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Ontario Frozen Plasma Audit 2: *Are we doing any better?*

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- Medical consultant for Canadian Blood Services
- Funded by CIHR for research studies on Frozen Plasma, Age of Red Blood Cells, and effect of donor characteristics.
- Consultant / local investigator for pharmaceutical companies including Amgen, Novartis, Bayer, Rigel, GlaxoSmithKlein



Overview

1. Overview of Frozen Plasma Utilization
2. Review of 2008 Ontario audit of Frozen Plasma
3. 2013 Frozen Plasma audit results
4. Draft recommendations from 2013 audit



Why transfuse Frozen Plasma?

FP reduces bleeding

Elevated INR/PT increases risk of bleeding



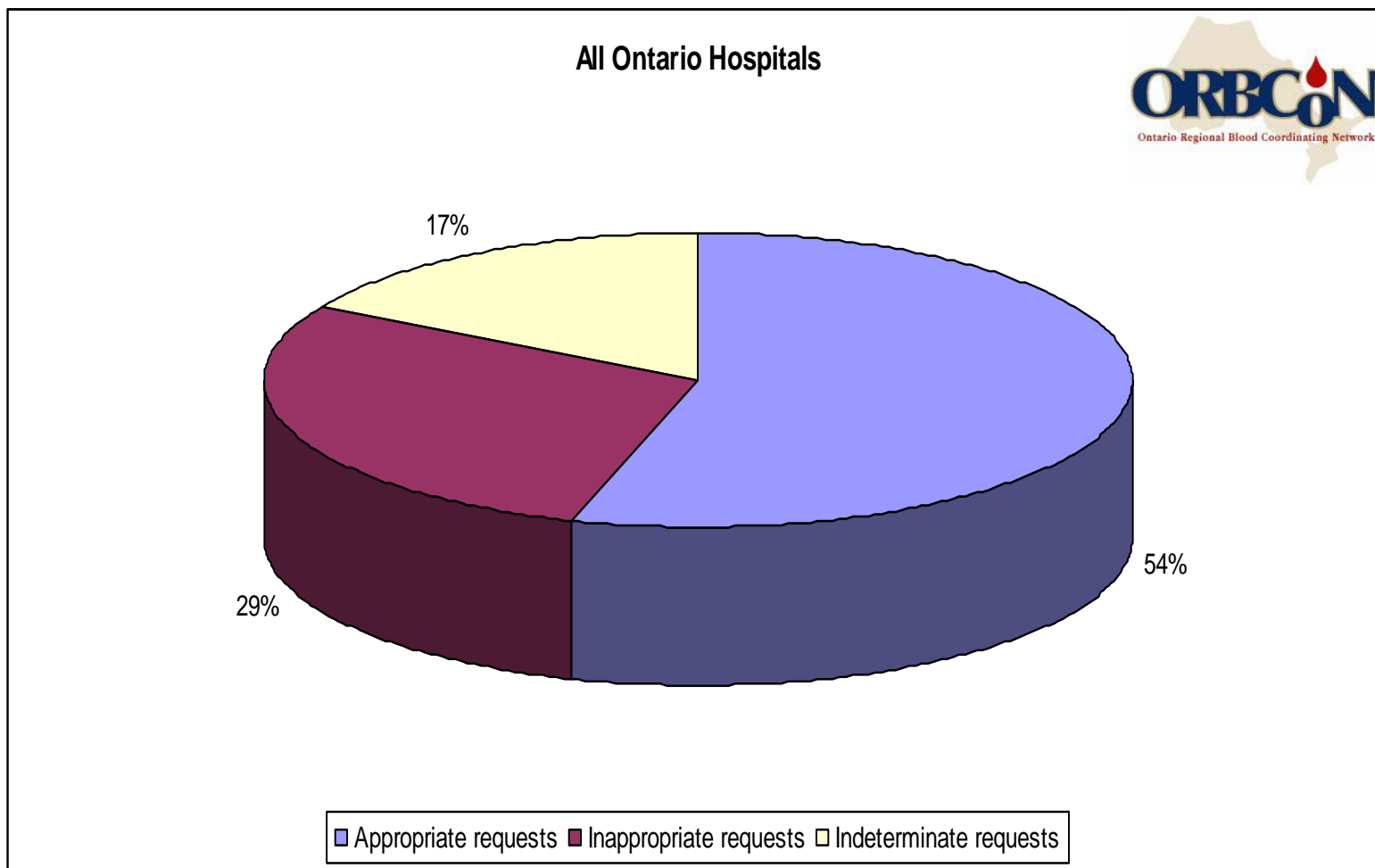
Transfusing FP will correct the INR/PT



Correcting the INR/PT will reduce bleeding



Appropriateness of Frozen Plasma Use in Ontario in 2008





Appropriateness of Frozen Plasma Use in Ontario in 2008

Total no of appropriate Frozen Plasma requests	314 (54.8%)
Coagulopathy (not warfarin / vit K deficiency) Bleeding <i>and</i> INR >1.5 and/or PTT >1x normal .	96 (16.8)
Peri-surgical bleeding INR>1.5 and/or PTT>1x normal.	80 (14.0)
Coagulopathy (not warfarin / vit K deficiency) Urgent intervention or surgery INR >1.5 and/or PTT>1x upper limit of normal.	43 (7.5)
Reversal of warfarin or vitamin K deficiency. Bleeding INR >1.5 and/or PTT >1x normal.	37 (6.4)
“Massive transfusion” INR>1.5 and/or PTT >1x normal.	35 (6.1)



Appropriateness of Frozen Plasma Use in Ontario in 2008



Total no of inappropriate Frozen Plasma requests	164 (28.6%)
INR < 1.5 and normal PTT Irrespective of bleeding status or procedure status	97 (16.9 %)
Reversal of warfarin or vitamin K deficiency Absence of bleeding	41 (7.2 %)
Reversal of other coagulation defect INR >1.5 and PTT>1x upper limit of normal. No bleeding or surgery/procedure planned	15 (2.6 %)
Heparin reversal (regardless of INR)	10 (1.7 %)
INR ≤ 1.0 and normal PTT Irrespective of bleeding status or procedure status	7 (1.2 %)



ORBCoN Recommendations for FP Transfusions

Situations in which the transfusion of FP is reasonable:

Clinical Indication	Reason
Bleeding	Liver disease or DIC with INR above 1.5
	Massive transfusion (expect more than 10 RBC units transfused in 24 hours) with INR above 1.5 (or rapidity of bleeding does not allow for MD to wait for results)
	Reversal of warfarin or vitamin K deficiency only where intravenous vitamin K would not suffice and prothrombin complex concentrate (Octaplex®) is unavailable
	Inherited or acquired single factor deficiencies where specific factor concentrate is unavailable
Emergency surgery or major procedure (within 6 hours)	Reversal of warfarin or vitamin K deficiency only where intravenous vitamin K would not suffice and prothrombin complex concentrate (Octaplex®) is unavailable
Surgery or major procedure	Liver disease or DIC with INR above 1.5
	Inherited or acquired single factor deficiencies where specific factor concentrate is unavailable
Plasma exchange	Thrombotic thrombocytopenic purpura (TTP)

Situations in which transfusion of FP is NOT useful:

- INR 1.5 or less (including major or minor procedure/surgery)*
- Use of 1:1 (FP:RBC) replacement when patient is unlikely to require massive transfusion
- Coagulopathy in the absence of bleeding or need for emergency surgery
- Elective reversal of warfarin where time allows for warfarin cessation and/or use of vitamin K
- Reversal of anticoagulants other than warfarin (eg: heparin/LMWH, rivaroxaban)
- Volume expansion or "nutrition support"



Methodology

- Prospective 5-day audit of Frozen Plasma and Prothrombin Complex Concentrate
 - Non-consecutive days
 - November 18th – December 13th, 2013
- All Ontario hospitals with transfusion services invited to participate
- Web based audit tool
 - Completed by transfusion technologists
- All transfusions adjudicated by 2 hematologists
 - Pre-determined appropriateness criteria



Data Collection

- Hospital site
- Patient care area
- Date of transfusion
- Patient age (year of birth) and sex
- Number of plasma units ordered and transfused
- Number of prothrombin complex concentrate vials ordered and infused
- Ordering physician specialty
- Indication for transfusion/infusion
 - Bleeding, Procedures, Coagulopathy
- Pre and post transfusion coagulation testing results



Ontario Frozen Plasma 2013

Plasma *Appropriateness Ratings*

Code	Appropriate
A1	<ul style="list-style-type: none">• Coagulopathy other than warfarin, vitamin K deficiency, heparin, or other anticoagulants• Urgent surgery or invasive procedure• Pre- or post- transfusion INR >1.5 and/or PTT > 1.5x upper limit of normal
A2	<ul style="list-style-type: none">• Coagulopathy other than warfarin, vitamin K deficiency, heparin, or other anticoagulants• Bleeding• Pre- or post- transfusion INR > 1.5 and/or PTT > 1.5x upper limit of normal
A3	<ul style="list-style-type: none">• “Massive transfusion”• Pre- or post- transfusion INR > 1.5 and/or PTT > 1.5x upper limit of normal or no laboratory coagulation data available at the time of product issue
A4	<ul style="list-style-type: none">• Apheresis/plasma exchange or TTP• Regardless of coagulation status
A5	<ul style="list-style-type: none">• Peri-surgical bleeding not due to any anticoagulant medication• Minor bleeding• Pre- or post- transfusion INR > 1.5 and/or PTT > 1.5x upper limit of normal.
A6	<ul style="list-style-type: none">• Peri-surgical bleeding not due to any anticoagulant medication• Major bleeding• Pre- or post-transfusion INR > 1.5 and/or PTT > 1.5x upper limit of normal or no coagulation data available
A7	<ul style="list-style-type: none">• Congenital coagulation factor deficiency other than Factor II, VII, VIII, IX, X, XIII• Bleeding and or surgery/procedure• No factor concentrates available
A8	<ul style="list-style-type: none">• Reversal of coagulation defect due to warfarin or vitamin K deficiency• Bleeding or urgent surgery or invasive procedure• Contraindication to PCCs (e.g. history of heparin induced thrombocytopenia)



Ontario Frozen Plasma 2013

Appropriateness Ratings

Code	Inappropriate
I1	<ul style="list-style-type: none">• Reversal of coagulation defect due to warfarin or vitamin K deficiency,• Absence of bleeding and/or no urgent surgery/procedure
I2	<ul style="list-style-type: none">• Reversal of coagulation defect due to warfarin or vitamin K deficiency• Bleeding or surgery or invasive procedure• No contraindication to PCC
I3	<ul style="list-style-type: none">• $INR \leq 1.5$ and $PTT \leq 1.5x$ upper limit of normal pre- transfusion• Irrespective of bleeding status or procedure status
I4	<ul style="list-style-type: none">• Heparin reversal (regardless of INR)
I5	<ul style="list-style-type: none">• Reversal of other anticoagulants (Dabigatran/Pradaxa, Rivaroxiban, Apixaban, etc)
I6	<ul style="list-style-type: none">• Volume replacement
I7	<ul style="list-style-type: none">• Reversal of coagulation defect other than coumadin/warfarin or vitamin K or heparin• Pre or post transfusion $INR \geq 1.5$ and/or $PTT \geq 1.5x$ upper limit of normal• No bleeding or surgery/procedure
Code	Indeterminate
M1	<ul style="list-style-type: none">• No laboratory coagulation data pre- or post- transfusion
M2	<ul style="list-style-type: none">• No laboratory coagulation data pre- transfusion (with normal coags post-procedure)



Ontario Frozen Plasma 2013 PCC Appropriateness Ratings

Code	Appropriate
PCC-A1	<ul style="list-style-type: none">• Reversal of warfarin or vitamin K deficiency• Bleeding• Pre- or post-transfusion INR >1.5
PCC-A2	<ul style="list-style-type: none">• Reversal of warfarin or vitamin K deficiency• Urgent surgery or invasive procedure (within 6 hours)• Pre- or post-transfusion INR >1.5
PCC-A3	<ul style="list-style-type: none">• Congenital deficiency of Factors II, VII, IX, or X• Bleeding, surgery or invasive procedure
Code	Inappropriate
PCC-I1	<ul style="list-style-type: none">• Reversal of coagulopathy other than warfarin, vitamin K deficiency or congenital deficiency of factors II, VII, IX, or X• Regardless of bleeding status or surgical/procedure
PCC-I2	<ul style="list-style-type: none">• Reversal of warfarin, vitamin K deficiency• Absence of bleeding• Non-urgent surgery or invasive procedure (>6 hours)
PCC-I3	<ul style="list-style-type: none">• Reversal of congenital factor deficiency other than factors II, VII, IX, or X
Code	Indeterminate
PCC-M1	<ul style="list-style-type: none">• Reversal of other anticoagulants, Fondaparinux, Dabigatran, Rivaroxaban, Apixaban)• Bleeding and/or surgery/procedure



Ontario Plasma Audit 2013

Results

- 51 of 158 (32%) eligible hospitals participated
 - Approximately 60% of the plasma transfused in province
 - 3 small hospitals
 - 37 community hospitals
 - 11 teaching hospitals
- 329 orders for Frozen Plasma
- 113 orders for PCCs



Ontario Plasma Audit 2013

Results - Plasma

Total number of reported FP orders	329 (7 apheresis/plasma exchange)
Total number of FP units ordered (250 mL equivalents)	969
Total number of FP units transfused (250 mL equivalents)	922
FP (250 mL) units transfused	724
Apheresis (250 mL) transfused	2
Apheresis (500 mL) transfused	98
Total number of Cryosupernatant units ordered	88
Total number of Cryosupernatant transfused	88



Ontario Plasma Audit 2013

Results - Plasma



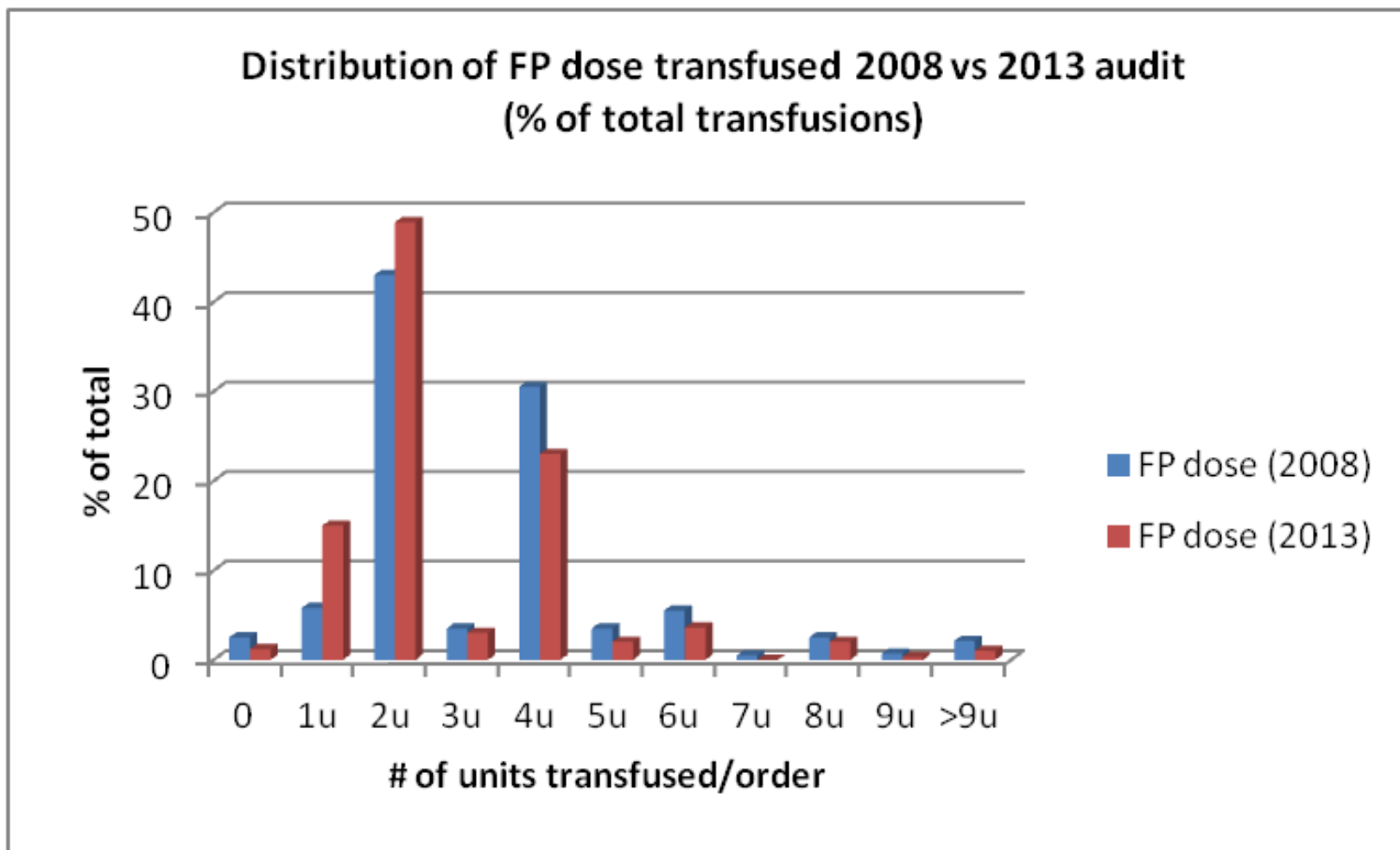
Procedure/Indication	Total # (%)	Community # (%)	Teaching # (%)
Surgery	108	49	59
Unknown	45	30	15
Other	32	17	15
Image guided therapy	7	1	6
Scope	6	1	5
Central line placement	2	2	0
Liver biopsy	2	1	1
Thoracentesis	1	1	0



Ontario Plasma Audit 2013

Results - Plasma

Dose of FP transfused





Indications for FP

A. Coagulopathy

- Anticoagulant 71 (21.4%)
- Coagulopathy 147 (44.4%)

A. Bleeding

- 198 (59.8%)

A. Procedures

- 144 (43.5%)



Ontario Plasma Audit 2013

Results - Plasma



Coagulopathy	Total # (%)	Community # (%)	Teaching # (%)
Yes	175 (54.3)	87 (46.0)	88 (66.2)
Liver disease	53 (30.3)	40 (46.0)	13 (14.8)
Massive transfusion	46 (26.3)	7 (8.0)	39 (44.3)
Unknown	34 (19.4)	21 (24.1)	13 (14.8)
Sepsis	25 (14.3)	12 (13.8)	13 (14.8)
DIC	10 (5.7)	2 (2.3)	8 (9.1)
Trauma	6 (3.4)	4 (4.6)	2 (2.3)
Vit K deficiency	1 (0.6)	1 (1.1)	0 (0.0)
No	98 (30.4)	70 (37.0)	28 (21.0)
Unknown	49 (15.2)	32 (17.0)	17 (12.8)



Ontario Plasma Audit 2013

Anticoagulant Reversal

Type of anticoagulant	# of orders
Warfarin	55
LMWH	22
Heparin	18
Dabigatran (Pradaxa)	3
Rivaroxaban (Xarelto)	3
Don't know	3



Ontario Plasma Audit 2013

Results - Plasma



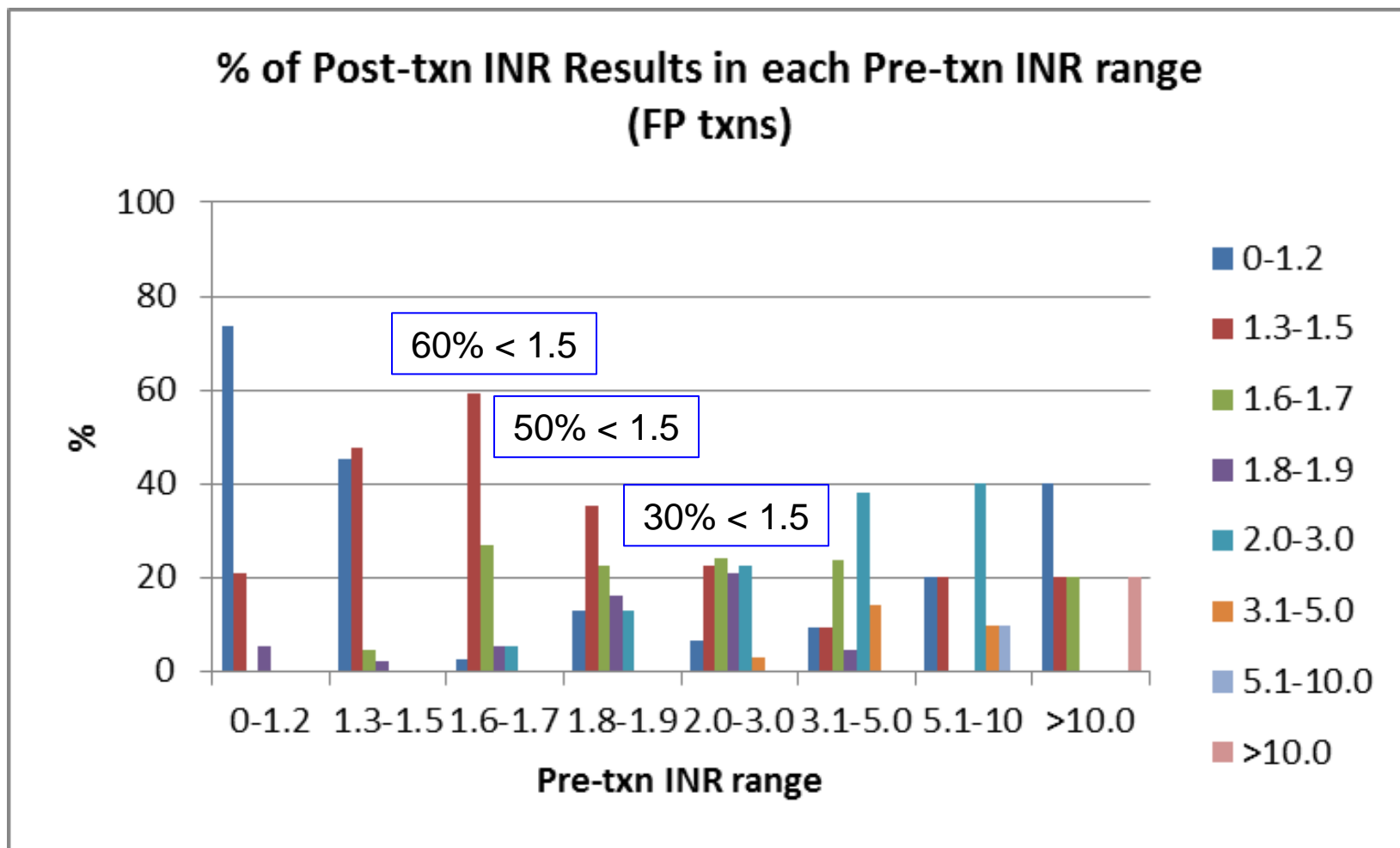
	All (n=49)	Community Hospitals (n=38)	Teaching Hospitals (n=11)
Total # FP orders	322	189	133
# of units ordered	955	538	417
Median # units ordered (min-max)	2 (1-18)	2 (1-16)	2 (1-18)
# of units transfused	908	514	394
Median # units transfused (min-max)	2 (1-18)	2 (1-15)	2 (1-18)



Ontario Plasma Audit 2013

Results - Plasma

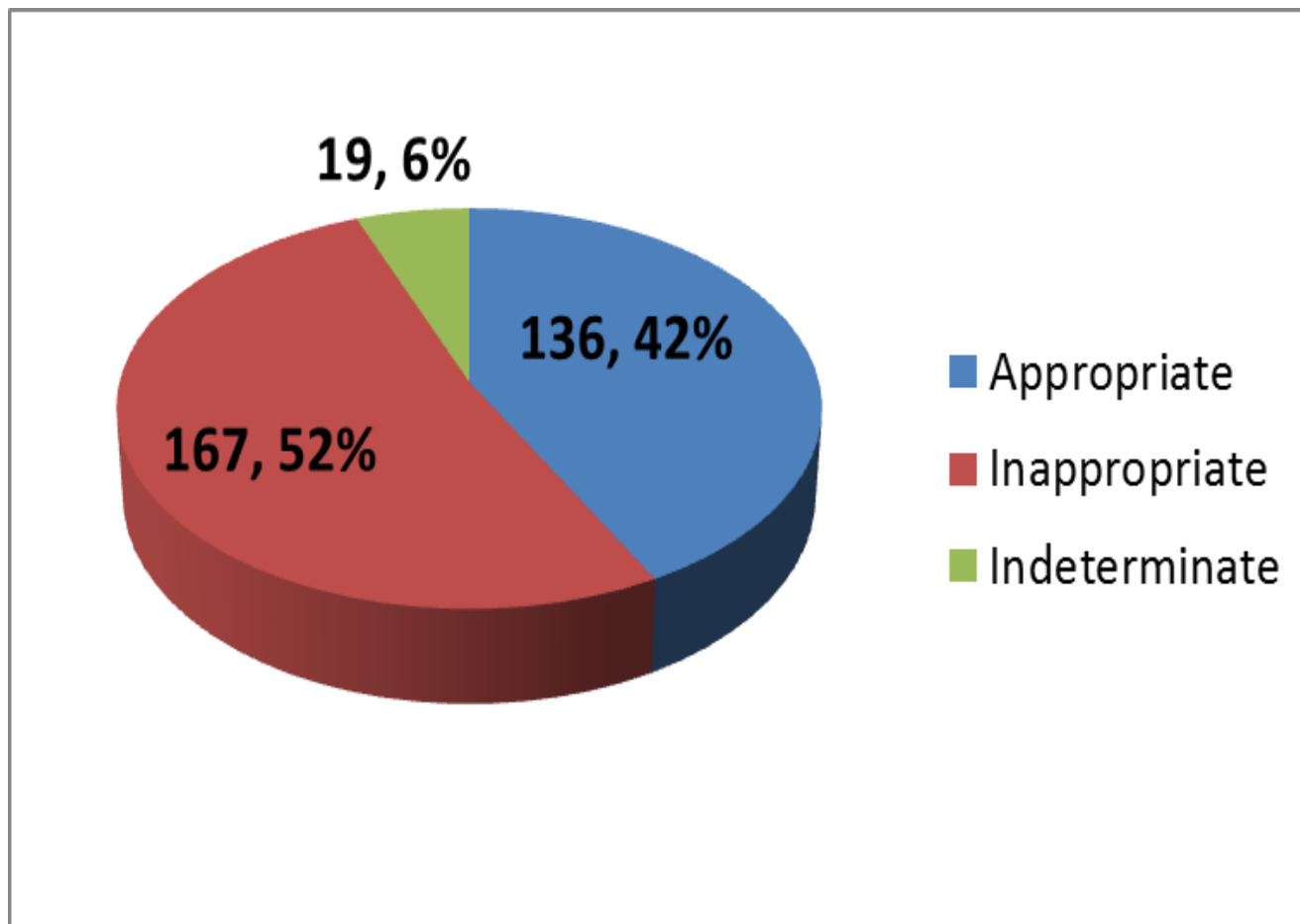
Change in INR with FP transfusion





Ontario Plasma Audit 2013

Results - Plasma





Ontario Plasma Audit 2013

Results - Plasma

Appropriate Uses

Code	# of orders (%)	Code Description
A2	86 (26.1)	<ul style="list-style-type: none">• Coagulopathy other than warfarin, vit K deficiency, heparin, or other anticoagulants• Bleeding• INR > 1.5 and/or PTT > 1.5x normal
A3	29 (8.8)	<ul style="list-style-type: none">• “Massive transfusion”• INR > 1.5 and/or PTT > 1.5x normal or no laboratory coagulation data available at the time of product issue
A1	20 (6.1)	<ul style="list-style-type: none">• Coagulopathy other than warfarin, vit K deficiency, heparin, or other anticoagulants• Urgent surgery or invasive procedure• INR >1.5 and/or PTT > 1.5x normal
A4	7 (2.1)	<ul style="list-style-type: none">• Apheresis/plasma exchange or TTP• Regardless of coagulation status
A6	1 (0.3)	<ul style="list-style-type: none">• Peri-surgical bleeding not due to any anticoagulant medication• Major bleeding• INR > 1.5 and/or PTT > 1.5x normal or no coagulation data available



Ontario Plasma Audit 2013

Results - Plasma

Inappropriate Uses

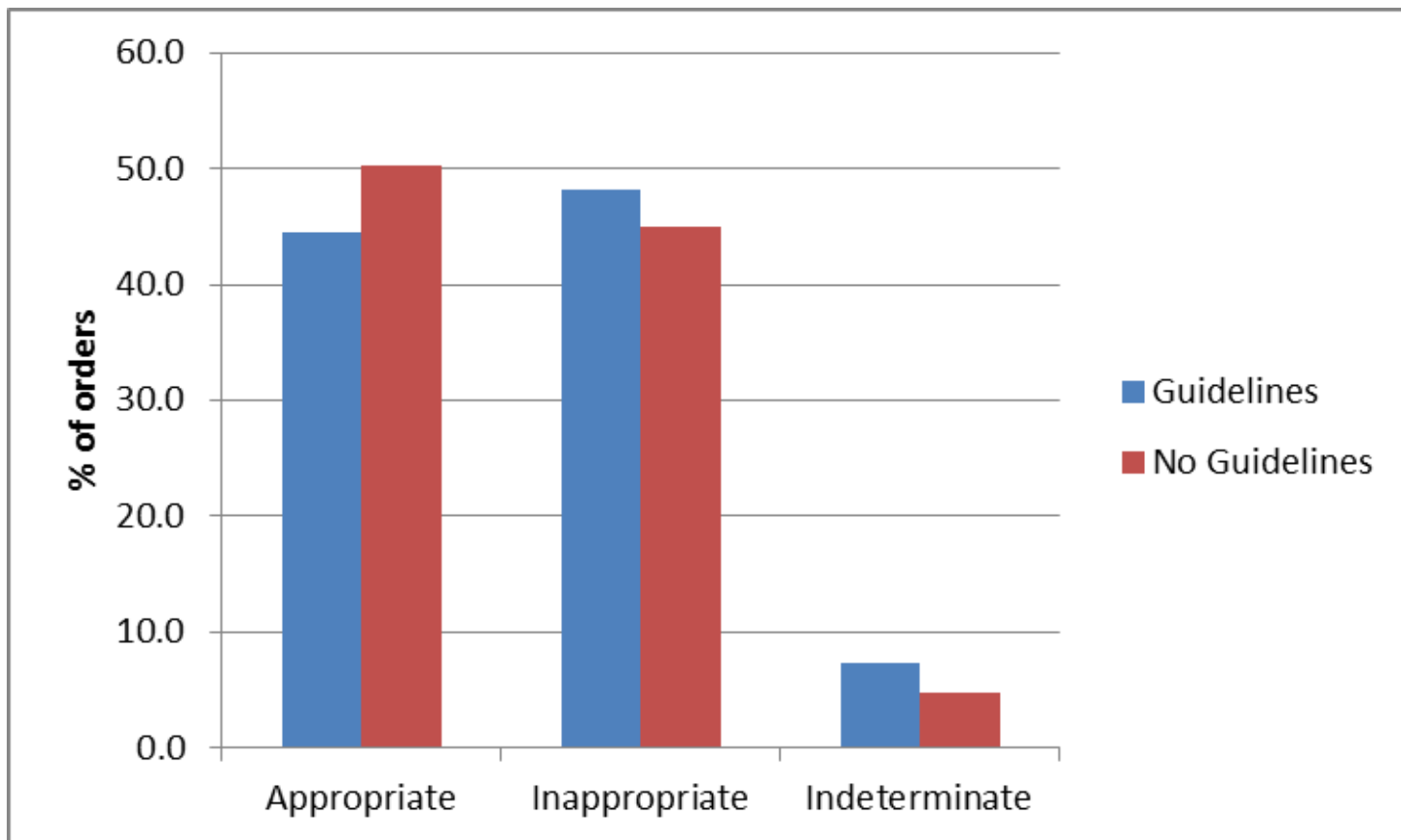
Code	# of orders (%)	Code Description
I3	76 (23.1)	<ul style="list-style-type: none">• $INR \leq 1.5$ and $PTT \leq 1.5x$ normal• Irrespective of bleeding status or procedure status
I2	38 (11.6)	<ul style="list-style-type: none">• Reversal of coagulation defect due to warfarin or vit K deficiency• Bleeding or surgery or invasive procedure• No contraindication to PCC
I7	21 (6.4)	<ul style="list-style-type: none">• Reversal of coagulation defect other than coumadin/warfarin or vitamin K or heparin• Pre or post transfusion $INR \geq 1.5$ and/or $PTT \geq 1.5x$ normal• No bleeding or surgery/procedure
I4	18 (5.5)	<ul style="list-style-type: none">• Heparin reversal (regardless of INR)
I5	8 (2.4)	<ul style="list-style-type: none">• Reversal of other anticoagulants (eg. Dabigatran, Rivaroxiban, etc)
I1	6 (1.8)	<ul style="list-style-type: none">• Reversal of coagulation defect due to warfarin or vit K deficiency,• Absence of bleeding and/or no urgent surgery/procedure



Ontario Plasma Audit 2013

Results - Plasma

Effect of Guidelines





Ontario Plasma Audit 2013

Results - PCCs



Total number of reported orders	113
Total number of vials ordered	410
Total number of vials infused	402
Average number of vials ordered (min-max)	4 (1-6)
Average number of vials infused (min-max)	4 (1-6)



Ontario Plasma Audit 2013

Results - PCCs

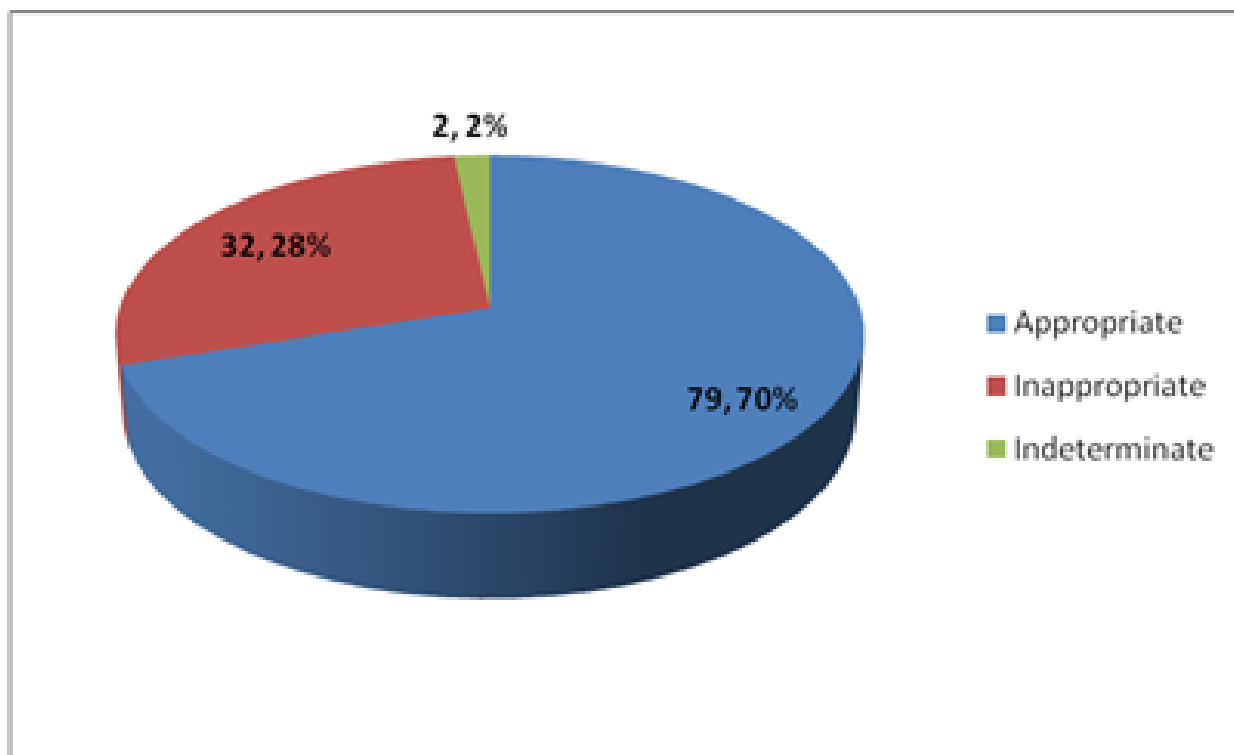


PCC Issued to	Total # (%)	Community # (%)	Teaching # (%)
Emergency Room	57 (50.4)	46 (51.1)	11 (47.8)
Medical Ward	19 (16.8)	16 (17.8)	3 (13.0)
Intensive Critical Care Unit	14 (12.4)	13 (14.4)	1 (4.3)
Surgical Ward	10 (8.8)	6 (6.7)	4 (17.4)
Operating Room	5 (4.4)	3 (3.3)	2 (8.7)
Unknown	4 (3.5)	2 (2.2)	2 (8.7)
Coronary Care Unit	2 (1.8)	2 (2.2)	0 (0.0)
Recovery Room	1 (0.9)	1 (1.1)	0 (0.0)
Cardiovascular ICU	1 (0.9)	1 (1.1)	0 (0.0)
Total	113	90	23



Ontario Plasma Audit 2013

Results - PCCs

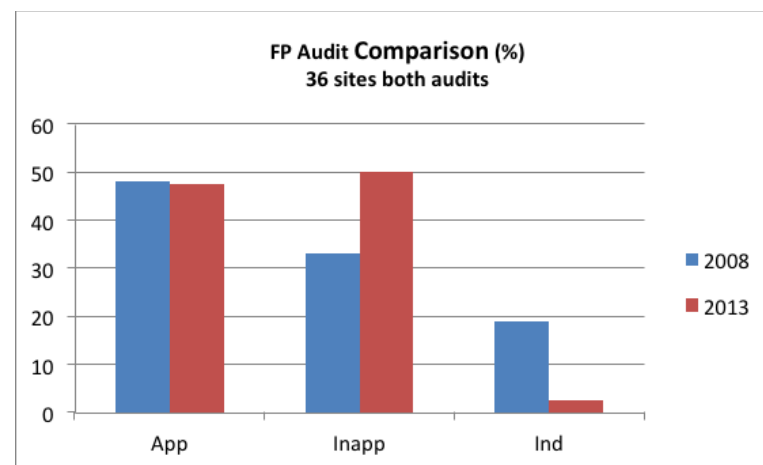




FP Audit – 2013 vs. 2008

	2013	2008
FP transfusions for warfarin reversal	2%	7%
FP transfusions for INR \leq 1.5	23%	18%
FP use for non-bleeding patients not requiring procedure	6%	3%
FP use for heparin or other anticoagulant reversal	8%	2%

- 36 sites participated in both audits
- Less than 50% of transfusions appropriate in both 2008 & 2013





CONCLUSIONS

- No improvement in FP utilization since 2008
- Continued high inappropriate FP use
- Continued inappropriate dose for FP
- Higher rates of appropriate use with PCCs

“We can do better”



Ontario Plasma Audit 2013

Draft Recommendations

Recommendation 1

Develop formal clinical practice recommendations for use of FP in Ontario which could then be adopted by all hospitals.

- Guidelines alone not sufficient to change practice
- Required first step to implement further recommendations to change practice



Ontario Plasma Audit 2013

Draft Recommendations

Recommendation 2

Develop a Quality Improvement plan for Frozen Plasma transfusion in Ontario.

- Traditional “knowledge translation” activities left to local institutions have not been effective
- Incorporate into overall Quality Improvement plan for transfusion which has begun with red blood cell transfusions



Ontario Plasma Audit 2013

Draft Recommendations

Recommendation 3

Develop a standardized, template order form for Frozen Plasma, which would include mandatory relevant pre-transfusion information to allow assessment of appropriateness of transfusion request.

- Adopt or modify local existing transfusion request forms to capture relevant clinical data
- Include in development of computerized order entry (CPOE)



Ontario Plasma Audit 2013

Draft Recommendations

Recommendation 4

Develop a standardized, template order form for Frozen Plasma, which would include mandatory relevant pre-transfusion information to allow assessment of appropriateness of transfusion request.

- Adopt or modify local existing transfusion request forms to capture relevant clinical data
- Include in development of computerized order entry (CPOE)



Ontario Plasma Audit 2013

Draft Recommendations



Recommendation 5

All hospitals would be required to perform annual audit of FP audits using standardized metrics.

- Metrics from standardized data to allow for interhospital comparisons
- Results of annual audits from all hospitals should be reported to provincial body (e.g. BPCO or ORBCON),
- Results would be distributed to all hospitals for peer comparison.



Ontario Plasma Audit 2013

Draft Recommendations

Recommendation 6

Develop specific criteria/algorithm for auditing FP transfusions specifically including coumadin reversal by transfusion technologists be.

- Developed provincially and be implemented by local hospitals
- The algorithm should include decision tree for referral of specific inappropriate FP requests to transfusion medicine physicians for review



Ontario Plasma Audit 2013

Draft Recommendations

Recommendation 7

Develop educational tools and resources that target the largest users of FP and those with highest inappropriate use.

- These tools can then be used by local transfusion medicine physicians to influence/change practice.



Thank you



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