

# *Review of Prothrombinex Use*

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SAAS MedSTAR Emergency Medical Retrieval



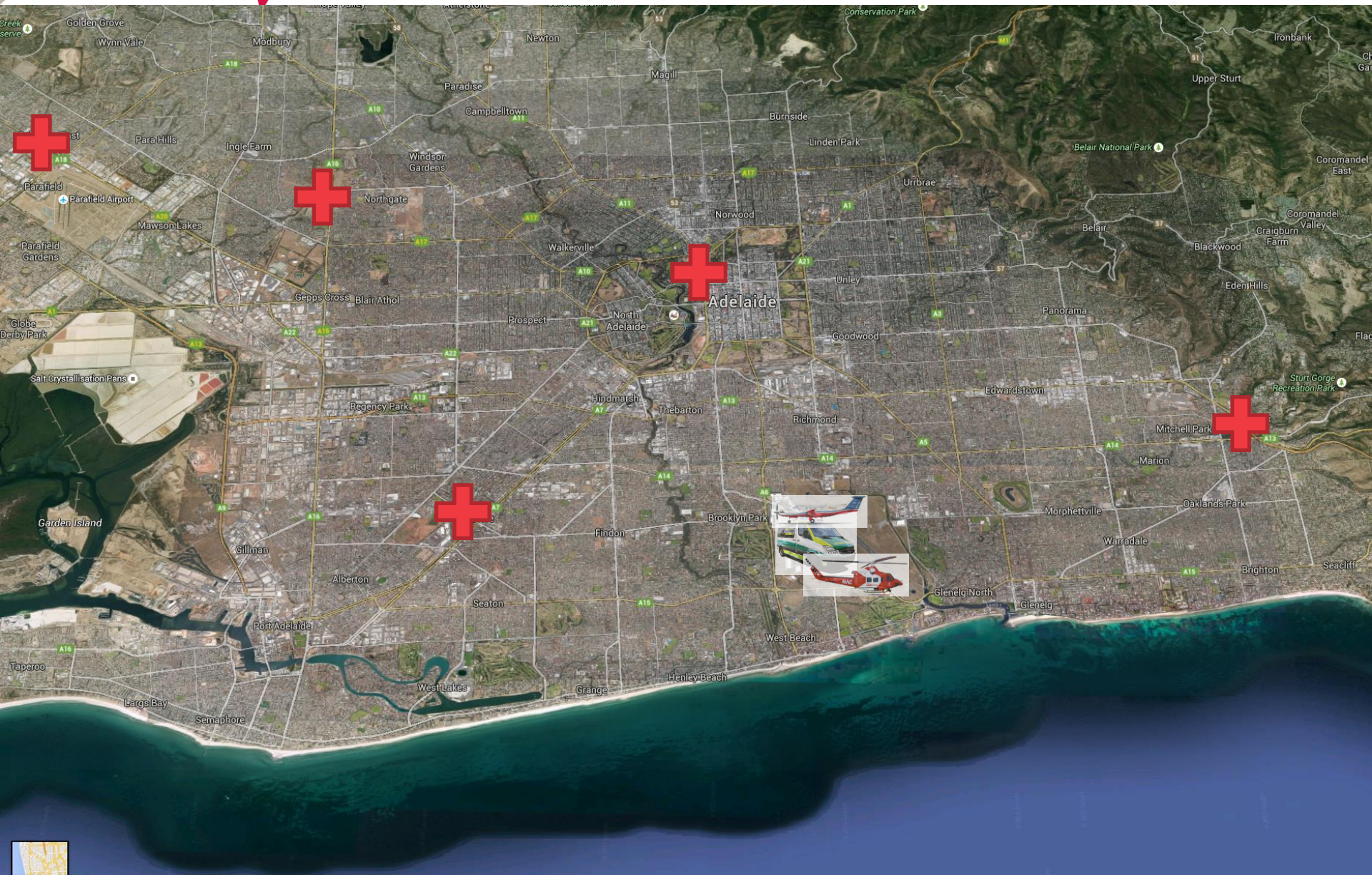
# Overview

- > SAAS MedSTAR
- > Prothrombinex
- > The Audit
- > Results
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  - Time
  - Effectiveness
- > Comparison to Other Australian Data
- > Limitations
- > Conclusions



# SAAS MedSTAR

- > Medical retrieval directorate of SA Ambulance
- > Cover large geographic area
  - Fixed wing
  - Rotary wing
  - Rapid response vehicles
- > Based at airport
  - Response times improved
  - Remote from hospital resources, including blood bank



SAAS MedSTAR Emergency Medical Retrieval



# Prothrombinex

- > The 3 factor prothrombin complex concentrate available in Australia
- > Prepared from pooled human donor plasma
- > Contains
  - factors II, IX and X; and
  - low levels of factors V and VI
- > Relatively easy to store
  - 6 month shelf life at room temperature
- > Relatively low bulk

# Prothrombinex continued

- > Packaged as powder with water for reconstitution
- > Each package contains 500iu
- > Dose 15-50iu/kg





# Prothrombinex

## > Indications

- Treatment or prophylaxis of bleeding in acquired deficiency of prothrombin complex factors, such as deficiency caused by treatment with vitamin K antagonists.
- Treatment or prophylaxis of bleeding in patients with single or multiple congenital deficiency of factor IX, II or X when purified specific coagulation factor product is not available

## > Other uses

- Some evidence suggesting efficacy in other bleeding with prolonged INR



## Prothrombinex governance

- > Stored in drug fridge on base
- > Total of 6 ampules 3000iu total
- > Decision to take made by the tasking retrieval consultant
- > Removed into esky if required
- > Once removed from fridge marked with 6 month expiry date and stored in air conditioned room
- > Option to rotate back to a hospital if approaching expiry





## The Audit

- > Ethics approval was obtained from the Southern Adelaide Clinical Human Research Ethics Committee.
- > Cases where Prothrombinex was administered by the retrieval team were identified from the retrieval service patient database.
- > The paper case cards of the identified patients were then manually reviewed
- > Finally, the data matched to patients in the state-wide electronic laboratory record.

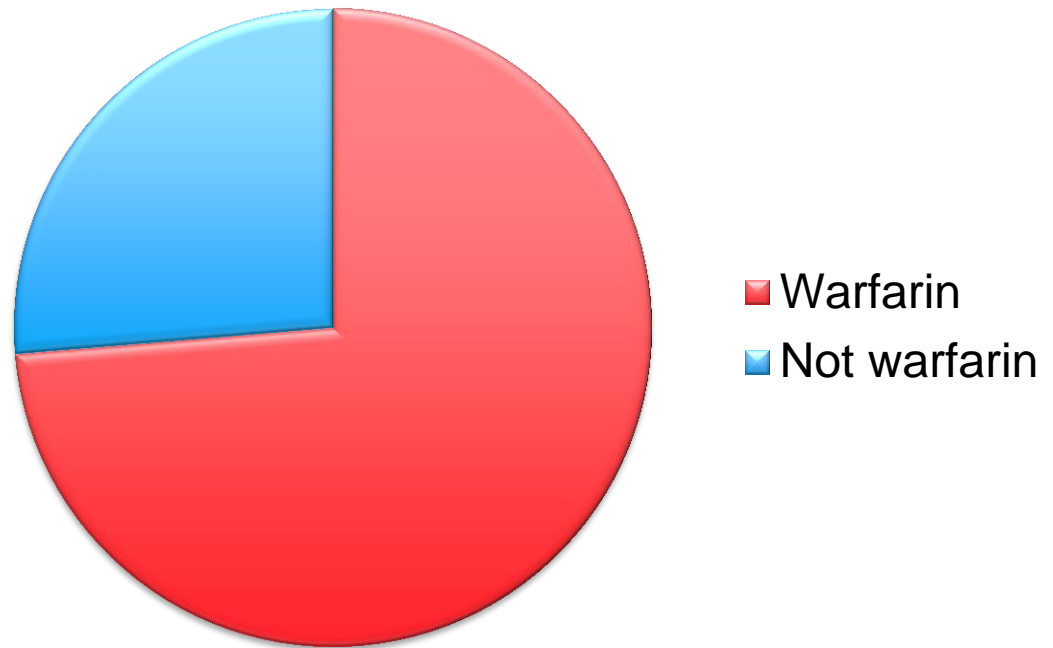


## Results

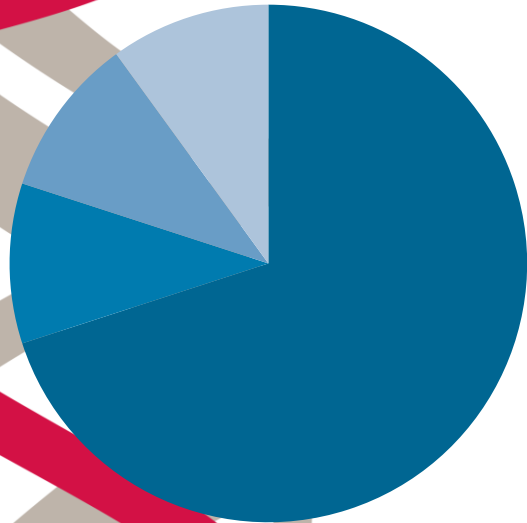
- > Between 1 January 2010 and 31 November 2013 thirty-eight cases were identified.
- > Over the same period there were 4402 adult retrievals
- > Paired INR's were available for 33 or the 38 patients

# Usage

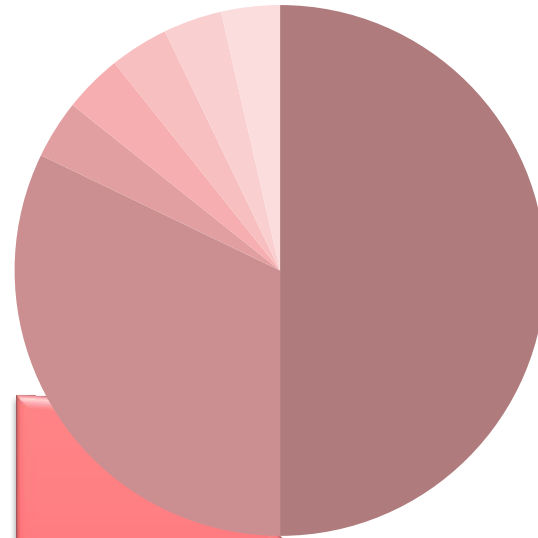
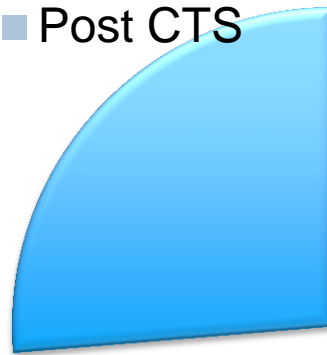
- > 28/38 (74%) on warfarin
- > 10/38 (26%) not on warfarin



# Usage



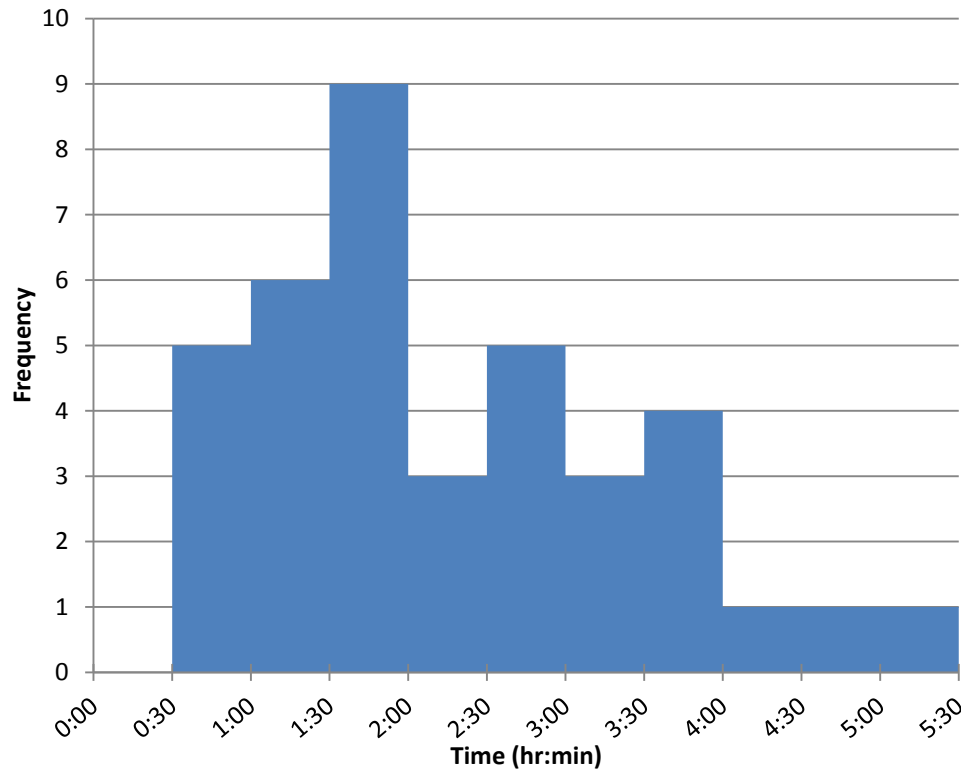
- Liver
- PPH
- PR bleed
- Post CTS



- ICH
- GI bleed
- Trauma
- CTS
- PPH
- AAA
- Epistaxis

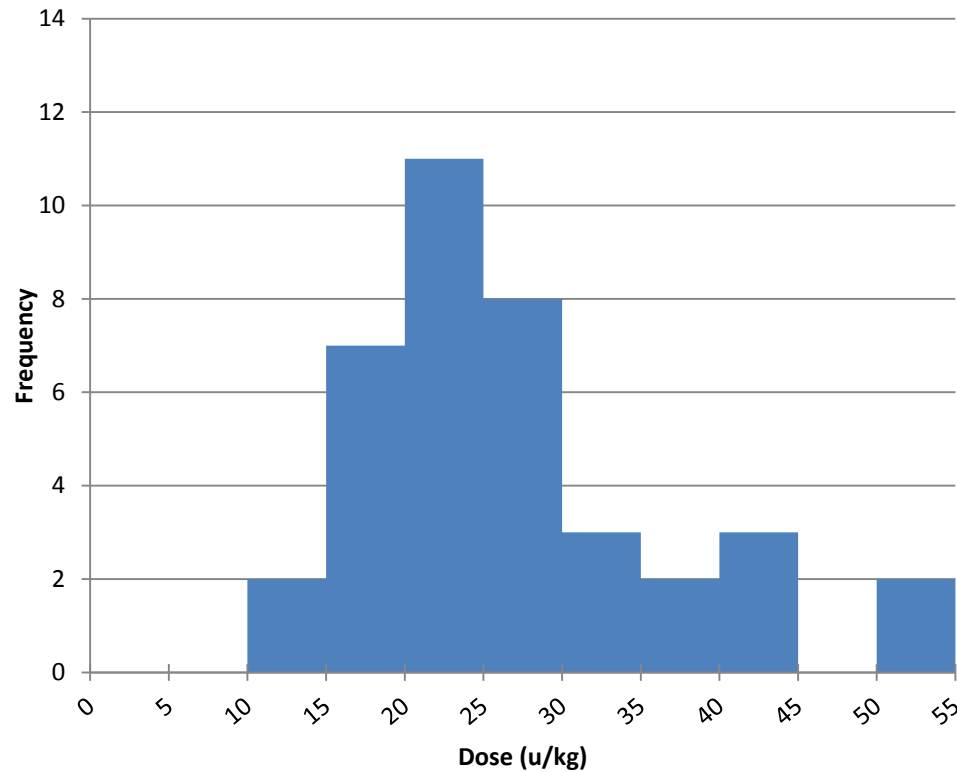
# Time Saved

- > The median time saved was 120 minutes (range 40 - 285 mins)



# Dose given

- > The median dose of Prothrombinex administered was 26.5 iu/kg (range 13.3 – 54.5 iu/kg)





# Effectiveness

- > 33/38 Had both pre and post INR's available
  - 5 no pre INR available
  - Died
  - Unable to be data matched
- > Effectiveness defined as receiving  $\text{INR} \leq 1.5$



## Effectiveness

- > There was no significant difference between starting and destination INR's in the non warfarin group
- > There was a significant difference between starting and destination INR's in the warfarin group ( $p < 0.005$  Related samples wilcoxon signed rank test)



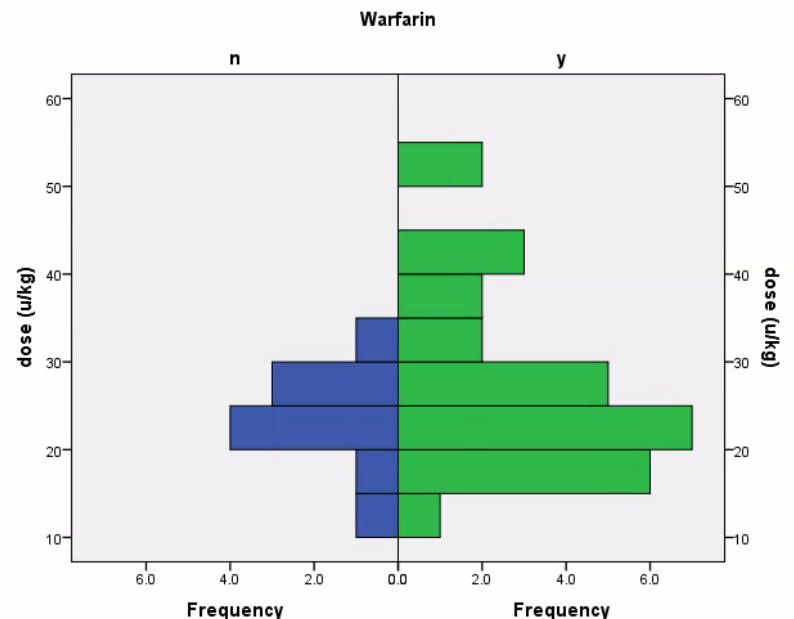
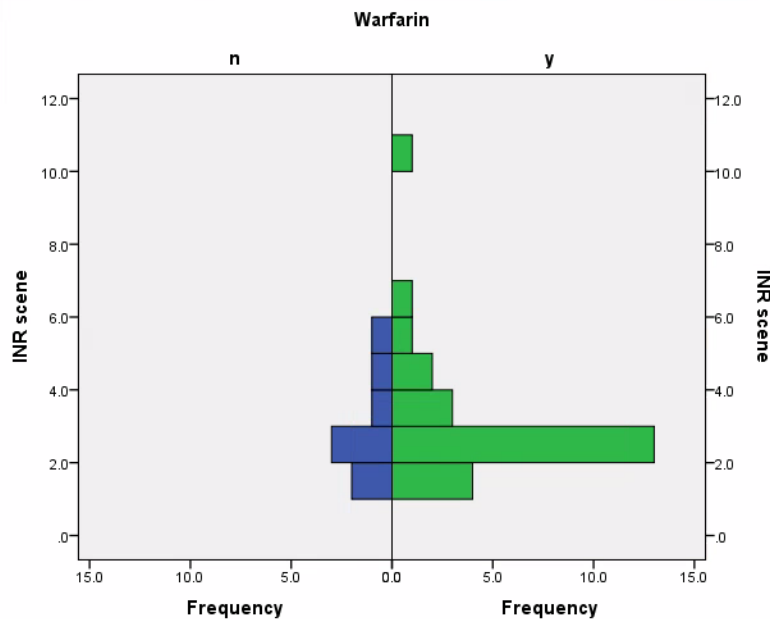
# Effectiveness

	Reversal	Not reversal	
Warfarin	23	4	27
Not warfarin	2	7	9
	25	11	36

P <0.001 Fisher's Exact Test

# Confounders

- > There was no significant difference between starting INR and dose given between the warfarin and no-warfarin groups (Mann-Whitney U test)



# Comparison to other data

- > Our usage is similar to Royal Perth hospital usage:
  - 35/47 uses were for warfarin reversal
  - Mean dose given 18 iu/kg
  - Was most effective in correcting INR in the warfarin group

## Prothrombinex-VF use in warfarin reversal and other indications

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**P**rothrombinex-VF powder for injection (PTX-VF; CSL Biotherapies, Melbourne, Vic) is a prothrombin complex concentrate (PCC). Each vial contains 500 IU factor II, 500 IU factor IX, 500 IU factor X, 25 IU antithrombin III, 192 IU heparin sodium and  $\leq$  500 mg human plasma proteins. PTX-VF is indicated in the treatment and perioperative prophylaxis of bleeding in acquired deficiency of coagulation factors caused by vitamin K antagonists (ie, warfarin), and the treatment and prophylaxis of bleeding in patients with congenital coagulation factor deficiency. However, clinical data on the efficacy of PTX-VF are limited and the optimal dose is yet to be determined.<sup>1-3</sup> Locally, the Australasian Society of Thrombosis and Haemostasis Warfarin Reversal Consensus Group recommends 25-50 IU/kg of

### Abstract

**Objective:** To assess the use of Prothrombinex-VF powder for injection (PTX-VF) at Royal Perth Hospital and analyse the efficacy and safety profile of PTX-VF.

**Design, setting and patients:** A prospective observational audit of PTX-VF use, conducted by reviewing medical records and laboratory and imaging results for all patients prescribed PTX-VF from 1 November 2009 to 1 May 2010.

**Main outcome measures:** Data on indication, diagnosis, comorbidities, dose of PTX-VF, fresh frozen plasma (FFP) and vitamin K, coagulation parameters before and after PTX-VF administration, and adverse effects.

**Results:** 334 vials of PTX-VF were administered to 84 patients over 107 prescriptions. Indications were warfarin reversal, intraoperative bleeding and coagulopathy (66, 20 and 21 prescriptions, respectively). PTX-VF with FFP was compared with PTX-VF alone for warfarin reversal and there was a significant decrease in international normalised ratio (INR) that was independent of group ( $P < 0.001$ ). Lower doses of PTX-VF ( $< 25$  IU/kg) were compared with higher doses (25-50 IU/kg) for warfarin reversal and decrease in INR was significant, independent of group ( $P = 0.002$ ). PTX-VF was administered for intraoperative bleeding in 18 patients who had not been treated with warfarin. No hypersensitivity reactions, thrombotic complications or worsening of disseminated intravascular coagulation occurred during 7-day follow-up.

**Conclusion:** For warfarin reversal, lower doses of PTX-VF ( $< 25$  IU/kg) and PTX-VF without FFP were effective. PTX-VF was also used in intraoperative bleeding and non-warfarin coagulopathy. No adverse events were associated with PTX-VF.



# Limitations

- > Retrospective audit
  - Potential to have missed cases
  - Some data not available
- > Guidelines changed
- > NOAC
- > Can this be extrapolated to other products?



## Conclusions

- > With a robust, but relatively simple, governance process prothrombinex can be managed remotely from a hospital blood bank.
- > Usage pattern was similar to other hospital case series
- > 25iu/kg represents a reasonable balance of effectiveness vs bulk
- > Effectiveness in non-warfarin related bleeding is less clear