Experience with phlebotomy for people with Hepatitis C virus: a Systematic Review

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ABSTRACT

Background

Hepatitis C Virus (HCV) remains a major challenge and is characterised by the requirement for repeated phlebotomy but low uptake of treatment.

Aims and methods

The aims of this systematic review were to locate and synthesise evidence regarding:

(i) the impact of phlebotomy experience on access to treatment for HCV and (ii) interventions used to improve phlebotomy experience for people with HCV.

Abstracts were reviewed for 100 articles; full text review was undertaken of 16 articles and four papers were subjected to quality appraisal.

Findings

Synthesis of the studies revealed three findings: access to phlebotomy characterised by perceptions of stigma and fear of blood sampling; the impact of poor phlebotomy experience on treatment access and the lack of communication between service users and service providers.

Conclusions

Recent treatment developments have potential to impact on mortality and morbidity. However, in order to introduce appropriate interventions, it is essential to engage service users.

KEYWORDS

Hepatitis C, phlebotomy, specialist nursing, treatment, service users

BACKGROUND

The blood borne virus Hepatitis C (HCV) is a major cause of morbidity and mortality worldwide and poses an important public health challenge (Nelson et al 2011); as emphasised recently by Public Health England '*...in an era of curative treatments and prevention options, we must question whether this is acceptable*' (Public Health England 2015). Intravenous drug users account for the majority of cases of HCV yet low uptake of treatment persists across settings (Mehta et al 2008, Swan et al 2010, Bruggman and Grebely 2015), even when tailored services are developed (Grebely et al 2008). As treatments for HCV evolve, it becomes increasingly important, from a public health perspective, to improve uptake of services (Nelson et al 2011).

Treatment patterns and efficacy vary according to HCV genotype; however, treatment has improved over the last 2 or 3 years with cure rates for some HCV genotypes increasing to 80-90%. Modelling has shown that if treatment was doubled especially within the population of people who inject drugs (PWID) hepatitis C could be eradicated within a generation (Martin et al 2013).

HCV treatment requires regular blood tests before, during and following a course of treatment; however, prolonged intravenous drug use leads to damaged veins and poor circulation. This patient group reports poor experiences of blood sampling (Harris et al 2013) and fear of iatrogenic vein damage (Olsen et al 2014) hence attendance for monitoring and treatment is often poor (Grebely et al 2008). In addition fear of investigations and treatment has been identified by patients as a key barrier to accessing care (Swan et al 2010). However, Islam et al (2013) found that intravenous drugs users do access health services, although this is frequently not

related to their drug problem, hence there is an opportunity for health professionals to develop proactive strategies.

Current guidelines emphasise the efficacy and cost-effectiveness of testing procedures and treatments (for example, Scottish Intercollegiate Guidelines network (SIGN) 2013). Strategies to explore the patient experience and improve uptake of treatment are less frequently addressed. This systematic review was designed to address this gap.

Objective of the review

The objective of the systematic review was to locate and synthesise evidence regarding:

1. Impact of phlebotomy experience on decisions to access testing and treatment for HCV
2. Interventions used to improve phlebotomy experience for people with HCV

METHOD

A protocol outlining the processes used for the selection and analysis of the papers was developed and conducted in accordance with PRISMA guidelines (Moher et al 2009). The review question was formatted using PICOS:

Participants – patients with hepatitis C and poor venous access

Interventions/exposure – blood sampling interventions

Comparator – usual phlebotomy practice

Outcomes – decision to access treatment for HCV, treatment adherence, patient experience of phlebotomy

Studies – quantitative, qualitative, mixed methods and Systematic Reviews

Inclusion and exclusion criteria are presented at Table 1.

INSERT TABLE 1

Search strategy

The databases and search terms are presented at Table 2; a number of databases were included to maximise the identification of relevant studies. In addition a hand search of the *International Journal of Drug Policy* was undertaken; no new studies were identified via this route. The initial broad search yielded over 1000 results; after applying further exclusion criteria the search was reduced to 100 titles (see PRISMA flow chart at Figure 1). Each title and abstract was screened by two reviewers (FF, VS) and those that were clearly not relevant were excluded, resulting in 16 papers. Full text articles were reviewed by two authors (FF, VS) with the third reviewer involved for any disagreements (RE). Four papers met the inclusion criteria and were subjected to quality review by two authors (FF, VS) again with the third reviewer (RE) used to resolve any disagreements. The included studies are summarised at Table 3.

INSERT FIGURE 1

INSERT TABLES 2 & 3

Quality appraisal

As we were focusing on the patients experiences of seeking (or not seeking) treatment for HCV we expected most of the studies to take a qualitative approach. Hence all papers were evaluated using the critical appraisal scoring systems

developed for qualitative and quantitative methodologies by Kmet et al (2004). Calculation of scores is detailed in a footnote to Tables 4 and 5 and range from 0.0 to 1.0. The authors suggest a cut off summary score of between 0.55 and 0.75. The score for the quantitative paper was 0.625 and scores for the qualitative studies achieved ranged from 0.7 to 1.0 (see Tables 4 and 5) with an overall mean of 0.81 for both groups hence the studies were all included in the data synthesis.

INSERT TABLES 4 & 5

Data synthesis

Data was extracted from each of the papers into a summary table (see Table 3) to enable comparison across all studies. Irrespective of the methodology used in the study all findings were subject to a thematic review in an attempt to identify commonalities and differences between the papers. The papers were assessed across study characteristics which included comparison of interventions identified, methodologies, geographical origin, limitations, participant characteristics, and any outcomes or themes identified. Thematic analysis was used to identify themes and synthesise findings from the qualitative and quantitative studies (Mays et al 2005).

FINDINGS

Four studies met the inclusion criteria: three qualitative studies and one quantitative study. Studies were carried out in Australia, the Republic of Ireland and England (n=2). Sample sizes ranged from 10 – 39 and studies were conducted in hepatology clinics held in the secondary care or community setting. Data was collected in the three qualitative studies through in-depth interviews; the quantitative study used a survey and audit of medical records.

In each of the studies, problems with phlebotomy were explored as part of wider problems with treatment access and the findings from all studies identified that, although the highest prevalence of HCV occurs amongst people who inject drugs (PWID's), this is the group who are the least likely to access treatment. Populations studied were similar across the four papers - current or former PWIDs - and from developed countries with very similar prevalence and the same transmission route/ risk factors for HCV.

Thematic analysis revealed five themes across the studies: stigma, fear of phlebotomy, poor phlebotomy experience, trust, disconnection between service users and service providers. The way in which these factors affected the pathway from HCV risk to treatment is illustrated at Figure 2.

INSERT FIGURE 2

HCV treatment requires frequent venous blood sampling but poor experience with phlebotomy was directly linked to decisions to access treatment in all studies. In all the 3 qualitative papers, participants perceived stigma from staff, for example:

'[y]a can't get past the triage nurse (service user, Swan et al 2010)

'as soon as I told the consultant what drugs... I was on, he sort of, like, recoiled' (service user, Harris et al 2013)

This also extended to disapproval of practices such as self-phlebotomy (Clements et al 2015). Fear of having blood taken was prevalent across the study; service users described how phlebotomy makes them *'petrified'* (Swan et al 2010) or *'makes me want to cry...'* (Clements et al 2015). Of note, across the studies most participants

were happy to undergo initial testing but the requirement for repeated phlebotomy associated with treatment led them to leave the treatment pathway.

The extent of poor phlebotomy practice was described by service users in Clements study as akin to being used as a '*dart board*' or '*pin cushion*' with one service user describing the stress he experienced after nine unsuccessful attempts to find a vein (Clements et al 2015). A nurse participant in Harris' study described the consequences of the hospital phlebotomist '*stick(ing) them six or seven times in a hopeless attempt to get blood out of them and then they [service users] won't turn up again.*' (Harris et al 2013). Mason and colleagues (2007) reported that '36% of liver clinic patients and 59% of drug health service users had difficulty with venous access and 24% and 63% respectively were reluctant to have blood taken'.

All studies showed strong joint working between providers of services, for example an established partnership between a hospital hepatology service, specialist drug and alcohol service and regional blood borne virus service (Harris et al 2013), between nursing and medical staff (Clements et al 2015) and between primary and secondary care (Mason et al 2007). There is evidently the will to give patients the opportunities to access care. However the findings across the four studies also highlighted a disconnection between service users and service providers. This was most evident when service users sought to advise health care workers on the best way to access their veins (Clements et al 2015) or had to circumvent the GP in order to find out about treatment (Swan et al 2010). By contrast there was evidence of much communication between PWID, particularly related to 'war stories' about phlebotomy and treatment experiences (Swan et al 2010). Success stories from others with HCV, and witnessing the death of HCV sufferers were also motivators to

get service users (back) onto a treatment pathway. The double jeopardy of two way mistrust was illustrated by a service user in Harris' study: '*they know I'm lying anyway.... I didn't bother with it [HCV treatment].*' (Harris et al 2013). However, there were also examples of interaction: '*I listen to them ... because they use their veins to inject so they know which vein to use*' (Nurse, Harris et al 2013).

DISCUSSION

The small number of studies meeting the inclusion criteria indicates the paucity of evidence available. Synthesis of the studies revealed three key findings: access to phlebotomy characterised by perceptions of stigma and fear of blood sampling; the impact of poor phlebotomy experience on treatment access and the lack of communication between service users and service providers.

The problem of access to HCV treatment is predominantly identified in secondary care, where treatment is provided (Ferguson et al 2015). The main role of most primary care and drug services is the identification of HCV, which is predominately through dry blood spot testing. Institutional barriers to treatment access for PWID include perceptions by service users that clinicians are reluctant to allow access to treatment for current intravenous drug users (Coupland et al 2009), including General Practitioners not referring for specialist testing and treatment (Cullen et al 2007). Perceptions of stigma have also been reported by women who developed iatrogenic HCV (Dunne & Quayle 2002). In the wider context, intravenous drug users have also reported stigma in the healthcare environment and negative staff attitudes (Neale et al 2008), which has been associated with poorer quality of life (Zickmund et al 2004).

Participants with chronic HBV or HCV reported phlebotomy continuing despite their obvious distress or pain (Drazic and Caltabiano 2013). In our review the single quantitative study meeting the inclusion criteria was the only study examining an intervention to improve phlebotomy for people with HCV and was of moderate quality only (Mason et al 2007).

Zickmund and colleagues (2004) conducted semi structured interviews with 322 people diagnosed with HCV and found that 41% (n=131) reported communication problems with the physician responsible for their care. Perceptions of dis-engagement between services have been reported previously: clients of an opiate substitute treatment program in Australia reported concerns that HCV treatment was not perceived by clinicians as a legitimate activity (Treloar et al 2010). In their mapping of social factors mediating HCV treatment access, Harris & Rhodes (2013) found that integrated delivery of multidisciplinary care was a key facilitating factor.

Limitations

The small number of studies meeting the inclusion criteria is both a strength, reflecting the rigour of the systematic review method, and a limiting factor. We focus specifically on experience of, and interventions to improve, phlebotomy in people with HCV. A recent systematic review examining interventions to improve treatment (Meyer et al 2015) only identified a single study related to phlebotomy, which was a comparison of standard phlebotomy and point of care testing for HCV screening (Morano et al 2014). We limited our search to studies reported in English. Whilst there are conflicting views about the bias this may introduce (Higgins & Green 2011), we took a pragmatic view based on the different profile of people with HCV in

developed and developing countries, with the latter more likely to be due to iatrogenic causes (Shepard et al 2005).

CONCLUSIONS

Recent developments with treatment indicate shorter duration, with less phlebotomy experiences for the service user, hence there is the potential to have a real impact on mortality and morbidity. However, findings from synthesis across these studies identifies that the people who need treatment frequently do not access or engage with services. The one intervention study using an improved phlebotomy approach (Mason et al 2007) showed positive impact for people who previously did not engage; given that it is almost a decade since this study was published, this area of work does not appear to have borne further fruit. Figure 2 identifies areas for future study, in particular development of interventions which may bring service users back onto the treatment pathway. In order to introduce interventions that are acceptable to the patient, it is essential to engage service users during the development stage and identify outcome measures that are important to service users and service providers.

References

- Bruggmann P, Grebely J (2015) Prevention, treatment and care of hepatitis C virus infection among people who inject drugs. *International Journal of Drug Policy* **26**: S22-S26.
- Clements A, Grose J, Skirton H (2015) Experiences of UK patients with hepatitis C virus infection accessing phlebotomy: a qualitative analysis. *Nursing & Health Sciences* **17**(2): 214-222.
- Coupland H, Day C, Levy MT, Maher L (2009) Promoting equitable access to hepatitis C treatment for Indo-Chinese injecting drug users. *Health Promotion Journal of Australia* **20**(3): 234-40.
- Cullen W, Stanley J, Langton D, Kelly Y, Bury G (2007) Management of hepatitis C among drug users attending general practice in Ireland: baseline data from the Dublin Area Hepatitis C in General Practice initiative. *European Journal of General Practice* **13**: 5-12.
- Drazic YN, Caltabiano ML (2013) Chronic hepatitis B and C: Exploring perceived stigma, disease information, and health-related quality of life. *Nursing & Health Sciences* **15**(2), 172-178.
- Dunne E, Quayle E. (2002) Pattern and process in disclosure of health status by women with iatrogenetically acquired hepatitis C. *Journal of Health Psychology* **7**: 565-82.
- Ferguson C, Higgs P, Olsen A (2015) Jugular venipuncture and other innovative approaches to phlebotomy among people who inject drugs. *Nursing & Health Sciences* **17**: 539–541.
- Grebely J, Genoway KA, Raffa JD et al (2008) Barriers associated with the treatment of hepatitis C virus infection among illicit drug users. *Drug and Alcohol Dependence* **93**: 141-147.
- Harris M, Rhodes T, Martin A (2013) Taming systems to create enabling environments for HCV treatment: negotiating trust in the drug and alcohol setting. *Social Science and Medicine* **83**: 19-26.
- Harris M, Rhodes T (2013) Hepatitis C treatment access and uptake for people who inject drugs: a review mapping the role of social factors. *Harm Reduction Journal* **10**(1): 1.
- Higgins JPT, Green S (eds.) (2011) *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Islam MM, Topp L, Iversen J, Day C, Conigrave KM, Maher L (2013) Healthcare utilisation and disclosure of injecting drug use among clients of Australia's needle and syringe programs. *Australian & New Zealand Journal of Public Health* **37**(2):148-154.

Kmet LM, Lee RC, Cook LS (2004) *Standard Quality Assessment Criteria for Evaluating Primary Research Papers from a Variety of Fields*. Alberta Heritage Foundation for Medical Research. Canada

Martin NK, Vickerman P, Grebely J et al (2013) Hepatitis C virus treatment for prevention among people who inject drugs: modelling treatment scale-up in the age of direct-acting antivirals. *Hepatology* **58**(5): 1598-1609.

Mason S, Watts A, Sheils S, Koorey D. (2007) Improving access to HCV treatment: external jugular venepuncture can overcome problems with difficult venous access. *International Journal of Drug Policy* **18**(5): 433-436

Mays N, Pope C, Popay J (2005) Systematically reviewing qualitative and quantitative evidence to inform management and policy-making in the health field. *Journal of Health Services Research and Policy*, **10** Suppl 1, 6-20.

Mehta SH, Genberg BL, Astemborski J, et al. (2008) Limited uptake of hepatitis C treatment among injection drug users. *Journal of Community Health* 2008; **33**(3):126-133.

Meyer JP, Moghimi Y, Marcus R, Lim JK, Litwin AH, Altice FL (2015) Evidence-based interventions to enhance assessment, treatment, and adherence in the chronic Hepatitis C care continuum. *International Journal of Drug Policy* **26**(10), 922-935.

Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009) Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Med* **6**(6): e1000097. doi:10.1371/journal.pmed1000097

Morano JP, Zelenev A, Lombard A, Marcus R, Gibson BA, Altice FL (2014). Strategies for hepatitis C testing and linkage to care for vulnerable populations: point-of-care and standard HCV testing in a mobile medical clinic. *Journal of Community Health* **39**(5): 922-934.

Neale J, Tompkins C, Sheard L (2008) Barriers to accessing generic health and social care services: a qualitative study of injecting drug users. *Health & Social Care in the Community* **16**(2): 147-54.

Nelson PK, Mathers BM, Cowie B, Hagan H, Des Jarlais D, Horyniak D, Degenhardt L (2011) Global epidemiology of hepatitis B and hepatitis C in people who inject drugs: results of systematic reviews, *The Lancet* **378**:571-583.

Olsen A, Banwell C, Harley D, Welsh L, Petersons C. (2014) Treating hepatitis C: Does gender matter? *Australasian Viral Hepatitis Conference*. Alice Springs, Australia, 17–19 Sep. 2014.

Public Health England (2015) *Hepatitis C in the UK: 2015 report*. Accessible at https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/448710/NEW_FINAL_HCV_2015_IN_THE_UK_REPORT_28072015_v2.pdf (accessed 26/05/2016)

Scottish Intercollegiate Guidelines Network (SIGN) (2013) Management of Hepatitis C. Edinburgh: SIGN (SIGN Publication no. 133). Available at: <http://www.sign.ac.uk> Date last accessed: 21/02/2016

Shepard CW, Finelli L, Alter MJ. (2005) Global epidemiology of hepatitis C virus infection. *Lancet Infect Dis.* **5**:558–67.

Swan D, Long J, Carr O, et al (2010) Barriers to and facilitators of hepatitis C testing, management, and treatment among current and former injecting drug users: a qualitative exploration. *AIDS Patient Care STDS.* **24**(12):753-62.

Treloar C, Newland J, Rance J, Hopwood M. (2010) Uptake and delivery of hepatitis C treatment in opiate substitute treatment: perceptions of clients and health professionals. *Journal of Viral Hepatitis* **17**(12): 839-844.

Zickmund S, Hillis SL, Barnett MJ, Ippolito L, LaBrecque DR (2004). Hepatitis C virus-infected patients report communication problems with physicians. *Hepatology*, **39**(4): 999-1007.

Figure 1 PRISMA flow chart

Figure 2 Reasons why people with HCV leave the treatment pathway

References: 1=Harris et al 2013; 2= Swan 2010; 3=Mason et al 2007; 4= Clements et al 2015

Figure 2 Reasons why people with HCV leave the treatment pathway

Table 1 Inclusion and Exclusion criteria applied to systematic review papers

Inclusion criteria	Exclusion criteria
<ul style="list-style-type: none">• Papers published in English• All countries• Primary research evidence• All treatments for illicit drug users	<ul style="list-style-type: none">• Subjects not illicit drug users• HCV due to iatrogenic causes• Study not about access to treatment• Professional opinion or consensus• Screening only• Prevention or harm reduction strategies rather than treatment

Table 2 Databases and search terms

Databases	Search terms
PsycInfo, Medline, Pubmed, Cinahl, BNI, ASSIA, Social Care Online, Cochrane, Embase, HMIC and NHS Evidence.	Drug misuse/ drug abuse [+NT]/ OR INTRAVENOUS DRUG USAGE/ OR exp DRUG PWID/ IVDU ADDICTION Phlebotomy, testing for HepC, treating hep C HCV Poor venous access, vascular/venous access

Table 3 Summary of the studies included in the narrative synthesis

	<i>Reference/country</i>	<i>Aim</i>	<i>Study Design</i>	<i>Participants and sample</i>	<i>Findings</i>
1	Mason et al (2007) Australia	To evaluate success of a new means of collecting blood (external jugular vein EJV) for people with HCV	Observational design: <u>Phase 1</u> : phlebotomy audit in HCV infected patients, <u>Phase 2</u> : assessment of EJV in this population.	<u>Phase 1</u> : n=39 service users <u>Phase 2</u> : n=29 service users	All patients reported high levels of satisfaction compared to previous venous access attempts. EJV improves access to antiviral therapy and is a safe and effective technique for patients with difficult venous access (DVA).
2	Harris, Rhodes & Martin (2013) UK	To explore accessibility of HCV treatment provision in two drug and alcohol services	Qualitative interviews	Service user group: people with HCV (n= 35) Service provider group: providers of HCV treatment in London (n=14)	Service providers employed strategies to 'tame' the treatment system so as to create an environment in which trust was a critical feature. This was enacted through practices of 'negotiated flexibility', in relation to appointments, eligibility, and phlebotomy. Service users (i) placed greater trust in familiar environments and known health providers and (ii) emphasised the potentially stigmatising effects of negotiating treatment in unfamiliar territory, especially hospital settings.
3	Swan et al. (2010) Ireland	To explore IDUs experiences of what enables or prevents them engaging at every level of HCV care, including testing, follow-up, management and treatment	Qualitative interviews	N= 36 service-users across a range of primary and secondary care services	Barriers included perceptions of HCV infection as relatively benign, fear of investigations and treatment, and feeling well. Difficulties accessing HCV care included limited knowledge of testing sites, not being referred for specialist investigations and ineligibility for treatment. Relationships with health care providers

		processes.			influenced engagement with care: trust in providers, concern for the service-user, and continuity of care fostered engagement. Education on HCV infection, investigations, and treatment altered perceptions.
4	Clements et al (2015) UK	To explore the experiences of I.V. drug users with phlebotomy services and perceptions of staff attitudes and care delivery.	Qualitative interviews	N= 10 IV drug users with Hep C virus	Four themes were identified: conflicts associated with phlebotomy, emotional responses to phlebotomy, patients as expert, and offering solutions.

Table 4 Quality appraisal scores for Quantitative Study

Paper	Mason et al (2007)
Question / objective sufficiently described?	2
Study design evident and appropriate?	0
Method of subject / comparison group selection or source of information / input variables described and appropriate?	1
Subject (and comparison group, if applicable) characteristics sufficiently described?	2
If interventional and random allocation was possible, was it described?	N/A
If interventional and blinding of investigators was possible, was it reported?	N/A
If interventional and blinding of subjects was possible, was it reported?	N/A
Outcome and (if applicable) exposure measure(s) well defined and robust to measurement / misclassification bias? Means of assessment reported?	1
Sample size appropriate?	1
Analytic methods described / justified and appropriate?	N/A
Some estimate of variance is reported for the main results?	N/A
Controlled for confounding?	N/A
Results reported in sufficient detail?	2
Conclusions supported by the results?	2
Summary score	0.625

The summary score for quantitative studies is calculated by determining the total sum of scores, then subtracting it from the total possible sum (28- number of NA x 2), and then dividing the total sum by the total possible sum. Items are scored for the degree that they meet the criteria for each question detailed by the authors of the quality appraisal guidance: 2=yea, 1-partial, 0-no, NA=not applicable.

Table 5 Quality appraisal scores for Qualitative Studies

Papers	Harris & Rhodes (2011)	Swan et al. (2010)	Clements et al (2015)
Question / objective sufficiently described?	2	2	2
Study design evident and appropriate?	2	2	2
Context for the study clear?	2	2	2
Connection to a theoretical framework / wider body of knowledge?	2	2	2
Sampling strategy described, relevant and justified?	2	2	2
Data collection methods clearly described and systematic?	1	2	2
Data analysis clearly described and systematic?	1	2	2
Use of verification procedure(s) to establish credibility?	0	2	2
Conclusions supported by the results?	2	2	2
Reflexivity of the account?	0	0	2
Summary score	0.7	0.9	1.00

The summary score for qualitative studies is calculated by dividing the sum of scores by the total possible sum (20). Items are scored for the degree that they meet the criteria for each question detailed by the authors of the quality appraisal guidance: 2=yes, 1= partial, 0= no. For these studies an assessment of this measure as being 'not applicable' is not permitted.