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Homelessness and Hepatitis A—San Diego County, 2016–2018

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Abstract

Background.—Hepatitis A is a vaccine-preventable viral disease transmitted by the fecal-oral route. During 2016–2018, the County of San Diego investigated an outbreak of hepatitis A infections primarily among people experiencing homelessness (PEH) to identify risk factors and support control measures. At the time of the outbreak, homelessness was not recognized as an independent risk factor for the disease.

Methods.—We tested the association between homelessness and infection with hepatitis A virus (HAV) using a test-negative study design comparing patients with laboratory-confirmed hepatitis A with control subjects who tested negative for HAV infection. We assessed risk factors for severe hepatitis A disease outcomes, including hospitalization and death, using multivariable logistic regression. We measured the frequency of indications for hepatitis A vaccination according to Advisory Committee on Immunization Practices (ACIP) guidelines.

Results.—Among 589 outbreak-associated cases reported, 291 (49%) occurred among PEH. Compared with those who were not homeless, PEH had 3.3 (95% confidence interval [CI], 1.5–7.9) times higher odds of HAV infection, 2.5 (95% CI, 1.7–3.9) times higher odds of hospitalization, and 3.9 (95% CI, 1.1–16.9) times higher odds of death associated with hepatitis A. Among PEH, 212 (73%) patients recorded other ACIP indications for hepatitis A vaccination.

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Author contributions.

C. M. P. and S. S. S. analyzed the information. Y. L. and S. R. performed molecular testing and analysis. C. M. P., S. S. S., and E. C. M. wrote the initial draft. All authors contributed to the writing, revision, and finalization of the manuscript.

Disclaimer.

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Potential conflicts of interest.

The authors report no potential conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

Conclusions.—PEH were at higher risk of infection with HAV and of severe hepatitis A disease outcomes compared with those not experiencing homelessness. Approximately one-fourth of PEH had no other ACIP indication for hepatitis A vaccination. These findings support the recent ACIP recommendation to add homelessness as an indication for hepatitis A vaccination.

Keywords

hepatitis A; homelessness; hepatitis A vaccine

Infection with hepatitis A virus (HAV) is characterized by acute onset of jaundice, fatigue, diarrhea, and other signs and symptoms of acute liver infection. Transmission of HAV follows the fecal-oral route through person-to-person contact or ingestion of contaminated water or food, but can be interrupted through improvements in drinking water, sanitation, hygiene, and vaccination [1]. During 1994–1998, the County of San Diego Health and Human Services Agency (COSD) reported approximately 500 hepatitis A cases per year [2]. After the introduction of routine childhood hepatitis A vaccination in California in 1999 and nationwide in 2006, the number of cases decreased to 40 or fewer cases each year, most of which were travel associated [2].

During November 2016–May 2018, San Diego County experienced an outbreak of hepatitis A notable for a high proportion of cases among people experiencing homelessness (PEH) or people who used illicit drugs (injection or noninjection) during their exposure period [3]. At the time of the outbreak, the Advisory Committee on Immunization Practices (ACIP) recommended hepatitis A vaccination for certain people recognized to be at increased risk of HAV infection or severe outcomes attributable to illness, including children, men who have sex with men (MSM), people who travel to countries with high or intermediate rates of HAV, people who use illicit drugs, and people who have chronic liver diseases [4]. Although homelessness was not recognized as an independent risk factor for HAV infection at the time [4, 5], outbreaks of hepatitis A in 2016–2018 in California, Michigan, Utah, Kentucky, and other states among similar risk groups prompted consideration of homelessness as an independent risk factor for HAV infection [6, 7]. On 24 October 2018, the ACIP voted to recommend adding homelessness to the list of hepatitis A vaccine indications [8].

We investigated to assess whether homelessness was an independent risk factor for HAV infection and increased severity of hepatitis A disease during the outbreak in San Diego County. Additionally, we determined whether patients had 1 or more known ACIP indications other than homelessness for hepatitis A vaccination.

METHODS

Case Reporting and Investigation

The COSD received reports of hepatitis A through routine clinical and laboratory surveillance and contacted patients while hospitalized or by personal phone for interview. Upon detection of an increase in hepatitis A reports in March 2017, a supplemental hypothesis-generating questionnaire was developed with targeted questions on homelessness and illicit drug use to complement routine surveillance questions on clinical symptoms,

contact history, and other exposure information. Homelessness was defined as self-reported lack of reliable housing during the 2–7 weeks before illness onset. Vaccination indications according to ACIP at the time were assessed using information on history of international travel, illicit drug use, sexual exposures, and coinfection with either hepatitis B virus (HBV) or hepatitis C virus (HCV) documented by hepatitis B surface antigen positivity, HCV antibody positivity, or HCV RNA detection.

Serum specimens positive for immunoglobulin M (IgM) antibody to HAV were requested from the hospital or diagnostic laboratory to test for the presence of HAV RNA using reverse transcriptase–polymerase chain reaction (RT-PCR), the most sensitive and widely used method for assessing HAV viremia [9]. Serum specimens collected within 4 weeks after symptom onset were considered for testing. Next-generation sequencing was used to amplify a 315–base-pair fragment of the VP1-P2B region to differentiate the *IB* genotype attributed to the outbreak from the genotypes common in North America, such as *IA* [10, 11]. Molecular characterization and genotype assessment were conducted by the Centers for Disease Control and Prevention (CDC) Division of Viral Hepatitis Branch Laboratory, the California Department of Public Health Viral and Rickettsial Disease Laboratory, and the San Diego Public Health Laboratory.

Case Assessment

We defined a confirmed case as isolation of HAV genotype *IB* in a resident of San Diego County with acute onset of hepatitis A symptoms during 1 November 2016–23 May 2018 (Table 1). In the absence of serum available for RT-PCR testing, we defined a probable case as signs or symptoms consistent with acute viral hepatitis, evidence of either jaundice or elevated aminotransferase levels, and either positive IgM antibody to HAV or an epidemiologic link to a laboratory-confirmed case [12]. We defined a control subject as a patient reported by routine surveillance to COSD for suspicion of hepatitis A but who tested negative for HAV by RT-PCR.

Risk Factor Analysis: Hepatitis A Virus Infection

To test for an association between homelessness and infection with HAV, we used a test-negative study design comparing confirmed case-patients with control subjects. Because of the strict use of RT-PCR criteria, probable cases were excluded from the test-negative study. We calculated crude and adjusted infection odds ratios (ORs) for homelessness using univariate and multivariable logistic regression models built by backwards stepwise selection (retention $P < .10$) of known risk factors for HAV infection (ie, international travel, MSM, or illicit drug use) and age and sex. This time- and resource-efficient study design has been used to study risk factors for dengue [13] and more broadly for estimating vaccine efficacy against influenza [14–16], rotavirus [17], cholera [18, 19], and pneumococcus [20]. The method reduces misclassification bias through use of strict laboratory criteria and reduces bias attributable to differential health-seeking behavior by including only those patients who sought care.

Risk Factor Analysis: Hepatitis A Disease Severity

To test for an association between homelessness and clinical severity of hepatitis A, we assessed 2 outcomes as follows: hospitalization and death from causes associated with hepatitis A. We determined if death was associated with hepatitis A through expert review of cause of death and contributing conditions listed on death certificates. Among confirmed and probable cases, we calculated crude and adjusted ORs between homelessness and each outcome using univariate and multivariable logistic regression models built by backwards selection ($P < .10$) of age, sex, illicit drug use, MSM, and coinfection with either HBV or HCV.

The CDC reviewed this study for human subjects protection and deemed it to be nonresearch. Patient data were collected confidentially by epidemiology program staff for public health response activities and stored in a secure Confidential Morbidity Report system by COSD.

RESULTS

During 1 November 2016–23 May 2018, a total of 589 hepatitis A cases were reported; 502 (85%) were confirmed by RT-PCR to match 1 of the genotype *IB* strains (Table 2). Median patient age was 43 years (range, 5–87 years), 400 (68%) were male, and 404 (69%) were hospitalized. Among 20 (3%) patients who died of causes associated with hepatitis A, 19 (95%) had underlying factors (eg, cirrhosis, diabetes, or cardiomyopathy) that may have contributed to increased risk of severe outcomes, 14 (70%) reported homelessness, and 2 (10%) had relapsing HAV infection, defined as recurrent disease within 6 months of last recovery [21]. No patients reported having received the full, 2-dose vaccination series before becoming infected. Among the 589 confirmed and probable cases, outbreak risk factor data were available for 535 (91%), 200 (37%) of whom reported both homelessness and illicit drug use, 91 (17%) reported homelessness only, and 77 (14%) reported illicit drug use only.

Among the 291 patients who reported experiencing homelessness, 79 (27%) did not report any other ACIP indications for vaccination (Table 2). Of the 212 (73%) PEH with at least 1 known indication, 200 (94%) reported illicit drug use, 72 (34%) were coinfected with HBV or HCV, 6 (2.8%) were MSM, and 4 (1.9%) reported recent international travel to Mexico, which is a country with intermediate or high rates of HAV.

Risk Factor Analysis: Hepatitis A Virus Infection

In total, 502 RT-PCR–confirmed case-patients and 96 control subjects with negative RT-PCR results were included for test-negative case-control analysis. Homelessness was reported by 251 (50%) case-patients and 23 (24%) control subjects; the crude OR for infection was 2.4 (95% confidence interval [CI], 1.4–4.1) (Table 3). This association increased to 3.3 (95% CI, 1.5–7.9) after adjustment for age, sex, and international travel in the multiple logistic regression model.

Risk Factor Analysis: Hepatitis A Disease Severity

Among the 589 confirmed and probable cases, 404 (68%) patients were hospitalized and 20 (3%) died. The OR for hospitalization was 3.1 (95% CI, 2.1–4.5) comparing patients reporting homelessness with those not reporting homelessness (Table 4). The adjusted OR for hospitalization was 2.5 (95% CI, 1.7–3.9) after adjustment for illicit drug use and age. Hospitalization and death were more common as patient age increased (Figure 1). The OR for death associated with hepatitis A was not statistically significantly elevated at 2.5 (95% CI, .9–7.8), but after adjusting for age and coinfection with HBV or HCV, the odds of death were 3.9 (95% CI, 1.1–16.9) times higher for patients reporting homelessness than for those not reporting homelessness (Table 5).

DISCUSSION

During a hepatitis A outbreak in San Diego County with approximately 600 reported cases, we identified homelessness as an independent risk factor for HAV transmission and severe hepatitis A disease. Homelessness is a recognized risk factor for a range of health conditions and diseases [22] and has been associated with outbreaks of hepatitis A in the past [23–25], but homelessness was not recognized by the ACIP as an independent risk factor for hepatitis A infection at the time of the outbreak [4, 5].

PEH, especially those who are unsheltered, may be at increased risk of HAV infection because of high population density and inadequate facilities for sanitation and hygiene and at increased risk of severe outcomes because of a high prevalence of associated comorbidities, malnutrition, and alcohol-related liver disease [26]. Studies have reported that homelessness may be an independent risk factor for HAV antibody positivity [27], and targeted vaccination of PEH is feasible [28] and helped control previous outbreaks among PEH [25]. Using the framework of a recent consensus report from the National Academy of Sciences [29], further research should assess whether hepatitis A is a “housing-sensitive condition” from a public health perspective because of risks for PEH acquiring and transmitting HAV.

San Diego City and County, with an estimated 9116 people who were homeless in 2017, ranks fourth highest among US city areas and second only to Los Angeles in the number of people who are homeless and unsheltered [30]. The relatively high burden of homelessness may have contributed to the size and severity of this outbreak. Therefore, COSD targeted interventions toward PEH beginning with the recommendation to vaccinate PEH in the first health alert sent by the county on 10 March 2017 [3]. To reach this population, approximately 2500 HAV vaccination events occurred through stationary points of dispensary, mobile vans, and vaccination foot teams consisting of a nurse and law enforcement officer [31]. Hepatitis A virus vaccinations were also administered by other community partners at homeless shelters, jails, emergency departments, and during influenza vaccination drives. Beyond vaccination, other interventions for this risk group included transitional housing in tent cities, 24-hour public bathrooms and handwashing stations, enhanced street sanitation, targeted health messaging, personal hygiene kits, and temporary convalescent housing after hospital discharge [31].

Case-fatality ratios from recent outbreaks, including San Diego County, are higher than historical outbreaks and may result in part from a shifting case demographic toward older patients [11]. The increasing risk of hospitalization and death among older patients in this outbreak is consistent with previous studies that reported that case fatality increased with age from 0.1% among children aged less than 15 years, 0.3% among people aged 15–39 years, and 2.1% among adults aged 40 years or older [5, 32].

The median age of 43 years among confirmed and probable cases is similar among patients reporting homelessness (median, 44 years) and not reporting homelessness (median, 42 years) and is consistent with contemporaneous outbreaks in other states [11]. While the occurrence of hepatitis A has decreased nationally in all age groups since 2000, incidence of the disease is lowest among persons aged 0–9 years and 10–19 years compared with older age groups as of 2016 [33].

Our study limitations include possible misclassification of sensitive topics including homelessness status and history of illicit drug use, although we expect such misclassification to be independent of case-control status because of the delayed receipt of confirmatory RT-PCR test results. Self-reported vaccination history was cross-referenced and supplemented using the San Diego Immunization Registry, although vaccinations received outside San Diego County are more likely to be missed. The prevalence of comorbidities may be underestimated by using coinfection status with HBV or HCV as an incomplete surrogate for chronic liver disease caused by risk factors such as chronic alcoholism.

In this investigation, we suspect that the measured association between homelessness and HAV infection is likely underestimated, because associations between homelessness and other causes of symptoms consistent with viral hepatitis infection may inflate the prevalence of homelessness among the test-negative control subjects. Additionally, PEH may be preferentially hospitalized for reasons beyond those measured [34, 35], but we expect that the outcome of case fatality is robust to this potential bias.

These findings strongly support the ACIP recommendation to add homelessness as an indication for hepatitis A vaccination [8], as well as the need to improve adult hepatitis A vaccination rates among groups who are at risk and to address the underlying causes of homelessness [26]. Approximately half of all patients in this outbreak, and three-quarters of PEH, had at least 1 previously known ACIP indication for vaccination (Table 2), yet none received the 2-dose HAV vaccination series before infection. Outbreak response vaccination with 1 dose of HAV vaccine was found to be feasible in San Diego County and elsewhere [31, 36, 37], and previous studies have shown that the single vaccine can confer protection for 4–11 years [38, 39].

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References

1. Centers for Disease Control and Prevention. Hepatitis A. In: Hamborsky J, Kroger A, Wolfe S, eds. Epidemiology and prevention of vaccine-preventable diseases. 13th ed. Washington, DC: Public Health Foundation, 2015.
2. County of San Diego Health and Human Services Agency. San Diego County Annual Communicable Disease Report. 2016.
3. County of San Diego Health and Human Services Agency. Hepatitis A virus outbreak associated with homelessness, drug use in San Diego County. 2017; Available at: https://www.sandiegocounty.gov/content/dam/sdc/hhsa/programs/phs/cahan/communications_documents/03-10-17.pdf. Accessed 21 August 2019.
4. Centers for Disease Control and Prevention. Prevention of hepatitis A through active or passive immunization: recommendations of the Advisory Committee on Immunization Practices (ACIP). Morb Mortal Wkly Rep 2006; 55:1–23.
5. World Health Organization. WHO position paper on hepatitis A vaccines—June 2012. Wkly Epidemiol Rec 2012; 87:261–76. Available at: https://www.who.int/wer/2012/wer8728_29/en/. Accessed 21 August 2019. [PubMed: 22905367]
6. Centers for Disease Control and Prevention. Advisory Committee on Immunization Practices (ACIP) summary report. 2017. Available at: https://stacks.cdc.gov/view/cdc/58894. Accessed 21 August 2019.
7. Centers for Disease Control and Prevention. Outbreak of hepatitis A virus (HAV) infections among persons who use drugs and persons experiencing homelessness. 2018. CDC Health Alert Network. Available at: https://emergency.cdc.gov/han/han00412.asp. Accessed 21 August 2019.
8. Doshani M, Weng M, Moore KL, Romero JR, Nelson NP. Recommendations of the Advisory Committee on Immunization Practices for use of hepatitis A vaccine for persons experiencing homelessness. Morb Mortal Wkly Rep. 2019; 68:153–6.
9. Nainan OV, Xia G, Vaughan G, Margolis HS. Diagnosis of hepatitis a virus infection: a molecular approach. Clin Microbiol Rev 2006; 19:63–79. [PubMed: 16418523]
10. Association of Public Health Laboratories. Hepatitis A virus testing and resources. 2018;1–3. Available at: https://www.aphl.org/programs/infectious_disease/Documents/2018_HAV_DiagnosticUpdate.pdf. Accessed 21 August 2019.
11. Foster M, Ramachandran S, Myatt K, et al. Hepatitis A virus outbreaks associated with drug use and homelessness—California, Kentucky, Michigan, and Utah, 2017. Morb Mortal Wkly Rep 2018; 67:2017–9.
12. Council of State and Territorial Epidemiologists. Public health reporting and national notification for hepatitis A. 2011. Available at: www.cste.org/resource/resmgr/PS/11-ID-02.pdf. Accessed 21 August 2019.
13. Yung CF, Chan SP, Thein TL, Chai SC, Leo YS. Epidemiological risk factors for adult dengue in Singapore: an 8-year nested test negative case control study. BMC Infect Dis 2016; 16:323. [PubMed: 27390842]
14. Fukushima W, Hirota Y. Basic principles of test-negative design in evaluating influenza vaccine effectiveness. Vaccine 2017; 35:4796–800. [PubMed: 28818471]
15. Sullivan SG, Tchetgen Tchetgen EJ, Cowling BJ. Theoretical basis of the testnegative study design for assessment of influenza vaccine effectiveness. Am J Epidemiol 2016; 184:345–53. [PubMed: 27587721]
16. Belongia EA, Simpson MD, King JP, et al. Variable influenza vaccine effectiveness by subtype: a systematic review and meta-analysis of test-negative design studies. Lancet Infect Dis 2016; 16:942–51. [PubMed: 27061888]
17. Bar-Zeev N, Kapanda L, Tate JE, et al. Effectiveness of a monovalent rotavirus vaccine in infants in Malawi after programmatic roll-out: an observational and case-control study. Lancet Infect Dis 2015 15(4):422–8. [PubMed: 25638521]
18. Azman AS, Parker LA, Rumunu J, et al. Effectiveness of one dose of oral cholera vaccine in response to an outbreak: a case-cohort study. Lancet Glob Health 2016; 4:e856–63. [PubMed: 27765293]

19. Franke MF, Jerome JG, Matias WR, et al. Comparison of two control groups for estimation of oral cholera vaccine effectiveness using a case-control study design. Vaccine 2017; 35:5819–27. [PubMed: 28916247]
20. Broome CV, Facklam RR, Fraser DW. Pneumococcal disease after pneumococcal vaccination: an alternative method to estimate the efficacy of pneumococcal vaccine. N Engl J Med 1980; 303:549–52. [PubMed: 6995835]
21. Glickson M, Galun E, Oren R, Tur-Kaspa R, Shouval D. Relapsing Hepatitis A: review of 14 cases and literature survey. Medicine 1992; 71: 14–23. [PubMed: 1312659]
22. Aldridge RW, Story A, Hwang SW, et al. Morbidity and mortality in homeless individuals, prisoners, sex workers, and individuals with substance use disorders in high-income countries: a systematic review and meta-analysis. Lancet 2018; 391:241–50. [PubMed: 29137869]
23. Syed NA, Hearing SD, Shaw IS, et al. Outbreak of hepatitis A in the injecting drug user and homeless populations in Bristol: control by a targeted vaccination programme and possible parenteral transmission. Eur J Gastroenterol Hepatol 2003; 15:901–6. [PubMed: 12867801]
24. Tjon GMS, Götz H, Koek AG, et al. An outbreak of hepatitis A among homeless drug users in Rotterdam, The Netherlands. J Med Virol 2005; 77:360–6. [PubMed: 16173016]
25. James TL, Aschkenasy M, Eliseo LJ, Olshaker J, Mehta SD. Response to hepatitis A epidemic: emergency department collaboration with public health commission. J Emerg Med 2009; 36:412–6. [PubMed: 18359602]
26. Kushel M. Hepatitis A outbreak in California—addressing the root cause. N Engl J Med 2018; 378:211–3. [PubMed: 29211622]
27. Hennessey KA, Bangsberg DR, Weinbaum C, Hahn JA. Hepatitis A seroprevalence and risk factors among homeless adults in San Francisco: should homelessness be included in the risk-based strategy for vaccination? Public Health Rep 2009; 124:813–7. [PubMed: 19894423]
28. Poulos RG, Ferson MJ, Orr KJ, et al. Vaccination against hepatitis A and B in persons subject to homelessness in inner Sydney: vaccine acceptance, completion rates and immunogenicity. Aust N Z J Public Health 2010; 34:130–5. [PubMed: 23331355]
29. National Academy of Sciences. Permanent supportive housing. Washington, DC: National Academies Press, 2018. Available at: https://www.nap.edu/catalog/25133/permanent-supportive-housing-evaluating-the-evidence-for-improving-health-outcomes. Accessed 21 August 2019.
30. Regional Task Force on the Homeless. WeALLCount annual comprehensive report. San Diego, 2017. Available at: http://www.rtfhsd.org/wp-content/uploads/2017/07/comp-report-final.pdf. Accessed 21 August 2019.
31. County of San Diego. Hepatitis A outbreak after action report. 2018. Available at: https://www.sandiegocounty.gov/content/dam/sdc/cosd/SanDiegoHepatitisAOutbreak-2017-18-AfterActionReport.pdf. Accessed 21 August 2019.
32. Hollinger F, Ticehurst J. Hepatitis A. In: Fields virology. Philadelphia: Lippincott-Raven, 1996:735–82.
33. Centers for Disease Control and Prevention. Viral hepatitis surveillance—United States, 2016. Available at: https://www.cdc.gov/hepatitis/statistics/2016surveillance/pdfs/2016HepSurveillanceRpt.pdf. Accessed 21 August 2019.
34. Salit SA, Kuhn EM, Hartz AJ, Vu JM, Mosso AL. Hospitalization costs associated with homelessness in New York City. N Engl J Med 1998; 338:1734–40. [PubMed: 9624194]
35. Feigal J, Park B, Bramante C, Nordgaard C, Menk J, Song J. Homelessness and discharge delays from an urban safety net hospital. Public Health 2014; 128:1033–5. [PubMed: 25443103]
36. McMahon BJ, Beller M, Williams J, Schloss M, Tanttila H, Bulkow L. A program to control an outbreak of hepatitis A in Alaska by using an inactivated hepatitis A vaccine. Arch Pediatr Adolesc Med 1996; 150:733–9. [PubMed: 8673200]
37. Zamir C, Rishpon S, Zamir D, Leventhal A, Rimon N, Ben-Porath E. Control of a community-wide outbreak of hepatitis A by mass vaccination with inactivated hepatitis A vaccine. Eur J Clin Microbiol Infect Dis 2001; 20:185–7. [PubMed: 11347668]
38. Hatz C, van der Ploeg R, Beck BR, Frösner G, Hunt M, Herzog C. Successful memory response following a booster dose with a virosome-formulated hepatitis A vaccine delayed up to 11 years. Clin Vaccine Immunol 2011; 18:885–7. [PubMed: 21411599]

39. Iwarson S, Lindh M, Widerström L. Excellent booster response 4–6 y after a single primary dose of an inactivated hepatitis A vaccine. Scand J Infect Dis 2002; 34:110–1. [PubMed: 11928839]

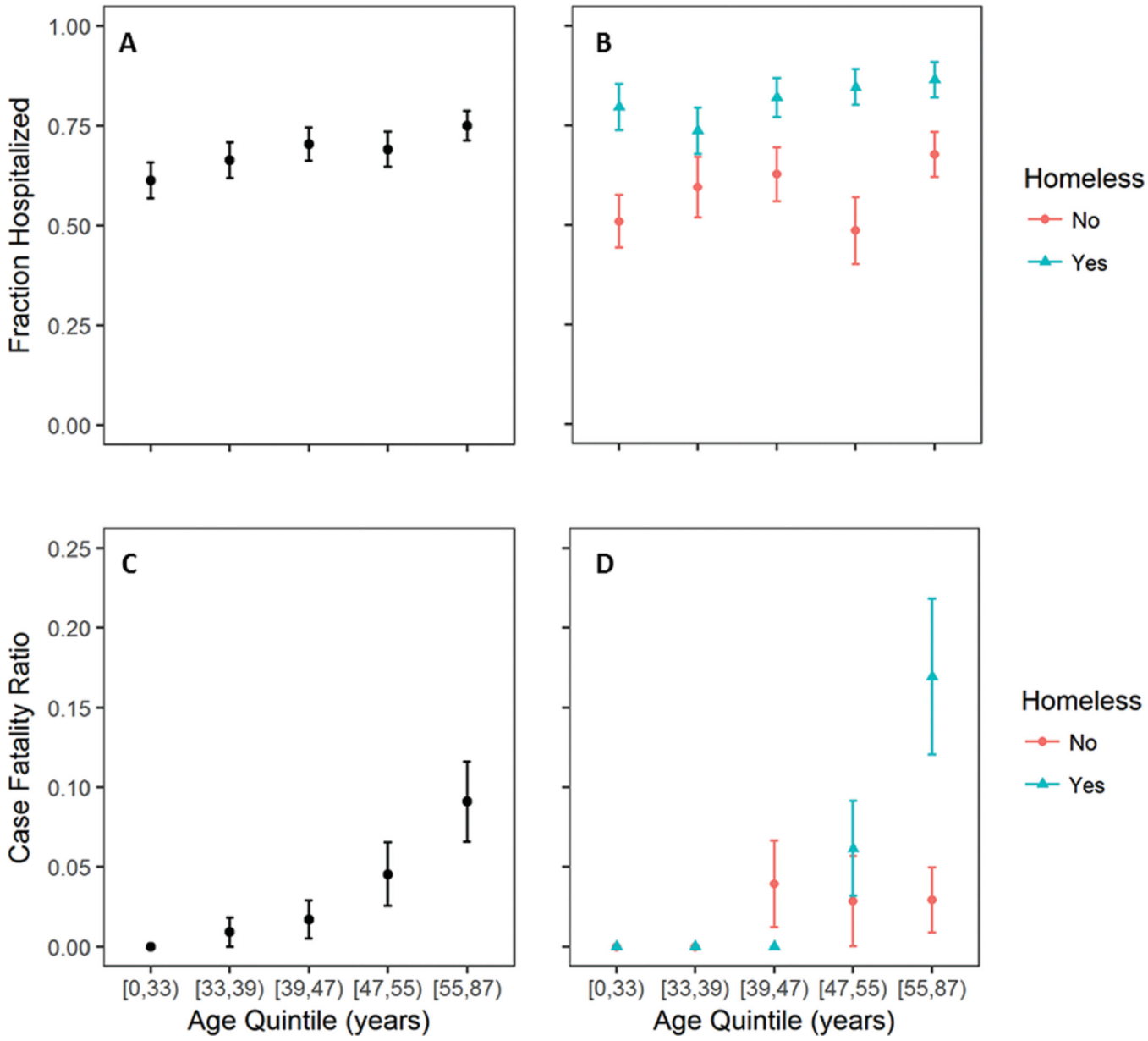

Figure 1.

Risk of hospitalization (*A, B*) and death (*C, D*) among confirmed and probable cases by homelessness and age quintile (ie, 0 to <33, 33 to <39, 39 to <55, and ≥55 years).

Table 1.

Assessment Criteria for Case Status and Inclusion in Risk Factor Analyses

	Clinical Presentation[a]	Positive for IgM Antibody to HAV or Epi-link[b]	RT-PCR Testing for HAV RNA	Risk Factor Analysis	
				HAV Infection	Disease Severity
Control subject		Either	Tested, negative	Included	…
Confirmed case	Positive	Positive	Tested, positive[c]	Included	Included
Probable case	Positive	Positive	Not tested	…	Included

Abbreviations: HAV, hepatitis A virus; IgM, immunoglobulin M; RT-PCR, reverse transcriptase–polymerase chain reaction.

[a]Acute illness with a discrete onset of any sign or symptom consistent with acute viral hepatitis (eg, fever, headache, malaise, anorexia, nausea, vomiting, diarrhea, and abdominal pain) and either (1) jaundice or (2) elevated serum alanine aminotransferase or aspartate aminotransferase.

[b]Epidemiologic link with a person who has laboratory-confirmed hepatitis A (ie, household or sexual contact with an infected person during the 15–50 days before the onset of symptoms).

[c]HAV RNA genotype IB only.

Table 2.

Patient Characteristics and Risk Factors Among Confirmed and Probable Cases—San Diego County, 2016–2018

	All Confirmed and Probable Case-patients (N = 589)		Patients Reporting Homelessness (N = 291)		Patients Not Reporting Homelessness (N = 253)[a]	
	No.	%	No.	%	No.	%
Sex (male)	400	67.9	210	72.2	159	62.8
Case classification						
Confirmed	502	85.2	251	86.3	218	86.2
Probable	87	14.8	40	13.7	35	13.8
Clinical outcome						
Hospitalized	404	68.6	237	81.4	149	58.9
Died	20	3.4	14	4.8	5	2.0
Risk group						
Homeless and illicit drug use	200	34.0	200	68.7	…	…
Homeless only	91	15.4	91	31.3	…	…
Illicit drug use only	77	13.1	…	…	66	26.1
Neither	167	28.4	…	…	167	66.0
Unknown	54	9.2	…	…	20	7.9
Signs and symptoms						
Dark urine	410	69.6	196	67.4	197	77.9
Jaundice	391	66.4	182	62.5	181	71.5
Vomiting	318	54.0	155	53.3	142	56.1
Fever	293	49.7	128	44.0	147	58.1
Diarrhea	223	37.9	134	46.0	81	32.0
Hepatitis coinfection						
HBV	25	5.1	16	6.5	6	2.9
HCV	83	17.5	61	25.0	14	7.2
ACIP vaccine indication						
Any	324	54.6	212	72.9	95	37.5
Illicit drug use	277	47.0	200	68.7	66	26.1
Coinfection with HBV or HCV	101	20.1	72	28.6	19	9.0
International travel	23	5.3	4	1.9	18	8.0

	All Confirmed and Probable Case-patients (N = 589)		Patients Reporting Homelessness (N = 291)		Patients Not Reporting Homelessness (N = 253)[a]	
	No.	%	No.	%	No.	%
MSM[b]	14	3.5	6	2.1	8	5.0
Aged <18 years	2	0.3	0	0.0	2	0.8
	Median	**IQR**	**Median**	**IQR**	**Median**	**IQR**
Age, years	43	34–52	44	35–52	42	33–55
Laboratory results						
ALT, IU/L	1735	905–2801	1613	804–2635	1974	1090–3044
AST, IU/L	1226	417–2357	1328	412–2424	1234	435–2213
Total bilirubin, mg/dL	6.0	3.4–9.0	5.8	3.1–8.9	6.4	3.9–9.2

Abbreviations: ACIP, Advisory Committee on Immunization Practices; ALT, alanine aminotransferase; AST, aspartate aminotransferase; IQR, interquartile range; HBV, hepatitis B virus; HCV, hepatitis C virus; MSM, men who have sex with men.

[a] Data on homelessness was not available for 45 (7.6%) patients.

[b] Percentage of males.

Table 3.

Crude and Adjusted Logistic Regression Results from Risk Factor Analysis for Hepatitis A Virus Infection

	Confirmed Case-patients (N = 502)		Control Subjects (N = 96)			
	No.	%	No.	%	Odds Ratio (95% CI)	Ratio[a] (95% CI)
Homelessness						
Yes	251	50.0	23	24.0	2.40 (1.43–4.14)[b]	3.28 (1.52–7.90)[b]
No	218	43.4	48	50.0	Ref	Ref
Missing	33	6.6	25	26.0	…	…
Age, years						
Median	43		49		0.97 (.95–.98)[b] per year	0.97 (.95–.99)[b] per year
Sex						
Male	334	66.5	46	47.9	2.17 (2.46–3.39)[b]	2.31 (1.20–4.53)[b]
Female	167	32.3	50	52.1	Ref	Ref
Other	1	0.2	0	0.0	…	…
International travel						
Yes	36	7.2	9	9.4	0.23 (.10–0.57)[b]	0.29 (.12–.75)[b]
No	360	71.7	36	37.5	Ref	Ref
Missing	106	21.1	51	53.1	…	…
Illicit drug use						
Yes	232	46.2	24	25.0	2.58 (1.59–4.30)[b]	…
No	197	39.2	35	36.5	Ref	…
Missing	73	14.5	37	38.5	…	…
MSM						
Yes	11	2.2	1	1.0	2.46 (.47–45.5)	…
No	259	51.6	58	60.4	Ref	…
Missing	232	46.2	37	38.5	…	…
HBV or HCV coinfection						
Yes	81	16.1	11	11.5	1.08 (.68–1.82)	…
No	350	69.7	53	55.2	Ref	…
Missing	71	14.1	32	33.3	…	…

Abbreviations: CI, confidence interval; HBV, hepatitis B virus; HCV, hepatitis C virus; MSM, men who have sex with men; Ref, reference.

[a]Multivariable model including homelessness, age, sex, and history of international travel.

[b]Association significant at $P < .05$.

Table 4.

Crude and Adjusted Logistic Regression Results From Risk Factor Analysis for Hospitalization Associated With Hepatitis A Among Confirmed and Probable Cases

	Hospitalized (N = 404)		Not Hospitalized (N = 185)			
	No.	%	No.	%	Odds Ratio (95% CI)	Adjusted Odds Ratio[a] (95% CI)
Homelessness						
Yes	237	58.7	54	29.2	3.06 (2.09–4.54)[b]	2.53 (1.66–3.88)[b]
No	149	36.9	104	25.8	Ref	Ref
Missing	18	6.7	27	6.7	…	…
Age, years						
Median	44		40		1.01 (1.00–1.03) per year	1.02 (1.00–1.03)[b] per year
Illicit drug use						
Yes	215	53.2	62	33.5	2.26 (1.58–3.26)[b]	1.66 (1.07–2.57)[b]
No	142	35.1	78	42.2	Ref	Ref
Missing	47	11.6	45	24.3	…	…
HBV or HCV coinfection						
Yes	83	20.5	18	9.7	1.70 (1.17–2.55)[b]	…
No	275	68.1	126	68.1	Ref	…
Missing	46	11.4	41	22.2	…	…
Sex						
Male	277	68.6	123	66.5	1.12 (.77–1.62)	…
Female	125	30.9	62	33.5	Ref	…
Other	2	0.5	0	0.0	…	…
MSM						
Yes	6	1.5	6	3.2	0.62 (.21–1.92)	…
No	199	49.3	92	49.7	Ref	…
Missing	199	49.3	87	47.0	…	…

Abbreviations: CI, confidence interval; HBV, hepatitis B virus; HCV, hepatitis C virus; MSM, men who have sex with men; Ref, reference.

[a]Multivariable model including homelessness, age, and illicit drug use.

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[b] Association significant at $P < .05$.

Table 5.

Crude and Adjusted Logistic Regression Results From Risk Factor Analysis for Death Associated With Hepatitis A Among Confirmed and Probable Cases

	Died (N = 20)		Survived (N = 569)			
	No.	%	No.	%	Odds Ratio (95% CI)	Adjusted Odds Ratio[a] (95% CI)
Homelessness						
Yes	14	70.0	277	48.7	2.51 (.94–7.85)	3.91 (1.14–16.9)[b]
No	5	25.0	248	43.4	Ref	Ref
Missing	1	5.0	44	7.7	…	…
Age, years						
Median	58		42		1.07 (1.04–1.11)[b] per year	1.11 (1.07–1.17)[b] per year
HBV or HCV coinfection						
Yes	7	35.0	94	16.5	1.99 (.96–3.91)	2.52 (1.11–5.75)[b]
No	11	55.0	390	68.7	Ref	Ref
Missing	2	10.0	85	15.0	…	…
Illicit drug use						
Yes	4	20.0	273	48.0	0.34 (.09–1.07)	…
No	9	45.0	211	37.1	Ref	…
Missing	7	35.0	85	14.9	…	…
Sex						
Male	17	85.0	383	67.3	2.72 (.90–11.8)	…
Female	3	15.0	184	32.3	Ref	…
Other	0	0.0	2	0.4	…	…

Abbreviations: CI, confidence interval; HBV, hepatitis B virus; HCV, hepatitis C virus; Ref, reference.

[a]Multivariable model including homelessness, age, and HBV or HCV coinfection.

[b]Association significant at $P < .05$.