ClinicalTrials.gov and Addressing Challenges in Finding Evidence

Deborah A. Zarin, M.D.
Director, ClinicalTrials.gov
February 2014
Evidence Based Regulatory Decision Making

• Requires access to all relevant evidence
  – Not just those data submitted by a sponsor
  – Not just those analyses submitted by a sponsor

• Barriers to complete access to evidence:
  – Missing (invisible) trials or other studies
  – Unreported or changed outcome measures
  – Unreported (or obscured) AEs
  – Incomplete or changed analyses
Systematic, Searchable Sources of Data
(Beyond those submitted by sponsor)

• PubMed
• ClinicalTrials.gov
• Other registries
Problems with Published Literature

- Missing many trials
- Incomplete reporting of trials that are published
  - Prespecified outcome measures may be omitted
  - AEs omitted
- Lack of fidelity to protocol for some analyses; e.g.
  - Unacknowledged changes to outcome measures
  - Deviations from analysis plan
Fig 2 Cumulative percentage of studies published in a peer reviewed biomedical journal indexed by MEDLINE during 100 months after trial completion among all NIH funded clinical trials registered within ClinicalTrials.gov

Kaplan-Meier estimates for ulcer complications according to traditional definition. Results are truncated after 12 months, no ulcer complications occurred after this period. (Adapted from Lu 2001.)
Trial Registration and Results Reporting

• Registration (prior to trial initiation)
  – Public list of all relevant trials with key protocol details

• Results Reporting
  – Structured, curated summary data
    • Ensures minimum data set: (participant flow, baseline characteristics, prespecified outcome measures, AEs)
    • Independent of journal publication
ClinicalTrials.gov

• Registry: Over 160,000 studies
  – 500 new studies/week
  – 18% (over 29,000) observational studies

• Results database: Over 11,000 studies
  – 100 new sets of results/week

• International in scope
  – Fewer than half are in US only

• All phases, all study models, all intervention types
Content of ClinicalTrials.gov Record

• One record per trial
• Registration section
  – Submitted at trial initiation
  – Summarizes information from trial protocol
    – Condition
    – Interventions
    – Outcomes
    – Design, etc
  – Includes recruitment information (e.g., eligibility, locations)
• Results section
  – Submitted after trial completion
  – Summarizes trial results
    • Participant flow
    • Baseline characteristics
    • Outcome measures (including statistical analyses)
    • Adverse events
Key Policies

• ICMJE (Registration only)
  – Interventional trials
    • All intervention types
  – All phases; all jurisdictions; enforced by journal editors

• FDAAA (Registration and Results)
  – Interventional trials
    • Drugs, biologics, devices
  – **Not** phase 1
  – US FDA jurisdiction (e.g., IND/IDE or US site)
  – Specific enforcement mechanisms

• EMA (Registration and Results)
“Invisible” Trials

• Not all trials legally required to register
  – E.g., non-IND studies with no US sites
• Registration only helps if there is an accessible, searchable database
• Features of search engine determine the utility
  – Even best search engines have challenges with drug and device names, other features of trials
• Many registries around the world
  – Varying quality of search engines
  – No systematic de-duplication
Not All Trials are Registered
Number of Trials First Registered in 2014 at ClinicalTrials.gov and Listed as “Completed” or “Terminated” by Start Year

- **Industry** (n = 35 trials)
- **Non-Industry** (n = 124 trials)
Not All Registered Trials Can Be Found
Drug Serial #s = “Hidden” Trials
ClinicalTrials.gov Gardasil® Search

Gardasil® was approved on June 8, 2006
PubMed Gardasil® Search

One month after approval (and promotion)
Study NCT00378560

**Gardasil (V501) Study in Adult Women**

This study is currently recruiting patients.
Verified by Merck September 2006

<table>
<thead>
<tr>
<th>Sponsored by:</th>
<th>Merck</th>
</tr>
</thead>
<tbody>
<tr>
<td>Information provided by:</td>
<td>Merck</td>
</tr>
<tr>
<td>ClinicalTrials.gov Identifier:</td>
<td>NCT00378560</td>
</tr>
</tbody>
</table>

**Purpose**

A study to evaluate the efficacy, immunogenicity, safety and tolerability of Gardasil (V501) in adult women.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Intervention</th>
<th>Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Papillomavirus</td>
<td><strong>Vaccine: V501, Gardasil, human papillomavirus (types 6,11,16,18) recombinant vaccine</strong> / <strong>Duration of Treatment: 7 Months</strong></td>
<td>Phase II</td>
</tr>
<tr>
<td>Infections</td>
<td><strong>Vaccine: Placebo (unspecified) / Duration of Treatment: 7 Months</strong></td>
<td></td>
</tr>
</tbody>
</table>
Names/Identifiers Are Critical

• Search engines depend on known names, lists of synonyms, and hierarchies: e.g., Paxil
  – Aropax
  – Asimia
  – brl-29060
  – fg-7051
  – Ldmp
  – Paroxetine
  – Pexeva
  – Seroxat

• “Code” names, without “de-coders,” lead to “hidden” trials

• Non-specific names may also prevent the search engine from retrieving a useful list of trials

• Biologic, device, and other irregular intervention names challenge the system:
  – Vaccine: ALVAC-HIV MN120TMG (vCP205)
  – Device: IT LEISH (rK39); Device: galyfilcon AP 8.3 BC; Device: BD/33G
Naming Drugs

• After Approval
  - Generic name (USAN, USP), links to chemical structure

• Before Approval
  - Chemical structure (name, drawing)
  - Company serial number
    - No public record or oversight
    - No guaranteed one-to-one correspondence
Does the Search Engine Enable You to Find the Trials You Want?

- Spelling correction and relaxation of search terms
- Use of synonymy
- Fielded search
- Use of hierarchy from MeSH
- Relevancy ranking
There Are Many Trial Registries of Varying Quality

Insufficient Coordination Leads to “World Chaos”
## Protocol Registration Status

<table>
<thead>
<tr>
<th>Mandatory for Registrant to Post (in effect)</th>
<th>Non-voluntary Post by EC or Government (in effect)</th>
<th>Mandatory for Registrant to Post (pending)</th>
<th>Non-voluntary Post by EC or Government (pending)</th>
<th>Legislation / Regulations (ongoing activity)</th>
<th>Voluntary Registry (in effect)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Argentina_EfC</td>
<td>Argentina_EfC</td>
<td>KenyinaEffC</td>
<td>Croatia <strong>Integrated Platform</strong></td>
<td>Canada</td>
<td>Africa</td>
</tr>
<tr>
<td>Chile</td>
<td>Mexico_Switzerland</td>
<td></td>
<td>Spain <strong>Integrated Platform</strong></td>
<td>China</td>
<td>Australia/New Zealand</td>
</tr>
<tr>
<td>Colombia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>China_CFDA</td>
</tr>
<tr>
<td>Czech Republic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>China_ChiCTR</td>
</tr>
<tr>
<td>France</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Cuba</td>
</tr>
<tr>
<td>Germany <strong>PharmNet.Bund</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Euro. Union_ENCePP</td>
</tr>
<tr>
<td>Korea <strong>MFDS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Germany_DRKS</td>
</tr>
<tr>
<td>Netherlands <strong>CCMO</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Hong Kong</td>
</tr>
<tr>
<td>Norway</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Iran</td>
</tr>
<tr>
<td>Peru</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Japan</td>
</tr>
<tr>
<td>Russia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Korea_CRIS</td>
</tr>
<tr>
<td>Serbia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Sri Lanka</td>
</tr>
<tr>
<td>Singapore</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Tanzania</td>
</tr>
<tr>
<td>Slovakia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>United Kingdom</td>
</tr>
<tr>
<td>Venezuela</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Argentina_ReNIS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Austria NIS1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brazil2</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Euro. Union <strong>EU PAS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>India</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Israel3</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malaysia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>New Zealand4</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Philippines5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>South Africa</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Taiwan</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>United States</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- This table is not intended to be exhaustive
- It is not guaranteed to be accurate
- Red indicates changes since April 2012
- Last updated April 2013

1 Non-interventional studies
2 Register Phase 1 - 4 trials in ReBEC
3 Register in ClinicalTrials.gov
4 Required for ethics approval (WHO/CTgov)
5 Register Phase 1 - 4 trials in PHRR
6 Posts PDF lists of trials
7 Replaced database with PDF file
8 In any WHO/ICMJE registry plus national database
9 NCA loads XML; sponsor adds summary
10 Post-marketing studies
11 In public user test phase (since Jul 2011)
12 NRES, ISRCTN, and PROSPERO

Copyright © 2013 SEC Associates, Inc.
Welcome

- The Clinical Trials Search Portal provides access to a central database containing the trial registration data sets provided by the registries listed on the right. It also provides links to the full original records.

- To facilitate the unique identification of trials, the Search Portal bridges (groups together) multiple records about the same trial. [More information]

- Please note: This Search Portal is not a clinical trials registry. [How to register a trial]

- For mobile users, please use this link [http://apps.who.int/trialsearch/ictrmob.aspx](http://apps.who.int/trialsearch/ictrmob.aspx). It can be opened from any smartphone.

- It is now possible to export the results of the search into XML. [More information]

- Crawling the ITRP database now requires a username/password. To request access to the crawling pages please send an email to ictrinfo@who.int

Data Providers

Data sets from [data providers](#) are updated every Tuesday evening according to the following schedule:

**Every week:**

- Australian New Zealand Clinical Trials Registry, last data file imported on 3 February 2014
- ClinicalTrials.gov, last data file imported on 3 February 2014
- EU Clinical Trials Register (EU-CTR), last data file imported on 3 February 2014
- ISRCTN, last data file imported on 3 February 2014

**Every 4 weeks:**

- Brazilian Clinical Trials Registry (ReBec), last data file imported on 3 February 2014
- Chinese Clinical Trial Registry, last data file imported on 2 February 2014
- Clinical Trials Registry - India, last data file imported on 3 February 2014
- Clinical Research Information Service - Republic of Korea, last data file imported on 3 February 2014
- Cuban Public Registry of Clinical Trials, last data file imported on 3 February 2014
- German Clinical Trials Register, last data file imported on 3 February 2014
- Iranian Registry of Clinical Trials, last data file imported on 2 February 2014
- Japan Primary Registries Network, last data file imported on 2 February 2014
- Pan African Clinical Trial Registry, last data file imported on 3 February 2014
- Sri Lanka Clinical Trials Registry, last data file imported on 2 February 2014
- The Netherlands National Trial Register, last data file imported on 3 February 2014
- "New" Thai Clinical Trials Register (TCTR), last data file imported on 3 February 2014
88 Registered Clinical Studies of Tysabri:
ClinicalTrials.gov & WHO Search Portal

ClinicalTrials.gov Search
Intervention = “Tysabri”
Synonyms Searched:
  • Natalizumab
  • Antegren
  • Anti-vla4

WHO Search Portal Search
Intervention = “Tysabri” OR “Natalizumab”

29 studies
43 studies
16 studies
Names for 3 SSRI Drugs Recognized by ClinicalTrials.gov Search Engine

<table>
<thead>
<tr>
<th>Zoloft</th>
<th>Prozac</th>
<th>Paxil</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Altruline</td>
<td>• Fluoxetine</td>
<td>• Aropax</td>
</tr>
<tr>
<td>• Aremis</td>
<td>• Lilly 110140</td>
<td>• Asimia</td>
</tr>
<tr>
<td>• Besitran</td>
<td>• Rapiflux</td>
<td>• Brisdelle</td>
</tr>
<tr>
<td>• Gladem</td>
<td>• Reconcile</td>
<td>• brl-29060</td>
</tr>
<tr>
<td>• Lustral</td>
<td>• Sarafem</td>
<td>• fg 7051</td>
</tr>
<tr>
<td>• Sealdin</td>
<td>• Selfemra</td>
<td>• Ldmp</td>
</tr>
<tr>
<td>• Sertraline</td>
<td></td>
<td>• Paroxetine</td>
</tr>
</tbody>
</table>

25
Case Study – the GAS Study

• Registered in (at least) three registries
  – ISRCTN, ClinicalTrials.gov, ANZCTR

• Three different PIs (US, UK, Aus); three different “sponsors.”

• ANZCTR and ClinicalTrials.gov records have same title; ISRCTN lists ANZCTR as secondary ID

• WHO portal lists two records, but does not recognize them as duplicates; does not have the ISRCTN record
On WHO Portal Site:
Basic Search for “The GAS Study”

<table>
<thead>
<tr>
<th>Recruitment status</th>
<th>Main ID</th>
<th>Public Title</th>
<th>Date of Registration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recruiting</td>
<td>ACTRN12606000441516</td>
<td>A multi-site randomised controlled trial comparing regional and general anaesthesia for effects on neurodevelopmental outcome and apnoea in infants</td>
<td>16/10/2006</td>
</tr>
</tbody>
</table>

Disclaimer: Trials posted on this search portal are not endorsed by WHO, but are provided as a service to our users. In no event shall the World Health Organization be liable for any damages arising from the use of the information linked to in this section. None of the information obtained through use of the search portal should in any way be used in clinical care without consulting a physician or licensed health professional. WHO is not responsible for the accuracy, completeness and/or use made of the content displayed for any trial record.
On WHO Portal Site: Title Field Search for “Neurodevelopmental Outcome”

<table>
<thead>
<tr>
<th>Recruitment status</th>
<th>Main ID</th>
<th>Public Title</th>
<th>Date of Registration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recruiting</td>
<td>NCT00809055</td>
<td>Magnetic Resonance Imaging (MRI) and Neurodevelopmental Outcomes in Preterm Infants Following Administration of High-Dose Caffeine</td>
<td>15/12/2008</td>
</tr>
<tr>
<td>Recruiting</td>
<td>NCT00756600</td>
<td>A Multi-Site Randomized Controlled Trial Comparing Regional and General Anesthesia for Effects on Neurodevelopmental Outcome and Apnea in Infants</td>
<td>18/09/2008</td>
</tr>
<tr>
<td>Recruiting</td>
<td>NCT00713635</td>
<td>Prenatal Effects of Congenital Heart Disease (CHD) on Neurodevelopmental Outcome</td>
<td>09/07/2008</td>
</tr>
<tr>
<td>Recruiting</td>
<td>NCT00464100</td>
<td>Near-Infrared Spectroscopy (NIRS) Neurodevelopmental Outcomes</td>
<td>18/04/2007</td>
</tr>
<tr>
<td>Recruiting</td>
<td>ACTRN12606000441516</td>
<td>A multi-site randomised controlled trial comparing regional and general anaesthesia for effects on neurodevelopmental outcome and apnoea in infants</td>
<td>16/10/2006</td>
</tr>
<tr>
<td>Recruiting</td>
<td>NTR364</td>
<td>Effect of early fatty acid status on neurodevelopmental outcome at 9 years,</td>
<td>12/09/2005</td>
</tr>
<tr>
<td>Recruiting</td>
<td>NTR305</td>
<td>The effect of treatment of neonatal electrographic seizures, detected with the continuous cerebral function monitoring, with respect to occurrence of postneonatal epilepsy and neurodevelopmental outcome.</td>
<td>09/09/2005</td>
</tr>
</tbody>
</table>
Problems with Published Studies

• Incomplete reporting of Outcome Measures
  – Unacknowledged changes
  – Omissions

• Unacknowledged changes to Analysis Population
  – “missing participants”

• Incomplete reporting of AEs, e.g.,
  – Only “attributable” or “clinically significant”
4 Scientific Modules

- Participant Flow
- Baseline Characteristics
- Outcome Measures
- Adverse Events
- Other, including “Certain Agreements”
## Serious Adverse Events

<table>
<thead>
<tr>
<th></th>
<th>Intravitreal Afibercept Injection (IAI) (Baseline to Week 24)</th>
<th>Sham Treatment (Baseline to Week 24)</th>
<th>IAI to IAI (Week 24 to Week 100)</th>
<th>Sham Treatment to IAI (Week 24 to Week 100)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total # participants affected/at risk</strong></td>
<td>6/114 (5.26%)</td>
<td>6/74 (8.11%)</td>
<td>20/110 (18.18%)</td>
<td>14/60 (23.33%)</td>
</tr>
<tr>
<td><strong>Blood and lymphatic system disorders</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anaemia * A [1]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td># participants affected/at risk</td>
<td>1/114 (0.88%)</td>
<td>0/74 (0%)</td>
<td>0/110 (0%)</td>
<td>1/60 (1.67%)</td>
</tr>
<tr>
<td>Neutropenia * A [2]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td># participants affected/at risk</td>
<td>0/114 (0%)</td>
<td>0/74 (0%)</td>
<td>0/110 (0%)</td>
<td>1/60 (1.67%)</td>
</tr>
<tr>
<td>Pernicious anaemia * A [3]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td># participants affected/at risk</td>
<td>0/114 (0%)</td>
<td>0/74 (0%)</td>
<td>0/110 (0%)</td>
<td>1/60 (1.67%)</td>
</tr>
<tr>
<td><strong>Cardiac disorders</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td># participants affected/at risk</td>
<td>0/114 (0%)</td>
<td>1/74 (1.35%)</td>
<td>0/110 (0%)</td>
<td>0/60 (0%)</td>
</tr>
</tbody>
</table>

* Indicates events were collected by non-systematic methods.

A Term from vocabulary, MedDRA Version 13.1

[1] Non-Ocular AE
[2] Non-Ocular AE
[3] Non-Ocular AE
[4] Non-Ocular AE
Timing and Completeness of Trial Results Posted at ClinicalTrials.gov and Published in Journals

Carolina Riveros¹,²,³, Agnes Dechartres¹,²,³*, Elodie Perrodeau¹,³, Romana Haneef¹,³, Isabelle Boutron¹,²,³,⁴, Philippe Ravaud¹,²,³,⁴,⁵

¹INSERM U738, Paris, France, ²Université Paris Descartes—Sorbonne Paris Cité, Paris, France, ³Centre d’Épidémiologie Clinique, Hôpital Hôtel-Dieu, Assistance Publique-Hôpitaux de Paris, Paris, France, ⁴French Cochrane Centre, Paris, France, ⁵Mailman School of Public Health, Columbia University, New York, New York, United States of America

Findings: “Reporting was significantly more complete at ClinicalTrials.gov than in the published article for the flow of participants (64% versus 48% of trials, p < 0.001), efficacy results (79% versus 69%, p = 0.02), adverse events (73% versus 45%, p < 0.001), and serious adverse events (99% versus 63%, p < 0.001).”

Conclusions: “Our results highlight the need to search ClinicalTrials.gov for both unpublished and published trials. Trial results, especially serious adverse events, are more completely reported at ClinicalTrials.gov than in the published article.”
24% of trials reported analyzing 90% or fewer participants for the first primary outcome measure.

~70% of trials reported analyzing fewer than 100% of participants for the first primary outcome measure.
Haphazard reporting of deaths in clinical trials: a review of cases of ClinicalTrials.gov records and matched publications—a cross-sectional study

Amy Earley,¹ Joseph Lau,² Katrin Uhlig,¹,³

ABSTRACT

Context: A participant death is a serious event in a clinical trial and needs to be unambiguously and publicly reported.

Objective: To examine (1) how often and how numbers of deaths are reported in ClinicalTrials.gov records; (2) how often total deaths can be determined per arm within a ClinicalTrials.gov results record and its corresponding publication and (3) whether counts may be discordant.

Design: Registry-based study of clinical trial results reporting.

Setting: ClinicalTrials.gov results database searched in July 2011 and matched PubMed publications.

Selection criteria: A random sample of ClinicalTrials.gov results records. Detailed review of records with a single corresponding publication.

ARTICLE SUMMARY

Article focus

- We hypothesised that the lack of clear expectations for reporting all deaths in clinical trials give rise to discrepancies in the number of deaths reported across reports of a trial.

Key message

- There is a lack of clarity, consistency and agreement in reporting of deaths in clinical trials which highlights the need for unambiguous templates to standardise reporting of total number of deaths per arm in ClinicalTrials.gov records and more explicit reporting guidelines for peer-reviewed publications.

Strengths and limitations of this study...
Some Suggestions

• Enforce registration and use NCT # in communications
• Ask sponsors for listings of all trials, along with registration numbers
• Signal seriousness of registration details; follow-up on discrepancies
• Consider methods of disseminating “code names” and other informal naming conventions
Unambiguous Identification of Obesity Trials

TO THE EDITOR: Colman et al. (Oct. 25 issue) describe trial results underlying approval of two weight-management drugs by the Food and Drug Administration. However, their table included noninformative terms (e.g., “study 1”) without citing publications or ClinicalTrials.gov records. The materials that were referenced used only acronyms (e.g., BLOOM) and internal identifiers (e.g., OB-301) — neither of which could be linked to the terms in the table. Using ClinicalTrials.gov (www.clinicaltrials.gov), we identified six studies of lorcaserin for obesity and nine studies of phentermine and topiramate for obesity (as of October 15, 2012). Only Colman et al. could confirm the likely matches (Table 1).

This is an important example of why listing ClinicalTrials.gov identifiers (NCT numbers) would provide unambiguous access to trial-design infor-

Table 1. Different Identifiers for the Same Clinical Studies.

<table>
<thead>
<tr>
<th>Drug, Identifier Used by Colman et al., and Identifier Used in References Cited by Colman et al.</th>
<th>Probable ClinicalTrials.gov Identifier</th>
<th>Publication (PubMed Identifier) Associated with Probable ClinicalTrials.gov Identifier</th>
</tr>
</thead>
<tbody>
<tr>
<td>Qsymia</td>
<td>Study 1</td>
<td>OB-301</td>
</tr>
</tbody>
</table>

*BLOOM denotes Behavioral Modification and Lorcaserin for Overweight and Obesity Management, BLOOM-DM Behavioral Modification and Lorcaserin for Obesity and Overweight Management in Diabetes Mellitus, BLOSSOM Behavioral Modification and Lorcaserin Second Study for Obesity Management, and NA not applicable.