Contemporary Clinical Trials 72 (2018) 146–157

Contents lists available at ScienceDirect

Contemporary Clinical Trials

journal homepage: www.elsevier.com/locate/conclintrial

Deception in clinical trials and its impact on recruitment and adherence of study participants

Chuen Peng Lee[a,*], Tyson Holmes[b], Eric Neri[c], Clete A. Kushida[d]

[a] Department of Respiratory and Critical Care Medicine, Tan Tock Seng Hospital, 11 Jalan Tan Tock Seng, 308433, Singapore
[b] Stanford University Human Immune Monitoring Center, Institute for Immunity Transplantation and Infection, Stanford University School of Medicine, Stanford, United States
[c] Stanford University School of Medicine, Palo Alto, CA, United States
[d] Stanford Sleep Medicine Center, Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, 450 Broadway Street, MC 5704, Pavilion C, 2nd Floor, Redwood City, CA 94063-5704, United States

ABSTRACT

Deceptive practices by participants in clinical research are prevalent. It has been shown that as high as 75% of participants withheld information to avoid exclusion from studies. Self-reported adherence has been found to be largely inaccurate. Overcoming deception is a critical issue, since the safety of study participants, the integrity of research data and research resources are at risk. In this review article, we examine deception from the perspective of investigators conducting clinical trials; we describe the types (concealment, fabrication, drug holidays and collusion), prevalence, risks, and predictors of deception, and propose an approach to reduce the impact of deception, especially on adherence, in clinical trials.

1. Introduction

"Everybody lies" so said actor Hugh Laurie in his former role as Dr. Gregory House in the Emmy Award-winning American television series – "House" [1]. This is far from fiction in clinical practice [2]. The New York Times bestseller, "Everybody Lies - Big Data, New Data, and What the Internet Can Tell Us About Who We Really Are," unravels deception through big data aggregated by online search engines [3]. Data generated by clinical trials is as likely as any other aspects of our lives to be contaminated by lies and partial truths [4].

1.1. Prevalence

Deceptive practices are prevalent [4–8]. The deceit rate in healthy volunteers range from 3 to 25% across multiple studies [9–14]. Devine and colleagues studied the use of deception by experienced research participants who reported an average participation in 12 studies in the past year and a lifetime-reported income as a study participant of more than $20,000 USD [4]. One in four of the 99 surveyed participants self-reported exaggeration of a symptom (fabrication) to enter a trial. One in three participants fabricated by pretending to have a health problem, providing false information, or inflicting self-harm to qualify for a study. Seventy-five percent of participants withheld information to avoid exclusion.

1.2. Risks

1.2.1. Overcoming deception is a critical issue

1.2.1.1. The integrity of research data is at risk. Deceptive behavior may lead to invalidation of studies. Multiple simultaneous activations of inhalers, recorded by electronic monitoring devices, were detected in multiple patients in two asthma trials [15]. Because of this deception (fabrication) and poor overall adherence, valid conclusions could only be made in 6 out of 34 patients. In intention-to-treat analyses, undetected non-adherence may lead to biased estimates of treatment effects when analyses are misinterpreted as assessments of treatment as received [16]. Rebound effects (due to sudden uncounteracted physiologic responses to the actions of the withdrawn drug) and recurrent first dose effects from drug holidays may confound efficacy and side effects of a new drug [17]. White coat compliance may lead to therapeutic paradoxes, i.e., progression of glaucoma despite normal intraocular pressure in the clinic [18].

1.2.1.2. The safety of study participants is at risk. Deaths have been reported from deceit in clinical trials. A bulimic trial participant had concealed her medical history in a clinical study where the interaction between bulimia-led hypokalemia and the study drug, lithium, led to her demise [19]. Study participants who are chronic substance abusers may experience severe withdrawal symptoms, e.g., delirium tremens, which could be life-threatening or confound the side effect profile of the

* Corresponding author.
E-mail address: chuen_peng_lee@ttsh.com.sg (C.P. Lee).

https://doi.org/10.1016/j.cct.2018.08.002
Received 31 May 2018; Received in revised form 27 July 2018; Accepted 14 August 2018
Available online 21 August 2018

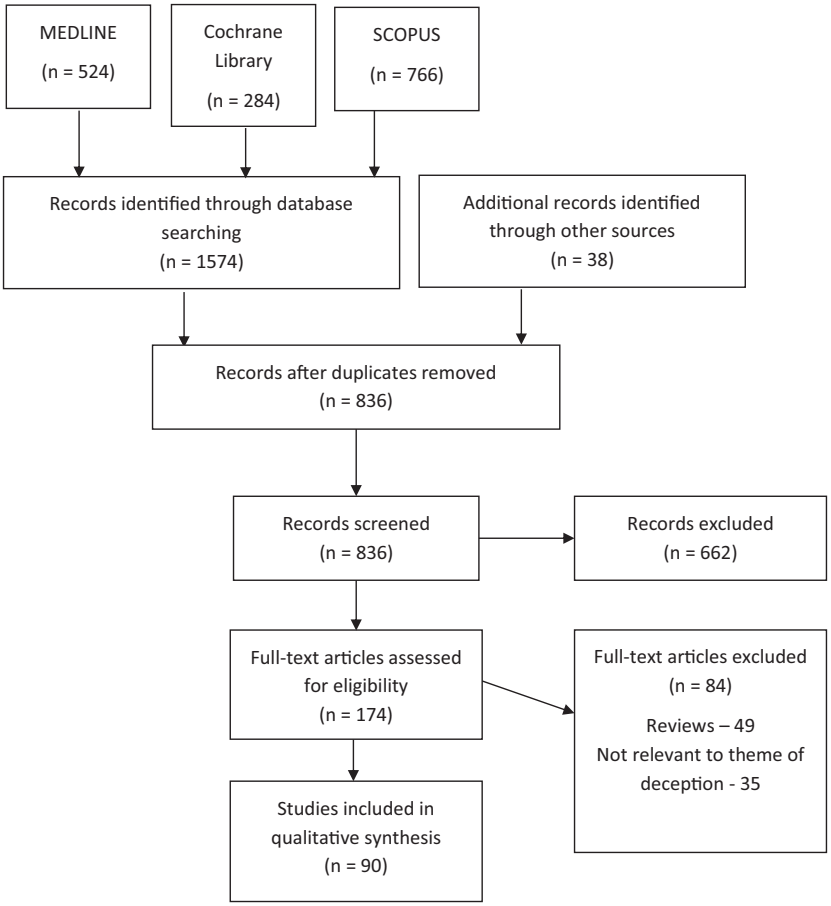

Fig. 1. Identification of studies on deception.

study drug. Unreported Drug holidays have led not only to false positive viral load but also to the emergence of drug resistant organisms [20]. Deception in drug adherence, i.e., pill dumping, could underestimate the efficacy and side effects of a drug or overestimate its minimally effective dose [21].

1.2.1.3. Research resources are at risk. Pharmaceutical and biological companies spend an estimated 23 million hours each year just on recordkeeping for a new drug application [22]. It takes an average of 12 years for a new drug and 3 to 5 years for a new device from inception to approval by the Food and Drug Administration (FDA) [23]. The widely held belief that larger trials lead to more accurate results may not hold true as it has been shown that there was greater medication nonadherence in such studies [24]. These hidden costs of deception remained largely unexplored.

By reviewing current literature, we hope that we could inform the research community of the burden of deception by participants in clinical research, thereby increasing awareness and collaborative efforts to stunt its growth.

2. Methods

2.1. Key Definitions

"Deception" is defined as the act of causing someone to accept as true or valid what is false or invalid [25]. Deception can be classified into the following categories: Concealment is defined as intentional non-disclosure [25]. Commonly intentionally-withheld information such as participant nondisclosure of tobacco use, illicit drug abuse, alcohol consumption, pre-existing medical conditions, and concurrent enrollment in other clinical trials are examples of concealment [4,8]. Fabrication is defined as the act of invention aimed at achieving deception [25]. Examples of fabrication includes participant exaggeration of symptoms, falsification of current health status, and over-reporting of adherence. Collusion is defined as participant sharing of privileged information pertaining to study recruitment among fellow participants in order to gain study admission [26] and sharing of study drugs [27]. These types of deception by participants to ensure their recruitment or continued participation in clinical trials have been reported [4]; this deceptive behavior by participants may result in bias and lead to uninterpretable study outcomes.

Non-adherence to a research protocol represents a violation of the contract and a breach of trust between the investigator and participant, which yields misleading or erroneous research outcomes, and may result in harm when translated to clinical practice. Over-reporting of adherence can be regarded as an expression of guilt for non-adherent behaviour. Drug holidays (i.e., periods of consecutively missed drug dosages), excluding periods of reduced or no use per clinician advice, can be considered as a form of intentional non-adherence.

We conducted a literature search on all studies reported in the English language in MEDLINE, Cochrane library, and SCOPUS from inception till 10 December 2017 using a combination of the following search terms: "deception", "deceit", "professional research subjects", "simultaneous enrolment", "co-enrolment", "undue inducements", "subversive subjects", "veteran volunteers", "repeat participation", "inhaler dumping", "nebulizer dumping", "pill dumping", "white coat compliance", "self-report and CPAP", "drug holidays", and "smoking and deception". Relevant references cited in selected manuscripts were pearled and were also included in this review. Studies on non-adherence (except for drug holidays) and those without an objective test