

Section 1

Introduction and methods

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Background

Hepatitis D is a viral hepatitis that can only replicate with Hepatitis B. Hepatitis D infection may occur simultaneously with hepatitis B (coinfection), or can occur in chronic Hepatitis B (superinfection)¹. Coinfection is often acute and will clear within 6 months, however, there is risk of acute liver failure². Superinfection is the most common form of hepatitis, and has a higher risk of cirrhosis and liver cancer²⁻⁴.

Hepatitis D is transmitted through broken skin or blood, transmission can occur from mother to child but it is rare⁵. The majority of hepatitis D patients are asymptomatic, symptoms can include fever, abdominal pain, nausea, vomiting, jaundice, confusion, bruising, or bleeding, loss of appetite, dark urine, and pale-coloured stools^{5,6}.

Hepatitis is more common in the Middle East, West and Central Africa, Amazonian river basin, Mongolia, Romania, Russia, Pakistan, Georgia, and Turkey⁷.

In Australia 2016, 61 cases of hepatitis D were notified, with an average of 48 cases annually in the period 2011-2015, most cases were reported from New South Wales, Victoria, and Queensland⁸. In Australia, hepatitis D is more common in people born in Vietnam, Sudan, and Afghanistan, and there is a higher risk for anyone who has ever been in prison⁹. More males than females have hepatitis D in Australia, at a rate of 2:1⁸.

Personal Experience, Expectations and Knowledge (PEEK)

Patient Experience, Expectations and Knowledge (PEEK) is a research program developed by the Centre for Community-Driven Research (CCDR). The aim of PEEK is to conduct patient experience studies across several disease areas using a protocol that will allow for comparisons over time (both quantitative and qualitative components). PEEK studies give us a clear picture and historical record of what it is like to be a patient at a given point in time, and by asking patients about their expectations, PEEK studies give us a way forward to support patients and their families with treatments, information and care.

The research protocol used in PEEK studies is independently driven by CCDR. PEEK studies include a quantitative and qualitative component. The quantitative component is based on a series of validated tools. The qualitative component is the result of two years of protocol testing by CCDR to develop a structured interview that solicits patient experience data and provides patients with the opportunity to provide advice on what they would like to see in relation to future treatment, information and care. The structured interview has also been designed so that the outcomes of PEEK studies can inform policy, research, care, information, supportive care services and advocacy efforts.

Position of this study

A search was conducted in Pubmed (March 6, 2023) to identify studies of hepatitis D, or hepatitis B with patient reported outcomes, or patient experience conducted in the past five years worldwide (Table 1.1). Meta-analysis studies, studies with children, studies in developing countries, and studies of less than five participants were excluded. There were 2 studies identified that included participants with hepatitis D, and 21 studies that included participants with hepatitis B

There were two studies that included participants with hepatitis D, one study was a multi-national study that reviewed emails or social media queries from 65 people with hepatitis D focused on information¹⁶. The second study included 43 participants with hepatitis D, 82 participants with hepatitis B and collected health-related quality of life by survey¹⁷.

There were 6 studies that collected qualitative data from participants with hepatitis D, there was one study that reviewed emails or social media queries from 338 participants that was focused on information¹⁸. There were 28 participants that took part in focus groups that described health literacy¹⁹. There were four studies that

interviewed between 11 and 23 people with hepatitis B that were focused on stigma²⁰, decision making²¹, quality of life²² and symptoms²³

This is the only hepatitis D study of patient reported outcomes, or patient experience conducted in the last 5 years in Australia, and the only study world wide to interview people with hepatitis B about their experiences. In addition, PEEK is a comprehensive study covering all aspects of disease experience from symptoms, diagnosis, treatment, healthcare communication, information provision, care and support, quality of life, and future treatment and care expectations.

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validated tools. The qualitative component is the result of two years of protocol testing by CCDR to develop a structured interview that solicits patient experience data and provides patients with the opportunity to provide advice on what they would like to see in relation to future treatment, information and care. The structured interview has also been designed so that the outcomes of PEEK studies can inform policy, research, care, information, supportive care services and advocacy efforts.

Participants

To be eligible for the study, participants needed to have been diagnosed with Hepatitis D, have experienced the healthcare system in Australia, be 18 years of age or older, be able to speak English, Cantonese or Mandarin, and be able to give consent to participate in the study.

Recruitment was difficult in this rare patient population however was possible through clinicians and groups such as LiverWELL, Hepatitis NSW, Hepatitis Queensland, and Vietnamese and Chinese community groups.

Ethics

Ethics approval for this study was granted (as a low or negligible risk research study) by the Centre for Community-Driven Research Ethics Committee (Reference CS_Q4_03).

Data collection

Data for the online questionnaire was collected using Zoho Survey (Zoho Corporation Pvt. Ltd. Pleasanton, California, USA, www.zoho.com/survey).

There were five researchers who conducted telephone interviews and used standardised prompts throughout the interview. The interviews were recorded and transcribed verbatim. Identifying names and locations were not included in the transcript. All transcripts were checked against the original recording for quality assurance.

Online questionnaire (quantitative)

The online questionnaire consisted of the 36-Item Short Form Health Survey (SF36) (RAND Health)¹⁰, a modified Cancer Care Coordination Questionnaire for Patients (CCCQ)¹¹, the Short Fear of Progression Questionnaire (FOP12)¹², and the Partners in Health version 2 (PIH)¹³. In addition, investigator derived

questions about demographics, diagnosis, treatment received and future treatment decisions making were included.

Structured Interview (qualitative)

Interviews were conducted via telephone by registered nurses who were trained in qualitative research. The first set of interview questions guided the patient through their whole experience from when symptoms were noticed up to the present day.

Questionnaire analysis

Statistical analysis was conducted using R included in the packages “car”, “dplyr” and “ggplot2” (R 3.3.3 GUI 1.69 Mavericks build (7328)). The aim of the statistical analysis of the SF36, CCCQ, FOP12, and PIH responses was to identify variations by gender, age, location of residence, education status and socio-economic status. Scales and subscales were calculated according to reported instructions¹⁰⁻¹³.

The Location of participants was evaluated by postcode using the Australian Statistical Geography Maps (ASGS) Remoteness areas accessed from the Australian Bureau of Statistics¹⁴.

The level of socio-economic status of participants was evaluated by postcode using the Socio-economic Indexes for Areas (SEIFA) accessed from the Australian Bureau of Statistics¹⁵.

For comparisons between groups, a two-sample t-test was used when assumptions for normality and variance were met, or when assumptions were not met, a Wilcoxon rank sum test with continuity correction was used. Questions where participants were asked to rank preferences were analysed using weighted averages. Weights were applied in reverse, the most preferred option was given the largest weight equal to the number of options, the least preferred option was given the lowest weight of 1.

Structured interviews analysis

A content analysis was conducted using conventional analysis to identify major themes from structured interviews. Text from the interviews were read line-by-line by the lead researcher and then imported into CCDR’s custom database. Each question within the interview was individually analysed. Initial categories and definitions were identified and registered in CCDR’s custom database. The minimum coded unit

was a sentence with paragraphs and phrases coded as a unit.

A second researcher verified the codes and definitions, and the text was coded until full agreement was reached using the process of consensual validation. Where a theme occurred less than 5 times it was not included in the study results, unless this result demonstrated a significant gap or unexpected result.

Data were collected between April 2022 and July 2023. Analysis and final reporting was completed in August 2023.

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Table 1.1: PEEK position

Author, Year	Location	Conditions	Qualitative data collection	Surveys	Study focus								
						2: Health status, co-morbidities	3: Diagnosis experience	4: Decision making	5: Treatment, healthcare system use	6: Information, communication and self-management	7: Care, support and navigating healthcare system	8: Quality of life, mental health, relationships	9: Expectations, preferences and messages
Buti et al, 2021 ¹⁷	Spain	HBV,HDV		43 HDV, 82 HBV	HRQOL	X						X	
Kumar et al, 2020 ¹⁶	Multi-national	HDV	65 (Email/ social media queries)		Information		X		X	X		X	
Freeland et al, 2021 ¹⁸	Multi-national	HBV	338 (Email/ social media queries)		Information		X		X	X		X	
Hyun et al, 2021 ¹⁹	USA	HBV	28 (Focus groups)		Health literacy		X		X	X		X	
Alber et al, 2020 ²⁰	USA	HBV	23 (Interviews)		Stigma					X		X	
Freeland et al, 2021 ²¹	USA	HBV	19 (Interviews)		Decision making			X	X				
Freeland et al, 2021 ²²	USA	HBV	19 (Interviews)		Quality of life		X		X			X	
Jang et al, 2018 ²³	Korea	HBV	11 (Interviews)	147	Symptoms		X					X	
Evon et al, 2021 ²⁴	USA	HBV		1,576	Symptoms		X						
Daida et al, 2020 ²⁵	USA	HBV		969	HRQOL	X							
Evon et al, 2020 ²⁶	USA	HBV		876	HRQOL	X	X						
Chen et al, 2021 ²⁷	Taiwan	HBV		503	HRQOL	X	X						
Cortesi et al, 2020 ²⁸	Italy	Liver conditions		284 HBV	HRQOL	X	X						
Younossi et al, 2019 ²⁹	Multi-national	HBV		229	HRQOL	X						X	
Roche et al, 2022 ³⁰	Multi-national	HBV		195	HRQOL	X			X				
Höner Zu Siederdisen et al, 2018 ³¹	Germany	HBV		174	HRQOL	X							
Younossi et al, 2019 ³²	Multi-national	Liver conditions		132 HBV	HRQOL	X							

Volpes et al, 2020 ³³	Italy	HBV		86	HRQOL	X	X				X		
Ekerfors et al, 2019 ³⁴	Sweden	Liver conditions		57 HBV	HRQOL		X						
McPhail et al, 2020 ³⁵	Australia	Liver conditions		33 HBV	HRQOL	X							
Westermann et al, 2019 ³⁶	Germany	Liver conditions		31 HBV	HRQOL	X			X			X	
Dirks et al, 2019 ³⁷	Germany	Liver conditions		22 HBV	HRQOL	X	X						

Abbreviations and terminology

ASGS	The Australian Statistical Geography Standard from the Australian Bureau of Statistics, defines remoteness and urban/rural definitions in Australia
CCDR	Centre for Community-Driven Research
dF	Degrees of Freedom. The number of values in the final calculation of a statistic that are free to vary.
f	The F ratio is the ratio of two mean square values, used in an ANOVA comparison. A large F ratio means that the variation among group means is more than you'd expect to see by chance.
HER2	Human epidermal growth factor receptor 2
FOP	Fear of Progression. Tool to measure anxiety related to progression
IQR	Interquartile range. A measure of statistical dispersion, being equal to the difference between 75th and 25th percentiles, or between upper and lower quartiles.
p	Probability value. A small <i>p</i> -value (typically ≤ 0.05) indicates strong. A large <i>p</i> -value (> 0.05) indicates weak evidence.
PEEK	Patient Experience, Expectations and Knowledge
PIH	Partners in Health
SD	Standard deviation. A quantity expressing by how much the members of a group differ from the mean value for the group/
SEIFA	Socio-Economic Indexes for Areas (SEIFA) ranks areas in Australia according to relative socio-economic advantage and disadvantage. This is developed by the Australian Bureau of Statistics.
SF36	Short Form Health Survey 36
t	t-Statistic. Size of the difference relative to the variation in your sample data.
Tukey HSD	Tukey's honestly significant difference test. It is used in this study to find 5 significantly different means following an ANOVA test.
W	The W statistic is the test value from the Wilcoxon Rank sum test. The theoretical range of W is between 0 and (number in group one) x (number in group 2). When W=0, the two groups are exactly the same.
χ^2	Chi-squared. Kruskal-Wallis test statistic approximates a chi-square distribution. The Chi-square test is intended to test how likely it is that an observed distribution is due to chance.

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