Burnet Institute
Medical Research. Practical Action.

High uptake of treatment and cure rates in a decentralized community-based general practitioner-led hepatitis C model of care for people who inject drugs and people affected by liver disease in Yangon, Myanmar

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Funding support & implementing partners

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Disclosure of Interest

This study was supported by Unitaid. MH has received investigator-initiated grant funding from Gilead Sciences and Abbvie for unrelated work. AP has received investigator-initiated grant funding from Gilead Sciences, MSD and Abbvie and speaker fees from Gilead Sciences for unrelated work. JH has received investigator-initiated grant funding and speaker fees from Gilead Sciences for unrelated work. WLY has received Gilead Sciences Fellowship for related work. KPK has received non-financial support from Mylan, Hetero and Royal Ruby. YYS and WA have received non-financial support from Mylan. WN has received non-financial support from Mylan and Cipla. All others declare no potential competing interests.

Background

- Access to direct-acting antivirals (DAAs) for hepatitis C treatment is restricted to tertiary hospitals
- Increasingly, GPs are providing DAAs in primary care settings
- Growing evidence to support decentralization of care into community settings and task-shifting to GPs and other non-specialist providers
- But data from low-and middle-income countries (LMICs) is still limited

Table 1 Summary of characteristics of 142 included studies

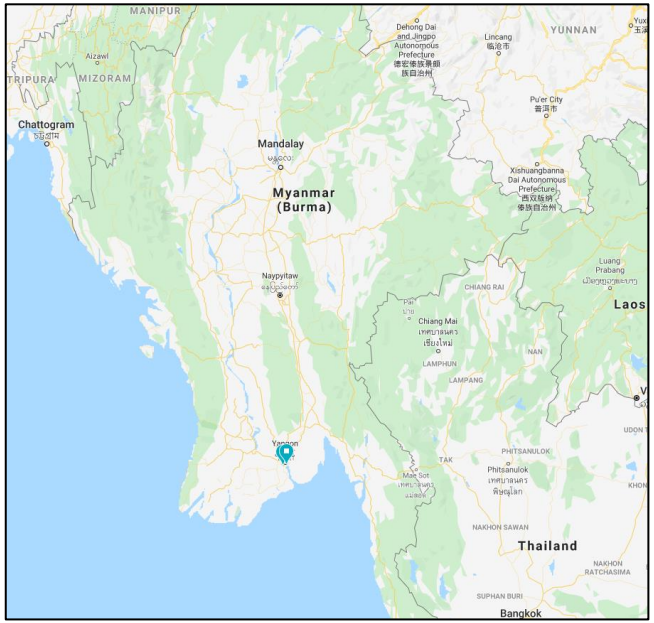
		Total (142 studies)	People who inject drugs (80 studies, 56%)	General population (37 studies, 26%)	People in prisons (20 studies, 14%)	People living with HIV (5 studies, 4%)
Low-income and middle-income countries		20 (14%)	7 (9%)	10 (27%)	1 (5%)	2 (40%)

Oru, E., et al (2021). Decentralisation, integration, and task-shifting in hepatitis C virus infection testing and treatment: a global systematic review and meta-analysis. *The Lancet Global Health*. https://doi.org/10.1016/S2214-109X(20)30505-2

Background – Myanmar

Hepatitis C in Myanmar

- 2.7% anti-HCV antibody positive
- Most common genotypes: GT1, GT3, GT6
- Transmission through formal/informal healthcare settings & injecting drug use
- 56% anti-HCV antibody positive among people who inject drugs



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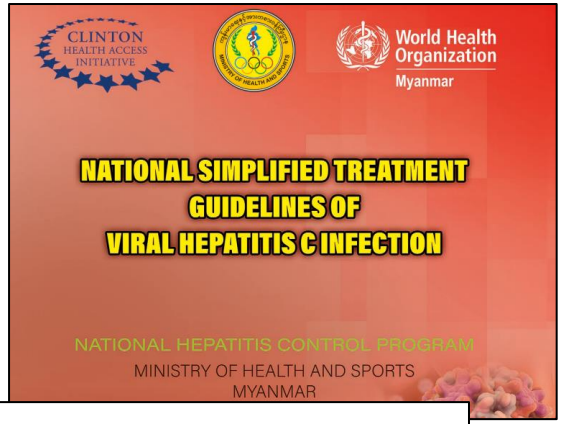
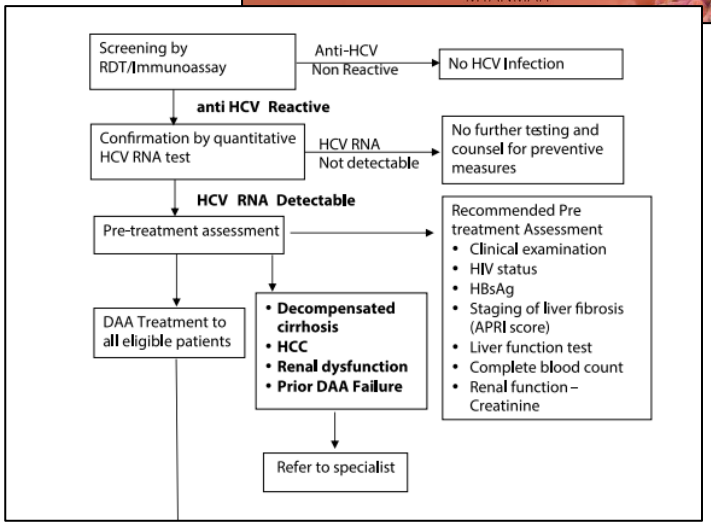
Background- Myanmar

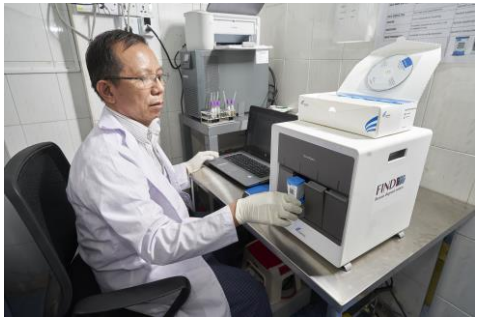
- Guidelines allow for:
  - HCV testing using RDTs and GeneXpert HCV VL assay
  - Use of pan-genotypic DAA regimens, no need for genotyping
  - GPs to treat most patients, only refer for decompensation, HCC, prior DAA failure, and renal dysfunction





Study Design

- Decentralized
- Community-based
- ‘one-stop-shop’
- Simplified clinical pathway:
  - point-of-care diagnostic testing
  - GP-led pan-genotypic DAA therapy



Note: All photos included were taken and are shared with permission from those featured. Photos were taken by Kyaw Win Hlaing

Study Recruitment

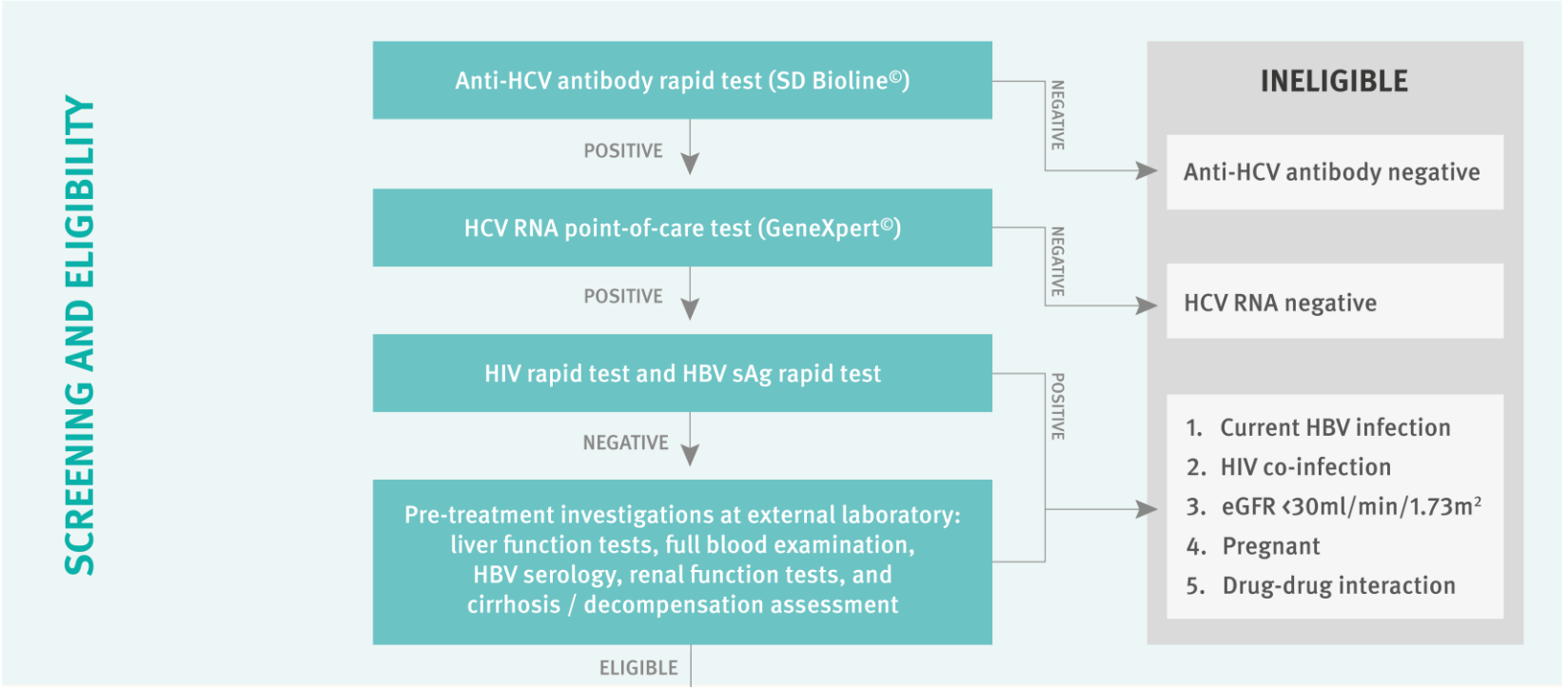
Recruitment & Eligibility Criteria

- Aged 18 years and over
- Not known RNA positive
- Registered for enrolment and recalled *OR* Presented during study recruitment

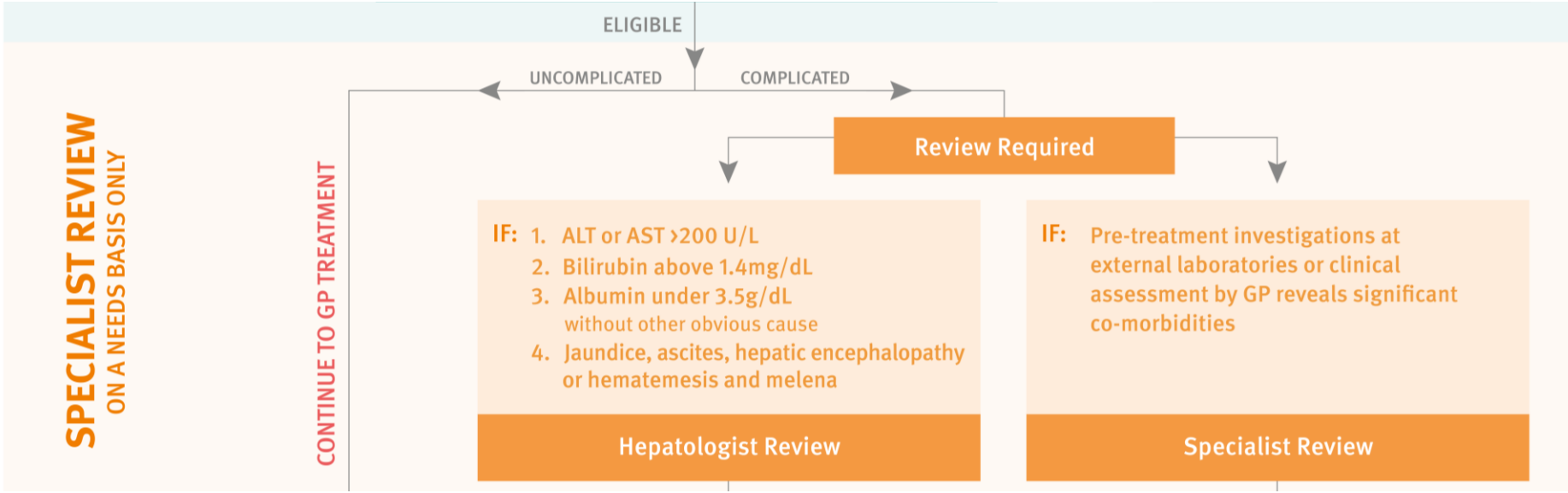
Exclusion criteria

- HIV infection
- HBV infection
- eGFR <30
- Active TB/ on treatment for TB
- Previous HCV treatment
- Current pregnant/breast-feeding
- Serious drug-drug interaction with sofosbuvir/daclatasvir

Clinical Pathway

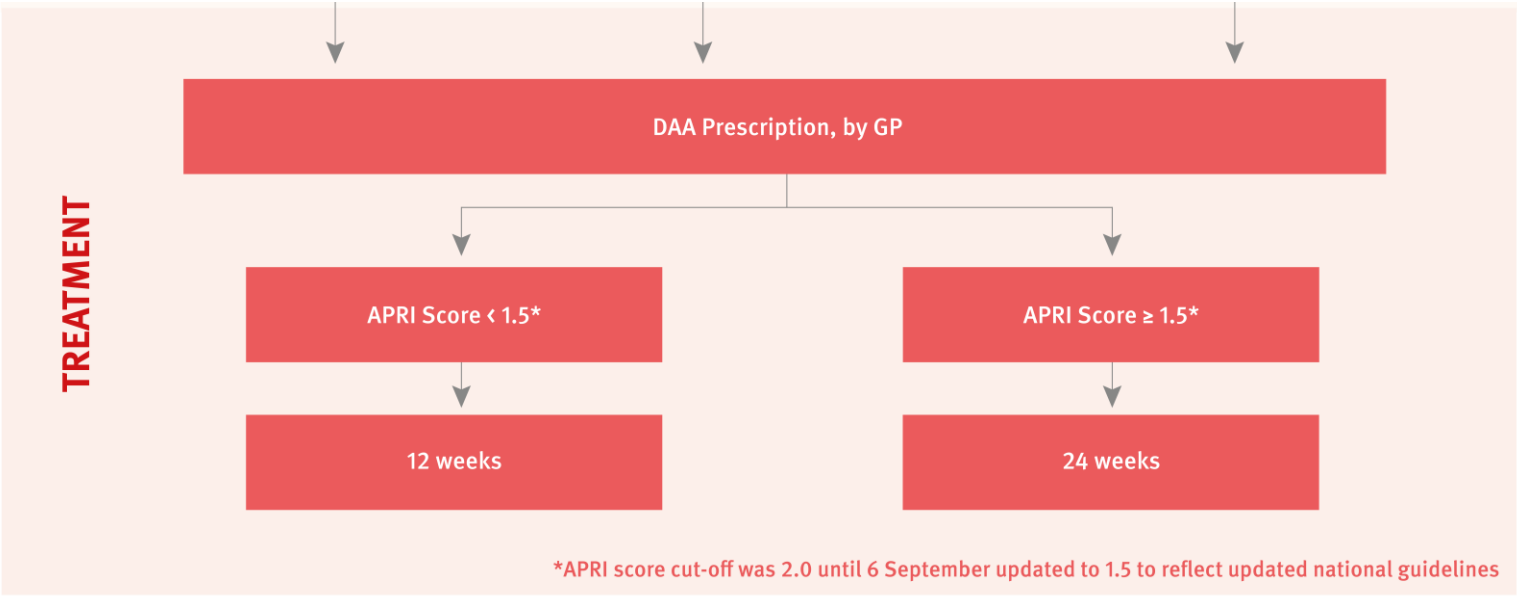


Clinical Pathway



Clinical Pathway

sofosbuvir (400mg) +
daclatasvir (60mg)



Monitoring, SVR12

Monitoring

- Treatment dispensed every four weeks at site
- No routine blood testing for monitoring
- Adherence and side-effects monitored at each visit

SVR12

- SVR12 conducted on-site using GeneXpert machine

Results – Participant Characteristics

	Total N= 633 n (%)	MLF Clinic N = 380 n (%)	Burnet Clinic N = 253 n (%)
Sex, male	405 (64)	166 (44)	239 (95)
Age, years (median, IQR)	42 (31, 53)	50.5 (39, 59)	32 (27, 40)
Residence location			
Yangon	466 (74)	223 (59)	243 (96)
Outside of Yangon	167 (26)	157 (41)	10 (4)
Ever injected drugs	265 (42)	12 (3)	253 (100)
Injected drugs in the past six months	236 (89)	1 (8)	235 (93)
Prescribed methadone (at enrolment)	161 (25)	0 (0)	161 (64)
Previously tested for anti-HCV antibodies (self-report)			
Never tested	91 (14)	12 (3)	79 (31)
Tested previously	542 (86)	368 (97)	174 (69)

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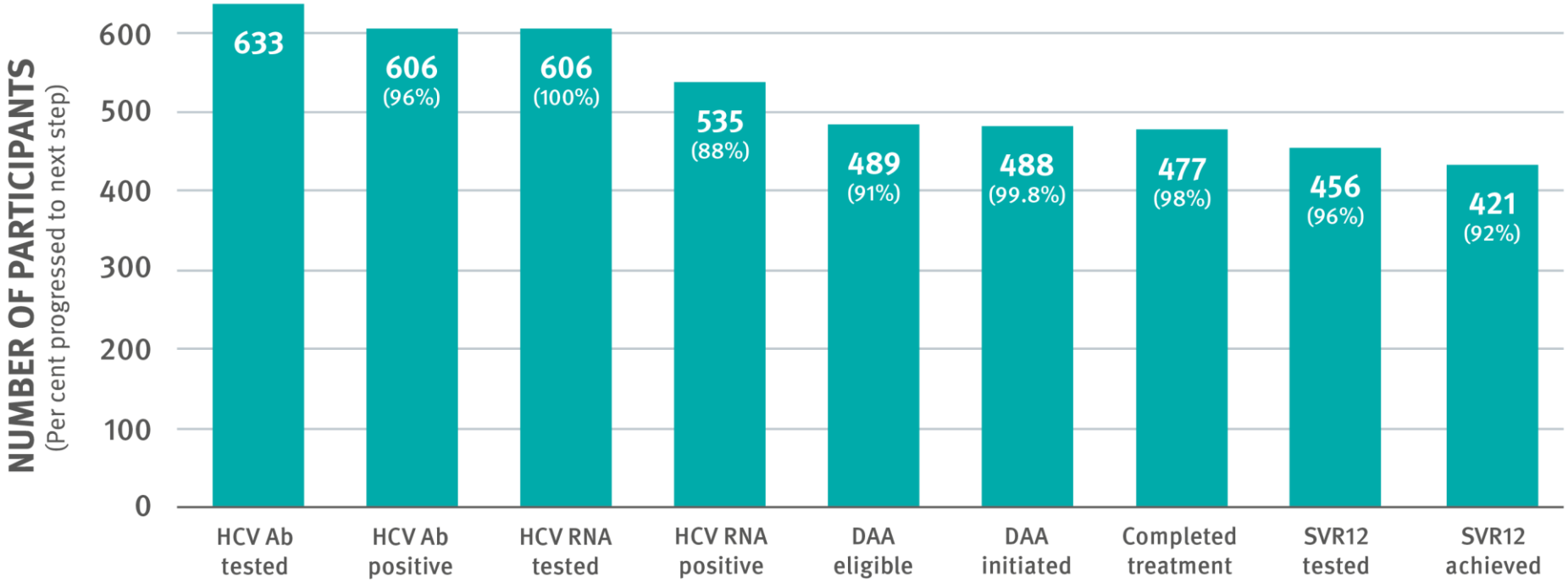
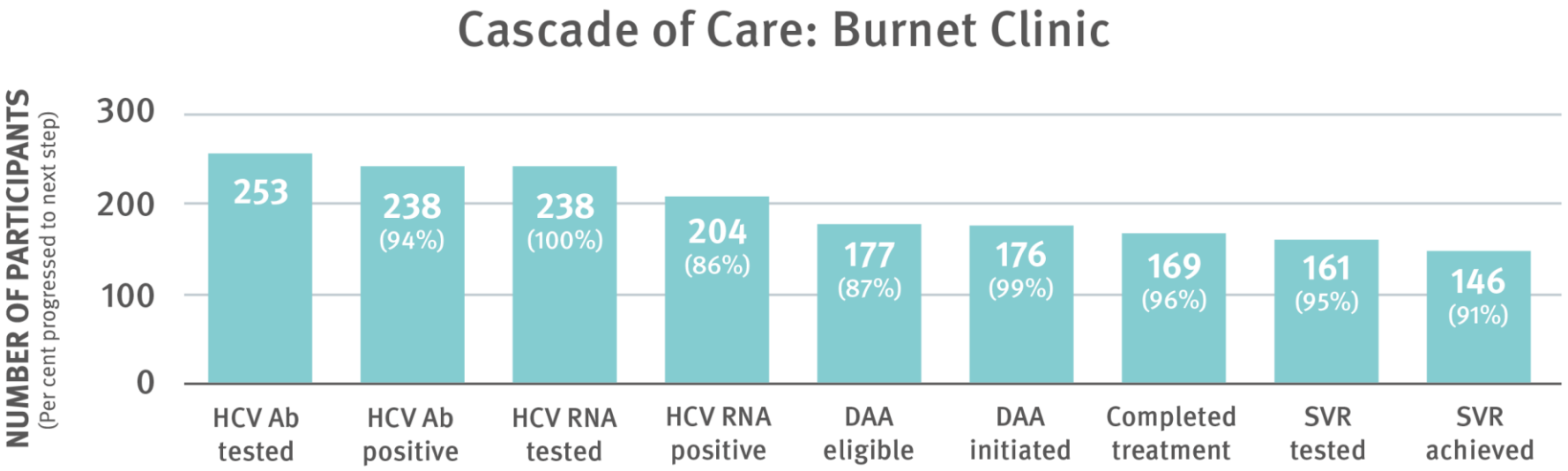
Results – Cascade of Care



Results – Cascade of Care (BI Clinic)



Results – Cascade of Care, by site

Table 3: Cascade of Care, by site	Total N = 535 n (%)	MLF Clinic N = 331 n (%)	Burnet Clinic N = 204 n (%)
Patients who underwent specialist review	30 (5%)	13 (4%)	17 (8%)
Patients eligible for DAA treatment	489 (91%)	312 (94%)	177 (87%)
Patients who completed treatment (per protocol)	N=489 477 (98%)	N=312 308 (99%)	N=177 174 (96%)
Patients who tested for SVR12	N=477 456 (96%)	N=308 295 (96%)	N=169 161 (95%)
Patients who achieve SVR12	N=456 421 (92%)	N=295 275 (93%)	N=161 146 (91%)

Results – Referral to specialist

Protocol for referral to hepatologist

- any physical signs of decompensation
- liver enzymes (AST, ALT) >200 U/L
- bilirubin above upper limit of normal (1.14mg/dL)
- albumin <3.5g/dL without other obvious cause

Reason for referral

	Hepatologist	Other specialist
	N = 26	N = 4
Elevated liver enzymes	22	
Low platelet count	1	
DDI advice	1	
Cardiac issue		1
Chest X-ray required		2
Abnormal abdomen ultrasound	1	
Review for gallstones	1	
Referral to urosurgeon		1

Results – Monitoring, Loss to Follow Up

- One serious adverse event, unrelated to DAA therapy
- Four participants were lost to follow up during treatment
- Most participants reported taking all DAA doses
- Most participants reported experiencing no side effects
- 27 participants were lost to follow up at SVR12
- 35 participants did not achieve SVR12
  - 4 were cirrhotic, vs 31 were non-cirrhotic
  - 5 reported at least one missed DAA doses

Results - Number of Visits, Turn Around Time

- 91% of participants had two visits to start onto treatment
  - 1 combined screening / diagnosis visit
  - 1 review / treatment initiation visit

- Time (in days) from RDT test date to DAA prescription date was a median of 3 days (IQR: 2, 5)

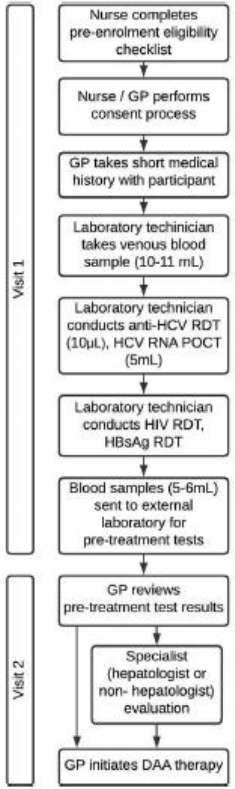
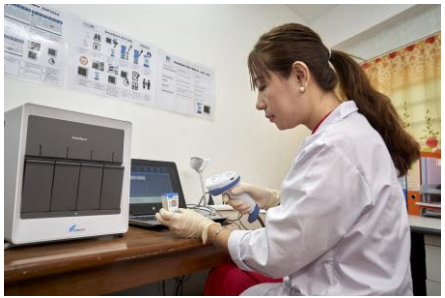
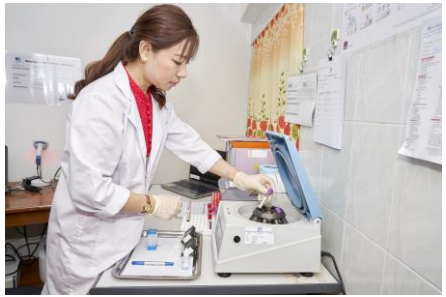


FIGURE 1 Study procedures diagram. Study procedure steps from pre-enrolment screening to initiating DAA therapy

Results – Operational Considerations

- GeneXpert requires:
  - Sturdy table, with space for device, printer, barcode scanner
  - Centrifuge, if using whole blood sample cartridges
  - Airconditioning, clean room
  - Stable electricity supply, facilitated by UPS
  - Training in running tests, pipetting plasma sample, responding to errors
  - Continuous error monitoring, troubleshooting
  - Regular maintenance, and access to technicians for module replacements





Results – Operational Considerations (Error rate / module replacement)

- The BI site experienced an error rate of 3% and the MLF site 6%
  - most common type of error at the BI site was user/procedural error (6/13, 46%)
  - most common type of error at the MLF site was 'other errors' (17/42, 41%), followed by user/procedural errors (11/42, 26%) and cartridge errors (8/42, 19%)
- The two Xpert machines required six module replacements, one at the BI and five at the MLF site, during 19 month study period

Reporting & Dissemination

- Online dissemination meeting in October 2020 - summary report and brochure made available online and to stakeholders in Myanmar via mail

- Started to work with network of GPs on how to scale-up similar model of care

- Currently work is paused, due to Covid-19 pandemic and political unrest

ORIGINAL ARTICLE | Open Access

Outcomes of the CT2 study: A 'one-stop-shop' for community-based hepatitis C testing and treatment in Yangon, Myanmar

Bridget Louise Draper, Hla Htay, Alisa Pedrana, Win Lei Yee, Jessica Howell, Khin Pyone Kyi, Win Naing, Khin Sanda Aung, Jessica Markby, Philippa Easterbrook, Anna Bowring, Win Aung ... See all authors

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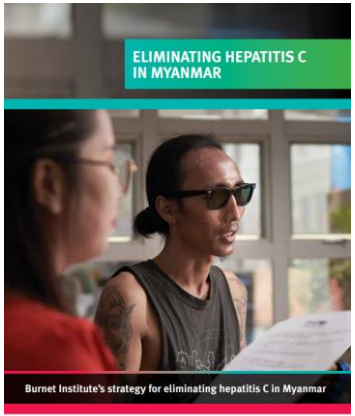

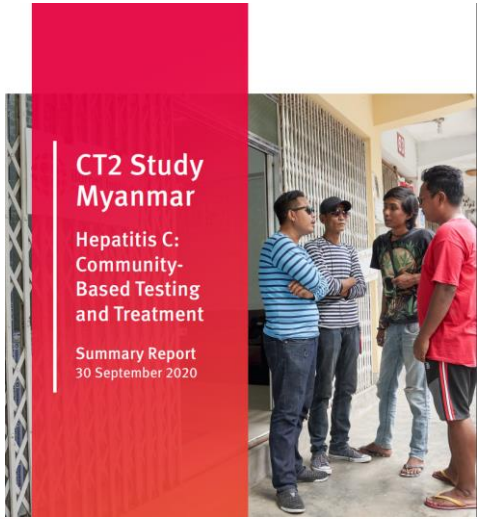

Conclusions & What Next

The CT2 model of care was:

- Feasible
- Effective: retention in care, SVR12
- Acceptable to providers
- Acceptable to patients
- Cost-effective

Conclusions & What Next

- Decentralized, non-specialist led care is critical to expanding access to care

- ‘one-stop-shop’ model of care had high retention in care & reducing loss to follow up is important in providing cost-effective care

- Now, our challenge is getting countries to invest in this upfront

Acknowledgements

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- Professor Margaret Hellard
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