Doran, J, Hope, V, Wright, T, Scott, J, Ciccarone,, D and Harris, M

Prevalence and factors associated with chronic venous insufficiency, leg ulceration and deep-vein thrombosis among people who inject drugs in London, United Kingdom

Prevalence and factors associated with chronic venous insufficiency, leg ulceration and deep-vein thrombosis among people who inject drugs in London, United Kingdom

Running title: Prevalence and associations of vascular conditions among PWID

Jason Doran[1,2], Vivian Hope[3], Talen Wright[4], Jenny Scott[5], Daniel Ciccarone[6], Magdalena Harris[1]

1. Faculty of Public Health and Policy, London School of Hygiene & Tropical Medicine, London, United Kingdom.

2. National Infection Service, Public Health England, London, United Kingdom.

3. Public Health Institute, Liverpool John Moores University, Liverpool, United Kingdom.

4. Division of Psychiatry, University College London, London, United Kingdom.

5. Department of Pharmacy and Pharmacology, University of Bath, Bath, United Kingdom.

6. Department of Family and Community Medicine, University of California, San Francisco, USA

Jason Doran MSc, Epidemiologist and Research Fellow, Vivian Hope PhD, Professor, Talen Wright MSc, PhD student, Jenny Scott PhD, Senior Lecturer, Daniel Ciccarone PhD, Professor, Magdalena Harris PhD, Professor.

Correspondence to: Dr Jason Doran, North West Field Epidemiology Service, Public Health England, Cunard Building, Water St., Liverpool L3 1DS, UK. Tel: +447415273958; Email: doranja@tcd.ie

Declaration of Competing Interests

No conflicts to declare.

Abstract

Introduction. People who inject drugs (PWID) are vulnerable to a range of harms, including vascular conditions such as chronic venous insufficiency (CVI), leg ulcers and deep-vein thrombosis (DVT). The extent of vascular conditions has rarely been studied, despite contributing to considerable illness and disability among PWID. We assess the prevalence and associations of vascular conditions in PWID in London, UK.

Methods. Survey-data from the community-recruited Care and Prevent Study of PWID in London were analysed. Participants were asked about CVI and leg ulcers using pictorial-questions, and if they had ever been diagnosed with DVT. Associations between vascular-conditions and demographic/drug-use information were explored using univariate and multivariable logistic regression.

Results. Among participants (n=455), the prevalence of CVI, leg ulcers and DVT was 13% (n=57), 10% (n=46) and 23% (n=105), respectively. CVI and DVT were positively associated with injecting into the groin, while injecting into the leg was positively associated with leg ulcers and DVT. CVI was also associated with not cleaning injection sites and diagnosed hepatitis C virus; and DVT with hepatitis C virus.

Discussion and Conclusion. The prevalence of vascular problems among PWID in London is very high in comparison to the general population. These conditions are primarily associated with injection into the femoral vein. Use of these injection sites indicate peripheral venous access problems. There is a need to reinvigorate safe injection information provision in harm reduction services, with attention to reducing risk practices associated with venous-damage and transitions to femoral injection.

Key words: people who inject drugs; CVI; leg ulcers; deep-vein thrombosis; harm reduction

1. Introduction

There are an estimated 15 million people who inject drugs (PWID) worldwide [1], with the United Kingdom (UK) having one of the highest levels of injection drug-use in Western Europe [2]. Illicit drug injection is associated with high levels of morbidity and premature mortality and increases susceptibility to a range of injecting-related harms, including blood-borne viral infections, such as hepatitis C (HCV) and HIV, skin and soft tissue infections, overdoses and vascular damage [3,4].

Injecting-drug use is a risk factor for venous damage, including deep vein thrombosis (DVT), chronic venous insufficiency (CVI) and leg ulceration. DVT, where occlusion of the vein occurs due to the formation of a thrombus on the vein wall, can cause irreversible damage, including peripheral oedema and post-thrombotic limb symptoms, such as ulcers and varicose eczema [5-7]. A study of people receiving treatment for opioid use in Middlesbrough, UK estimated a DVT prevalence of 14% [7], compared to approximately 0.1% in general adult populations [8,9], indicating that DVT is more common among PWID. DVT in PWID may be due to endothelial damage from injecting, potentially related to the overuse of acidifiers in drug preparation [10], as well high levels of coagulative factors as a result of injecting-related infections [11,12].

CVI, a consequence of venous damage in the lower extremities [13], has not been systematically studied among PWID, but is reported as common, with 87% of those examined at a treatment centre in the United States exhibiting clinical evidence of CVI [14]. Clinical manifestations of CVI include the appearance of varicose veins, oedema and darkened, dry skin on the lower extremities [14]. CVI and the ensuing vascular hypertension can give rise to the development of chronic leg ulceration [15-17]. Leg ulcers, defined as ‘breaks in the skin

between the knee and the ankle, present for four weeks or more' [18] appear to disproportionately impact PWID. A Scottish study, for example, reported a 15% prevalence of leg ulceration among PWID [19] in comparison with a 1-2% prevalence in the general population studies in high-income countries [20-22].

As well as posing a substantive cost to healthcare systems [23], venous complications can be severely damaging to both physical and mental health. PWID with leg ulceration are frequently subject to chronic pain, mobility restrictions and also stigma and shame, including in relation to the management of open and odoriferous wounds [24,25]. Subsequently, this can act to restrict social mobility and employment options, compromise access to health care and exacerbate self-medication with illicit opioids for pain relief [13,25-27].

Harm reduction research, policy and practice has traditionally oriented around the prevention and treatment of blood-borne viral infections and, more recently, skin and soft tissue infections [28]. Given the significant individual and social burden of injecting-related vascular issues, there is an urgent need to develop acceptable, accessible and effective preventative interventions. In order to implement such interventions, a greater understanding of the prevalence and risk factors for vascular issues among PWID is required, yet these have rarely been studied. In this study, we aimed to estimate the prevalence of vascular issues among PWID in London, UK and examine the associated factors, through the analysis of data from an in-depth cross-sectional survey exploring injecting practices and harms among PWID in London.

2. Materials and Methods

2.1 Data

Anonymised quantitative survey data from the mixed-methods Care and Prevent Study (C&P) were used. Detailed methods and study rationale for C&P have previously been published [29]. The in-depth survey included questions surrounding injection-related comorbidities, drug-use history, injecting practices, sociodemographic characteristics and healthcare access. Participants completed a detailed researcher-administered, computer-assisted survey.

2.2 Ethical approval

Ethical approvals were obtained from the London Bridge Research Ethics Committee [17/LO/0872] and the London School of Hygiene and Tropical Medicine Observational Research Ethics Committee [12021]. Written consent was obtained from all participants in the study.

2.3 Study sample recruitment and eligibility

Participants were recruited from six treatment centres, homeless hostels and outreach services across London, UK. Eligibility to participate in the survey was restricted to those aged 18+, who had ever injected psychoactive drugs and who were assessed as being able to provide informed consent. Participants were not approached directly for the study but were fully informed about the study through a detailed participant information sheet and researchers were present at the sites to provide further information on specified days. Interested participants then contacted the research team directly. Participants received a £10 voucher as reimbursement for their time. In total, 455 PWID completed the survey between October 2017 and March 2019.

2.4 Study measurements

The C&P study questionnaire was carefully developed through extensive consultation with a panel of experts. The survey asked participants questions surrounding sociodemographic details; drug use history, injection preparation and administration practices (lifetime and

previous 12 months); reuse and cleaning of injecting equipment (lifetime); experience of skin and soft tissue infections, vascular conditions and other health conditions, including HIV and HCV. Questions pertaining to ever having CVI and leg ulceration were accompanied by pictures of typical condition presentation, to indicate their type and severity. Participants were also provided with a verbal description of symptoms in order to aid identification and nomination of severity, minimising misclassification bias. Participants were asked if they had ever been diagnosed by a healthcare worker as having had deep vein thrombosis (DVT).

Participants answered detailed questions on reuse of injecting equipment, injecting hygiene practices, primary drugs injected, type and amount of acidifier used to prepare injection solutions, number of injections per day, week or month, body sites injected and number of times taken to achieve an injection. The latter question was included as it provides a strong indication of peripheral venous damage [30].

Participants who reported a lifetime history of CVI or leg ulcers were asked about the duration of the condition, how long it took them to seek care and if they had ever been hospitalised for that condition. Participants who reported a previous diagnosis of DVT were asked how long it took them to seek care prior to diagnosis. Measures pertaining to care seeking were informed by prior epidemiological injecting-related infection risk factor and hospitalisation research [31], which used five or more days as an indicator of health care delay. We also specified 10 or more days to measure of the extent of delay, in recognition of the multiple barriers many PWID face in seeking care [4].

2.5 Case definitions

The dependent variables in this study were a lifetime history of CVI, leg ulcers and diagnosed DVT. A lifetime history of CVI was defined as participants who reported ever having CVI based on pictures of the typical CVI presentation included in the survey. A lifetime history of leg

ulcers was defined as participants who reported ever having a leg ulcer based on pictorial guidance included in the survey. Finally, a lifetime history of DVT was defined as participants who reported ever being diagnosed with DVT in the past.

2.6 Statistical analysis

Data analysis was performed in Stata 16.1. Unless otherwise stated, all variables included in this analysis are reported across the participants' history of injecting. Descriptive statistics, including means, medians and ranges were used to present demographic and background characteristics of the entire sample and of those reporting a lifetime history of CVI, leg ulcers and diagnosed DVT. Univariate logistic regression was performed to investigate the associations between demographic and substance-use characteristics (independent variables) and lifetime history of CVI, leg ulcers and DVT (dependent variables), estimating unadjusted odds ratios and their 95% confidence intervals. Characteristics associated with vascular issues from the univariate analysis, where the *P*-value was <0.1, were included in the multivariable logistic regression model. Separate models for each of the three vascular issues were built including the likely confounding variables age and gender, *a priori*. A forward's stepwise entry multivariable logistic regression was built to estimate adjusted odds ratios and their 95% confidence intervals. At each forward step, retention in the model was dependent either on the factor having the largest confounding effect or the strongest evidence of being an independent risk factor. Multivariable associations were deemed significant if *P*-values obtained by the Wald tests were <0.05.

3. Results

3.1 Prevalence of CVI, leg ulcers and DVT

Of the 455 participants, 13% (n=57) reported lifetime history of CVI, 10% (n=46) reported leg ulceration and 23% (n=105) had been diagnosed with DVT (Table 1). Of those reporting CVI,

37% (n=21) had lived with this for 5 or more years, 46% (n=26) had received related medical care and 16% (n=9) were hospitalised as a result. Of those reporting leg ulceration, 11% (n=5) had lived with this for 5+ years, 74% (n=34) had received related medical care and 37% (n=17) were hospitalised. The proportion of participants who reported taking 10 or more days to seek medical advice from first noticing symptoms of the condition was 28% (n=16) in those with CVI and 20% (n=9) in those with leg ulcers.

INSERT TABLE 1

3.2 Socio-demographic characteristics and unadjusted associations with venous issues

The mean age of participants was 46 years and 75% (n=341) identified as male. More than half of participants (54%, n=244) self-reported an HCV diagnosis and the majority (78%, n=355) reported a lifetime history of street homelessness, with a mean duration of four years (Table 2). The percentage of participants who were ever homeless was 86%, 85% and 83% among those with a lifetime history of CVI, leg ulcers and DVT, respectively. Diagnosed HCV and increasing number of years homeless were crudely associated with all three conditions. In addition, increasing age in years was crudely associated with CVI, while female gender was protective against CVI (Table 2).

INSERT TABLE 2

3.3 Substance use characteristics and unadjusted associations with venous issues

As shown in Table 3, 42% (n=192) of participants injected drugs for 15 or more years and 59.5% (n=271) primarily injected either heroin, crack or heroin and crack combined in the

previous 12 months. Table 3 shows 70% (n=317) reported injecting 1+ times per day, and the use of higher-risk body sites for injection was common: 60.5% (n=275) had ever injected into their leg, 41.5% (n=189) had ever injected into their groin and 37.1% (n=169) had ever injected into their neck. Twenty-five percent of participants (n=113) typically took four or more attempts (skin punctures) to achieve an injection. Two-thirds (67%, n=306) sometimes or always reused needles and almost one-quarter (22.6%, n=103) never wiped the injection site prior to injecting. Crude associations showed that CVI was positively associated with injecting for 15+ years; ever injecting into the leg, groin or neck; and never cleaning the injection site prior to injecting (Table 3). Leg ulcers were more likely in PWID who reported: injecting for 15+ years; injecting heroin, crack or heroin and crack combined as a main drug in the previous 12 months; ever injecting into the leg, groin or neck; and taking 4+ attempts to achieve an injection (Table 3). Finally, DVT was more likely in those who reported injecting for 15+ years; injecting heroin, crack, or heroin and crack combined as a main drug in the previous 12 months; injecting more than once per day; and ever injecting into the leg, groin or neck (Table 3).

INSERT TABLE 3

3.4 Factors associated with CVI, leg ulcers and DVT: multivariable analysis results

Factors associated with CVI, leg ulcers and DVT among PWID in this study are shown in Table 4 as adjusted odds ratios. Following adjustment, ever injecting into the groin and leg was associated with DVT and ever injecting into the leg was associated with leg ulcers. CVI was also associated with never cleaning the injection site before injecting and diagnosed HCV. Finally, DVT was associated with diagnosed HCV (Table 4).

INSERT TABLE 4

4. Discussion

This study found a high prevalence of vascular damage among PWID in London. The prevalence of CVI, leg ulceration and DVT are markedly higher than the levels in the general adult population. DVT was the most common venous issue reported in this sample of PWID, with a lifetime prevalence of 23%. Given participants were only asked about diagnosed DVT, actual prevalence might be higher. In comparison, general population studies report DVT incidence of 1 per 10,000 in the adults aged under 40 years to 5-6 per 1000 in those aged 80 and over [8,9]. Leg ulceration was reported by 10% of our PWID participants, considerably higher than an approximately 1% lifetime prevalence reported among the general populations in high-income countries [20-22]. CVI prevalence, at 13% among our sample, also indicates disproportional impact on PWID, in comparison with a 6-9% prevalence among in the few available studies pertaining to general populations in high-income countries [32]. This high prevalence of DVT, CVI and leg ulceration among our community sample of PWID accord with the few published estimates, primarily generated from samples of PWID receiving treatment for their drug use [33-35].

While the factors associated with each of the vascular conditions in this study varied, the strongest association for all was having ever injected into the femoral vein. Participants who reported ever using the femoral vein (42%) had almost 10-, seven- and two- times the odds of reporting DVT, CVI and leg ulcers, respectively, than those who never injected into the femoral vein. As damage to the femoral vein through injecting will likely impact returning blood flow in the area, this finding is expected. Transitions to using the femoral vein

commonly occur due to difficult peripheral venous access – also indicated by our sample. We asked how many attempts (skin punctures) it took to achieve a typical injection, with 25% reporting four or more attempts. This, a clear marker of compromised venous access, is a risk for transition to the use of deeper veins such as the femoral or jugular veins, with potentially dangerous health consequences [10,36-38].

Compromised venous access and damage among PWID is likely due to scarring from repeated injections, including the possible overuse of acidifiers when injecting and/or compromised filtration practice [10,30]. Interventions to promote and maintain peripheral venous health are a key preventative measure for the vascular conditions described in this study. Harris *et al*., for example, have detailed the role of structural and educational interventions in alerting the link between overuse of acidifier in injection preparation and venous damage [30]. Interventions orientated toward promoting venous care and safe injection preparation practice are also likely to resonate with PWID and provide a point of connection for other health and social care interventions [39].

As more broadly reported, difficulty in maintaining injecting related hygiene (such as cleaning sites prior to injection) can exacerbate risk of bacterial infection and related complications [40]. People who are unstably housed, rough sleeping and/or have difficulty accessing fresh, clean water are likely to be most at risk of injection related injuries and infections [41]. Therefore, it is crucial that interventions practically orientate toward providing sufficient equipment to support hygienic injection practice (such as clean water, hand wipes, alcohol wipes, injection preparation mats) as well as information on how to do so. Advocacy for the introduction of environments that support safe, hygienic injection practice is essential, particularly in countries that currently legislate against safe or supervised injection facilities.

We note high levels of hospitalisation for venous issues (16% for CVI and 37% for leg ulcers) in this sample of PWID and have published elsewhere on the association between the time taken to seek medical care, condition severity and hospitalisation [4]. Delaying or avoiding medical attention for venous conditions can be extremely dangerous. Untreated DVT, for example, can lead to potentially fatal pulmonary embolisms [42]. Although this particular analysis did not seek to identify specific barriers to the treatment of vascular issues, qualitative data from the Care and Prevent Study highlight the multiple barriers PWID face to healthcare access, such as stigma, discrimination, poverty, limited geographical mobility, competing demands and fear of drug withdrawal if confined as an inpatient [43]. These and other barriers have been widely reported globally [44-46]. As we argue elsewhere [43], there is an urgent need for health care system transformation so that PWID are able to engage early with a diversity of welcoming, flexible and accessible services.

Given the high prevalence of venous complications in PWID, screening for DVT, CVI and leg ulcers should be offered to PWID as part of general healthcare provision. As self-care of injecting related injuries and infections is reportedly high among PWID [4], supporting best practice can reduce complication development. This could include provision of wound-care training, bandages and dressings. Although supporting self-care for venous ulcers is compromised by the need for specialist compression bandaging application, it might support wound healing for PWID unable to attend regular wound care appointments. As noted, PWID face multiple barriers to health care access, particularly in relation to specialist services. It is therefore crucial that financial and policy support is provided for a range of innovative accessible interventions, such as in-reach wound care nurses at drug treatment and homeless hostel services and outreach wound care services for people living on the street [47].

4.1 Strengths and limitations

This study measured wide-ranging injecting-related conditions, however, the inherent nature of a cross-sectional study meant we were unable to investigate temporal-relationships between factors associated with the conditions and thus we cannot eliminate the possibility of reverse causality. Additionally, the nature of the study meant that only current injecting related behaviour could be explored in detail, and past practices and risks may be different from current ones. However, in contrast to longitudinal studies which use healthcare records, our study captures a community-based sample, who were not necessarily accessing healthcare or drug treatment services and who have conditions that may not have been clinical recognised or recorded. Survey data may be subject to reporting bias as self-reporting of conditions, including those diagnosed, was used. Previous studies have, however, indicated that self-reporting of injecting-related infections is reliable among PWID [48]. In addition, this study used photographs to aid recall and self-diagnosis (see [49]). However, although some participants might have incorrectly reported their conditions, we believe such errors to be minimal. Answers relating to questions surrounding injection practices and hygiene may have been influenced by social desirability bias, though this is unavoidable and likely minimal.

The study aimed to be as representative as possible. Recruitment took place in community settings, thus aiming to engage a range of PWID – including those who might have difficulty accessing clinical services or hospitals. Although recruitment of participants was solely in London, comparative analysis demonstrates high comparability between characteristics of C&P participants and those of PWID recruited to a large national surveillance study in the UK [40]. This indicates the generalisability of PWID in the UK, with the acknowledgement of potential participant selection bias.

4.2 Conclusion

The lifetime prevalence of vascular issues in PWID in London, UK is considerably higher than in the general population. Considering the associated healthcare costs, distress and disability, interventions are urgently needed to reduce their occurrence, including removing the barriers to safe injecting practice, and improving access to care. Interventions which prevent vascular damage early in the causal pathway and help to promote safe injecting preparation and practice are likely to yield significant harm reduction benefits.

Role of Funding Source

MH was funded by a National Institute for Health Research (NIHR) Career Development Fellowship [CDF-2016-09-014] for the Care and Prevent Study. The views expressed are those of the authors and not necessarily those of the National Health Service, the National Institute for Health Research or the Department of Health and Social Care.

Acknowledgements

We thank Care and Prevent study collaborators, study sites and participants for their excellent contribution to this study.

Declaration of Competing Interests

No conflicts to declare.

References

1. Degenhardt L, Peacock A, Colledge S, Leung J, Grebely J, Vickerman P, et al. Global prevalence of injecting drug use and sociodemographic characteristics and prevalence of HIV, HBV, and HCV in people who inject drugs: a multistage systematic review. Lancet Glob Health 2017;5:e1192-e207.

2. EMCDDA. United Kingdom- Country Drug Report. European Monitoring Centre for Drugs and Drug Addiction; 2019.

3. Cornford C, Close H. The physical health of people who inject drugs: complexities, challenges, and continuity. Br J Gen Pract 2016;66:286-7.

4. Doran J, Harris M, Hope VD, Wright T, Edmundson C, Sinka K, Heinsbroek E. Factors associated with skin and soft tissue infections among people who inject drugs in the United Kingdom: A comparative examination of data from two surveys. Drug Alcohol Depend 2020;213:108080.

5. Baldeweg SE. Arterial and venous disease and deep vein thrombosis. Injecting drug use is major risk factor for deep vein thrombosis. BMJ 2000;321:1018.

6. Lisse JR, Davis CP, Thurmond-Anderle ME. Upper extremity deep venous thrombosis: increased prevalence due to cocaine abuse. Am J Med 1989;87:457-8.

7. Cornford C, Mason J, Inns F. Deep vein thromboses in users of opioid drugs: Incidence, prevalence, and risk factors. Br J Gen Pract 2011;61:e781-6.

8. Cushman M. Epidemiology and risk factors for venous thrombosis. Semin Hematol 2007;44:62-9.

9. White RH. The epidemiology of venous thromboembolism. Circulation 2003;107(Suppl 1):I4-8.

10. Ciccarone D, Harris M. Fire in the vein: Heroin acidity and its proximal effect on users' health. Int J Drug Policy 2015;26:1103-10.

11. McColl MD, Tait RC, Greer IA, Walker ID. Injecting drug use is a risk factor for deep vein thrombosis in women in Glasgow. Br J Haematol 2001;112:641-3.

12. Mackenzie AR, Laing RB, Douglas JG, Greaves M, Smith CC. High prevalence of iliofemoral venous thrombosis with severe groin infection among injecting drug users in North East Scotland: successful use of low molecular weight heparin with antibiotics. Postgrad Med J 2000;76:561-5.

13. Pieper B. Nonviral Injection-related injuries in persons who inject drugs: skin and soft tissue infection, vascular damage, and wounds. Adv Skin Wound Care 2019;32:301-10.

14. Pieper B, Templin T. Chronic venous insufficiency in persons with a history of injection drug use. Res Nurs Health 2001;24:423-32.

15. O'Meara S, Cullum NA, Nelson EA. Compression for venous leg ulcers. Cochrane Database Syst Rev 2009(1):CD000265.

16. Anderson I. Compression bandaging in patients with venous insufficiency. Nurs Stand 2008;23:49-55; quiz 6.

17. Mekkes JR, Loots MA, Van Der Wal AC, Bos JD. Causes, investigation and treatment of leg ulceration. Br J Dermatology 2003;148:388-401.

18. SIGN. The care of patients with chronic leg ulcers. A National Clinical Guideline. Scottish Intercollegiate Guidelines Network; 1998.

19. Coull AF, Atherton I, Taylor A, Watterson AE. Prevalence of skin problems and leg ulceration in a sample of young injecting drug users. Harm Reduct J 2014;11:22.

20. Graham ID, Harrison MB, Nelson EA, Lorimer K, Fisher A. Prevalence of lower-limb ulceration: a systematic review of prevalence studies. Adv Skin Wound Care 2003;16:305-16.

21. Vowden KR, Vowden P. The prevalence, management and outcome for patients with lower limb ulceration identified in a wound care survey within one English health care district. J Tissue Viability 2009;18:13-9.

22. Dale JJ, Callam MJ, Ruckley CV, Harper DR, Berrey PN. Chronic ulcers of the leg: a study of prevalence in a Scottish community. Health Bull (Edinb) 1983;41:310-4.

23. Lewer D, Hope VD, Harris M, Kelleher M, Jewell A, Pritchard M, et al. Incidence and treatment costs of severe bacterial infections among people who inject heroin: A cohort study in South London, England. Drug Alcohol Depend 2020;212:108057.

24. Palfreyman SJ, Tod AM, King B, Tomlinson D, Brazier JE, Michaels JA. Impact of intravenous drug use on quality of life for patients with venous ulcers. J Adv Nurs 2007;58:458-67.

25. Devey T. Using an outreach service to meet the needs of users of intravenous drugs with leg ulceration. Nurs Times 2010;106:22-3.

26. Green J, Jester R, McKinley R, Pooler A. The impact of chronic venous leg ulcers: a systematic review. J Wound Care 2014;23:601-12.

27. Pieper B. A retrospective analysis of venous ulcer healing in current and former users of injected drugs. J Wound,Ostomy Continence Nurs 1996;23:291-6.

28. Boucher LM, Marshall Z, Martin A, Larose-Hébert K, Flynn JV, Lalonde C, et al. Expanding conceptualizations of harm reduction: results from a qualitative community-based participatory research study with people who inject drugs. Harm Reduct J 2017;14:18.

29. Harris M, Brathwaite R, McGowan CR, Ciccarone D, Gilchrist G, McCusker M, et al. 'Care and Prevent': rationale for investigating skin and soft tissue infections and AA amyloidosis among people who inject drugs in London. Harm Reduct J 2018;15:23.

30. Harris M, Scott J, Wright T, Brathwaite R, Ciccarone D, Hope V. Injecting-related health harms and overuse of acidifiers among people who inject heroin and crack cocaine in London: a mixed-methods study. Harm Reduct J 2019;16:60.

31. Hope VD, Ncube F, Parry JV, Hickman M. Healthcare seeking and hospital admissions by people who inject drugs in response to symptoms of injection site infections or injuries in three urban areas of England. Epidemiol Infect 2015;143:120-31.

32. Ruckley CV, Evans CJ, Allan PL, Lee AJ, Fowkes FGR. Chronic venous insufficiency: Clinical and duplex correlations. The Edinburgh Vein Study of venous disorders in the general population. J Vasc Surg 2002;36:520-5.

33. Pieper B, Templin T. Lower extremity changes, pain, and function in injection drug users. J Subst Abuse Treat 2003;25:91-7.

34. Kwiatkowska W, Knysz B, Gąsiorowski J, Witkiewicz W. Deep vein thrombosis of the lower limbs in intravenous drug users. Postepy Hig Med Dosw (Online) 2015;69:510-20.

35. Coull AF, Kyle RG, Hanson CL, Watterson AE. Risk factors for leg ulceration in people who inject drugs: A cross-sectional study. J Clin Nurs 2021;30:1623-32.

36. Summers PJ, Struve IA, Wilkes MS, Rees VW. Injection-site vein loss and soft tissue abscesses associated with black tar heroin injection: A cross-sectional study of two distinct populations in USA. Int J Drug Policy 2017;39:21-7.

37. Wright NM, Allgar V, Tompkins CN. Associations between injecting illicit drugs into the femoral vein and deep vein thrombosis: A case control study. Drug Alcohol Rev 2016;35:605-10.

38. Hoda Z, Kerr T, Li K, Montaner JS, Wood E. Prevalence and correlates of jugular injections among injection drug users. Drug Alcohol Rev 2008;27:442-6.

39. Harris M, Rhodes T. Venous access and care: harnessing pragmatics in harm reduction for people who inject drugs. Addiction 2012;107:1090-6.

40. Doran J, Harris M, Hope VD, Wright T, Edmundson C, Sinka K, et al. Factors associated with skin and soft tissue infections among people who inject drugs in the United Kingdom: A comparative examination of data from two surveys. Drug Alcohol Depend 2020;213:108080.

41. Harris M, Scott J, Hope V, Wright T, McGowan C, Ciccarone D. Navigating environmental constraints to injection preparation: the use of saliva and other alternatives to sterile water among unstably housed PWID in London. Harm Reduct J 2020;17:24.

42. Min S-K, Kim YH, Joh JH, Kang JM, Park UJ, Kim H-K, et al. Diagnosis and Treatment of Lower Extremity Deep Vein Thrombosis: Korean Practice Guidelines. Vasc Specialist Int 2016;32:77-104.

43. Harris M. Normalised pain and severe health care delay among people who inject drugs in London: Adapting cultural safety principles to promote care. Soc Sci Med 2020;260:113183.

44. Harris M, Rhodes T, Martin A. Taming systems to create enabling environments for HCV treatment: negotiating trust in the drug and alcohol setting. Soc Sci Med 2013;83:19-26.

45. Paquette CE, Syvertsen JL, Pollini RA. Stigma at every turn: Health services experiences among people who inject drugs. Int J Drug Policy. 2018;57:104-10.

46. Biancarelli DL, Biello KB, Childs E, Drainoni M, Salhaney P, Edeza A, et al. Strategies used by people who inject drugs to avoid stigma in healthcare settings. Drug Alcohol Depend 2019;198:80-6.

47. Robinowitz N, Smith ME, Serio-Chapman C, Chaulk P, Johnson KE. Wounds on wheels: implementing a specialized wound clinic within an established syringe exchange program in Baltimore, Maryland. Am J Public Health 2014;104:2057-9.

48. Morrison A, Eliott L, Gruer L. Injecting-related harm and treatment-seeking behaviour among injecting drug users. Additction 1997;92:1349-52.

49. Wright T, Hope V, Ciccarone D, Lewer D, Scott J, Harris M. Prevalence and severity of abscesses and cellulitis, and their associations with other health outcomes, in a community-based study of people who inject drugs in London, UK. PLoS One 2020;15:e0235350.

Table 1. Prevalence and treatment of CVI, leg ulcers and DVT among PWID (n=455)

	CVI	**Leg ulcers**	**DVT**
Prevalence (%)	13% (n=57)	10% (n=46)	23% (n=105)
Duration with venous issue			
<5 years (%)	63% (n=36)	89% (n=41)	*
5+ years (%)	37% (n=21)	11% (n=5)	*
Received medical attention for the condition (%)	46% (n=26)	74% (n=34)	*
Hospitalised with this condition (%)	16% (n=9)	37% (n=17)	*
Took 10+ days to seek medical advice for the condition (%)	28% (n=16)	20% (n=9)	25% (n=26)

* Participants were not asked about this in relation to DVT. CVI, chronic venous insufficiency; DVT, deep-vein thrombosis.

Table 2. Demographic and health characteristics among people who inject drugs (n=455) stratified by CVI, leg ulcers and DVT

	Entire sample (n=455)	CVI (n=57)			Leg ulcers (n=46)			DVT (n=105)		
Variable	**N (%) /Mean (IQR)**	**N (%)**	**Crude OR (95% CI)**	***P*-value**	**N (%)**	**Crude OR (95% CI)**	***P*-value**	**N (%)**	**Crude OR (95% CI)**	***P*-value**
Age										
Mean (IQR)	45.7 (44.9,46.5)	48 (45.9,50)	1.03 (1.01,1.07)	0.04	46 (43.8,48.7)	1.0 (0.97,1.04)	0.65	46 (44.2,47.6)	1.0 (0.98,1.03)	0.77
Gender										
Male	341 (75)	50 (88)	1	0.01	35 (76)	1		83 (79)	1	0.26
Female	114 (25)	7 (12)	0.38 (0.14,0.88)		11 (24)	0.93 (0.41,1.97)	0.85	22 (21)	0.74 (0.42,1.29)	
Diagnosed hepatitis C										
No	211 (46)	16 (28)	1	0.003	15 (33)	1		32 (30)	1	<0.001
Yes	244 (54)	41 (72)	2.46 (1.3,4.9)		31 (67)	1.9 (0.96,3.91)	0.05	73 (70)	2.39 (1.47,3.93)	
Number of years homeless										
Mean (IQR)	4.1 (3.4,4.7)	6.8 (3.9,9.6)	1.1 (1.02,1.1)	0.002	6.2 (3.0,9.5)	1.05 (1.0,1.1)	0.03	5.7 (4.1,7.3)	2.23 (1.18,4.43)	0.001

CI, confidence interval; CVI, chronic venous insufficiency; DVT, deep-vein thrombosis; IQR, interquartile range; OR, odds ratio.

Table 3. Substance use characteristics among people who inject drugs (n=455) stratified by CVI, leg ulcers and DVT

Variable	Entire sample (n=455)	CVI (n=57)			Leg ulcers (n=46)			DVT (n=105)		
	N (%)	N (%)	Crude OR (95% CI)	*P*-value	N (%)	Crude OR (95% CI)	*P*-value	N (%)	Crude OR (95% CI)	*P*-value
Years injecting										
<15 years	263 (58)	23 (40.3)	1	0.004	16 (35)	1	0.001	43 (41)	1	<0.001
15+ years	192 (42)	34 (59.7)	2.25 (1.23,4.15)		30 (65)	2.86 (1.45,5.79)		62 (59)	2.44 (1.53,3.91)	
Injected heroin, crack or heroin and crack combined in previous 12 months										
No	184 (40.5)	23 (40.3)	1	0.99	10 (22)	1	0.006	31 (30)	1	0.001
Yes	271 (59.5)	34 (59.7)	1.0 (0.6,1.9)		36 (78)	2.67 (1.25,6.18)		74 (70)	1.85 (1.14,3.07)	
Typical injecting frequency										
Inject less than once per day	138 (30)	15 (26.3)	1	0.48	17 (37)	1		23 (22)	1	0.03
Inject 1+ times per day	317 (70)	42 (73.7)	1.25 (0.7,2.5)		29 (63)	0.72 (0.37,1.45)	0.302	82 (78)	1.74 (1.02,3.06)	
Ever injected into the leg										
No	180 (39.5)	12 (21.1)	1	0.002	5 (10.9)	1	<0.001	12 (11.4)	1	<0.001
Yes	275 (60.5)	45 (78.9)	2.74 (1.37,5.86)		41 (89.1)	6.13 (2.35,20.2)		93 (88.6)	7.15 (3.7,14.8)	
Ever injected into the groin										
No	266 (58.5)	11 (19.3)	1	<0.001	15 (32.6)	1	<0.001	16 (15.2)	1	<0.001
Yes	189 (41.5)	46 (80.7)	7.46 (3.65,16.4)		31 (67.4)	3.28 (1.65,6.75)		89 (84.8)	13.9 (7.61,26.5)	
Ever injected into the neck										
No	286 (62.9)	21 (36.8)	1	<0.001	19 (41.3)	1	0.001	40 (38.1)	1	<0.001
Yes	169 (37.1)	36 (63.2)	3.42 (1.85,6.4)		27 (58.7)	2.67 (1.37,5.26)		65 (61.9)	3.84 (2.38,6.23)	
Typical number of attempts to achieve injection										
1-4 times	342 (75)	37 (65)	1	0.05	28 (61)	1	0.02	75 (71)	1	0.31
4+ times	113 (25)	20 (35)	1.8 (0.9,3.3)		18 (39)	2.12 (1.1,4.18)		30 (29)	1.29 (0.76,2.15)	
Typically wipe injection site before injecting										
Always or sometimes	352 (77)	31 (54)	1	<0.001	31 (67)	1	0.088	78 (74)	1	0.39

Never	103 (23)	26 (46)	3.5 (1.9,6.5)		15 (33)	1.77 (0.8,3.54)		27 (26)	1.25 (0.72,2.12)	
Ever reuse needles/syringes										
Never	149 (33)	13 (23)	1	0.08	12 (26)	1	0.3	26 (25)	1	0.05
Sometimes or always	306 (67)	44 (77)	1.8 (0.9,3.7)		34 (74)	1.43 (0.7,3.1)		79 (75)	1.65 (0.98,2.82)	

CI, confidence interval; CVI, chronic venous insufficiency; DVT, deep-vein thrombosis; OR, odds ratio.

Table 4. Factors associated with CVI, leg ulcers and DVT among people who inject drugs (n=455): multivariable regression results

Variable	CVI		Leg ulcers		DVT	
	aOR (95% CI)	*P*-value	aOR (95% CI)	*P*-value	aOR (95% CI)	*P*-value
Sex						
Male	1	0.09	1	0.58	1 0.94 (0.49,1.77)	0.84
Female	0.47 (0.19,1.1)		1.23 (0.58,2.62)			
Age, years	1.03 (0.99,1.07)	0.08	0.99 (0.95,1.03)	0.68	0.99 (0.97,1.02)	0.93
Diagnosed HCV						
No	1	0.03	¥	-	1	
Yes	2.1 (1.10,3.99)				1.83 (1.1,3.13)	0.02
Ever injected into the groin						
No	1		1		1	
Yes	6.69 (3.28,13.63)	<0.0001	1.96 (0.98,3.93)	0.05	9.57 (5.2,17.6)	<0.001
Ever injected into the leg						
No	¥	-	1 3.92 (1.41,10.86)	0.009	1 3.2 (1.57,6.48)	<0.001
Yes						
Typically wipe injection site before injecting						
Always or sometimes	1		¥	-	¥	-
Never	3.03 (1.62,5.68)	0.001				
Years injecting						
<15 years	¥	-	1		1	
15+ years			1.95 (0.98,3.93)	0.06	1.58 (0.98,2.56)	0.07

¥ This variable was not included in the final model. aOR, adjusted odds ratio; CI, confidence interval; CVI, chronic venous insufficiency; DVT, deep-vein thrombosis; HCV, hepatitis C virus.