RESEARCH LETTER

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Expanding access to hepatitis C treatment by improving linkage to care: Establishing a cascade of care and active linkage program for the South Karelia region in Finland

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1 | INTRODUCTION

Chronic infection with hepatitis C virus (HCV) is associated with significant morbidity and all-cause mortality. Recent advances in treatment have made the disease curable for all patient groups, including those previously considered uncurable.¹ To treat patients in need of care, those with chronic HCV must be identified with adequate testing methods. However, to conduct testing and subsequently refer patients to treatment, the relevant individuals must be first linked and attached to care.

Finland's Hepatitis C Strategy has estimated that there are more than 30 000 persons infected with HCV living in Finland as of 2019 (Finland's Hepatitis C Strategy for 2017-2019, available online). By the end of 2018, 31 647 HCV-antigen-positive cases had been entered into Finland's National Infectious Diseases Register since the establishment of the register in 1998 (Infectious Diseases Register, accessed April 2020). In Finland, around 1150 persons are infected each year, and the disease burden is slowly increasing because the amount of treatment given has fallen behind the number of persons requiring treatment.² In a recent meta-analysis by Fraser et al,³ it was suggested that the rate of treatment should be increased 200 times in Finland to reduce HCV prevalence to 30% by 2030. In a global review by Razavi et al,⁴ it was concluded that 80% of high-income countries are not on track to meet HCV elimination targets by 2030, and 67% are off track by at least 20 years. Immediate action to improve HCV screening and treatment globally was suggested to make HCV elimination attainable.

Drug use has previously prevented the provision of treatment, but this barrier was lifted in 2018. A national strategy (Finland's Hepatitis C Strategy for 2017-2019, 2016) and national recommendation on the cascade of care² determined that all persons should be tested and treated regardless of their drug user status.

Finland has a very low population density of 39 people per square mile (15 people per square kilometer), which ranks 171st in the world and makes Finland one of the most sparsely populated countries of the European Union (World Population Review, 2020). For this reason, the national recommendation is to establish regional treatment plans and programs. South Karelia (population: 130 000) is region located by the Russian border, with the highest reported incidence for HCV in Finland (Infectious Diseases Register, accessed April 2020).

This paper reviews the real-life outcome of the South Karelia Linkage to Care program, which combined data from the National Infectious Diseases Register and social registries to identify living HCV-antigen-positive persons still residing in the region. These persons were tracked down, contacted, and finally motivated for testing to identify individuals with chronic HCV and provide them with a treatment plan. In addition, the persons' data were entered into an electronic regional Hepatitis C register, and the experience gained in the program was used to create a regional cascade of care, in harmony with the global WHO goals.

2 | SUBJECTS AND METHODS

2.1 | Linking patients to care

This retrospective real-world register analysis was approved by the committee of the Southern Karelia Central Hospital, decision number

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EKS/1392/13.01.05/2019. At the beginning of the project, national social welfare and infectious disease registers were used to identify all HCV-antigen-positive persons (name, social security number, address or other identification parameters) still residing in the area. In addition, the cause of death register was used to exclude those who had deceased. The second step was to check the HCV RNA status of those identified in the previous phase based on their medical records and to recognize patients who had already received treatment or were HCV RNA negative. Those whose HCV RNA status was unknown were contacted either by telephone, letter, or social media. Newspaper announcements and posters on various kinds of addiction service sites were also used to invite persons for testing if they had any suspicion of an HCV infection. If no contact information was found, persons using services relevant based on the missing individuals' medical records (opioid substitution therapy or needle exchange programs) were utilized to reach the missing individuals or forward the request to them. When the individuals were found, they were invited to visit the clinic so that a treatment plan could be prepared or their HCV RNA status determined if previously unknown. In addition, the individuals were provided with information about the disease and the change in treatment policies in Finland. Information about those who could not be reached by any method was provided to the local health centers based on their latest known residence to test them for HCV RNA later if they visited the health services.

The regional cascade of care was adapted from the national recommendation. All health service providers (primary care, specialized hospital care, substance addiction, and social services) in the region were notified, enrolled in the program, and trained to provide information about the patients' right to get tested for their HCV antigen status as well as general information about the disease. Patient data collected from the medical records available in all of the sources were used to establish an electronic regional HCV registry.

3 | RESULTS

The demographic and clinical characteristics of the HCV-antigenpositive subjects are presented in Table 1. Male gender was more frequent among the population, and the median age was 40.7 years. Due to removal for the requirement to define the genotype, genotype had been defined from only 118 subjects and was similar to national prevalence (Finland's Hepatitis C Strategy for 2017-2019, available online). Fibroscan measurements were rare, as APRI, according to recommendations, APRI score (AST to Platelet Ratio Index) is used as the primary diagnostic method to investigate the state of liver health. In total, 97 patients had initiated treatment, of which 81 received SVR12. Thirteen patients were lost to follow-up or did not attend SVR12 testing. Seventy-four patients experienced a spontaneous recovery.

Figure 1 summarizes the study results. In the beginning of the project, 525 persons with an HCV-antigen-positive status were identified as alive and still residing in the South Karelia region. Of those persons, 81 had been treated and 74 had experienced a spontaneous recovery. Totally, 370 people were identified as potentially HCV RNA

TABLE 1 Clinical and demographic characteristics

Total HCV antigen positive	539
Male gender	366 (67.9%)
Median age	40.7
Genotype	n = 118
1a	25 (21.2)
1b	20 (15.6)
1a/1b	6 (5.1)
1 not specified	12 (10.2)
2	14 (11.9)
3	40 (33.9)
3a/1b	1 (0.01)
Fibroscan	n = 42
FO	10
F1	15
F2	7
F3	7
F4	3
Treatment initiated	97/539 (18.0)
Spontaneous recovery	74/539 (13.6)
Received SVR12	81/94 (86.2)
Lost to follow-up	13/94 (13.8)

Note: % given in parenthesis.

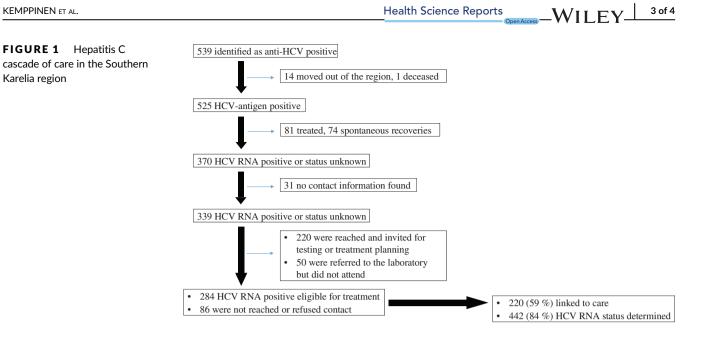
positive and invited for either further testing if their HCV RNA status was unknown, or for treatment evaluation if they were found to be HCV RNA positive. Of these 370 individuals, some type of contact information was obtained for 339 individuals. Of these 339, a total of 220 individuals could be reached. Information on some of the individuals' HCV RNA status was obtained from their medical records without establishing contact with the person. Additional testing was conducted on a proportion of the individuals whose HCV RNA status was previously unclear or who were determined to continue high-risk behavior such as IV drug use. Fifty of the individuals who had been referred to the laboratory did not attend testing and contact with them was lost. Finally, at least 284 individuals were confirmed to be HCV RNA positive and remained untreated at the time. All of those motivated to start treatment received a treatment plan.

At the end of the project, 220 out of the potential 370 HCV RNApositive individuals were linked to care. Eighty-six individuals could either not be reached or had no record of their HCV RNA status. HCV RNA status was determined for 442 individuals out of the 525 HCVantigen-positive people identified at the beginning of the project.

4 | DISCUSSION

Our program aimed to clarify the HCV RNA status of HCV-antigenpositive individuals living in the Southern Karelia region and link all traced HCV RNA-positive people to care. At the end of the project,

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the HCV RNA status of 84% of the HCV-antigen-positive population had been determined. In addition, 59% of the patients were linked to care. Lack of motivation to get tested and start treatment was identified as the biggest barrier for linking patients to care. Persons identified as actively using drugs emerged as the subpopulation requiring more extensive psychosocial interventions to achieve attachment to care. Ninety individuals in our cohort reported having used IV drugs during the previous year. Individuals aged 20 to 25, 25 to 30, and 30 to 35 years were less motivated to start treatment in comparison with other age groups.

The barriers for linking individuals to care involved many traditional aspects reported elsewhere.⁵⁻⁹ Disease awareness was generally low among the individuals, with some of them commenting that since they had no symptoms, they were not motivated to start treatment. Most individuals still thought that drug abstinence was a requirement for receiving treatment and were not aware of directacting antivirals. Prejudices and previous negative experiences of using healthcare services were also frequently described. Fear of stigmatization was given as a reason by many of those individuals who were currently employed and not actively using drugs. They reported wanting to avoid additional entries on HCV in their medical records. By contrast, many were motivated to start treatment after receiving information about the current treatment policy and options as well as general information about the disease. Many had been waiting for an opportunity to be treated.

Long geographical distances have traditionally posed a challenge for healthcare in Finland and other sparsely populated countries. For this reason, networking within the healthcare system and collaboration between the service providers essential to reaching the goals even at a regional level. Primary health service providers would generally need additional resources to initiate HCV treatments because of a lack of centralized funding in Finland. For this reason, their contribution to this program was limited and not in harmony with the national recommendation.

This program successfully established a cascade of care for linking, testing, and treating HCV-positive persons in the Southern Karelia region. An electronic HCV register was established and deemed essential for following and maintaining treatment goals and continuing to support those treated with regular follow-ups and counseling.

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CONFLICT OF INTEREST

The authors do not have any conflicts or competing interests to declare.

AUTHOR CONTRIBUTIONS

Conceptualization: Juha Kemppinen, Sauli Vuoti, Pekka Suomalainen Formal analysis: Juha Kemppinen, Hanna-Kaisa Anttila, Sauli Vuoti Writing - original draft: Sauli Vuoti, Hanna-Kaisa Anttila, Juha Kemppinen Writing - review and editing: Sauli Vuoti, Juha Kemppinen, Pekka Suomalainen

All authors have read and approved the final version of the manuscript.

Sauli Vuoti had full access to all of the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis.

DATA AVAILABILITY STATEMENT

The authors confirm that the data supporting the findings of this study are available within the article.

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