Updates from National Advisory Committee on Blood and Blood Products

ORBCON update

January 23, 2021

Alan Tinmouth, NAC Vice-chair

National Advisory Committee on Blood and Blood Products | Comité consultatif national sur le sang et les produits sanguins

Overview

- Subcommittee updates
- Blood Shortages Working Group
- Ig shortages
- CBS PRPR Review Process
- CBS Plasma Protein Products (PPP) and Fresh Blood Components highlights

National Advisory Committee on Blood and Blood Products (NAC)

- NAC collaborates with and provides advice on the utilization management of blood and blood products and transfusion medicine practice to the provincial and territorial (PT) Ministries of Health and Canadian Blood Services (CBS).

Chair: Dr. Oksana Prokopchuk-Gauk

Vice-Chair: Dr. Alan Tinmouth

NAC Work Plan

- The NAC Work Plan is developed following direction of the PTBLC and CBS to NAC
- Documents arising out of the Work Plan have a 3-year schedule for review
  - Schedule reviewed and we confirmed which documents are due for update, including:
    - PCC Recommendations
    - RBC Transfusion Policy Framework
    - National Plan for Shortages of Labile Components

Active NAC Sub Committees

- Guideline Endorsement
- Fibrinogen Concentrate
- Solvent Detergent Plasma
- Prothrombin Complex Concentrates
- National Plan for the Management of Labile Blood Components
- Patient Blood Management
- Immunoglobulin Shortages Plan
- Website Maintenance

Guideline Endorsement Subcommittee

https://www.nacblood.ca/resources/indexendorse.html

Endorsed

- **ICTMG Guidance on platelet transfusion for patients with hypoproliferative anemia**
- **ICTMG Guidance on RBC Specifications for patients with hemoglobinopathies**

Under review

- **Fetal and neonatal alloimmune thrombocytopenia: recommendations for evidence-based practice, an international approach**

NAC Statement on Fibrinogen Replacement (April 2020)

https://www.nacblood.ca/resources/guidelines/downloads/FC%20Statement%20Update%20Final2020.pdf

Indications for fibrinogen replacement in acquired hypofibrinogenemia:

- Bleeding obstetrical patient and fibrinogen level <2.0g/L
- Massive bleeding or preoperative patient with fibrinogen < 1.5g/L

Suggested adult doses for fibrinogen replacement in acquired hypofibrinogenemia:

  - Fibrinogen Concentrate (FC): 2-4g*
  - Cryoprecipitate: 10 units (1 unit/10 kg)
  - Frozen Plasma: 3-4 units (10-15 mL/kg)
- Pediatric: In published studies, FC dosing has ranged between 30-60 mg/kg.

Products:

- No evidence of superiority of different products (Different FC products; FC vs. Cryoprecipitate).
- FC has a preferred safety profile (decreased transmissible disease risk)
- FC offers logistical advantages, including: a more precise fibrinogen dose, simple preparation without need for thawing, and efficiency of administration.

**off label indication but supported by literature*

NAC Statement on Fibrinogen Replacement

https://www.nacblood.ca/resources/guidelines/downloads/FC%20Statement%20Update%20Final2020.pdf

SUMMARY OF REVISIONS

Revision Date	Detail
Next revision - 2021	Expected Spring 2021
February 2020	Added discussion on RiaSTAP and FIBRYGA as two brands of fibrinogen concentrate now available from CBS
	Added reference for the FIBRES study
	Added statement on fibrinogen concentrate having a favorable safety profile over cryoprecipitate or frozen plasma for fibrinogen replacement
July 2018	Addition of dosing recommendations for pediatric patients
	Clarified suggested fibrinogen replacement threshold for obstetrical patients

Recommendations for Use of Prothrombin Complex Concentrates in Canada

- Recommendation from 2014
- Literature reviewed since last version and determined that no update needed
- Subcommittee meeting to revise document
  - External experts to be identified and invited
- Will consider addressing use of PCCs outside of warfarin reversal:
  - PCC for reversal of direct oral anticoagulants (DOACs)
  - PCC for other coagulopathies

NAC Blood Shortage Working Group

Interim update posted in March 2020 at start of pandemic.

https://www.nacblood.ca/resources/shortages-plan/20200320%20The%20National%20Plan%20for%20Management%20of%20Shortage%20of%20Labile%20Blood.pdf

- Further revisions in progress based on feedback from March 2020 update

Solvent Detergent Plasma – Revised Framework

Revised criteria based on original CADTH report (May 2011). Updated to reflect current clinical practice , but continue to follow original principles outlined by by the CADTH Panel of Experts.

S/D Plasma should be considered for:

1. Patients who require a high volume or chronic plasma transfusions (primary qualifier) :
   a. Congenital TTP or,
   b. Need for plasmapheresis with plasma as a replacement fluid for conditions such as acquired TTP and HUS or,
   c. Clotting factor deficiencies for which specific licensed concentrates not be readily available

   And who have one of the following secondary qualifiers:
   - Have experienced a recurrent clinically significant allergic reaction to plasma
   - Have an existing lung disorder that would make them more susceptible to effects of TRALI react ion.
2. Any patient who requires plasma but a blood group compatible product is not available in a timely manner.
3. Patients who have had a previous life-threatening reaction to plasma that could be avoided by the use of S/D plasma, where no alternative therapies are available.

Requests outside the above listed would be subject to review by local TM experts and CBS.

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And who hav…

- Have ex…
- Have ar… …l react ion.

2. Any patie… …timely manner.
3. Patients who have had a previous life-threatening … …by the use of S/D plasma, where no alternative therapies are ava…

CBSdeveloping new form and customer letter to incorporate changes.

Requests outside the above listed would be subject to review by local TM experts and CBS.

Patient Blood Management

- Request to CBS-PTBLC to include PBM within the scope of the NAC work plan (Aug 2020)
- Development of a Patient Blood Management Position Statement and Guidance Document as a new initiative on the NAC Work Plan approved (Sept 2020)
- Patient Blood Management Subcommittee formed
  - Dr. Ryan Lett from Saskatchewan as chair
  - Will draw upon expertise and existing groups in Canada
  - Review of recent European guidelines

Immunoglobulin Shortage Plan

Development of National Plan for Management of Shortage of Immunoglobulin Products is needed

- 2018 Expert Panel recommended development of priority list of patients / conditions
- Shortage of SCIg in Summer 2019
- COVID-19 has led to high likelihood of IVIg shortage in short to medium term
- Accelerated the development of a National Ig Shortages Plan
  - Interim shortage plan approved in July 2020
  - Development of full plan over following 18 months

Interim Immunoglobulin Shortage Plan

- Interim guidance released July 2020 (4-month development)
- Model of green / green advisory / amber / red phase from labile blood components
- Green phase - follow provincial / regional guidelines
- Based on Quebec framework for Ig shortage
- Input from stakeholders across Canada

The National Plan for Management of Shortages of Immunoglobulin Products (Ig) – Interim Guidance

Amber	Ig supply/inventory levels are low for a short or prolonged period. **Reduce use by 20 to 50%:**
	• Continue to follow all the actions outlined in Green phase and Green Advisory phase.
	• Limit Ig use to clinical circumstances when there are:
	  ○ No viable alternatives; **and/or**
	  ○ the condition is life-threatening or there is a risk for irreversible disability as identified in the table below.
	• Use the lowest Ig dose for the shortest duration required to achieve the desired outcome.
	• Implement screening of all Ig orders within the hospital transfusion service/blood bank.

Red	There is a critical and prolonged Ig shortage. **Reduce use by over 50%:**
	• Limit Ig use to clinical circumstances when there are:
	  ○ No viable alternatives; **and/or**
	  ○ the condition is life-threatening or there is a risk for irreversible disability as identified in the table below.
	• Have each case and dose approved by a formally established peer committee as per local jurisdictional guidance*.
	• File a written copy of the decision in the patient's medical record and send another copy to Transfusion Medicine Services (blood bank).

https://www.nacblood.ca/resources/shortages-plan/The National Plan for Management of Shortages of Immunoglobulin Products (Ig) Interim Guidance_July 27 2020.Published.pdf

Considerations for Full National Ig Shortage Plan

- Roles and responsibilities of all stakeholders
- Data sharing including inventory levels
- Adjudication Committees
- Ethical framework
- Allocation criteria
- Medico-legal implications

- Assessement of the effectiveness of inventory phase activities
- Guidance for product switching
- Guidance for use of Ig in research
- Availability and accessibility ofa lternative therapies
- Tools to document decisions or use

Immunoglobulin Update - October 2020

S. Grenier, Canadian Blood Services

- Potential shortfall of IVIg identified for 2021-22 and 2022-23
  - NEBMC communication in Dec 2020 outlining possible shortage
- Expected disruptions in supply of some brands and vial sizes in 2021

- Pending contract finalization, identified gap for 21/22 and 22/23 were filled by alternative Ig
- Major changes
  - *GGL ↓ 50%*
  - *Gammunex ↑ 33%*
  - *Privigen ↔ however vial sizes will be impacted (10g and 40g)*
  - *Panzyga ↑ 100%*
  - *Octagam* to fill the rest of the gap*

Immunoglobulin Update - October 2020

- All options for additional sources IVIg exhausted
- Readiness to switch IVIG brands will be required
- CBS will work with hospitals especially large users for potential brand switches
- Provinces responsible for developing local strategies for IVIg management using the Interim National Ig Shortages Plan as a framework
  - NAC is preparing a statement supporting the use of Ig utilization appropriateness guidance documents endorsed within jurisdictions

Overview – Interim review process

CADTH

Clinicians

Med/Sci Review

P'economic review

Patient groups

Patient consultation

CPEC

CBS health care professionals and scientists provide feedback on clinical and pharmacoeconomic reports.

Canadian Blood Services

Clinician groups

Patient groups

Blood banks

CBS as formulary manager

CDM for listing decision

Products under review:

- Hemlibra – CADTH Final Recommendations (Dec)
- Vonvendi- Expert committee recomendation
- Haegarda

CBS PPP utilization

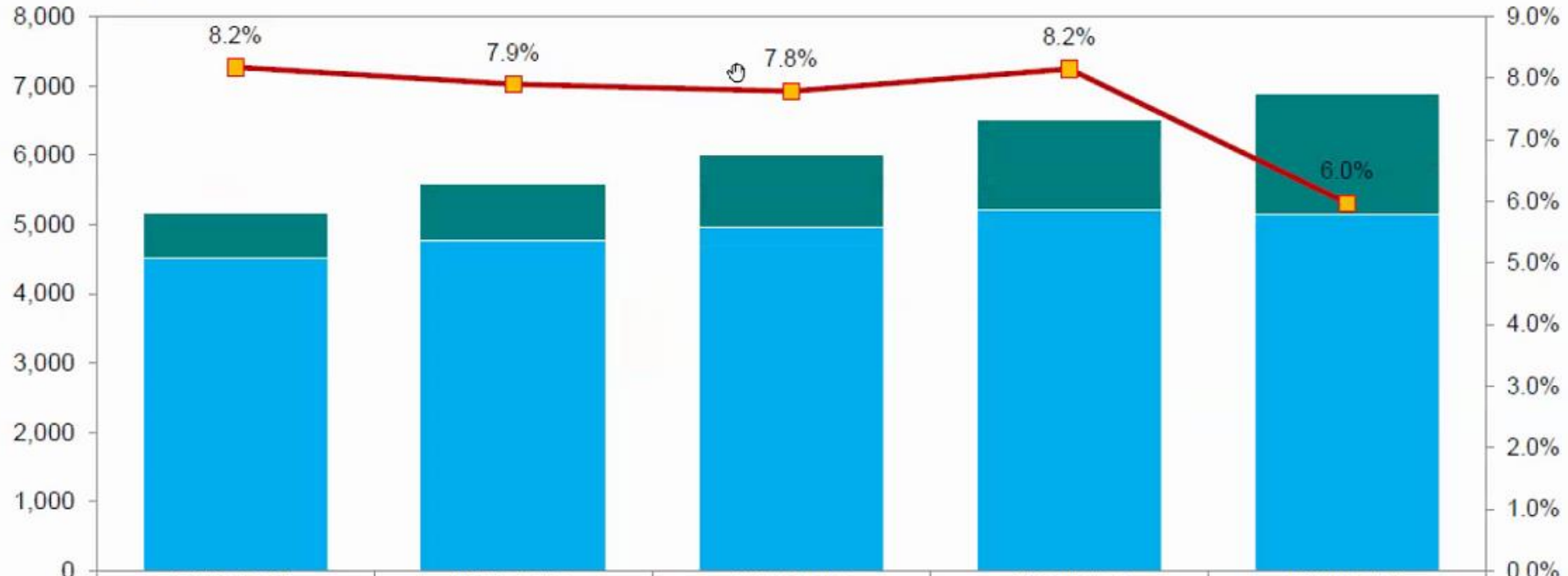
- Immunoglobulin increased by 6.0%
- FVIII utilization decreased by 6.5%
- FEIBA decrease by 52.1%
- Fibrinogen concentrate increase by 30% (71% increase in 2019/20)
- Decrease in cryoprecipitate demand by -57.7% (-39.1% in 2019/20)

Analysis of Immune Globulin

Immune Globulin 5 year trend by grams

* FY2020/21 Forecast is based on Sep 30 year-to-date actuals

Total thousands of grams | Year on Year % Growth

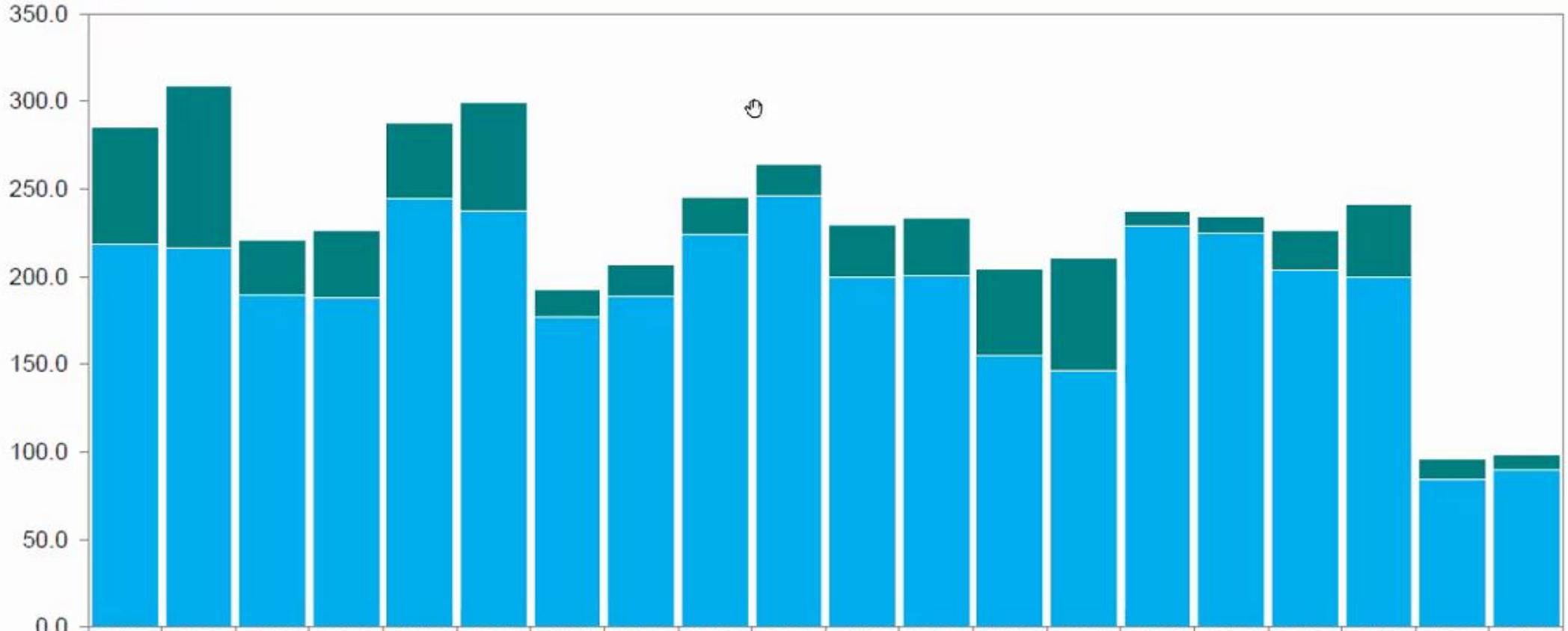


	FY2016/17	FY2017/18	FY2018/19	FY2019/20	FY2020/21
Subcutaneous	660	802	1,058	1,298	1,753
Intravenous	4,511	4,778	4,957	5,207	5,140
Growth %	8.2%	7.9%	7.8%	8.2%	6.0%

Immune Globulin provincial comparison by population - FY2020/21 vs. FY2019/20

Total grams per 1,000 population

* FY2020/21 Forecast is based on Sep 30 year-to-date actuals



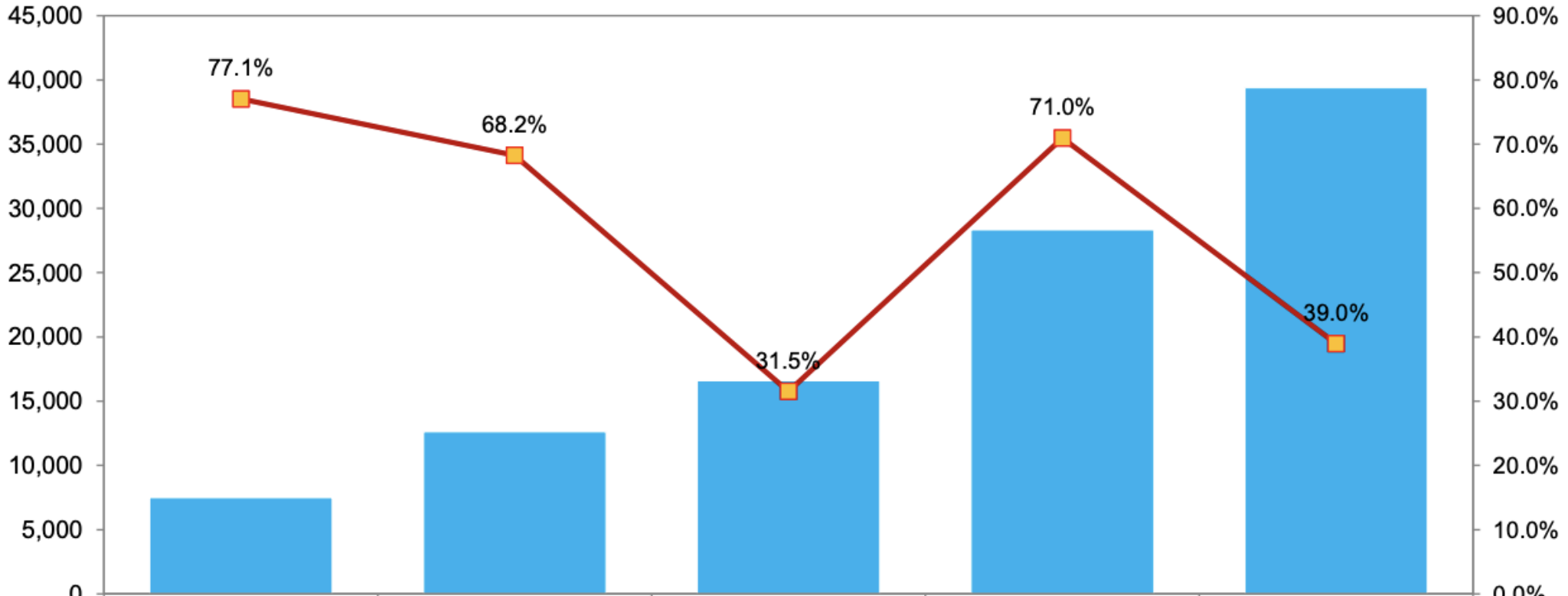
	19/20	20/21	19/20	20/21	19/20	20/21	19/20	20/21	19/20	20/21	19/20	20/21	19/20	20/21	19/20	20/21	19/20	20/21	19/20	20/21
	AB		BC		MB		NB		NL		NS		ON		PE		SK		Territories	
Subcutaneous	66.4	93.0	31.0	38.4	43.3	62.1	16.0	17.9	20.5	17.7	30.1	33.0	49.4	64.8	8.6	9.5	22.8	42.3	11.8	8.3
Intravenous	218.9	215.8	189.9	187.6	244.3	237.8	176.7	189.0	224.4	246.0	199.4	200.8	155.1	145.9	228.6	224.5	203.7	199.3	84.0	90.1

Analysis of Fibrinogen

Fibrinogen 5 year trend by grams

Total grams | Year on Year % Growth

* FY2020/21 Forecast is based on Sep 30 year-to-date actuals

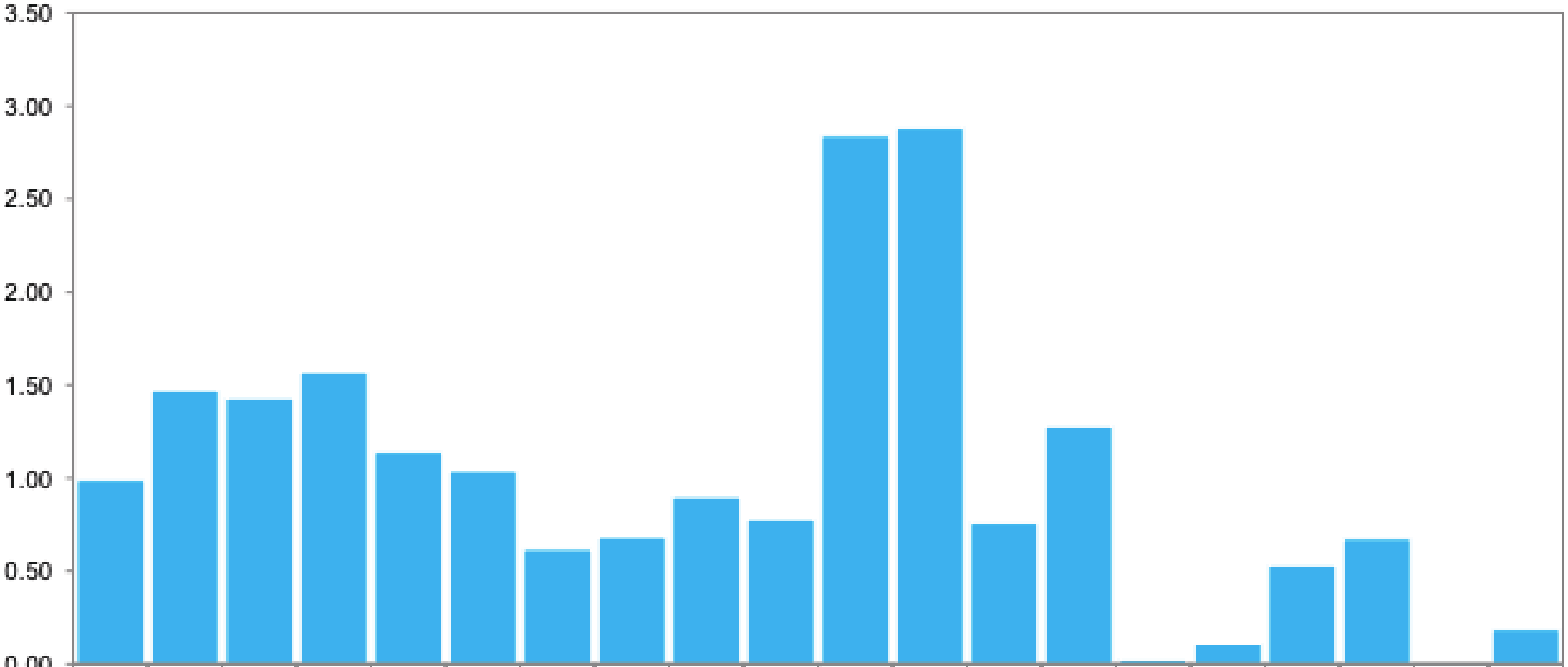


	FY2016/17	FY2017/18	FY2018/19	FY2019/20	FY2020/21
Fibrinogen	7491	12603	16575	28335	39375
Growth %	77.1%	68.2%	31.5%	71.0%	39.0%

Fibrinogen provincial comparison by population - FY2020/21 vs. FY2019/20

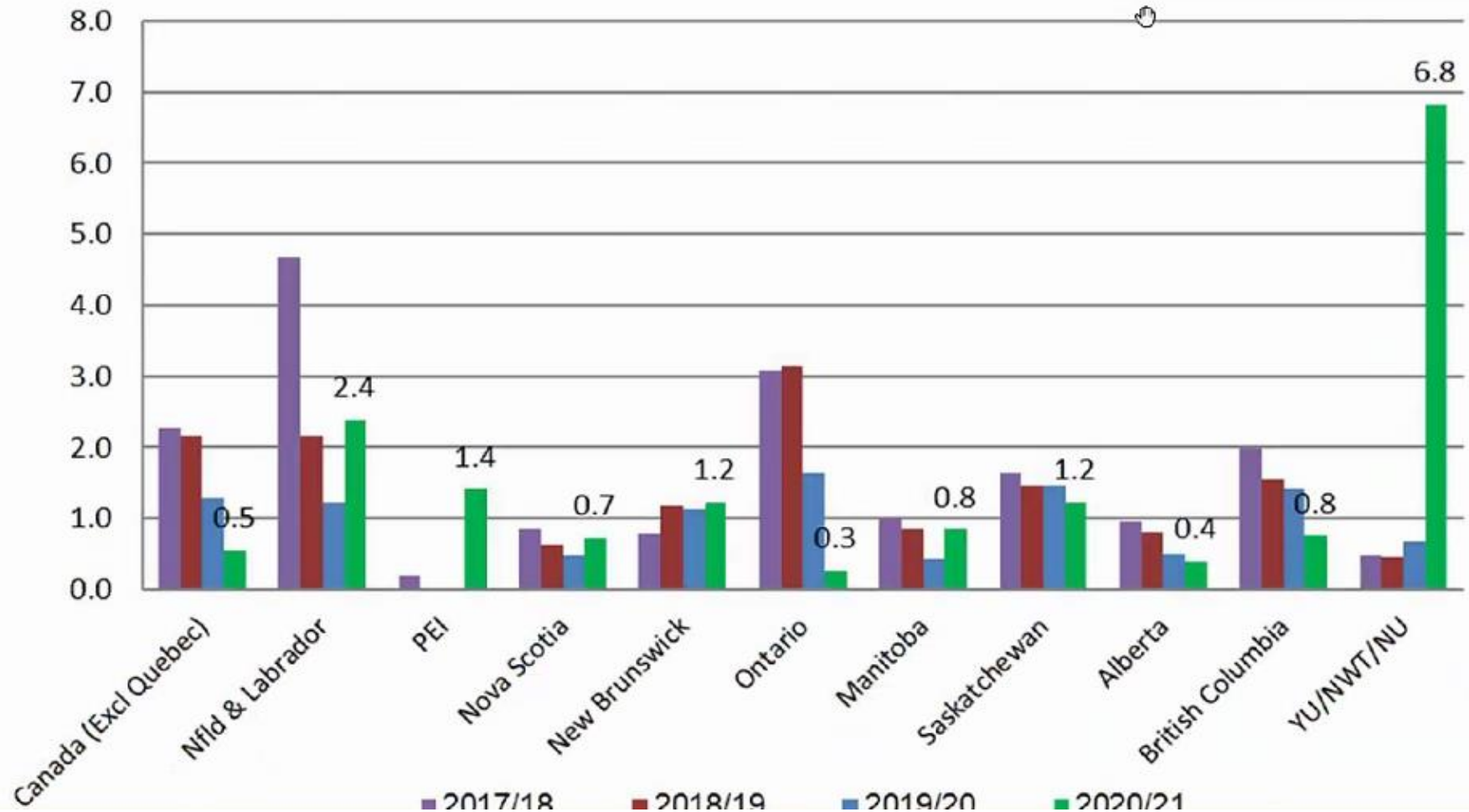
Total grams per 1,000 population

* FY2020/21 Forecast is based on Sep 30 year-to-date actuals



	19/20 AB	20/21 AB	19/20 BC	20/21 BC	19/20 MB	20/21 MB	19/20 NB	20/21 NB	19/20 NL	20/21 NL	19/20 NS	20/21 NS	19/20 ON	20/21 ON	19/20 PE	20/21 PE	19/20 SK	20/21 SK	19/20 Territories	20/21 Territories
Fibrinogen	1.0	1.5	1.4	1.6	1.1	1.0	0.6	0.7	0.9	0.8	2.8	2.9	0.8	1.3	0.0	0.1	0.5	0.7	0.0	0.2

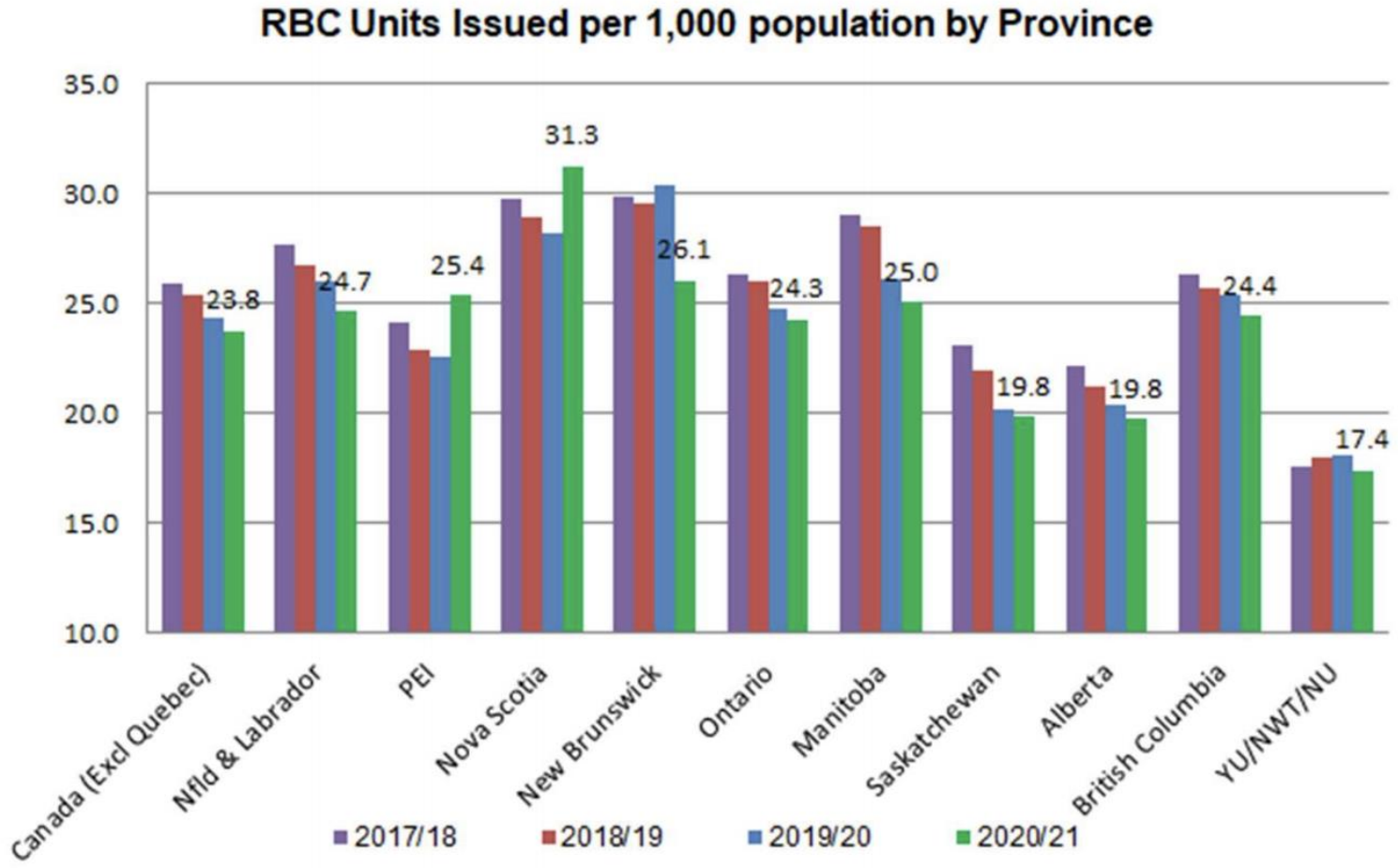
Cryoprecipitate Units Issued per 1,000 population by Province



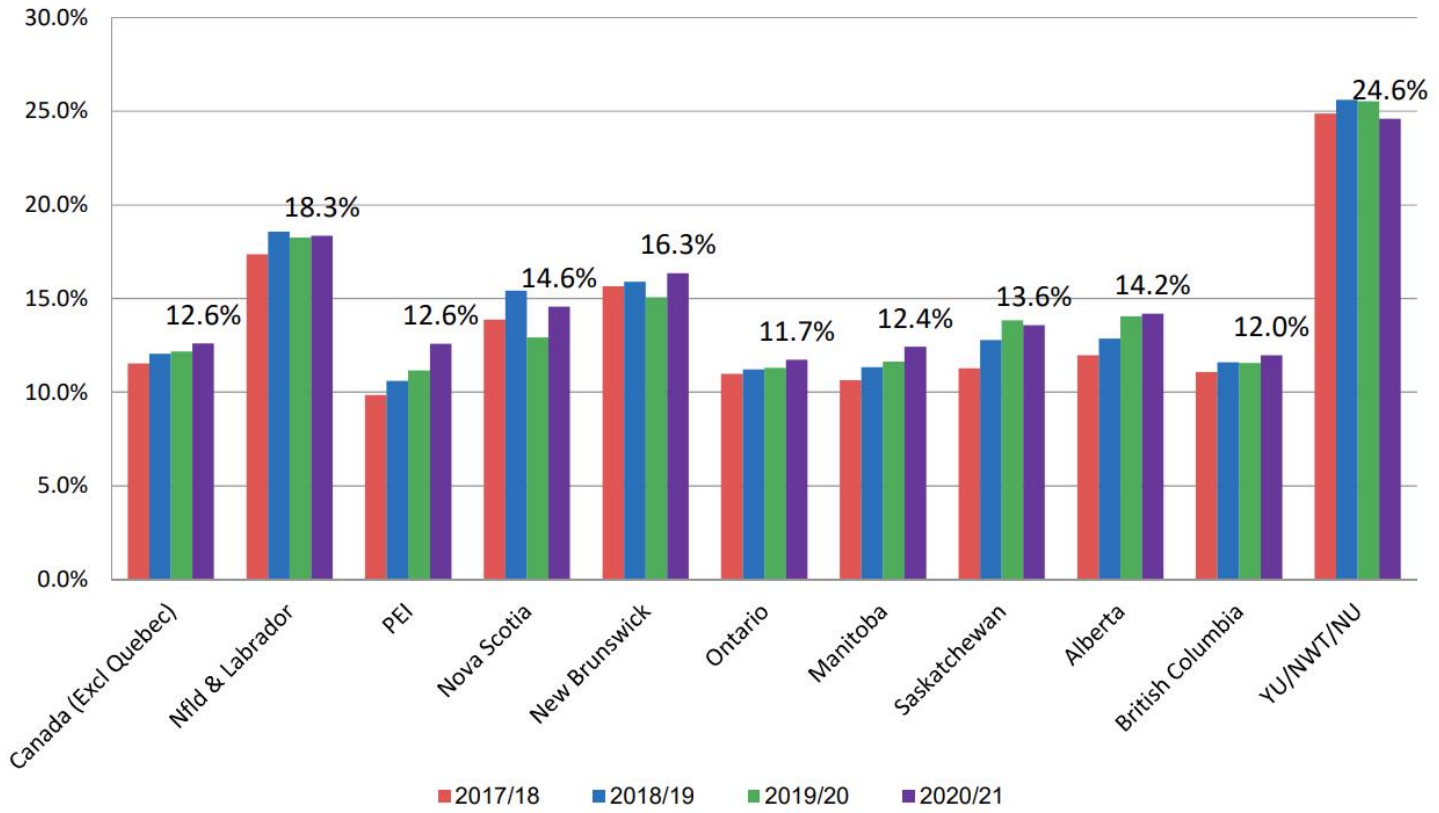
CBS Fresh Blood Component

- Overall decrease in RBC issues
  - O negative percentage increased by from 12.2% to 12.6%
  - Ontario 11.7%
- Platelet units issued stable (-0.7%)
- Frozen plasma issued continues to decrease (-8.4%)
  - AB percentage increased from 16.7% to 19.3%
  - Ontario 20.3%

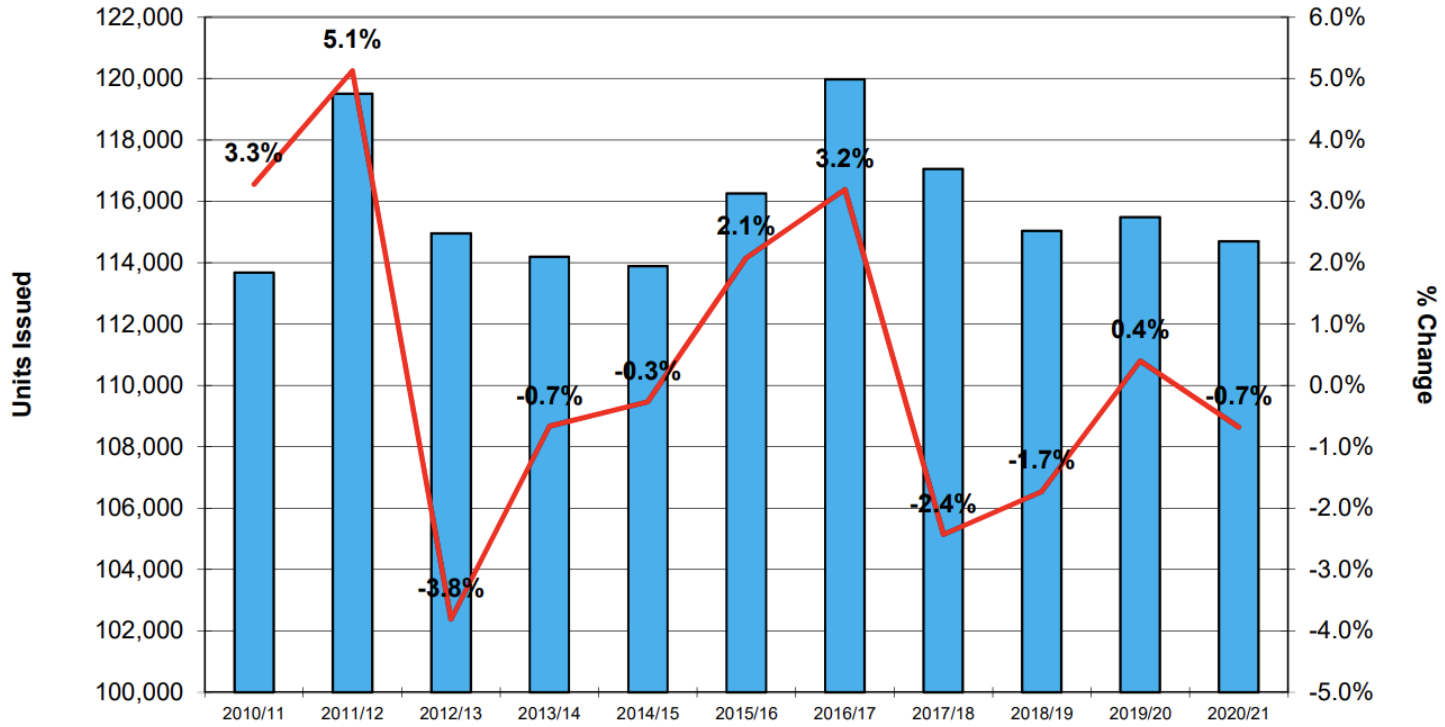
RBC Units Issued per 1,000 population by Province



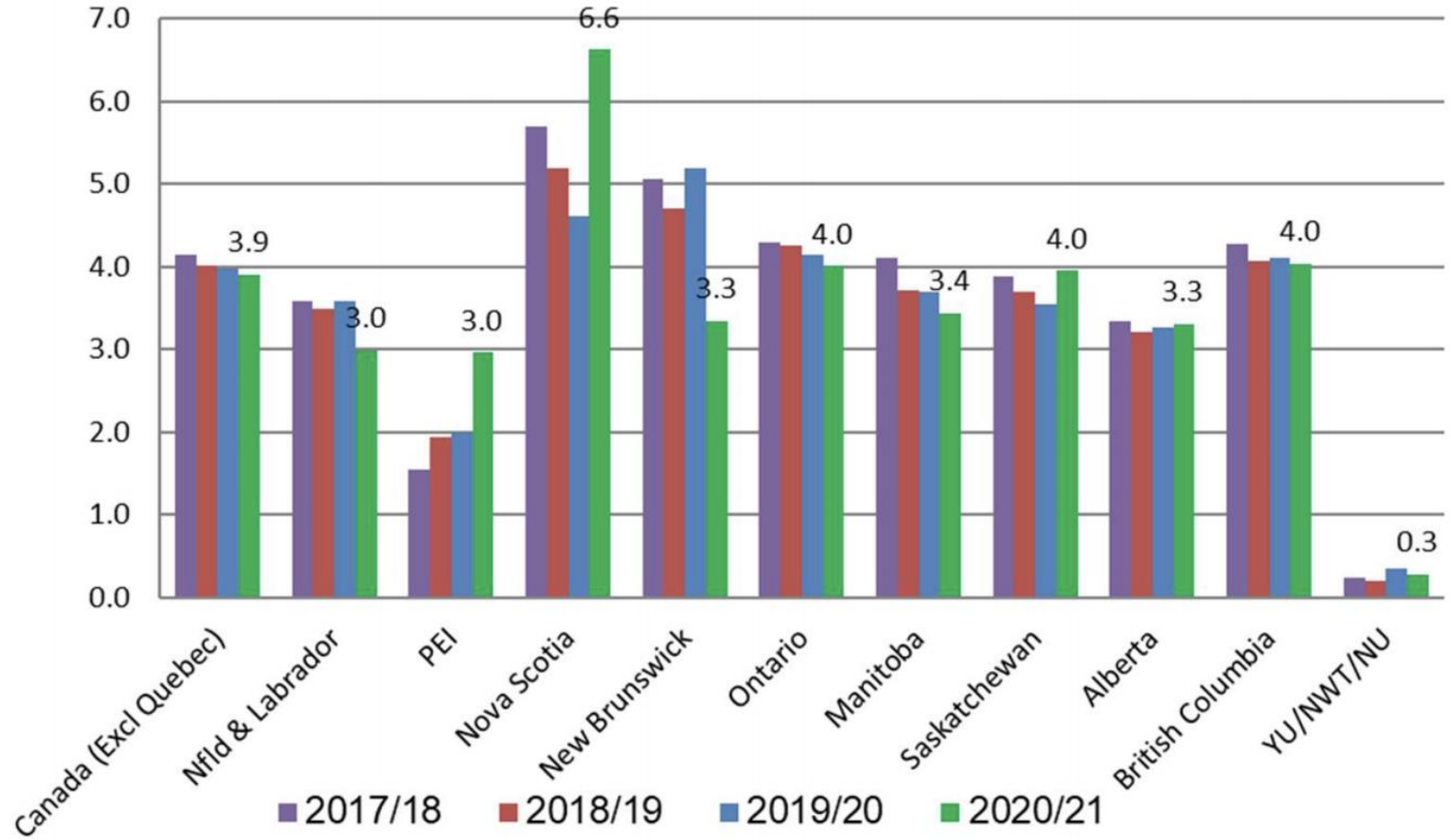
% O-Neg RBC Issues of Total RBC Issues by Province



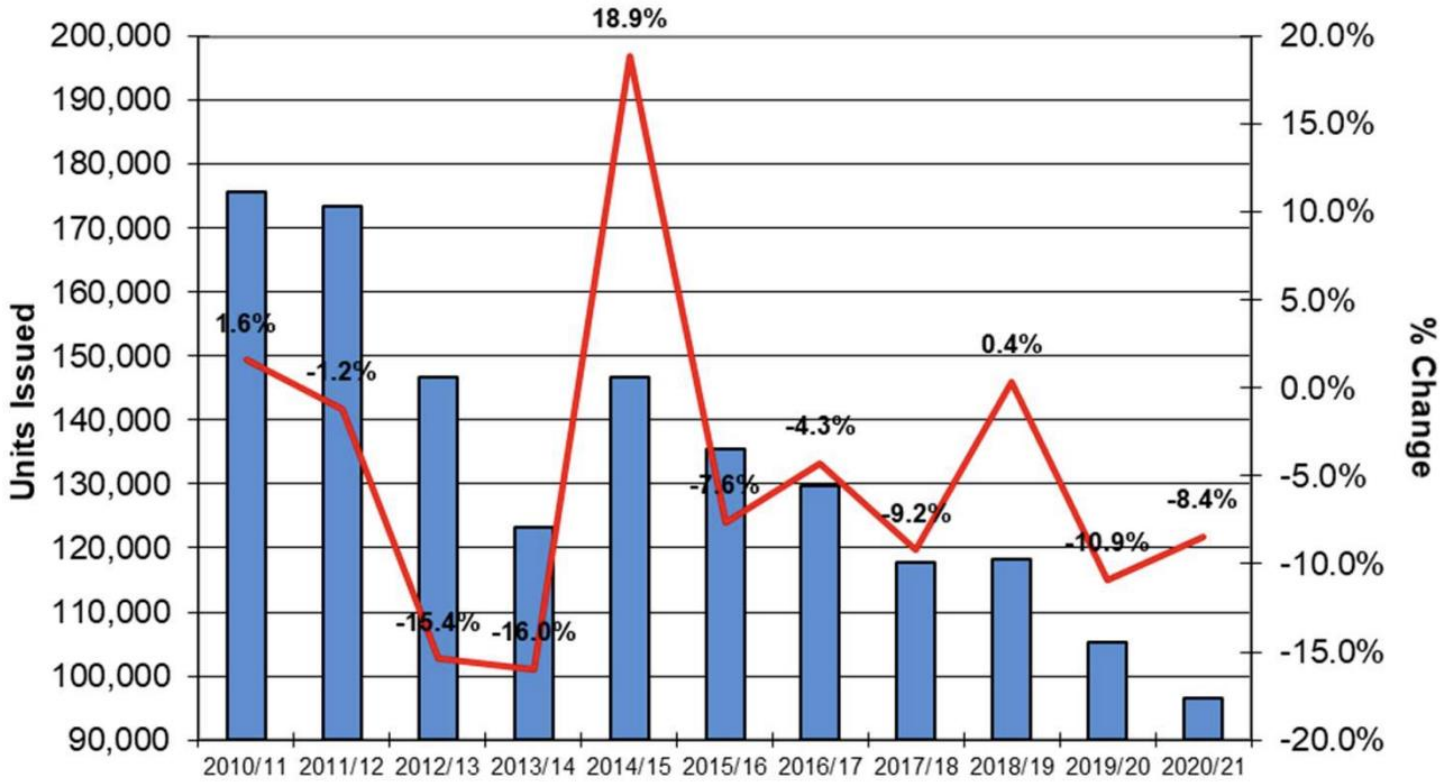
Platelet Units Issued & Fiscal Period Growth Rates



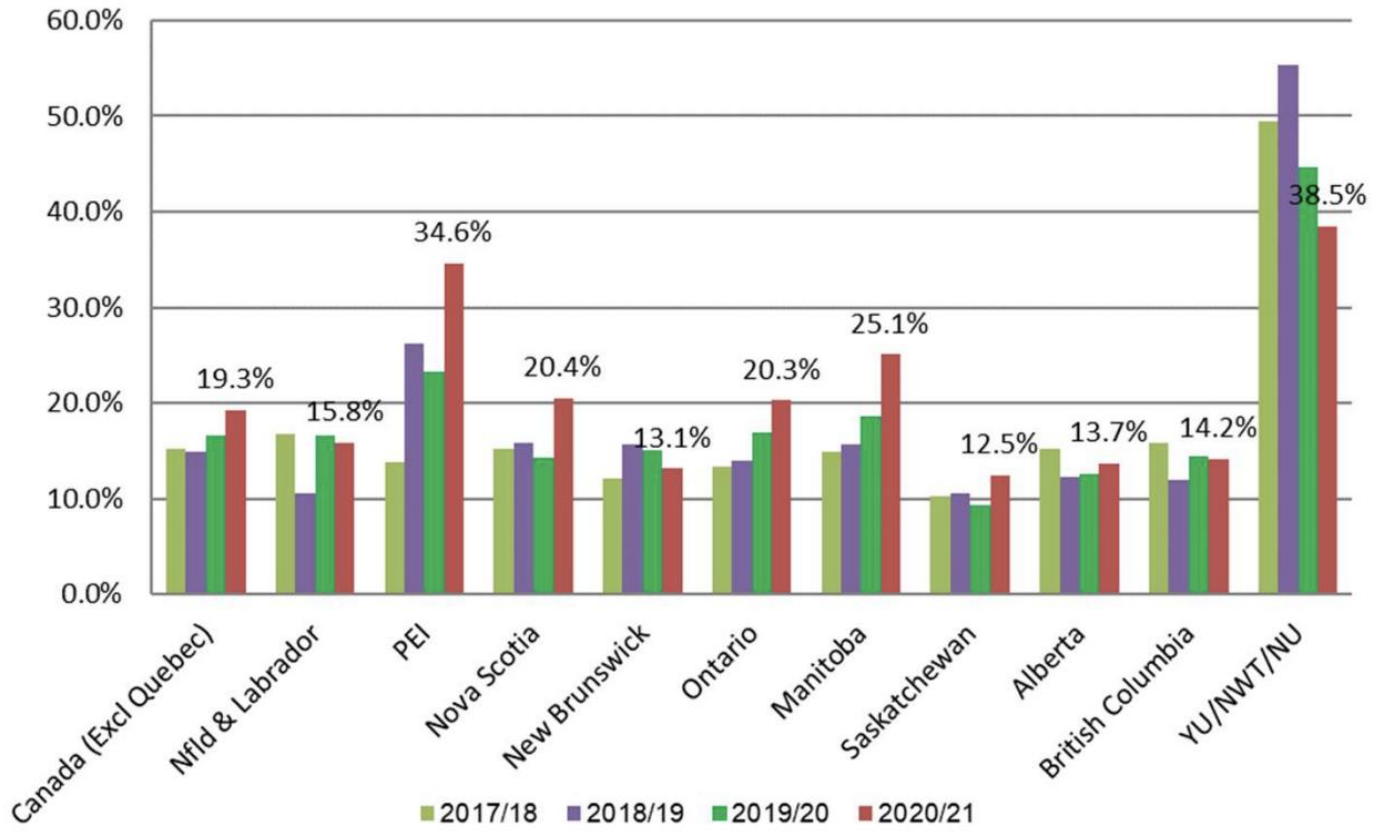
Platelet Units Issued per 1,000 population by Province



Plasma Units Issued & Fiscal Period Growth Rates



% AB Plasma Issues of Total Plasma Issues by Province



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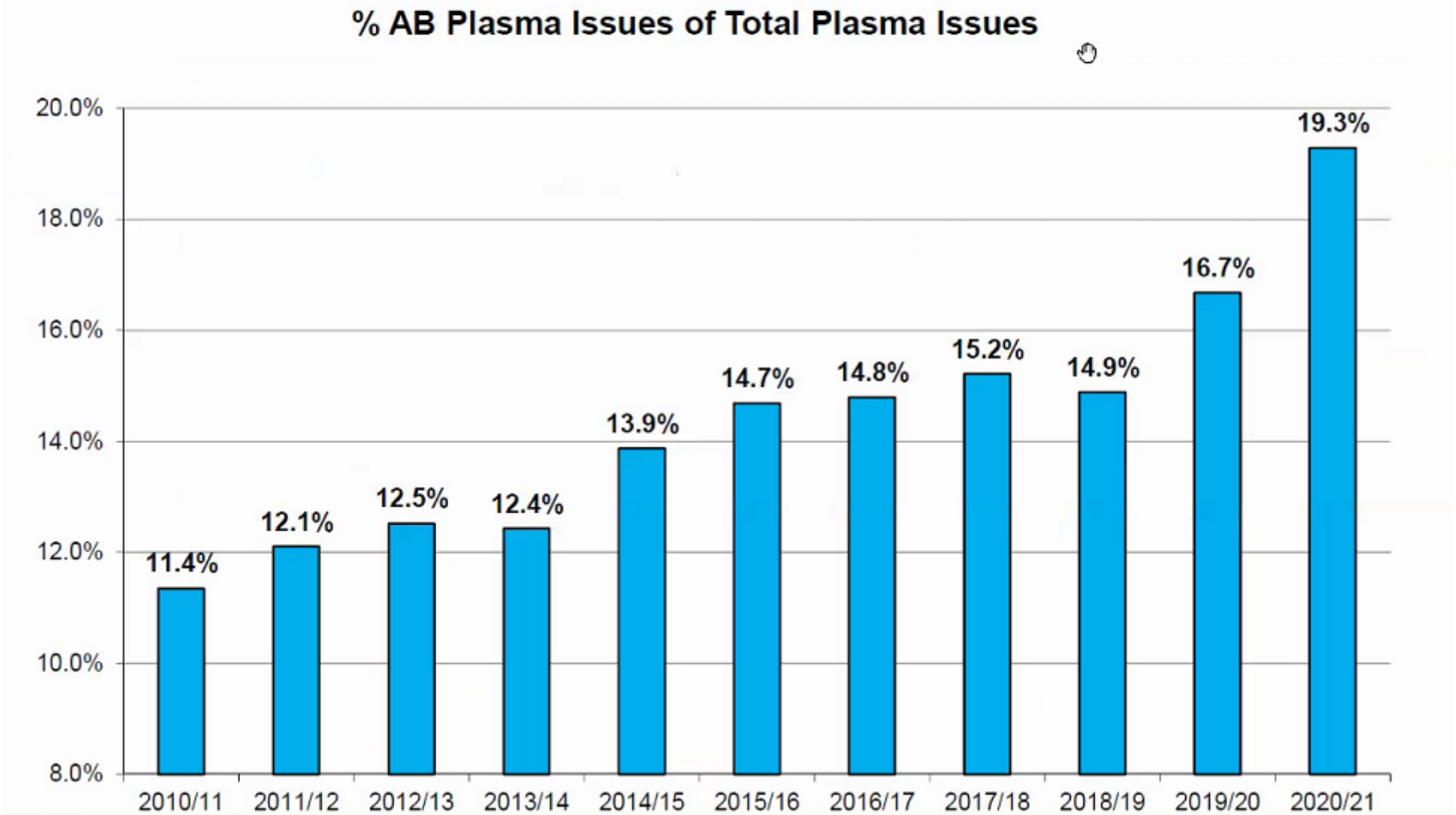

National Blood Portfolio Lead: Background

- Since the establishment of the Canadian Blood Services (CBS) in 1998, the following provinces have functioned as the National Blood Portfolio lead:

Jurisdiction	Timeframe
Saskatchewan (Transition from Canadian Red Cross Society)	To 1998
Ontario	1998-2001
British Columbia	2001-2005
Nova Scotia	2005-2008
Alberta	2008-2010
Newfoundland and Labrador	2010-2013
Manitoba	2013-2015
New Brunswick	2015-2017
Saskatchewan	2017-2019
Prince Edward Island	2019-2021

Going forward:

Jurisdiction	Timeframe
Ontario	**2021-2023**
British Columbia	2023-2025
Nova Scotia	2025-2029


QUESTIONS