



OTHER TRANSACTION AUTHORITY

Presented By:

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US National Debt as of October 26, 2017



NATIONAL DEBT OF UNITED STATES

\$ 20,446,131,495,881

Includes Intragovernmental Holdings and allowance of one day delay in banks reporting to treasury

Source: USA Gov. Note, you may see our USA debt clock jump. To give you the most accurate live figures, we are continually monitoring the situation and manually adding the new lump sums of government debt.

\$20 Trillion and Counting



What types of contracts are efficient, cost effective, bridges new partnerships, and can be used to improve public preparedness and response?





- **Commercial Firms**
- **New R&D Players**
- **Consortia**
- **Corporations that never held a government contract**

Companies on the cutting edge of technology







- Joint Decision Making
- Team
- Accountability

Joint Decision Making

- Interrogate Risks
- Assess Progress
- Agree on Next Steps



- Universities
- Nonprofit Organizations
- Large Businesses
- Small Businesses



Team

Team

ARTICLES OF COLLABORATION

3.4 Two main reasons for using overviews of properly randomized trials to assess MODERATE treatment effects: avoiding selection biases and reducing random errors

Reliable detection (or refutation) of treatment effects that are only moderate in size requires the reliable evaluation of (i) moderate biases and (ii) moderate random errors, either of which might obscure (or mimic) moderate treatment effects. Each of these selection biases may be difficult to assess adequately without a proper overview of the appropriately randomized trials.⁴

First, without a systematic search for all relevant randomized trials, an unbiased selection of the trials to be reviewed is unlikely. The selection biases caused by this search process may be moderate, but they may be difficult to assess and other selection biases (to be discussed below) may be more serious.

Second, unless comparisons are made among overviews based on trials that are similar in design (or, preferably, several different comparisons are made), the chance can be produced for random errors that are comparable in size to moderate treatment effects. Such errors may be avoidable in an overview of all relevant randomized trials.

3.5 Overviews of trials with no data-dependent selection bias: statistical difficulties

A complete and exhaustive review (not of the results of trials, but of the results of the review) of all published trial results that could be relevant, and of unpublished results of particular trials that remain unpublished unless those results are exceptional,¹¹ makes overviews based only on the published literature likely to be moderately biased results.¹² Moreover, even a complete review of nothing but the published literature might be such a time-consuming task (especially if additional information needs to be sought by investigators) that only a few determined investigators would be likely to achieve it. Others may be satisfied with an incomplete review that excludes some of the better known publications, but this might introduce some further selection bias since even among published studies the favorable or unfavorable play of chance in the results of a trial may substantially influence how well known that trial becomes, and trials that appear to have particularly promising results (or, for some treatments, particularly unpromising results) are likely to be among the best known. Even if any selective biases of this published literature are only moderate in size, moderate biases may add moderate to moderate treatment effects impossible to assess reliably. The biases that can be introduced by selective exclusion of certain randomized trial results can, however, be avoided by systematic review of all (or of an unbiased subset) of the randomized trials ever undertaken.

3.6 Other selection biases within or in design or in analysis of trials

Overviews may also be of some limited help in consulting other selection biases in the design or in the analysis of trials. Selection biases in design can be produced not only by failure to allocate treatment properly at random, but also by post-randomization withdrawal of selected patients (see below). Selection bias in analysis can be produced not only by undue emphasis on just a limited number of trials, but also by undue data-dependent emphasis on the relevant effects of treatment in particular subgroups of patients (for real examples, see Table 1 and the associated discussion on "Selection bias from subgroup analyses").

3.7 Proper randomization to avoid selection bias: statistical difficulties in the assessment of MODERATE treatment effects

Comparisons of two treatments (or two "treatment efficacy" hypotheses) or comparisons of two treatments (or two "treatment efficacy" hypotheses) with moderate biases, the effect size of which is moderate, are difficult to assess reliably. For example, in a randomized trial with a treatment (P=0.002) in mortality was compared with a control (P=0.002) in mortality, if half of the same population had been specifically instructed to follow the control, then a statistically significant "evaluation" of the treatment would have been produced.

Proper randomization to avoid selection bias is only possible if the next treatment allocation before patient entry is unknown (or, for example, where randomization data are publicly available, allowing foreknowledge, or where allocation is otherwise based on address, distance, or other non-random factors) that are unassociated with the original sequence of treatments was completely random. Trials that permit foreknowledge to bias patient entry are not, in fact, properly randomized, although they are often mistakenly described as such.

Non-randomized methods may sometimes suffice as a crude means of deciding whether or not large therapeutic effects exist, but they are generally of little value for reliable detection, or refutation, of moderate therapeutic effects. Hence, the present overviews are restricted to properly randomized trials.

3.8 Selection biases from subgroup analyses: statistical difficulty in the assessment of qualitative "interactions" and of quantitative "interactions"

Patients with early breast cancer may be very different from each other, and the treatment appropriate for one may not be appropriate for another. Ideally, therefore, what is wanted is not only an answer to the question "Is this treatment good on average for a wide range of patients?", but also an answer to the question "For which recognizable categories of patient is this treatment good?". In other words, the ideal would be a reliable description of the categories most likely to benefit from treatment. This ideal is, however, difficult to attain.

"Interactions" — that is, differences between the effects of treatment in different categories of patients — may be of two types that can have quite different practical consequences. If treatment improves the prognosis appreciably in one category of patients but does so to a negligible extent, or not at all, in another category then this is a qualitative interaction. If, however, treatment improves the prognosis appreciably in one category but in the other then this is a quantitative interaction. Unfortunately, the direct use of clinical trial results in particular subgroups of patients to refute or to demonstrate any type of interaction is often extremely difficult — and, even if statistically significant evidence of an interaction is found, this may still fall far short of providing reliable evidence of a qualitative interaction.¹⁵⁻¹⁸

One possible determinant of the size of the absolute benefits of any therapy in some particular category of patient is the absolute risk of death (or recurrence) without treatment. For example, the number of regional lymph nodes containing breast cancer deposits, divided into three standard categories (N0, N1-3, N4+), is an important prognostic feature. If, therefore, some treatment reduces the risk of death by a similar proportion in all patients, the absolute benefit in the earliest stages of the first few years after treatment may be greater in poor-prognosis patients (e.g. 40% dead reduced to 30%) than in good-



Accountability



Offerors IP Concerns



- Ensure IP for Mission
- Respect and Protect IP
- Identify IP Vs License deliverables
- Creative IP solutions

Offerors IP Concerns

1. Ensure IP for the Mission

- Meet the need

2. Respect and Protect IP

- Valuable intangible property
- Maintain assurance that IP rights are exclusive

3. IP Vs License Deliverables

- Identify IP issues early
- Identify mutually agreeable terms
- Identify IP Vs License rights



Offerors IP Concerns

4. Identify IP

Vs

License Deliverables

- Creative IP Solutions
- No One size fits all
- Scientific solution w/limited regulations
- Delivery of technical data necessary to the mission



Cost Share

Allowable Cost Share

- Cash Contributions
- In-Kind Contributions
- Third party
- Commercial Software

Unallowable Cost share

- Patent Cost
- Copyrighted Material
- Developing Software
- Funding from another Gov't Agency



Questions?



ASPR: Saving Lives... Protecting America

