의학교육연구의 질을 향상시키기 위한 '연구보고의 표준' 의 활용

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Using of the "Consolidated Standards of Reporting Trials : CONSORT" to heighten quality of Medical Education study

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=Abstract=

Using of the "Consolidated Standards of Reporting Trials :CONSORT" to heighten quality of Medical Education study

Objectives: Through using of the strong research method like a Randomized Controlled Trial: RCT, we have to heighten quality of Medical Education study. I 'd like to introduce "CONSORT", which stands for Consolidated Standards of Reporting Trials.

Contents: Preventive Service Task Force(2001) in USA proposed Levels of evidence for enlarging evidence-based Practice: EBP. And the CONSORT was introduced, which encompasses various initiatives developed by the CONSORT Group to alleviate the problems arising from inadequate reporting of randomized controlled trials (RCTs). the CONSORT has 13 guides like these: 1. How participants were allocated to interventions 2. Scientific background and explanation of rationale 3. Eligibility criteria for participants, The settings and locations where the data were collected. 4. Precise details of the interventions intended for each group and how and when they were actually administered 5. Specific objectives and hypotheses 6. Clearly defined primary and secondary outcome measures,

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When applicable, any methods to enhance the quality of measurements (e.g., multiple observations, training of assessors) 7. How sample size was determined, When applicable, explanation of any interim analyses and stopping rules 8. Method used to generate the random allocation sequence, Details of any restriction [of randomization] 9. Method used to implement the random allocation sequence 10. Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups 11. Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment, If done, how the success of blinding was evaluated 12. Statistical methods used to compare groups for primary outcome(s), Methods for additional analyses, such as subgroup analyses and adjusted analyses 13. Flow of participants through each stage (a diagram is strongly recommended) Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome.

Results and Conclusion: Randomized Controlled Trial: RCT guided of CONSORT will contribute to do stronger evidence-based medical studies.

Key Words: CONSORT, Randomized Controlled Trial: RCT, quality of Medical Education study

서론

근거기반한 의학 및 의료실무의 변화가 의미있게 이루어지기 위해서는 관련연구의 질이 향상되어야 할 것이다. 특히 여러 연구 방법 중에서 무작위 통제 실험 연구(Randomized Controlled Trial: RCT)가 가장 강력하고 효율적인 연구방법이 될 것이다. 이하에서는 무작위통제실험 연구의 의의와 무작위통제실험 연구를 보고할 때, 질을 보장하기 위해 추천되고 있는 연구 보고의 통합 표준(Consolidated Standards of Reporting Trials :CONSORT)의 연구지침을 소개하고자 한다.

무작위 통제 실험 연구의 의의

근거기반 실무 (Evidence-Based Practice: EBP)라는 용어는 1990년대 초부터 흔히 사용 되고 있다.1-3) 이는 건강관리문제를 해결하기 위해 과학적인 접근방법인 연구를 통해 그 결과에 근거하여 건강관리의 질을 향상시키려는 의도를 갖고 있다.

어떠한 근거가 실무로 전환되어야 하는가? 미국의 Preventive Service Task Force(2001)는 근거의 질의 순위를 다음과 같이 정했다:4)

즉 의학 및 건강관련 실무를 안내하는 대부분의 근거는 무작위 통제 실험 연구

〈Table 1〉. Levels of evidence

Level I	evidence obtained from at least one properly designed RCT
Level II-1	evidence obtained from well-designed controlled trials without randomization
Level II-2	evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than on e center or research group
Level II-3	evidence obtained from multiple time series with or without the intervention or dramatic results in uncontrolled trials
Level III	opinion of respected authority based on clinical experience, descriptive studies or reports of expert committees

(Randomized Controlled Trial: RCT) 연구로 부터 나오며, 매우 적은 근거가 기관의 의견으로부터 나온다.

무작위 통제 실험 연구로 부터 나오는 근거에 전적으로 의지하려는 근본적 이유는 이와 같은 연구가 원인과 결과의 인과관계를 분명히 해주기 때문이다.3,5) 더군다나 무작위통제실험 연구는 독립변수의 조작(Manipulation), 연구 참여자의 무작위 할당(Randomization)과 통제군(Control group)을 두어 인간과 환경적 편견(Bias)을 조정하고 연구의 내적타당도(Internal validity)를 향상시키기 때문이다. 무작위통제실험에서 종종 사용되는 맹검(blinding)은 편견을 제거하는데 도움을 준다.6,7) 그러므로 편견을 제거하는데 힘쓰지 않는 연구들은 그릇된 결론으로 이어질 수 있으며 결과의 정당성 및 유용성에 위험을 내포하게 된다.8-10)

건강관련 과학자들이 무작위통제실험 연구의 결과를 제대로 평가하고 실무에 적용하기 위해서, 설계에 대한 세부적인 정보를 제공해야 하며, 무작위 할당이 어떻게 이루어졌는지, 맹검(blinding), 데이터 관리, 분석 및 해석이 어떻게 이루어졌는지 알려줘야 한다. 다시 말해, 무작위통제실험 연구가 기준에 맞게 진행되고, 명확하게 보고될 때 근거기반 실무(EBP)에 강한 영향을 줄 수 있으며 나아가 환자의 건강관리를 질적으로 향상 시킬 수 있을 것이다.11)

그러나 수십 년 간의 노력에도 불구하고 무작위통제실험 연구는 아직도 적절하게 보고되지 않고 있다12-15). 부정확한 보고는 무작위통제실험 연구의 결과 해석을 어렵게 또는 불가능하게 할 뿐만 아니라 잘못된 결과가 받아들여지게 하는 비윤리적 행위와 맞닿아 있다.

현재 건강관련 논문집에 보고된 대다수의 연구들에 무작위통제실험가 적용되지는 않았지만, 그 수는 점점 증가하고 있고 중재의 효과에 있어서 가장 강력한 결과를 제공하고 있다. 이러한 결과는 명확하고 이해하기 쉬운 방법으로 보고될 때 최고의 효과가 있을 것이다.

연구보고의 통합표준(CONSORT)의 활용

1990년대 중반에 무작위통제실험 보고의 질을 향상시키려는 두 독자적 그룹이 '연구 보고의 통합 표준 (Consolidated Standards of Reporting Trials: CONSORT)' 양식을

낳게 되었다16). 여기에는 국제적 규모의 임상 연구가, 통계학자, 역학자, 의학 학술지 편집자들이 참여하였다. 이 '연구 보고의 통합 표준'의 양식은 점차로 많은 의학 및 보건 분야 학술지17-20)와 CMJE21)(International Committee of Medical Journal Editors, Vancouver group으로도 알려져 있다), CSE (Council of Science Editors), WAME (World Association of Medical Editors)와 같은 편집인 협의회의 지지를 얻게 되었다.

Figure1. 무작위 임상 연구의 순서(참가자 선정, 치료군 배정, 추적 관찰, 결과분석)에 따른 흐름도

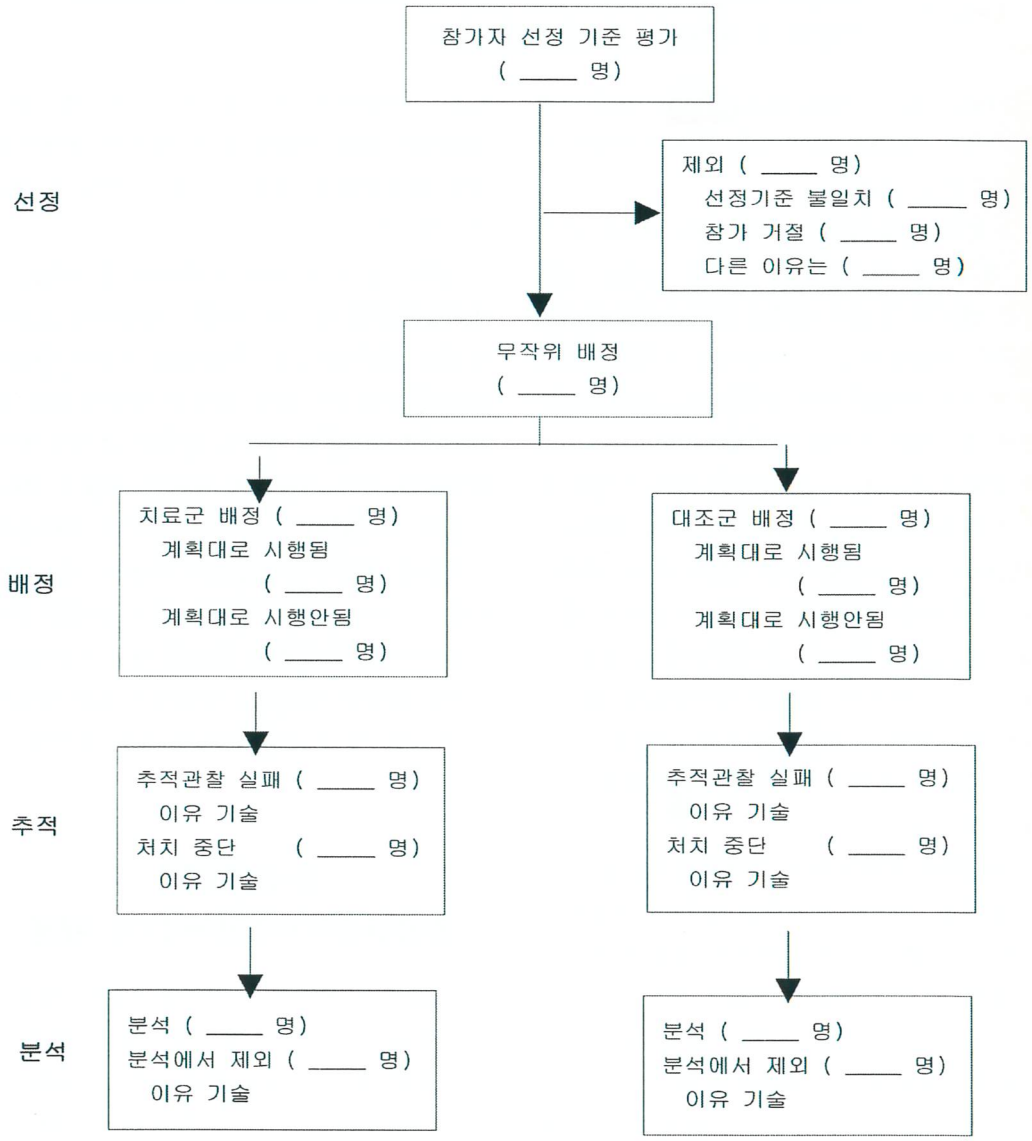

Table2. 무작위통제실험를 보고할 때 포함시킬 항목의 체크리스트

항 목	번호	기술내용	기술된 페이지
제목 및 초록	1	참가자가 어떻게 치료군에 배당되었는가?(예: 무작위 배당 등)	
서론 배경	2	과학적 배경 및 근거 설명	
방법 참가자	3	연구 참여 기준, 자료 수집 장소 및 환경	
처치	4	각 군에 의도된 처치를 자세히 언급. 언제 어떻게 해당 처치가 실제로 행해졌는지	
목표	5	연구 목표와 가설을 구체적으로 기술	
결과	6	일차적, 이차적 결과 변수 측정 방법을 명확히 하고 측정의 질을 향상시킬 수 있는 방법(반복 측정, 평가자 교육 등)을 기술	
환자수 계산	7	대상 환자 수가 어떻게 결정되는가. 가능하다면 연구의 중간평가나 중단 기준을 설명	
무작위 배당			
배당의 순서	8	치료군과 대조군의 순서를 무작위 결정하는 방법을 기술, 층화(stratification)나 차폐(blocking)등의 제한 방법을 기술	
배당의 눈가림	9	무작위 배당을 시행하는 방법을 기술(예, 숫자가 적힌 상자 또는 전화로 문의). 환자가 배당될 때까지 소속된 군을 비밀로 했는지를 명확히 기술	
배당의 실행	10	누가 배당의 순서를 결정하는가. 누가 참가자를 연구에 포함시키는가, 누가 참가자를 각 군에 배정하는가를 기술	
맹점	11	참가자, 처치 제공자, 결과 분석자에게 배당된 소속군이 비밀로 유지되었는가, 비밀 유지 여부의 평가는 어떻게 이루어졌는가를 기술	
통계 방법	12	일차적 결과 변수(들)을 비교하기 위한 통계 방법, 소그룹 분석 또는 보정 분석(adjustment analysis) 등의 추가적 분석 방법을 기술	
결과 참가자 흐름도	18	참가자의 흐름을 가능하면 도표로 표시. 구체적으로는 각 군의 무작위 배당된 숫자, 계획된 처치를 시행받은 숫자, 연구를 계획하고 끝마친 숫자, 일차적 결과 변수를 분석한 숫자를 기술	
모집	14	참가자 모집 기간과 추적 관찰 기간을 명시	
시작 시점의 자료	15	연구 시작 시점에서 각 군의 역학적, 임상적 특징 기술	
분석된 숫자	16	결과 분석에 포함된 각 군의 참가자 숫자를 기술. 분석이 치료 의도의 원칙(intention to treat)에 의해 시행되었는지 여부기술. 가능하면 결과를 정대 숫자로 기술할 것(예, 50% 보다는 20명 중 10명으로)	
결과의 추정치	17	일차, 이차 변수에 대하여 각 군의 결과치를 요약하고 추정치 및 정확도를 기술(예, 95% 신뢰구간)	
부차적 분석	18	소그룹 분석, 보정 분석 등의 추가 분석 결과를 기술. 그것이 사건에 계획된 것인지 여부를 기술	
부작용	19	각 군의 모든 중요한 부작용을 기술	
고찰 해석	20	연구 가설을 염두에 둔 결과의 해석. 판결이 개입될 소지는 없었는지, 결과 해석의 주의점을 기술	
일반화	21	연구 결과를 다른 집단에 일반화할 수 있는가	
전체적 근거	22	최근까지의 근거에 비추어 볼 때 연구 결과의 일반적인 해석을 기술	

'연구 보고의 통합 표준'은 영어, 불어, 독일어, 일본어, 스페인어, 네델란드어, 한국어로도 출판되었다. 인터넷으로도 '연구 보고의 통합 표준'은 다른 정보와 함께 공개되어 있다. (http://www.consort-statement.org/Translation/translation.htm). 여기에는 무작위통제실험 보고를 위한 체크리스트와 순서도로 구성되어 있다. 편의상 이 체크리스트와 순서도를 간단히 CONSORT 라고도 부른다. CONSORT는 논문 작성, 심사 및 평가에 사용하기 위한 것이다.

아래의 순서도(Flowchart)는 연구자나 독자들이 무작위통제실험 연구를 통해 연구참여자/대상자를 추적하는 지침이 되며(figure1. 참조), 체크리스트는 연구자들이 무작위통제실험 연구의 질을 높이기 위해 설정한 기준들을 명확하게 빠짐없이 기술하도록 하는 지침이 된다(Table2 참조). 첨부1과 2에 이에 관련된 내용이 원문으로 소개되어 있다.

이와 같은 흐름과 체크리스트의 확인을 통해, 즉 CONSORT의 사용으로 무작위통제실험의 부적절한 보고를 줄일 수 있을 뿐 만 아니라22,23) 연구의 진행 과정에도 긍정적인 영향을 줄 수 있다. 연구비 지원 기관 또한 이러한 영향을 인정하고 있다.24) 연구비 신청 시 계획서에 CONSORT 항목을 반영하는 것은 계획서 선정 과정에 유익하게 작용할 것이다.

CONSORT 개발 과정에서 채택한 근거 중심 접근법은 무작위통제실험25), 관찰 연구26), 그리고 진단 연구의 메타분석을 보고하기 위한 표준 양식을 개발하는 과정에도 이용되고 있다.

결론

근거기반한 의학교육이 이루어지기 위해서도 관련연구의 질이 향상되어야 할 것이다. 의학교육분야에서도 무작위 통제 실험 연구(Randomized Controlled Trial: RCT)는 의미있는 근거를 제공하는 강력하고 효율적인 연구방법이 될 것이다. 의학교육분야에서도 근거에 기반하여 교육의 효과를 검증하기 위해 CONSORT에서 제안하는 무작위통제실험 연구의 평가 기준에 부합된 질적인 연구를 시행할 것을 제안한다.

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첨부1. Consort 웹사이트 소개

Welcome to the CONSORT Statement Website

CONSORT, which stands for Consolidated Standards of Reporting Trials, encompasses various initiatives developed by the CONSORT Group to alleviate the problems arising from inadequate reporting of randomized controlled trials (RCTs). The main product of CONSORT is the CONSORT Statement, which is an evidence-based, minimum set of recommendations for reporting RCTs. It offers a standard way for authors to prepare reports of trial findings, facilitating their complete and transparent reporting, and aiding their critical appraisal and interpretation. The CONSORT Statement comprises a 22-item checklist and a flow diagram, along with some brief descriptive text. The checklist items focus on reporting how the trial was designed, analyzed, and interpreted; the flow diagram displays the progress of all participants through the trial.

첨부2. 무작위통제실험결과를 보고할 때 포함시킬 항목과 예문

1. How participants were allocated to interventions

(e.g., "random allocation", "randomized" or "randomly assigned").

Examples

- In title: "Smoking reduction with oral nicotine inhalers: double blind, randomized clinical trials of efficacy and safety ..."
- In abstract:"Design: Randomized, double-blind, placebo-controlled trial"

2. Scientific background and explanation of rationale

Example

"The carpal tunnel syndrome is caused by compression of the median nerve at the wrist and is a common cause of pain in the arm, particularly in women. Injection with corticosteroids is one of the many recommended treatments.

One of the techniques for such injection entails injection just proximal to (not into) the carpal tunnel. The rationale for this injection site is that there is often a swelling at the volar side of the forearm, close to the carpal tunnel, which might contribute to compression of the median nerve. Moreover, the risk of damaging the median nerve by injection at this site is lower than by injection into the narrow carpal tunnel. The rationale for using lignocaine (lidocaine) together with corticosteroids is twofold: the injection is painless, and diminished sensation afterwards shows that the injection was properly carried out.

We investigated in a double blind randomised trial, firstly, whether symptoms disappeared after injection with corticosteroids proximal to the carpal tunnel and, secondly, how many patients remained free of symptoms at follow up after this treatment"

3(a). Eligibility criteria for participants

Example

"…all women requesting an IUCD [intrauterine contraceptive device] at the Family Welfare Centre, Kenyatta National Hospital, who were menstruating regularly and who were between 20 and 44 years of age, were candidates for inclusion in the study. They were not admitted to the study if any of the following criteria were present: (1) a history of ectopic pregnancy, (2) pregnancy within the past 42 days, (3) leiomyomata of the uterus, (4) active PID [pelvic inflammatory disease], (5) a cervical or endometrial malignancy, (6) a known hypersensitivity to tetracyclines, (7) use of any antibiotics within the past 14 days or long-acting injectable penicillin, (8) an impaired response to infection, or (9) residence outside the city of Nairobi, insufficient address for follow-up, or unwillingness to return for follow-up"

3(b). The settings and locations where the data were collected

Example

"Volunteers were recruited in London from four general practices and the ear, nose, and throat outpatient department of Northwick Park Hospital. The prescribers were familiar with homoeopathic principles but were not experienced in homoeopathic immunotherapy"

4. Precise details of the interventions intended for each group and how and when they were actually administered

Example

"Patients with psoriatic arthritiswere randomised to receive either placebo or etanercept (Enbrel) at a dose of 25 mg twice weekly by subcutaneous administration for 12 weeks ... Etanercept was supplied as a sterile, lyophilised powder in vials containing 25 mg etanercept, 40 mg mannitol, 10 mg sucrose, and 1·2 mg tromethamine per vial. Placebo was identically supplied and formulated except that it contained no etanercept. Each vial was reconstituted with 1 mL bacteriostatic water for injection"

5. Specific objectives and hypotheses

Example

"In the current study we tested the hypothesis that a policy of active management of nulliparous labour would : 1. reduce the rate of caesarean section, 2. reduce the rate of prolonged labour; 3. not influence maternal satisfaction with the birth experience"

6(a). Clearly defined primary and secondary outcome measures

Example

"The primary endpoint with respect to efficacy in psoriasis was the proportion of patients achieving a 75% improvement in psoriasis activity from baseline to 12 weeks as measured by the PASI [psoriasis area and severity index]. Additional analyses were done on the percentage change in PASI scores and improvement in target psoriasis lesions"

6b. When applicable, any methods to enhance the quality of measurements (e.g., multiple observations, training of assessors)

Examples

"The clinical end point committee ··· evaluated all clinical events in a blinded fashion and end points were determined by unanimous decision"

"Blood pressure (diastolic phase 5) while the patient was sitting and had rested for at least five minutes was measured by a trained nurse with a Copal UA-251 or a Takeda UA-751 electronic auscultatory blood pressure reading machine (Andrew Stephens, Brighouse, West Yorkshire) or with a Hawksley random zero sphygmomanometer (Hawksley, Lancing, Sussex) in patients with atrial fibrillation. The first reading was discarded and the mean of the next three consecutive readings with a coefficient of variation below 15% was used in the study, with additional readings if required"

7(a). How sample size was determined

Examples

"We believed that ···the incidence of symptomatic deep venous thrombosis or pulmonary embolism or death would be 4% in the placebo group and 1.5% in the ardeparin sodium group. Based on 0.9 power to detect a significant difference (P = 0.05, two-sided), 976 patients were required for each study group. To compensate for nonevaluable patients, we planned to enroll 1000 patients per group"

"To have an 85% chance of detecting as significant (at the two sided 5% level) a five point difference between the two groups in the mean SF-36 general health perception scores, with an assumed standard deviation of 20 and a loss to follow up of 20%, 360 women (720 in total) in each group were required"

7b. When applicable, explanation of any interim analyses and stopping rules

Examples

"The results of the study···were reviewed every six months to enable the study to be stopped early if, as indeed occurred, a clear result emerged"

"Two interim analyses were performed during the trial. The levels of significance maintained an overall P value of 0.05 and were calculated according to the O'Brien-Fleming stopping boundaries. This final analysis used a Z score of 1.985 with an associated P value of 0.0471"

8(a). Method used to generate the random allocation sequence

Example

"Independent pharmacists dispensed either active or placebo inhalers according to a computer generated randomization list"

8(b). Details of any restriction [of randomization]

■ (e.g. blocking, stratification).

Example

"Women had an equal probability of assignment to the groups. The randomization code was developed using a computer random number generator to select random permuted blocks. The block lengths were 4, 8, and 10 varied randomly . . ."

9 Method used to implement the random allocation sequence

■ (e.g., numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned.

Example

"Women were assigned on an individual basis to both vitamins C and E or to both placebo treatments. They remained on the same allocation throughout the pregnancy if they continued in the study. A computer-generated randomisation list was drawn up by the statistician ··· and given to the pharmacy departments. Theresearchers responsible for seeing the pregnant women allocated the next available number on entry into the trial (in the ultrasound department or antenatal clinic), and each woman collected her tablets direct from the pharmacy department. The code was revealed to the researchers once recruitment, data collection, and laboratory analyses were complete"

10. Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups

Example

"Determination of whether a patient would be treated by streptomycin and

bed-rest (S case) or by bed-rest alone (C case) was made by reference to a statistical series based on random sampling numbers drawn up for each sex at each centre by Professor Bradford Hill; the details of the series were unknown to any of the investigators or to the co-ordinator and were contained in a set of sealed envelopes, each bearing on the outside only the name of the hospital and a number. After acceptance of a patient by the panel, and before admission to the streptomycin centre, the appropriate numbered envelope was opened at the central office; the card inside told if the patient was to be an S or a C case, and this information was then given to the medical officer of the centre."

11(a). Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment

Example

"All study personnel and participants were blinded to treatment assignment for the duration of the study. Only the study statisticians and the data monitoring committee saw unblinded data, but none had any contact with study participants."

11(b). If done, how the success of blinding was evaluated

Example

"To evaluate patient blinding, the questionnaire asked patients to evaluate which treatment they believed they had received (acupuncture, placebo, or don't know) at 3 points in time…If patients answered either acupuncture or placebo, they were asked to indicate what led to that belief …"

12(a). Statistical methods used to compare groups for primary outcome(s)

Example

"All data analysis was carried out according to a pre-established analysis plan. Proportions were compared by using Chi-squared tests with continuity correction or Fisher's exact test when appropriate. Multivariate analyses were conducted with logistic regression. The durations of episodes and signs of disease were

compared by using proportional hazards regression. Mean serum retinol concentrations were compared by t test and analysis of covariance ... Two sided significance tests were used throughout."

12(b). Methods for additional analyses, such as subgroup analyses and adjusted analyses

Examples

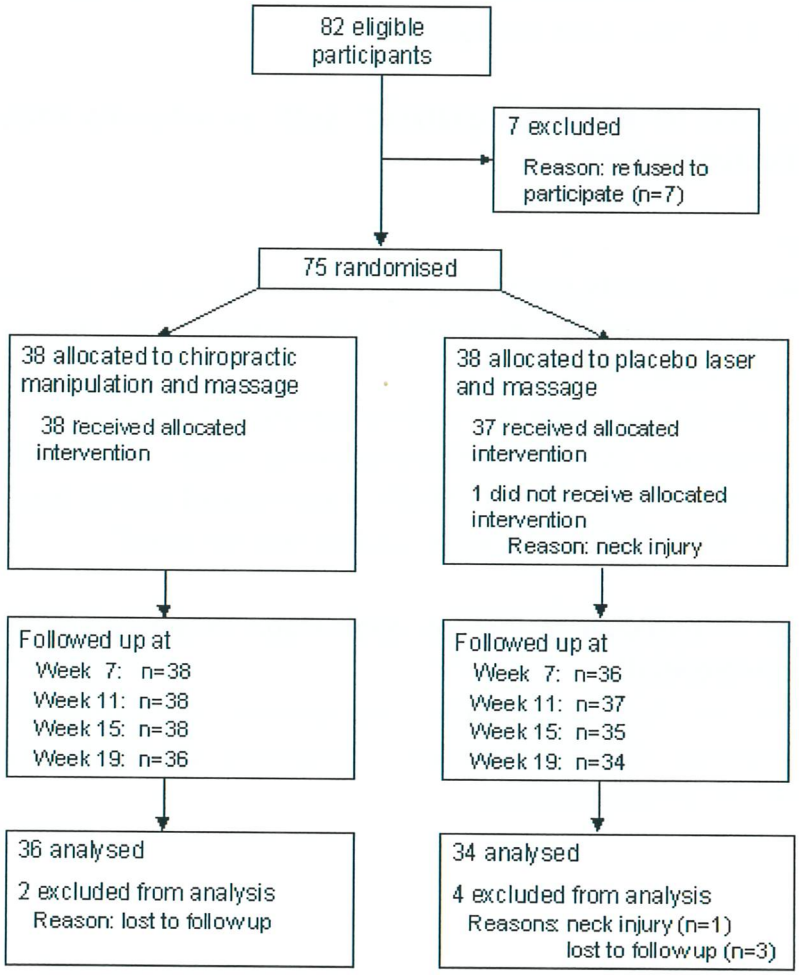
"Proportions of patients responding were compared between treatment groups with the Mantel-Haenszel Chi-squared test, adjusted for the stratification variable, methotrexate use"

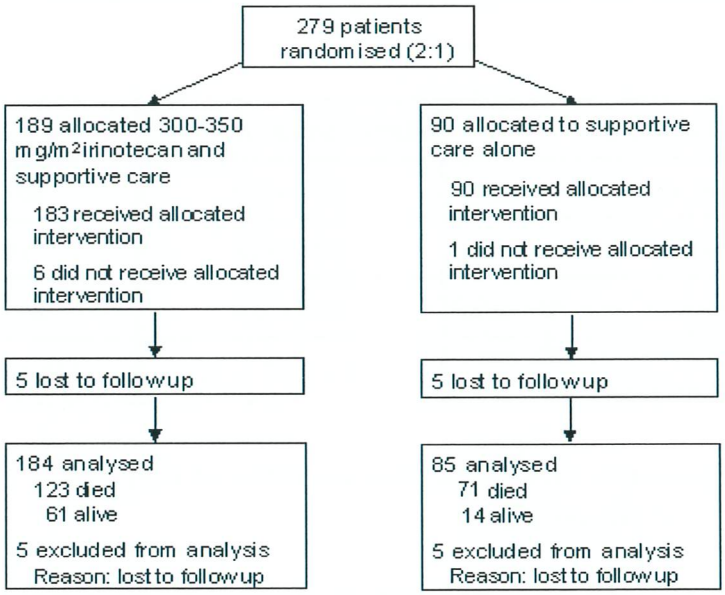
"…it was planned to assess the relative benefit of CHART in an exploratory manner in subgroups: age, sex, performance status, stage, site, and histology. To test for differences in the effect of CHART, a chi-squared test for interaction was performed, or when appropriate a chi-squared test for trend"

13(a). Flow of participants through each stage (a diagram is strongly recommended)

Specifically, for each group report the numbers of participants randomly assigned, receiving intended treatment, completing the study protocol, and analyzed for the primary outcome.

Examples


82 eligible participants
7 excluded
Reason: refused to participate (n=7)
75 randomised
38 allocated to chiropractic manipulation and massage
38 received allocated intervention
38 allocated to placebo laser and massage
37 received allocated intervention
1 did not receive allocated intervention
Reason: neck injury
Followed up at
Week 7: n=38
Week 11: n=38
Week 15: n=38
Week 19: n=36
Followed up at
Week 7: n=36
Week 11: n=37
Week 15: n=35
Week 19: n=34
36 analysed
2 excluded from analysis
Reason: lost to followup
34 analysed
4 excluded from analysis
Reasons: neck injury (n=1)
lost to followup (n=3)



13(b). Describe protocol deviations from study as planned, together with reasons

Examples

"There was only one protocol deviation, in a woman in the study group. She had an abnormal pelvic measurement and was scheduled for elective caesarean section. However, the attending obstetrician judged a trial of labour acceptable; caesarean section was done when there was no progressin the first stage of labour"

"The monitoring led to withdrawal of nine centres, in which existence of some patients could not be proved, or other serious violations of good clinical practice had occurred"

14. defining the periods of recruitment and follow-up

Example

"Age-eligible participants were recruited … from February 1993 to September 1994… Participants attended clinic visits at the time of randomization (baseline) and at 6-month intervals for 3 years"

15. demographic and clinical characteristics of each group

Example

Characteristic	Vitamin group (n = 141)	Placebo group (n = 142)
Mean age ± SD, y	28.9 ± 6.4	29.8 ± 5.6
Smokers, n (%)	22 (15.6)	14 (9.9)
Mean body mass index ± SD, kg/m^2	25.3 ± 6.0	25.6 ± 5.6
Mean blood pressure ± SD, mm HgSystolicDiastolic	112 ± 1567 ± 11	110 ± 1268 ± 10

Baseline demographic and clinical characteristics of trial groups [adapted from part of Table 1 of Chappell et al .

16. Number of participants (denominator) in each group included in each analysis and whether the analysis was by "intention to treat". State the results in absolute numbers when feasible (e.g., 10 of 20, not 50%)

Examples

"The primary analysis was intention-to-treat and involved all patients who were randomly assigned ···"

"One patient in the alendronate group was lost to follow up; thus data from 31 patients were available for the intention-to-treat analysis. Five patients were considered protocol violators ... consequently 26 patients remained for the per-protocol analyses"

17. For each primary and secondary outcome, a summary of results for each group, and the estimated effect size and its precision (e.g. 95% confidence interval)

18. Address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those prespecified and those exploratory

Example

"Another interesting finding was the evidence of some interaction between treatment with vitamin A and severity of disease on presentation, with results slightly in favour of the vitamin A group among patients initially admitted to hospital, the opposite occurring among those treated as outpatients. Although this finding comes from a subgroup analysis which was preplanned, in no case did the different response between the treatment groups reach significance at the 5% level"

19. important adverse events or side effects in each intervention group

Example

"The proportion of patients experiencing any adverse event was similar between the rBPI21 and placebo groups: 168 (88·4%) of 190 and 180 (88·7%) of 203, respectively, and it was lower in patients treated with rBPI21 than in those treated with placebo for 11 of 12 body systems. … the proportion of patients experiencing a severe adverse event, as judged by the investigators, was numerically lower in the rBPI21 group than the placebo group: 53 (27·9%) of 190 versus 74 (36·5%) of 203 patients, respectively. There were only three serious adverse events reported as drug-related and they all occurred in the placebo group"

20. Interpretation of the results, taking into account study hypotheses, sources of potential bias or imprecision, and the dangers associated with multiplicity of analyses and outcomes

21. (external validity) of the trial findings

Example

"Despite the size and duration of this trial, the populations of patients with OA and RA are much larger and therapy continues for substantially longer than 6 months. Moreover, many patients with OA and RA have comorbid illnesses (e.g., active GI [gastrointestinal] disease) that would have excluded them from the current study. Consequently, the results of this study do not address the occurrence of rare adverse events, nor can they be extrapolated to all patients seen

in general clinical practice"

22. General interpretation of the results in the context of current evidence

Example

"Studies published before 1990 suggested that prophylactic immunotherapy also reduced nosocomial infections in very-low-birth-weight infants. However, these studies enrolledsmall numbers of patients; employed varied designs, preparations, and doses; and included diverse study populations. In this large multicenter, randomized controlled trial, the repeated prophylactic administration of intravenous immune globulin failed to reduce the incidence of nosocomial infections significantly in premature infants weighing 501 to 1500 g at birth"