

Chapter 2.4.2

CLINICAL RANDOMISED CONTROLLED TRIALS IN RURAL PRIMARY HEALTH CARE SETTINGS

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Introduction

There has been a continuous discussion about the effectiveness of primary care and family medicine in the literature. Research in rural primary health care has received negligible attention, although important developments in Australia, Canada and some European countries have been reported during the past years. Although the body of published rural research in Australia is growing steadily, a bibliometric analysis of Australian rural research indicated that only 1% of the total number of Australian health publications between 1990 and 2007 addressed rural health (1).

While the issue of research capacity is essential to explaining the limited number of published research papers in rural primary care (2, 3, 4, 5, 6), other issues on conducting and reporting rural health research also need to be identified and addressed in order to ensure the robustness of the results in rural primary care randomised control trials (RCTs). Key points needing prompt attention, as reported by an Australian paper, include privacy of participants, collection of data, cultural traditions of indigenous communications, dissemination of results, and giving something back to the community (7). Meanwhile a thorough look into the type of interventions assessed in RCTs which are conducted in the rural field is suggested, so that investigators may be aware of specific issues that need to be considered to enhance the validity of their trials.

In this chapter, we focus on RCTs conducted in rural primary care settings worldwide. We aim to identify the interventions in rural primary care settings that have been evaluated in at least one RCT and we describe certain characteristics of these trials. Among the study's objectives is to raise a discussion regarding what may be lacking in clinical research in rural practice and the types of efforts and actions required to build research capacity.

Methods

We searched Pubmed (from inception to May 2011) to identify RCTs conducted in rural primary care settings, limiting our search to English articles on human subjects. We used the following algorithm: 'Rural AND ('Family Practice'[Mesh] OR 'Primary Health Care'[Mesh] OR 'Physicians, Family'[Mesh] OR 'family medicine'[tiab] OR 'family practice'[tiab] OR 'general medicine'[tiab] OR 'general practice'[tiab] OR 'general internal medicine'[tiab] OR 'family physician'[tiab] OR 'general practitioner'[tiab] OR 'primary care'[tiab]) AND ('Clinical Trials as Topic'[Mesh] OR 'randomised controlled trial'[pt] OR 'controlled clinical trial'[pt] OR randomised[tiab] OR placebo[tiab] OR randomly[tiab] OR trial[tiab])'. Electronic search was complemented by perusal searches of the references of the included articles as well as the references of review articles.

We excluded studies that were not conducted exclusively in rural areas, i.e. trials that included both rural and semi-rural or urban settings. We also excluded trials that did not explicitly state that they were conducted in rural primary care settings as well as those that compared an intervention between a primary care with a secondary or tertiary care setting, e.g., myocardial infarction thrombolysis performed at home vs. thrombolysis performed at hospital. In addition, articles that described only the study protocol without reporting the results of the trial were not included.

We extracted the following items from each article: first author, year of publication, country where the RCT was conducted, sample size, number of arms, design (parallel, crossover), randomisation unit (individual or cluster), intervention, comparison (another active intervention; standard or usual care; placebo or no treatment), primary outcomes, and follow-up period. We also recorded how the authors interpreted the results of the trial. Specifically, we categorised studies in three groups - i.e. studies reporting that the intervention was effective; studies reporting that the intervention had no effect; and studies which reported that the intervention was harmful. Finally, we determined whether trials reported any funding sources.

We described the data using absolute numbers and percentages for binary and categorical outcomes; we calculated median and interquartile range (IQR) for continuous variables.

Results

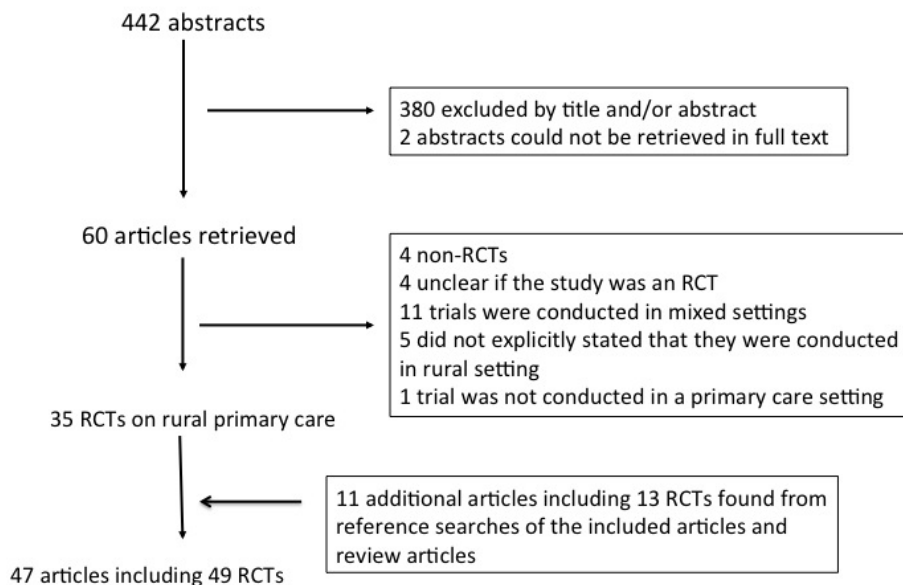
Our initial search retrieved 442 abstracts. We excluded 380 by title or abstract and we retrieved 62 articles in full text. Out of these, we excluded 25 due to the following reasons:

- the trial was not an RCT (n= 4);
- the study design was unclear (n=4);
- the trial was not conducted only in a rural setting (n=11);
- the trial was unclear about the setting it was conducted (n=5);
- the study was not conducted in a primary care setting (n=1).

We were not able to retrieve two articles published in 1982 and 1978 respectively in full text.

After searching the references of the included studies and the references of the reviews, we found 11 additional papers. Therefore, we finally included 49 RCTs reported in 47 articles (Figure 1).

**Figure 1:
Flow chart of the eligible studies**



- The median year of publication was 2002 (IQR 1996-2005).
- Nineteen (40%) out of the 47 studies were conducted in US, seven in Canada (15%), seven in European countries (15%), five in Africa (11%), five in Australia (11%), and from one trial in Israel, Thailand, Honduras, and Costa Rica.
- Median sample size was 182 (IQR 74-727) participants.
- Thirty (65%) out of the 49 trials used the individual (physician, patient, health care worker) as their randomisation unit, one RCT used the family, while 18 (33%) were designed as cluster RCTs, randomising clinical settings or practices, and communities or towns.
- There was only one RCT with a cross-over design. Seven trials (15%) included more than two arms.
- The median follow-up period for the 49 trials was 12 (IQR 6-18) months.

The RCTs evaluated a diversity of multi-faceted interventions rather than single pharmaceutical treatments (Appendix A). There were only two trials that specifically examined the efficacy of a single drug intervention; one of them compared the use of anistreplase at home with placebo for acute coronary artery disease and the other evaluated the effectiveness of an antacid tablet vs. placebo for lowering LDL. RCTs reported either the use of standard and usual care (13/49) or another intervention (22/49) as control. Fourteen (28%) trials used placebo or no intervention in their control group.

There were only two RCTs that reported hard outcomes such as survival or mortality; the rest of the trials used surrogate markers to measure efficacy of interventions, health services use outcomes, and questionnaires to measure the performance of interventions by comparing the score change between the arms.

Outcomes were relevant to physicians' performance in one third of the trials while the rest of the RCTs referred to patients' health care endpoints (Appendix B).

Twenty-nine (59%) out of the 49 RCTs suggested that the intervention was significantly effective; however, 18 (39%) studies suggested that there was no effect difference between the intervention arm and the controls. There was only one trial that found the intervention harmful.

Thirty-two (65%) out of the 49 trials reported funding sources.

Discussion

Our overview on RCTs in rural primary care revealed few published trials, half of which were conducted between 1997 and 2005. Less than 25% of the trials were published after 2005. While half of the trials were performed in North America (US and Canada), there were RCTs conducted in rural settings on all five continents.

The majority of these trials followed the standard parallel two-arm design for RCTs. One third of them were designed as cluster randomised trials, using practices, communities, or towns instead of individuals as the unit of randomisation. They evaluated a diversity of multi-faceted interventions and reported a variety of outcomes. Hard outcomes were lacking. However, a high proportion of interventions were found to be effective. The duration of follow-up was moderate. Funding sources were reported in most of the trials.

There was a limited number of RCTs in rural primary health care. This has been supported previously for research in primary care in general. Current literature on community orientation is mainly descriptive and most papers correspond rather poorly to the Wonca definition of general practice (GP) or family medicine (FM) (8).

While there is an important body of opinion papers and non-systematic reviews in terms of person-centred care using a comprehensive and holistic approach, 'person-centred care' remains poorly defined and examined (9). With regards to specific problem solving skills, pragmatic comparative effectiveness studies on new and established drugs or non-pharmaceutical therapy are needed (8).

The limited number of RCTs that our study identified highlighted the lack of research capacity especially in rural primary health care settings. Even in countries where rural research has been translated into experimental research, limitations in rural capacity and especially in educational programmes (10) have been reported, and developing strategies are suggested (2; 3). This finding is also in line with the European General Practice Research Network (EGPRN) study (9), which endorses the recommendations of Wonca that they have been included in the Kingston Report (11).

RCTs in rural primary care included certain characteristics, for which guidelines for their reporting need to be clarified. Besides the specific guidelines that were issued for cluster randomised and pragmatic trials, the reporting of randomised trials comparing multi-faceted interventions would need further guiding from specific recommendations. In addition, outcomes used in rural primary care - such as measures of health services utilisation or questionnaire scores - need to be validated before their use.

An extremely high proportion of the included trials supported significant efficacy for the experimental intervention. Whether all multi-faceted approaches used in rural primary care are indeed efficacious, or compromised internal validity of these trials led to these results, remains to be further investigated. In addition, potential effective interventions will need to be confirmed by subsequent studies before their use in practice could be recommended. Researchers, who will participate in rural primary health care projects, need to be adequately trained to meet the challenges of experimental research (12).

Limitations

Our overview had several limitations.

We limited our search only to one electronic database and we did not consider journals of the rural primary care field that may not be registered in Pubmed. As such, we may have not included a number of RCTs that were not indexed in Pubmed. However, after hand-searching the references of the included and the review articles, the additional retrieved RCTs were also indexed in Pubmed. Our searches were restricted up to 2011. Updated searches need to be performed to clarify whether there was an increase in the number of rural RCTs after May 2011.

We excluded RCTs that compared interventions between rural and urban settings, as well as trials that were conducted in urban, semi-rural, and rural settings simultaneously. However, even after including trials in these settings, the total number of RCTs would not dramatically increase.

In addition, we did not evaluate the quality of these trials, and therefore cannot address quality issues pertaining to the design of these papers. Moreover, we cannot reach any conclusion on the robustness of the results for the eligible trials.

Conclusion

Our study showed that published RCTs conducted in rural primary health care were very limited. They invariably assessed multi-faceted approaches in primary care using a variety of outcomes, and most of them reported that their experimental intervention was more effective when compared to controls. Further investigation is needed to evaluate the methodological quality of these trials and acknowledge issues that may pertain to the design of RCTs in rural primary care.

This overview can contribute further to the efforts that have been undertaken by Wonca in building research capacity and provide some essential input to the Wonca Working Party on Rural Practice.

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Further reading

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Appendix A

Interventions of rural RCTs

First author	Year	Intervention	Comparison group
Noknoy S	2010	Motivational Enhancement Therapy	No intervention
Hogg W	2009	Anticipatory and Preventive Team Care (APTCare)	Usual care
Ellerbeck EF	2009	arm1: pharmacotherapy supplemented with up to 2 counseling calls (moderate-intensity disease management); arm2: pharmacotherapy supplemented with up to 6 counseling calls (high-intensity disease management)	Pharmacotherapy alone
Oak K	2008	arm1: unscheduled visit to the practice by a librarian; arm2: a brief e-mail to each GP, giving a link to the library homepage	No intervention
Ely AC	2008	Chronic Care Model Model Program (+standard care)	Standard care
Weber V	2008	Electronic Medical Record Intervention for fall prevention	Usual care
McCrae CS	2007	Multicomponent behavioral treatment	Sleep hygiene education
Majoko F	2007	Five-visit antenatal care (ANC) model with specified goals	Usual care
Tessaro I	2007	Cookin' Up Health, a computer-based interactive nutrition intervention	No intervention
Ahles TA a	2006	Information and physician feedback tailored to their management needs	Usual care
Ahles TA b	2006	arm1: information and physician feedback tailored to their pain management needs; arm2: with nurse-educator telephone contact	Usual care
Clarke	2005	Community-based health workers	No treatment
Bergus GR	2005	Providers were given completed PHQ-9 questionnaires (depression screening) at the baseline visit	Providers not aware of patients' screening results
Samore MH	2005	Community intervention plus clinical decision support that were targeted toward primary care clinicians for antimicrobial use	Community intervention alone
Pavlidis C	2005	Earwax removal: instillation of water into the ear canal for 15 minutes before syringing	Syringing immediately
Morris SS	2004	arm1: household-level package alone; arm2: service-level package alone; arm3: both packages	Standard services

First author	Year	Intervention	Comparison group
Askim T	2004	Extended service for rehabilitation after stroke	Ordinary stroke unit service (ordinary service)
Rockwood K	2003	Comprehensive Geriatric Assessment (CGA)	Usual care by family physicians
Taylor CT	2003	Pharmacist intervention for improving certain chronic disease management	Standard medical care
Myer L	2003	Rapid plasma reagin test (Macro-Vue RPR Card Test, Becton-Dickinson, USA) was performed on site by nursing staff	Blood specimens sent to the provincial reference laboratory; all women were counseled to return 2 weeks later to receive their results
Kronick J	2003	Educational intervention: individualised 3-hour training session on using the World Wide Web to research patient-related questions	No intervention
Goldhaber-Fiebert JD	2003	Community based nutrition and exercise intervention	Standard medical care from physician
Arthur AJ	2002	Health check	Personal letter
Bernal-Delgado E	2002	Educational outreach visit, conveying data based on a systematic review of the literature that was reinforced with printed material	Placebo /no treatment
Young JM	2002	Distance learning module for smoking prevention	Preventive care guideline
Elliott TE	2002	Lake Superior Rural Cancer Care Project	No intervention
Hammond CS	2001	A combination of targeted information for patients coupled with a personalised distribution practice guideline information for physicians	No intervention
Ahles TA	2001	Information and physician (+/-nurse) feedback tailored to their pain management needs	Usual care
Mayer-Davis EJ	2001	Intensive lifestyle (reduced fat and calorie intake and increased activity)	Intensive lifestyle plus ongoing formal evaluation for continuous quality improvement
Harrison A	2000	Health worker training and STD syndrome packets (containing recommended drugs, condoms, partner notification cards and information leaflets)	No intervention

First author	Year	Intervention	Comparison group
Rockwood K	2000	Specialised procedure known as Comprehensive Geriatric Assessment (CGA), which consists of initial evaluation and subsequent multidisciplinary management of clinical problems	Usual care by family physicians
Dietrich AJ	2000	The primary care component of SunSafe consisted of a continuing education meeting at local hospitals on sun protection education followed by 2 visits to each participating practice by a research assistant	No intervention
Chan DH	1999	Two months discussing the topic of depression in the elderly with the help of a facilitator and two geriatric psychiatrists	Similar educational resources via the Internet but without the benefit of the small-group interaction
O'Connell DL	1999	Two sets of graphical displays (6 months apart) of their prescribing rates for 2 years, relative to those of their peers, were posted to participants	No intervention
Kinsinger LS	1998	Office system to increase breast cancer screening	No intervention
Hogg WE	1998	arm1: computer-generated customised letters as reminders to patients of outstanding preventive procedures/ one paragraph per family member; arm2: form letter, which outlined all the recommended preventive procedures for all ages and both sexes	Usual care
Davies-Adetugbo AA	1997	Individual, focused breast-feeding counselling	Counseling for diarrhea
Clover K a	1996	Mass media promotion to recruit wome for mammography	Community participation to recruit women for mammography
Clover K b	1996	Community participation to recruit wome for mammography	Family physician involvement to recruit women for mammography

First author	Year	Intervention	Comparison group
Rawles J	1996	Anistreplase 30 units iv (thrombolysis)	Placebo
Turner RC	1994	Computer-generated prompt sheet placed on the front of patients' charts to remind physicians to perform selected health maintenance items	Patient-carried prompt card to remind physicians to perform selected health maintenance items
Frame PS	1994	Computer-based health maintenance tracking system that generated annual provider and patient reminders for all patients regardless of appointment status	Manual flowchart-based tracking system in which patient reminders were triggered by provider request
Brunham S	1992	Videotaped discharge summaries in communicating patient information to rural physiotherapists	Written discharge summaries in communicating patient information to rural physiotherapists
Hempel RJ	1992	6-minute videotape explaining reasons to wear seat belts	Espousing general preventive health care guidelines with no mention of seat belts
Sperber AD	1991	Chewable antacid tablet containing simethicone, magnesium hydroxide, and 113 mg of aluminum hydroxide per tablet	Placebo
Charlton I	1990	Peak flow asthma management	symptom only asthma management
Leke RJ	1988	Training and supervision of local nurses and Community Women's Organisation leaders were recruited to urge women to attend antenatal clinic	Training and supervision of local nurses
Curry RW Jr	1980	Referral form accompanied by a request for feedback and a return mailer	Referral form only

Appendix B

Reported primary outcomes evaluated in rural RCTs

First author	Year	Primary outcomes
Noknoy S	2010	Alcohol consumption
Hogg W	2009	Chronic disease management score
Ellerbeck EF	2009	Self-reported, point-prevalence smoking abstinence at 24 months
Oak K	2008	Use of the Cornwall Health Library Service
Ely AC	2008	Weight change
Weber V	2008	Medication use (drop); falls
McCrae CS	2007	Insomnia
Majoko F	2007	Number of visits, referrals from RHC for antenatal, intrapartum or post- partum problems, place of delivery and low birthweight infant (<2500 g)
Tessaro I	2007	Scores on knowledge of dietary fats, food label reading, and readiness to eat 5 fruits and vegetables a day and foods lower in fat
Ahles TA a	2006	Medical Outcomes Study 36-Item Short-Form
Ahles TA b	2006	Medical Outcomes Study 36-Item Short-Form
Clarke	2005	Successful treatment completion in new smear positive pulmonary TB patients
Bergus GR	2005	Change in PHQ-9 scores; proportion of subjects who were actively managed with medication or by referral to a mental health specialists
Samore MH	2005	Community-wide antimicrobial usage; diagnosis-specific antimicrobial use
Pavlidis C	2005	Attempts to remove wax
Morris SS	2004	Rates of use of preventive health services by pregnant women and young children (specifically, the proportion of pregnant women attending at least five antenatal checkup visits; the proportion of new mothers going for a check-up within 10 days of delivery, and the proportion of children younger than 3 years of age going to the health centre at least once during the month preceding the interview)
Askim T	2004	Proportion of patients who were independent according to Modified Rankin Scale (mRS) (independence, mRS≤/ =2)
Rockwood K	2003	Goal Attainment Scaling (GAS)
Taylor CT	2003	Goal achievement for : BP; HbA1c; INR; LDL
Myer L	2003	Perinatal death
Kronick J	2003	Frequency of access; comfort with on-line medical information (Likert scale)
Goldhaber-Fiebert JD	2003	Weight, BMI, HbA1c, BP, fasting Glu, TCHOL, TROGL, HDL, LDL (calculated)
Arthur AJ	2002	Flu vaccination received

First author	Year	Primary outcomes
Bernal-Delgado E	2002	Proportional change in the number of packages prescribed during the six months before intervention and the six months afterwards
Young JM	2002	Improvement in knowledge, attitudes, and skills (questionnaire)
Elliott TE	2002	Physician practice behaviors regarding cancer diagnosis, staging, treatment, clinical trial participation, and post-treatment surveillance
Hammond CS	2001	Health status, urinary symptoms and bother, treatments received, and prostate-related knowledge; power calculation for 10% difference in patient knowledge and anxiety
Ahles TA	2001	Medical Outcomes Study 36-Item Short-Form
Mayer-Davis EJ	2001	Differences in weight, BMI, and fasting blood glucose
Harrison A	2000	Proportion of simulated patients given recommended drugs; correctly case managed (given recommended drugs plus condoms and partner cards); adequately counselled; reporting good staff attitude; and consulted in privacy
Rockwood K	2000	Survival; assessment of individualised goals attained (clinometric tool): < 35 (much worse than expected) to > 65 (much better than expected)
Dietrich AJ	2000	Sun protection promotion activities of primary care clinicians as determined by their self report, research assistant observation, and parent interviews
Chan DH	1999	Multiple Choice Questions (MCQ) test (feasibility, keys to success, utility of Internet-assisted education from an education and evaluation perspective)
O'Connell DL	1999	Reduction in prescribing rates for five main drug categories
Kinsinger LS	1998	Increase in mammograms
Hogg WE	1998	Family Received Index= the proportion of all procedures for which a family was overdue that they received; Family Received Index and Family End-of-study Up-to-date Index= the proportion of procedures for which the family was eligible and for which they were up-to-date at the end of the study
Davies-Adetugbo AA	1997	Prevalence of exclusive breast feeding
Clover K a	1996	Proportion of women attending for mammography
Clover K b	1996	Proportion of women attending for mammography
Rawles J	1996	Mortality
Turner RC	1994	Performance of influenza vaccinations, stool for occult blood, pap smears, breast examinations performed by the physicians, and mammograms
Frame PS	1994	Provider compliance with the health maintenance protocol for 11 procedures determined by chart audits, costs of computer-based tracking, and response of inactive patients to health maintenance reminders

First author	Year	Primary outcomes
Brunham S	1992	Multiple choice questions regarding the patients' problems, goals and treatment for physiotherapy
Hempel RJ	1992	Seat belt use
Sperber AD	1991	LDL; HDL; HDL/LDL
Charlton I	1990	Number of doctor consultations, courses of oral steroids, short term nebulised salbutamol; number of patients with doctor consultations, courses of oral steroids, short term nebulised salbutamol
Leke RJ	1988	Attendance at antenatal clinics
Curry RW Jr	1980	Percentage of consultant feedback; median time interval between a patient's contact with a consultant and receipt of that consultant's report by the rural clinics

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