

Table 2. Discordant Primary Efficacy Outcome Results Reported in FDA Reviews and Peer-Reviewed Publications

Trial ID	Primary Efficacy Outcome	FDA-Reported Results	Publication-Reported Results	Why Results Differed	Whether Interpretation Altered
NCT00739102 (STROLL study)	Stent primary patency at 12 mo	66.5% (95% CI, 60%-72.5%) (minimum prespecified effect of 66%)	71.2% (95% CI, 64.8%-76.8%) (no minimum prespecified effect)	More lenient definition of primary patency in publication-reported results	Yes, study interpreted as negative in FDA review, positive in publication
NCT01094678 (Zilver PTX-single arm)	Stent primary patency at 12 mo	82.7% in the Zilver PTX group	86.2% in the Zilver PTX group	More lenient definition of primary patency in publication-reported results	No, primary efficacy outcome event rate similar in FDA review and in publication
NCT00209274 (Everest II RCT)	Freedom from death, mitral valve surgery (for device group) or reoperation (for control group), and grade 3+ or 4+ mitral regurgitation at 12 mo	72.4% in the percutaneous repair group vs 87.8% in the surgical repair group ($P = .001$ for noninferiority)	55% in the percutaneous repair group vs 73% in the surgical repair group ($P = .007$)	Publication reported intention-to-treat analysis for primary outcome; FDA reported per-protocol analysis for primary outcome	Unlikely, while freedom from primary efficacy outcome event rate was substantially greater in FDA review than in publication, both the intention-to-treat and per-protocol analyses were presented in the publication

Abbreviations: FDA, US Food and Drug Administration; RCT, randomized clinical trial; STROLL, S.M.A.R.T. Nitinol Self-Expandable Stent in the Treatment of Obstructive Superficial Femoral Artery Disease.

Improved publication rates, particularly among public companies, are probably a consequence of the explicit inclusion of medical devices in the 2007 FDA Amendment Act expansion of clinicaltrials.gov registration and reporting requirements. However, recent failures of high-profile cardiovascular devices may also have led patients and physicians to more frequently ask about the evidence supporting newly approved devices, prompting publication by companies seeking clinical adoption of their products.⁶ Although we found that results of the vast majority of clinical studies supporting recent FDA approval of high-risk cardiovascular devices are now being made available to the clinical and research communities, efforts to improve the accessibility of results through online FDA resources and within medical device labels may still be needed to ensure dissemination of historical studies.

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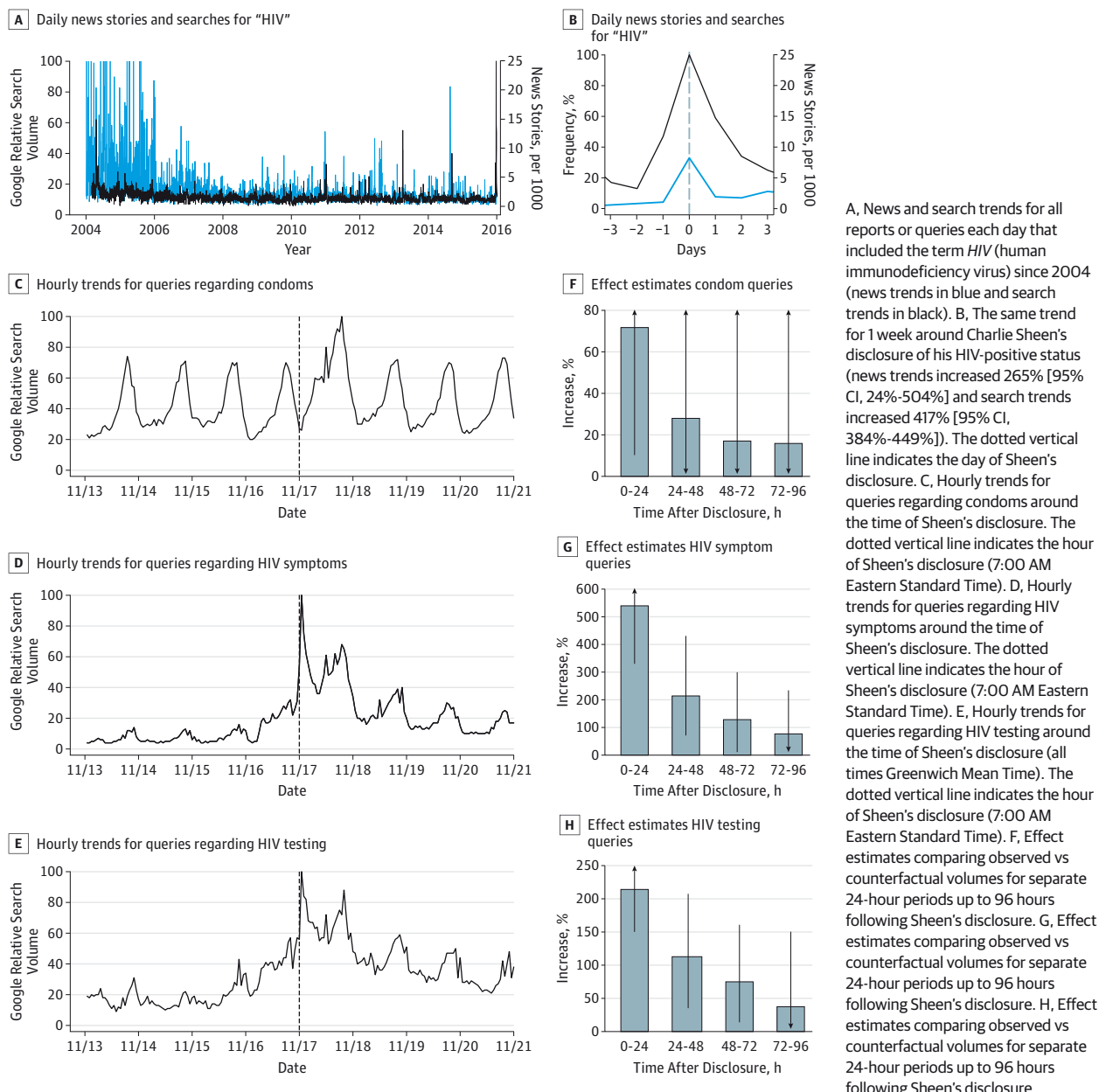
News and Internet Searches About Human Immunodeficiency Virus After Charlie Sheen's Disclosure

Celebrity Charlie Sheen publicly disclosed his human immunodeficiency virus (HIV)-positive status on November 17, 2015. Could Sheen's disclosure, like similar announcements from celebrities,¹ generate renewed attention to HIV? We provide an early answer by examining news trends to reveal discussion of HIV in the mass media and Internet searches to reveal engagement with HIV-related topics² around the time of Sheen's disclosure.



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Figure. News and Internet Searches Related to Human Immunodeficiency Virus



A, News and search trends for all reports or queries each day that included the term *HIV* (human immunodeficiency virus) since 2004 (news trends in blue and search trends in black). B, The same trend for 1 week around Charlie Sheen's disclosure of his HIV-positive status (news trends increased 265% [95% CI, 24%-504%] and search trends increased 417% [95% CI, 384%-449%]). The dotted vertical line indicates the day of Sheen's disclosure. C, Hourly trends for queries regarding condoms around the time of Sheen's disclosure. The dotted vertical line indicates the hour of Sheen's disclosure (7:00 AM Eastern Standard Time). D, Hourly trends for queries regarding HIV symptoms around the time of Sheen's disclosure. The dotted vertical line indicates the hour of Sheen's disclosure (7:00 AM Eastern Standard Time). E, Hourly trends for queries regarding HIV testing around the time of Sheen's disclosure (all times Greenwich Mean Time). The dotted vertical line indicates the hour of Sheen's disclosure (7:00 AM Eastern Standard Time). F, Effect estimates comparing observed vs counterfactual volumes for separate 24-hour periods up to 96 hours following Sheen's disclosure. G, Effect estimates comparing observed vs counterfactual volumes for separate 24-hour periods up to 96 hours following Sheen's disclosure. H, Effect estimates comparing observed vs counterfactual volumes for separate 24-hour periods up to 96 hours following Sheen's disclosure.

Methods | News trends, gathered via the Bloomberg Terminal (<http://www.bloomberg.com/professional/>), included counts of global English-language reports with the term *HIV*. Internet searches, gathered via Google Trends (<https://google.com/trends/>), included counts of searches originating from the United States for 4 categories: HIV (all searches with "HIV"), condoms ("condom" or "condoms"), HIV symptoms ("symptom," "symptoms," or "signs of" and "HIV"), and HIV testing ("test," "tests," or "testing" and "HIV"). News about HIV was measured per 1000 reports. To compare relative search popularity, queries about HIV were divided by the total number of searches for each day or hour and then scaled to range from 0 to 100. Approximate raw search counts were from Google Adwords (<http://www.google.com/adwords/>). All measures

from January 1, 2004 (when Google began data collection), through November 24, 2015, were analyzed. As these analyses are based on public meta-data, institutional board review was not required.

Our approach was quasi-experimental, comparing outcomes around Sheen's disclosure with counterfactual estimates for expected news about and search volumes for HIV if Sheen's disclosure had not occurred. Data analysis was conducted from November 17 to December 8, 2015. Expected volumes were calculated using an autoregressive integrated moving average algorithm by Hyndman and Khandakar³ and data from all days since 2004 for daily analyses or all hours in the 4 days preceding Sheen's disclosure for hourly analyses (both after excluding 1-day or 24-hour washout when Sheen's HIV

status was rumored). The ratio of observed and counterfactual volumes with *t* tests was computed using R, version 3.2.1 (R Foundation for Statistical Computing).

Results | Since 2004, news reports about HIV decreased from 67 (95% CI, 57-77) stories per 1000 to 12 (95% CI, 11-13) stories per 1000 in 2015. The day of Sheen's disclosure, however, coincided with a 265% (95% CI, 17%-500%; $P < .01$) increase in news reports mentioning HIV (97% of which also mentioned Sheen), with more than 6500 stories on Google News alone, which placed Sheen's disclosure among the top 1% of HIV-related media days in the past 7 years (Figure).

Sheen's disclosure also corresponded with the greatest number of HIV-related Google searches ever recorded in the United States. About 2.75 million more searches than expected included the term *HIV*, and 1.25 million searches were directly relevant to public health outcomes because they included search terms for condoms, HIV symptoms, or HIV testing.

All searches regarding HIV were 417% (95% CI, 383%-450%; $P < .001$) higher than expected the day of Sheen's disclosure. Hourly trends suggested that searches related to condoms were 72% (95% CI, 10%-171%; $P < .048$) higher than expected 24 hours after Sheen's disclosure, first increasing the evening following the disclosure and remaining higher for 48 hours. Searches related to HIV symptoms were 540% (95% CI, 332%-808%; $P < .001$) higher than expected and searches related to HIV testing were 214% (95% CI, 151%-358%; $P < .001$) higher, both of which spiked the hour of Sheen's disclosure and remained higher 72 hours later.

Discussion | Just as with celebrities Rock Hudson's and Magic Johnson's disclosures of their HIV-positive status,⁴ Sheen's disclosure may be similarly reinvigorating awareness and prevention of HIV. News and search trends are only proxies for awareness and healthy behaviors, respectively, and sentinel surveillance (such as rates of HIV testing) is needed to clarify these early findings. Yet, our findings can still inform practice, building on theories where availability of and seeking information foreshadow action.⁵ Efforts to leverage the "Charlie Sheen effect," such as coordination of prevention-focused press with coverage related to Sheen as with celebrity Angelina Jolie's prophylactic mastectomy,⁶ may be prudent.

While no one should be forced to reveal HIV status, Sheen's disclosure may benefit public health by helping many people learn more about HIV infection and prevention. More must be done to make this benefit larger and lasting.

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Editor's Note

Adapting Health Education for the Internet Age

Prurient interest in the lives of prominent persons flourished long before the electronic age. However, intimate details about the lives of celebrities now go viral in an explosive e-minute.

The implicit challenge posed by the article by Ayers et al¹ in this issue of *JAMA Internal Medicine*, about Charlie Sheen's announcement that he is human immunodeficiency virus-positive, is how to take advantage of such moments to educate the public about health issues. This news not only caused people to read news articles about Sheen but also prompted them to perform Internet searches concerning human immunodeficiency virus testing and symptoms.

The job of public health is to be certain that the right information is easily available when people seek it. People need to know where to go to obtain the services they need in the language they speak in the community in which they live. Health educators have long known the importance of context and opportunity: an episode of bronchitis is a good moment to address smoking cessation; an attack of chest pain is the right time to talk about obesity. We can provide more effective messages about public health if we adapt traditional methods of health education to our increasingly social media-driven world and make sure the messages are available in advance of the next celebrity disclosure.

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Medical End-of-Life Practices in Switzerland: A Comparison of 2001 and 2013

Physician-assisted suicide, but not euthanasia, is legal in Switzerland.¹ The Netherlands and Belgium, where euthanasia is legal, regularly monitor the incidence of medical end-of-life practices.^{2,3} As part of a study in 6 European countries, reliable data on medical end-of-life practices were collected in the German-speaking part of Switzerland in 2001.⁴ To assess trends in physician-assisted suicide and other medical end-of-life practices, we conducted an identical study in Switzerland in 2013.



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Methods | A detailed description of the methods used in our study has been published elsewhere.^{2,4} On the basis of a random sample of death certificates in the German-speaking part of Switzerland (containing 70% of the country's total 8.1 million residents and the major cities of Zurich, Basel, and Bern)

filed between August 2013 and January 2014, we mailed 4998 questionnaires to the decedents' attending physicians under conditions of strict anonymity, of which 3173 (63.5%) were returned. All data from 2001 and 2013 were weighted to adjust for age- and sex-related differences in response rates and were age-standardized to the age distribution of Swiss residents at death in 2013. Two-sided *P* values for the comparison of 2001 and 2013 data were calculated using the Pearson χ^2 test for 2-way contingency tables (STATA survey tables for weighted data; STATA Corp LP).

Results | In 2013, a total of 71.4% of all deaths in our study population from the German-speaking part of Switzerland were nonsudden and expected and therefore eligible for end-of-life decisions. In 58.7% of all sampled deaths, at least 1 end-of-life decision was made, compared with a corresponding 52.0% in 2001 (*P* < .001) (Table).

The percentage of deaths in which life-prolonging treatment was forgone increased from 28.7% of all deaths in 2001 to 35.2% of all deaths in 2013 (*P* < .001). The percentage of deaths that were preceded by intensified alleviation of pain and symptoms remained stable (22.3% in 2001 vs 21.3% in 2013).

Physician-assisted death increased from 1.0% in 2001 to 2.2% in 2013 (*P* < .001), with assisted suicide increasing in the

Table. Frequency of Medical End-of-Life Practices in the German-Speaking Part of Switzerland, 2001 and 2013

Characteristic	Values ^a		P Value
	2001 ^b	2013	
Sampled cases, No.	4991	4998	
Studied cases (response rate), No. (%)	3355 (67.2)	3173 (63.5)	
Nonsudden, expected deaths	69.9 (68.3-71.4)	71.4 (69.8-72.9)	.19
Deaths preceded by at least 1 end-of-life practice ^c	52.0 (50.3-53.8)	58.7 (57.0-60.4)	<.001
Forgoing life-prolonging treatment ^d	28.7 (27.2-30.4)	35.2 (33.6-36.9)	<.001
Intensified alleviation of symptoms ^e	22.3 (20.9-23.8)	21.3 (19.9-22.7)	.31
Physician-assisted death	1.0 (0.7-1.4)	2.2 (1.8-2.8)	<.001
Assisted suicide ^f	0.3 (0.2-0.5)	1.1 (0.8-1.5)	<.001
Euthanasia ^g	0.2 (0.1-0.5)	0.3 (0.2-0.6)	.41
Ending of life without the patient's explicit request ^h	0.5 (0.3-0.8)	0.8 (0.5-1.2)	.08
Continuous deep sedation until death ⁱ	4.7 (4.0-5.4)	17.5 (16.2-18.8)	<.001
Without end-of-life decision	0.9 (0.6-1.3)	1.2 (0.9-1.6)	.26
Combined with			
Forgoing life-prolonging treatment	2.0 (1.6-2.6)	10.9 (9.8-12.0)	<.001
Intensified alleviation of symptoms	1.6 (1.2-2.1)	4.9 (4.1-5.7)	<.001
Physician-assisted death	0.1 (0.1-0.3)	0.5 (0.3-0.9)	.005

^a Data are presented as percentage (95% CI) unless otherwise noted.

^b Data for 2001 are age standardized to 2013. This may entail slight differences to previously published figures.

^c All data regarding these practices are weighted percentages (95% CIs) of all studied cases.

^d Affirmative answer to the question, "Did you or another physician withhold or withdraw a medical treatment while taking into account the possible hastening of death?"

^e Affirmative answer to the question, "Did you or another physician intensify the alleviation of pain and/or symptoms while taking into account the possible hastening of death?"

^f Affirmative answer to the question, "Was death the consequence of the use of a drug that was prescribed or supplied by you or another physician with the

explicit intention of enabling the patient to end his or her life?"

^g Affirmative answer to the question, "Was death the consequence of the use of a drug that was administered by you or another physician with the explicit intention of hastening the patient's death?" AND affirmative answer to the question, "Was this decision made at the explicit request of the patient?"

^h Affirmative answer to the question, "Was death the consequence of the use of a drug that was administered by you or another physician with the explicit intention of hastening the patient's death?" AND negative answer to the question, "Was this decision made at the explicit request of the patient?"

ⁱ Affirmative answer to the question, "Did the patient receive drugs, such as benzodiazepines and/or other sedative substances, to keep him or her in deep sedation or coma until death?"