Randomisation in REDCap

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Agenda

- What is randomisation?

    - Definitions
    - Why do we do it?
    - Study designs

- Methods of randomisation

- Randomisation in REDCap
    - Project configuration
    - Different allocation options

- Into Production: controlling the process
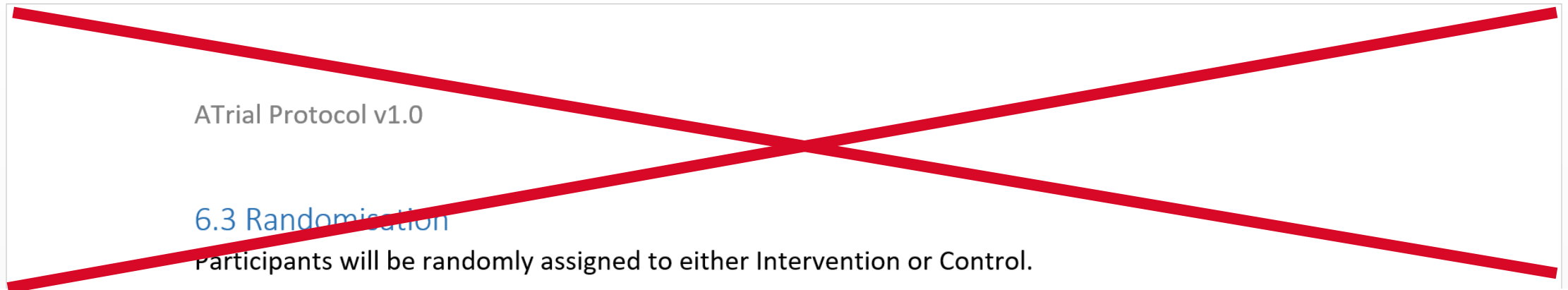
- Alternatives for "randomness"

What is Randomisation?

ATrial Protocol v1.0

6.3 Randomisation

Participants will be randomly assigned to either Intervention or Control.

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Participants will be randomly assigned to either Intervention or Control.

- No! Allocation to group is not random!

- Aim to balance the number of participants allocated to each group, e.g. intervention vs. control.
    - "balance the number", or rather "control the potential imbalance".
    - Random process like coin flip does not protect against imbalance, e.g. 5 heads in a row.

- Allocate sequentially from a randomisation schedule generated in advance.

What is Randomisation?

- "Stratified permuted blocks"

    - "**blocks**": Allocations are arranged in blocks according to the allocation ratio
      e.g. for 1:1 blocks will be size
      2 (1 of each), 4 (2 of each), 6 (3 of each) etc.

    - "**permuted**": The sequence of allocations within each block varies. Each block contains allocations ordered according to one of the possible permutations, e.g. for block size 4:
      `IICC ICIC CICI CCII`

    - "**stratified**": balance within subgroups by using a different schedules for each group of participants
      e.g. female/site1, female/site2, male/site1, male/site2

- Maximal imbalance is the half the size of the largest block:
  Schedule: IIICCC CCCIII
  Count I : 123333 333
  Count C : 000123 456
          ^   ^

sequence	site	sex	block	block_entry	allocation
1	site1	f		1	1 intervention
2	site1	f		1	2 control
3	site1	f		2	1 intervention
4	site1	f		2	2 control
5	site1	f		2	3 control
6	site1	f		2	4 intervention
7	site1	f		3	1 intervention
8	site1	f		3	2 intervention
9	site1	f		3	3 control
10	site1	f		3	4 control
11	site1	f		4	1 control
12	site1	f		4	2 intervention
13	site1	f		5	1 control
14	site1	f		5	2 control
15	site1	f		5	3 intervention
16	site1	f		5	4 intervention
17	site1	f		6	1 intervention
18	site1	f		6	2 control
19	site1	f		6	3 control
20	site1	f		6	4 intervention
21	site1	f		7	1 control
22	site1	f		7	2 intervention
23	site1	f		7	3 control
24	site1	f		7	4 intervention
25	site1	f		8	1 intervention
26	site1	f		8	2 control
27	site1	f		9	1 control
28	site1	f		9	2 control
29	site1	f		9	3 intervention
30	site1	f		9	4 intervention

murdoch children's research institute

What is Randomisation?

ATrial Protocol v2.0

6.3 Randomisation

Participants will be randomised to either the Intervention or Control group with an allocation ratio of 1:1, using a web-based randomisation procedure. The randomisation schedule and web-based service will be provided by the Clinical Epidemiology and Biostatistics Unit (CEBU) at the Murdoch Children's Research Institute. The randomisation will be in randomly permuted blocks of variable length, stratified by study centre, and by sex, that is, either male or female.

What is Randomisation?

Why We Do It

- Minimising imbalance in allocations.

- Minimise any potential for bias (or any potential for the appearance of bias)

- Stratification – balancing within subgroups – controls confounding enabling causal inference:

  - Can say:
    "Exposure X is causally linked to outcome Y"

  - Not just:
    "Exposure X is associated with outcome Y"

Study Designs

- Parallel group

- Cross-over (I → C, C → I)

- Cluster-randomised (randomise e.g. the site, school etc. not individuals)

- Open-label

  - Everyone is aware of the allocation

- Single-blind

  - Study team know allocation, participant does not

- Double-blind

  - Neither study team nor participant aware of allocation (e.g. active vs. placebo)

Randomisation Methods

- Traditional: secure envelopes

  - Tamper-proof envelopes

  - Open in sequence to reveal allocation

  - Still sometimes used, especially as emergency backup

- Electronic, centralised

  - IVR (telephone)

  - Web-based

  - Easier than preparing & managing envelopes

  - Less potential for (appearance of) bias

  - May still require backup, contingency process in the event of forgotten passwords, connectivity problems etc.
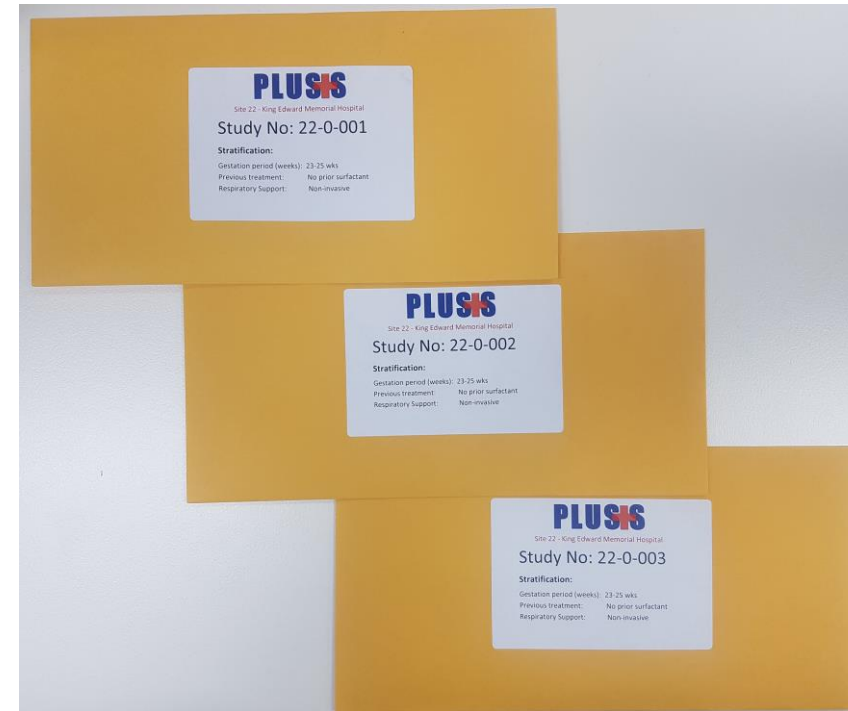
Randomisation in REDCap

- Set up fields for stratification and allocation (including Data Access Groups, if required).

- Enable "Randomization" on the Project Setup page.

- Set up the Randomization Model on the Randomisation page.

- Generate and upload a test randomisation schedule csv file

  - E.g. from the "5x all possible combos" example

- Enable the "Randomize" permission for the User Roles that require it.

- Test it!

- A new record can be created by randomising but only stratification and allocation values get saved.

Randomisation in REDCap: Into Production

Controlling the Process

- Different version of randomisation schedule used for project in Production.

  - Administrators may add new records if required e.g. for
    > Additional strata such as a new site
    > Extending the number of records for existing strata

- Generate schedule using a **<u>reproducible</u>** process.

  - Stats package script, NOT just hacked together in Excel!

  - Stats group have SOP – independent statistician generates as per protocol wording, checked

- Mis-randomisations…

  - Mistakes can occur but allow them to stand.

  - You do not - cannot! - update stratification values in the database or delete/re-randomise.

  - Make corrections in data cleaning / analysis scripts.

RandList_ATrail_20190603.do

```stata
31    ralloc Block BlkSize Alloc, ///
32        ntreat(2) /// number of allocation groups
33        strata(4) /// number of strata
34        osize(2)  /// number of different block sizes
35        nsubj(50) /// number of allocations per stratum
36        trtlab("Intervention" "Control") /// labels for allocations 1 and 2
37        seed(20190603) /// seed for random nuumber generator, ensures reproducibility
38        saving("ATrial_rand")
39
40    sort StratID Block SeqInBlk
41    gen Seq=_n
42    bysort StratID (Seq): gen StratSeq=_n
43    drop if StratSeq>50 // drop unneeded entries (partial blocks remain)
44
45    * Stratification factor fields
46    gen site=""
47    replace site="Site 1" if StratID==1 | StratID==2
48    replace site="Site 2" if StratID==3 | StratID==4
49    assert site!=""
50    gen sexlbl=""
51    replace sexlbl="f" if StratID==1 | StratID==3
52    replace sexlbl="m" if StratID==2 | StratID==4
53    assert sexlbl!=""
54
55    * Process for REDCap upload
56    gen redcap_data_access_group=""
57    replace redcap_data_access_group="9951" if site=="Site 1"
58    replace redcap_data_access_group="9952" if site=="Site 2"
59    assert redcap_data_access_group=="9951" | redcap_data_access_group=="9952"
60
61    gen sex=""
62    replace sex="2" if sexlbl=="f"
63    replace sex="1" if sexlbl=="m"
64    assert sex=="1" | sex=="2"
65
66    gen randalloc=Alloc
67    assert randalloc==1 | randalloc==2
68
69    save "ATrial_rand.dta", replace
70
71    keep randalloc sex redcap_data_access_group
72    order randalloc sex redcap_data_access_group
73
74    export delimited "ATrial_rand.csv"
```

Alternative Randomised Assignments

- Display of the group allocation is not always desired e.g. for double blind randomisations.

- Allocate to a randomisation number.
  - Study team member takes number to Pharmacy, who have a code-break sheet and can dispense appropriate blinded treatment
  - May require emergency code-break mechanism
  - Set up allocation field with randomisation numbers as field choices.

- Display allocated number and group.
  - Not recommended!
  - Online Designer/Codebook access reveals allocation sequence!
  - Max length of data dictionary cell contents in Excel is 65k characters.

- Minimisation, dynamic randomisation algorithms...

Other (Uncontrolled!) Ways to "Randomise"

- Sometimes the randomisation module is not what you need, e.g. "randomising" questions in a survey or in the mobile app.

- Record ID in public survey, modulo 3 gives 0, 1 or 2 essentially "at random"
  Use the result in branching logic.
  ```
  [record_id] – (rounddown([record_id]/3, 0) * 3)
  ```

- Administrators may use JavaScript functions for on-form calculations.
  Generate a random number and prevent it being reset once saved:
  ```
  if([rnd]='', Math.random(), [rnd])
  ```

- Or use the datediff() function to calculate seconds between two times
  ```
  if([secsince]='', datediff("01-06-2019 00:00:00", [now], "s", "dmy", false), [secsince])
  ```

- Example of Fizz Buzz for multiples of 3 and 5: https://is.gd/anzadminforum2019_fizzbuzz

Thank you. Any questions?

And thanks to the REDCap team at Vanderbilt University