for diagnosis of hypertension and dyslipidemia were considered for this study. According to the Eighth Joint National Committee and European Society of Hypertension (ESH)/European Society of Cardiology (ESC) guideline 2018, hypertension was defined as the percentage of respondents having an average systolic blood pressure (SBP) ≥140 mmHg and/or average diastolic blood pressure (DBP) ≥90 mmHg. Hypercholesterolemia is defined as total cholesterol (TC) level ≥5.0 mmol/L or ≥200.0 mg/dL. The rest of the definitions used in the review are described in Appendix 2.
Selection of Studies
Inclusion criteria were articles quantifying patient journey stages for hypertension and hypercholesterolemia in adults (≥18 years) of Argentina published in English, whose full text was available. Among structured search results, studies published in the last 11 years were selected, while in unstructured search, there were no date or language limits applied. Included study types from structured search were systematic review and/or meta-analysis, randomized controlled study, observational study (including case-control, cohort, cross-sectional, longitudinal, retrospective chart review, survey study types), and narrative reviews (both full articles and conference abstracts). Thesis abstracts, letters to the editor, editorials, case studies, and articles not representing the national population including population sub-groups were excluded. All the articles obtained through the structured and unstructured search were first screened using title and abstract, followed by full-text screening by independent reviewers based on these exclusion criteria.

Extraction and Validation of Data
Locally relevant data regarding the care of hypertension and dyslipidemia were extracted from the eligible studies. Data extracted from the studies included report characteristics, such as year of publication, language, and type of article, characteristics of the population studied, outcomes captured, and qualitative data presented in the paper regarding prevalence, awareness, screening, control, diagnostic and management practices, and various determinants in adherence to medication. The data were further validated by local experts before inclusion in the final analysis. To address any gaps in the availability of data, relevant local language studies or anecdotal data solicited from local experts or provided by authors were included in the review.

Statistical Analysis
Quantitative data on the patient journey stages for hypertension and dyslipidemia were extracted and analyzed from the included studies. Weighted means were calculated in the case of multiple data points for a patient journey stage.

Results
Details of Included Records
In the analysis of hypertension, 296 articles were obtained from the structured search, of which 284 articles were screened for eligibility and three were included in the final review. Four articles were obtained from the unstructured search including three articles provided by authors; of these, two were included in the final review. Overall, a total of five articles were included in the final analysis for hypertension. In the analysis of hypercholesterolemia, 1257 articles were obtained during the structured search. These included articles from Latin American countries due to the paucity of data from Argentina. Out of these, 190 articles from Argentina were screened, and four articles were used in the final analysis. Four articles were obtained during the unstructured search including two articles suggested by authors, of these one was included in the final analysis. Overall, five records were included in the final review of hypercholesterolemia. The final analysis included anecdotal data from the local experts for screening and control of hypercholesterolemia. The prevalence of hypertension and hypercholesterolemia in Argentina was 46.6% and 30.7% 23%.

The review revealed estimates for hypertension and hypercholesterolemia in Argentina were 61.6% and 37.3% for awareness, 97.5% and ≥80% for screening, 64.1% and 28.9% for diagnosis, 49.7% and 36.6% for treatment, and 19.9% and 20% for overall control. Adherence data were not available for hypercholesterolemia, while the same for hypertension was 50.4%. The flow of the studies through the review is depicted in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) diagram (Figure 1A and B) and the detailed characteristics of the included studies are mentioned in Table 1.

Pooled Analysis of Outcomes of Quantification of Patient Journey Stages
The total population of Argentina is estimated to be 45.2 million in 2020. According to the 4th Encuesta Nacional de Factores de Riesgo (ENFR) 2018, the prevalence of hypertension was 46.6% hypercholesterolemia was 30.7%. The data on the prevalence of hypertension mentioned in other articles were based on ENFR 1/2/3 surveys. As ENFR 2018 data
are now available, this reflects the most updated hypertension prevalence and has been included in the paper. Various patient journey stages were mapped as shown in Table 2.

Awareness, diagnosis, and treatment were lower for hypercholesterolemia compared with hypertension. Authors think that the higher rate of screening observed for both conditions may mostly be contributed by opportunistic screening in peripheral hospitals. Overall control of both the conditions was estimated to be very low.

**Discussion**

Argentina is a socially, culturally, and economically diverse country in Latin America. It has the largest aging population in Latin America.\(^{30}\) Similar to other countries in the region and other LMICs, the increasing burden of hypertension, hypercholesterolemia, and other NCDs in Argentina is a serious concern. As with other countries in the region, and also other LMICs, there is a growing threat of hypertension and hypercholesterolemia. The age- and gender-adjusted prevalence ratio of hypertension in Argentina (0.61) is comparable to Colombia (0.7) and Peru (0.65), but lower than Chile (1.48), Costa Rica (1.15), Dominican Republic (1.31), Puerto Rico (1.19), and Venezuela (1.49). Whereas, the age- and gender-adjusted
prevalence ratio of hypercholesterolemia in Argentina (0.84) was higher than in Dominic Republic (0.83), Peru (0.75), and Venezuela (0.78). However, fewer patients with hypertension and hypercholesterolemia are put on multiple drug regimens in Argentina as compared to other countries in Latin America.

A lack of awareness among the Argentine population regarding their status of hypertension and hypercholesterolemia was observed in this study, although awareness was better for hypertension than hypercholesterolemia. A possible reason may be the easier accessibility to hypertension screening without needing a lab investigation. Screening for hypertension and hypercholesterolemia is often dependent upon contact with the healthcare system when seeking treatment for other diseases. As a result, most of the patients remain undiagnosed. Even when diagnosed, patients are not aggressively treated by the health-care providers for tight control of hypertension and hypercholesterolemia. Further, following the initiation of the treatment, patient’s reluctance and behavioural issues lead to low adherence. All these result into low
### Table 1 Characteristics of the Included Studies in the Review

| S. No. | Title                                                                 | Authors                                      | Year of Publication | Patient Journey Data |
|-------|----------------------------------------------------------------------|---------------------------------------------|---------------------|----------------------|
|       | **Hypertension**                                                     |                                             |                     |                      |
| 1     | Prevalence, awareness, treatment and control of hypertension in rural and urban communities in Latin American countries | Lamelas et al                                | 2019                | Awareness (56.2%), Treatment (50.8%), Control (16.2%) |
| 2     | Trends in prevalence of hypertension in Argentina in the last 25 years: a systematic review of observational studies | Diaz et al                                   | 2015                | Awareness (57.9%), Treatment (49.5%), Control (20.5%) |
| 3     | National registry of hypertension. Epidemiological characteristics of hypertension in Argentina. the renata-2 study | Delucchi et al                               | 2017                | Awareness (61.2%), Treatment (55.5%), Adherence (50.4%), Control (24.2%) |
| 4     | Hypertension in seven Latin American cities: the cardiovascular risk factor multiple evaluation in Latin America (CARMELA) study | Hernandez-Hernandez R et al                  | 2010                | Screening (97.5%), Diagnosis (64.1%), Control (18%) |
| 5     | 4°ta Encuesta Nacional de Factores de Riesgo – Informe definitivo | Ministerio de Salud de la Nación, Instituto Nacional de Estadísticas y Censos | 2019                | Prevalence (46.6%), Awareness (68%), Treatment (48.3%) |
|       | **Dyslipidaemia**                                                    |                                             |                     |                      |
| 1     | Educational intervention to improve effectiveness in treatment and control of patients with high cardiovascular risk in low-resource settings in Argentina: study protocol of a cluster randomised controlled trial | Gulayin et al                                 | 2017                | Awareness (37.3%), Treatment (54.8%) |
| 2     | Inequalities in the use of secondary prevention of cardiovascular disease by socioeconomic status: evidence from the PURE observational study | Murphy et al                                 | 2018                | Treatment (17.7%) |
| 3     | Comparing Strategies for Lipid Lowering in Argentina: An Analysis from the CVD Policy Model–Argentina. Journal of general internal medicine | Konfino et al                                 | 2017                | Treatment (34%) |
| 4     | 4°ta Encuesta Nacional de Factores de Riesgo – Informe definitivo | Ministerio de Salud de la Nación, Instituto Nacional de Estadísticas y Censos | 2019                | Prevalence (30.7%), Diagnosis (28.9%) |
| 5     | Unusual genetic variants associated with hypercholesterolemia in Argentina | Corral et al                                  | 2018                | Treatment (40%) |
| 6     | Anecdotal Data by Key Opinion Leaders                                |                                             |                     | Screening (≥80%), Control (20%) |

### Table 2 Hypertension and Dyslipidaemia Pooled Estimates for Quantification of Patient Journey Stages from the Included Studies

| Condition   | Awareness | Screening | Diagnosis | Treatment | Adherence | Control |
|-------------|-----------|-----------|-----------|-----------|-----------|---------|
| Hypertension| 61.6%     | 97.5%     | 64.1%     | 49.7%     | 50.4%     | 19.9%   |
| Dyslipidaemia| 37.3%     | ≥80%      | 28.9%     | 36.6%     | No data   | 20%     |

**Notes:** † = Weighted Average, ‡ Simple Average. Source of data: † = Published Data; ‡ = Expert Opinion Only.
control rates (20%) for both the conditions (Table 2). A poor control predisposes most patients with hypertension and dyslipidaemia to a greater risk of cardiovascular morbidity and mortality.  

Limited data were available on adherence of hypercholesterolemia. Similarly, data regarding the contributory factors for poor quantification of patient journey stages were also lacking. Another major limitation encountered was the heterogeneity in the definition of awareness, adherence, diagnosis, treatment, since there is no universal definition of these. Further, quality appraisal of included studies was not done. Although there was a data validation step by local experts to evaluate the quality and relevance of data from the shortlisted studies, it did not follow a stringent quality appraisal checklist. Despite the limitations, the study could bring out various barriers in ensuring adherence and could inform regarding the actual situation of hypertension and dyslipidaemia care in Argentina and ways to improve the same.

-reported Barriers in Ensuring Adherence to Hypertension and Hypercholesterolemia

Based on the review, low adherence was found to be the major issue in ensuring optimal patient care. Besides quantification of patient journey stages, the review also gathered information from the included studies and from the opinion of the experts (authors) regarding barriers in adherence more prevalent in Argentina.

Patient-Level Barriers

At the level of patients, barriers consisted of socio-economic inequality, where poor strata had lower access and lower adherence, especially for high-cost medicines.  

Reluctance of the patients, economic reasons, access to the health system, forgetfulness, and lifelong nature of medication were factors that impacted adherence to the treatment. Lack of awareness about the disease and the need for its treatment were encountered as a barrier in multiple studies, particularly in rural areas.

Modifiable behavioural factors associated with low adherence were unhealthy habits followed by the patients, which included excessive salt consumption, smoking, and alcohol consumption. Obesity and physical inactivity introduced complacency to continue treatment as the results were not immediately visible. Comorbidities like diabetes needed multiple drugs to be consumed daily (polypharmacy) which affected motivation and remembrance. Psychosocial factors led to reduced support from family and society to avail health-care services and to continue treatment. Behavioural risk factors predisposed individuals to discontinuation of the medication. Persistent stress could also contribute to reduced adherence to the prescription.

Physician-Related Barriers

Physician-related barriers were medical and therapeutic inertia, limited consultation time for preventative counseling and screening of hypertension and dyslipidaemia, lack of knowledge on guideline-recommended values for detecting elevated blood pressure and cholesterol levels, improper prescription practices, and lack of empathy with the patient.

Primary care physicians (PCPs) are the primary point of contact for most patients seeking CVD care. As brought out by the review, PCPs frequently do not adhere to the standards of care for hypertension and dyslipidaemia. They may commit errors and irrational omissions while prescribing medicines due to a lack of time and motivation as a result of overwork in the outpatient settings. PCPs do not prescribe intensive therapies as recommended in guidelines for achieving more stringent control targets for hypertension and dyslipidaemia. This further leads to ignorance towards pre-hypertension and borderline dyslipidaemia.

Physicians face multiple competing demands within the given time. This lack of time along with the lack of reimbursement for preventive counseling makes them spend less time with the patient discussing other important aspects of the management of these conditions, especially encouraging important non-pharmacologic strategies such as consuming a healthy diet and increasing physical activity. This eventually leads to a lack of adherence on part of the patients, who fail to understand the importance of adhering to medication and modifying their unhealthy behaviour. Moreover, the practitioners have their own misbeliefs about blood pressure cut-offs and cholesterol levels, due to which they fail to prioritize these conditions among multiple chronic diseases.

Health System-Related Issues

Systemic issues also reportedly contributed to low adherence. These included poor health systems and lack of access to the health-care system in rural areas, evident from poor infrastructure and inadequate manpower. Cost of medications
and poor insurance coverage posed a significant challenge in continuing lifelong medication after initiation of treatment.\textsuperscript{32} Patients faced regular out-of-pocket expenditure to source refill of prescriptions from far-located health facilities which often lacked conveyance facilities.\textsuperscript{36} Health-care providers encountered conflicting guidelines for hypertension and dyslipidaemia, which created confusion in providing optimal care. The lack of a standardized referral pathway between primary care and secondary care for patients with complications affected the continuum of care.\textsuperscript{32}

**Suggested Interventions for Improving Hypertension and Hypercholesterolemia Care in Argentina**

The Health-care system and scientific societies should conduct awareness campaigns and programs for hypercholesterolemia and hypertension for patients with a lack of access to the health system.\textsuperscript{18} Strategies to optimize care and outcomes at various stages of the CVD patient journey include continual physician education (CPE), task shifting, and opportunistic screening. Task-shifting for screening hypertension can be done by training nurses or other non-physician staff in operating digital blood pressure (BP) apparatus and frequently calibrating the instruments.\textsuperscript{37,38} Continual physician education on the importance of screening and early detection, and nationwide campaign to sensitize care givers regarding the importance of tight control of hypertension and hypercholesterolemia will help improve the overall control of these conditions.\textsuperscript{18,35} Encouraging opportunistic screening is another proposed strategy to overcome poor patient turnaround. Due to the multifactorial and chronic nature of CVDs, patients must be provided with repeated counseling to improve their adherence to medications and recommended lifestyle modifications. A more frequent snapshot of NCDs is required in the population to identify the target intervention groups and to track the progress of the efforts made in the field.

**Conclusion**

The review revealed that the overall control of hypertension (19.9\%) and hypercholesterolemia (20\%) was poor in the adult population in Argentina. There was a dearth of data on patient journey stages despite a comprehensive search. This study provides a quantitative mapping of the various stages of a patient’s journey in the Argentine population with hypertension and hypercholesterolemia. The major gaps highlighted by the review were regarding the awareness, diagnosis, treatment, and adherence for both hypertension and hypercholesterolemia. These gaps were perceived in addition to poor prescribing practices by PCPs. Optimizing these factors such as patient-level barriers, physician-related barriers, and health system-related issues could be useful to improve adherence. Both national-level policymakers and health officials will be able to utilize the data obtained and make provisions for improving the practices of health-care workers and devising awareness strategies to ensure adherence to medication among the patients.

**Key Points**

1. Current knowledge: Around 34\% of all deaths in Argentina are attributed to cardiovascular diseases. Prevalence of hypertension and dyslipidaemia is one of the highest in Argentina among Latin American countries and increasing. There is a dearth of Argentina-specific data regarding status-of-care for these conditions, especially with respect to patient journey stages.

2. Contribution of the article to current knowledge: The article highlighted poor awareness, diagnosis, treatment, and adherence, which affected overall control of the conditions. Forgetfulness and unawareness of the patients; high cost and lifelong nature of medication; outdated knowledge and poor prescription practices of physicians; and lack of access to healthcare and insurance contributed to the sub-optimal state of care.

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Disclosure
Carlos R Yarleque is an employee of Upjohn – A Division of Pfizer. The authors declare no other potential conflicts of interest in relation to this work.

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