Optimizing point-of-care testing strategies for diagnosis and treatment of hepatitis C virus infection in Australia: A model-based cost-effectiveness analysis

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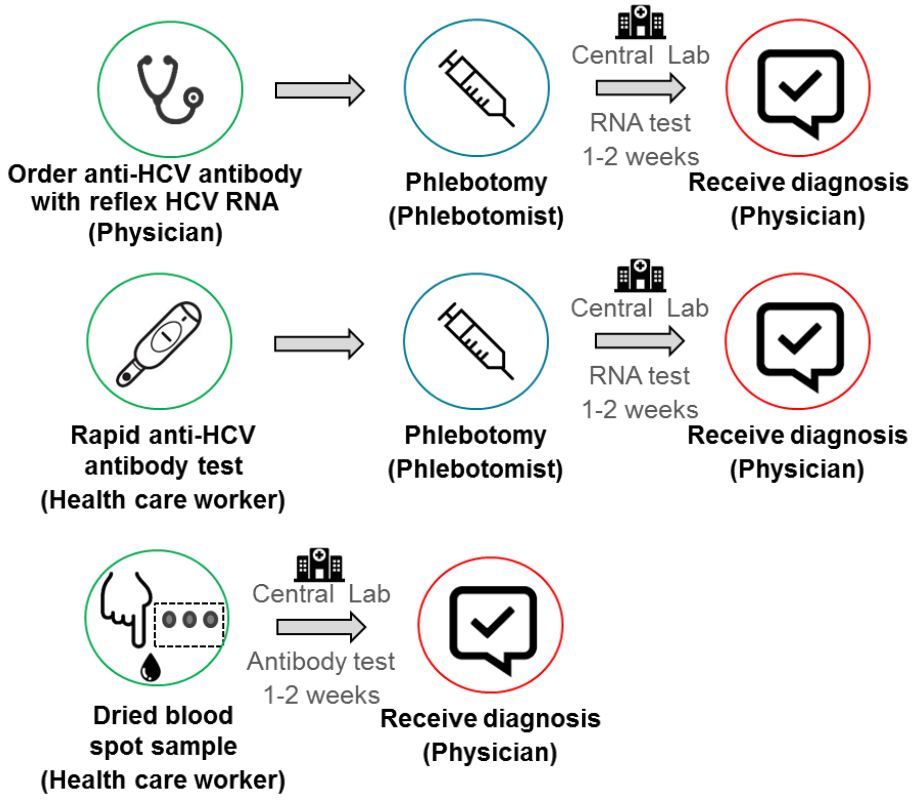
HCV Elimination Goals

- World Health Organisation (WHO) goal to eliminate hepatitis C virus (HCV) infection by 2030
- Direct-acting antiviral (DAA) HCV therapies >95% cure rates led to the HCV elimination goal possible
- Globally, low diagnosis (23%) and treatment (5%) of people diagnosed
- Hampered by current diagnostic pathways requiring multiple visits and resulting in loss to follow-up in key populations

What options do we have to improve HCV testing?



HCV antibody testing with reflex RNA testing

Rapid HCV antibody testing

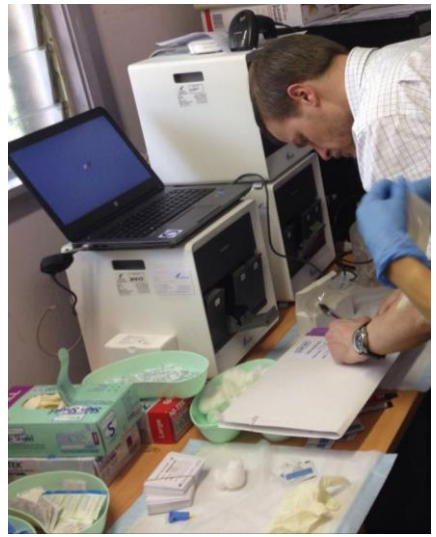
Dried blood spot testing

Finger-stick POC testing for HCV RNA detection

Source: Grebely J et al. Expert Review of Molecular Diagnostics 2017

POC HCV antibody (exposure) & RNA (active infection)

60 mins



- Real-world performance for HCV RNA quantification of active infection
  - Xpert® HCV Viral Load Fingerstick Sensitivity – 100%, Specificity 100%[3]

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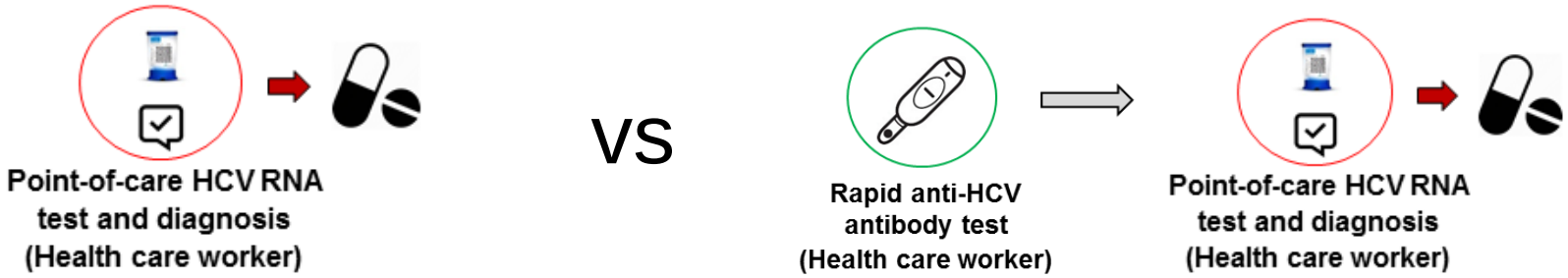
McHugh J Clin Micro 2017, Grebely Lancet Gastro Hep 2017, Lamoury Journal of Infectious Diseases 2018

Rationale and Aim



- POC RNA testing more expensive and thus its cost-effectiveness to be determined
- Aim to evaluate the cost-effectiveness of different testing strategies in relation to HCV prevalence to optimize testing and treatment outcomes to inform policy/practice

Source: Prof J Grebely

Economic analysis framework key elements

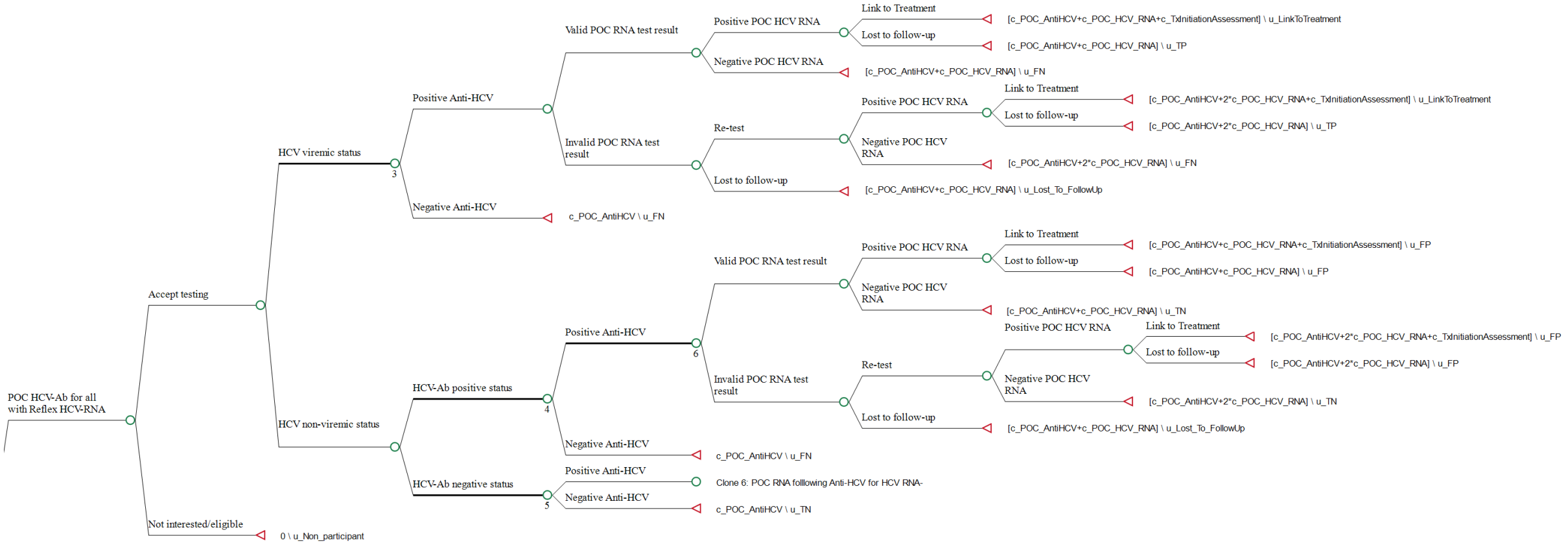
- *Study perspective:* Australian Governments (Commonwealth and States)
- *Study population:* people at risk of HCV infection in key service settings (e.g. prison, NSP, drug treatment clinic)
- *Outcomes modelled:*
  1. Detection of active infection
  2. Treatment initiation in the active infection cases
- *Costs assessed:*
  1. Based on real program financial information
  2. Time and motion pilot data collected from testing sites to estimate labour cost
  3. Costs estimated at three levels

Diagnostic strategies

1. POC HCV RNA testing for everyone
2. POC antibody screening for everyone with reflex POC HCV RNA testing among HCV antibody positive people
3. POC antibody screening for treatment-naïve people with reflex POC HCV RNA testing and immediate POC HCV RNA testing for treatment-experienced individuals
4. Standard of care with on-site sample collection: HCV antibody and HCV RNA testing through standard laboratory mechanisms (with on-site blood collection by venepuncture).

Decision Analytical Models

Point of Care HCV Ab with reflex POC HCV RNA testing



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Model key parameters - Epi

Parameter	Setting			Source
	Prison	NSP	Drug Treatment	
Proportion of people tested	1	1	1	Assumption
HCV Ab prevalence	0.37	0.61	0.69	SToP-C, ETHOS Engage
HCV RNA+ in HCV-Ab+	0.32	0.30	0.20	SToP-C, ETHOS Engage
HCV RNA prevalence	0.12	0.18	0.14	SToP-C, ETHOS Engage
HCV Ab (+) in HCV RNA (-)	0.28	0.53	0.64	SToP-C, ETHOS Engage
Self-report history of HCV Treatment	0.10	0.35	0.40	SToP-C, ETHOS Engage
Self-report history of HCV Treatment/Diagnosis in RNA (+)	0.14	0.18	0.26	SToP-C, ETHOS Engage
Self-report history of HCV Treatment/Diagnosis in RNA (-)	0.09	0.39	0.43	SToP-C, ETHOS Engage
Treatment-Naïve in HCV Ab (+)	0.74	0.43	0.42	SToP-C, ETHOS Engage
Treatment-Naïve in HCV RNA (+)	0.86	0.83	0.74	SToP-C, ETHOS Engage
HCV Ab (+) and RNA (-) in Treatment-Naïve	0.17	0.23	0.38	SToP-C, ETHOS Engage

Model key parameters - Operation

Parameter	Setting			Source
	Prison	NSP	Drug Treatment	
POC RNA invalid test due to operation error	0.03	0.03	0.03	Assumption
Sensitivity of test				
- POC anti-HCV	0.993	0.993	0.993	Bioline HCV, Abbott
- POC HCV RNA	1.00	1.00	1.00	Grebely et al 2017, Lamoury et al 2018
- Laboratory anti-HCV	1.00	1.00	1.00	
- Laboratory HCV RNA	1.00	1.00	1.00	
Specificity of test				
- POC anti-HCV	0.981	0.981	0.981	Bioline HCV, Abbott
- POC HCV RNA	1.00	1.00	1.00	Grebely et al 2017, Lamoury et al 2018
- Laboratory anti-HCV	1.00	1.00	1.00	
- Laboratory HCV RNA	1.00	1.00	1.00	
Lost to follow-up				
- POC RNA re-test	0.25	0.25	0.25	Grebely et al 2014
- SOC RNA test	0.31	0.31	0.31	Yousafzai, MT. et al 2021
Linkage to treatment				
- POC	0.93	0.81	0.81	Yousafzai, MT. et al 2021
- SOC	0.60	0.59	0.59	Yousafzai, MT. et al 2021

Model key parameters – costs (base case)

Test	Mean			Source
Point-of-care RNA test	Testing Variable Cost	Direct Cost (including variable and fixed costs)	Total Cost	Cepheid National POCT Program TEMPO Study
	$96	$129	$153	
Point-of-care combined HCV Ab and RNA tests	Anti-HCV only	Anti-HCV Reflex RNA	RNA only (1)	Grebely et al 2021
	$34	$163	$129	
Standard of care laboratory HCV tests	Anti-HCV only	Anti-HCV & RNA	RNA only (1)	MBS 2021
	$38	$153	$115	
Treatment initiation assessment	$180			Hajarizadeh, et al. 2021 MBS 2021

(1) Tx-experienced

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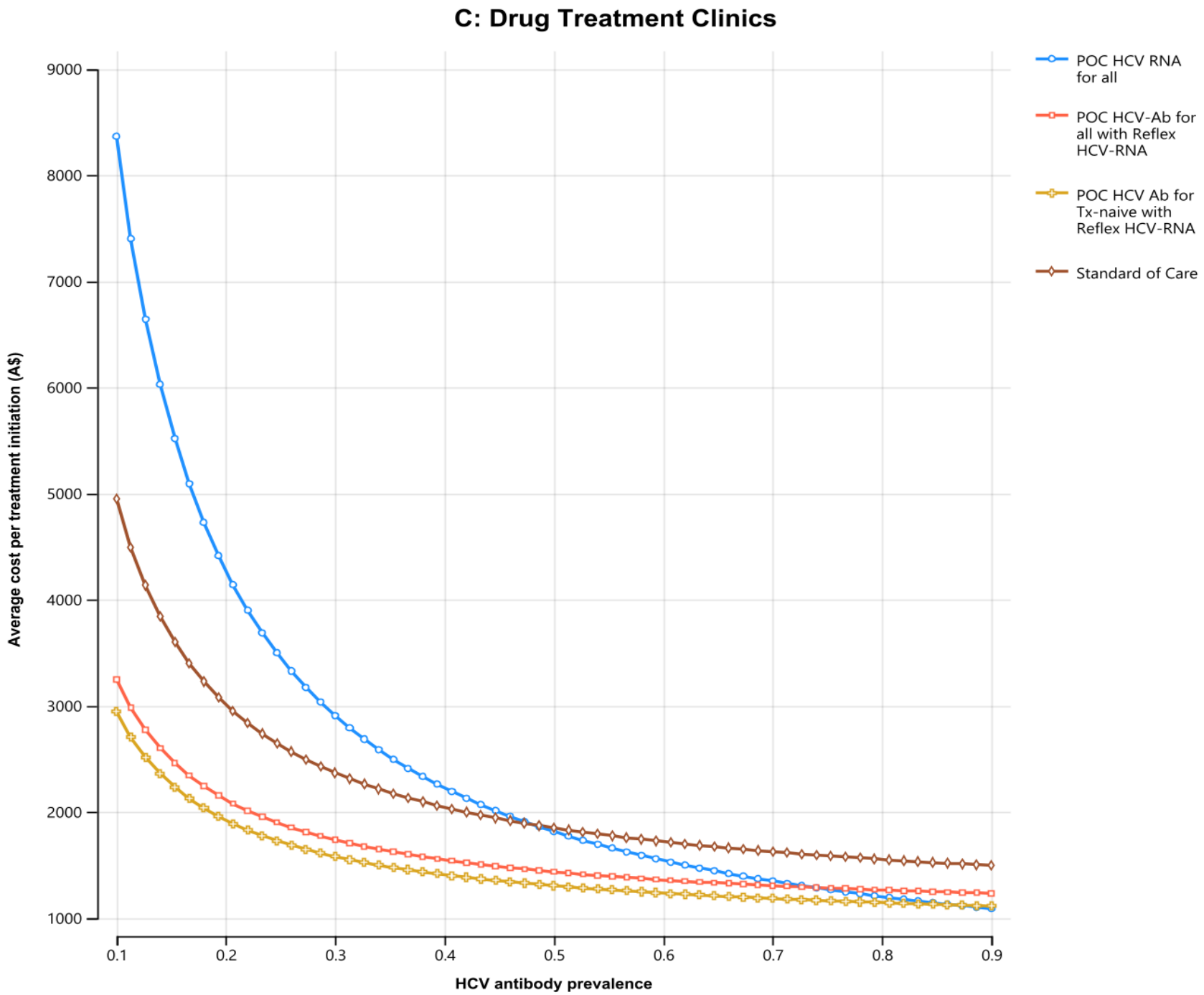
Base case cost-effectiveness – Tx Initiation

Strategy	Average cost per person tested	Incremental Cost	Effectiveness (HCV case)	Incremental Effectiveness	ICER	Average cost per HCV case treated	Number to test for one HCV case
Prison Setting							
Standard of Care	$76		0.0531			$1426	18.8
POC HCV RNA for all	$152	$76	0.1078	0.0547	$1386	$1406	9.3
POC HCV-Ab for all with Reflex HCV-RNA	$123	$27	0.1071	0.0539	$500	$960	9.3
POC HCV Ab for Tx-naive with Reflex HCV-RNA	$99	$23	0.1072	0.0541	$424	$921	9.3
NSP Setting							
Standard of Care	$100		0.0802			1248	12.5
POC HCV RNA for all	$159	$59	0.1468	0.0666	$879	1080	6.8
POC HCV-Ab for all with Reflex HCV-RNA	$141	$41	0.1458	0.0656	$630	970	6.9
POC HCV Ab for Tx-naive with Reflex HCV-RNA	$130	$30	0.1460	0.0658	$455	890	6.9
Drug Treatment Setting							
Standard of Care	$103		0.0633			$1632	15.8
POC HCV RNA for all	$152	$49	0.1118	0.0486	$1010	$1362	8.9
POC HCV-Ab for all with Reflex HCV-RNA	$146	$42	0.1111	0.0478	$884	$1310	9.0
POC HCV Ab for Tx-naive with Reflex HCV-RNA	$132	$29	0.1113	0.0480	$605	$1189	9.0

Average cost / person treated by Ab prevalence

49%, 74%, 86%



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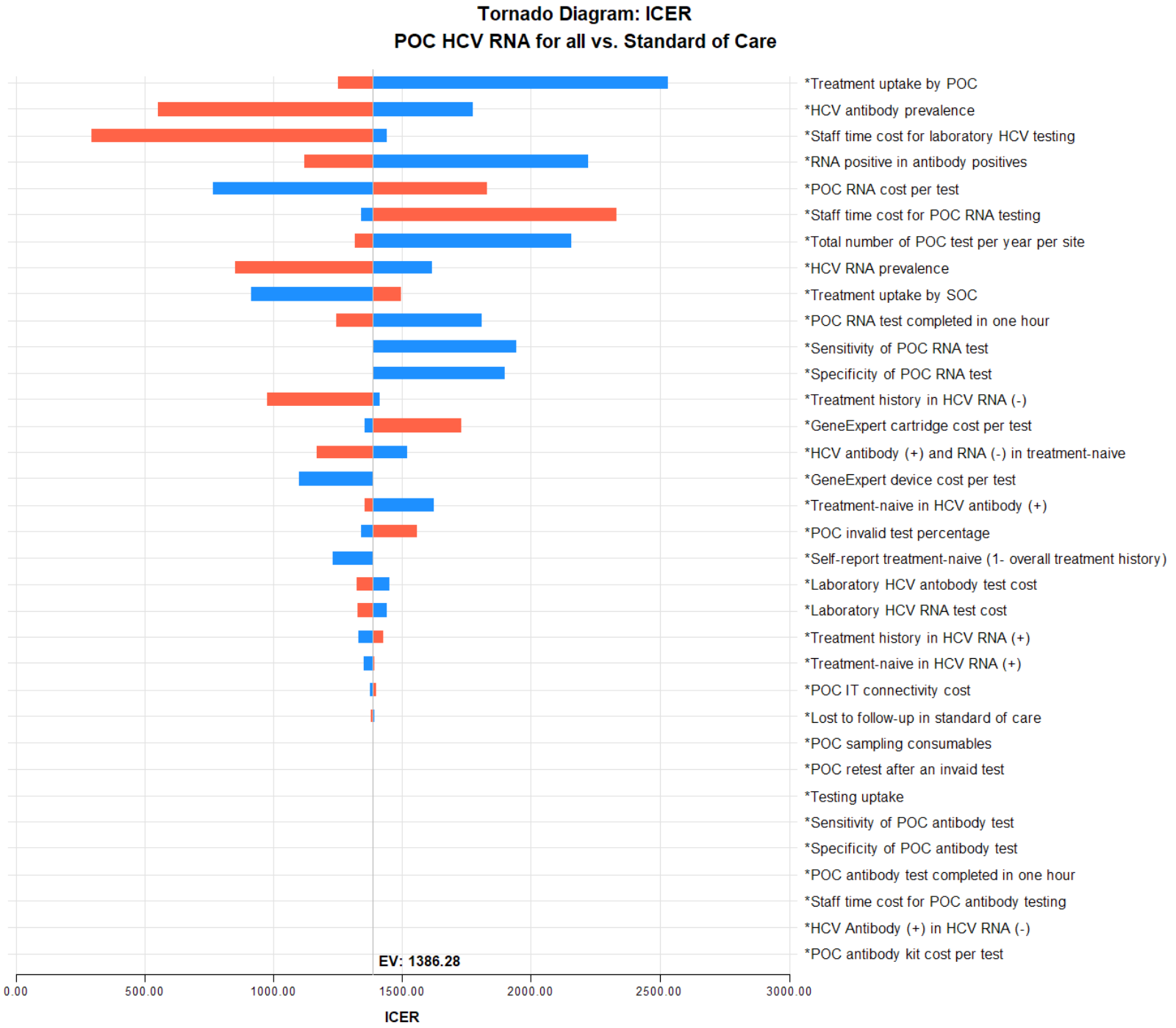
One-way Sensitivity Analysis - Prison

POC HCV RNA testing for all



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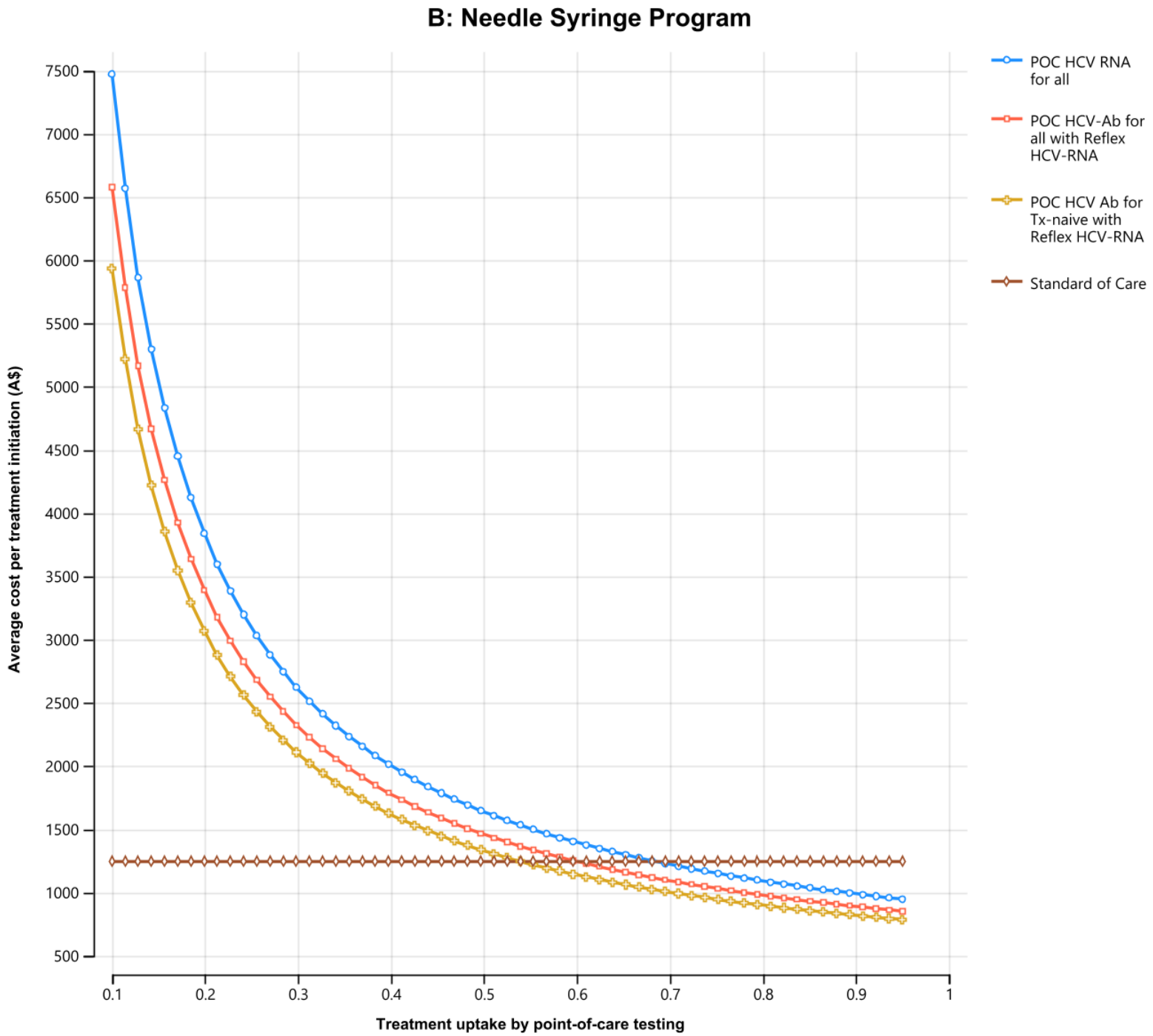
Average cost / person treated by POC Tx uptake

54%, 60%, 68%



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Threshold of POC Tx uptake

Best Testing strategy	Treatment uptake in the base case		Threshold of POC Tx uptake for equal average cost per case treated to SOC		
Setting	**SOC**	**POC**	**POC HCV-Ab for treatment-naïve with reflex POC RNA**	**POC HCV-Ab for all with reflex POC RNA**	**POC HCV RNA for all**
Prison	60%	93%	55%	58%	91%
NSP	59%	81%	54%	60%	68%
Drug Treatment	59%	81%	57%	64%	67%

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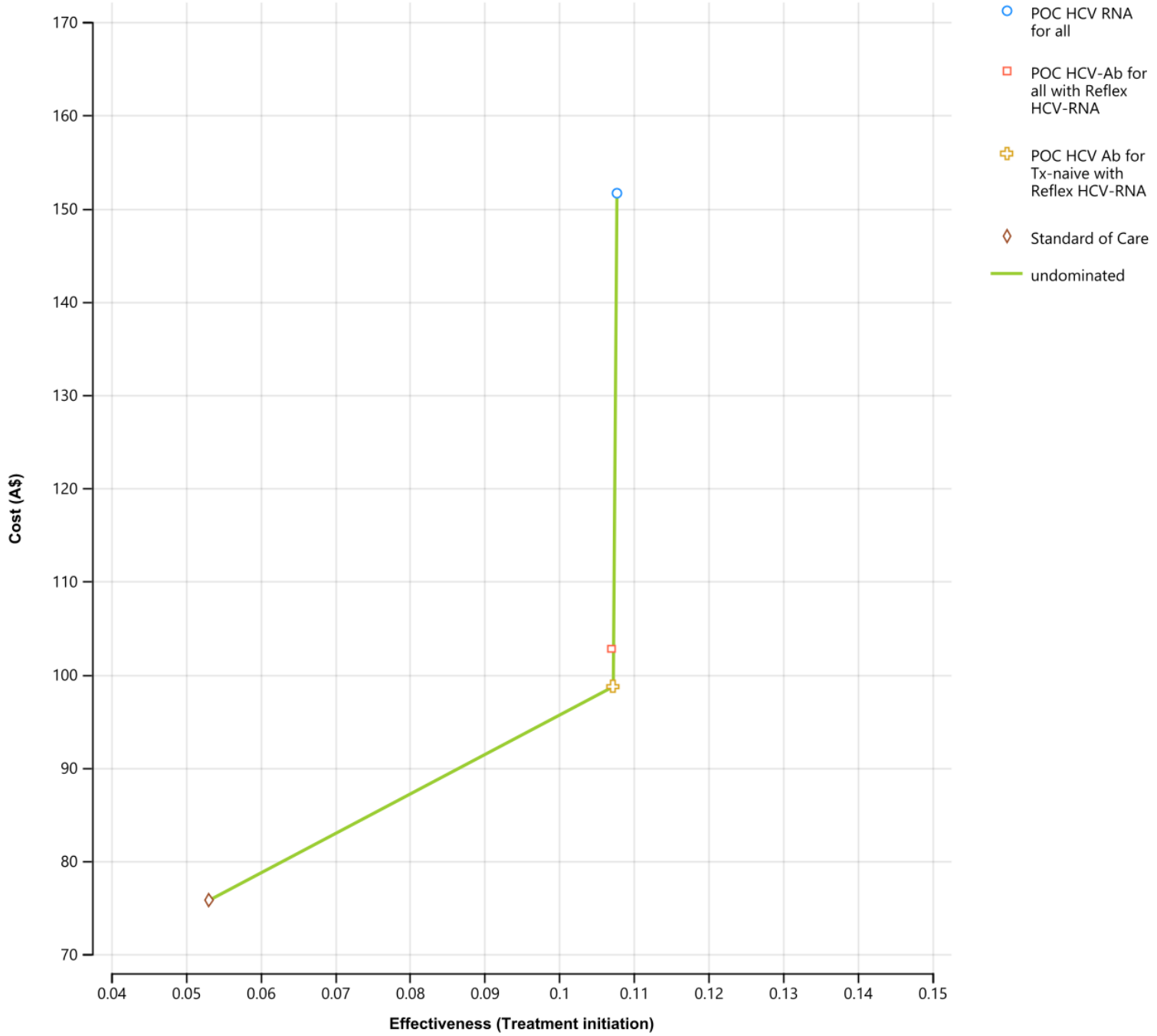
Cost-effectiveness planes for the base case

A: Prison



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Summary

- The average cost per treatment initiation is ~35% lower for point-of-care testing strategies compared to standard of care. By average cost per treatment initiation:
  - Two-step POC testing (Ab reflex RNA) with consideration of treatment history is most cost-effective across all settings in HCV antibody prevalence <79% in prison, <86% in community.
  - In high HCV antibody prevalence populations/settings (>86%), a one-step point-of-care HCV RNA testing strategy is most effective
  - In low HCV antibody prevalence populations/settings (e.g. prison <35%, NSP<45%, DrugTx <49%), one-step point-of-care HCV RNA testing is the least cost-effective due to its high cost

Conclusions and Implications

- POC testing would perform better with modest improvement in treatment uptake by 9%~31%, where pilot shows significant increases (PIVOT 93% vs. 22%; TEMPO 81% vs. 27%).
- Future data from the National HCV Point-of-Care Testing Program across a range of real-world settings will further inform health economic analyses
- Long-term QALY is needed

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