

ALEATORIZACIÓN



Aleatorizar no es suficiente!

La aleatorización debe ser
Segura
Impredecible
Registrada

ALEATORIZACIÓN

- è Simple
- è Bloques permutados
- è Estratificada
 - é Bloques permutados dentro del estrato
 - é Minimización
 - é Por centro / institución

Probabilidad de desbalance en una aleatorización simple con dos tratamientos

N°de Sujetos	Diferencia	
	$p \leq 0.05$	$p \geq 0.01$
10	2:8	1:9
20	6:14	4:16
50	18:32	16:34
100	40:60	37:63
200	86:114	82:118
500	228:272	221:279
1000	469:531	459:541

ASIGNACIÓN A GRUPOS

Método para asignación aleatoria balanceada

Para estar seguro que el número de sujetos incluidos en cada grupo de estudio es aproximadamente el mismo durante el curso del estudio



Se asegura que no habrá variaciones en la asignación de sujetos a lo largo del estudio

CÓMO?

- è Se determina el número de sujetos a ser estudiados en cada bloque
- è Los tratamientos son aleatoriamente asignados dentro de cada bloque



ASIGNACIÓN A GRUPOS (Primer Paso)

- è Liste todos los posibles bloques de permutaciones de “A” y “B” (para x número de sujetos en cada bloque)
- è Numere los bloques listados

ASIGNACIÓN A GRUPOS (Primer Paso)

- è Cada bloque tendrá el mismo número de sujetos que reciban cada tipo de tratamiento
- è Cada bloque tendrá la misma probabilidad de selección

EJEMPLO

- è Hay una lista de bloques permutados para los tratamientos “A” y “B” de forma que cada bloque tiene el mismo número de sujetos que reciben cada tratamiento.
- è De esta forma la asignación aleatoria es balanceada cada 6 pacientes (bloques de 6).
- è Para este caso, hay 20 bloques diferentes, y 5 números fueron asignados a cada bloque.
- è Ejemplo: números 00, 01, 02, 03 y 04 fueron asignados al primer bloque (AAABBB)

EJEMPLO

Number	Sequence	Number	Sequence	Number	Sequence	Number	Sequence
00-04	AAABBB	25-29	ABABAB	50-54	BAAABB	75-79	BABBAA
05-09	AABABB	30-34	ABABBA	55-59	BAABAB	80-84	BBAAAB
10-14	AABBAB	35-39	ABBAAB	60-64	BAABBA	85-89	BBAABA
15-19	AABBBA	40-44	ABBABA	65-69	BABAAB	90-94	BBABAA
20-24	ABAABB	45-49	ABBBAA	70-74	BABABA	95-99	BBBAAA

ASIGNACIÓN A GRUPOS (Segundo Paso)

- è Seleccione al azar un número de 2 dígitos en la Tabla de Números Aleatorios (con los ojos cerrados, marque al azar un punto con un lápiz y seleccione el número más próximo a ese punto)
- è Liste la serie de números de 2 dígitos siguiendo la columna hacia debajo de ese punto
- è N° de números de 2 dígitos = $\frac{\text{Muestra total}}{\text{Tamaño del Bloque}}$

Para 60 sujetos = $60 / 6 = 10$

TABLA DE NÚMEROS ALEATORIOS

41	82	79	37	00	45	98	54	52	89	26	34
66	18	76	82	11	18	61	90	90	63	78	57
42	34	00	49	97	53	33	16	26	91	37	58
90	84	22	16	26	96	54	11	01	96	58	91
33	43	01	32	58	39	19	54	56	37	23	28
17	89	37	04	18	32	13	45	59	03	91	08
36	87	98	73	77	64	75	19	05	61	11	64
15	58	19	68	95	47	25	69	11	90	26	19
45	52	27	35	86	81	16	20	37	60	39	35
72	72	81	84	36	58	05	10	70	50	31	04
06	68	52	50	39	35	92	28	18	89	64	37
95	73	80	92	26	49	54	30	41	21	06	62
96	23	16	46	15	51	60	31	55	27	84	14
34	96	32	68	48	22	40	17	43	25	33	31
07	19	94	46	17	51	03	73	99	89	28	44
37	08	08	46	56	76	29	48	33	87	70	79
18	01	67	19	29	49	58	67	08	56	27	24
08	79	18	78	00	32	86	74	78	55	55	72

ASIGNACIÓN A GRUPOS (Tercer Paso)

- è Reemplace cada número de dos dígitos por la correspondiente secuencia de tratamientos A y tratamientos B.

EJEMPLO

(33) ABABBA	(54) BAAABB	(19) AABBBA	(13) AABBAB	(75) BABBAA
(25) ABABAB	(16) AABBBA	(05) AABABB	(92) BBABAA	(54) BAAABB

Number	Sequence	Number	Sequence	Number	Sequence	Number	Sequence
00-04	AAABBB	25-29	ABABAB	50-54	BAAABB	75-79	BABBAA
05-09	AABABB	30-34	ABABBA	55-59	BAABAB	80-84	BBAAAB
10-14	AABBAB	35-39	ABBAAB	60-64	BAABBA	85-89	BBAABA
15-19	AABBBA	40-44	ABBABA	65-69	BABAAB	90-94	BBABAA
20-24	ABAABB	45-49	ABBBAA	70-74	BABABA	95-99	BBBAAA



ASIGNACIÓN A GRUPOS (Cuarto Paso)

- è Enumere consecutivamente sobres opacos sellados (uno por cada sujeto de su muestra)
- è Inserte el tratamiento correspondiente en cada sobre siguiendo la secuencia generada de A's y B's

EJEMPLO

Número de sobre	Secuencia	Número de sobre	Secuencia	Número de sobre	Secuencia
1	(33) A	9	A	17	B
2	B	10	A	18	A
3	A	11	B	19	A
4	B	12	B	--	-
5	B	13	(19) A	--	-
6	A	14	A	--	-
7	(54) B	15	B	59	B
8	A	16	B	60	B



Características de las mujeres al ingreso al estudio según grupo de tratamiento

	Misoprostol	Ocitocina
	N= 9.238	N= 9.264
	%	%
Edad materna (media y DS)	26·5 (5·5)	26·3 (5·4)
Paridad = 0	44·8	45·8
Paridad igual o mayor de 5	5·2	5·2
Edad gestacional < 37 sem.	12·2	11·7
Ocitocina o prostaglandina previa al parto	38·0	37·8
Analgesia peridural	6·2	6·0
Parto vaginal asistido	9·1	8·2
Sutura perineal	66·4	66·1

Assessing the Quality of Randomization From Reports of Controlled Trials Published in Obstetrics and Gynecology Journals

Kenneth F. Schulz, MBA; Iain Chalmers, MBBS, MSc; David A. Grimes, MD; Douglas G. Altman

Objective.—To assess the methodologic quality of approaches used to allocate participants to comparison groups in randomized controlled trials from one medical specialty.

Design.—Survey of published, parallel group randomized controlled trials.

Data Sources.—All 206 reports with allocation described as randomized from the 1990 and 1991 volumes of four journals of obstetrics and gynecology.

Main Outcome Measures.—Direct and indirect measures of the adequacy of randomization and baseline comparisons.

Results.—Only 32% of the reports described an adequate method for generating a sequence of random numbers, and only 23% contained information showing that steps had been taken to conceal assignment until the point of treatment allocation. A mere 9% described both sequence generation and allocation concealment. In reports of trials that had apparently used unrestricted randomization, the differences in sample sizes between treatment and control groups were much smaller than would be expected due to chance. In reports of trials in which hypothesis tests had been used to compare baseline characteristics, only 2% of reported test results were statistically significant, lower than the expected rate of 5%.

Conclusions.—Proper randomization is required to generate unbiased comparison groups in controlled trials, yet the reports in these journals usually provided inadequate or unacceptable information on treatment allocation. Additional analyses suggest that nonrandom manipulation of comparison groups and selective reporting of baseline comparisons may have occurred.

BJOG would be of better quality than those published in the other three journals because a concerted editorial effort had been made to improve the quality of reporting in the *BJOG*,¹⁶ (2) the numbers of patients in the comparison groups of trials in which unrestricted randomization was used would be more similar than would be expected by chance, and (3) the percentage of reported statistically significant differences in baseline characteristics would be less than the expected 5%.

METHODS

We collected data from all reports (N=206) of trials published in the 1990 and 1991 volumes of the *AJOG*, the *BJOG*, the *JOG*, and *OG*. To identify eligible reports, we handsearched the journals and then cross-checked that search using the Oxford Database of Perinatal Trials¹¹ (issue 8) and MEDLINE. We included articles in which authors reported that individuals had been randomly allocated to parallel (un-

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Dimensions of Methodological Quality Associated With Estimates of Treatment Effects in Controlled Trials

Kenneth F. Schulz, PhD, MBA; Iain Chalmers, MBBS, MSc; Richard J. Hayes, MSc; Douglas G. Altman

Objective.—To determine if inadequate approaches to randomized controlled trial design and execution are associated with evidence of bias in estimating treatment effects.

Design.—An observational study in which we assessed the methodological quality of 250 controlled trials from 33 meta-analyses and then analyzed, using multiple logistic regression models, the associations between those assessments and estimated treatment effects.

Data Sources.—Meta-analyses from the Cochrane Pregnancy and Childbirth Database.

Main Outcome Measures.—The associations between estimates of treatment effects and inadequate allocation concealment, exclusions after randomization, and lack of double-blinding.

Results.—Compared with trials in which authors reported adequately concealed treatment allocation, trials in which concealment was either inadequate or unclear (did not report or incompletely reported a concealment approach) yielded larger estimates of treatment effects ($P < .001$). Odds ratios were exaggerated by 41% for inadequately concealed trials and by 30% for unclearly concealed trials (adjusted for other aspects of quality). Trials in which participants had been excluded after randomization did not yield larger estimates of effects, but that lack of association may be due to incomplete reporting. Trials that were not double-blind also yielded larger estimates of effects ($P = .01$), with odds ratios being exaggerated by 17%.

Conclusions.—This study provides empirical evidence that inadequate methodological approaches in controlled trials, particularly those representing poor allocation concealment, are associated with bias. Readers of trial reports should be wary of these pitfalls, and investigators must improve their design, execution, and reporting of trials.

ditionally, they suspected that methodologically inferior trials might produce bias in both directions, thereby causing greater variability in estimates of treatment effects. In neither analysis, however, did they detect a relationship.

Using a database of systematic reviews of controlled trials in pregnancy and childbirth,¹² we sought evidence of bias related to use of inadequate methodological approaches to trial design and execution. Rather than using quality scores, we investigated specific aspects that we believed might be influential.¹³ We hypothesized that estimates of treatment effects would be larger in trials in which (1) adequate measures had not been taken to conceal treatment allocation; (2) adequate measures had not been taken to generate the allocation schedule; (3) some allocated participants had been excluded from the analysis; and (4) measures had not been taken to implement double-blinding. Furthermore, we examined whether treatment effects varied more in trials in which allocation schedules had not been adequately concealed.

MATERIALS AND METHODS

Derivation of Study Material



Centro Rosarino de Estudios Perinatales

Centro Rosarino de Estudios Perinatales

