Retrieval of patients with hepatitis C who were lost to follow-up in Southern Denmark

Dröse, Sandra; Hansen, Janne Fuglsang; Røge, Birgit Thorup; Øvrehus, Anne Lindebo Holm; Christensen, Peer Brehm

Published in:
Infectious Diseases

DOI:
10.1080/23744235.2023.2189298

Publication date:
2023

Document version:
Accepted manuscript

Document license:
CC BY-NC

Citation for pulished version (APA):
Dröse, S., Hansen, J. F., Røge, B. T., Øvrehus, A. L. H., & Christensen, P. B. (2023). Retrieval of patients with hepatitis C who were lost to follow-up in Southern Denmark. *Infectious Diseases*, *55*(5), 361-369. https://doi.org/10.1080/23744235.2023.2189298

Retrieval of patients with hepatitis C who were lost to follow-up in Southern Denmark

Sandra Dröse[1,2], Janne Fuglsang Hansen [1], Birgit Thorup Røge[3], Anne Lindebo Holm Øvrehus[1,2] & Peer Brehm Christensen[1,2]

1. Department of Infectious Diseases, Odense University Hospital, Odense, Denmark
2. Department of Clinical Research, Faculty of Health Sciences, University of Southern Denmark, Odense, Denmark
3. Department of Medicine, Lillebælt Hospital, Kolding, Denmark

Abstract

Background

The goal of the C-Free-South project is to eliminate hepatitis C (HCV) in the Region of Southern Denmark (1.2 million inhabitants). One target group consists of people with HCV who had received care but were lost to follow-up. The study aim was to evaluate program efficacy in locating these patients and getting them into care.

Methods

Patients were contacted if they were HCV-RNA positive and age 18+ years, registered in the clinical hepatitis database as of November 1, 2019, and had no scheduled HCV-related appointment. They were contacted at 2-month intervals by phone or letter. For patients who did not respond, we asked their general practitioner to refer them, if possible.

Results

We identified 69 (7%) patients in the database who were listed as untreated and not being followed up. We successfully contacted 54 (78%), and the remaining 15 (22%) did not respond to our contacts. To date, 45 (65%) had initiated treatment, one (1%) had rejected treatment, and eight (12%) did not show up to their appointments. Among those receiving treatment, 20 (44%) responded after the first contact, 18 (40%) after the second contact, and 7 (16%) after informing the general practitioner.

Conclusion

An intensified and persistent effort made it possible to reach most HCV patients lost to follow-up. All new contact attempts increased the possibility that patients would receive treatment. Nevertheless, 22% of HCV patients lost to follow-up did not respond to repeated contact attempts.

Keywords: Hepatitis C, micro-elimination, lost to follow-up, direct-acting antivirals, retrieval

Introduction

Hepatitis C (HCV) is a viral infection that globally causes more deaths than HIV and malaria (1). Worldwide, 56.8 million people are infected with HCV, which entails a risk of liver cirrhosis and ultimately hepatocellular carcinoma (HCC) (2). The World Health Organization aims to eliminate HCV by 2030. Targets are defined as a 90% reduction in new infections and initiation of treatment in 80% with HCV. In absolute numbers, these goals mean decreasing incidence to <5 per 100,000 persons and <2 per 100 of people who inject drugs (1, 3).

Denmark is on track to HCV elimination according to the latest global updates (4). The estimated prevalence of HCV in Denmark is 0.21%, and 85% with HCV acquired their infection through injection drug use. According to a capture-recapture analysis, only 37% of the 9975 people estimated to live with chronic HCV in Denmark in 2016 have attended specialized care, and the proportion of undiagnosed HCV patients is estimated to be 24% (5). Direct-acting antivirals (DAAs) have been used in Denmark for the treatment of HCV regardless of concurrent injection drug use, and since November 1, 2018, regardless of fibrosis stage (6). Treatment is genotype specific according to the medical council's recommendations, and pan-genotypic treatment may be used in selected populations. Prescription of DAAs is the responsibility of specialists in infectious diseases and gastroenterology. The Danish healthcare system is tax paid and organized at a regional level, and all citizens are assigned to a private practitioner serving as the entry point for all secondary care.

In the Region of Southern Denmark (RSD), which accounts for 21% of the Danish population, a micro-elimination plan for HCV, the C-Free-South project, was initiated in March 2019 (7). An important part of the elimination program is to track patients who are lost to follow-up (LTFU). Patients can be lost at all steps in the cascade of care, such as before receiving test results, prior to referral for treatment, before treatment initiation, and during follow-up (8-11). Thus, in different studies the term "LTFU" may not necessarily cover the same population (12). In this study, we focus on the last steps in the cascade, on HCV patients who at some point attended a hepatitis clinic in the RSD and then became LTFU without receiving treatment for HCV. These patients were mainly LTFU before the introduction of DAA treatment without restrictions and might not know that they had become eligible for treatment. Previous LTFU studies have highlighted different methods of re-engaging patients, with contact made through the hepatitis clinic or through other departments, in combination with contact by phone and/or letter (electronically, physical mail), with several repetitions and in different combinations (10, 11, 13). The aim of this study was to evaluate the efficacy and success of the C-Free-South project intervention in re-engaging HCV patients who had contact with a specialized HCV clinic and then were LTFU.

Methods

Setting

In the RSD, HCV treatment has been handled by two clinics: the Department of Infectious Diseases at Odense University Hospital and the Department of Medicine at Sygehus Lillebælt in Kolding. During the retrieval of LTFU patients, the C-Free-South project established another simultaneous outreach intervention with decentralized HCV treatment provided by substance use treatment centers delivering opioid agonist therapy (OAT) (7). Patients LTFU who had enrolled with a substance use treatment center could receive HCV treatment assessment and initiation in an outreach setting without traveling to one of the two hepatitis clinics. The patients in the outreach clinics were linked with one of the two clinics depending on location.

Data sources

All patients diagnosed with hepatitis in the RSD were registered in a clinical database, "InfCare Hepatitis," after the first clinical contact in each of the two clinics and after providing informed consent (14). This database contained information about patient demographics, co-infection with hepatitis B and HIV, use of injection drugs and alcohol, liver stiffness measures (LSMs), liver disease staging including pathology and markers of liver function, treatment, and outcome. The database contains data from 2002 onwards. Most of the data have been manually updated except for HCV-RNA and HCV-Ab results. Patients were registered as "discharged" in the database when they achieved cure without a requirement for follow-up, died, or were transferred to another center. If patients did not appear after three scheduled appointments and repeated contact attempts failed before DAA treatment became an option for all people with HCV, they were "discharged" in the hepatitis database without a reason for discharge being noted. Patients were always welcome to be referred again.

Study design and population

Retrospective phase: registry-based case finding

In October 2019, a review of all HCV patients registered in the InfCare database was performed. If the reason for "discharged" was not stated, the patients were located in the electronic medical record. If they were still living in the region and without a negative HCV-RNA as their last test result, patients were classified as LTFU and were eligible for the study. In addition to the "discharged" LTFU patients, we found persons registered in the database without discharge or cure who had a positive HCV-RNA without a scheduled appointment for outpatient clinic HCV care. These LTFU patient also were eligible for the interventional phase of the study. Patients LTFU who were contacted in this study are also referred to as "call-back" patients (Figure 1).

Interventional phase: "call back" of LTFU patients

The intervention phase started in November 2019, when LTFU patients from the Department of Infectious Disease, Odense University Hospital, received a letter informing them of the new HCV treatment possibilities and offering a treatment appointment. At the Infectious Disease outpatient clinic in Kolding, Sygehus Lillebælt the first contact attempt was by phone; if patients did not respond, they received a letter. A specialist in infectious diseases made the phone call. If patients did not respond within 2 months after the first contact attempt, a reminder was sent. In case of non-response, correspondence was sent to their general practitioner (GP) with information about the treatment possibilities and asking for a referral if the

patient was interested. The letters to the GPs were sent in May 2021. Because of the COVID-19 pandemic, the process was delayed by several months.

Patients who responded had the opportunity to receive a full laboratory assessment including HCV-RNA testing, HCV genotyping and FIB4 before the medical check-up and treatment assessment. When blood tests were available, patients were invited for a clinical appointment, including a FibroScan, and treatment was initiated at the first visit. The only planned follow-up was at 12 weeks after completed treatment, and if sustained virological response (SVR) was obtained, the patients were discharged. Patients with suspected or confirmed cirrhosis were offered post-treatment HCC screening according to standard of care. DAA treatment complied with the national guidelines defined by the Danish Medicines Council and was genotype specific. The Council was responsible for the national procurement and use of DAAs. Treating physicians could deviate from the guidelines at their discretion without any delay or inconvenience to the patient. During the study period, recommended treatments were 12 weeks of elbasvir/grazoprevir for patients with genotype 1/4, 8 weeks of glecaprevir/pibrentasvir for patients with genotype 2/3, and 12 weeks of velpatasvir/sofosbuvir for patients with cirrhosis.

Ethics approval

According to Danish law, doctors cannot contact patients once they have been discharged from their clinic. In these cases, because the contact was deemed to be in the best interest of the patients, the Legal Office at the RSD (21/27031) authorized the intervention. The study was approved by the Danish Data Protection Agency (j.nr.: 21/27949).

Data collection and analysis

The characteristics of the 69 individuals eligible for call back were defined through the data in the InfCare hepatitis database. For patients in the non-treated group, the last available data including FibroScan results were used from the database before “discharge.” For patients in the treatment group, the latest FibroScan results before treatment initiation were used.

Descriptive data are reported as absolute numbers, percentages or medians (with interquartile ranges; IQRs). Differences between subgroups were tested for statistical significance using the chi-square test, Mann–Whitney U test, or Kruskal–Wallis test. Analyses were performed using STATA 16.

Results

Retrospective phase

The review of the InfCare database yielded 69 patients with HCV in RSD who were LTFU and eligible for retrieval. Of this group, 19 were associated with the Department of Medicine, Sygehus Lillebælt, Kolding, and 50 patients were from the Department of Infectious Diseases at Odense University Hospital (Figure 2).

Interventional phase

Contact was achieved with 54 (78%) of the 69 eligible call-back patients. Treatment was initiated in 45/69 (65%). Thirteen of the successful contacts (29%) received their medical checkup and treatment through outreach care in a substance use treatment center near their place of residence. One (1%) patient rejected treatment, and 8/69 (12%) expressed interest in treatment but did not attend appointments. No contact was achieved with 15 (22%) of the patients with HCV who were LTFU after two attempts and a letter to

their GP. Of those who initiated treatment, 20 (44%) responded after the first contact by phone or letter, and 18 (40%) responded after the second contact by letter. Seven (16%) patients responded after a letter was sent to their GP (Figure 3). Among those who were treated after the first, second and third contacts, an analysis for differences in age, ethnicity, mode of transmission, use of alcohol or injection drugs, stage of fibrosis, and genotype showed a significant difference only for genotype.

No major differences were found between the treated (n=45) and non-treated groups (n=24), (no contact, n=15; with contact but no treatment started, n=8; rejection of treatment, n=1). The only significant difference between the groups was the availability of a FibroScan result. Both groups were majority male, and the median age for the whole group was 43.1, but the treatment group was numerically older (median, 44 years). The main mode of transmission was drug use, which was the same in both groups and related to the use of injection drugs. The majority of patients in the treatment group had no reporting of heavy alcohol use (>14 weekly units for women and 21 for men), whereas the non-treated group was evenly split between those who did and did not report heavy use. Overall, nine patients (13%) had significant fibrosis (LSM >10 kpa), seven (10%) had LSM compatible with cirrhosis (>12 kpa) (Table 1) (15). The first patient initiated treatment 3 days after first contact, whereas the latest patient who initiated treatment did so at 977 days (2.7 years) after the first contact attempt. Seventeen patients (37.8%) initiated treatment one year after first contact (Table 2).

Cascade of care

None of the LTFU patients had ever received HCV treatment before call back. Of the initial 69 patients who were LTFU, 43 of 45 who initiated treatment had completed treatment to date, and the remaining two were still in ongoing treatment. Eight patients expressed an interest in treatment but repeatedly did not appear for treatment assessment. Most of this group (6/8) had indicated interest in treatment when contacted by phone. The “response on contact” between the clinics did not differ significantly and 34 of 50 patients (68%) started treatment at Odense University Hospital compared with 11 of 19 (58%) initiating treatment at Kolding. No patient discontinued treatment, and no relapse has been registered so far. Of the 43 patients who completed treatment, 34 achieved SVR, 3 SVR results were pending, 4 were LTFU, and 2 patients died after treatment and before SVR was achieved (Figure 4). The two clinics did not differ significantly in contact efficacy or treatment initiation rates.

Discussion

To our knowledge, this effort is the first HCV call-back project in the Nordic region. We re-traced 78% (n=54) patients and initiated treatment in 65% (n=45). This proportion is higher than previously reported in LTFU studies (10, 16). In the Netherlands, which has a lower HCV prevalence than Denmark, a national program for retrieving LTFU patients has been implemented, and studies have shown that it is feasible in terms of achieving HCV elimination (17, 18). In several regions of the Netherlands, patients have been “called back” for treatment. In a study from the South Limburg region 308 HCV patients were contacted and 29% responded (10). In a study from the Utrecht province, 269 HCV patients were contacted, but only 17.4% (n=47) responded. Of those, 42 had chronic HCV and 25 were cured, had results pending, or were scheduled for treatment (16).

The high call-back efficacy in our study may relate to several factors. We contacted only individuals who had been patients in our outpatient clinics. We did not systematically ask about the reason for dropout, but

our impression is that the vast majority did so because of the lack of accessible treatment options before the DAA era. Nevertheless, it was probably easier for LTFU patients to return for treatment if they were invited by letter to the clinic they had previously attended instead of to an unfamiliar department (16).

The option to be treated at a local substance use treatment center probably contributed to the high treatment uptake in our study. Of 45 treated patients, 29% (n=13) were treated through this outreach intervention. The longer distance to HCV treatment clinics is linked to decreased treatment uptake. Simpson et al found that people living within <4 km from their HCV treatment clinic had a 1.22 higher odds of being treated compared with those living further away (19). One LTFU study from Spain, which examined factors related to non-attendance at a HCV treatment clinic, showed that OAT was a predictor of non-attendance (20). By offering treatment at a local substance use treatment center, we eliminated the distance obstacle and integrated hepatitis treatment with regular OAT (21).

Multiple visits to initiate treatment are a known risk factor for dropping out of the cascade of care, but at the time of this study, we had to allow for 4–6 weeks of processing time for HCV genotyping. With complete blood work available at a local laboratory immediately after contact, the patient only needed one visit at the clinic that initiated treatment. This factor might also have been important in retaining patients in care once contact was made (22). In the latest national guidelines (2022), pan-genotypic treatment is now allowed if patients are at high risk for being LTFU, allowing the physician to treat at the first encounter (23).

Our findings indicate that repeated contact attempts improved call-back efficiency considerably. We contacted patients by phone or letter in several attempts. In a comparison of the two contact strategies, contact by phone seems to have been easier but did not seem to have been an advantage in terms of treatment response. The group who received a letter had taken the effort to make an appointment, whereas the phone group did not. The fact that eight patients indicated an interest in treatment, but never attended clinic could indicate that showing interest in treatment is easier than attending clinic. Supporting this inference is the fact that all LTFU patients who did attend clinic after their retrieval initiated treatment and fulfilled it. If we could engage other healthcare settings that patients contact or could identify peers who could motivate patients to enter treatment, we might be able to reach even more of them, especially the 12% who indicated interest in treatment (24).

Our study had 22% non-respondents to our repeated contact attempts. We believe that reaching this "hard-to-reach" group requires dedicated and experienced HCV staff. We have therefore engaged an outreach mobile clinic with dedicated personnel to increase uptake further (25). A major limitation of this study, however, is that the reason patients did not respond is a matter of speculation. In other studies, a high alcohol intake has been a barrier to treatment initiation, and we had a numerically but non-significantly higher intake of alcohol in the non-treated group (26). The InfCare database contains no information about living conditions, which is another study limitation and reduces knowledge about the patient's background.

We included only patients who had attended our clinic in this study. There remains a large group of individuals who once had a positive HCV test but never attended clinical care. This group could not be contacted for legal reasons at the time, but fortunately, the ministry of health overruled this prohibition in 2020. Now more than 3000 possible HCV patients in Denmark have been contacted and are in the process of being offered treatment in the so-called "call-in" initiative. Thus far, the efficacy of "call in" in RSD has

been somewhat lower than for call back, but we hope that the data we present here can be used to improve the ongoing call-in process (Peer Brehm Christensen, personal communication).

The call-back intervention took place during the COVID-19 pandemic, which significantly prolonged its duration. Our outpatient clinics were partially closed for HCV patients during 2020-2021, and it is possible that we might have had even higher efficacy if treatment had not been deferred for patients (27).

In a low-prevalence HCV setting, it is very efficient to treat identified patients with HCV who have been LTFU. However, this effort should be made in combination with other initiatives trying to detect the group of undiagnosed, e.g., by screening in the general population (28). To trace those diagnosed with HCV infection and initiate treatment is an important milestone, however, and on the road to HCV elimination by 2030, every patient counts.

Acknowledgments

The authors thank nurses Trine Sølund Bager and Mie Rønnebæk in the hepatitis outpatient clinic, Department of Infectious Disease, Odense University Hospital, and Department of Medicine, Sygehus Lillebælt, Kolding, for their great commitment.

Disclosure statement

SD has received speaker fees from Gilead, Abbott and AbbVie, travel support from Gilead and AbbVie, and research grants from Gilead. PBC has received research grants from Gilead, AbbVie, and MSD. ALHØ has received research grants from Gilead and speaker fees and travel support from Gilead, AbbVie, and MSD. JFH has received travel support from Gilead, AbbVie, and MSD. BTR has no conflicts of interest.

Funding

The C-Free South Project is funded by the C.H.I.M.E. grant by Gilead Sciences (ISR-DK-18-10469). The Region of Southern Denmark and the University of Southern Denmark, Odense, have supported the work. The financial supporters have not been involved in this work.

ORCID

Sandra Dröse 0000-0002-0282-595X

Janne Fuglsang Hansen 0000-0002-8039-0699

Birgit Thorup Røge 0000-0003-2170-7665

Anne Lindebo Holm Øvrehus 0000-0002-2594-6500

Peer Brehm Christensen 0000-0003-1394-058X

1. WHO. Global Health Sector Strategy on Viral Hepatitis, 2016-2021: towards ending viral hepatitis.; 2018 Publication date: June 2016. Report No.: WHO reference number: WHO/HIV/2016.06.
2. Global change in hepatitis C virus prevalence and cascade of care between 2015 and 2020: a modelling study. The lancet Gastroenterology & hepatology. 2022.
3. WHO. Interim Guidance for country validation of viral hepatitic elimination. World Health Organization 2021: WHO; 2021 June 2021.
4. Foundation C. Countries/ Territories achieving relative or absolute impact and programmatic targets - HCV 2023 [Available from: https://cdafound.org/polaris-countries-maps/.
5. Nielsen S, Hansen JF, Hay G, Cowan S, Jepsen P, Omland LH, et al. Hepatitis C prevalence in Denmark in 2016-An updated estimate using multiple national registers. PLoS One. 2020;15(9):e0238203.
6. lægemiddelrekommandation M. Medicinrådets fælles regionale behandlingsvejledning med lægemiddelrekommandation for kronisk hepatitis C - valg mellem lægemidler. 2018.
7. Dröse S, Øvrehus ALH, Holm DK, Madsen LW, Mössner BK, Søholm J, et al. A multi-level intervention to eliminate hepatitis C from the Region of Southern Denmark: the C-Free-South project. BMC infectious diseases. 2022;22(1):202.
8. Safreed-Harmon K, Blach S, Aleman S, Bollerup S, Cooke G, Dalgard O, et al. The Consensus Hepatitis C Cascade of Care: Standardized Reporting to Monitor Progress Toward Elimination. Clin Infect Dis. 2019;69(12):2218-27.
9. Aleman S, Soderholm J, Busch K, Kovamees J, Duberg AS. Frequent loss to follow-up after diagnosis of hepatitis C virus infection: A barrier towards the elimination of hepatitis C virus. Liver international : official journal of the International Association for the Study of the Liver. 2020;40(8):1832-40.
10. Heil J, Soufidi K, Stals F, Frantzen H, Robroek-Schaecken A, Bakker CM, et al. Retrieval and re-evaluation of previously diagnosed chronic hepatitis C infections lost to medical follow-up in the Netherlands. Eur J Gastroenterol Hepatol. 2020;32(7):851-6.
11. Francesca Romana P, Francesco S, Massimo S, Antonio Giulio B, Annalisa T, Vincenzina M, et al. Missed linkage to care for patients who screened positive for Hepatitis C in a tertiary care center: results of the Telepass project. J Viral Hepat. 2021.
12. van Dijk M, Drenth JPH. Loss to follow-up in the hepatitis C care cascade: A substantial problem but opportunity for micro-elimination. J Viral Hepat. 2020;27(12):1270-83.
13. Yen HH, Su PY, Liu, II, Zeng YH, Huang SP, Hsu YC, et al. Retrieval of lost patients in the system for hepatitis C microelimination: a single-center retrospective study. BMC Gastroenterol. 2021;21(1):209.
14. Mössner B HJ, Øvrehus A, Nymark A, Christensen PB. Patienter med Viral Hepatitis B og C Region Syd, Midt og Nord Årsrapport 2016.

Report of patients with Viral hepatitis in the West of Denmark 2016 from the clinical database Infcare Hepatitis. (in Danish). 2017.
15. Afdhal NH, Bacon BR, Patel K, Lawitz EJ, Gordon SC, Nelson DR, et al. Accuracy of fibroscan, compared with histology, in analysis of liver fibrosis in patients with hepatitis B or C: a United States multicenter study. Clin Gastroenterol Hepatol. 2015;13(4):772-9.e1-3.
16. Kracht PAM, Arends JE, van Erpecum KJ, Thijsen SFT, Vlaminckx BJM, Weersink AJL, et al. REtrieval And cure of Chronic Hepatitis C (REACH): Results of micro-elimination in the Utrecht province. Liver international : official journal of the International Association for the Study of the Liver. 2019;39(3):455-62.
17. Isfordink CJ, Brakenhoff SM, van Dijk M, van der Valk M, de Knegt RJ, Arends JE, et al. Hepatitis C elimination in the Netherlands (CELINE): study protocol for nationwide retrieval of lost to follow-up patients with chronic hepatitis C. BMJ open gastroenterology. 2020;7(1):e000396.

18. Isfordink CJ, van Dijk M, Brakenhoff SM, Kracht PAM, Arends JE, de Knegt RJ, et al. Hepatitis C Elimination in the Netherlands (CELINE): How nationwide retrieval of lost to follow-up hepatitis C patients contributes to micro-elimination. Eur J Intern Med. 2022.
19. Simpson H, Manley P, Lawler J, Morey S, Buchanan E, Hewett M, et al. Distance to treatment as a factor for loss to follow up of hepatitis C patients in North East England. Journal of Public Health. 2018;41(4):700-6.
20. Del Pino Bellido P, Guerra Veloz MF, Cordero Ruíz P, Bellido Muñoz F, Vega Rodriguez F, Caunedo Álvarez Á, et al. CHRONIC HEPATITIS C PATIENTS LOST IN THE SYSTEM: PREDICTIVE FACTORS OF NON-REFERRAL OR LOSS OF FOLLOW UP TO HEPATOLOGY UNITS. Rev Esp Enferm Dig. 2021.
21. Dröse S CP, Holm DK, Røge BT, Øvrehus A. Baseline capability for hepatitis test and treatment in drug treatment clinics in the

Region of Southern Denmark- a pre-elimination intervention assessment. INHSU; Sydney, Australia2021.
22. Cunningham EB, Wheeler A, Hajarizadeh B, French CE, Roche R, Marshall AD, et al. Interventions to enhance testing, linkage to care, and treatment initiation for hepatitis C virus infection: a systematic review and meta-analysis. The lancet Gastroenterology & hepatology. 2022;7(5):426-45.
23. Medicinrådet. Medicinrådets lægemiddelrekommandation og behandlingsvejledning vedrørende lægemidler til hepatitis C. 2022.
24. Silano JA, Treloar C, Leadbeatter K, Davidson S, Doidge J. Peer-facilitated treatment access for hepatitis C: the Live Hep C Free project. Harm Reduct J. 2022;19(1):40.
25. Droese S, Madsen LW, Harvald GB, Grinderslev S, Kofoed K, Kræmer L, et al. Screening for hepatitis C in Denmark-the effect of a mobile outreach intervention. Journal of hepatology. 2022;77:S550.
26. Mason K, Dodd Z, Guyton M, Tookey P, Lettner B, Matelski J, et al. Understanding real-world adherence in the directly acting antiviral era: A prospective evaluation of adherence among people with a history of drug use at a community-based program in Toronto, Canada. The International journal on drug policy. 2017;47:202-8.
27. Blach S, Kondili LA, Aghemo A, Cai Z, Dugan E, Estes C, et al. Impact of COVID-19 on global hepatitis C elimination efforts. Journal of hepatology. 2020.
28. Wentworth JJ, Øvrehus ALH, Hansen JF, Biesenbach P, Christensen PB. Emergency department testing is feasible but ineffective to eliminate hepatitis C in Denmark. Infect Dis (Lond). 2021;53(12):930-41.

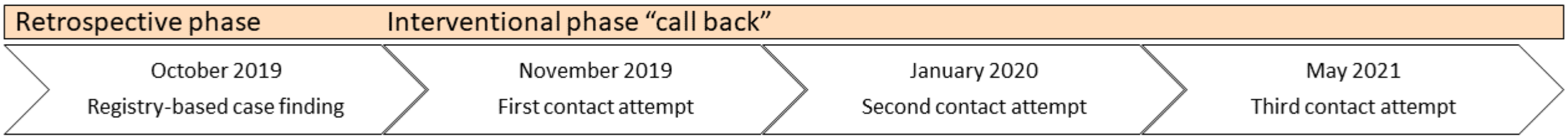

Figure 1. Flow of study design

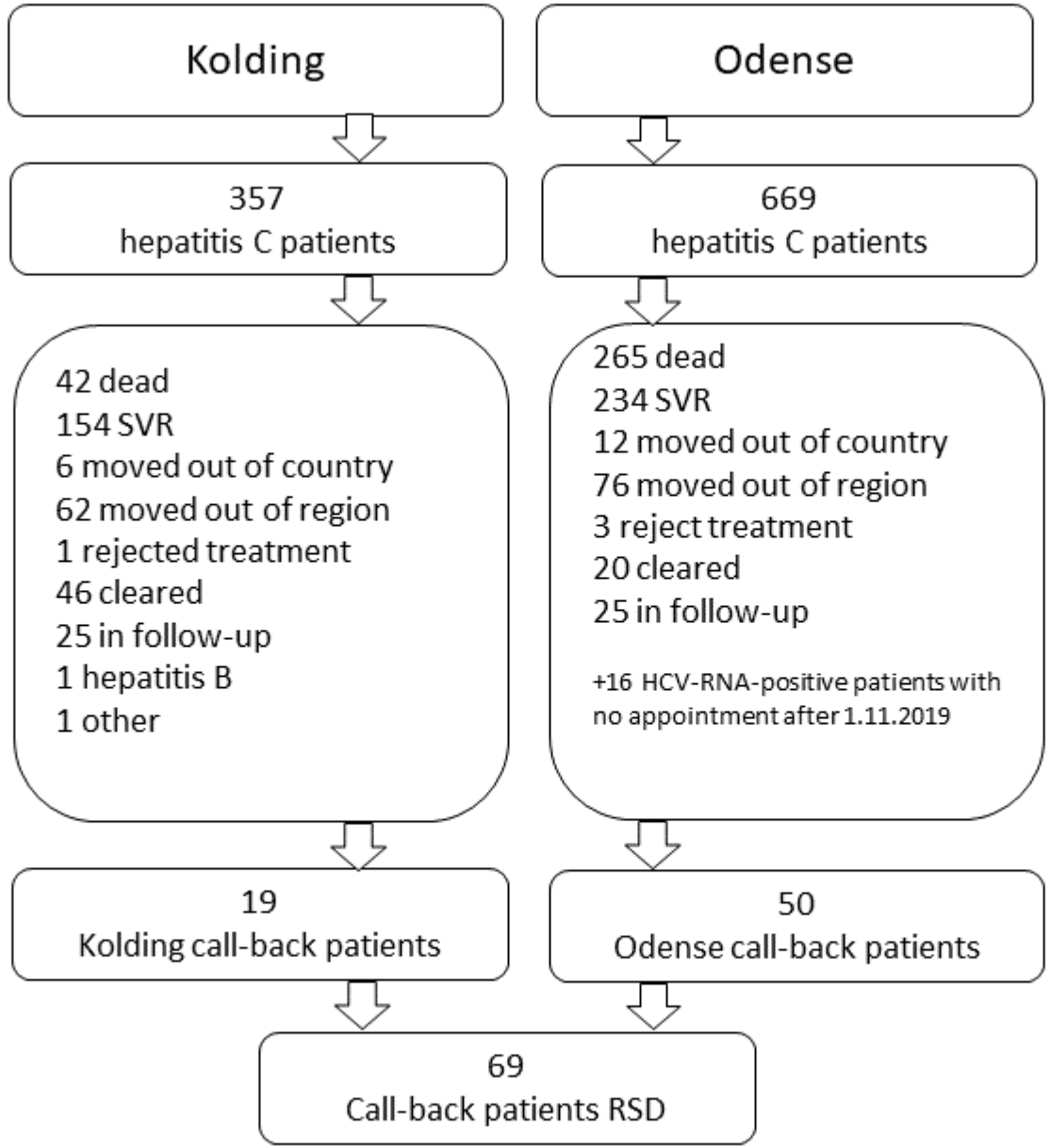

Figure 2 Flowchart of the identification in the database of patients lost to follow-up

- RSD: Region of Southern Denmark; SVR: Sustained virological response

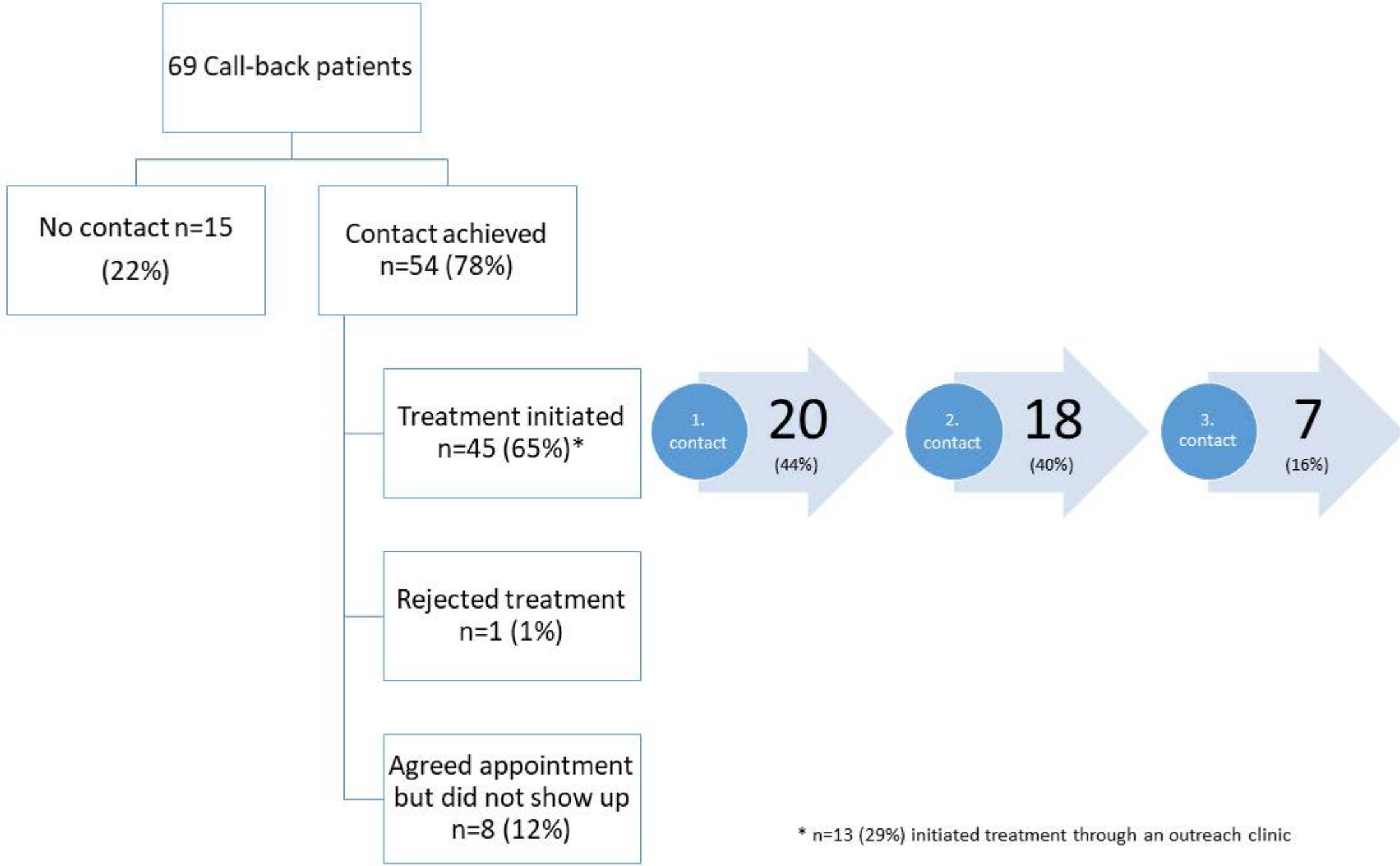

Figure 3. Flowchart of call-back patients and an overview of how many persons initiated treatment after each contact attempt

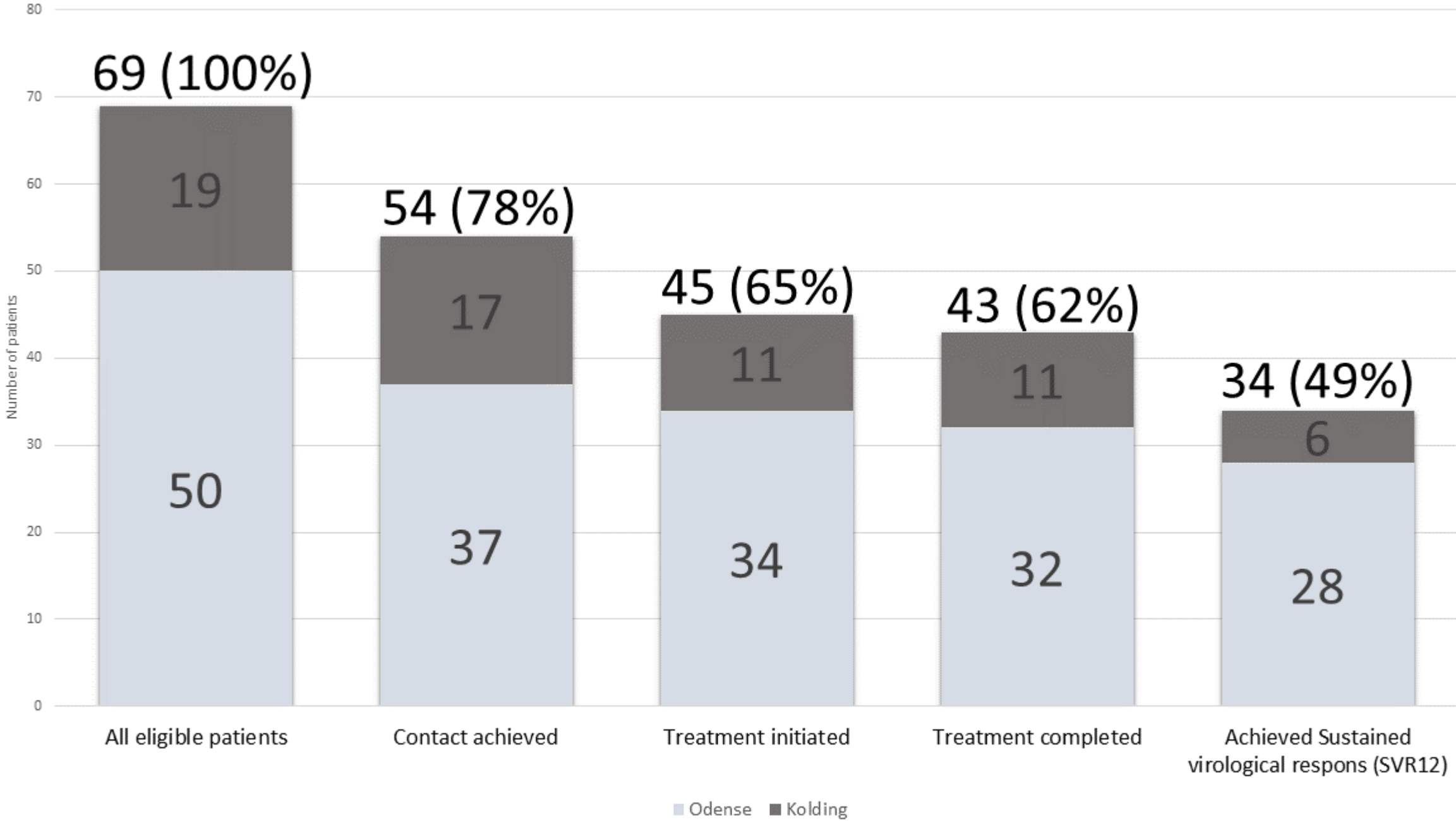

Figure 4. Cascade of care of traced call-back patients

Table 1. Characteristics of hepatitis C patients lost to follow-up

	All (N=69)	Treated (n=45)	Non-treated (n=24)	P value
Age in years, median (IQR)	43.1 (34.8–49.4)	44.0 (33.2–49.5)	42.8 (36.7–48.3)	.239[M]
Male sex, n (%)	51 (74)	33 (73)	18 (75)	.881[C]
Ethnicity, n (%)				.862[K]
White	46 (66.7)	28 (62.2)	18 (75)	
Non-white	5 (7.2)	3(6.7)	2 (8.3)	
Unknown	18 (26.1)	14 (31.1)	4 (16.7)	
Last day of registration in the InfCare database before retrieval, n (%)				.858 [C]
<January 1, 2015	13 (18.9)	8 (17.8)	5 (20.8)	
>January 1, 2015 < October 31, 2018	33 (47.8)	21 (46.7)	12 (50)	
>November 1, 2018	23 (33.3)	16 (35.5)	7 (29.2)	
Mode of HCV transmission, n (%)				.942[K]
Drug use	44 (63.8)	30 (66.7)	14 (58.3)	
Sexual route (no other risk)	4 (6.4)	3 (6.7)	1 (4.2)	
Tattoo or drug use	1 (1.4)	1 (2.2)	0	
Sexual route or drug use	2 (2.9)	0	2 (8.3)	
Other	1 (1.4)	1 (2.2)	0	
Unknown	17 (38.6)	10 (22.2)	7 (29.2)	
Heavy alcohol consumption (ever >14 units weekly for women, 21 units weekly for men), n (%)				.487[C]
Yes	23 (33.3)	14 (31.1)	9 (37.5)	
No	30 (43.5)	21 (46.7)	9 (37.5)	
Unknown	16 (23.2)	10 (22.2)	6 (25.0)	
History of injection drug use, n (%)				.812[C]
Yes	40 (58.0)	28 (62.2)	12 (50.0)	
No	15 (21.7)	10 (22.2)	5 (20.8)	
Unknown	14 (20.3)	7 (15.6)	7 (29.2)	
FibroScan LSM examination in database, n (%)				.001[C]
Yes	64 (93.0)	45 (100)	19 (79.2)	
No	5 (7)	0	5 (20.8)	
FibroScan LSM in kpa, median (IQR)	5.6 (4.8–7.9)	5.6 (5.0–7.6)	5.6 (4.5–8.1)	.791[M]

LSM ≤10 kpa, n	55	36	19	.110[C]
LSM >10 kpa <12 kpa, n (%)	2 (3)	2 (4)	0	
LSM >12 kpa, n (%)	7 (10)	7(16)	0	
Genotype				.256[C]
1	28	18	10	
2	4	4	0	
3	21	15	6	
4	2	2	0	
6	1	0	1	
Unknown	13	6	7	

M=Mann–Whitney U test; C=Chi-square test; K=Kruskal–Wallis test

LSM: Liver stiffness measure

	All treated	<12 weeks	>12 weeks <12 month	>12 month
Initiated HCV treatment, n (%)	45 (100)	12 (26.7)	16 (35.5)	17 (37.8)
Days from first contact until treatment initiation, median (IQR)	230 (41–734)	43 (23–68)	164 (113–239.5)	601 (459–734)

Table 2. Time in days from first contact attempt until treatment initiation divided in groups