Letters

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

<table>
<thead>
<tr>
<th>Trial ID</th>
<th>Primary Efficacy Outcome</th>
<th>FDA-Reported Results</th>
<th>Publication-Reported Results</th>
<th>Why Results Differed</th>
<th>Whether Interpretation Altered</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCT00739102 (STROLL study)</td>
<td>Stent primary patency at 12 mo</td>
<td>66.5% (95% CI, 60.0%-72.5%) (minimum prespecified effect of 66%)</td>
<td>71.2% (95% CI, 64.8%-76.8%) (no minimum prespecified effect)</td>
<td>More lenient definition of primary patency in publication-reported results</td>
<td>Yes, study interpreted as negative in FDA review, positive in publication</td>
</tr>
<tr>
<td>NCT01094678 (Zilver PTX-single arm)</td>
<td>Stent primary patency at 12 mo</td>
<td>82.7% in the Zilver PTX group</td>
<td>86.2% in the Zilver PTX group</td>
<td>More lenient definition of primary patency in publication-reported results</td>
<td>No, primary efficacy outcome event rate similar in FDA review and in publication</td>
</tr>
<tr>
<td>NCT00209274 (Everest II RCT)</td>
<td>Freedom from death, mitral valve surgery (for device group) or reoperation (for control group), and grade 3+ or 4+ mitral regurgitation at 12 mo</td>
<td>72.4% in the percutaneous repair group vs 87.8% in the surgical repair group (P = .001 for noninferiority)</td>
<td>55% in the percutaneous repair group vs 73% in the surgical repair group (P = .007)</td>
<td>Publication reported intention-to-treat analysis for primary outcome; FDA reported per-protocol analysis for primary outcome</td>
<td>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</td>
</tr>
</tbody>
</table>

**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. 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.

Adam T. Phillips, MD
Vinay K. Rathi, BA
Joseph S. Ross, MD, MHS

**Author Affiliations:** Department of Internal Medicine, Yale University School of Medicine, New Haven, Connecticut (Phillips); medical student, Yale University School of Medicine, New Haven, Connecticut (Rathi); Robert Wood Johnson Foundation Clinical Scholars Program, Section of General Internal Medicine, Department of Internal Medicine, Yale University School of Medicine, New Haven, Connecticut (Ross); Department of Health Policy and Management, Yale University School of Public Health, New Haven, Connecticut (Ross); Center for Outcomes Research and Evaluation, Yale–New Haven Hospital, New Haven, Connecticut (Ross).

**Corresponding Author:** Joseph S. Ross, MD, MHS, Robert Wood Johnson Foundation Clinical Scholars Program, Section of General Internal Medicine, Department of Internal Medicine, Yale University School of Medicine, PO Box 208093, New Haven, CT 06520 (joseph.ross@yale.edu).

**Published Online:** February 22, 2016. doi:10.1001/jamainternmed.2015.8590.

**Author Contributions:** Drs Phillips and Ross had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

- **Study concept and design:** All authors.
- **Acquisition, analysis, or interpretation of data:** All authors.
- **Drafting of the manuscript:** Phillips, Rathi.
- **Critical revision of the manuscript for important intellectual content:** All authors.
- **Statistical analysis:** Phillips, Rathi.

**Study supervision:** Ross.

**Conflict of Interest Disclosures:** Dr Ross reported receiving support through Yale University from Medtronic, Inc and Johnson & Johnson to develop methods of clinical trial data sharing, from the Centers of Medicare & Medicaid Services to develop and maintain performance measures that are used for public reporting, from the Blue Cross Blue Shield Association to better understand medical technology evidence generation, and from the US Food and Drug Administration to develop methods for postmarket surveillance of medical devices. No other disclosures were reported.


**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, 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 topics around the time of Sheen’s disclosure.

© Copyright 2016 American Medical Association. All rights reserved.
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 were 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 Khandakar 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 disclosure had not occurred). Data analysis was conducted from November 17 to December 8, 2015.
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 of health education to our next celebrity: 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.

John W. Ayers, PhD, MA
Benjamin M. Althouse, PhD, ScM
Mark Dredze, PhD
Eric C. Leas, MPH
Seth M. Noar, PhD

Author Affiliations: Graduate School of Public Health, San Diego State University, San Diego, California (Ayers); Santa Fe Institute, Santa Fe, New Mexico (Althouse); New Mexico State University, Las Cruces (Althouse); Human Language Technology Center of Excellence, Johns Hopkins University, Baltimore, Maryland (Dredze); Bloomberg LP, New York, New York (Dredze); University of California-San Diego School of Medicine, La Jolla (Leas); School of Media and Journalism, University of North Carolina, Chapel Hill (Noar).

Corresponding Author: John W. Ayers, PhD, MA, Graduate School of Public Health, San Diego State University, 9245 Sky Park Ct, Ste 230, San Diego, CA 92123 (ayers.john.w@gmail.com).


Author Contributions: Dr Ayers had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: All authors.

Acquisition, analysis, or interpretation of data: Ayers, Althouse, Dredze, Leas.

Drafting of the manuscript: All authors.

Critical revision of the manuscript for important intellectual content: All authors.

Conflict of Interest Disclosures: Drs Ayers and Althouse reported sharing an equity stake in Directing Medicine LLC, which advises how to implement some of the methods embodied in this work. Dr Dredze reported receiving consulting fees from Directing Medicine LLC and Sickweather LLC, who use social media for public health surveillance. The methods described in this article are not proprietary. No other disclosures were reported.

Additional Contributions: Kurt Ribisl, PhD, and Diana Francis, BA, University of North Carolina, provided feedback but were not compensated for their contribution.


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 job of public health is to be certain that the right information arrives when it is needed. Yet, prurient interest in prominent persons is needed to clarify early findings. Yet, our findings can still inform practice of health education if we adapt traditional methods of health education to our next celebrity: 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.

Mitchell H. Katz, MD
Conflict of Interest Disclosures: None reported.


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.

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) 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.

Results | In 2013, a total of 71.4% of all deaths in our study population from the German-speaking part of Switzerland were non-sudden 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>
<thead>
<tr>
<th>Table. Frequency of Medical End-of-Life Practices in the German-Speaking Part of Switzerland, 2001 and 2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristic</td>
</tr>
<tr>
<td>---------------------------------</td>
</tr>
<tr>
<td>Sampled cases, No.</td>
</tr>
<tr>
<td>Studied cases (response rate), No. (%)</td>
</tr>
<tr>
<td>Nonsudden, expected deaths</td>
</tr>
<tr>
<td>Deaths preceded by at least 1 end-of-life practice*</td>
</tr>
<tr>
<td>Forgoing life-prolonging treatment*</td>
</tr>
<tr>
<td>Intensified alleviation of symptoms*</td>
</tr>
<tr>
<td>Physician-assisted death</td>
</tr>
<tr>
<td>Assisted suicide</td>
</tr>
<tr>
<td>Euthanasia</td>
</tr>
<tr>
<td>Ending of life without the patient’s explicit request*</td>
</tr>
<tr>
<td>Continuous deep sedation until death</td>
</tr>
<tr>
<td>Without end-of-life decision</td>
</tr>
<tr>
<td>Combined with</td>
</tr>
<tr>
<td>Forgoing life-prolonging treatment</td>
</tr>
<tr>
<td>Intensified alleviation of symptoms</td>
</tr>
<tr>
<td>Physician-assisted death</td>
</tr>
</tbody>
</table>

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

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

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

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?”

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?”

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?”

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?”

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?”

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?”