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## Clinical Trials

Part 8

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### Clinical Trials Course Wrap-Up Session

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- Bring together concepts of design & analysis learned in course by:
  1. Reviewing consort statement for reporting and evaluation of clinical trials
  2. Evaluation of 2 articles with respect to consort statement – did they follow the concepts of consort?

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## CONSORT

(Consolidated Standards Of Reporting Trials)

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- Quality and adequacy of reporting RCTs has been quite variable, by time & specialty
- 1996 – first CONSORT statement published to remedy this; updated in 2001
- Supported by growing number of journal editors and editorial groups

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## CONSORT (continued)

- Consists of:
  1. 22 – item checklist
  2. Flow diagram of reporting trial participants
- Intended for use in writing and reviewing clinical trials
- Preliminary data indicate that CONSORT has improved the quality of RCT reports
- CONSORT movement has also encouraged similar developments in reporting of meta analyses, diagnostic studies and health economics studies.

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## 22 – Item CONSORT Checklist

1. Title and abstract - randomized
  2. Introduction, background – scientific background rationale for trial
- **Methods**
    3. Participants – eligibility criteria settings
    4. Interventions – details for each group, how and when administered
    5. Objectives – specific objectives / hypotheses
    6. Outcomes – primary, secondary, methods to enhance quality

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## CONSORT Checklist (continued)

- **Methods**
  7. Sample Size – How determined, interim analyses / stopping rules
  8. Randomization – sequence generation (blocking, stratification)
  9. Randomization – allocation concealment; was allocation concealed until after patient entry?
  10. Randomization – implementation (sequence, enrollment, assignments)

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## CONSORT Checklist (continued)

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- **Methods**
  11. Blinding (masking) – participants, health care providers, evaluators, measures of success of blinding
  12. Statistical methods – for primary outcomes, subgroups, covariate adjustment
- **Results**
  13. Participant flow – diagram (screened, randomized, treated, analyzed by arm)
  14. Recruitment – dates of recruitment, FU

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## CONSORT Checklist (continued)

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- **Results**
  15. Baseline data – demographics, clinical characteristics by arm
  16. Numbers analyzed – was analysis by ITT
  17. Outcomes and estimation – primary, secondary, results for each arm, effect size and CI
  18. Ancillary analysis – subgroups, covariate adjustments (pre-specified, exploratory)
  19. Adverse events

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## CONSORT Checklist (continued)

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- **Comments**
  20. Interpretation – sources of potential bias, multiplicity
  21. Generalization – external validity of findings
  22. Overall evidence – general interpretation of results in context of current evidence

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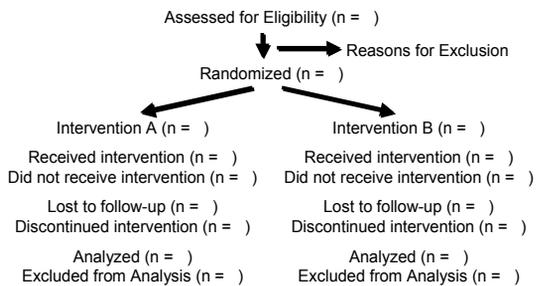
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## CONSORT Flow Diagram




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## Application of Consort Checklist to Following Article

Weinberger, Morris, et. al., "Does Increase Access to Primary Care Reduce Hospital Readmissions?", New England Journal of Medicine, 334: May 30, 1996, 1441-1447

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## CONSORT Checklist (Weinberger, et al.)

1. Title and abstract – randomization stated in abstract
2. Introduction & background – rationale for trial, p.1441 – costs for hospitalization, readmissions high; readmissions potential marker for poor quality of care; pressure to reduce hospitalizations
- **Methods**
3. Participants – p.1441 Hospitalized in GMS; DM / CHF / COPD; exclusions – already in primary care, dialysis, chemotherapy, radiation therapy, from nursing home, admitted for procedure, in another study, CA rule-out, non-English, score ≤ 5 in MSQ and no caregiver, refused consent, no telephone.

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## CONSORT Checklist (Weinberger, et al.)

- **Methods**
  4. Interventions - p.1442 – nurse, physician background on PC team
    - Table 1 – Compliance with inpatient and outpatient components
    - Control – usual care
  5. Objectives - p. 1441 – Primary hypothesis: PC program would reduce readmission rate and hospital days
  6. Outcomes – p.1442
    - Primary – readmission rate, # hospital days
    - Secondary – time to readmission, % patients readmitted, number of emergency visits, number of outpatient visits, SF-36, patient satisfaction

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## CONSORT Checklist (Weinberger, et al.)

- **Methods**
  7. Sample size – p.1443, 2-sided test, alpha = 0.05, power = 0.85, 28% reduction in readmission rate and hospital days, n = 1400
  8. Randomization sequence generation – p. 1442, stratified by study site, entitlement status, index disease; generation method not given
  9. Randomized allocation concealment – telephoning statistical center, p. 1442
  10. Randomization implementation – p. 1442, stratified, call to statistical center
  11. Blinding – p. 1442, RA, unaware of patient assignment, telephoned patient at 30 & 180 days for SF-36, satisfaction, use of non-VA care

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## CONSORT Checklist (Weinberger, et al.)

- **Methods**
  12. Statistical methods – p. 1443, baseline comparisons, intention to treat, Wilcoxon rank-sum test, chi-square test, Kaplan-Meier & log rank test, analysis of variance and covariance (stratification factors, number of hospital days in 180 days prior to randomization)
- **Results**
  13. Participant flow – p. 1443, 10,129 screened; 3209 eligible; 1396 randomized; reasons for not randomizing patient decision (971), discharge before randomization (446)
  14. Recruitment dates – p. 1443, 11/93 – 7/94

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## CONSORT Checklist (Weinberger, et al.)

- Results
  - 15. Baseline data – p.1443, Table 2 (demographics, clinical character), p. 1444, Table 3 (SF-36 and patient satisfaction)
  - 16. Numbers analyzed – in each table
  - 17. Outcomes – p. 1444, Table 4, readmission rate, hospital days, % readmitted
  - 18. Ancillary analysis – diagnosis subgroups, Table 4, p. 1444 covariate adjustment (stratification variable, number of hospital days before randomization), SF-36, satisfaction with care (Figure 2, p. 1445)
  - 19. Adverse events – N/A

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## CONSORT Checklist (Weinberger, et al.)

- Discussion
  - 20. Interpretation – p. 1445, potential reasons for findings
    - Premise may be wrong
    - Detection of undetected problems
    - Improved communication
  - 21. Generalizability, p. 1446 – disadvantaged men, differences between randomized vs. eligible nonrandomized
  - 22. Overall evidence – current findings compared to previous trials, p. 1445-6

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## CONSORT Checklist (Weinberger, et al.)

- Summary
  - 1. Randomization not in title, but in abstract
  - 2. Generation of randomization scheme not described
- 20 of 22 elements adequately addressed, in spite of fact that not checklist was used.

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## Summary Comments

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- DVA is not unique position in world to conduct clinical trials, particularly multi-center
- Involve statistical colleagues early in the process. They can provide valuable input in protocol design, and conduct of trial, as well as analysis.
- Use CONSORT statement to plan, report, and evaluate, trials
- Don't forget the KISS Principle – Keep It Simple

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## Application of Consort Checklist to Larson Article

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Larson, Vernon, et. al., 'Efficacy of 3 Commonly Used Haring Aid Circuits, JAMA, Vol. 284, No. 14 October 11, 2000, pp. 1806 - 1813

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