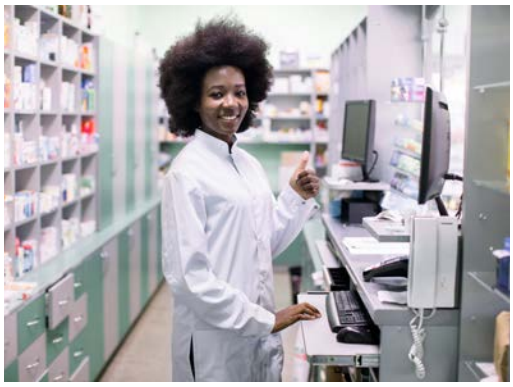
# NIRMATRELVIR/ RITONAVIR IMPLEMENTATION IN CANADA

## SUMMARY EVALUATION REPORT: JANUARY TO AUGUST 2022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*Rapport d'évaluation sommaire : de janvier à août 2022*

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# EXECUTIVE SUMMARY

On January 17, 2022, Health Canada approved nirmatrelvir/ritonavir (N/R; PAXLOVID™) as a COVID-19 therapeutic for use in adults with mild to moderate symptoms who are at high risk of disease progression. This was the first oral treatment for COVID-19, which facilitated administration in outpatient settings across the country. The goal of the Government of Canada's COVID-19 therapeutics actions as a key component of the national pandemic emergency preparedness and response[1] is to prevent hospitalizations and deaths, thus protecting the population and the health care system. The availability of this new treatment required jurisdictions to pivot resources and innovate to provide large quantities of COVID-19 therapeutics quickly to populations at higher risk of disease progression. In this context, various stakeholders identified important questions about best practices for the use of this new treatment, which led the Public Health Agency of Canada (PHAC) to develop an evaluation framework in collaboration with jurisdictions. Identifying best practices and documenting the implementation process across the country were established as priority elements for the evaluation framework and constitute the focus of this report.

From July to August 2022, PHAC held a series of discussion sessions with provinces, territories (PT) and federal departments that had received allocations of N/R for use in their populations. The format—based on qualitative methodology—aimed to explore their experiences on various dimensions of implementation. This report summarizes the experiences of managers and health care professionals involved in the planning of COVID-19 therapeutics' health service delivery at PT or federal departmental levels and as such may not have captured some dimensions of implementation such as patient or provider perspectives.

The roll out of N/R can be described in two main phases. In the first months after the drug was authorized, supply was constrained, scientific evidence was limited, and health systems were forced to organize service delivery rapidly. This period also coincided with surges in COVID-19 cases due to the spread of the new more transmissible Omicron variant of concern (VOC), which appeared to be associated with less severe disease than earlier VOCs. Jurisdictions were also transitioning from PCR testing—which required laboratory services—to self-administered rapid antigen tests (RAT) that were widely accessible in community settings. Given the short timelines between the drug's availability and initiation of distribution, jurisdictions had little opportunity for advance planning. These contextual elements impacted the early phases of the roll out in terms of establishment of eligibility criteria, service delivery models and communication strategies. To ensure adherence to eligibility criteria and manage a limited drug supply, service delivery models tended to be more centralized with limited access points. During this phase, significant efforts were made to ensure equitable geographical distribution of N/R across the country.

[1] Government of Canada. COVID-19 pandemic guidance for the Health Care Sector. Accessed online October 25th 2022: https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/health-professionals/covid-19-pandemic-guidance-health-care-sector.html

By the end of the spring, the supply had increased, and RATs were more widely used, facilitating the diagnosis of COVID-19. In this second phase, most jurisdictions expanded eligibility criteria and access points for N/R assessment and provision. The majority of jurisdictions transitioned to decentralized or mixed service delivery models, with complementary services—mostly virtual intake centres—for patients without access to a regular health care provider (HCP). During this phase, jurisdictions adapted their implementation strategies based on their experience to date, and uptake of the drug increased. Nevertheless, patient demand and uptake of N/R was described as lower than anticipated.

Inherent characteristics of N/R contributed to uptake challenges, namely the short number of days during which the drug can be administered following symptom onset, the numerous drug-drug interactions (DDIs) and the requirement for dose modification in the case of kidney failure. Raising patient awareness, training of HCPs and support of specialists served to alleviate some of these challenges. Additional activities to further support HCPs may be considered in some settings in the future. A continuing challenge is the lack of high quality scientific evidence on the optimal usage of the drug; it is hoped that forthcoming results from adaptive platform trials, both international and domestic (CanTreatCOVID trial[2]) will address this.

Demand and uptake continue to be influenced by population awareness of drug availability, eligibility criteria, and where it can be accessed. Jurisdictions have used varied strategies to optimize uptake including communications, support to providers and adjustments to health care service organization. Potential strategies that could further optimize uptake include additional communication activities and facilitated accessibility. Reach and overall uptake of N/R could be further improved by identifying population groups with low uptake, and developing focused strategies designed with social and economic determinants of health in mind. Individuals eligible for N/R may still choose not to take this drug despite a provider's recommendation, due to their perception of risk from COVID-19 or concerns about the implications of DDI management.

The evaluation identified specific challenges associated with uptake and accessibility for Indigenous peoples. While some were related to the availability of primary care (a systemic issue, particularly in remote communities), there are other areas that could be explored: facilitation of COVID-19 testing, management of DDIs, engagement with the communities (including urban Indigenous populations) while ensuring culturally safe care and support for self-determination. Of note, low levels of SARS-CoV-2 transmission and very high vaccination rates may have contributed to a lower need for therapeutics in some communities.

The procurement process for N/R was led by federal authorities in the context of global supply constraints of COVID-19 therapeutics. Satisfaction with this process was generally high and jurisdictions appreciated the collaborative processes and problem-solving approaches that ensured equitable access to N/R and other COVID-19 therapies. Additional improvements could include: greater centralized distribution and storage capacity; Federal, Provincial, and Territorial (FPT) engagement during the planning phases; and increased opportunities for FPT discussion of clinical recommendations.

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[2] Canadian adaptive trial of treatments for COVID in community settings. Accessed online on October 25th 2022: https://cantreatcovid.org/

The challenges experienced by Canadian jurisdictions and the service delivery strategies they deployed appear comparable to those of other high-income countries using N/R. When considering selected international experiences, closer integration of care with clinical trials to offer treatment while fostering research and exploring additional accessibility measures from an equity-seeking lens could be further explored in Canada.

# CONTEXT

On January 17, 2022, Health Canada approved nirmatrelvir/ritonavir (PAXLOVID™) as a COVID-19 therapeutic for use in adults at high-risk of disease progression. This was the first oral treatment for COVID-19, which facilitated administration in outpatient settings. In Canada, public health/health care is a shared responsibility between federal, provincial/territorial and regional/local health authorities. Each has their specific defined role, and all must work together effectively to provide the most effective and efficient public health programming. Although therapeutic procurement is traditionally the responsibility of provinces/territories, the federal government took responsibility for procurement and allocation of COVID-19 therapeutics as a component of Canada's pandemic emergency preparedness and response. The goal of the Government of Canada with respect to COVID-19 therapeutics is to identify, secure and manage a supply of safe and effective COVID-19 therapeutics for use in Canada's health care systems. This prevents hospitalizations and deaths, thus protecting the population and the health care system. These actions have required jurisdictions to pivot resources and innovate in order to provide significant quantities of COVID-19 therapeutics quickly to service providers, permitting rapid administration to those who need them.

After the Health Canada authorization of this new therapeutic option, public health, health care stakeholders and clinicians identified important questions about best practices for its use in the context of limited scientific evidence. An evaluation framework was developed at the onset of the rollout to assess and help address any concerns that might arise during implementation. One of the priority areas identified was how to optimize implementation. As such, this report focuses on the evaluation of implementation: to better understand how N/R has been distributed and administered across Canada; to hear from jurisdictions/organizations about their experiences with the rollout; and to identify lessons learned and the most promising strategies to deliver N/R (and other COVID-19 therapeutics) moving forward. The overarching aim of this component of the evaluation was to answer the following questions:

1. How has N/R been administered across Canada?
2. What are the most promising strategies to deliver N/R in outpatient settings?

The topics that are explored in this report include: eligibility criteria, distribution and prescription mechanisms, health care service delivery models, communication strategies, favourable factors, challenges in the deployment of N/R and experiences with the procurement process. The report summarizes the experiences of provincial, territorial and federal departments that were shared with PHAC during discussion sessions on these topics, as well as some experiences from other countries. One section also focuses on Indigenous health perspectives.

# METHODOLOGY

A qualitative methodology approach was used to answer the above questions. All jurisdictions that were part of the FPT therapeutics allocation process were invited to participate in discussion sessions organized by PHAC from July 8th to August 31st. The invitations were sent to participant lists of existing FPT working groups and were intended for managers or health care professionals involved in the planning and implementation of COVID-19 therapeutics at the jurisdictional level. Representatives from the following PTs and federal departments participated: British Columbia (BC), Alberta (AB), Saskatchewan (SK), Manitoba (MB), Ontario (ON), New Brunswick (NB), Newfoundland and Labrador (NL), Nova Scotia (NS), Prince Edward Island (PE), Northwest Territories (NT), Nunavut (NU), Yukon (YK), Correctional Service Canada (CSC) and Indigenous Services Canada (ISC). The Department of National Defense (DND) provided information in writing as their experience with administering N/R was very limited at the time of the evaluation.

Jurisdictions were free to choose participants as appropriate for their jurisdiction's organizational model(s). As such, some participants were working in regional health authorities while others were in active clinical practice. During the course of the discussion sessions, a few jurisdictions recommended that additional participants be contacted to provide more information: this was done through email, phone call, or an additional discussion session.

A pre-established questionnaire was used during the discussion sessions, which lasted an hour on average. Participants were sent written information in advance, to explain the main topics that would be covered during the discussion. Three PHAC staff attended to host the meeting, ask questions and collect the information shared by participants.

The PHAC policy on research activities was followed: a consultation with the Research Ethics Board was not required, given the nature of the evaluation. Consultations took place with the Privacy Management Division to ensure any personal information that might be disclosed during the evaluation was handled as per federal regulations and departmental policies. A privacy notice was shared with participants at the start of the discussion session and was available in writing. After obtaining consent from participants, the discussion sessions were transcribed using the transcription feature in Microsoft Word. These transcriptions were reviewed for accuracy and used to draft a summary of the discussion session for each jurisdiction. The summaries were sent to participants for review, and the final version was used to prepare this report. Jurisdictions also provided some information in the form of documents, particularly for their eligibility criteria. Transcription recording files were deleted once the verbatim transcriptions were finalized. Verbatim transcriptions were deleted after completion of consultations on this report.

The questionnaire was inspired by health services organization frameworks as described by Donabedian et al., the Consolidated Framework for Implementation Research, RE-AIM and behavioral science theory models of healthcare utilization[3,4,5,6.] According to Lévesque et al., availability of services (access) for patients can be defined by five dimensions of accessibility for patients: approachability, acceptability, availability and accommodation, affordability, and appropriateness[7]. A logic model also served as a basis for the development of the questionnaire. Consideration was given to include questions that stakeholders identified frequently. Figure 1 provides a visual representation of the framework that was developed to support the evaluation methodology.

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[3] Donabedian A. Evaluating the quality of medical care. 1966. Milbank Q. 2005;83(4):691–729.

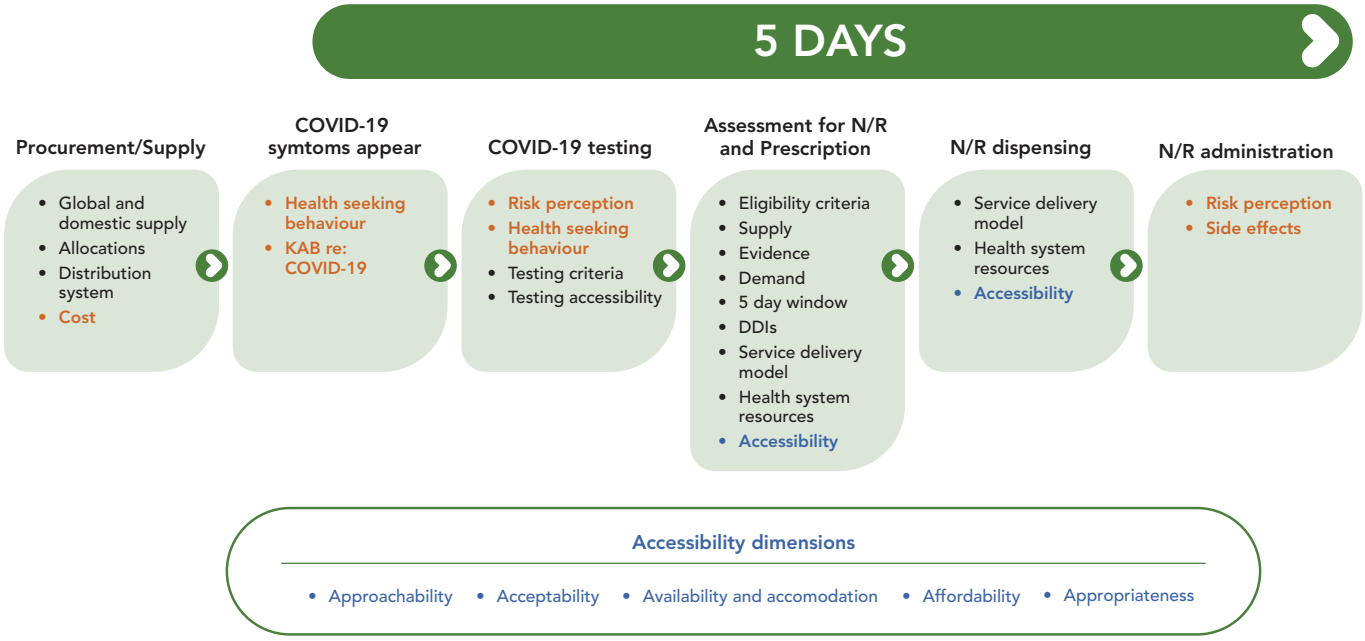
[4] Damshroder LJ, Aron DC, Keith RE, Kirsh SR, Alexander JA, Lowery JC. Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science. Implementation Science 4, article number 50: (2009). Accessed online June 2022: Fostering implementation of health services research findings into practice: a consolidated framework for advancing implementation science | Implementation Science | Full Text (biomedcentral.com)

[5] RE-AIM, accessed online in June 2022: What is RE-AIM?—RE-AIM

[6] Glanz K, Bishop DB. The role of behavioral science theory in development and implementation of public health interventions. Annu Rev Public Health, 2010;31:399–418

[7] Levesque JF, Harris MF, Russell G. Patient-centered access to health care: Conceptualising access at the interface of health systems and populations. International Journal for Equity in Health. 2013;12(1):18

**FIGURE 1:** Patient trajectory framework for the implementation of N/R in Canada




**LEGEND:** Orange text indicates dimensions that were not explored in this evaluation due to methodology limitations or inapplicability (e.g., cost of drugs is currently covered by PHAC). Blue text indicates dimensions that were partially explored in this evaluation: although access was explored in the discussion sessions, since the experiences of the patients were not part of the methodology, accessibility dimensions could only be partially assessed, through the lens of discussion participants. KAB: Knowledge, attitudes and beliefs. DDIs: drug-drug interactions. Eligibility criteria, service delivery model characteristics and testing criteria are presented in tables, by jurisdiction. Content and thematic analysis was performed for all the other topics.

Limitations of this evaluation include:

- Self-selection of participants;
- Non-participation of some jurisdictions;
- Incomplete capture of factors that may have impacted the roll out;
- Exclusion of patient and front-line provider experiences;
- Potential for desirability bias.

# ELIGIBILITY CRITERIA

At the beginning of the roll-out, most jurisdictions established their eligibility criteria for N/R based on guidance from PHAC and Canada's drug and health technology agency (CADTH), the product monograph, as well as expert opinion from internal advisory committees (when available). In the context of limited supply, the eligibility criteria (described in Table 1) were initially formulated to ensure that priority access to treatment would be given to those who would benefit the most from N/R, namely those with the highest risk of severe outcomes.

**TABLE 1:** Eligibility criteria by jurisdiction at the beginning of the roll out

| JURISDICTION | ACCORDING TO VACCINATION STATUS (VS) | | INDIGENOUS PEOPLES | LTCF | PREGNANCY | IMMUNO-SUPPRESSION | COMORBIDITIES |
|---|---|---|---|---|---|---|---|
| | UV OR PV | FV | | | | | |
| BC | ≥60 yo w.≥3RF<br>≥70 yo w.≥1RF | ≥70 yo w. ≥3RFs | ≥ 60 yo and UV or PV | N/A | Y | ≥18 yo | DM, BMI ≥30, Smoking, heart failure, stroke |
| AB | ≥65 yo<br>≥18 yo w. 1 RF | N/A | N/A | N/A | Y | ≥18 yo | DM, CKD, COPD, moderate to severe asthma, CHF, BMI ≥30 |
| SK | 18–55yo w/ ≥1 RF<br>OR<br>≥55 yo | N/A | N/A | N/A | N | Regardless of A or VS | DM, BMI ≥30, CKD, COPD, CHF, Asthma |
| MB | 18–40 yo w. ≥1 RF | ≥50 yo w. ≥1 RF | V[1], ≥ 40 yo, w. ≥1 RF | N/A | N/A | ≥18 yo | DM, CKD, CVD, Cancer |
| ON | T1: ≥70 yo UV<br>≥60 yo UV with ≥1RF<br>T2: ≥60 yo UV<br>≥50 yo UV with ≥1RF | N/A | T1: ≥60 yo<br>T2: ≥50 yo | N/A | Y | ≥18 yo | DM, BMI ≥30, CHF, CVD, HTN, LD |
| NB | 60–79 yo | ≥80 yo | 60–79 yo | 60–79 yo | N/A | ≥18 yo | N/A |
| NS | ≥18 yo w. ≥1 RF | ≥18 w. ≥1 RF | N/A | N/A | Y | ≥18 yo | CKD, DM, BMI ≥30, CVD, HTN, CRD, SCA, NDD, Frailty |
| PEI | ≥ 60 yo | ≥60 yo | >60 | >60 | N/A | ≥18 yo | DM, HTN, CHF, COPD, BMI≥30 |
| NL | ≥80 yo | N/A | PV, ≥60 yo | PV, ≥60 yo | N/A | ≥18 yo | |
| YK | ≥60 yo<br>≥50 yo w≥1 RF | N/A | N/A | N/A | N/A | ≥18yo | BMI ≥30, CKD, DM, CD, CVD, CHF |

| JURISDICTION | ACCORDING TO VACCINATION STATUS (VS) | | INDIGENOUS PEOPLES | LTCF | PREGNANCY | IMMUNO-SUPPRESSION | COMORBIDITIES |
|---|---|---|---|---|---|---|---|
| | UV OR PV | FV | | | | | |
| **NT** | ≥18 yo<br>w. ≥1 RF | ≥50 yo[2] w. ≥1 RF<br>18–49 yo w. ≥2 RFs | N/A | N/A | N/A | N/A | BMI ≥40<br>DM, COPD, CKD, CD |
| **NU**[+] (risk stratification) | T1: ≥70 yo UV<br>≥60 yo UV with ≥1RF<br>T2: ≥60 yo UV<br>≥50 yo UV with ≥1RF | N/A | ≥55 yo | N/A | Y | Regardless of A | |
| **CSC** | ≥80yo<br>≥55 yo w.≥1RF | N/A | N/A | N/A | N/A | ≥18yo | |
| **ISC**[++] | ≥60 yo | ≥80 yo | UV, PV ≥60 yo | UV, PV ≥60 yo | N/A | ≥18 yo | |
| **DND** | T1: PV, ≥80 yo<br>T2: PV, ≥70 yo; PV, ≥ 60 w. ≥2RFs<br>T3: PV, ≥60 yo;PV, ≥50 yo w.≥2RFs | | T1:PV ≥60 yo<br>T2: PV ≥50 yo | PV ≥60 yo | N/A | ≥18 yo | |

**LEGEND:**

IS: Immunosuppression; UV: unvaccinated; PV: Partially vaccinated; FV: Fully Vaccinated; LTCF: Long-term care facility residents; yo: years old; N/A: Not applicable; A: age; VS: Vaccination status; RF: Risk factor; Y: Yes; N: No; T1: Tier 1; T2: Tier 2.

[1] having received 2/2 or 1/1 doses

[2] have not received 3rd booster dose

[+] NU closely followed ON's guidelines with the exception of the eligibility age for the Indigenous community

[++] ISC's eligibility criteria varied from region to region, the eligibility criteria listed above is that of the National Office.

Immunosuppression includes patients on an active treatment or recent cancer treatment, those with a solid organ transplant or recent stem cell transplant, moderate to severe primary immunodeficiency, advanced or untreated HIV infection, on moderate to severe immunosuppressive treatment (e.g., rituximab, high dose systemic corticosteroids). Duration of treatment and time since treatment varied between jurisdictions.

RFs include but are not limited to: obesity (BMI ≥ 30kg/m$^2$); diabetes (DM); cardiovascular disease (CVD), heart disease (CD), hypertension (HTN), congestive heart failure (CHF); chronic respiratory disease (CRD—including cystic fibrosis and chronic obstructive pulmonary disease); Neurodevelopmental disorders (NDD, including cerebral palsy (CP)), intellectual or developmental disability (IDD); sickle cell anemia (SCA); moderate to severe kidney disease (Mod-Sev KD—eGFR <60mL/min); moderate to severe liver disease (Mod-Sev LD, e.g., Childs Pugh class B or C cirrhosis).

At the outset of the roll out, there was general alignment across jurisdictions in eligibility criteria for these broader categories: older under—or unvaccinated individuals, Indigenous populations and individuals with immunosuppression or other comorbidities. Within these categories however, there was significant inter-jurisdictional variability in threshold for age when combined either with vaccination status (unvaccinated, undervaccinated, or vaccinated) or the presence of comorbidities (ranging from one to three). This variation may be explained in part by the limited scientific information concerning the effectiveness of the drug in vaccinated individuals: the pivotal trial—unpublished when distribution began—was focused on unvaccinated individuals. Despite variability in the definition of immunosuppression and included conditions, this was a consistent criterion and almost all jurisdictions set the age at 18 years. With respect to other comorbidities, there was general consistency in eligibility for BMI ≥ 30, diabetes, lung and cardiovascular diseases, however there were variations in the pulmonary or cardiac conditions. There was also more variability in how smoking, hypertension and chronic kidney disease were included. Pregnancy was a criterion in four jurisdictions, some did not include it and most guidance did not comment on this criterion. For residents of long-term care facilities (LTCF), some jurisdictions allowed N/R for all residents (regardless of age or vaccination status), while the majority applied the same criteria as for other groups. The information on LTCF was not described in all the guidance documents, however other policies may have covered this group. Indigenous populations were prioritized for eligibility in almost all jurisdictions, generally using broader age / vaccination status criteria than for other groups.

## CHANGES TO ELIGIBILITY CRITERIA OVER TIME

As supply increased, 12 jurisdictions expanded their N/R eligibility criteria. The expansion included a lowered age of eligibility and the inclusion of vaccinated populations (for example, those living in LTCF settings). Definitions for criteria were refined (e.g., immunosuppression) and the definition of fully vaccinated was further clarified to reflect the addition of booster doses. Two jurisdictions moved from relying on strict eligibility criteria to providing clinical guidance recommendations for prescribers (MB and ON). Two jurisdictions (YK and DND) have not changed their eligibility criteria since the beginning of the rollout (Table 2). While ISC did not change their national guidance, each ISC region has adapted their eligibility criteria with time (more details can be found in the "Indigenous health perspectives" section of the report). Overall, later updates to guidance resulted in less variability for age criteria in combination with vaccination status or risk factors, although some remain. Pregnancy criteria have not changed and interjurisdictional variations in comorbidities and immunosuppression are similar to what was observed with the earlier recommendations.

**TABLE 2:** Eligibility criteria by jurisdiction at the time of the evaluation (July–August 2022)

| JURISDICTION | ACCORDING TO VACCINATION STATUS (VS) | | INDIGENOUS PEOPLES | LTCF | PREG-NANCY | IMMUNO-SUPPRESSION | COMORBIDITIES |
|---|---|---|---|---|---|---|---|
| | UV OR PV | FV | | | | | |
| BC | **UV** ≥18 yo w. ≥3 RF<br>≥50 yo<br>**PV** ≥50 yo w. ≥3RF<br>≥70 w.≥1RF | ≥70 yo w. ≥3RFs | ≥ 18yo and UV<br>≥50 yo and PV<br>≥70 yo | N/A | Y | ≥18 yo | DM, BMI ≥30, Smoking, heart failure, stroke |
| AB | ≥55 yo<br>≥18 yo w.≥1 RF<br>≥70 yo w. ≥2 RF | ≥70 yo w. ≥2 RF | ≥60 yo w. ≥2 RF<br>**UV or PV** ≥45 yo<br>≥50 yo w. ≥1 RF | Regardless of A or VS | Y | Regardless of A or VS | DM, CKD, COPD, moderate to severe asthma, CHF, BMI ≥30 |
| SK | 18–55yo w/ ≥1 RF<br>OR<br>≥55 yo | ≥70 yo with ≥3 RF | ≥2 RF | N/A | N | Regardless of A or VS | CKD, CVD, CAD, DM, |
| MB (recommendations) | 18–40 yo w. ≥1 RF | ≥50 yo w. ≥1 RF | V[1], ≥ 40 yo, w. ≥1 RF | N/A | N/A | ≥18 | DM, CKD, CVD, Cancer |
| ON (recommendations) | <20 yo UV w. ≥3 RF<br>20–39 yo UV or PV ≥3 RF<br>40–69 yo: UV, ≥1 RF<br>PV≥ 3 RF<br>≥70 yo UV OR PV with ≥1RF | ≥70 with ≥3 RF | Priority population | 40–49 yo UV w. ≥1 RF<br>50–69 UV or PV w. ≥3 RF;<br>≥70 UV or PV w. ≥ 1 RF or<br>V w. ≥3 RF | Y | Regardless of A | DM, BMI ≥30, CHF, CVD, HTN, CP, CRD, SCA, Mod-Sev KD, Mod-Sev LD, IDD |
| NB | 50–79 yo | ≥80 yo | 50–79 yo | 50–79 yo | N/A | ≥18 yo | N/A |
| NS | ≥18 yo w.≥1 RF | ≥18 yo w. ≥1 RF | N/A | N/A | Y | ≥18 yo | CKD, DM, BMI ≥30, CVD,HTN, CRD, SCAD, NDD, Frailty |
| PEI | ≥ 50 yo | ≥50 yo | >50 | >50 | N/A | ≥18 yo | DM, HTN, CHF, COPD, BMI≥30 |
| NL | ≥80 yo | ≥80 yo | ≥60 yo | ≥60 yo | N/A | ≥18 yo | |
| YK | ≥60 yo<br>≥50 yo w≥1 RF | N/A | N/A | N/A | N/A | ≥18yo | BMI ≥30, CKD, DM, CAD, CDV, CHF |
| NT | ≥50 yo<br>OR<br>18–49 yo w. ≥ 1 RF | ≥70 yo[2]<br>OR<br>50–69 yo[3] w. ≥ 1 RF | N/A | Regardless of A or VS | N/A | Regardless of A or VS | Regardless of A or VS |

| JURISDICTION | ACCORDING TO VACCINATION STATUS (VS) | | INDIGENOUS PEOPLES | LTCF | PREG-NANCY | IMMUNO-SUPPRESSION | COMORBIDITIES |
|---|---|---|---|---|---|---|---|
| | UV OR PV | FV | | | | | |
| **NU**[+] (risk stratification) | ≤20 yo w. ≥ 3 RF[3]<br>20–39 yo w. ≥ 3 RF[3]<br>40–64 yo w. ≥ 1 RF<br>40–64 yo w. ≥ 3 RF[3] | ≥65 yo w. ≥ 3 RF | PV/UV: ≥55 yo<br>FV: ≥55 yo w. ≥ 3 RF | N/A | Y | Regardless of A or VS | DM, BMI ≥30, CHF, CVD, HTN, LD, |
| **CSC** | ≥80yo<br>≥55 yo w.≥1RF | N/A | N/A | N/A | N/A | ≥18yo | |
| **ISC**[++] | ≥60 yo | ≥80 yo | UV, PV ≥60 yo | UV, PV ≥60 yo | N/A | ≥18 yo | |
| **DND** | T1: PV, ≥80 yo<br>T2: PV, ≥70 yo; PV, ≥ 60 w. ≥2RFs<br>T3: PV, ≥60 yo;PV, ≥50 yo w.≥2RFs | N/A | T1:PV ≥60 yo<br>T2: PV ≥50 yo | PV ≥60 yo | N/A | ≥18 yo | |

**LEGEND:**

IS: Immunosuppression; UV: unvaccinated; PV: Partially vaccinated; FV: Fully Vaccinated; IP: Indigenous Persons; LTC: Long-term care residents; yo: years old; N/A: Not applicable; A: age; VS: Vaccination status; RF: Risk factor; Y: Yes; N: No; T1: Tier 1; T2: Tier 2; T3: Tier 3.

[1] having received 2/2 or 1/1 doses

[2] have not received 4th booster dose

[3] have not received 3rd booster dose

[+] NU closely followed ON's guidelines with the exception of the eligibility age for the Indigenous community

[++] ISC's eligibility criteria varied from region to region, the eligibility criteria listed above is that of the National Office.

Immunosuppression includes patients on an active treatment or recent cancer treatment, those with a solid organ transplant or recent stem cell transplant, moderate to severe primary immunodeficiency, advanced or untreated HIV infection, on moderate to severe immunosuppressive treatment (e.g., rituximab, high dose systemic corticosteroids. Duration of treatment and time since treatment varied between jurisdictions.

RFs include but are not limited to: obesity (BMI ≥ 30kg/m$^2$); diabetes (DM); cardiovascular disease (CVD), heart disease (CD), hypertension (HTN), congestive heart failure (CHF); chronic respiratory disease (CRD—including cystic fibrosis and chronic obstructive pulmonary disease); Neurodevelopmental disorders (NDD, including cerebral palsy (CP)), intellectual or developmental disability (IDD); sickle cell anemia (SCA); moderate to severe kidney disease (Mod-Sev KD—eGFR<60mL/min); moderate to severe liver disease (Mod-Sev LD, e.g., Childs Pugh class B or C cirrhosis).

## BASIS FOR CHANGES TO ELIGIBILITY CRITERIA

The main factors having influenced modifications to the eligibility criteria were described as follows:

- Increased supply of N/R;
- Changes based on the World Health Organization (WHO) Therapeutics and Covid-19: living guidelines;
- Clinical considerations from consultations with physicians (such as booster dose availability and new infections after 90 days etc.);
- Emerging evidence from research such as the EPIC-SR clinical trial results;
- Loss of effectiveness of neutralizing monoclonal antibodies (mainly sotrovimab) as Omicron VOCs evolved;
- Epidemiology studies within the jurisdiction.

# SERVICE DELIVERY MODELS

The service delivery models varied between jurisdictions as a result of health system infrastructure. Table 3 provides an overview of selected characteristics for each jurisdiction. There were three main service delivery models that jurisdictions used to prescribe N/R to their populations: a centralized prescription model, a decentralised model, and a mixed model combining both approaches. At the start of the N/R implementation, seven jurisdictions and two federal departments used a centralized prescription model: after the initial rollout, two of the seven PTs moved to a decentralized model, and four moved to a mixed model (keeping the centralised model in place for unaffiliated patients or patients that could not access their HCPs in a timely manner). Three jurisdictions and one federal department used a decentralized model initially. Two jurisdictions used a mixed model initially; one of them transitioned to a decentralized prescription model.

Authorized prescribers varied between jurisdictions based on their regulations. Physicians (MD), nurse practitioners (NP) and in some cases pharmacists (RPh) were authorized, with some PTs amending regulations to allow designated HCPs to prescribe. Five jurisdictions have authorized prescriptions by RPhs, and one jurisdiction has allowed community nurses to prescribe in an expanded role.

## PATIENT TRAJECTORIES: CENTRALIZED PRESCRIPTION MODELS

A centralized prescription model permits patients to access N/R through virtual or physical intake centres with designated access points. In this model, N/R provision is available in designated locations such as regional health authority (RHA) pharmacies, community pharmacies, and assessment centres. Given the limited N/R supply at the start of the rollout, seven PTs (SK, NB, MB, PE, ON, AB, NS) and two federal departments (CSC and DND) established a centralised model whereby patients could access N/R in set assessment centres, or through virtual intake centres, telephone health lines and/or designated prescribers.

Authorized prescribers in this model varied from designated core prescribers comprised of MDs, NPs and/or RPhs in NS, AB, PEI, SK, and MB; to MDs and NPs in ON. N/R is dispensed from a centrally located pharmacy at DND, and from regional pharmacies at CSC. NB put in place a collaborative prescribing agreement for RPhs. Six PTs (SK, NB, MB, PEI, ON, and AB) later expanded to decentralised or mixed models (described in the sections below) as supply increased. NS is currently using a centralised N/R prescription model through a virtual intake system. NS also offers home delivery services for N/R when needed. CSC and DND are also currently using a centralized N/R service delivery model.

## PATIENT TRAJECTORIES: DECENTRALIZED PRESCRIPTION MODELS

A decentralized prescription model is a model whereby the assessment of eligibility criteria and prescription of N/R is carried out autonomously by primary care providers, and multiple access points are distributed across the jurisdiction. In this model, N/R may be available in community pharmacies, community health centres or usual primary health care settings such as clinics and emergency departments (EDs). In this model, N/R is provided in community pharmacies, clinics, EDs, or community health centres.

YK, NT, and NU have used a decentralized prescription model for N/R since the start of the rollout, and patients could access treatment by self-identifying through community health centres, and/or hospitals (including EDs) or health lines. NB and MB decentralised their process as supply increased, with N/R becoming available for prescription by any HCP with prescriptive authority and through community pharmacies. NL is currently using a decentralized model, expanding their process from a mixed model as described below. Information about the ISC model is described in the "Indigenous health perspectives" section of the report.

## PATIENT TRAJECTORIES: MIXED PRESCRIPTION MODEL

A mixed prescription model incorporates both a centralised and decentralised patient trajectories for N/R. In this model, the decentralized access points are generally the most used and the centralized access points offer an alternative for unaffiliated patients or those who cannot access their primary care provider (PCP) within the 5-day eligibility timeframe. Two jurisdictions (BC and NL) used a mixed model from the onset of the rollout; NL later decentralized their model. Four provinces expanded from a centralized model to include a decentralized prescription model system with prescription and access to N/R available through PCPs or any HCP with prescriptive authority, with community pharmacies providing the treatment. This was the case for ON, AB, SK, and PEI.

BC had a mixed model from the onset of the rollout. In addition to enabling all authorized prescribers (e.g., MDs, NPs) to prescribe N/R, the province also introduced a centralized pathway for unaffiliated patients or those who are not able to access their PCP in a timely manner. N/R can be dispensed through any community pharmacies, although not all pharmacies stock the medication.

NL used a mixed prescription model at the onset, with provision of N/R initially limited to a number of RHA pharmacies; and assessment and prescription open to any primary care provider (MDs and NPs) through a screening tool. With time NL's model was decentralized and expanded to include NPs through the 811 Healthline; and in May 2022 assessment and provision moved to community pharmacies with RPhs able to assess and dispense N/R.

**TABLE 3:** Service delivery model characteristics and testing criteria to access N/R by jurisdiction—July to August 2022

| JURISDICTION | CENTRALIZED, DECENTRALIZED OR MIXED PRESCRIPTION MODELS (CDM) | AUTHORIZED PRESCRIBERS (MD, NP, RPH) | ACCESS POINTS FOR PATIENTS WITHOUT A REGULAR PROVIDER | TESTING CRITERIA FOR ELIGIBILITY (MOLECULAR TESTING INCLUDES PCR AND POINT OF CARE MOLECULAR TESTS) |
|---|---|---|---|---|
| BC | M | Any authorized prescribers (MD, NP, etc.) | Service BC | Mostly RATs<br>Molecular testing can be prescribed for therapeutic indications |
| AB | M | MD, NP, and community based RPh | Outpatient COVID-19 treatment program (phone line); any HCP | Mostly RATs<br>Molecular testing if prescribed by clinician for therapeutic indications |
| SK | M | MD, NP, and RPh | 811 health line | Mostly RATs<br>Molecular testing for specific indications only<br>If symptoms present and RAT negative, PCR can be accessed through 811 |
| MB | D | MD, NP | Any HCP | Positive test recommended at the discretion of the prescriber (RAT or PCR) |
| ON | M | MD, NP | Clinical assessment centre, Health Connect Ontario (811), community health centres | RATs<br>Molecular testing for specific indications only<br>If RAT negative but meet criteria for PCR testing and test is positive on PCR, also eligible |
| NB | D | MD, NP, RPh | ER, 811 | Mostly RATs<br>Molecular testing for specific indications only |
| NS | C | RPh, and MD (designated prescribers) | Self-report to centralized system | Mostly RATs<br>Molecular testing only for specific indications |
| PEI | M | MD, NP, RPh since July | 811 Health Line Stats Can | Molecular confirmation is preferred, RATs accepted |
| NL | D | MD, NP, RPh | Community pharmacy, ER, 811 NPs | Mostly RATs<br>Molecular testing for specific indications only |
| YK | D | MD, NP, nurse in community | ER, community health centres | Molecular tests recommended; RATs accepted |
| NT | D | MD, NP | Health centres | Molecular tests recommended |

| JURISDICTION | CENTRALIZED, DECENTRALIZED OR MIXED PRESCRIPTION MODELS (CDM) | AUTHORIZED PRESCRIBERS (MD, NP, RPH) | ACCESS POINTS FOR PATIENTS WITHOUT A REGULAR PROVIDER | TESTING CRITERIA FOR ELIGIBILITY (MOLECULAR TESTING INCLUDES PCR AND POINT OF CARE MOLECULAR TESTS) |
|---|---|---|---|---|
| **NU** | D | MD, NP | Healthline, ER (in Iqaluit), community health centres | Molecular tests or RATs |
| **CSC** | C | MD, NP | N/A | Molecular test confirmation |
| **ISC** | D | Varied by region | N/A, however PT modalities can be accessed if available | Molecular test or RATs |
| **DND** | C | MD | N/A | Unknown |

## TESTING CRITERIA TO ACCESS OUTPATIENT THERAPEUTICS

At the start of the N/R rollout, a positive COVID-19 test was required in all jurisdictions for its prescription. A molecular COVID-19 test (either by PCR or NAAT) was required for seven jurisdictions; the other seven allowed N/R prescriptions with a positive rapid antigen test (RAT) result—whether self-administered (6) or HCP administered (1)—with one jurisdiction also accepting verbal confirmation of a positive COVID-19 test. Although not recommended (per jurisdictional guidance), in some instances, N/R could be prescribed on the basis of presentation and clinical judgement if symptoms were persistent or if SARS-CoV-2 infection (COVID-19) was highly suspected and there were barriers to testing (e.g., family members with SARS-CoV-2 infection, presence of symptoms).

Testing requirements later changed for 10 jurisdictions, with two moving to clinical testing guidelines for HCPs (in lieu of criteria established by the jurisdiction), and the others accepting self-administered RATs. These changes occurred largely due to a tightening of PCR testing eligibility criteria as a result of limited testing capacity as the underlying issue. Four jurisdictions also documented concerns around timely access to PCR results, as some were shipping to out-of-province laboratories. This led to a wider use of RATs instead of PCR tests to ensure patients could be diagnosed and receive N/R in a timely manner. At the time of the evaluation, four jurisdictions require/prefer a form of positive molecular test, either laboratory-based PCR or Abbott's ID Now, to receive N/R; and 11 jurisdictions use self-administered RATs as the primary testing method.

Access to tests and testing varied: seven jurisdictions documented wide distribution and access to RATs, with RATs available free of charge in pharmacies, libraries, and even (in one case) gas stations. One jurisdiction also had services to transport their populations to testing centres.

Increased testing and the wide availability of RATs had a positive impact on the rollout. One jurisdiction noted the sparse access to test centers at the onset and how the move to RATs increased the number of patients assessed. Similarly, owing to issues relating to the timeliness of laboratory-based PCR results, the inclusion of positive RATs in the eligibility for N/R facilitated the rollout for jurisdictions.

# ACCESSIBILITY AND UPTAKE

During the discussion sessions with the jurisdictions, participants were asked if they were aware of patient groups or populations within the eligibility criteria that may have had more difficulties accessing the drug during the rollout. The overall uptake was generally described by jurisdictions as being lower than initially anticipated or consistent with the expectations that N/R would not be widely used due to inherent characteristics of the drug. The most common themes reported by the participants about access considerations were:

- Geographical considerations: In the earlier stages of the roll out, ensuring equal access in remote sparsely populated areas was challenging due to the allocation process, bulk packaging of courses of treatment while needing to send the drug to multiple small localities that were geographically dispersed. Ensuring supply to LTCFs also presented challenges for some jurisdictions. However, these geographical access challenges were mostly described as being temporary and resolved quickly with increasing drug supply.
- Unaffiliated patients (without a regular family physician or other first line HCPs);
- Information on access issues was unknown or unavailable for some jurisdictions;
- Presence of technological barriers to be able to analyze inequities in prescribing N/R to subgroups of the population.

In this context, it is possible that the information presented in this section is limited by the participants' awareness of accessibility considerations or by inherent (technological) limitations of information systems in use by each jurisdiction. In addition, the identification of an appropriate denominator or availability of data linkage to perform such analyses posed significant methodological challenges. Access considerations that were reported may be anecdotal in nature and based on frontline experiences, and some potential issues might not have been identified. Some jurisdictions reported no access issues.

Additional reported themes associated with access include:

- Healthcare organization:
  - Sufficient prescribing resources
  - Drug not stocked in all pharmacies
  - Access to primary care more generally
- Health care providers:
  - Level of comfort of prescribers, especially for complex clinical situations
  - Knowledge about best use scenarios or drug access points
- No costs for patients, both for testing and treatment
- Testing:
  - Timelines for PCR results (in earlier phases of the roll out when PCR was required)
  - Accessibility of testing
- Patients:
  - Health seeking behaviour (fear of consequences from a positive test, late presentation)
  - Level of demand
  - Awareness of availability/existence of the drug or eligibility criteria
- Availability of the formulation ("renal pack") for patients with kidney failure

Finally, high demand from patients at low risk of complications (i.e., not meeting eligibility criteria) was reported to impact access for those at higher risk. For example, this could hinder the efficient assessment of higher risk groups or divert resources to low-risk individuals, with a potential for reduced access.

## Strategies to increase accessibility and uptake

To ensure access for unaffiliated patients, jurisdictions have implemented a virtual centralized intake option via a phone line (with virtual prescribing), maintained COVID-19 assessment clinics, or decentralized prescription authority to a wider range of HCPs. One jurisdiction reported a significant increase in weekly numbers of prescriptions once community pharmacists started to assess and prescribe. These approaches are not mutually exclusive, and some jurisdictions are using multiple strategies for unaffiliated patients. These services are also available to patients who can't be assessed by their regular provider within five days of symptom onset.

In terms of geographical access, some jurisdictions worked with community pharmacies or other related stakeholders to ensure coverage (with reasonable travel times) across the entire territory, as well as availability of stock within LTCF. Maps of access points and pharmacies that stock the medication are available for several jurisdictions.

One jurisdiction analyzed prescribing by neighbourhood. Compared to other communities, prescribing was substantially (58%) lower in disadvantaged, marginalised, and racialized communities. Networks established earlier in the pandemic were leveraged to engage directly with both the communities and health care workers to raise awareness. Following these interventions, the prescribing difference fell to less than 7%.

To enhance uptake, one jurisdiction developed a web based self-reporting tool for any person testing positive for COVID-19, to let patients self-identify to the virtual intake centre as a priority for treatment. The instructions for this tool are inserted in testing kits. It is also possible to call the provincial health line for assistance in filling out the tool if the person is not comfortable with the web platform. With the use of data linkage and available metrics of PCR testing, it was possible to ascertain an increase of the use of this tool over time.

Additional strategies that were reported include:

- Systematic electronic notification about eligibility criteria for treatments and how to access them at the same time as tests results are communicated
- Translation of materials in multiple languages
- Engagement and outreach with community organizations
- Supporting local public health units or health care organizations in their efforts
- Education or awareness activities for patient groups with specific conditions (organized by medical specialty groups, patient groups, treatment units, etc.)
- Transportation support for testing and obtaining prescriptions

# COMMUNICATIONS AND TRAINING

Communication and training varied by jurisdiction. All jurisdictions deployed several communication activities for stakeholders, HCPs and the public as well as training and tools for HCPs. Many indicated not having a formal communications plan specific to N/R, while three jurisdictions indicated significant involvement of a communications team in the planning and operationalization of the N/R rollout. The communications generally encompassed all COVID-19 therapies and COVID-19 messaging more generally. Patient and provider perceptions and responses to N/R had not been formally evaluated or studied by jurisdictions at the time of the discussion sessions. However, several participants had firsthand experiences interacting with HCPs or the public on the virtual intake lines, through HCP committees or within their clinical practice. A few jurisdictions had some metrics from their centralized assessment processes.

## FOR THE POPULATION

Jurisdictions employed a mix of the following communication activities, to varying degrees:

- Publication of eligibility criteria and information on public facing government websites
- Press and media releases by the Chief Medical Officer of Health
- Social media
- News reports and media appearances by physicians
- Town halls
- Community outreach efforts
- Text messages (linked to testing results)

One jurisdiction reported restricting messaging to the public at the onset of the rollout, given the limited supply of N/R. This changed as supply increased. Some jurisdictions provided anecdotal and metrics-based reports of patients' response to N/R. Four jurisdictions reported that assessed patients expressed gratitude for having received treatment, or for being followed up despite not being eligible for N/R. There were some reports of adverse reactions to N/R, including dysgeusia (a persistent bad taste) and gastrointestinal events (three jurisdictions), with some patients discontinuing treatment because of the adverse reactions. As well, two jurisdictions reported apprehension from eligible patients who refused treatment, either due to symptoms not being severe enough or because of DDIs requiring adjustments to their medications. There were anecdotal reports of ineligible patients wanting the treatment (especially those on the cusp of eligibility) and jurisdictions reported adjusting their communications to manage expectations in those cases. As well, there were some instances that required the messaging to be adjusted to ensure that patients were taking the medication as prescribed and not discontinuing because they were feeling better. One jurisdiction reported having little request from its population for N/R while another reported keen demand.

## FOR HEALTHCARE WORKERS

The communication to HCPs varied based on the prescriber group and the health system of the jurisdictions. Overall, the main channels of communication to HCPs included information sessions delivered through pre-existing networks such as stakeholder groups (physician, pharmacists, and nurse practitioner associations). Many had continuing medical education sessions, with three jurisdictions reporting sessions attended by hundreds of HCPs. Three jurisdictions held grand rounds in hospitals. Five jurisdictions indicated having a task force or working group for COVID-19 that was also involved with the N/R rollout; as such, these groups aided in the knowledge dissemination efforts directed at HCPs.

Information was also disseminated through ministries of health. Two jurisdictions used their Firstline app to share information and updated guidance documents with providers. One jurisdiction indicated publishing in various peer-reviewed journals, and others used academic detailing to upskill their HCPs in assessing, prescribing and providing N/R. Based on the feedback survey in one jurisdiction, 95% of the participants felt more confident in prescribing N/R after receiving the academic detailing service and particularly appreciated having one designated space to access links to prescribing tools. Some provinces also leveraged their drug plan for communications.

There were also internal communications within the health authorities. Three jurisdictions created special communications for their LTCF providers with modified guidance documents; two communicated directly to specialist transplant and oncology teams (among others) to disseminate information to their patients. In addition, three jurisdictions reported communicating directly with providers through email, phone calls, or chat groups. Expert consultants from the working groups/task forces they'd established were available for questions as well.

In general, jurisdictions did not conduct formal evaluation activities to document the effects of the training activities on prescriber knowledge, attitudes and beliefs (KAB) surrounding N/R. However, there were anecdotal reports of some hesitancy and discomfort among prescribers, due to the limited evidence on the efficacy of N/R or the complexity of the DDIs. However, HCPs also expressed appreciation for the availability of the treatment, and uptake of N/R through HCPs has increased over time and with increasing experience. As an oral antiviral, N/R was positively perceived by some HCPs as reducing treatment barriers in more remote and rural areas without the same access to intravenous therapies like remdesivir.

# FAVOURABLE FACTORS

The most commonly reported factors/themes favouring implementation related to collaboration, gradual increases in drug supply and availability, and use of rapid antigen tests in community settings.

Identified collaborations included vertical and horizontal partnerships within the healthcare structures of the jurisdictions and with HCPs. Interprofessional collaboration between nurses, physicians and pharmacists (Colleges, associations and other stakeholders) was a key enabler. Participants made specific mention of support from pharmacist organizations and associations, either in their role concerning the management of DDIs, the provision of the drug or—where applicable—implementation of prescription authorisation. In this regard, willingness to change legislation was instrumental.

In the first weeks following Health Canada's authorization of the drug, the quantities of treatment courses shipped were characterised by the participants as being limited, small or less than patient demand. The situation improved quickly, with larger quantities being available for shipment allocations. Participants considered the stabilization of supply to be a major factor facilitating the roll out.

At the time N/R became available in mid-January 2022, most jurisdictions were experiencing significant surges of COVID-19 cases. The combination of high volumes of symptomatic patients and PCR testing led to pressures on testing capacity and increased times required to analyze and communicate the results to the patients. This led to a transition from a reliance on molecular/PCR tests to the wider use of rapid antigen tests accessible in community settings. Since treatment with N/R must be started within five days of symptom onset, the large-scale deployment of accessible rapid antigen tests that took place in the following months—shortening the time to obtain a positive COVID-19 test result—was highlighted as a very important enabler to the roll out of N/R and other COVID-19 therapies.

Other frequent themes relating to favourable factors that emerged during the discussions include:

- Health care provider factors:
  - Scientific support and clear guidance (expert groups or advisory panels)
  - Dedicated COVID-19 therapeutics clinical working groups
  - Expert consultants available for prescribers (internal medicine, infectious disease specialists, dedicated prescribers and pharmacy consultation)

    - Preparation and dissemination of training and tools for prescribers (education sessions, cheat sheets, academic detailing, standardized forms, etc.)
    - Adjustments to billing
- Communication factors:
    - Pre-existing communication pathways and structures or—if not available—implementation of dedicated therapeutics steering committees/networks with good stakeholder representation.
    - Clear and frequent communication at all levels of the health system, with HCPs and the public
- Organizational factors:
    - Support from senior policy makers
    - Leveraging earlier experiences from the roll-out of other therapeutics
    - Responsiveness of teams, problem solving
    - Organizations and stakeholders working towards common goals, coordinated teams.
    - Technology/IT solutions (e.g., linkages between testing and notification for patient eligibility, linkages with pharmacy databases, monitoring of distribution, dashboards etc.)
    - Dedicated access pathway for unaffiliated patients

# CHALLENGES

The rollout was not without its challenges, particularly in the first weeks following authorization. Jurisdictions were able to rollout N/R in a matter of days, and the main challenges resulted from: the initial limited supply; scientific uncertainty; inherent characteristics of the drug; added pressure on health care resources; infrastructure and systems to support the rollout; and testing considerations. Jurisdictions adapted to these challenges with various strategies and several reported that they were significantly alleviated as of six months into the rollout.

## Limited scientific evidence

Several jurisdictions reported that the limited evidence on the efficacy of N/R was an obstacle. The lone clinical trial had been conducted by the manufacturer in a selected population of unvaccinated patients, and the drug was distributed prior to publication of the study results in a peer reviewed journal. This led to challenges in decision making (e.g., eligibility criteria) and provider apprehension or discomfort to prescribe N/R as evidenced in the "Communications and training" section. Some participants expressed concerns about the lack of research infrastructure to start high quality effectiveness studies at the same time as the beginning of the rollout. However, significant training opportunities, support for providers and the publication of additional studies, increased confidence and familiarity with the treatment, as well as prescribing.

## Drug-drug interactions

The complexity of the DDIs and contraindications that are mostly attributed to ritonavir, an antiviral developed for the treatment of HIV, were also highlighted as a barrier to uptake. The assessment of DDIs required a significant amount of time and therefore put pressures on pharmacist and prescribing resources. Moreover, managing the DDIs required first line HCPs to acquire a new knowledge base for a drug that they prescribed rarely (ritonavir) prior to the large-scale deployment of N/R. Opportunities for HCPs to appropriate the information before N/R was distributed were limited given the rapidity of the authorization and distribution. Some participants highlighted that at the beginning of the rollout, a number of prescribers did not recommend N/R after assessing DDIs although they could be addressed with some medication adjustments. With training and time, prescriber proficiency and comfort improved significantly. However, DDIs meant many patients who met other eligibility criteria, were not candidates for treatment with N/R. One jurisdiction analyzed metrics from their virtual intake centre and described that between 20–30% of patients who self-identified for treatment were ineligible due to DDIs.

## Infrastructure

Given the short lead-time from Health Canada approval to the availability of N/R, the rollout required the creation of new systems and infrastructures, and one jurisdiction noted the pressure added by the public announcement of the treatment availability. This limited opportunity for advanced planning to support the rollout created challenges for several jurisdictions, at the outset. This was due to such reasons as not having centralized patient records or an electronic system to effectively track administration of N/R. This required the creation of new processes and—in some instances—modifications of regulations. Jurisdictions worked with networks and associations to amend regulations, streamline approval processes, and create new documentation and labelling systems for N/R.

## Strained resources

Aside from needing to implement new infrastructure, the added pressure on health care resources (and in some situations an underlying lack of primary care resources more generally) was identified as a major factor impacting the rollout. Many jurisdictions reported shortages of HCPs; this, coupled with the ongoing strain COVID-19 placed on the health care systems, impacted the rollout, and hindered access. This was especially true for unaffiliated patients or those that could not access their primary HCP in a timely manner. Although jurisdictions have put in place safeguards to ensure that unaffiliated patients could access N/R through designated access points, health lines, or emergency departments, the ongoing resource pressures on primary care in general remain a challenge to the administration of COVID-19 therapeutics as well as the provision of other health services. Jurisdictions reported that the lack of healthcare professionals negatively impacted patient access to N/R. COVID-19 surges exacerbated this further, due to limited resources to assess the influx of referred patients. Given that the assessment and prescription process could take up to an hour, some jurisdictions created billing codes for providers to compensate for the workload.

### Additional challenges

Additional themes related to challenges also emerged in the discussion sessions and are described in more detail in other sections of the report. The most frequent were:

- Timeliness and access to COVID-19 tests, and getting PCR results within the required 5-days;
- Testing considerations (more details are provided in the Service Delivery Models section);
- Lack of awareness of treatment availability and the need for increased communication (more details are available in the Access and Uptake section);
- The need to manage expectations for a treatment that is not appropriate for everyone;
- Low uptake in LTCF due to high vaccination rates (prior to expansion of eligibility to vaccinated individuals);
- Delay in accessing renal packs necessitating manipulation of N/R by RPhs and NPs;
- Challenges related to procurement and distribution (more details are available in the following section).

## PROCUREMENT AND DISTRIBUTION

To support the public health emergency response to the pandemic, the Government of Canada assumed a procurement role for COVID-19 therapeutics to secure timely access to safe and effective treatments through equitable distribution to health systems across the country. In consultation with PTs and relevant federal departments, procurement decisions were based on available evidence, global supply constraints and jurisdictional need for assistance to ensure equitable access. Federal procurement of therapeutics was also contingent on Health Canada authorization. This section of the report will focus on FPT experience with the Federal procurement and distribution of N/R.

Overall, jurisdictions described their experience with the federal procurement of N/R as positive. Jurisdictions expressed appreciation for the federal government's role in ensuring access to the treatment, especially in the context of a global supply shortage. Negotiating individual contracts for the procurement of N/R at the jurisdictional levels would not have been feasible and would have resulted in disparities in access and pricing. By contrast, federal procurement allowed equitable and swift access to treatment across Canada. As well, the transparency in allocation and coordination with PTs through the working groups fostered collaboration and trust. Representation of all jurisdictions at the table was appreciated. Furthermore, as supply increased, jurisdictions were able to share with each other.

## Challenges

Given the unique circumstances of the procurement situation, jurisdictions did face some challenges. The initial ordering process was challenging as it was manual (through Excel); emails concerning allocation arrived at irregular intervals and were sent to selected individuals on short notice, which sometimes result in missed communications. As well, because the communications were combined for all COVID-19 therapies, there was a potential to miss the information about N/R allocations. The ordering system for N/R differed from that for previously procured therapeutics, which at times required quite significant adjustments in PT processes. The switch to VaccineConnect for ordering did mitigate these challenges, although some jurisdictions felt a need for additional adjustments or training opportunities. Moreover, availability of centralized storage space, or lack thereof, was identified as a challenge by eight jurisdictions, owing in part to:

- the ordering mechanism by which all allocated products had to be accepted locally;
- the lack of a centralized distribution process (some were not able to secure timely alternative arrangements with wholesalers within their jurisdiction); and
- the overestimation of need.

Insufficient storage space within the jurisdictions themselves also compounded this issue, sometimes locally (e.g., pharmacies being unable to offer the drug due to lack of storage space). Two jurisdictions documented the temperature of the product had fallen outside of the recommended range (15–25°C) during transportation, requiring communication with the manufacturer to ensure viability of the product. Furthermore, one jurisdiction indicated having significant industry involvement and pressure which was difficult to navigate.

Overall, jurisdictions felt like these concerns were addressed and facilitated through prompt communication from the PHAC team.

## Adjustments and moving forward

### PROCUREMENT AND ORDERING PROCESSES

Although VaccineConnect simplified the ordering process, a few jurisdictions suggested some adjustments to further facilitate the ordering process. Suggestions include linking the system to a wholesaler to streamline ordering at the jurisdictional level or by designating a person to communicate the allotment for ordering. Alternatively, some jurisdictions suggested having the distribution of N/R to jurisdictions through a wholesaler as an option part of the national contract, as well as the alignment of the processes with existing contracts with group purchasing organisations. Lastly, some jurisdictions raised questions about the possibility of accessing molnupiravir in the future, which will depend on the Health Canada authorization decision and evolving scientific evidence.

#### REPRESENTATION AND FORA

Having jurisdictions' clinical teams involved in the decision-making process was also suggested to better assess predicted role and use of therapies being considered for procurement. This would also provide more time to plan and organize their services or guidance, and alleviate the pressure that jurisdictions are currently facing to use all supply (i.e., if available supply exceeds actual clinical need). Reinstatement of an FPT working group/forum to discuss emerging topics and clinical issues was suggested. Moreover, it was also suggested that PHAC facilitate discussions with jurisdictions regarding eligibility criteria and coordinate rollout from the outset. Providing guidance documents on eligibility criteria prior to the announcement of product availability could alleviate pressure on jurisdictions and facilitate decision making processes.

#### BUDGETARY CONSIDERATIONS

Jurisdictions are cognisant of the special circumstances in the procurement of N/R and as such budgetary considerations have emerged as usage of COVID-19 therapeutics continues. As well, the cost-effectiveness of implementation was raised by one jurisdiction, i.e., whether it is justified to treat low-risk populations unlikely to significantly benefit from N/R. Some jurisdictions asked questions about the long-term plan for procurement of COVID-19 therapies and whether the model would revert to the usual processes for therapeutics (with jurisdictions being responsible for cost and procurement). Finally, questions were also raised about minimum quotas for purchasing.

# INDIGENOUS HEALTH PERSPECTIVES

This section of the report summarises information gathered from discussion sessions with participants from provinces, territories and ISC, which also gave written feedback. ISC was consulted on the questionnaire prior to the discussion session with their representatives. As described in the methodology section, perspectives from primary care providers, communities and patients are not included in this report, therefore the information presented may not reflect the full scope of the Indigenous health perspectives and experiences related to the rollout of N/R.

## ELIGIBILITY CRITERIA

Provinces and territories generally prioritized Indigenous populations in their eligibility criteria (more details are available in tables 1 and 2), in consideration of social and other determinants of health. The age threshold for eligibility was frequently lower for Indigenous populations than for the non-Indigenous population of the jurisdictions. Criteria varied to some degree in each province and territory, and the ISC national pharmacy office (NPO) within the Office of Primary Care also established guidelines for the communities they serve. Using the NPO guidelines in consultation with their jurisdictional guidelines, the various ISC regions devised their own regional criteria, leading to variability in eligibility criteria between regions. These eligibility criteria were also updated over time by various jurisdictions.

ISC NPO formulated their guidance for N/R using the recommendations from CADTH and PHAC, as well as results from clinical trials. Epidemiological data and input from physicians were also used to determine populations that would benefit the most from treatment with N/R. Some jurisdictions specifically reported including representation from the primary care teams providing care to members of the Indigenous communities or Indigenous leaders in the process of establishing their criteria.

This overall context was described as being complex and challenging for healthcare organizations and prescribers. In addition, variability across the country may have led to some frustration and confusion within the population as the eligibility criteria varied across the jurisdictions.

# SERVICE DELIVERY MODELS

Provision of health care services for Indigenous Peoples across Canada is a shared responsibility between health care systems of Provinces and Territories, ISC and in some situations additional stakeholders (e.g., self-governing First Nations, Métis and Inuit governments)[8]. For services related to COVID-19 therapeutics, the same general model applies and experiences in this section will be described for PTs and ISC.

## Indigenous Services Canada

ISC directly delivers services in 50 remote and isolated First Nations communities of varying sizes located in four regions and provides funding to 29 additional First Nations communities who employ their own workforce to deliver their primary health care services. N/R is available at the nursing stations within the remote and rural communities. Most nursing stations have access to NP or physician services, either on site or remotely; some regions may have communities that do not have onsite access to designated providers. Prescription of N/R requires access to medical information and lab work to check for renal function. Authorized prescribers include NPs and MDs. Typically, a person who develops COVID-19 symptoms will go to the nursing station to be tested and assessed for therapies (if the test is positive). Prescribing and provision of the medication is also carried out at the nursing station.

### TESTING CRITERIA

Results from molecular tests (PCR and ID NOW) as well as RATs are accepted to receive N/R. Obtaining PCR results often took longer, therefore, RATs were built into the guidance over time.

[8] https://www.sac-isc.gc.ca/eng/1626810177053/1626810219482

## Provinces and Territories

Participants of the discussion sessions generally described the models for Indigenous populations as being "not different" than for the overall population, but allowed for flexibility to meet the needs of the communities and provide equitable access to therapies across their respective jurisdictions. For jurisdictions that implemented "hotlines" or other virtual assessment modalities, these services were generally described as available for all residents, including Indigenous peoples. In Indigenous communities, testing, assessment, prescription and provision of the medication were available through nursing stations (either through ISC services or other modalities), Aboriginal Health access centres, Indigenous health teams, primary care teams already working with the communities and with prior experience administering monoclonal antibodies, etc.

Supply of N/R was either provided by community pharmacies (near or within the Indigenous communities) or stored at local health care facilities. Most jurisdictions reported working with various partners to ensure that there were access points close to the communities.

Some jurisdictions reported specific service delivery models for urban Indigenous populations. One jurisdiction described active mobilization and outreach activities through pre-established health care networks aiming to ensure awareness of N/R availability, eligibility criteria and access for Indigenous populations. Another jurisdiction reported setting up clinics for COVID-19 testing and care in the largest city of the jurisdiction, within areas that serve the urban Indigenous population and adjusting the service delivery model to facilitate access of Indigenous communities more generally within the jurisdiction.

### TESTING CRITERIA

The criteria for testing were generally aligned with the eligibility criteria for N/R established within the scope of each jurisdiction. PCR, other molecular tests and RATs were generally accepted (more details are available in table 3). Tests were available in nursing stations, health centres, community pharmacies or other local sites, depending on the service delivery models in each community. Some Indigenous communities opted to set up their own immunization and testing centres for COVID-19, sometimes with public health support. One jurisdiction reported using mobile testing clinics for some communities.

Access to testing was challenging in some circumstances. In areas where PCR tests needed to be transported a long distance to the laboratory or to another jurisdiction for analysis, delays in obtaining results past the five-day window occurred. Some jurisdictions reported that PCR test results were often delayed. Although there may have been other molecular point of care testing options available for these communities (e.g., ID NOW or Lucira), the supplies were limited and at times there were shortages of these tests, with direct shipping from the manufacturers taking up to four weeks in some circumstances. Given these challenges, several jurisdictions opted to change their policies to incorporate RATs for Indigenous communities, while others allowed an HCP to prescribe N/R for a patient at high risk of disease progression based on clinical presentation and judgement, when testing was a significant barrier.

# COMMUNICATIONS AND TRAINING

## For healthcare workers

The ISC teams collaborated with the pharmacy teams to work on guidance and clinical protocols, which were utilized for communications. There were ongoing communications with nursing staff at the nursing stations; as well, through collaboration with the pharmacy team, training was provided to HCPs on safe provision of N/R, including the mechanisms of prescription and the required blood work for kidney function, through educational materials and webinars. Provincial and territorial governments made available physicians to support the rollout at ISC. Communication was done through the respective province or territory and ISC had weekly follow up meetings with regional pharmacists to track the rollout. Ongoing updates were also provided within the ISC regional medical officers' group that is linked to remote HCPs in nursing stations.

For the PTs, in addition to the training activities described in the "Communications and training" section, some jurisdictions reported training sessions for partners with the First Nations and Inuit Health Branch and specific engagement with physicians and other providers working with Indigenous communities (more details are described in the "Accessibility and uptake" section).

In terms of provider perceptions, the initial response among HCPs was described as mixed: some were involved in the rollout and/or requested access to N/R before its availability, while others expressed apprehension in prescribing the medication given the complexity of the DDIs and limited support. This may have been due to a higher incidence of comorbidities and contraindications in some of the populations where these providers were practising.

As well, for more remote populations, the potential for complications from the medication and the limited access to emergency or tertiary care appeared to increase the apprehension, and the ability to treat adverse reactions locally was perceived as an additional factor needing to be considered before prescribing. The medication reviews and the blood work required for creatinine clearance (CrCl) also exacerbated the apprehension among providers, as well as the potential for language barriers when reconciling patients' medications.

As providers became more familiar with prescribing N/R and with increased training activities, these apprehensions appear to have lessened.

## For the population

It was noted that in some isolated communities, Facebook and local radio stations were used to disseminate information to the public advising on when to seek medical care, the symptoms of COVID-19, and the therapies available. Additional communication strategies were implemented as availability increased, to build patient awareness. Members of the public were urged to be tested and to go to nursing stations if they were ill.

Some PTs also distributed information to the population through the radio, issued public health memos for communication with the population or used community engagement activities. Participants noted that in the early stages, patient awareness of the availability of N/R was low in some settings, hindering access, and individuals were presenting too late after symptom onset to receive the treatment.

Participants described varying opinions within Indigenous communities regarding the clinical value of N/R. As such, further communication with Indigenous communities to understand their needs and experiences would be beneficial to better deploy COVID-19 therapies. As well, there may be a perception from some patients at the cusp of eligibility that they could have benefited from N/R but were unable to access treatment due to the limitations set by the eligibility criteria (e.g., age). Before N/R was available, one of the key messages to the population about COVID-19 was to stay home if experiencing symptoms. It was reported that this messaging might have contributed to patients presenting after the five-day window for prescription and therefore it would be important to continue communication efforts related to available therapeutics. Some participants perceived that less emphasis was being placed on communications about the availability of N/R than for vaccines or previous COVID-19 therapeutics, which may also have hindered demand.

## FAVOURABLE FACTORS

Facilitating factors identified included: ongoing communication with stakeholders; weekly pharmacy meetings to ascertain needs and progress, and to discuss any issues as they arose; sharing of documents; and positive strategies were described as facilitating factors. Some jurisdictions reported that their decentralized organizational model ensured accessibility across their territory and that the small size of their structures enabled their rollout.

Where applicable, the collaboration between public health medical officers and pharmacy leads to strategize on the distribution of N/R was key to the rollout, as this helped identify gaps in distribution. The rollout created new partnerships to widen reach and work in collaboration to close gaps, if any, in the service delivery of N/R.

The acquisition of iStat cartridges for point-of-care CrCl testing was important in the rollout for some communities as patients' files might not be up to date. As well, access to expert consultants (pharmacists, internist, infectious disease specialists)—including virtually—provided valuable support to manage complex clinical decisions.

## CHALLENGES

At the outset, the limited supply and other allocation and distribution considerations were described by most jurisdictions as a challenge in ensuring equitable distribution in remote, rural communities including Indigenous communities. Some jurisdictions reported having to manage temperature excursion (due to cold exposure) incidents with the supply during transportation.

Given the short lead-time from approval to distribution of N/R, there were challenges with disseminating the information on N/R, including educational information, and distributing the treatment. The timeliness of test results was a barrier for access; for example, patients who were not feeling sick enough to consider testing or delayed testing for any reason might not be eligible for N/R by the time they sought care. In general, wait times within the healthcare system are sometimes high, which can be a deterrent to seeking care in some communities. The ordering process for N/R was a deviation from normal ordering processes, which required some coordination to ensure access to N/R in communities spread across multiple jurisdictions.

Overall access to primary care in some jurisdictions was described as an ongoing challenge affecting capacity for the rollout and N/R access. Insufficient health care professional resources, in the wider context of national shortages of HCPs was described as a contributing challenge. For example, some service delivery locations may not have MDs or NPs on site. Furthermore, in some communities or regions there is limited or no access to primary care on weekends, therefore during those periods, patient access was restricted or may require consulting the Emergency Department of the hospital (where applicable). One jurisdiction described that some concerns were expressed from Indigenous communities, as well as critical care units that serviced them, that N/R was not effectively being delivered to the Indigenous population at the beginning of the rollout.

There have been challenges with DDIs, especially in terms of finding the appropriate person to consult for DDIs and clinical management of patients with reduced kidney function. As described in the communication section, some providers expressed discomfort related to DDIs that would be difficult to treat locally should a clinical emergency occur, due to a lack of availability of more specialized care. The clinical management of patients with reduced kidney function also posed challenges: nurses and pharmacists initially had to work out and modify the dosages themselves (until renal packs for N/R became available), which left room for human error in general. This also slowed down the process for administration and led to apprehension among nurses who needed to manipulate the packaging to adjust dosage for those clients.

Finally, the lack of consistent communication across the country may have confused patients seeking care; this, coupled with various levels of awareness of therapeutic availability and language barriers, may have contributed to a reduced access by patients.

## ACCESSIBILITY AND UPTAKE

Most participants described the uptake of N/R as being limited or low at the time of this evaluation, in First Nations and Inuit communities in the Territories, as well as in other Indigenous communities. In some cases, the uptake was described as lower than for previous therapeutic options (e.g., monoclonal antibodies). There was limited information about uptake for Indigenous Peoples living in urban areas and some participants described limited information in general, concerning Indigenous communities' satisfaction with access. The main factors reported by participants that were associated with the level of uptake were:

- High vaccination rates;
- Low levels of SARS-COV-2 transmission in communities/small number of COVID-19 cases;
- Risk perception about COVID-19;
- Perceptions about the medication (concerns about the effectiveness, side effects or drug interactions);

- Communication approaches (compared to the vaccination campaigns for example);
- Care for COVID-19 sought or available more than five-day from symptom onset;
- Complexity of DDIs;
- Ability to test for renal function in remote and isolated communities;
- Access to primary care in general or locally in remote communities;
- Access to treatment care outside of regular hours of operation (some jurisdictions).

The following strategies were deployed by various jurisdictions to facilitate access and uptake:

- Establish Indigenous peoples as priority population for access to COVID-19 therapeutics;
- Ensure geographical proximity of community pharmacies providing N/R with Indigenous communities or if not available, provide supply to other local providers present locally (e.g., nursing stations);
- Engage early with prescribers who are regular HCPs in Indigenous communities;
- Enlist clinicians from rural and remote settings involved in the delivery of N/R;
- Organize services to ensure access in Indigenous communities from the outset;
- Ensure alternative services are available for unaffiliated patients;
- Leverage telephone health lines for patient screening and assessment;
- Ensure alternate professions have prescribing authority in remote areas with limited access to usual prescribers;
- Ensure access to Infectious diseases specialists (or other medical specialists) as consultants for complex clinical situations;
- Engage with Indigenous health authorities;
- Outreach by Public Health with groups supporting Indigenous populations

## PROCUREMENT AND DISTRIBUTION

The experiences of the jurisdictions with procurement are detailed in the section on "Procurement and distribution". For Indigenous populations specifically, some jurisdictions commented that being part of the national process ensured they could access supply of N/R which would have been very challenging otherwise. The opportunity to participate in the working groups and discussions was appreciated, especially in securing treatment for remote and isolated populations. This allowed good collaboration between the jurisdictions to establish needs and secure treatment.

# INTERNATIONAL EXPERIENCES

A scan of published studies and grey literature did not produce evidence on research or evaluation of health care organizational models related to N/R (as of August 31st 2022). However, it was possible to document some information on eligibility criteria and characteristics of service delivery models through this scan. The following table summarizes eligibility criteria and some service delivery characteristics for selected countries.

**TABLE 4:** Eligibility criteria and service delivery strategies in selected countries

| STRATEGY | USA | AUSTRALIA | UK | FRANCE | ITALY | NZ |
|---|---|---|---|---|---|---|
| **Eligibility criteria / Target populations** | | | | | | |
| Lab confirmed (+ PCR / RAT) | √ | √ | √ | √ | √ | √ |
| Seniors | | √ | | | | √ |
| Adults with health related risk factors for progression to severe disease | √ (1+) | √ (2+) | √ | √ | √ (1+) | √ |
| Indigenous | √ | √ | | | | √ |
| Under/unvaccinated | √ | | | √ | | √ |
| **Service delivery strategies** | | | | | | |
| Centralized procurement systems | √ | √ | √ | √ | | |
| Includes pharmacists as authorized prescribers | √ | | | | | √ |
| Free testing (may be limited to eligible populations) | √ | X | √ (for high risk patients) | ? | ? | √ |
| Free N/R | √ | X | √ | √ | ? | √ |
| Home delivery of N/R | √ (limited to some jurisdictions) | √ | | | | √ (limited to some jurisdictions) |
| "Advance identification / prescriptions" for/of eligible people before they get COVID | | | √ | | | √ |
| Programs for residents with no access to primary care (e.g. uninsured, undocumented, without a family MD, etc.) | √ | √ | | √ | | |
| Programs for rural/remote population | | | √ | | | √ |

## ELIGIBILITY CRITERIA

All six countries included in this environmental scan required individuals to have laboratory confirmation of SARS-CoV-2 in order to be eligible for N/R. In terms of target populations, most countries specifically targeted adults 18 years and older with risk factors (specific comorbidities and/or immunosuppression or age-based criteria); one country (Australia) required 2 or more risk factors to be eligible. Three countries, Australia, New Zealand and the USA, specifically had programs targeting Indigenous populations; however this criterion might not be relevant for France, Italy and the UK. Only Australia and New Zealand had programs targeting senior citizens (age may vary depending on country), while only France and New Zealand had programs that specifically targeted unvaccinated populations. In the USA, the drug is authorized for use starting at the age of 12, and eligible patients should have at least one risk factor (age over 50, specific conditions or behaviours and unvaccinated or incompletely vaccinated against COVID-19[9].

## SERVICE DELIVERY STRATEGIES

Four countries, Australia, France, the UK and the USA had centralized procurement systems at the national or federal level. Centralized procurement systems provided the national/federal authorities to optimize pricing and support regional/local jurisdictions in equitable access to N/R. COVID-19 testing is available free of charge in New Zealand and the USA, while the UK limits free testing to certain populations, including high risk patients eligible for COVID-19 therapies. Four countries (US, UK, France and New Zealand) provided N/R at no charge to their citizens/residents, while Australia included N/R in their Pharmaceutical Benefits Scheme at substantially reduced cost to patients.

Several innovative strategies were identified that aimed to improve access. These included allowing community pharmacists to prescribe N/R and providing home delivery of N/R. Other strategies were aimed at identifying and targeting high risk patients. These included providing advance prescriptions for pre-identified high-risk patients and programs targeting rural or remote populations and populations without access to primary health care. For example, in New York City, mobile ("test and treat") clinics have been used, similar to those used for vaccination outreach[10]. There is evidence from the USA documenting inequities in N/R accessibility[11]. A retrospective study undertaken in the US assessing ethnic and racial disparities in outpatient COVID-19 treatments, including N/R, found lower prescription rates among racialized persons and ethnic minorities, especially in higher risk patients such as those over the age of 50 and the immunocompromised[12].

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[9] Accessed on October 3rd 2022: Interim Clinical Considerations for COVID-19 Treatment in Outpatients | CDC

[10] Accessed October 3rd 2022: N.Y.C. to Offer Paxlovid at Mobile Virus Test Sites, First in U.S.—The New York Times (nytimes.com)

[11] Gold J. et al. Dispensing of Oral Antiviral Drugs for Treatment of COVID-19 by Zip Code–Level Social Vulnerability—United States, December 23, 2021–May 21, 2022. MMWR June 24, 2022 / 71(25);825–829

[12] Boehmer TK, Koumans EH, Skillen EL, et al. Racial and Ethnic Disparities in Outpatient Treatment of COVID-19—United States, January–July 2022. MMWR Morb Mortal Wkly Rep 2022;71:1359–1365. DOI: http://dx.doi.org/10.15585/mmwr.mm7143a2

In the UK, there are two pathways to access N/R: one is via the National Health Service (NHS) and the second is via participation in the PANORAMIC[13] platform adaptive trial. This approach enabled the enrollment of very large number of patients in a real-life effectiveness trial for multiple COVID-19 outpatient therapies. The paucity of scientific information was a factor in the rollout in Canada as discussed above.

**IN SUMMARY**

Eligibility criteria for N/R were similar across the six jurisdictions studied. However, service delivery strategies varied. This was likely related to differing health care delivery structures and populations. PHAC participates in various fora with other countries in which the rollout of N/R was discussed. There were anecdotal reports of experiences similar to Canada's: volumes of courses of treatment administered were described as limited, paucity of scientific evidence impacted the roll out and management of DDIs were resource intensive and limited the number of candidates for treatment.

# NEXT STEPS AND POSSIBLE STRATEGIES TO FURTHER EXPLORE

## FUTURE PLANS

During the discussion sessions, participants were asked a) if they were planning additional changes to their N/R rollouts and b) about their contingency plans in case of a fall surge of COVID-19 leading to increased volumes of patients requiring treatment. Jurisdictions with decentralized or mixed service delivery models were planning to continue with the same approaches and were planning to hire additional designated prescribers to staff the virtual assessment centres. Jurisdictions with centralized models were considering further integration of N/R prescribing in primary care systems. New scientific evidence would be the main trigger to modify existing eligibility criteria. Furthermore, some jurisdictions were planning messaging for eligible groups or additional communication activities in the fall. Gathering ongoing scientific evidence has been identified as an important aspect moving forward and some participants were looking forward to the deployment of the CanTreatCOVID adaptive platform trial. In this regard, integration of patient recruitment in current N/R service delivery processes was under discussion in some jurisdictions. Three jurisdictions were actively planning evaluation activities to better inform their programs related either to drug effectiveness, patient experiences or to other gaps of interest to their context. Finally, some jurisdictions were contemplating adding pharmacists as N/R prescribers. At the time when the discussions took place, policy decisions were under consideration and decisions were yet to be made.

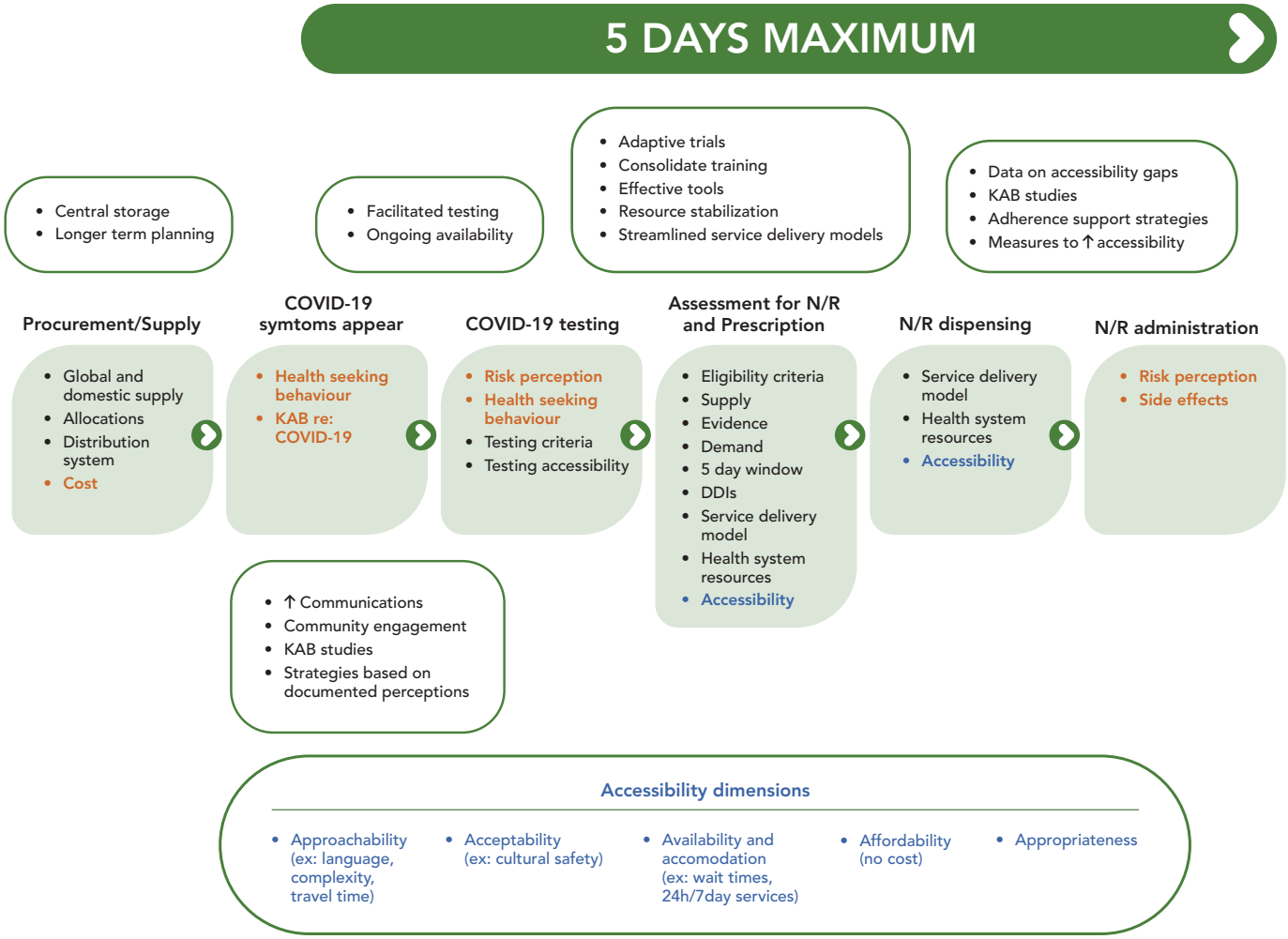
[13] Accessed October 3rd 2022: Homepage—apologies—PANORAMIC (panoramictrial.org)

## POSSIBLE STRATEGIES TO FURTHER EXPLORE

This section describes potential strategies to further optimize the uptake of N/R for patients at increased risk of disease progression; they reflect the ongoing challenges described by the jurisdictions, successful strategies related by participants and some international experiences. Factors influencing uptake and possible barriers differed for each jurisdiction depending on their respective health care systems, characteristics of their population and the capacity of information systems to analyze relevant data. Figure 2 provides a visual representation of possible strategies as they relate to patient trajectory components.

In terms of procurement and supply, facilitating central storage of supply and a centralized federal distribution process could be further explored. Expansion of the FPT coordination role to include evidence and clinical discussions would be appreciated by some jurisdictions.

**FIGURE 2:** Patient trajectory to access N/R in Canada and possible strategies to optimize uptake




**LEGEND:** KAB: Knowledge, attitudes and behaviours. DDIs: Drug-drug interactions. Orange text indicates dimensions that were not explored in this evaluation, blue text indicates dimensions that were partially explored in this evaluation

Health seeking behaviours of the target populations will be influenced by their knowledge and attitudes[14] (such as concerns about severe COVID-19, awareness that N/R is available, perceived self-efficacy), capacity to consult and the accessibility of the testing, assessment and distribution services. There is limited information at the moment about patients' perceptions of and experiences with N/R. Jurisdictions have indicated that for the most part, they had not yet conducted surveys, studies or analyzed these topic areas. Obtaining additional information on perceptions and experiences of the population and HCPs could help identify specific factors contributing to lower uptake as well as gaps in accessibility, and inform strategies aiming to optimize administration of N/R. Depending on the factors identified, strategies such as communication campaigns, engagement of communities or facilitated accessibility could be implemented as appropriate.

In terms of health care systems factors, it appears that the overall primary care capacity has impacted the roll out of N/R in several contexts. Although some of the considerations were described as systemic and not specific to COVID-19 therapeutics (and therefore complex to address), some strategies—such as consolidating training and tools for providers, streamlining patient trajectories and ensuring ongoing access to testing, particularly for easy-to-use rapid tests—may still be in reach. Barriers related to cost are known to be a major contributing factor to accessibility[15] and providing ongoing access to no-cost testing and treatment could be considered. It has been previously established that COVID-19 does not impact Canadians equally[16]. Literature findings and one jurisdiction's assessment of prescriptions rates in various communities suggest that inequities in N/R uptake may follow similar trends. These findings support the need for programs and communication efforts to ensure equitable access through increased awareness of—and access to—treatment in groups affected by health and social disparities. Finally, when considering selected international experiences as well as successful strategies used by some jurisdictions, accessibility could be further enabled by deploying services (including virtual consultations) to patients without a primary care provider, identifying and targeting high risk individuals, providing advance prescriptions, mobile testing and prescribing services (including home care) and furthering access measures for remote and isolated communities.

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[14] Glanz K, Bishop DB. The role of behavioral science theory in development and implementation of public health interventions. Annu Rev Public Health, 2010;31:399–418

[15] Schoen C, Osborn R, Squires D, Doty MM. Access, affordability, and insurance complexity are often worse in the United States compared to ten other countries. Health Affairs (Millwood). 2013;32(12):2205–2215

[16] Government of Canada. From risk to resilience : An equity approach to COVID-19. Chief Public health Officer of Canada's Report on the State of Public Health in Canada 2020. Accessed Online November 18th 2022. https://www.canada.ca/en/public-health/corporate/publications/chief-public-health-officer-reports-state-public-health-canada/from-risk-resilience-equity-approach-covid-19.html https://www.canada.ca/en/public-health/corporate/publications/chief-public-health-officer-reports-state-public-health-canada/from-risk-resilience-equity-approach-covid-19.html