Twitter As a Noninvasive Bio-Marker for Trends in Liver Disease

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With the success of hepatitis C virus (HCV) direct-acting antiviral therapies, there has been a shift in research focus to the other major chronic liver diseases (CLDs). The use of social media, specifically Twitter, has become a popular platform for understanding public health trends and for performing health care research. To evaluate this, we studied the areas of public interest and social media trends of the following three major CLDs: hepatitis B virus (HBV), HCV, and nonalcoholic fatty liver disease (NAFLD)/nonalcoholic steatohepatitis (NASH). Twitter activity data from January 1, 2013, through January 1, 2019, for HBV, HCV, and NAFLD/NASH were collected using the social media analytic tool Symplur Signals (Symplur LLC) software. Content and regression analyses were performed to understand and predict Twitter activity for each of the CLDs. Over the study period, there were 810,980 tweets generating 4,452,939,516 impressions. HCV tweet activity peaked in 2015 at 243,261 tweets, followed by a decline of 52.4% from 2015 to 2016 with a subsequent plateau through 2018. Meanwhile, NAFLD/NASH and HBV tweet activity has continued to increase, with projections that these two CLDs will surpass HCV by the second half of 2023 and 2024, respectively. Treatment and Management was the most popular content category for HCV and NAFLD/NASH, while Prevention was the most popular content category for HBV. Conclusion: Twitter is a useful social media tool to gauge public interest in liver disease over time. The information provided by Twitter can be used to identify gaps in public knowledge or highlight areas of interest that may need further research. Future studies on the use of Twitter in liver disease are warranted. (Hepatology Communications 2019;3:1271-1280).

he introduction of direct-acting antiviral (DAA) therapies in 2011 for the treatment of hepatitis C virus (HCV) has revolutionized the management of HCV, with sustained virologic response rates of greater than 95%.⁽¹⁻³⁾ However, other common chronic liver diseases (CLDs), such as nonalcoholic fatty liver disease (NAFLD)/nonalcoholic steatohepatitis (NASH) and hepatitis B virus (HBV), continue to carry a substantial liver disease burden worldwide.^(3,4) This is likely due to a lack of either effective or curative treatments despite numerous drugs in clinical development.^(5,6) Therefore, given the tremendous success of current HCV therapy, a shift in health care focus from HCV to the other major CLDs is expected.

The use of social media in health care has become popular in recent years as a way to provide public, emotional, and experiential support.⁽⁷⁾ Health care research involving social media has evolved as a way to characterize the interests of large populations and locate trends of interest. One of the most popular social media platforms that can be used for

Abbreviations: AASLD, American Association for the Study of Liver Diseases; CLD, chronic liver disease; DAA, direct-acting antiviral; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis; WHO, World Health Organization.

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this purpose is Twitter. Twitter is an American online news and networking service created in 2006 in which "users" post and interact with short messages (previously limited to 140 characters but increased to 280 characters since 2017) known as tweets. As of the third quarter of 2018, there were an estimated 326 million active monthly Twitter users.⁽⁸⁾

Twitter has been demonstrated to be a valid tool in performing research on topics such as content analysis, surveillance, and intervention.⁽⁹⁾ In addition, Twitter has proven to be an excellent way to expand the reach and influence of medical professionals.⁽¹⁰⁾ The utility of this platform continues to expand in the era of digital medicine and has been studied in various fields, such as hematology/oncology,⁽¹¹⁾ immunology,⁽¹²⁾ surgery,⁽¹³⁾ neurology,⁽¹⁴⁾ and cardiology.⁽¹⁵⁾ Thus far, the use of Twitter as a research modality has not been studied in hepatology. Given the increasing trends of social media use in medicine, the American Association for the Study of Liver Diseases (AASLD) has advocated for the increased use of social media to "advance and disseminate the science and practice of hepatology, and to promote liver health and quality patient care."⁽¹⁶⁾ The AASLD Twitter handle has become a regular source of key information regarding hepatology news and currently has over 13,000 followers (https:// twitter.com/AASLDtweets). The other major liver societies also have their respective Twitter handles: European Association for the Study of the Liver (https://twitter.com/EASLnews) with over 8,700 followers and Asian Pacific Association for

the Study of the Liver (https://twitter.com/APASL news) with over 400 followers.

Symplur Signals (Symplur LLC) is a social media analytic tool that organizes massive amounts of data published on Twitter in a way in which it can be analyzed based on hashtags. One of the associated projects on this platform is the Healthcare Hashtag Project, which is aimed at making Twitter more accessible for providers and the health care community.⁽¹⁷⁾ To date, analysis of Symplur data has been used in a variety of different diseases and medicine specialties, including rare hematologic malignancies,⁽¹⁸⁾ colon cancer,⁽¹⁹⁾ immunology,⁽¹⁰⁾ and urology.⁽²⁰⁾

In this study, we aimed to use a large database of tweets collected from Twitter by Symplur Signals to describe the shift in public interest among three of the major CLDs (HBV, HCV, and NAFLD/ NASH). Additionally, we aimed to characterize the social media content of each of these CLDs as it evolves yearly to determine the specific topics that are the driving force behind the shifts in public interest.

Materials and Methods

TWEET POPULATION AND HASHTAGS USED

Data were collected using the publicly available Twitter analytics platform Symplur Signals (Symplur LLC) (www.symplur.com). We used the hashtags

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"#Hepb,""#Hepatitisb," and "HBV" to search for tweets regarding HBV. The hashtags "#Hepc," "#Hepatitisc," and "HCV" were used to search for tweets regarding HCV. Similarly, the hashtags "Fattyliver," "NAFLD," and "NASH" were used to search for tweets regarding NAFLD/NASH. Tweets from January 1, 2013, to January 1, 2019, were analyzed for HBV and HCV. The hashtags for NAFLD/NASH were not registered until late in 2014 so tweets from January 1, 2015, to January 1, 2019, were analyzed for NAFLD/NASH. In addition, the keywords "HIV" and "obesity" were used to identify tweets about human immunodeficiency virus (HIV) and obesity from January 1, 2013, to January 1, 2019, to see if the trend of public interest toward HIV was occurring in the same fashion as HBV/HCV and obesity for NAFLD/NASH.

The tweet populations for each of the three CLDs were analyzed as they changed yearly. Tweet incidence rate was defined as the number of new tweets per person-year. Specific tweet information was collected, including how often there were attached mentions (tweets in which another username is stated), links (tweets with an attached web address), and media (tweets with attached photo or video). The frequency of retweets (repost or forward of a tweet) and replies to the original tweets were recorded as well as the number of unique users. The total number of impressions (number of times tweets about the search term were delivered to Twitter streams) was calculated by multiplying the number of tweets by the number of followers for every influencer (user on social media with a following). Impressions were evaluated in addition to tweet activity as they help illustrate the overall public exposure of the specific diseases analyzed. The top five influencers, ranked based on the total number of impressions and their respective social media influence, were also analyzed to identify the characteristics of the most active social media users for each disease.

CONTENT

The secondary objective was to analyze the change in content of each of the CLDs over time to explain the changes in Twitter activity with time. To assess the contents of the tweets as well as the change in content over time, 500 random tweets were selected per year per disease. Only tweets that were written in English and medically related were assessed for content. Tweets were categorized into one of eight content categories based on a prior study evaluating the content of tweets in cardiology research⁽¹⁵⁾ by one of six physicians (B.D., S.S., S.T., A.V., C.G., and N.J.). The categories were as follows: 1) Risk Factor, 2) Awareness, 3) Treatment and Management, 4) Mechanism, 5) Outcomes, 6) Symptoms, 7) Prevention, and 8) Support.

STATISTICAL ANALYSIS

Linear regression was performed to understand trends in Twitter activity and content analysis for each disease between the period January 1, 2013, and January 1, 2019, and between the period January 1, 2015, and January 1, 2019. The second period was chosen because that was when Twitter data for all three CLDs became available. The calculated regression equations were used to project future Twitter activity for each disease. All statistical analyses were performed using Microsoft Excel (Redmond, WA) and SAS 9.4 (Cary, NC).

Results

TWEET AND IMPRESSION ACTIVITY

From January 1, 2013, to January 1, 2019, there were 810,980 tweets from 189,184 users, generating 4,452,939,516 total impressions. The overall tweet summary for the three CLDs evaluated in this study is shown in Table 1. For HBV, there were 26,807 unique users who posted an average of 3.3 tweets per user, generating 25,847 impressions per user. For HCV, there were 144,760 unique users who posted an average of 4.5 tweets per user, generating 24,588 impressions per user. For NAFLD/ NASH, there were 17,617 unique users who posted an average of 4.3 tweets per user, generating 11,394 impressions per user. Interestingly, the proportion of HBV and HCV tweets with mentions (76.2%-79.9%) and retweets (63.1%-66.1%) appeared to be substantially higher than NAFLD/NASH (mentions, 60.5%; retweets, 52.4%). In addition, the proportion of HBV and HCV tweets with attached links (61.4%-69.0%) or media (43.2%-43.7%) also appeared to be higher than NAFLD/NASH (attached links, 56.9%; media, 38.6%).

	HBV*	HCV*	NAFLD/NASH [†]
Total tweets	87,779	647,865	75,336
Tweets with mentions	66,888 (76.2%)	517,644 (79.9%)	45,576 (60.5%)
Retweets	55,389 (63.1%)	428,239 (66.1%)	39,496 (52.4%)
Tweets with links	60,568 (69.0%)	397,789 (61.4%)	42,832 (56.9%)
Tweets with media	38,359 (43.7%)	279,878 (43.2%)	29,106 (38.6%)
Tweets with replies	1,492 (1.7%)	8,681 (1.34%)	925 (1.2%)
Unique users	26,807	144,760	17,617
Impressions	692,889,717	3,559,314,026	200,735,773

TABLE 1. TWEET SUMMARY OF HBV, HCV, AND NASH/NAFLD

*Tweets evaluated between January 1, 2013, and January 1, 2019; [†]Tweets evaluated between January 1, 2015, and January 1, 2019.

The trends of tweet and impression activity for each of the three CLDs are depicted in Figs. 1 and 2, respectively. The number of tweets and impressions for HCV increased dramatically between 2013 and 2015. Afterwards, HCV tweet activity decreased from 52.4% from 2015 to 2016 and then plateaued while HCV impression activity continued to fluctuate. Meanwhile, the tweet incidence rates for HCV peaked at 4.7 tweets per person-year in 2013 and then fluctuated between 2.9 and 3.9 tweets per person-year

(Supporting Fig. S1). The number of tweets and impressions for HBV increased gradually from 2013 to 2018 by an average of 46.4% and 66.8% per year, respectively, with an unexpected spike in activity in 2017. The HBV tweet incidence then remained relatively stable between 2.7 and 3.4 tweets per person-year. When we evaluated HIV, there appeared to be a similar trend to HCV, with a tweet activity peak in 2016 instead and a decline in the years following (Supporting Table S1). The tweet incidence rate for

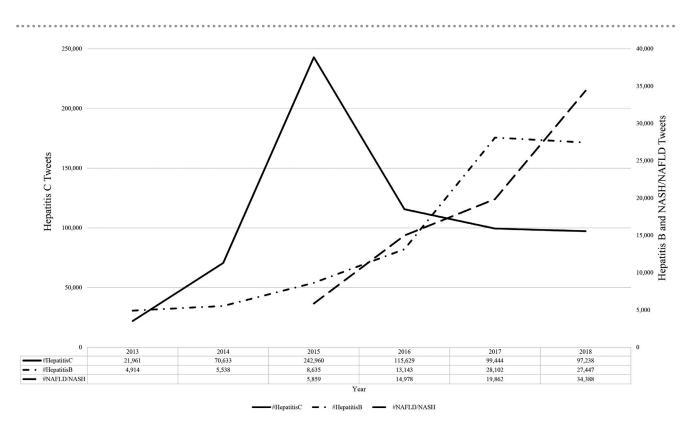


FIG. 1. Trend of tweet activity. The three CLDs evaluated: HBV versus HCV versus NAFLD/NASH. Hashtags used for HBV included #hepatitisb, #hepb, #hbv; HCV included #hepatitisc, #hepc, #hcv; NAFLD/NASH included #fattyliver, #nash, #nafld.

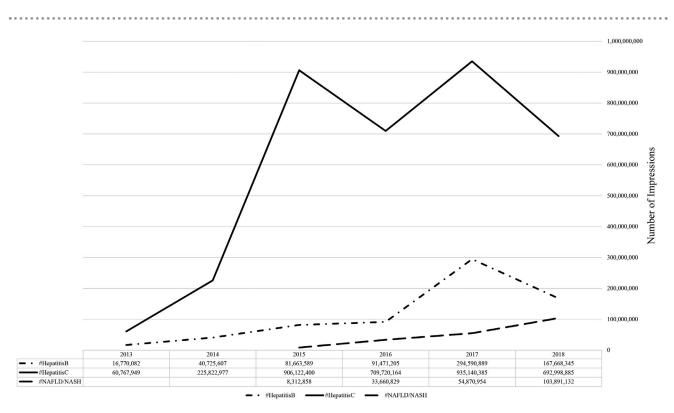


FIG. 2. Trend of impression activity. The three CLDs evaluated: HBV versus HCV versus NAFLD/NASH. Hashtags used for HBV included #hepatitisb, #hepb, #hbv; HCV included #hepatitisc, #hepc, #hcv; NAFLD/NASH included #fattyliver, #nash, #nafld.

HIV also fluctuated in a similar fashion (between 2.7 and 3.9 tweets per person-year) like HBV and HCV. Finally, the number of NAFLD/NASH tweets and impressions rapidly increased yearly by an average of 87.1% (tweets) and 152.4% (impressions) per year. However, the tweet incidence rate decreased from 4.5 tweets per person-year in 2015 to 3.3 tweets per person-year in 2018. Interestingly, the number of "obesity" tweets and impressions also increased yearly by an average of 18.2% (tweets) and 36.1% (impressions). Obesity tweets and impressions increased annually similar to NAFLD/NASH tweets and impressions. However, in contrast to NAFLD/NASH, the tweet incidence rate for obesity increased during the evaluated period from 2.9 tweets per person-year in 2013 to 3.7 tweets per person-year in 2015 to 4.2 tweets per person-year in 2018 (Supporting Table S2).

There was excellent linear correlation between time with HBV tweet ($R^2 = 0.875$; P < 0.0001) and NAFLD/NASH tweet ($R^2 = 0.955$; P < 0.0001) and impression ($R^2 = 0.9303$; P < 0.0001) activity. HBV impression activity and HCV impression activity demonstrated poor linear correlation with time (HBV $[R^2 = 0.6207; P = 0.0014]$ and HCV $[R^2 = 0.5298; P = 0.0047]$). There was no linear correlation between time and HCV tweet activity ($R^2 = 0.0719; P = 0.3712$).

Linear regression plots of tweet activity versus time (January 1, 2015, to December 31, 2018) in the three CLDs are shown in Fig. 3. HCV displays a negative slope, while HBV and NAFLD/NASH display a positive slope. In the second half of 2015, there was an unusual spike in the tweet activity of HCV up to 192,544 tweets. On the projection analysis of future Twitter activity for the three CLDs, this outlier was not included because it caused skewing of the trajectory. Based on this projection, NAFLD/NASH tweet activity will overtake HCV by the second half of 2023 and HBV will overtake HCV by the second half of 2024. Without removal of the outlier, both HBV and NAFLD/NASH will overtake HCV by the first half of 2020.

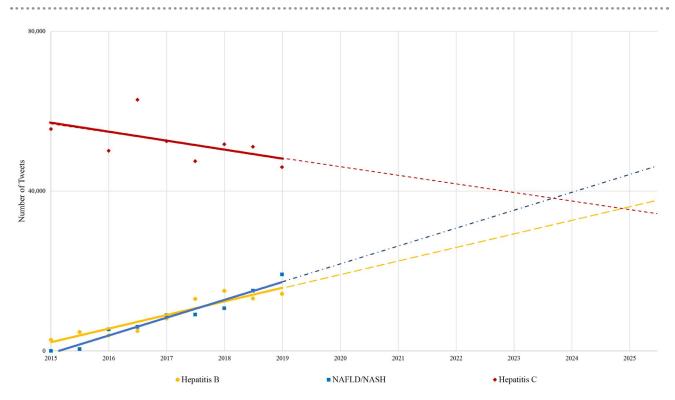


FIG. 3. Projected tweet activity. The three CLDs evaluated: HBV versus HCV versus NAFLD/NASH. Solid line denotes established trend line of disease tweet activity; dotted line denotes projected trend line of disease tweet activity.

TOP INFLUENCERS

The top five influencers for HBV, HCV, and NAFLD/NASH generated a total of 303,544,297 (44.3% of total HBV) impressions, 587,825,282 (18.7% of total HCV) impressions, and 54,589,163 (27.2% of total NAFLD/NASH) impressions (Table 2). The World Health Organization (WHO) (Twitter username @WHO) was the top influencer for HBV and HCV with 123,428,264 and 242,729,481 impressions, respectively. Neil Floch, M.D. (Twitter username @NeilFlochMD) was the top influencer for NAFLD/NASH with 18,398,868 impressions.

CONTENT ANALYSIS

Content about Treatment and Management was consistently the most popular among tweets pertaining to HCV (38.8%-58.6% of tweets from 2013 to 2018), followed in popularity usually by Awareness in every year, except for 2014 when Support was the second most tweeted content category (Supporting Table S3). However, Treatment and Management for HCV during the study period experienced the steepest decline (slope, -3.34%) noted for any of the content categories of any of the CLDs. This was followed by content about Prevention for NAFLD/NASH (slope, -2.41%). In contrast, content regarding Awareness for HCV had the greatest increase (slope, +3.33%), followed by Support also in the HCV category (slope, +2.86%). Treatment and Management and Awareness were the two most frequently tweeted content categories for NAFLD/NASH. Although content regarding Mechanism was rarely discussed in HCV and HBV, since 2016 it has been among the top three NAFLD/ NASH categories. Popular HBV content topics centered around Awareness, Prevention, and Support, except in 2013 and 2016 when Treatment and Management was among the top three categories. The least discussed content category among the three CLDs was Symptoms.

Discussion

In this study, we evaluated a large database of tweets regarding three of the major CLDs and showed that

Rank		HBV*	HCV*	NAFLD/NASH [†]
1	Impressions	123,428,264	242,729,481	18,398,868
	Username	@WHO	@WHO	@NeilFlochMD
	Name	WHO	WHO	Neil Floch, M.D.
	Health care stakeholder	Organization: other health care, professional	Organization: other health care, professional	Doctor, physician
	Website	http://www.who.int	http://www.who.int	www.endtheweight.com
	Followers	4,506,542	4,506,542	132,717
2	Impressions	78,650,740	121,658,149	16,204,844
	Username	@cdchep	@danialvesd2	@TreatFattyLiver
	Name	CDC Hepatitis	Daniel Alves	Treat Fatty Liver
	Health care stakeholder	Organization: government	Unknown	Organization: other health care
	Website	http://www.cdc.gov/hepatitis	http://www.danialves.com	http://bit.ly/fattyliverguide
	Followers	34,897	8,243,058	2,551
3	Impressions	39,077,376	83,209,696	9,015,475
	Username	@womenshealth	@cdchep	@LifeExtension
	Name	womenshealth.gov	CDC Hepatitis	Life Extension
	Health care stakeholder	Organization: government	Organization: government	Organization: other health care
	Website	http://www.womenshealth.gov	http://www.cdc.gov/hepatitis	http://www.lifeextension.com
	Followers	987,825	34,974	161,931
4	Impressions	28,102,431	71,867,370	6,041,588
	Username	@srbachchan	@Consalud_es	@JHepatology
	Name	Amitabh Bachchan	ConSalud.es	Journal of Hepatology
	Health care stakeholder	Individual: nonhealth	Individual: other health	Organization: media, journalist/media
	Website	http://srbachchan.tumblr.com	http://www.ConSalud.es	http://www.journal-of-hepatology.eu
	Followers	28,102,431	107,121	7,497
5	Impressions	25,285,486	68,360,586	4,928,388
	Username	@HepBFoundation	@womenshealth	@PierreMenes
	Name	Hep B Foundation	Womenshealth.gov	Pierre Ménès
	Health care stakeholder	Organization: advocate/support, patient advocacy	Organization: government	Unknown
	Website	http://www.hepb.org/	http://www.womenshealth.gov	http://www.canalplus.fr/pierrotfootballblog
	Followers	6,763	987,825	3,464,194

TABLE 2. TOP FIVE INFLUENCERS BY IMPRESSIONS

*Tweets evaluated between January 1, 2013, and January 1, 2019; [†]Tweets evaluated between January 1, 2015, and January 1, 2019.

the overall trend of social media interest, as represented on Twitter, appears to have shifted from HCV to HBV and NAFLD/NASH in recent years. The tweet activity of HCV peaked in 2015 after numerous DAAs were approved by the U.S. Food and Drug Administration (FDA) between 2013 and 2015 for the treatment of HCV infection.⁽²¹⁻²⁴⁾ Tweet content analysis for HCV during this time was heavily focused on treatment. Based on linear regression analysis, we project that the Twitter activity of NAFLD/NASH and HBV will overtake HCV by the first half of 2023 and 2024, respectively. We suspect that a major reason for these trends is that a significant proportion of the tweets is coming from the medical community as

research-related tweets, and there is currently much more NAFLD/NASH- and HBV-related research being conducted compared to HCV. Interestingly, the overall trend of HIV (used as a positive control) appears to mirror that of HCV.

The effectiveness of DAAs has led to a decline in the number of HCV-related additions to the liver transplant waiting list, liver transplant surgeries, and cirrhosis.^(25,26) Since 2015, the amount of social media interest in terms of the number of HCV-related tweets fell dramatically between 2015 and 2016 and then plateaued despite four additional drugs being approved by the FDA and multiple indication expansions.⁽²⁷⁾ The number of HCV-related impressions has fluctuated since 2015, which is more reflective of the significant variations in popularity of the influencers posting the tweets. In our content analysis, we identified a continued but declining interest in Treatment and Management that remains significantly higher than any other content category in HCV, despite the overall declining Twitter activity. Most of the HCV tweets on Treatment and Management could be split into either being about the efficacy of DAAs or commenting about the high cost of treatment. Moreover, Awareness and Support for HCV is growing at the most rapid rate, which is likely related to tweeters raising awareness about the high cost of treatment or helping patients afford these medications.

In contrast to HCV, the prevalence of NAFLD/ NASH and the occurrence of NAFLD/NASHrelated mortality have been rapidly increasing.⁽²⁸⁾ As of 2016, the number of transplants performed for NAFLD/NASH had already surpassed the number of transplants performed for HCV in the United States; this is projected to continue to increase over the next few decades due to the obesity epidemic.^(29,30) Consistent with that is our data showing a rapid and linear increase in NAFLD/NASH Twitter activity from 2015 to 2018 that is reflective of the rising interest in this disease. In our study, it was the only one of the three CLDs with Twitter activity that continued to increase yearly, correlating to the yearly increase in "obesity" Twitter activity. Interestingly, despite this growth, NAFLD/NASH tweets were less likely to have attached mentions, links, media, and retweets compared to HBV and HCV tweets. In the social media atmosphere, it is accepted that tweets with more attached content will attract greater attention. This suggests that HBV and HCV tweets may be more robust than NAFLD/NASH tweets. Additionally, it was the only one of the three CLDs with a tweet incidence rate that decreased every year, suggesting that the growth in tweet activity is due mostly to an increase in unique users. Interestingly, the tweet incidence rate of obesity increased yearly, which suggests that the growth in obesity tweet activity may be due to more individual users posting more often. This may be because NAFLD/NASH is still a relatively new and underrecognized disease in the public domain compared to obesity and perhaps even HBV/HCV. This also suggests that NAFLD/NASH tweet activity may still have room to grow once its user base

becomes more comfortable and individually post more tweets in support of their ideas. Treatment and Management was the predominant topic of discussion for NAFLD/NASH; however, Mechanism was also a top topic of discussion, which suggests a public interest in the pathogenesis of the disease. However, this topic was hardly ever discussed for HCV, which is likely due to the overarching success of DAA therapies, resulting in a lack of interest regarding the mechanism of the disease.

Although the rates of HBV-related mortality have been decreasing gradually due to the implementation of vaccination programs and effective viral suppression with nucleoside analog therapies, HBV remains an important global public health problem with significant mortality.^(3,31,32) In this study, we identified that HBV Twitter activity has increased gradually with a spike in activity in 2017. This spike can likely be explained by the approval of tenofovir alafenamide (Vemlidy, Gilead Sciences) on November 10, 2016, as well as an increasing amount of interest on the progress of several investigational HBV drugs in the later stages of clinical development.^(33,34) When we performed the content analysis, we saw an uptrend in the proportion of HBV tweets discussing Treatment and Management and Prevention in 2017 compared to prior years. During this year, we also saw an increase in the number of HBV tweets discussing Mechanism, which is probably related to the emerging HBV therapies.

Prevention was one of the hottest topics when it came to HBV; this reflects the implementation and success of the hepatitis B vaccination programs.⁽³⁵⁾ In contrast, the lack of discussion on this topic in NAFLD/NASH and HCV likely suggests an absence of current public interest. This is surprising given that the prevalence of NAFLD/NASH and the annual incidence rate of acute HCV infections are both increasing.^(28,36) The lack of interest in HCV prevention can be attributed to the lack of an approved (and successful) HCV vaccine and the continued strong attention to DAAs.⁽³⁷⁾

There are several strengths to this study. First, we were able to capture and characterize public interest within liver disease using a large data pool through the use of a well-known social media platform, Twitter. By evaluating the trends of tweet activity, impressions, and content over the past 6 years, we were also able to analyze the shift in social media interest of three of the major CLDs. In addition, we were able to characterize the top social influencers and found that some of the top influencers in each CLD are actually not medical professionals or represent medical societies. This illustrates the important point that nonmedical individuals can sway public opinion in medically related topics.

However, there are several limitations to our study. First, alcoholic liver disease was not investigated in this study because its associated hashtags have not been registered with the Symplur Signals database, preventing prospective tweet collection. However, we would expect a similar trend in tweet activity and impressions to NAFLD/NASH because alcoholic liver disease recently replaced HCV as the leading indication for liver transplantation.⁽²⁶⁾ Finally, we were unable to analyze the tweet content of the entire collected database due to the overwhelmingly large numbers of tweets (>800,000) as well as a portion of the tweets being written in other languages. However, we felt that 500 tweets per year per disease was an adequate sample to obtain a flavor of the relevant tweet topics.

In summary, Twitter is a useful social media tool to gauge public interest in liver disease. The analysis of social media trends can be used to generate critical information about specific areas of public interest within the field of liver disease along with understanding evolving interests over time. This information can then be used to identify gaps of public knowledge or highlight areas of increased public interest that may warrant further research. Finally, this study helps establish a background for future research on the use of social media in liver diseases, including the use of social media to assess the impact of interventions and therapy.

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Supporting Information

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