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Abstract

Improving the referral process for familial breast cancer genetic counselling: findings of three randomised controlled trials of two interventions

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Objectives: To evaluate the effectiveness and cost-effectiveness of two complementary interventions, using familial breast cancer as a model condition. The primary care intervention consisted of providing computerised referral guidelines and related education to GPs. The nurse counsellor intervention evaluated genetic nurses as substitutes for specialist geneticists in the initial assessment and management of referred patients.
Design: The computerised referral guidelines study was a pragmatic, cluster randomised controlled trial (RCT) with general practices randomised to intervention or control groups. The nurse counsellor intervention was tested in two concurrent RCTs conducted in separate UK health service locations, using predetermined definitions of equivalence.
Setting: The computerised referral guidelines trial took place in general practices in Scotland from November 2000 to June 2001. The nurse counsellor intervention took place in a regional genetics clinic in Scotland, and in two health authorities in Wales served by a single genetics service during 2001.
Participants: The computerised referral guidelines study involved GPs and referred patients. Both nurse counsellor intervention trials included women referred for the first time, aged 18 years or over and whose main concern was family history of breast cancer.
Interventions: The software system was developed with GPs, presenting cancer genetic referral guidelines in a checklist approach. Intervention GPs were invited to postgraduate update education sessions, and both intervention and control practices received paper-based guidelines. The intervention period was November 2000 to June 2001. For the nurse counsellor trial, trial 1 ran outpatient sessions with the same appointment length as the standard service offered by geneticists, but the nurse counsellor saw new patients at the first appointment and referred back to the GP or on to a clinical geneticist according to locally developed protocol, under the supervision of a consultant geneticist. The control intervention was the current service, which comprised an initial and a follow-up appointment with a clinical geneticist.
In trial 2, a nurse counsellor ran outpatient sessions with the same appointment length as the new consultant-based cancer genetics service and new patients were seen at the first appointment and referred as in trial 1. The control intervention was a new service, and comprised collection of family history by telephone followed by a consultation with a clinical assistant or a specialist registrar, supervised by a consultant. The intervention was implemented between 1998 and 2001.

Main outcome measures: In the software system trial, the primary outcome was GPs' confidence in their management of patients with concerns about family history of breast cancer. For the nurse counsellor trial, the primary outcome was patient anxiety, measured using standard scales.

Results: In the software system trial, 57 practices (230 GPs) were randomised to the intervention group and 29 (116 GPs) to the control group. No statistically significant differences were detected in GPs' confidence or any other outcomes. Fewer than half of the intervention GPs were aware of the software, and only 22 reported using it in practice. The estimated total cost was £3.12 per CD-ROM distributed (2001 prices). For the two arms of the nurse counsellor trial, 289 patients (193 intervention, 96 control) and 297 patients (197 intervention and 100 control) consented, were randomised, returned a baseline questionnaire and attended the clinic for trials 1 and 2 respectively. The analysis in both cases suggested equivalence in all anxiety scores, and no statistically significant differences were detected in other outcomes in either trial. A cost-minimisation analysis suggested that the cost per counselling episode was £10.23 lower in intervention arm than in the control arm and £10.89 higher in the intervention arm than in the control arm (2001 prices) for trials 1 and 2, respectively. Taking the trials together, the costs were sensitive to the grades of doctors and the time spent in consultant supervision of the nurse counsellor, but they were only slightly affected by the grade of nurse counsellor, the selected discount rate and the lifespan of equipment.

Conclusions: Computer-based systems in the primary care intervention cannot be recommended for widespread use without further evaluation and testing in real practice settings. Genetic nurse counsellors may be a cost-effective alternative to assessment by doctors. This trial does not provide definitive evidence that the general policy of employing genetics nurse counsellors is sound, as it was based on only three individuals. Future evaluations of computer-based decision support systems for primary care must first address their efficacy under ideal conditions, identify barriers to the use of such systems in practice, and provide evidence of the impact of the policy of such systems in routine practice. The nurse counsellor trial should be replicated in other settings to provide reassurance of the generalisability of the intervention and other models of nurse-based assessment, such as in outreach clinics, should be developed and evaluated. The design of future evaluations of professional substitution should also address issues such as the effect of different levels of training and experience of nurse counsellors, and learning effects.

Contents

List of abbreviations

ANCOVA	analysis of covariance
BRCA gene	breast cancer susceptibility gene
CGS	Cancer Genetics Service
CI	confidence interval
CMA	cost-minimisation analysis
CONSORT	Consolidated Standards of Reporting Trials
EAC	equivalent annual cost
FU1	follow-up 1 (following counselling episode)
FU2	follow-up 2 (6 months after FU1)
GUHT	Grampian University Hospital Trust
HADS	Hospital Anxiety and Depression Scale
ICC	intracluster correlation coefficient
IQR	interquartile range
IT	information technology
ITT	intention-to-treat
MRC	Medical Research Council
NA	not applicable
PDA	personal digital assistant
PGEA	Postgraduate Education Allowance
PP	per-protocol
RCT	randomised controlled trial
RR	relative risk
SD	standard deviation
SEHD	Scottish Executive Health Department
SF-36	Short Form 36 Health Survey
STAI	State Trait Anxiety Inventory

All abbreviations that have been used in this report are listed here unless the abbreviation is well known (e.g. NHS), or it has been used only once, or it is a non-standard abbreviation used only in figures/tables/appendices in which case the abbreviation is defined in the figure legend or at the end of the table.

Executive summary

Background

Clinical genetics services need to find cost-effective ways of meeting increasing demand resulting from advances in knowledge of genetic contribution to risk of common diseases. GPs need both to provide first line genetic assessment and to identify patients who would benefit from referral to genetics clinics.

This project evaluated the effectiveness and cost-effectiveness of two complementary interventions, using familial breast cancer as a model condition. The primary care intervention consisted of providing computerised referral guidelines and related education to GPs. The nurse counsellor intervention evaluated genetic nurses as substitutes for specialist geneticists in the initial assessment and management of referred patients.

Primary care trial

Objectives

This study aimed to evaluate a computer support system for breast cancer genetics within a general practice setting and to examine the factors influencing its implementation.

Methods

The design was a pragmatic, cluster randomised controlled trial (RCT) with general practices randomised to intervention or control groups. The trial took place in general practices in the Grampian region of Scotland. Data were collected from GPs and patients they referred.

Intervention

A software system was developed with GPs. It presented cancer genetic referral guidelines in a checklist approach, along with other features designed to enhance its utility. The software was disseminated as a CD-ROM to intervention practices by information technology technicians, by the research team or by post, followed by a letter to each intervention GP individually. Intervention GPs were invited to postgraduate update education sessions, which included a hands-on demonstration of the software. Both intervention and control practices received paper-based guidelines when the Scottish Executive mailed these to all GPs in Scotland. The intervention period ran from November 2000 to June 2001.

Main outcome measures

The primary outcome was GPs' confidence in their management of patients with concerns about family history of breast cancer. Secondary outcomes were changes in referral patterns, patients' perceptions of risk and understanding of breast cancer risk factors. An economic evaluation was conducted in parallel with the main trial.

Results

Fifty-seven practices (230 GPs) were randomised to the intervention group and 29 (116 GPs) to the control group. Three postgraduate education sessions were attended by 27 (11.9%) GPs from 20 (35.1%) intervention practices.

No statistically significant differences were detected in GPs' confidence or any other outcomes. Fewer than half of the intervention GPs were aware of the software, and only 22 reported using it in practice. It was not possible to assess effects in just these 22 GPs. The estimated total cost was £3.12 per CD-ROM distributed (2001 prices), largely reflecting development costs. This estimate was sensitive to the number of copies produced and the timing of updates.

Conclusions

The trial had sufficient statistical power to detect a meaningful difference in the primary outcome. However, no improvement in GP confidence was observed and too few women were referred to allow clear conclusions on referral patterns or patient outcomes. The pragmatic approach to dissemination of the software did not lead to high levels of awareness or uptake of the intervention. It is not possible to conclude that the policy of developing the software package and disseminating it within a pragmatic strategy was effective in promoting GP confidence in their management of women concerned about the genetic risk of breast cancer.

Nurse counsellor trial

Objectives

This study aimed to test whether trained genetics nurse counsellors are as effective as current models of service for familial breast cancer counselling and to explore factors influencing cost-effectiveness.

Methods

Two concurrent RCTs were conducted in separate UK health service locations in 1998–2001, using predetermined definitions of equivalence. Trial 1 took place in a regional genetics clinic serving Grampian in north-east Scotland, and trial 2 in two health authorities in Wales served by a single genetics service. Both trials included women referred for the first time, aged 18 years or over, whose main concern was family history of breast cancer.

Interventions

In trial 1, a nurse counsellor, based in the regional cancer genetics clinic in Aberdeen, ran outpatient sessions with the same appointment length as the standard service offered by geneticists. She saw new patients at the first appointment and referred back to the GP or on to a clinical geneticist according to locally developed protocol, under the supervision of a consultant geneticist. The control intervention was the current service, which comprised an initial and a follow-up appointment with a clinical geneticist.

In trial 2, a nurse counsellor based in the regional genetics service in Cardiff ran outpatient sessions with the same appointment length as the new consultant-based cancer genetics service. She saw new patients at the first appointment and referred back to the GP or on to a clinical geneticist according to locally developed protocol, under the supervision of a consultant geneticist. The control intervention was a new service, and comprised collection of family history by telephone followed by a consultation with a clinical assistant or a specialist registrar, supervised by a consultant.

Main outcome measures

The primary outcome was patient anxiety, measured using the short form of the Spielberger State Trait Anxiety Inventory, the Hospital Anxiety and Depression Scale and the mental health and role emotional domains of the Short Form 36 health status instrument. Secondary outcomes were other aspects of health status, satisfaction, risk perceptions and understanding of breast cancer risk factors. Acceptability to GPs was also assessed and a concurrent economic evaluation conducted.

Results

In trial 1, 289 patients (193 intervention, 96 control) consented, were randomised, returned a baseline questionnaire and attended the clinic. Their mean age was 40.9 years and eventual clinic assessment placed 28% in the highest genetic risk category. The analysis suggested equivalence in all anxiety scores, and no statistically significant differences were detected in other outcomes. These findings were not altered by the per-protocol analysis. A cost-minimisation analysis suggested that the cost per counselling episode of £10.23 (95% confidence interval –£1.69 to 22.15) was lower in the intervention arm than in the control arm (2001 prices)

In trial 2, 297 patients (197 intervention and 100 control) consented, were randomised, returned a baseline questionnaire and attended the clinic. Their mean age was 39.5 years and eventual clinic assessment placed 30% in the highest genetic risk category. The analysis suggested equivalence in all anxiety scores, and no statistically significant differences were detected in other outcome in either trial. These findings were not altered by the per-protocol analysis. A cost-minimisation analysis suggested that the cost per counselling episode was £10.89 higher in the intervention arm than in the control arm (2001 prices).

Taking the trials together, the costs were sensitive to the grades of doctors and the time spent in consultant supervision of the nurse counsellor, but they were only slightly affected by the grade of nurse counsellor, the selected discount rate and the lifespan of equipment.

Conclusions

Genetics nurse counsellors could be considered equivalent across a range of outcomes to the current model of cancer genetic counselling in both trial locations, providing evidence of generalisability. This approach can be a cost-effective alternative to physician-led care for breast cancer genetic counselling, depending on the grade of doctor being substituted and the extent of consultant supervision.

Implications for healthcare

The primary care intervention described here cannot be recommended for widespread use without further evaluation. Computer-based

systems must be tested in real practice settings, with realistic dissemination and implementation strategies.

Genetic nurse counsellors may be a cost-effective alternative to assessment by doctors, when working within a defined protocol under supervision and under the same constraints. This trial does not provide definitive evidence that the general policy of employing genetics nurse counsellors is sound, as it was based on only three individuals.

Recommendations for research

Primary care trial

- Future evaluations of computer-based decision support systems for primary care must first address their efficacy under ideal conditions.
- In-depth studies are required to identify barriers to the use of such systems in practice.
- The growing adoption of handheld computers (personal digital assistants) for clinical and administrative tasks suggests that they may be more attractive to busy clinicians than desktop-based systems, but they require rigorous evaluation.
- Strategies for disseminating and implementing decision-support systems that have been shown to have efficacy in exploratory studies should be based on the best available evidence. Pragmatic trials are required to provide evidence of the impact of the policy of offering or installing such systems in routine practice.

Nurse counsellor trial

- This study should be replicated in other settings to provide reassurance of the generalisability of the intervention.
- Other models of nurse-based assessment, such as in outreach clinics, should be developed and evaluated.
- The design of future evaluations of professional substitution should address issues such as the effect of different levels of training and experience of nurse counsellors, and learning effects.

Chapter 1
Introduction

The current organisation of specialist genetics services within the NHS reflects their historical evolution. They have developed from academic departments to regional centres, each of which serves a number of smaller districts and usually has integrated clinical and laboratory services.[1] Until the late 1980s, UK genetics services were concerned in the main with the diagnosis of fairly uncommon congenital and inherited disorders, and counselling generally concerned reproductive issues.[2] For many years, genetic counselling has been provided almost exclusively by physicians, with the introduction of genetic counsellors or associates with a science or nursing background a fairly recent development.[3,4] Clinical genetics services have therefore had limited capacity to deal with the increasing demand which resulted from the rapid expansion of molecular genetics knowledge.[2] New ways of dealing with patient demand have been suggested; for example, an increased role for GPs,[2,5–7] supported by guidelines[8] and computer support aids,[9,10] the introduction of intermediate levels of specialist advice[2,11] and an enhanced role for nurses.[2–4,12]

Familial cancer provides a typical example of an area in which knowledge has progressed rapidly over the past decade, and where patient demand for information, counselling and mutation testing has increased dramatically. This has affected the workloads in both primary care and specialist centres. On the one hand, GPs need to be able to provide first line genetic assessment, identify patients who would benefit from referral, and provide information and appropriate reassurance for those who are unlikely to be at high genetic risk. As genetics becomes more integrated with mainstream medicine, some argue that the primary care role must eventually expand to include activities that are now considered specialist. On the other hand, regional clinics are still faced with a challenge of increasing their ability to manage and meet increasing demand within their own resource constraints. Even with the introduction of guidelines, most clinics have faced year-on-year increases in referrals, each of which requires counsellor time. Many specialist centres have taken the apparently logical approach of expanding their counselling resource by employing genetic associates or nurses, trained in a variety of more or less structured programmes. Although these staffing patterns are increasingly widespread, no formal evaluation of their effectiveness has been undertaken.

This project was designed in response to widespread concerns about the ability of the NHS to cope with the genetics revolution, at a time when very little rigorous evidence existed about the effectiveness of different interventions to deal with increasing demand. The Health Technology Assessment (HTA) Programme requested proposals to develop and evaluate interventions related to genetics in the broad area of the primary–secondary care interface. The present study evaluated the effectiveness and cost-effectiveness of two interventions intended to be complementary, using familial breast cancer as a model condition. One intervention was primary care based and consisted of computerised referral guidelines presented with an educational intervention, and the other was focused on specialist care, evaluating genetic nurses as substitutes for specialist geneticists in the initial assessment and management of referred women.

Reflecting this, the report is split into three main sections. The first two sections describe the evaluations of the two interventions and the third section draws together conclusions. The first intervention was evaluated in the Grampian region of Scotland, and the second in the Grampian region and in Wales.

Chapter 2

Primary care intervention: background

Rationale

The lifetime risk for breast cancer in UK women is approximately 8%,[13] so many women have a sister, mother or cousin affected by the disease. It is inevitable that concerned patients will look to their GPs for credible information about their genetic risk, and for specific advice and counselling.[14–17] However, it is unrealistic to expect GPs to analyse scientific and media reports of genetic discoveries and translate them into meaningful information for their patient.[5] The evidence suggests that GPs tend to overestimate the risk of hereditary cancer.[9,18–20] When this study was conceived in 1997 it was estimated that up to half of the specialist referrals for breast cancer genetic counselling were of patients at little more than population risk. This represents a serious burden on services designed for the few patients at high risk.[21,22] Furthermore, the UK is not the only country where concerns have been raised about the ability of specialist genetics services to meet the increase in demand.[14,23]

It has been argued that GPs should be able to manage many low- to moderate-risk patients themselves, thereby preventing delays for appointments at genetics services for genuinely high-risk patients.[9] Women at low risk primarily need information, reassurance and advice regarding preventive care, all of which are well within the domain of primary care.[17] Surveys, qualitative studies and statements by professional bodies suggest that GPs identify a role for themselves in genetics that reflects traditional general practice activities,[9,24] for example, taking a family history, making appropriate referrals to specialist services, providing credible information and reassurance, and providing emotional support. However, they identify significant barriers to achieving this role,[5,25] including inadequate knowledge or confidence[9,18,26–30] and practical, ethical and legal issues.[9,31–35]

There is, then, a legitimate debate regarding how far GPs should take on genetic counselling roles that are currently regarded as specialist. However, it is inevitable that patients will come to them as the first source of advice and the decisions that they make have an important impact on specialist care. Until future cohorts of newly trained GPs emerge from undergraduate and postgraduate programmes with the knowledge and skills which permit them to integrate genetic counselling into routine primary care practice, current GPs need to be equipped with the means to meet the needs of their patients in an appropriate and cost-effective way.

The practical issue facing the NHS now is how to support GPs in their key role: correctly distinguishing the patients or families who would benefit from specialist assessment from the larger number of patients who are unlikely to be carrying a significant disease-causing mutation. For both groups, GPs need to be able to provide appropriate information, advice and reassurance.

A large body of evidence exists on interventions to promote the uptake and use of evidence within the NHS.[36] Potential interventions targeted at primary care include:

- educational interventions targeted at professionals (e.g. printed material, continuing medical education)
- educational interventions targeted at patients (e.g. patient leaflets, videos)
- clinical guidelines
- decision support tools (e.g. passive and active computerised clinical guidelines)
- structural/organisational changes (e.g. liaison nurses, genetic nurse outreach clinics, primary care genetics specialists)
- Other (e.g. family history tools, telephone and fax helplines).

To be sustainable in the long term, any intervention would need to be cost-effective, and flexible enough to adapt as necessary to the rapidly changing knowledge base of medical genetics and to fit within primary care patterns of activity. At the time of designing this study, there was no clear evidence on the likely effectiveness of any particular primary care-based intervention, although there was probably enough evidence to suggest that passive guideline dissemination was not enough and that some active strategy would be required.[37] Three factors emerged to suggest an intervention worth evaluating. The first was that guidelines for the referral and management of familial cancers were being developed by an

expert group of clinicians on behalf of the then Scottish Home and Health Department [now the Scottish Executive Health Department (SEHD)], independently of this study. These guidelines were to be disseminated in paper form to all GPs in Scotland. In their final form, these guidelines were relatively complex for non-specialists to understand and operationalise in routine practice.[38] The second factor was that a major information technology initiative by the SEHD to equip each general practice in Scotland with standard hardware and software was in the advanced stages of planning.[39] Together, these provided an opportunity to develop a user-friendly, computer-based version of the guidelines for use in primary care. The third factor lay with the subject itself: genetics represents an area where medical knowledge has changed dramatically and, for most GPs, this means genuinely new learning. This suggested that the intervention should be implemented within an educational context, so that recipients would understand the rationale for the guidelines, and be more confident in their own decisions and their ability to advise their patients. Thus, a computer guideline system with a concurrent educational component was evaluated in this study.

Aims and objectives

The aims of this component of the study were:

- to evaluate the benefits and costs of the intervention, in terms of improvements in the referral process and in patient information
- to examine factors influencing the successful implementation of such a system within the practice setting.

The specific objectives were to compare, in practices offered the intervention and in control practices:

- the appropriateness of referrals for familial breast cancer risk assessment and counselling
- the extent to which referred patients were well informed
- the usefulness of referral letters and completeness of family history information
- the usefulness and acceptability of the intervention within the general practice setting
- the ease of use of the software.

Chapter 3

Primary care intervention: methods

Intervention

Development

The aim of the active intervention was to help GPs:

- to make informed decisions about the management of women concerned about their genetic risk of breast cancer (including the decision of whether or not to refer)
- to understand the underlying rationale for the referral guidelines
- to feel more confident about the advice they gave to patients.

As originally conceived, this intervention was to comprise an educational session plus software for GPs and/or their nominated practice staff (e.g. practice nurses). The educational session would cover essential background on cancer genetics and GPs would be instructed how to use a commercially available genetics software application, Cyrillic™ (version 2,1; Oxford: Cherwell Scientific, 1997; supplied to them free of charge) to calculate a patient's provisional genetic risk. They could then compare this risk with the Scottish clinical guidelines and make an informed decision about further management. However, during early testing of the software with volunteer GPs, it became apparent that it was unsuitable for use in primary care, and that a simpler, more GP-orientated package would be more likely to be used. Therefore, we developed an application in-house, with input from clinical geneticists and GPs.

The software was made available in a CD-ROM format (Appendix 1) and contained the following elements:

- a referral guide based on the Scottish referral guidelines for breast, ovarian and colorectal cancer; the format for this guide was a short preamble describing the specific family history information that would be required to use the guide, followed by a set of short checklists; the specific referral guidance generated depended on which boxes were ticked
- background information on the genetic basis of these cancers for health professionals, including the rationale underlying the referral guidelines
- printable, locally relevant information sheets, one set for patients being referred and another for those who did not meet referral criteria
- direct download of data from the referral guide into the Scottish electronic referral document, for those GPs who wished to use this facility
- useful weblinks for professionals and patients
- a direct e-mail link to enable GPs to contact the Cancer Genetics Service (CGS) directly for advice. GPs were encouraged to submit queries, without individual patient-identifying data, with a guaranteed response time of 3 working days from a genetic counsellor or clinical geneticist.

All GPs in the intervention practices were invited to an educational session on cancer genetics and a demonstration of the software. The educational session was promoted by the local postgraduate medical centre and was accredited with Postgraduate Education Allowance (PGEA) points. Medical staff from the Genetics Department at Aberdeen Royal Infirmary managed the session. In parallel, all intervention practices were provided with a copy of the software, by a visit from a technician from the local primary care trust's information technology (IT) department who installed the software directly, by a visit from a member of the research team who installed the software directly and ran a short demonstration, or mailed through the post. This was followed by letter from the Head of the Regional Genetics Service (NEH) to each individual GP in the intervention group. The letter described the CGS and the software, and reminded the recipient that his or her practice had recently received it; enclosed with the letter was a short guide to the software's installation and use. GPs who attended the education session were provided with extra copies of the software. A helpline number was provided for those experiencing technical difficulties.

GPs were encouraged to use the software for prior assessment of possible referrals to the cancer genetic service. It was envisaged that the package would allow them to give rapid advice (and often reassurance) to patients, to include more extensive and useful information in their referral letters than would otherwise be the case, and to avert

some referrals of low-risk women. It was made explicit that all referrals to the genetics service would be accepted irrespective of whether or not the software had been used.

In summary, the intervention had three main components:

- the educational session, including all written materials distributed for GPs' own use
- the software
- the e-mail-based link with the cancer genetics clinic, with its guaranteed response time.

Evaluation

Design

The intervention was evaluated using a cluster randomised controlled trial (RCT) design, in which the level of allocation was the general practice. Baseline and follow-up process and outcome data were collected from both GPs and patients. A cluster randomised design was adopted to avoid potential contamination between intervention groups, which was likely to occur if individual patients had been randomised within participating general practices.

Study setting and participants

The study was based in the Grampian Health Board area in the north-east of Scotland. All practices in the area were eligible for inclusion. Patients were eligible for inclusion if they were referred for breast cancer genetics counselling in the defined preintervention or postintervention periods.

Control intervention

Practices in the control group were not offered any specific intervention. At the time of the evaluation the Scottish cancer genetics referral guidelines (those presented in the intervention software) were disseminated by the Scottish Executive by mail to all GPs throughout Scotland.

Allocation

Practices were allocated randomly to intervention or control groups. A statistician (JM) constructed a computer file of all practices in Grampian, ordered by location and number of referrals to the CGS in the previous year. Practices were allocated systematically (one control followed by two interventions), starting at a practice in the list selected using a random number table. Two practices that included GPs involved in the design and management of the study and the development of the study intervention were excluded from the randomisation. All of the remaining 86 GP practices in Grampian were stratified by number of referrals to the CGS in the previous year and by urban or rural practice location, and randomised in a 2:1 intervention:control ratio. Different practices occupying the same premises were allocated to the same arm of the trial to avoid potential contamination.

Outcomes

GP confidence

GP confidence in managing patients presenting with concerns about their genetic risk of breast cancer was chosen as the primary outcome, for the reasons outlined in the rationale. It was assessed by responses to the following items in a self-completion questionnaire (self-reported confidence, on a four-point scale: not at all, a little, moderately, very confident):

- taking a family history
- knowing which patients need to be referred to clinical genetics
- reassuring low-risk patients
- being able to answer patients' questions about breast cancer genetics.

Referral patterns

Referral patterns were assessed in two ways: by the number of referrals for breast cancer genetic counselling, and by the proportions of referred patients falling into the categories of elevated (high or moderate) and population risk. The number of referrals was calculated from routine data collated by the Medical Genetics Department at Grampian University Hospital Trust (GUHT). Risk was examined in two ways: the initial risk assessed on the basis of the referral letters, and the final risk attributed following the patient's attendance at the clinic.

Referred patients' risk perceptions and knowledge

Patients' self-perceptions of genetic risk were assessed using a self-completion questionnaire (see Appendix 2) in which respondents were asked to rate their own perceived risk in two ways, against a notional 'average' woman, and on a scale. Knowledge was assessed by patients' responses to a set of questions on the causes of breast cancer. GPs and specialists alike are concerned with the holistic management of patients, so the questions were not limited to genetic issues. The topics matched the areas that the consultant geneticists reported covering during genetic counselling sessions with

patients, although the risk advice was tailored to the individual patient; in three of the five questions a standard 'correct' answer exists (stress, having a relative with cancer, minor injury).

Completeness of family history information in referral letters

The completeness of family history information was assessed by scrutiny of anonymised copies of the referral letters relating to all patients identified as having been referred to the CGS by one of the participating GPs in the preintervention and postintervention phases. Referral letters are routinely reviewed by the CGS and a provisional patient risk is assigned based on the content. A referral letter was considered 'adequate' if there was sufficient information to allow a provisional risk to be assigned, allowance being given where the family history or clinical situation was more complex than usual.

Dissemination and implementation of the intervention

This was assessed by calculating the proportion of invited GPs who actually attended an educational session and the proportion of intervention practices that they represented. Implementation GPs' awareness was assessed by responses to a question in a self-completion questionnaire.

Use of the software

This was assessed by GPs' responses to a set of questions presented in a self-completion questionnaire.

Other data relevant to the potential wider implementation of the intervention

A questionnaire for GPs was developed to cover the following areas of interest:

- perceptions of patient demand for cancer genetics counselling
- relationship with the CGS
- attitudes towards the use of computers in routine general practice
- level of use of computers in routine practice.

Data collection

To accommodate the three educational sessions and the roll-out of the software, the implementation of the intervention took place over an 8-month period (1 November 2000 to 30 June 2001). Data collection for the postintervention period started on 1 July 2001, after the intervention had been rolled out to all practices.

General practitioners

A questionnaire was developed and piloted in the two Grampian practices that were later excluded from the main trial. After minor amendments it was mailed to all GPs before implementing the intervention, and at the end of the intervention period, 1 year later. The two questionnaires were identical, except for the inclusion of questions specific to the study software in the follow-up questionnaire for GPs in intervention practices.

Referrals

Retrospective data on referrals from intervention and control practices were assembled for the period 1 January 2000 to 31 October 2000. The CGS database was established in January 2000 and constitutes the available patient referral data for the preintervention period. Identical data were collected for the period 1 July 2001 to 30 June 2002 to represent the postintervention period. The CGS administrative staff maintained and updated the database as a routine activity independent of the study, and extracted the data blind to intervention status.

Total numbers of referrals by practice were obtained from the CGS database. The database manager provided the study team with information on study patients' provisional genetic risk of breast cancer, as assessed from the referral letter by the clinical geneticists before the clinic appointment. This was a routine CGS activity and was performed independent of the study.

Patients

Patients referred to the CGS from the study general practices and subsequently recruited to the nurse counsellor trial (see Chapters 7–11) completed precounselling questionnaires incorporating a set of questions regarding knowledge of the causes of breast cancer, including genetic predisposition and risk perception. The nurse counsellor trial began before the primary care trial, so to maximise the sample size for the preintervention period, questionnaire data were included on all eligible patients referred between 31 May 1998 and 31 October 2000. Postintervention patient data were available for the period following implementation of the intervention 1 July 2001 to 31 May 2002.

Sample size

The total possible sample size was limited to the number of practices operating independently or from shared premises in Grampian (88 practices).

Assuming 70% participation by practices, based on previous intervention studies in Grampian, the total achievable sample size was considered to be 60–65 practices. A decision was made a priori to include as many practices as possible, and randomise 2:1 intervention:control so that a relatively large number of GPs tried out the intervention. An upper limit was therefore placed on the sample size by practical constraints. The primary outcome measure was GP confidence in managing patients concerned about breast cancer genetic risk. This was measured by the proportion of GPs responding to the relevant questionnaire item as being 'moderately' or 'very' confident in making referral decisions. As GP responses are clustered within practices, an estimate of the intrapractice correlation coefficient was obtained from the preintervention survey. Using the observed intrapractice correlation of 0.05 and an average number of GPs per practice of four, 69 practices (46 intervention, 23 control) were required to have 80% power of detecting a difference of 20% in GPs' confidence in making referral decisions (e.g. a shift from 40% to 60% 'moderately' or 'very' confident).[40]

Statistical analysis

Categorical variables were analysed using the χ^2 test. When categories were ordered a χ^2 test for trend was adopted. Relative risks (RRs) were calculated for patient risk and 95% confidence intervals (CIs) computed using the Confidence Interval Analysis program.[41] All *p*-values are from two-sided tests.

Although the unit of randomisation was the general practice, the effectiveness of the intervention was based on data collected from GPs and women. The clustering of observations (patients and GPs) within practices should be accounted for in the analysis of cluster randomised trials.[42] Therefore, additional analyses were conducted to account for clustering in the primary outcomes (GP confidence and risk). Intracluster correlation coefficients (ICC) were estimated using the analysis of variance approach[43] and *p*-values adjusted using the group specific adjusted χ^2.[44] For questions relating to GP confidence, the four categories were dichotomised ('not at all/a little' as opposed to 'moderately/very') in the analysis adjusted for clustering. Where the observed ICC for GP confidence (dichotomised variable) was greater than zero, the *p*-values and 95% confidence intervals have been adjusted for clustering. Since the number of patients per practice (i.e. per cluster) was small, analyses of the secondary outcomes have not been adjusted for clustering.

Ethics

Approval for the study was obtained from the Joint Ethics Committee of the University of Aberdeen and Grampian Health Board, and from the general practice subcommittee of Grampian Health Board. Before the trial, all GPs who had previously referred to the CGS were circulated information about the study. The Caldicott Guardian was informed and patient consent was obtained from each referred patient who fulfilled eligibility criteria.

Chapter 4

Primary care intervention: results

There are two populations of interest in the following analyses: GPs in the intervention (n=230) and control groups (n=116) and the patients referred by them to the CGS for breast cancer genetic counselling in the defined preintervention and postintervention periods.

Study participants

All practices in the Grampian area (n=88) were randomised, with the exception of two practices whose GPs (n=17) were involved in the pilot study. Fifty-seven practices (230 GPs) were randomised to the intervention group and 29 practices (116 GPs) to the control group. Characteristics of the practices are shown in *Table 1*.

Personal computer use in clinical practice

Figures 1 and *2* summarise patterns of use of, and attitudes towards using, computers in clinical practice. In the preintervention period, and before the study allocation was known, around half of all respondents described themselves as 'enthusiastic users' of computers in practice, the proportion being higher amongst intervention GPs than control GPs (*Figure 1*). Over half of respondents

TABLE 1 *Characteristics of study population*

GP practices	**Intervention (n = 57)**	**Control (n = 29)**
Urban practice, *n* (%)	20 (35)	12 (41)
No. of GP partners >3, *n* (%)	28 (49)	12 (41)
Two or more referrals to cancer genetics in previous year, *n* (%)	28 (49)	15 (52)
Annual number of referrals per practice in the previous year, median (IQR)	1 (0–3.5)	2 (1.0–2.0)
Individual GPs	**Intervention (n = 230)**	**Control (n = 116)**
Urban practice, *n* (%)	93 (40.4)	49 (42.2)
No. of GP partners >3, *n* (%)	183 (79.6)	90 (77.6)

IQR, interquartile range.

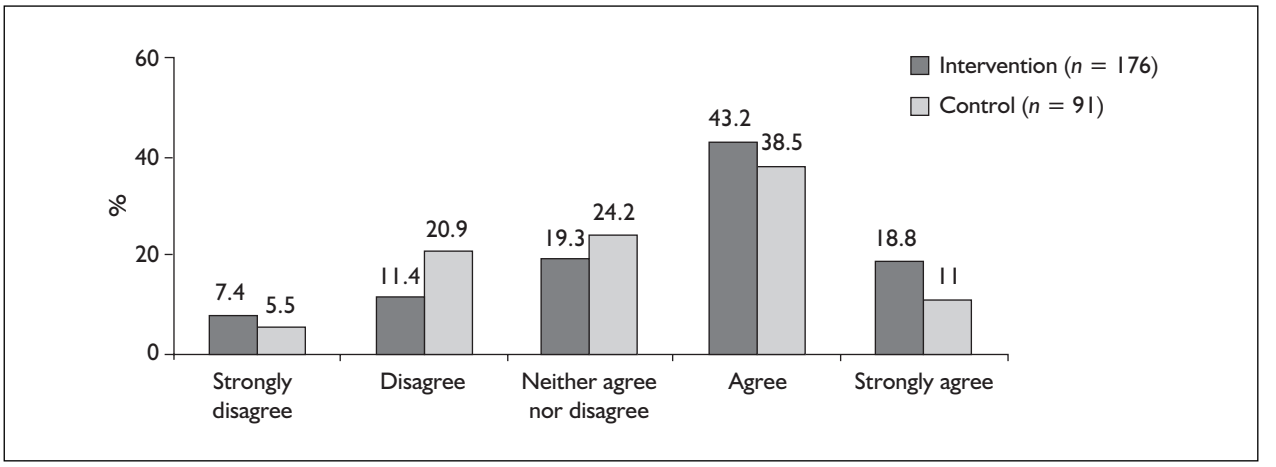

FIGURE 1 *Preintervention responses to the statement:* 'I am an enthusiastic user of computers in my clinical practice'. *Intervention vs control:* p = *0.07 (χ^2 test for trend).*

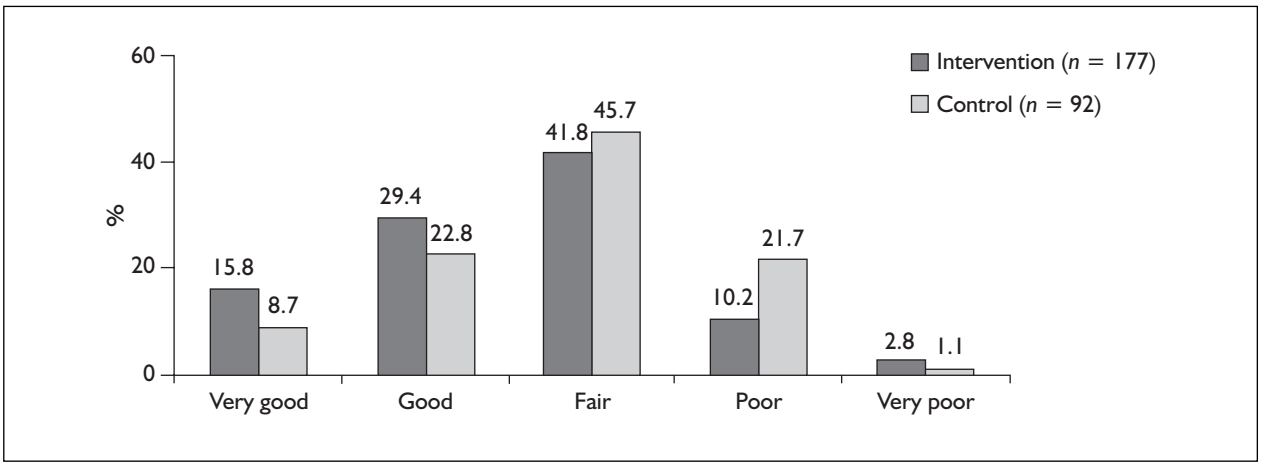

FIGURE 2 *Preintervention self-rating of computer skills. Intervention vs control:* p = *0.02 (χ^2 test for trend).*

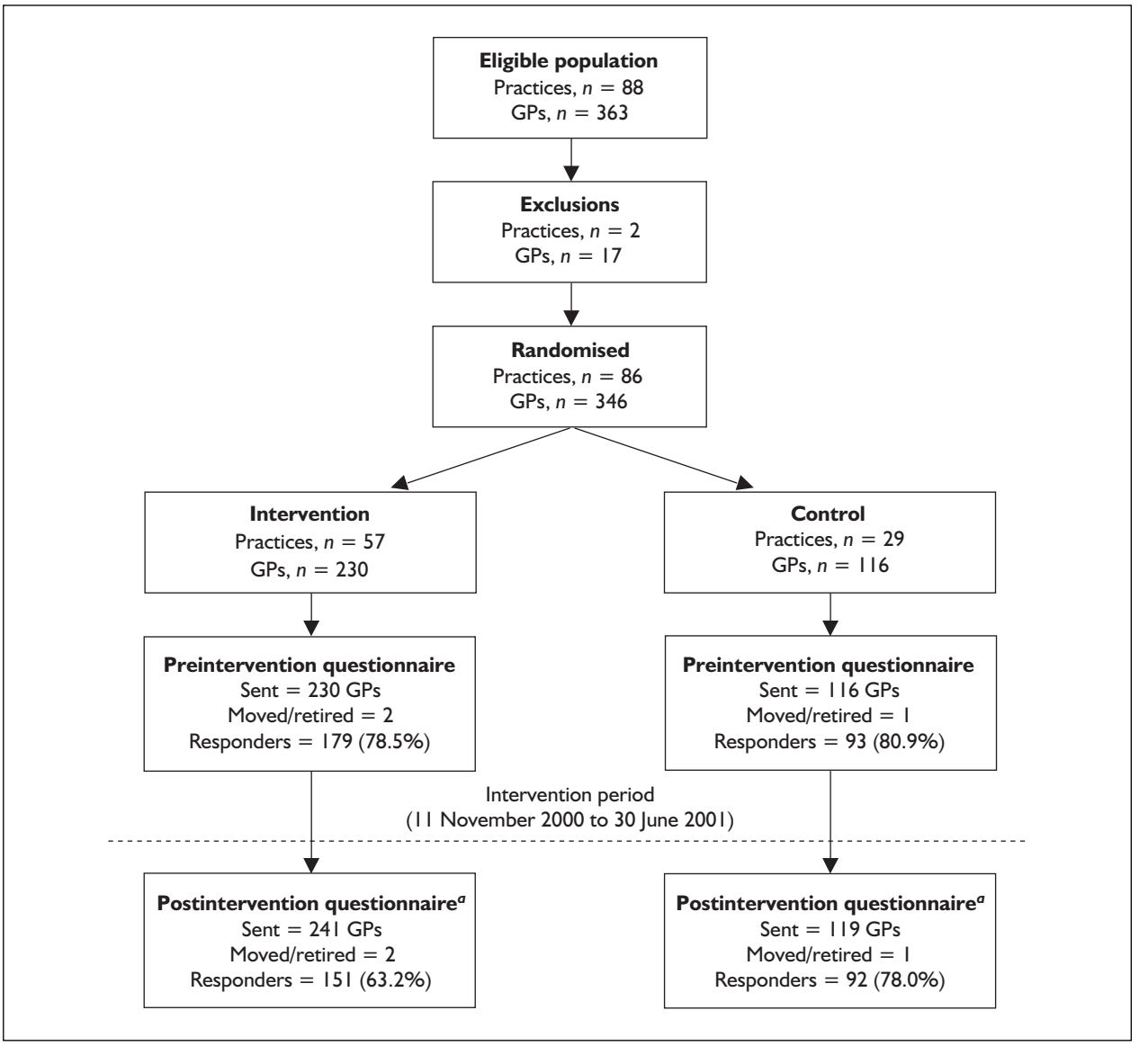

FIGURE 3 *CONSORT diagram: GP data.* [a] *The number of GPs in Grampian Health Board area changed during the trial. The follow-up questionnaire was mailed to all GPs practising in Grampian at the time.*

rated their own computer skills at least 'fair' in the preintervention period (*Figure 2*), with respondents from control practices apparently more confident than those from intervention practices.

The derivation of the data presented for the preintervention and postintervention periods is summarised in *Figures 3* and *4*.

Information from the CGS indicated that a total of 251 referrals was made to their service during the preintervention period, of which 140 (55.8%) were made from practices participating in this study. This compared with a total of 250 referrals in the postintervention period, 145 (58%) from practices participating in this study ($p = 0.61$). The remainder of referrals was made by non-participating practices ($n = 2$) and hospital specialists.

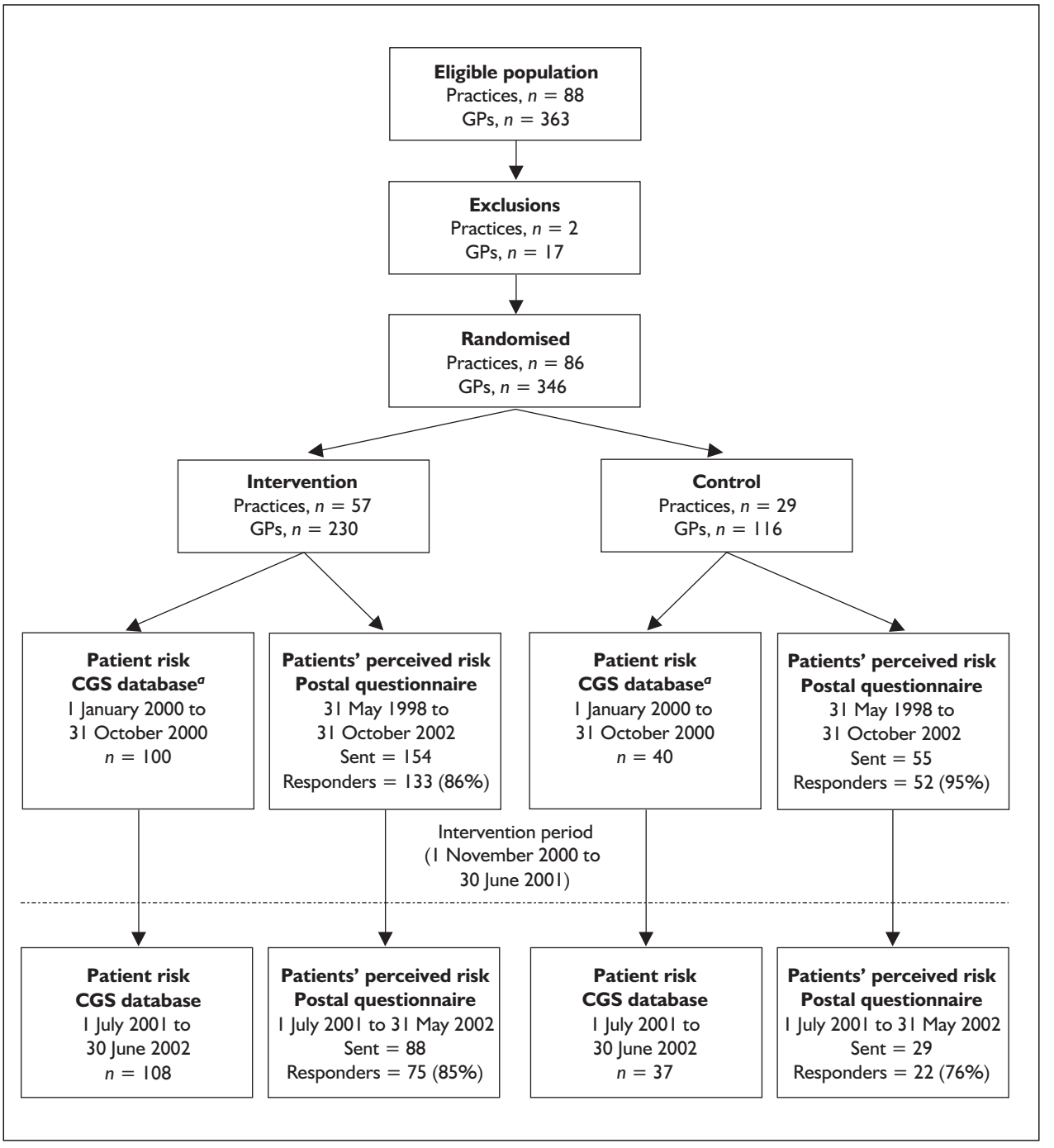

FIGURE 4 *CONSORT diagram: patient data. Flowchart of patient data.* [a] *Database established on 1 January 2000.*

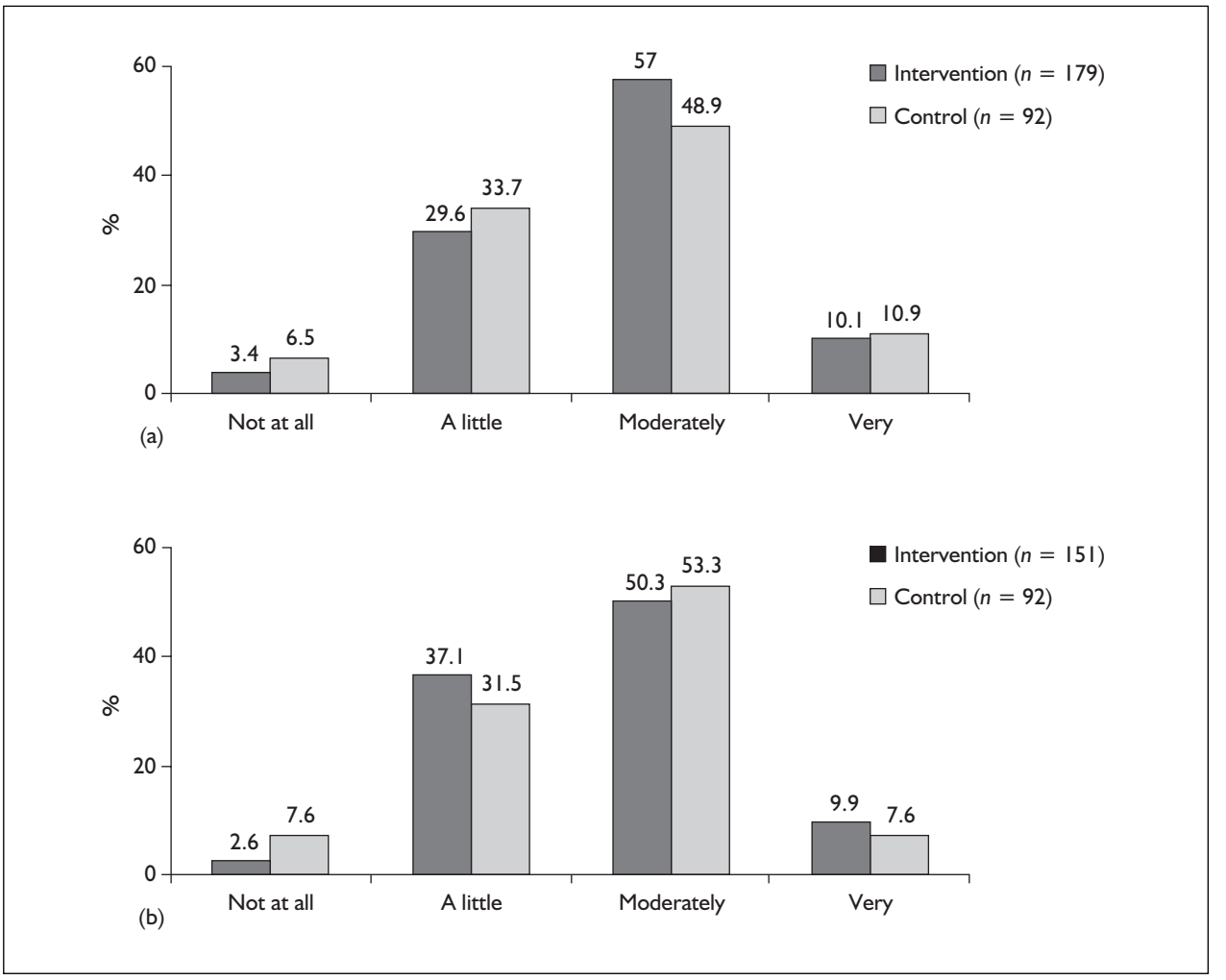

FIGURE 5 *Taking an appropriate family history. (a) Preintervention; (b) postintervention. Intervention vs control: (a)* p = *0.29; (b)* p = *0.56 (χ^2 test for trend).*

Outcomes

Confidence of GPs in management of patients concerned about familial cancer risk

Taken together, the data suggest only small effects of the intervention, at best, on GPs' confidence in their management of patients concerned about familial cancer risk (*Figures 5–8*). In the preintervention period, control and intervention GPs had similar patterns of responses to the four relevant questions. Respondents were most confident about taking an appropriate family history (65% were 'moderately' or 'very' confident) and least confident about answering patients' questions about familial cancer risk (23% 'moderately' or 'very' confident).

In the postintervention period, there was little difference between the intervention and control groups with respect to being 'moderately' or 'very' confident in taking an appropriate family history (60.3% and 60.9%, respectively, 95% CI for difference –12.9 to 12.0%, $p = 0.9$) and being able to answer patients' questions (23.3% and 21.7%, 95% CI for difference –10 to 13.3%, $p = 0.79$). Although the difference was not statistically significant, GPs in the intervention group were more confident at reassuring a patient who is low risk (57% versus 52%, 95% CI for difference –9.0 to 18.6%, $p = 0.49$) and knowing which patients need to be referred to clinical genetics (40% versus 33%, 95% CI for difference –5.4 to 18.9%, $p = 0.3$).

Referral patterns

Number of referrals

In the preintervention phase, intervention practices made 100 referrals (71.4% of all preintervention study population referrals) to the CGS and control practices made 40 referrals. In

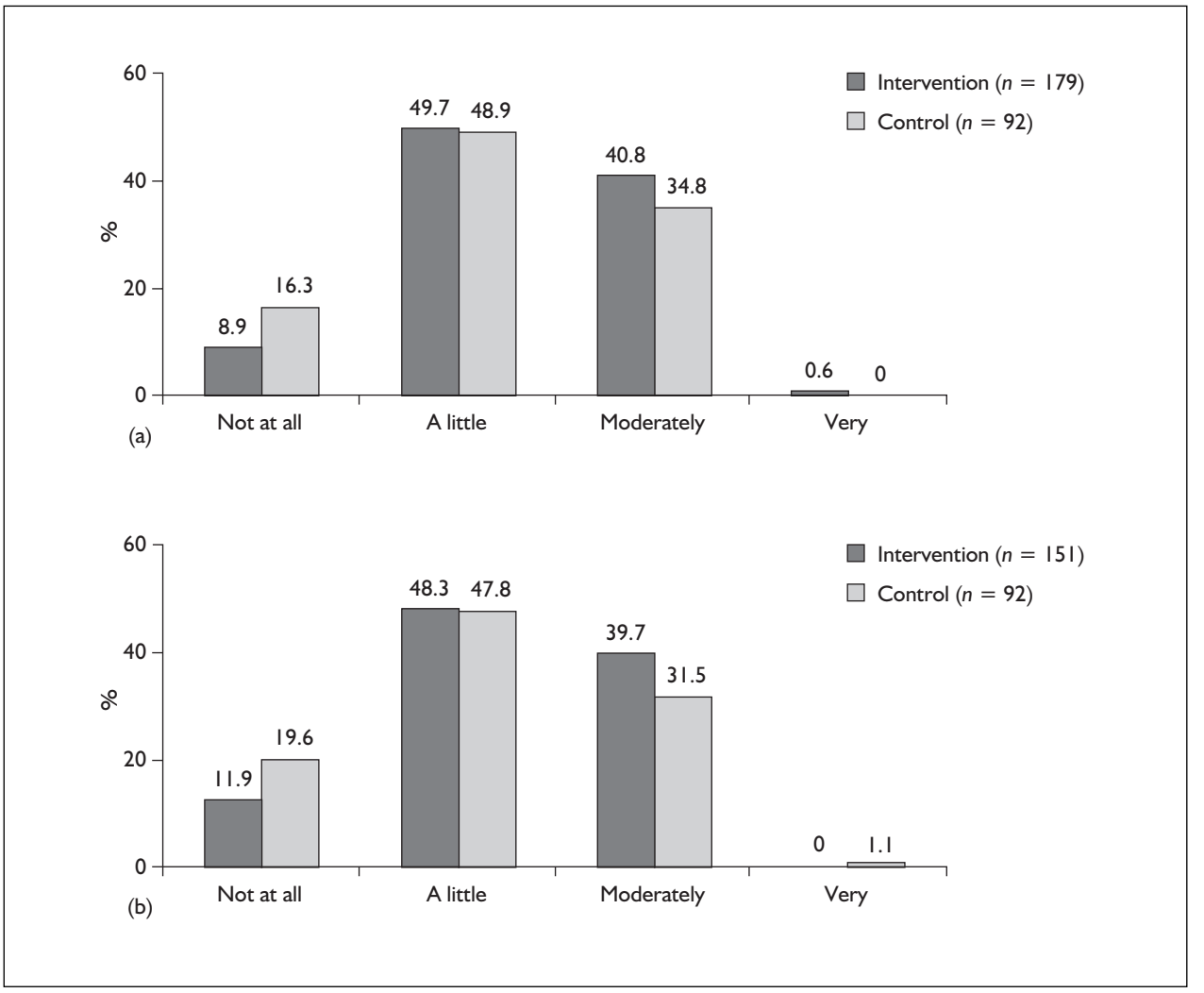

FIGURE 6 *Knowing which patients need to be referred to the CGS. (a) Preintervention; (b) postintervention. Intervention vs control: (a)* p = *0.09; (b)* p = *0.14 (χ^2 test for trend).*

the postintervention phase, intervention practices made 108 referrals (74.5% of all postintervention study population referrals) and control practices 37 referrals ($p = 0.56$).

Risk based on initial referral letter information

In the preintervention period, referral letters from GPs in the intervention practices were less likely to be categorised as elevated (high or moderate) risk than those from control practices (*Table 2*), with the converse being observed in the postintervention period. The differences were not statistically significant in the preintervention or postintervention phase. The intrapractice correlation coefficient was estimated to be 0.009 in the preintervention phase and zero in the postintervention phase. The p-value obtained after adjustment to the χ^2 statistic for clustering was similar to the unadjusted p-value. The comparisons involving control data were based on a small number of referrals in this group, and therefore should be interpreted with caution.

Final clinic risk

In the preintervention period, GPs in intervention practices were less likely than GPs in control practices to refer patients who were eventually assessed as having elevated risk (high or moderate) following assessment at the genetics clinic (*Table 3*). This result was of borderline statistical significance. The converse applied in the postintervention period. For final risk (preintervention and postintervention), no adjustment for clustering was required since the observed intrapractice correlation coefficient was zero.

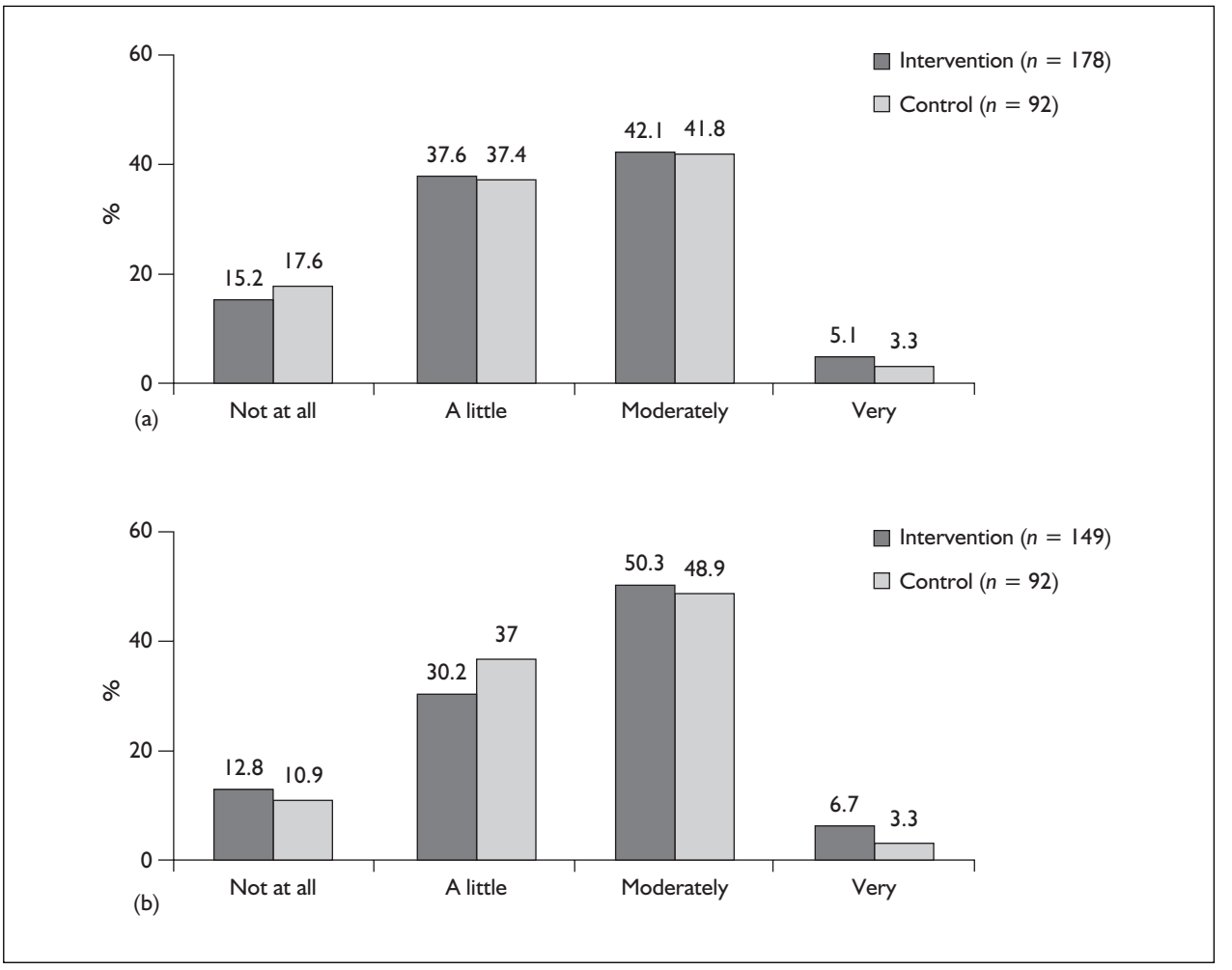

FIGURE 7 *Reassuring a patient who is at low risk according to the guidelines. (a) Preintervention; (b) postintervention. Intervention vs control: (a)* p = *0.54; (b)* p = *0.53 (χ^2 test for trend).*

TABLE 2 *Initial risk assessed on basis of referral letter*

	Intervention *n* (%)	**Control *n* (%)**	**RR (95% CI)**	***p*-Value[b]**
Preintervention period	(*n* = 96)	(*n* = 37)		
Low[a]	43 (44.8)	13 (35.1)		
Elevated	53 (55.2)	24 (64.9)	0.85 (0.63 to 1.15)	0.31 (0.31)[c]
High	5 (5.2)	4 (10.8)		
Moderate	48 (50.0)	20 (54.0)		
Postintervention period	(*n* = 102)	(*n* = 37)		
Low[a]	36 (35.3)	15 (40.5)		
Elevated	66 (64.7)	22 (59.5)	1.09 (0.80 to 1.47)	0.57
High	19 (18.6)	10 (27.0)		
Moderate	47 (46.1)	12 (32.4)		

[a] Reference group.
[b] Pearson χ^2.
[c] Pearson χ^2 adjusted for clustering of patients within practices.

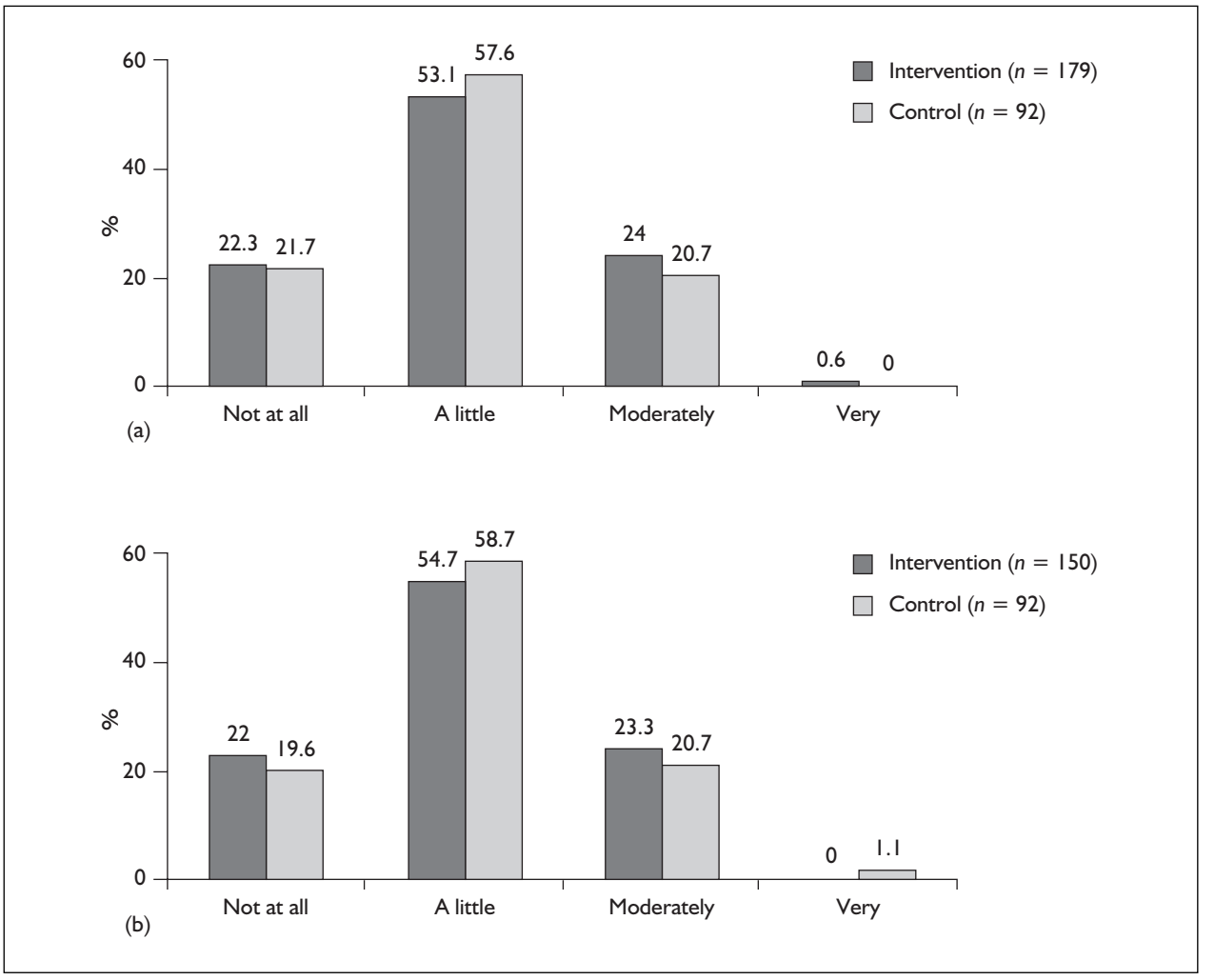

FIGURE 8 *Being able to answer patients' questions about family history and cancer. (a) Preintervention; (b) postintervention. Intervention vs control: (a)* p = *0.66; (b)* p = *0.83 (χ^2 test for trend).*

TABLE 3 *Final risk assessed at clinic*

	Intervention *n* (%)	**Control *n* (%)**	**RR (95% CI)**	***p*-Value[b]**
Preintervention period	(*n* = 88)	(*n* = 34)		
Low[a]	48 (54.5)	12 (35.3)		
Elevated	40 (45.5)	22 (64.7)	0.70 (0.50 to 0.99)	0.06
High	7 (8.0)	7 (20.6)		
Moderate	33 (37.5)	15 (44.1)		
Postintervention period	(*n* = 85)	(*n* = 29)		
Low[a]	36 (42.4)	15 (51.7)		
Elevated	49 (57.7)	14 (48.3)	1.18 (0.88 to 1.37)	0.38
High	14 (16.5)	7 (24.1)		
Moderate	35 (41.2)	7 (24.1)		

[a] Reference group.
[b] Pearson χ^2.

TABLE 4 *Patients' perceived risk*

	Intervention *n* (%)	Control *n* (%)	RR (95% CI)	*p*-Value[b]
Preintervention period	(*n* = 130)	(*n* = 48)		
Low[a]	37 (28.5)	15 (31.3)		
Elevated	93 (71.5)	33 (68.7)	1.04 (0.84 to 1.30)	0.72 (0.73)[c]
High	25 (19.2)	10 (20.8)		
Moderate	68 (52.3)	23 (47.9)		
Postintervention period	(*n* = 62)	(*n* = 18)		
Low[a]	12 (19.4)	4 (22.2)		
Elevated	50 (80.6)	14 (77.8)	1.04 (0.79 to 1.37)	0.79
High	11 (17.7)	2 (11.1)		
Moderate	39 (62.9)	12 (66.7)		

[a] Reference group.
[b] Pearson χ^2.
[c] Pearson χ^2 adjusted for clustering of patients within practices.

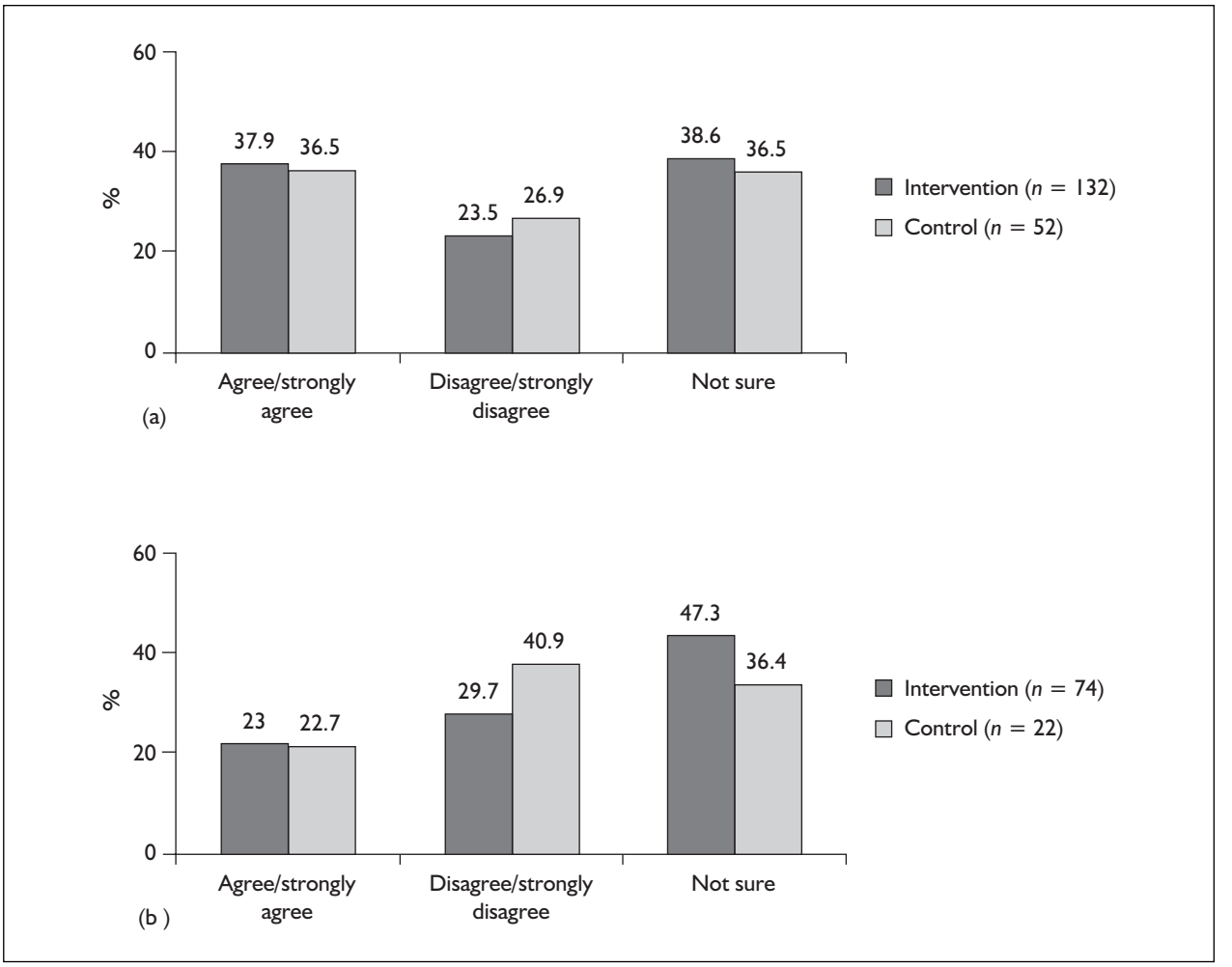

FIGURE 9 *Responses to the statement: 'Stress is a major cause of breast cancer'. (a) Preintervention; (b) postintervention. Intervention vs control: (a)* p = *0.89; (b)* p = *0.57 (χ^2 test for trend).*

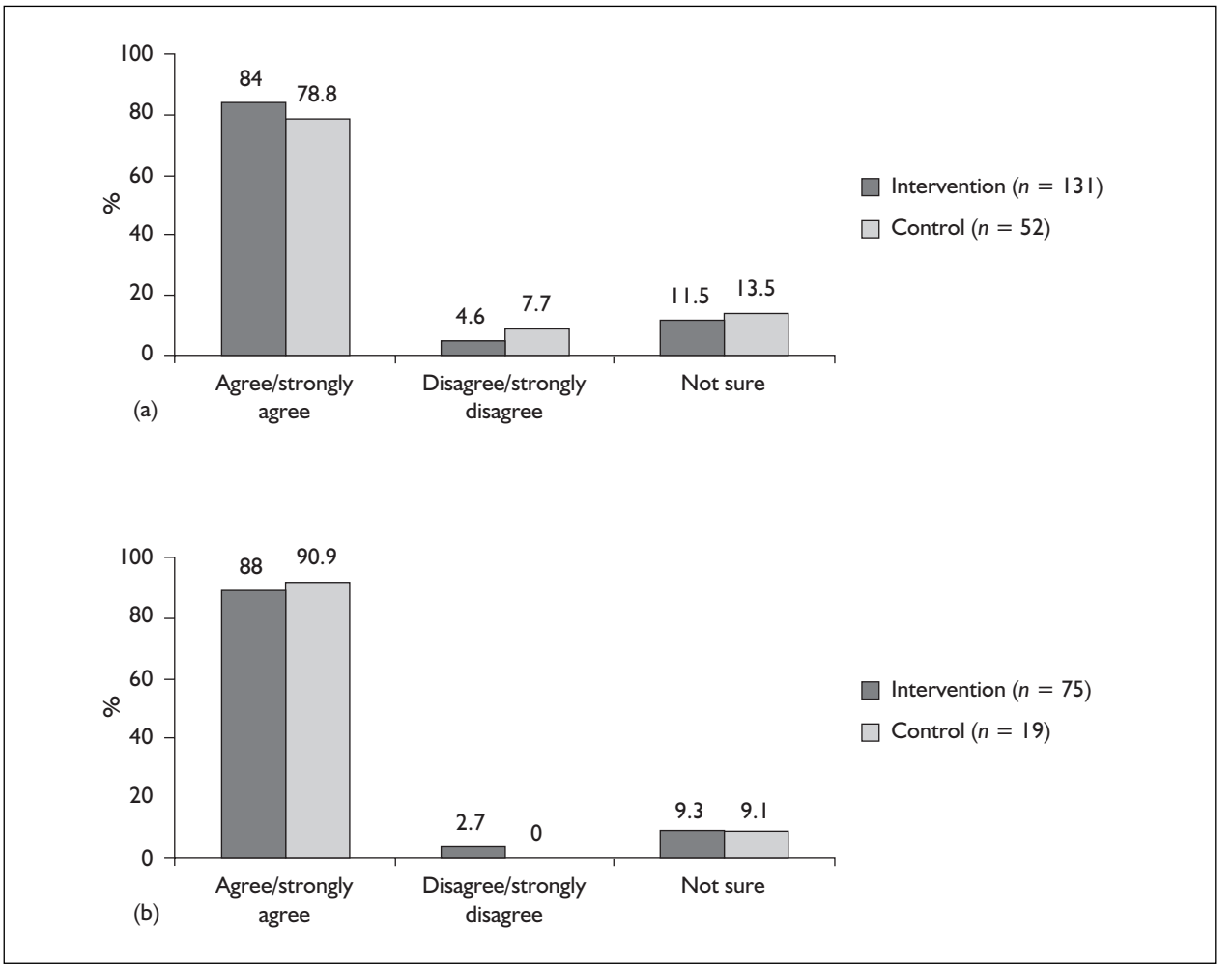

FIGURE 10 *Responses to the statement: 'Having one close relative with breast cancer always increases your risk considerably'. (a) Preintervention; (b) postintervention. Intervention vs control: (a)* p = *0.64; (b)* p = *0.74 (χ^2 test for trend).*

Referred patients' risk perceptions and knowledge

Perceived risk

Table 4 shows the patients' perceptions of their own risk, as assessed by self-completion questionnaire responses. In both the preintervention and postintervention periods, patients in intervention and control groups showed generally similar patterns of perceived risk when compared between groups, with relative risks close to unity. The intrapractice correlations estimated from the preintervention and postintervention data were 0.028 and zero, respectively. Adjustment for clustering had little impact on the *p*-value. Owing to a shorter data collection period in the postintervention phase, the number of referrals was smaller and thus the results should be interpreted cautiously.

Knowledge

Patients' beliefs about the causes of breast cancer, following referral but before the first clinic appointment, are presented in *Figures 9–13*. The 'appropriate' answer for each question depends partly on the advice given by the individual participant's GP, and this was not formally assessed. However, current evidence about breast cancer risk factors was presented in the educational session to intervention practices. If GPs in intervention practices were advising their patients in the same way as counsellors or clinicians in the CGS, and patients were heeding their advice, then the responses would be expected to cluster around 'disagree/strongly disagree' for some risk factors (stress, having one close relative with breast cancer, minor injury) and 'disagree/strongly disagree/not sure' for the other

two. Patients referred in the preintervention period showed generally similar patterns of responses relating to three of the suggested risk factors, but differed significantly in responses relating to diet and minor injury: patients in the intervention group were more likely to view a healthy diet as protective and less likely to perceive minor injury as an important cause of breast cancer. In both groups, a very high proportion (around 80%) was likely to perceive that having one close relative with breast cancer was an indicator of increased personal breast cancer risk.

In patients referred during the postintervention period, changes in the pattern of responses were seen in relation to some risk factor perceptions, but not others. Taken overall, the data do not suggest that the intervention produced an effect on the 'appropriateness' of perceptions among the patients referred by intervention GPs to the cancer genetics clinic. The only risk factor for which the data suggested a shift towards 'appropriate' perceptions was the risk from stress, and the change was observed in both intervention and control groups (*Figure 9*). Perceptions that having a close relative with breast cancer was an important risk factor were the most stable of all, and preintervention and postintervention responses were almost identical in both groups (*Figure 10*). The pattern relating to risk from oral contraceptives (*Figure 12*) was also generally similar, although less marked. In relation to diet (*Figure 11*), shifts were observed away from agreeing that it was an important risk factor in both intervention and control groups, but differences between the groups, as observed in the preintervention period, were still apparent although not statistically significant. In relation to the risk of minor injury to the breast, the preintervention differences between the groups became less marked, mainly because of a shift in the responses of the postintervention control patients.

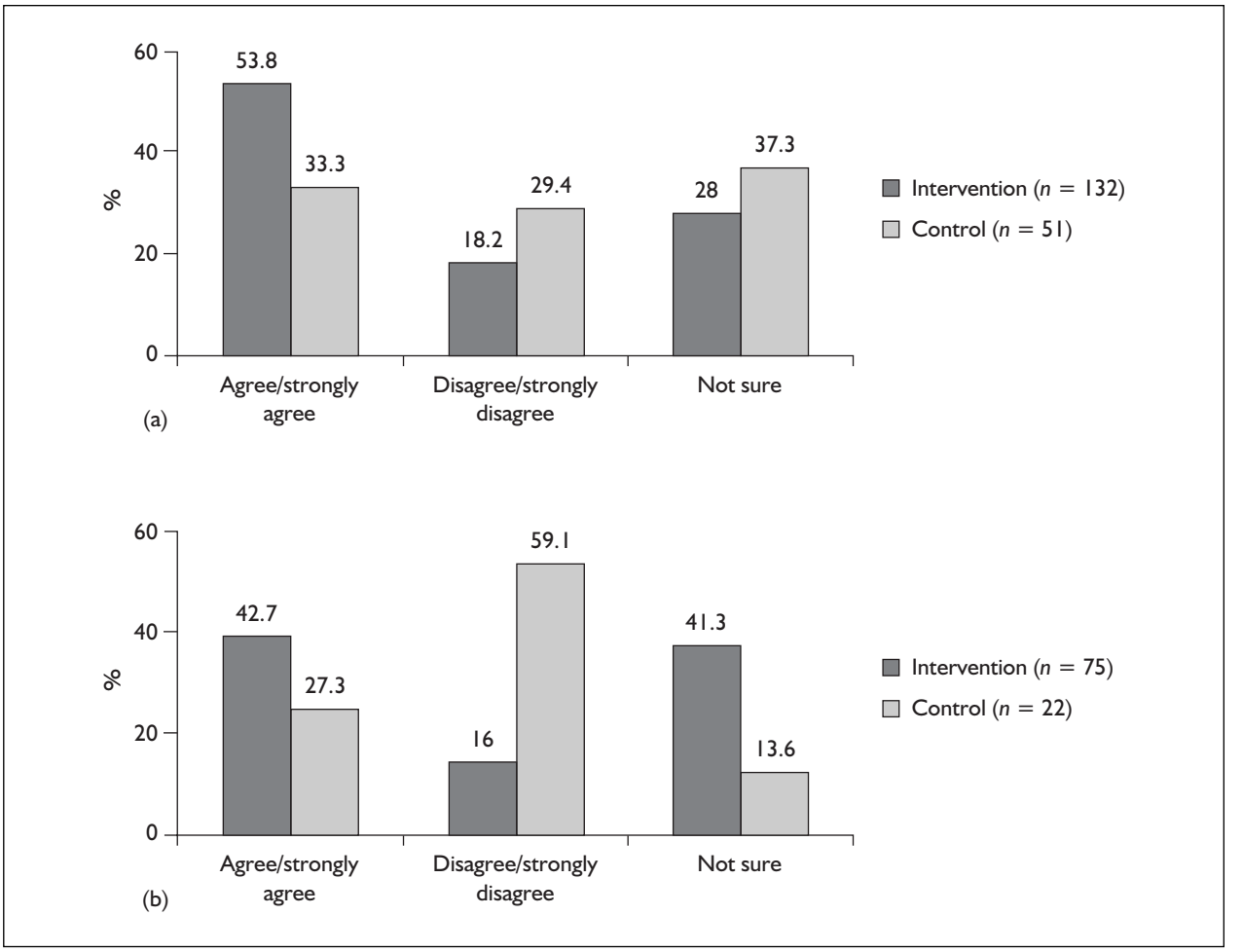

FIGURE 11 *Responses to the statement: 'A healthy diet can prevent breast cancer'. (a) Preintervention; (b) postintervention. Intervention vs control: (a)* p = *0.04; (b)* p = *0.32 (χ^2 test for trend).*

Completeness of family history information

In the preintervention phase, 96 out of 100 (96%) referral letters from intervention practices and 37 out of 40 (92.5%) letters from control practices were sufficiently complete for an initial risk assessment. In the postintervention period the comparable figures were 102 out of 108 (94.4%) for intervention and 37 out of 37 (100%) for control practices.

Dissemination and implementation of the intervention

A total of 27 (11.7%) GPs in intervention practices attended one of the three continuing medical educational sessions. These GPs represented 20 (35.1%) of the eligible GP practices. Of the 151/241 GP respondents in the intervention group, 64 (42.4%) were aware that their practice had the software. Of these 64, 22 (34.4%) had used it at least once. Frequency of use over the previous year ranged from once to six times, with a mean of 2 and a median of 2.6.

Use of the software

Table 5 summarises data on patterns of use among the 22 users. Under half reported using it in most or all patients, and the referral guidelines were the only component used by all respondents. Most respondents had used it with a patient present.

Figure 14 shows preintervention and postintervention data on GPs' usual responses to patients consulting with familial cancer concerns. The preintervention responses were very similar in control and intervention groups ($p = 0.95$). Most GPs suggested that they would make their own assessment before deciding to refer or take other action, and only a small proportion would automatically refer all such patients to a specialist. Postintervention data showed generally similar results and statistically non-significant differences between the groups ($p = 0.31$).

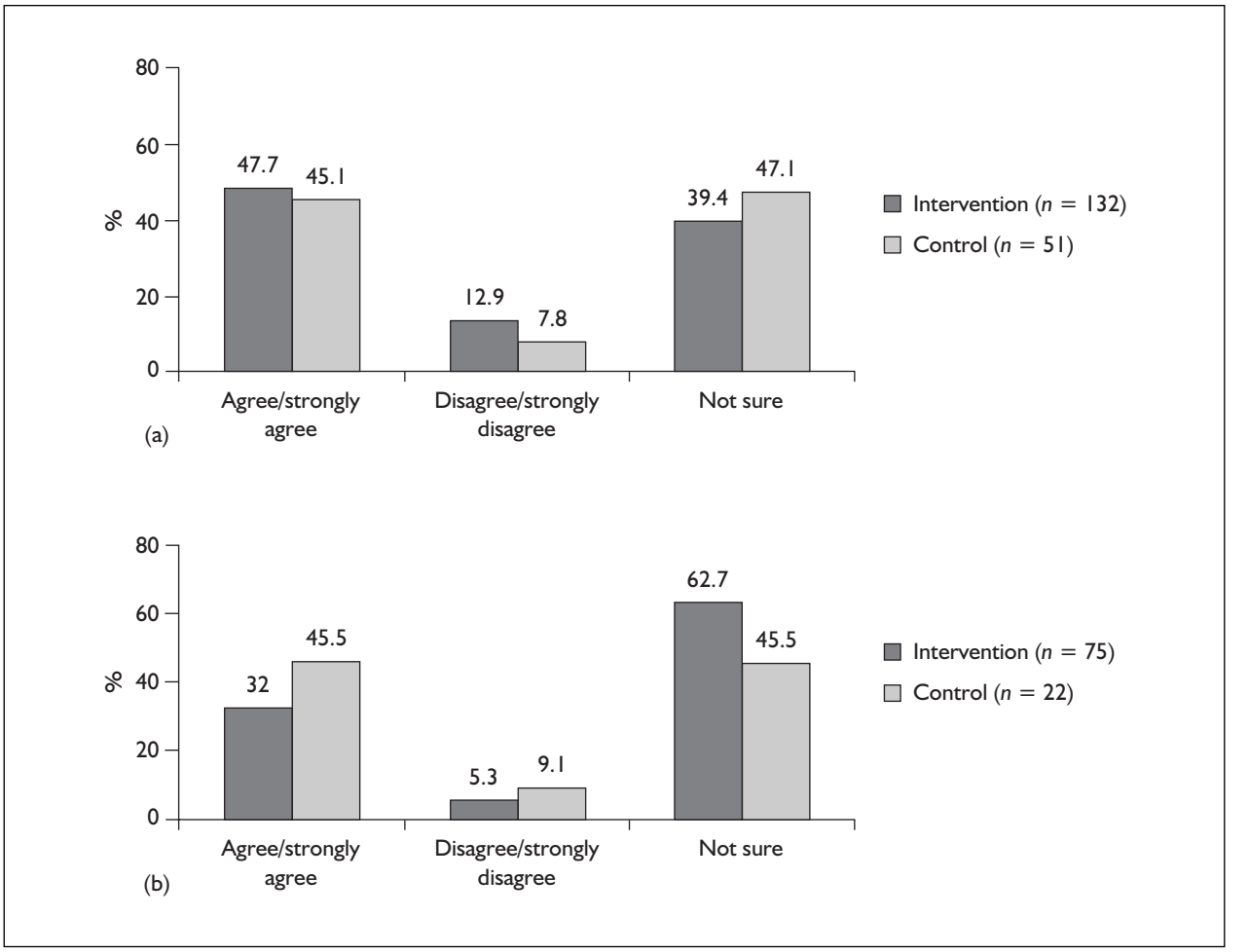

FIGURE 12 *Responses to the statement: 'Oral contraceptives can significantly increase the risk of breast cancer'. (a) Preintervention; (b) postintervention. Intervention vs control: (a)* p = *0.50; (b)* p = *0.35 (χ^2 test for trend).*

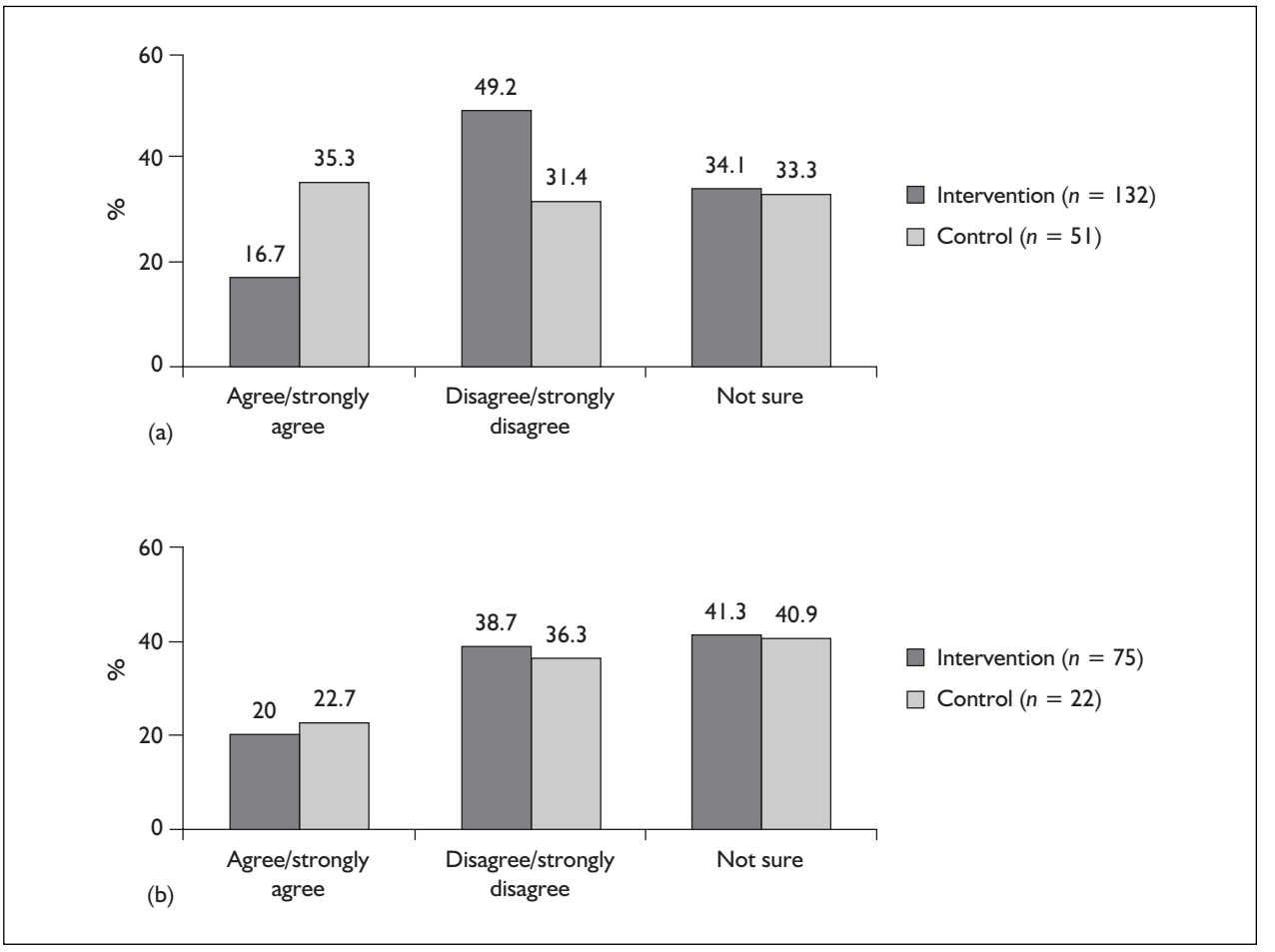

FIGURE 13 *Responses to the statement: 'Minor injury to the breast can cause breast cancer'. (a) Preintervention; (b) postintervention. Intervention vs control: (a)* p = *0.01; (b)* p = *0.96 (χ^2 test for trend).*

TABLE 5 *Pattern of use of intervention software among 22 users*

		n **(%)**
Used in presence of patient	Always	11 (50)
	Sometimes	7 (31.8)
	Never	4 (18.2)
How often software was used in managing patients	All patients	7 (31.8)
	Most patients	3 (13.6)
	Some patients	12 (54.5)
How long per patient consultation (minutes)	< 10	14 (63.8)
	10–20	8 (36.4)
Components used[a]	Referral guidelines	22 (100)
	Patient information leaflets	7 (31.8)
	Background information	7 (31.8)
	E-mail	1 (4.5)
	Weblinks	0

[a] Multiple responses permissible.

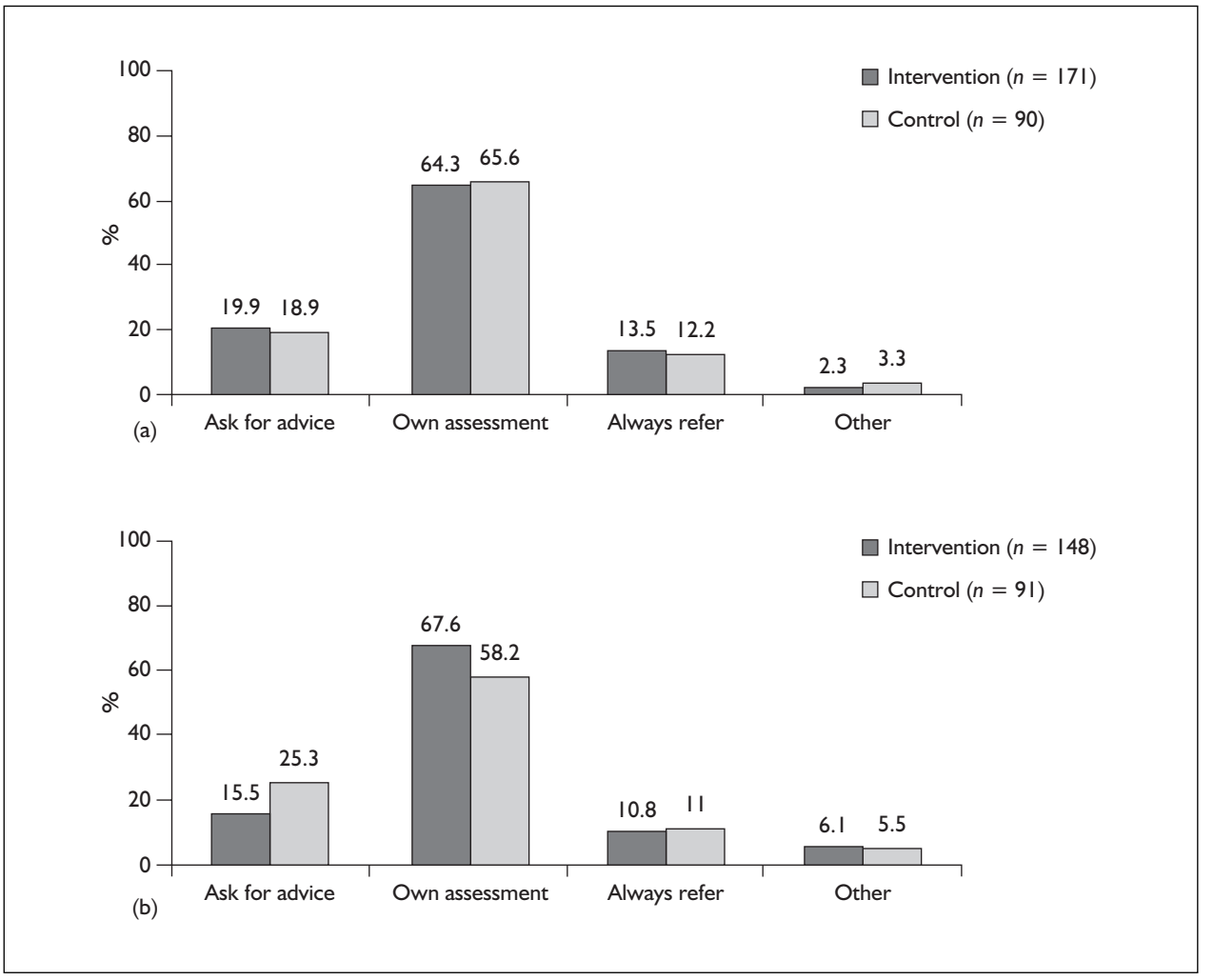

FIGURE 14 *What would you normally do when dealing with a patient who presented with concerns regarding a family history of cancer? (a) Preintervention; (b) postintervention. Intervention vs control: (a)* p = *0.95; (b)* p = *0.31 (χ^2 test for trend).*

Other factors influencing use and usefulness of intervention in practice

GPs were asked which types of interventions they thought would help in the management of patients seeking advice about familial cancer (*Figure 15*). In the preintervention phase, the most popular options were guidelines in some form, educational sessions or easier access to specialist services. Few respondents saw direct access to gene tests as appropriate. In the postintervention phase, the response pattern was very similar, although GPs in the intervention group were more likely to identify computer-based guidelines as helpful than those in the control group, and control GPs were more likely to identify educational sessions as being likely to be helpful.

Relationship with the cancer genetics service

A high proportion of respondents preintervention reported that they had sought the advice of the CGS at least once regarding familial cancer [164/179 (91.6%) respondents from intervention practices, 88/92 (95.7%) respondents from control practices; χ^2 test, $p = 0.53$]. The primary method of seeking advice was by letter (*Table 6*), with a small proportion of respondents reporting telephoning the service for advice. After the intervention, these patterns were almost unchanged. Only one respondent in the intervention group reported using the e-mail service, although records maintained by staff in the CGS indicate that four GPs used the e-mail services during the course of the study.

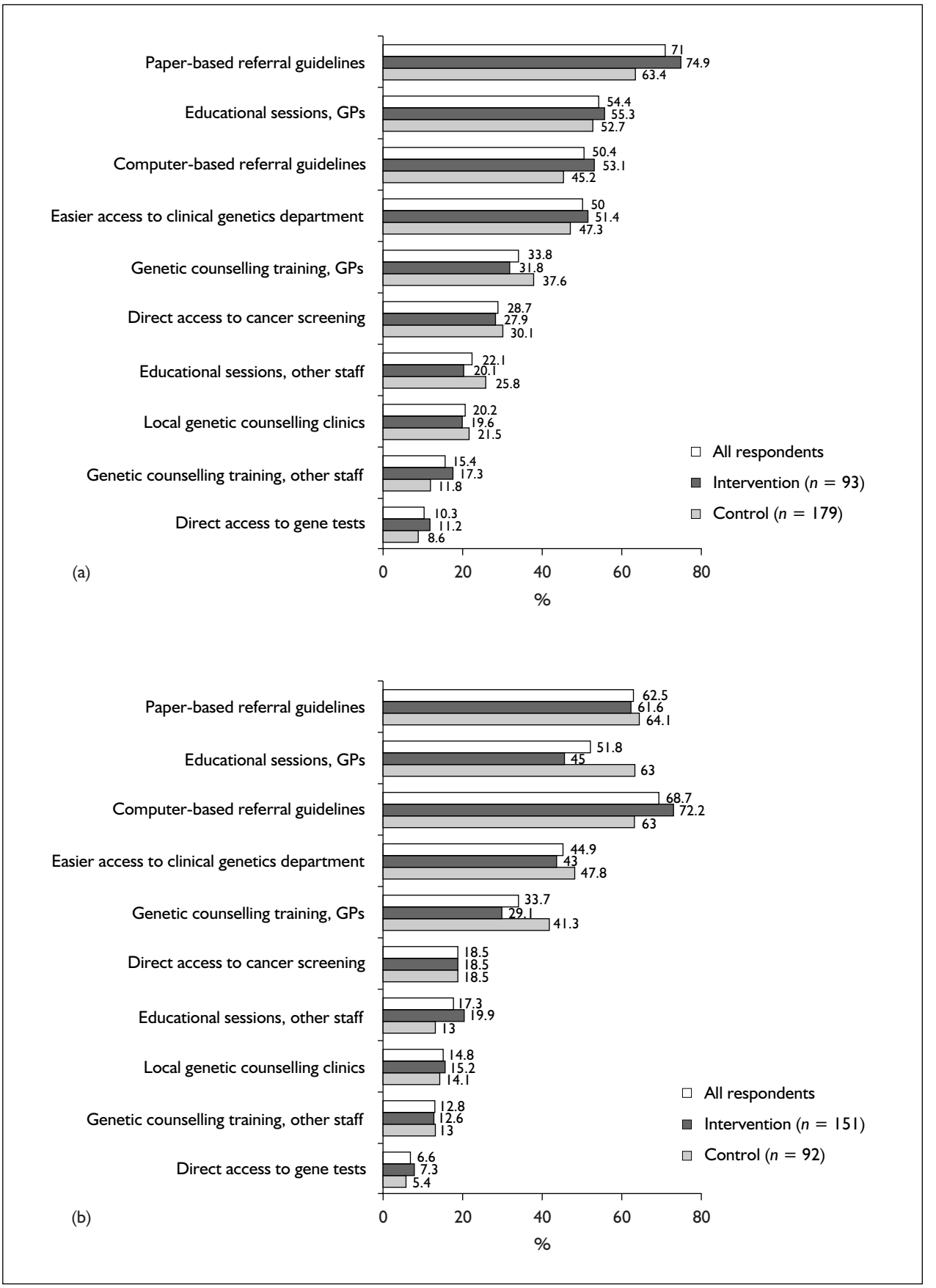

FIGURE 15 *Respondents' suggestions of interventions that would help in the management of patients concerned about familial cancer risk. (a) Preintervention; (b) postintervention.*

TABLE 6 *Method of seeking advice from the CGS*[a]

		Intervention *n* (%)	Control *n* (%)	*p*-Value[b]
Preintervention	*n*	179	93	
	Letter	153 (85.5)	75 (80.6)	0.53
	Telephone	27 (15.1)	18 (19.4)	0.47
	E-mail	N/A	N/A	–
Postintervention	*n*	151	92	
	Letter	133 (88.1)	80 (87.0)	0.95
	Telephone	28 (18.5)	23 (25.0)	0.3
	E-mail	1 (0.7)	0	–

[a] Multiple responses permissible.
[b] χ^2 test.
NA, not applicable.

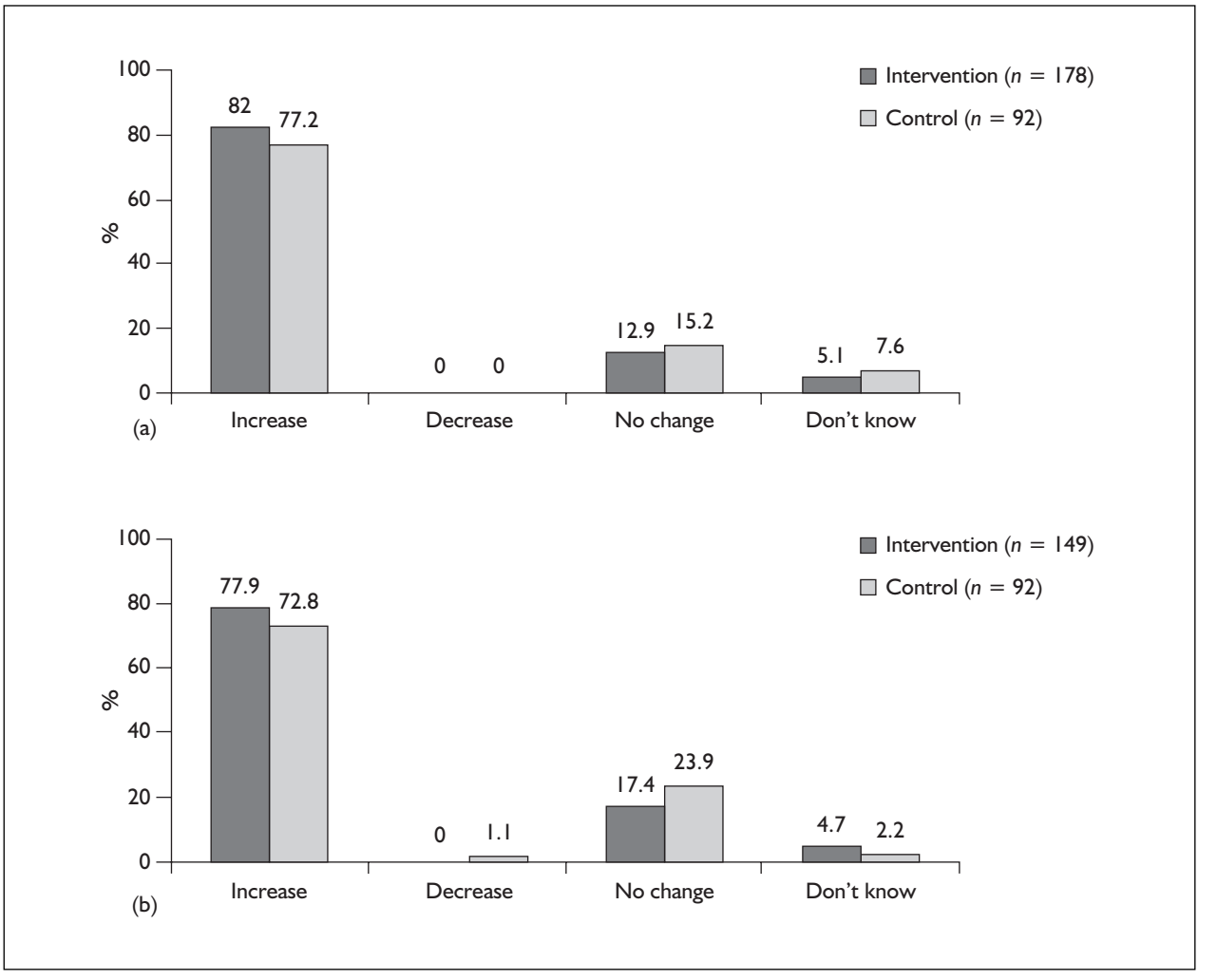

FIGURE 16 *In your opinion, have you noticed a change in the number of patients asking for information regarding family history of cancer in the past 3–5 years? (a) Preintervention; (b) postintervention. Intervention vs control: (a)* p = *0.58; (b)* p = *0.26 (χ^2 test for trend).*

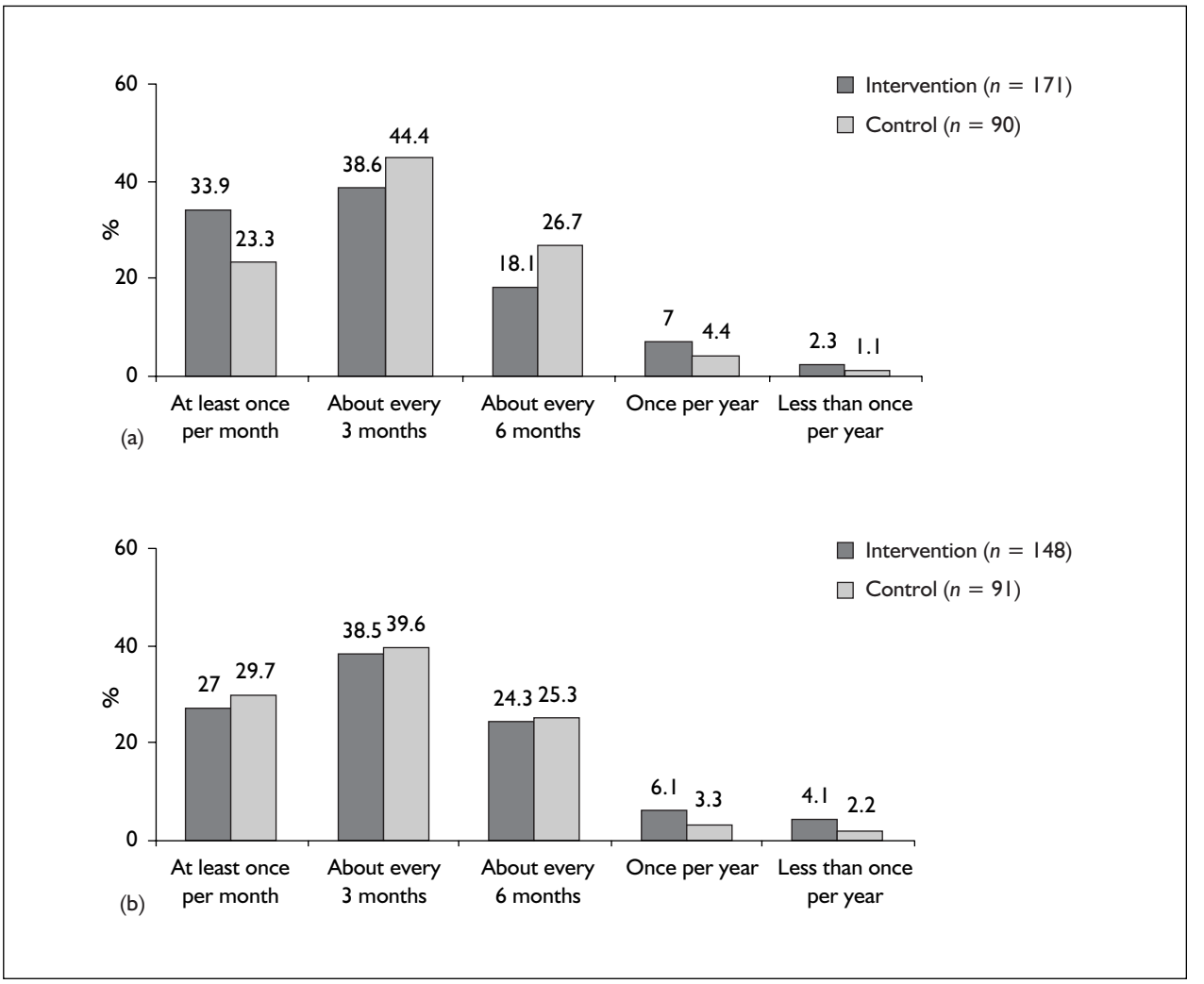

FIGURE 17 *Approximately, how often has the subject of family history of cancer been raised during a patient consultation in the past year? (a) Preintervention; (b) postintervention. Intervention vs control: (a)* p = *0.41; (b)* p = *0.34 (χ^2 test for trend).*

Perceptions of demand for cancer genetics counselling

In the preintervention period, around 80% of respondents reported an increase in the number of patients asking for advice about risk of familial cancer, with similar patterns in control and intervention groups (p = 0.58) and no respondents reporting a decrease (*Figure 16*). Responses in the postintervention period suggest that the perceptions were very stable (intervention versus control p = 0.26). In the preintervention period, the majority of respondents reported a frequency of consultations relating to familial cancer of at least once per 3 months, with intervention GPs more likely than control GPs to report a frequency of at least monthly (*Figure 17*), although the difference was not statistically significant (p = 0.21). In the postintervention period, the perceptions of demand were very similar in the two groups, with 27% and 29.7% of GPs in the intervention and control groups, respectively, reporting at least one patient per month raising the subject of a family history of cancer (95% CI for difference –14.6 to 8.7%).

Personal computer use in clinical practice

Responses to questions regarding personal use of a computer in day-to-day practice indicated a trend towards more frequent use postintervention in most respects (*Figures 18–21*). The activity for which this was most apparent was looking up clinical advice in the presence of a patient (*Figure 19*). The exception was using computers for decision support (e.g. guidelines or protocols) (*Figure 21*), where a statistically significant trend towards less frequent use was observed in both control and intervention groups.

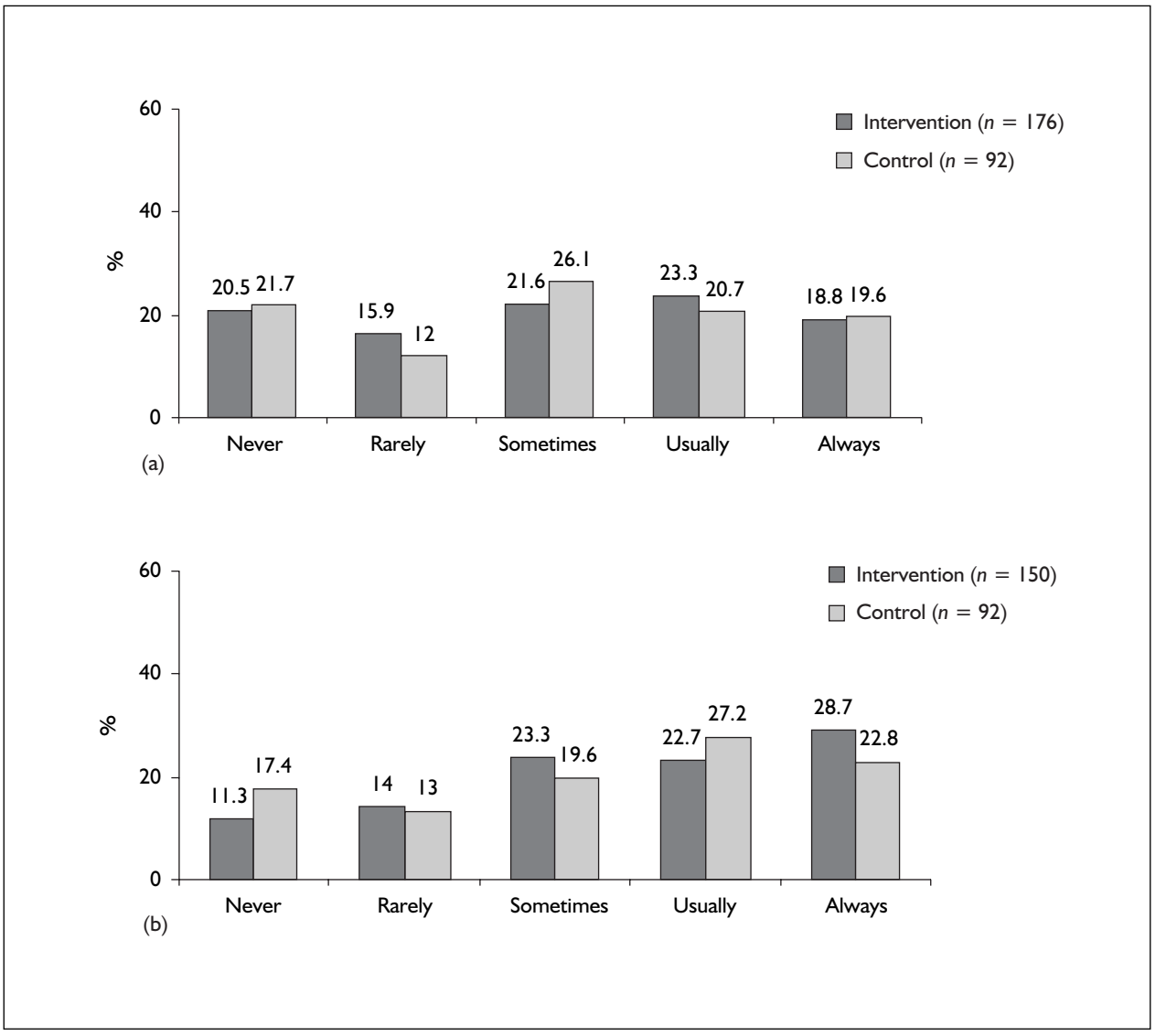

FIGURE 18 *Entering clinical data in the presence of the patient (i.e. during a consultation). (a) Preintervention; (b) postintervention. Intervention vs control: (a)* p = *0.98; (b)* p = *0.31 (χ^2 test for trend).*

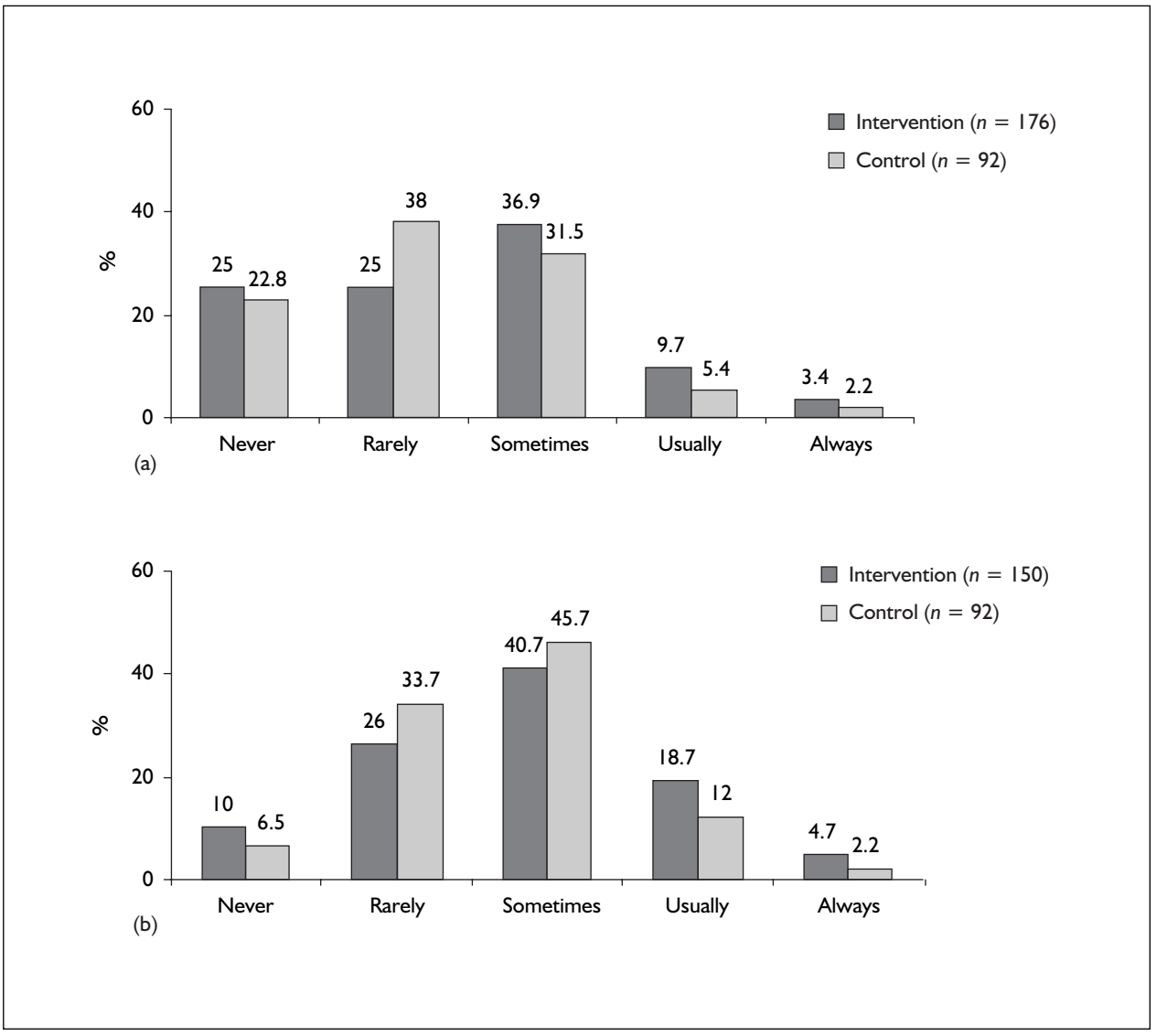

FIGURE 19 *Looking up clinical advice in the presence of the patient (i.e. during a consultation). (a) Preintervention; (b) postintervention. Intervention vs control: (a)* p = *0.25; (b)* p = *0.32 (χ^2 test for trend).*

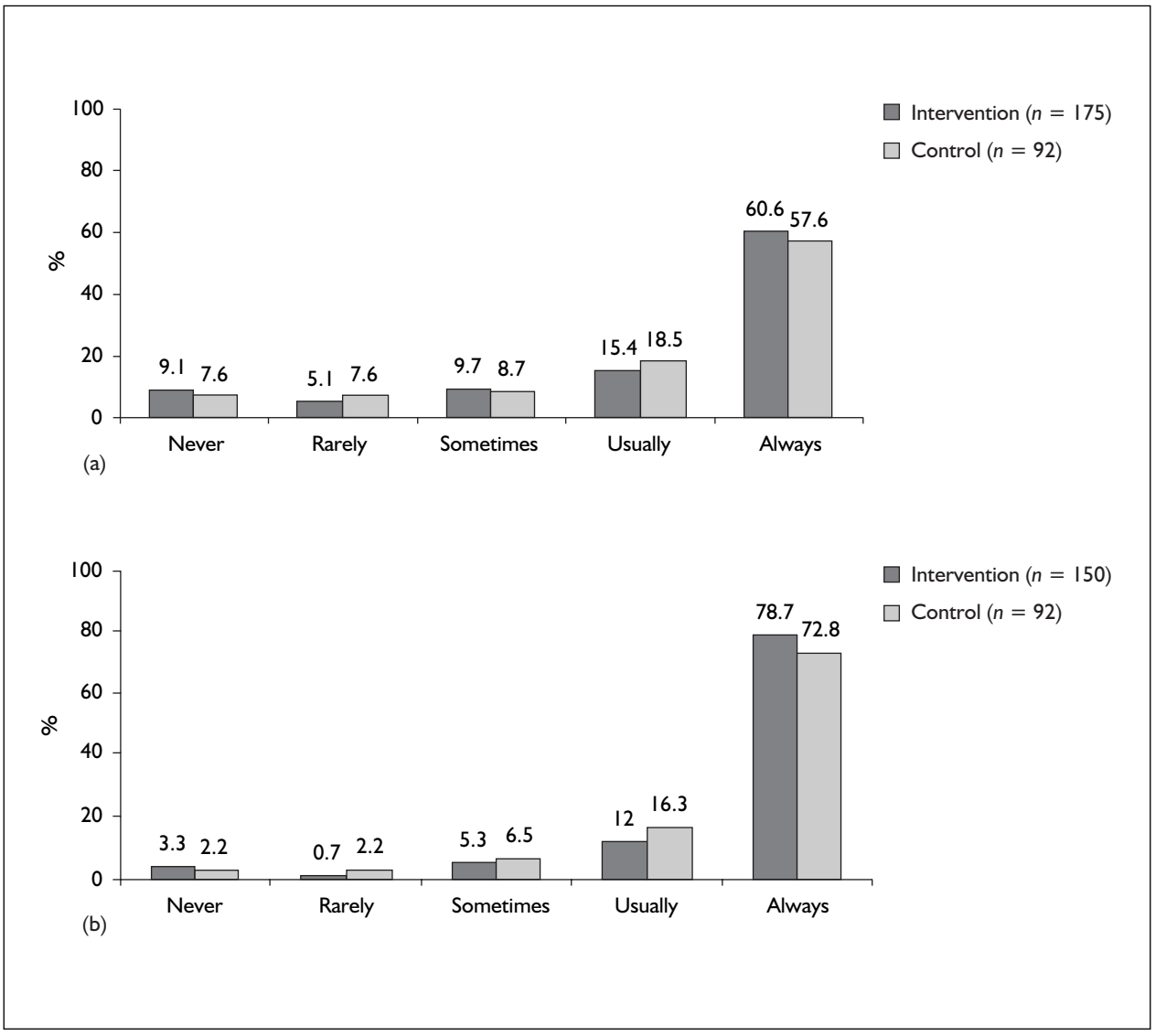

FIGURE 20 *Acute prescribing in the presence of the patient (i.e. during a consultation). (a) Preintervention; (b) postintervention. Intervention vs control: (a)* p = *0.89; (b)* p = *0.58 (χ^2 test for trend).*

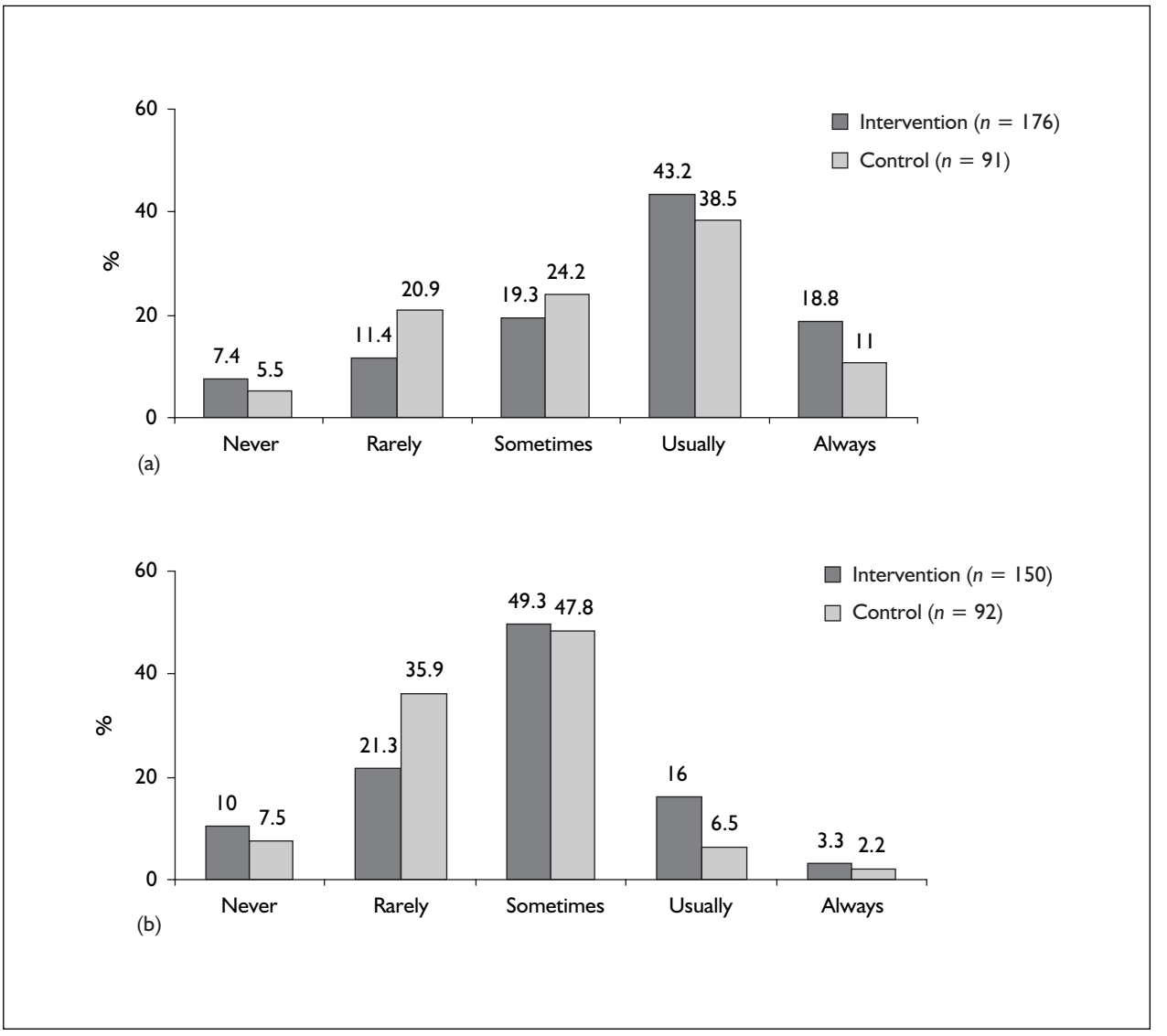

FIGURE 21 *Decision support (e.g. guidelines or protocols). (a) Preintervention; (b) postintervention. Intervention vs control: (a)* p = *0.22; (b)* p = *0.07 (χ^2 test for trend).*

Chapter 5

Primary care intervention: economic evaluation

Introduction

The economic component of the primary care intervention aimed to estimate the costs of the intervention from the perspective of the health service. As such, the objective was to cost three key areas:

- development of the software
- postgraduate education sessions
- use of the software in primary care.

Methods

Development of the software

This involved identifying all resources used to develop the software. Four categories of resource use were examined: staff, consumables, rooms and equipment.

Staff

It was anticipated that the majority of resource use was likely to be staff time. Staff costs were measured by estimating the amount of time staff devoted to developing the computer software. This comprised a dedicated computer programmer (12 weeks), who developed the program code, and a computing officer (8 hours), who copied the CDs. Also included were the costs of other staff (consultant geneticists, GPs and research staff from study) attending meetings necessary to plan, design and evaluate the software development. Non-GP staff costs for software development were valued using local unit costs from the GUHT Finance Department. The midpoint of the salary scale for each grade of staff was used to reflect a 'replacement' aspect, and employer's on-costs (National Insurance and Superannuation) at 13% were included.

Consumables

Consumable items for the software included the CDs and their labels (which displayed the study logo).

Room

In the development of software, room costs were based on the size of the floor space used for a new hospital building in Grampian. An equivalent annual cost (EAC) was then calculated, automatically incorporating both the depreciation and opportunity cost aspects of the capital item, with the opportunity cost of capital reflected in the discount rate.[45] A 6% discount rate was used for the EAC, as specified in the guidelines for conducting health technology assessments,[46] over a 50-year lifespan. Overheads are those costs shared by the entire hospital, such as heating, lighting and cleaning; these were calculated by measuring the amount of time for which rooms were required, combined with floor space, then valued using Grampian hospital finance data.

Equipment

Equipment costs included networked computers used by the computer programmer and computing officer. For computing costs an EAC was calculated at a 6% discount rate, over a 5-year lifespan, and network and maintenance costs were added.

The costing denominator was the number of CDs actually produced ($n = 70$). Marginal costing was performed on the software development to provide information on the cost of providing an extra unit of these activities (extra CDs produced).

Postgraduate educational sessions

Staff

This involved identifying all resources used to develop and deliver the educational sessions, and staff, consumables, rooms and equipment resources were examined.

Staff costs were calculated by estimating the amount of time staff devoted to the preparation and attendance at the three postgraduate educational sessions. Staff costs were estimated for those providing the session [consultant geneticists and the principal investigator for the study (clinical senior lecturer)], plus the costs for GPs attending and their travel costs.

Non-GP staff costs for attendance at educational sessions were valued using local unit costs from the GUHT Finance Department. GP salary and travel costs for attending the sessions were valued using a published source.[47]

Consumables
Stationery for the invitations and postage were included. Local unit costs were then applied to the consumable resources.

Room
The postgraduate educational sessions were conducted off the hospital site. However, overheads for an NHS setting are estimated here, as this is more likely to be generalisable to other settings.

Equipment
Computer time used in the preparation and presentation of the Microsoft Powerpoint slideshow was costed. For computing costs an EAC was calculated at a 6% discount rate, over a 5-year lifespan, and network and maintenance costs were added.

The costing denominator was the total number of GPs attending the three sessions (n = 27). Marginal costing was performed to provide information on the cost of providing an extra unit of postgraduate education (i.e. an additional GP attending an educational session).

Software use in primary care
The costs to the practices associated with the use of the software were estimated. Staff costs were measured by estimating the amount of GPs' time spent using the software to gather family history information. Questionnaire data were collected from intervention GPs, who were asked to estimate the average length of a consultation when the software was used. All costs were valued using published estimates, which included direct care staff costs and room costs, but excluded qualification costs.[47]

Results

All costs are reported for the year 2001 and are presented in pounds Sterling (£).

Development of the software
Table 7 presents the costs of software development.

TABLE 7 *Costs for the software development*

Cost category	Total average cost per CD (£)	Marginal cost[a] (£)
Staff	59.38	2.06[b]
Consumables	1.06	1.06
Equipment	1.38	
Rooms	9.87	
Total cost	71.69	3.12

[a] Additional CDs produced.
[b] Computing officer time to copy a CD.

TABLE 8 *Cost for each GP attending postgraduate education session*

Cost category	Total average cost per CD (£)	Marginal cost[c] (£)
Staff: software team[a]	21.20	
GP[b]	72.12	72.12
Consumables	1.09	1.09
Equipment	0.16	
Room	7.11	
GP travel costs	4.39	4.39
Total cost	106.07	77.60

[a] Includes costs for staff providing and preparing the educational session.
[b] Includes the cost of the GP's salary.
[c] Additional GPs attending the course in the short run (no extra staff required initially).

Postgraduate educational sessions

Table 8 presents the costs for the postgraduate education sessions.

Use of software in primary care

In total, 151 out of 241 GPs (63%) responded to the questionnaire, with 64 out of 151 (42%) stating that they were aware of the software and 22 out of 64 (34%) reporting that they had used the software at least once. For GPs who had used the software, 14 out of 22 (64%) estimated that 'on average' they spent up to 10 minutes for each patient when using the software. The remaining eight (36%) reported that they spent between 10 and 20 minutes with the patient when using the software. Based on a unit cost of £1.70 per minute, this implies that a shorter consultation would cost around £17.00 per patient and a longer consultation of up to 20 minutes would cost £34.00. When compared to published estimates of the units of time for GP consultations,[48] this suggests that the majority of GPs did not spend additional time during consultations in which they used the software, compared with all other consultations.

When interpreting the costing results of the primary care intervention, a potential limitation is related to the time estimates for risk assessment for GPs who did not use the software. This study did not collect information on the length of time 'on average' for advice on risk assessment from GPs who had not used the software. Therefore, the study could only indirectly compare GPs who used the software and those who did not, because estimates of time without the software were based on published estimates of average consultation lengths for UK GPs.

Chapter 6

Primary care intervention: discussion

An intervention was developed and evaluated which was designed to improve GPs' confidence in their management of patients concerned about genetic disease, using familial breast cancer as a model. It was designed to meet the expressed needs of GPs in a simple, sustainable manner, and it was deliberately disseminated in a pragmatic way. The primary outcome of interest was GP confidence, but data relating to referral patterns and patient outcomes were also collected. Taken as a whole, the evaluation could not distinguish a definite effect on the outcomes measured. The reasons may lie with the evaluation design, the intervention or its dissemination and related contextual factors.

The evaluation design

A pragmatic evaluation design was adopted; in other words, the study set out to measure what could be achieved by the policy of developing and offering the software to typical GPs. Although the trial was conducted in a real-life setting, a rigorous design was used. The cluster design successfully helped to minimise the chance of contamination between intervention and control groups. Nearly all practices in the Grampian region of Scotland took part and the trial, in principle, was large enough to identify a plausible effect size on confidence. As discussed below, the principal limitation was the small number of intervention GPs who actually used the system.

Several investigators have commented on the need for computer support systems to be evaluated in field settings[49,50] where many contextual factors may modify effectiveness in practice.[51] Very few computer-based systems have been evaluated in pragmatic primary care settings,[52–56] and their results have been mixed. In relation to genetics, Emery and colleagues have conducted extensive development work on a computerised intervention for primary care, but their reported evaluations so far, although very promising, have involved self-selected GPs assessing simulated patients with proxy outcomes.[10] The reported enthusiasm among GPs for computer systems[9,26] to assist them with genetics needs to be tested in the context of a busy surgery and normal workflow.

In this study outcomes were chosen that reflected the needs of the target population. Although referral rates and risk levels are important from a specialist perspective, confidence in management decisions and in advice given to patients more accurately reflects the GP's concern.[5,9,26] Choice of confidence as an outcome also had the advantage that the power of the study could be predicted (and maximised) more accurately, as it is dependent on the number of responding GPs, not the number of referrals. However, by also collecting data on referral and patient outcomes, some insight could be gained into possible broader effects of the intervention.

The intervention

GP surveys have indicated an enthusiasm for computer support to make genetics referral decisions.[9,26] The intervention developed and evaluated here evolved over the early stages of the project, as described in Chapter 3, specifically to meet the target population's needs.[10] It was originally planned to use the only available breast cancer risk assessment software program, Cyrillic, and to disseminate it to intervention practices in a series of small group educational sessions, involving GPs, practice nurses and other staff as GPs felt appropriate. The combination of a commercially available package (which would have already been through extensive development and testing) and the individualised implementation strategy (which would increase the chances of potential users integrating it into existing clinics or routines) was thought to represent a potentially sustainable, pragmatic intervention with a reasonable probability of success. However, as the researchers worked with GPs on the study team, they soon came to understand the software's limitations in a primary care setting, including its perceived complexity by potential users, the need to lengthen the consultation time if it were to be used during patient contact, the projected investment of time required by the average practitioner to learn its use and the type of output it produced: a computed risk of cancer. There was some doubt that GPs could be persuaded to invest the time to learn it and alter work routines to use

it, since breast cancer genetic risk assessment was only a very small part of their clinical activity. It was also concluded that a calculation of breast cancer risk was not the information that GPs sought; rather, their need was for guidance on the appropriate action to take for different risk levels.[9,10] A key issue was GP confidence, both in recognising family history patterns that clearly indicated a need for referral (detecting high risk) and in having sufficient knowledge to reassure convincingly those patients who were unlikely to be carrying a breast cancer susceptibility (BRCA) gene (reassuring low risk). The preliminary assessment was supported by the findings of the preintervention survey and by other published reports.[9,19,25,57] Ideally, the next step should have been to invest in an in-depth development and preliminary evaluation phase, in keeping with the Medical Research Council's (MRC's) framework for development and evaluation of complex interventions.[58] However, this was not within the resources of the study. Therefore, a decision was made to develop an in-house program, based on best available evidence at the time of factors likely to promote its effectiveness.

The authors were aware that cancer genetics guidelines were being developed by a central group for the SEHD and that they would be disseminated by mail to all GPs in the country. These guidelines were to be based on best available evidence, but were written by specialists; draft versions made available to the investigators suggested that they would be relatively complex for a non-specialist to interpret. Therefore, the software was designed to present the user with the guidelines as a set of questions that would elicit the necessary information on a patient's family history to allow a management recommendation to be made; no risk calculation was necessary.[9] As described in Chapter 3, elements were also incorporated into the software to enhance or expand its utility, by helping users to understand the evidence base of the guidelines, and by providing features that GPs might find useful once a management decision of some kind had been made.

The software

The software package had a local identity and took account of local circumstances, both of which are reported to improve the likelihood of effectiveness.[59–61] It was self-loading, demanded little learning time and was simple to navigate. The patient information leaflets and e-mail facility are tools that clinicians are said to appreciate,[9,26,51] and that enhance the relationship between GPs and specialist clinicians. The package could be described as a passive (on-demand) decision support system, in that it depended on the user deciding to activate it, rather than providing prompts in response to preset cues. It has been suggested that GPs value this approach, if presented in an accessible system.[51,62,63] However, a passive approach requires a user to remember that the system exists and to make the effort to use it, and these may be important barriers in a busy surgery, in a clinical situation that is relatively infrequent or where the system is not integrated with other practice systems.[64]

Dissemination and other contextual factors

The success of guideline-based interventions also depends on their dissemination strategy:[59] active educational intervention is more likely to be effective than passive dissemination.[61,65] A counter-argument is that a strategy that fits with existing systems, if effective, is likely to be more sustainable than one that depends on special, extensive or individualised interventions. While the aim was a dissemination strategy likely to support the use of the intervention, the researchers also wished to be as pragmatic (and therefore cost-effective and sustainable) as possible. To this end, they took advantage of systems already in place as far as possible: the software was bundled in with standard packages being installed on a contract basis by an IT company as part of a regional upgrading process; it was mailed out to practices and distributed at postgraduate education sessions. A few practices requested that the authors visit and demonstrate its use, which they did. Each GP was sent a letter from the head of the CGS alerting them to its arrival in the practice, with simple instructions on its installation. With the exception of the practice visits, these are all fairly passive dissemination methods, so the strategy was strengthened by running postgraduate education sessions for intervention practices. The format was still routine, comprising a standard evening postgraduate educational session, bearing PGEA points. However, these sessions were used as an opportunity to allow interaction between GPs and consultant geneticists (which improves the likelihood of effectiveness[61]) and hands-on demonstration of the software.

The intervention was designed with the aim of having the highest chance of effectiveness in the target group, taking into account GPs' perceptions

of what their own appropriate activities should be in relation to genetics.[5,9,24,57] The data suggest that the study GPs were reasonably comfortable with the use of computers in practice. Computers were used by many for routine tasks such as ordering prescriptions, although there were greater reservations about using computers for other areas of clinical activity in the presence of patients. However, the most telling finding of the evaluation was that only 22 of the 151 intervention GPs who responded actually used the software as intended. This is partly explained by the low level of awareness of the software: fewer than half of the intervention GPs were aware that their practice possessed it and, of those, about one-third reported using it. This suggests that the dissemination strategy was less effective than had been hoped, and that more active targeting of individual GPs might have led to greater use of the software in practice. Attendance at the education sessions was disappointing, but it was in keeping with the experience of guideline implementation trials in this and similar GP populations.[66–68] However, devoting greater resources to dissemination and implementation would have increased the costs of the intervention and limited both its sustainability and its generalisability.

The importance of the 'fit' of a passive, on-demand, system in the context of a busy general practice has already been noted. As well as being easy to use and accessible, an important consideration is the frequency with which GPs have the opportunity to use it. This is a reflection on how often patients present to them with concerns about breast cancer risk. There are no direct data on this, but the only UK study that has attempted to quantify consultation rates produced an average estimate of 0.6 consultations per GP per month[69] related to family history of breast cancer, with a slightly higher rate of consultations related to more general risk of breast cancer. Using the present data, it is possible to work backwards from the actual number of referrals made to the implications of different GP consultation rates. The data demonstrate that the overall referral burden, as viewed from the specialist clinic perspective, results from very low absolute numbers of referrals by individual GPs, perhaps one or two per year. It is unclear whether this reflects either the tip of the iceberg or the entire iceberg, although only around 15% of respondents reported that, by default, they referred all concerned patients for genetic counselling. This suggests that most GPs were making other kinds of management decisions for at least some patients. The smaller the number of patients consulting study GPs about breast cancer risk, the smaller the opportunity for the software to be used and, arguably, the lower the chance that it would be used and hence make an impact on the desired outcomes (assuming that it was an effective intervention). The greater the number of patients, the greater the opportunities for the software to make an impact, and possibly the higher probability that GPs would remember it and feel sufficiently familiar with it to use it. However, if a proportion of women with concerns was not being referred for specialist advice, this would also imply that GPs were already acting as very effective gatekeepers and that any intervention seeking to lower the number of low-risk referrals would be working very much at the margin. *Table 9* illustrates these issues. Using preintervention data on actual patient referral

TABLE 9 *Implications of underlying GP consultation rate on potential for software use*

Total no. of referrals per year in study population[a]	Assumed % of patients referred	Implied total no. of patients seen per year in study population	Implied potential frequency of use of software, per GP	Implied potential frequency of use of software, per practice	No. of low-risk patients referred[a]	Low risk, as % of all patients seen	% of all patients seen whose referral decision targeted
146	100	146	Once per 28 months	Once per 7 months	72	49	25
146	50	292	Once per 14 months	Once per 3.5 months	72	25	12
146	5	3048	Once per 5–6 weeks	Three times per month	72	2.4	1.2

[a] Derived from preintervention data, intervention and control groups combined; 346 GPs, 86 practices.

numbers in this study population (scaled up to 1 year for simplicity), the implication of different notional referral rates on the total number of patients consulting all the study GPs over a year was examined: this gives some indication of the potential for use of the software. From the specialist perspective, a key issue is low-risk referrals: using the same data, and assuming that the aim is to avert half of all low-risk referrals, the table indicates the proportion of total patients (not just referred patients) that these represent.

These hypothetical calculations assume that GPs are generally identifying and referring patients whose family histories are strongly suggestive of high-risk status, and that reducing referrals of low-risk patients is the more pressing policy goal.[9] From the clinic perspective, the issue is one of improving specificity (correctly identifying low-risk patients, so reducing the number referred) while maintaining high sensitivity (correctly identifying high-risk patients and maintaining their referral rate). From the GP's perspective, the issue is of being confident in the decisions made and advice given to those patients who are not referred.

Economic evaluation

The economic evaluation component of the intervention was essentially a cost analysis of three areas: software development, education sessions and the use of the software in practice. Over 80% of the total software development costs (£71.69) was accounted for by staff costs. These are sunk costs (one-off costs incurred in the development stage) and the unit cost of producing further CDs in the future would fall (assuming that no updating was required). In other words, the marginal cost of establishing the system in an additional practice is relatively small, at £3.12 per CD. Nevertheless, the results of the trial question whether this would be a useful investment, even if compliance with using the software increased.

The average cost of a GP attending one of education sessions was £106.07, of which the largest proportion (£72.12) was attributable to GP time. The sessions also incurred costs related to the preparation of the presentation and, if further similar sessions were run, these average costs would probably fall, assuming that the same set of slides was used and presenters were familiar with the material.

The cost of the use of the software in practices depended on the required length of the consultation, and around one-third of respondents reported longer consultations when they used the software, up to 20 minutes. The estimates are based on small numbers of users and survey respondents, so they need to be treated with caution. Other studies of computer-based interventions in primary care have also reported the need for longer consultation times.[10,70]

The total costs of the intervention are sensitive to the method of dissemination. Hypothetically, if it had been demonstrated that the software was effective without the need for education sessions, then it would appear to represent a very cheap intervention, especially if consultation times were not increased. Even with longer consultation times, the total extra costs would be fairly negligible for a relatively uncommon activity. There may also be practical ways in which GPs' use of the technology could be increased; for example, through dedicated sessions, perhaps by a particular GP specialising in giving advice about genetic risk.

Other important costs that have not been taken into account are those of extra referrals (if more high-risk patients were detected) or the savings associated with referrals averted (if a patient who would otherwise be referred was correctly identified as low risk and managed in primary care). These would also need to be set against the benefits of referral for the individual.

Contextual factors

Although there is a growing body of evidence on the effectiveness of interventions designed to promote improvements in patient management (including referral decisions) in primary care,[61] the area of genetics may present challenges that are not encountered in other clinical situations. There are two key issues: the pace of change of knowledge and GPs' perceptions of what their appropriate role is. Each of these is likely to influence the potential effectiveness and sustainability of an intervention such as the one reported here.

Pace of change of knowledge

Interventions need to take into account both the changing knowledge base in genetics and the fact that many practitioners are more or less learning the basics of the subject for the first time. This sets genetics apart from many other areas where interventions aim to promote evidence-based practice. Knowledge about the genetic basis of common conditions has changed fundamentally

over the past 10–15 years, and the evidence base is still developing. For example, as the evidence on the relative effectiveness of management interventions for patients at moderate and high risk of breast cancer becomes clearer,[71–76] the benefits of intervening with patients at different levels of risk may become more or less convincing and referral criteria may change. GPs may be expected to update their advice to concerned patients and counsel or manage greater or lesser numbers of patients themselves. The authors are unaware of any other clinical contexts where knowledge is changing so rapidly.

GPs' perceptions of their role

The importance of GPs' perceptions of their own appropriate role in relation to genetics has already been mentioned. The evidence suggests that, on the one hand, GPs are generally positive about this role[5,9,24,26,57] while, on the other, many are sceptical about the timescale, the types of benefits promised and just who should define their role.[25,34,77] If the key barriers are perceived as lack of knowledge or confidence,[26,57,78] or inadequate resources,[26] then an important issue may be overlooked: a suggested fundamental resistance among many GPs to taking on a role that is not coherent with an idea of generalist practice.[34,77] If this is the case, then interventions that are simplistic,[51] perceived as top–down or predicated on incorrect assumptions about GPs' perceptions of their own role in genetics[34] are unlikely to be effective or widely adopted in practice.

Chapter 7

Nurse counsellor intervention: background

Rationale

As described in Chapter 1, regional genetics clinics were faced with the challenge of increasing their ability to manage and meet increasing demand within their own resource constraints, in parallel with increasing patient interest in primary care. Even with the introduction of guidelines, most clinics faced year-on-year increases in referrals for breast cancer genetic counselling.[2,79,80] Each referred patient requires counsellor time to gather family history information, to contact relatives for consent to check their medical records, obtain and confirm diagnoses in family members, and to communicate risk assessments and counsel patients on their further management options. Assuming no reduction in demand or restriction in service, a major issue was how to increase counselling resources cost-effectively. In the 1990s, the bulk of genetic counselling was still provided by clinical geneticists, although it was becoming more common for specialist centres to include genetic associates, specialist nurses, liaison nurses or health visitors in a team approach.[3,7] The only recognised training path for non-medical counsellors was for science graduates wishing to become genetic associates, but training places at Master's level in the UK were very scarce. No particular training path existed for nurses, although many institutions provided postqualification courses in genetics of one sort or another.[4]

Recent UK policy statements have underlined the importance of nurse specialists and practitioners in a modernised service.[81] However, very little formal evidence of their effectiveness in practice currently exists, particularly where their role is that previously taken by a doctor (substitution). At the time this study was conceived and designed, few published controlled trials of substituting nurse specialists or practitioners for a traditional doctor's role[82,83] could be found.

Aims and objectives

The aims of this component of the study were:

- to evaluate whether trained nurse counsellors were equivalent to the current or likely services for familial breast cancer counselling in Grampian and Wales, in terms of effectiveness, acceptability and cost-effectiveness
- to explore further those factors influencing cost-effectiveness in the two trial settings.

The objectives were:

- to compare, in women having initial risk assessment carried out by a nurse counsellor or in the usual service setting, and relative to precounselling baselines,
  - postcounselling levels of anxiety and other psychological outcomes (immediately and 6 months after counselling)
  - postcounselling perceptions of general health status
  - postcounselling retention of specific risk information
  - patient satisfaction
  - acceptability of the service to referring GPs and other relevant health professionals
  - costs to the health service and patients.
- by the use of sensitivity analysis, to explore the effects of factors hypothesised to influence the cost-effectiveness of genetic counselling services for familial breast cancer.

Parallel trials in two geographical areas

Two separate evaluations of this intervention were conducted in two distant geographical areas in Britain (Grampian region and Wales). The intervention was similar in each, and an identical set of outcome data was collected. However, the trials were treated separately and distinctly. There were too many differences in other respects to combine differences in contextual factors, such as the patient population, the historical development of services, and pre-existing relationships between GPs and hospital specialists. In addition, the control arms reflected differences in current policy and practice in the two locations.

Chapter 8

Nurse counsellor intervention: methods

Current practice in the two trial locations

At the time the study was designed, a cancer genetics service had been available in Grampian for several years. Patients referred to the regional genetics centre were allocated two appointments with a clinical geneticist, each of approximately 45 minutes' duration. In the first appointment, family history and medical information would be obtained; following this, medical records, cancer registry information, and so on, would be sought to provide as complete information as possible for risk assessment. The patient would then return for a second appointment at which her risk status would be communicated and further management discussed. Because of the need to meet increasing demand, this practice evolved over the period of the trial. For referred patients not obviously at high risk, an appointment was only offered after a family history questionnaire had been returned, and often telephone contact was made to obtain specific information in advance of the first appointment. Many patients therefore attended for one appointment only. Thus, the control intervention in Grampian consisted of one or more appointments with a clinical geneticist.

In Wales, a cancer genetics service had not been provided before the trial, but started accepting referrals for familial breast cancer genetic counselling in December 1998. A clinical assistant conducted an initial patient assessment in the clinic or by telephone, followed by a search of medical records, and a face-to-face consultation in the clinic. He or she liaised with the supervising consultant geneticist as required.

Intervention

In Grampian, the intervention consisted of the nurse counsellor as first contact for newly referred patients. Her role was to gather family history and clinical information and to conduct a preliminary risk assessment, usually at an outpatient appointment, followed by the retrieval of medical records and any other relevant activities, a reassessment of the patient's genetic risk status and a discussion of further management with the supervising consultant geneticist. They would agree the follow-up option, either confirmation of low-risk status with no further specialist follow-up, or further follow-up at the cancer genetics service. The nurse counsellor then contacted the patient by telephone or arranged a clinic appointment to communicate the follow-up arrangements.

In Wales, the intervention consisted of the nurse counsellor as first contact for newly referred patients. As in the Grampian intervention, her role was to gather family history and clinical information and conduct a preliminary risk assessment, although it was more often conducted by telephone than in the clinic. This was followed by retrieval of medical records, a reassessment of the patient's risk status and agreement of further management with the supervising consultant geneticist. As in Grampian, the options were no further specialist follow-up or appointment at the cancer genetics clinic.

In both trials, the nurse counsellors worked to locally agreed protocols. Criteria for specialist follow-up generally included a lifetime cancer risk in excess of 20%, a complex family history requiring specialist interpretation and/or excessive anxiety or dissatisfaction with the service on the part of the patient. In both locations, the head of service was responsible for the decisions and actions of the nurse counsellors and was expected to supervise them actively, and to ensure the accuracy of risk assessments and other aspects of care. Training was delivered according to the needs of the nurse counsellors when they were appointed to their posts. For those without a background in genetics, a training programme already existed in Wales, and it was adapted for use in Grampian. The head of service in each locality was responsible for ensuring the competence of genetics nurses employed in the project.

Implementation

After the locally developed induction and training periods, the nurse counsellors took on outpatient loads with a set number of clinics per week. Appointments were arranged by administrative staff and care was taken to ensure that waiting times for new patients were generally the same for

control and intervention arms (as shorter waiting times for subjects in the intervention arm may directly influence the outcomes of interest). The decision to discharge or follow-up provided the boundary to the intervention; all activities from this point on were part of the usual cancer genetics service. All management decisions were the responsibility of the consultant geneticist, with the nurse counsellor acting on his or her behalf. Therefore, the intervention was considered to comprise:

- the first appointment with a new patient to gather clinical and family history information
- the communication of a provisional risk assessment
- the assembly of all available information to confirm the family history
- the communication with the responsible consultant regarding all the assembled information
- the communication with the patient regarding further follow-up or management.

Patient recruitment took place between 1998 and 2001 for the Grampian trial and 1999 and 2001 for the Wales trial.

Evaluation

Design

The intervention was evaluated using two RCTs, in which the level of allocation was the individual patient. The two trials were conducted concurrently. Baseline and follow-up data were collected from patients, and follow-up data were collected from their referring GPs. A parallel economic evaluation was conducted alongside the main data collection exercise (see Chapter 10).

Study settings and participants

The trials were conducted in two centres: the North of Scotland Regional Genetics Service based at GUHT in Aberdeen and the Institute of Medical Genetics, University Hospital of Wales in Cardiff.

Trial populations

Patients were eligible to take part if they lived within the Grampian Health Board Area or in one of two health authority areas in Wales (Bro Taf and Iechyd Morgannwg).

Inclusion criteria

- Aged 18 years or over
- first referral for genetic counselling
- main concern a family history of breast cancer
- literate in English
- willing to be randomised to the intervention or control group.

Exclusion criteria

- Previous attendance at genetic clinic
- known to the genetics service as a member of a gene-positive family
- unwilling to be randomised to the intervention group.

Recruitment

Recruitment was performed by the study research fellow in Grampian and by a research secretary in Wales. Potentially eligible patients were identified from referral letters and consent to contact was obtained from the referring GP (or patient's usual GP if referred by a hospital specialist). An opt-out system was used, whereby GP consent was assumed unless he or she contacted the study team within 1 week of notification. Patients for whom GP consent was not withheld were sent a letter describing the study (signed by the consultant in charge), a patient information sheet and a consent form. A reminder letter was sent if no response was obtained after 2–3 weeks. Ethics approval was received for this approach.

Control intervention

The control intervention in each arm was the routine practice, as described above.

Allocation

Allocation was performed by the Grampian-based research team for both trial locations. The random allocation schedule sequence for each trial was computer generated by the statistician (JM) and concealed within a Microsoft Access database. On receipt of a signed consent form, the research fellow (NT) entered the participant's name and date of birth into the database. Participants were randomised 2:1 to the intervention or control group (before their preclinic work-up, risk assessment and appointment). The allocation was concealed until the study number had been assigned. Following allocation, the CGS managed participants as they would any other patient, although in both trial locations the authors requested that appointments be scheduled with similar waiting times for intervention and control arms. In Grampian, this required building an artificial waiting list for the nurse counsellors. To prevent contamination, members of the same family were allocated to the same trial group.

Outcomes

Anxiety

Anxiety was chosen as the primary outcome. Change in anxiety is an important outcome in genetic counselling and is related to the appropriateness of subsequent risk perceptions and health behaviour.[84,85] Research on counselling following a diagnosis of breast cancer suggests that the counsellor–patient interaction is an important determinant of anxiety and coping styles.[86] Anxiety has several components, including cognitive, somatic and behavioural elements, all of which are relevant in the context of genetic counselling. The six-item short form of the state scale of the Spielberger State Trait Anxiety Inventory (STAI)[87] and the Hospital Anxiety and Depression Scale (HADS)[88] were used to measure anxiety. The STAI has been widely used in studies of women at risk of breast cancer,[89,90] and in studies of breast and ovarian cancer genetic counselling.[91–94] The score obtained from the short-form STAI is multiplied by 20 and divided by 6 to mirror scores obtained from the full 20-item version. These scores range from 20 to 80, with 80 indicating the worst possible anxiety score. The HADS ranges from 1 to 21, with a score of 21 indicating worst possible anxiety or depression.

General health status

Participants' perceptions of their general health were assessed using the Short Form 36 (SF-36) instrument,[95] which has been validated for use in the UK population.[96] For each dimension item scores are coded, summed and transformed on to a scale from 0 (worst possible health state measured by the questionnaire) to 100 (best possible health state).[97]

Knowledge of risk following counselling

Questions were identical to those used in the primary care trial (see Chapter 3). Knowledge was assessed by patients' responses to a set of questions on the causes of breast cancer. The topics matched the areas that the consultant geneticists reported covering during genetic counselling sessions with patients, although the risk advice was tailored to the individual patient; three of the five questions could be considered to have a standard 'correct' answer (stress, having a relative with cancer, minor injury). The study also assessed patients' self-perceptions of genetic risk using a self-completion questionnaire (see Appendix 2), in which respondents were asked to rate their own perceived risk in two ways, against a notional 'average' woman and on a scale. Concordance was assessed by comparing perceived personal risk with the risk communicated to the subject by the geneticist or nurse counsellor, and recorded in the case notes at the time of follow-up.

Acceptability of service to patients

A patient satisfaction questionnaire originally developed by Shiloh and colleagues was modified[98] for use in genetic counselling clinics (Appendix 3).

Acceptability of the service to referring GPs and other relevant professionals

A questionnaire was designed and administered to those GPs who referred patients for breast cancer risk assessment and who were randomised to an appointment with the nurse (Appendix 4).

Data collection

Patient data

The study instruments were combined as appropriate into a core questionnaire for administration at each of the three data collection stages. The baseline questionnaire also included items on patient expectations of the clinical encounter, the first follow-up questionnaire included items for the economic analysis, and the second follow-up questionnaire included patient satisfaction questions. The core questionnaire was piloted in non-study patients attending the CGS before the trial began. The baseline questionnaire was mailed to subjects who returned consent forms before attendance at the genetic clinic, with a covering letter signed by the consultant in charge. A reminder was sent 2 weeks later if no response was obtained. Following the initial episode of care, the first follow-up questionnaire was mailed to participants, with a reminder 2 weeks later for non-respondents. Six months later a second follow-up questionnaire was mailed to subjects who returned the first follow-up questionnaire, again with a reminder for non-respondents.

General practitioners

A cross-sectional postal questionnaire survey of all GPs who referred patients to the CGS, and who were randomised to the intervention group, was carried out after patient data collection was complete. To maximise the response rate, the questionnaire was kept very brief and included items on respondents' satisfaction with the intervention, whether they could tell that a referred patient had been seen in the intervention or in the control arm, and whether they would be prepared to refer future patients to see a nurse counsellor.

Data management

Returned questionnaires were checked for completeness and coded, and the data entered into a Microsoft Access database by an independent data officer, blind to the allocation. The data sets were checked for anomalies, which were corrected by checking the original questionnaires.

Sample size

The research question addressed equivalence rather than difference between the experimental and control interventions. Two-sided equivalence was chosen, rather than a non-inferiority (one-sided) hypothesis, the test hypothesis being that the intervention (nurse counsellors) was neither better nor worse than the control (current practice, namely a clinical geneticist-led clinic). The primary outcome was anxiety as assessed by the six-item (short) STAI. The sample size was based on an equivalence margin of ±4 units. For 80% power at the 5% significance level, and with an allocation ratio of 2:1, 214 participants were required in the intervention group and 107 in the control group to allow detection of equivalence within 4 units (assuming a standard deviation of 12 units). Towards the end of the recruitment phase the sample size calculations were revisited to test the original assumptions, using baseline STAI data from the study populations, and taking into account actual questionnaire response rates and clinic attendance rates. The actual standard deviation of baseline STAI scores was 14 units and the estimated overall study response rate was around 80%. The original sample size of 321, adjusted for a response rate of 80%, would enable a difference of 5.2 units to be shown as equivalent with 80% power. Increasing recruitment to 350 (to ensure follow-up data on 280 participants) would allow a difference of 5.0 units to be shown as equivalent. Increasing the sample size beyond this figure would not substantially decrease the equivalence margin towards the original equivalence margin of 4 units. Therefore, the sample size was adjusted upwards to recruit 350 women in each of the two linked trials.

Statistical analysis

The differences in outcome between the intervention and control group were adjusted for baseline scores using multiple linear regression. Multiple linear regression is a parametric approach which makes assumptions of normality. The primary outcome measures were known to demonstrate non-normal distributions. Linear regression is reasonably robust to departures from normality; however, to assess the impact of skewness bootstrap estimates were also calculated.[99] This was implemented in STATA 6.0 (College Station, TX: Stata Corporation; 1999), and bias corrected confidence intervals (2000 replications)[99] were compared with those produced from the linear regression model.

Equivalence limits

To demonstrate equivalence, the true difference in outcome should be shown to lie between a lower and an upper equivalence limit.[100] These equivalence limits were determined a priori by the trial steering group. The equivalence limit for the STAI, as adopted in the sample size calculation, was ±4 units. The short-form version of the STAI has six questions with four categories per question, and the score obtained from the short form is multiplied by 20 and divided by 6 to mirror scores obtained from the full 20-item version. Following a priori discussion with clinical colleagues, an equivalence limit of ±4 units was considered an overly strict level of equivalence, since the smallest possible difference in score is 3.3 units. This relates to a movement of one response category in a single question. Thus, an additional equivalence limit, ±10 units, was considered for STAI to indicate 'likely' equivalence. However, the original equivalence limit was considered when interpreting the results obtained.

For anxiety and depression as measured by HADS and the role–emotional and mental health scales of the SF-36, a difference smaller than one-third of a standard deviation in score was considered to indicate equivalence. Where the 95% confidence interval for the difference in outcome between the intervention and control arms fell completely within the equivalence limit, the outcome was considered 'equivalent' in both arms.[101] Where the 95% confidence interval for the observed difference fell completely outside the equivalence limit, the outcomes were considered to be non-equivalent. Where the 95% confidence interval for the observed difference overlapped the equivalence limit, the result was uncertain.

Intention to treat versus per-protocol analysis

In superiority trials, the most conservative analysis is by intention to treat (ITT). In an equivalence trial, however, an ITT analysis may blur the comparison between the groups and lead to an increased chance of declaring the two treatments as equivalent[101] when they are in reality non-equivalent, so a per-protocol (PP) (as-treated) analysis is usually considered statistically more conservative. However, the decision over which analysis (ITT or PP) should be primary in an

equivalence study is not straightforward[102] and depends on the particular characteristics of the study, including the definitions adopted for the ITT and PP analyses and the risk of bias.[103]

In this study, the ITT analyses included all women who were randomised, returned a baseline questionnaire and attended the clinic. Women who did not follow the randomisation (i.e. who were randomised to see a nurse counsellor but were seen by a clinical geneticist, or vice versa) or who returned for a second appointment with a clinical geneticist remained in the group to which they were randomly allocated. A number of women did not receive the counselling that they were allocated to receive. Most of the protocol deviations were due to staff illness, administration error and family appointments. These protocol deviations were unrelated to the intervention or the women and were unlikely to cause bias. However, in one of the trials, three women were randomised to a nurse counsellor but were seen by a clinical geneticist owing to specific factors associated with risk and therefore, potentially, with the outcome of interest (anxiety). In this situation, the inclusion of these subjects in the as-treated group was likely to introduce selection bias and, depending on relative performance of the experimental and control interventions in relation to the primary outcome, possibly lead to a PP analysis erroneously indicating equivalence. Therefore, the researchers decided on primary analysis in this study by ITT, with additional PP analyses on the key outcomes of interest to test the consistency of the data.

Subgroup analyses

One subgroup analysis was performed, based on participants' perceived risk of breast cancer at baseline. Participants selected one of six categories for their personal risk of cancer, which were then categorised into three subgroups (low, moderate, high) for analysis. The analysis was restricted to the primary outcome measures and, to test for a differential effect of the intervention across the subgroups, a formal statistical test of interaction was performed.[104] Analysis of covariance (ANCOVA) was carried out with baseline score as a covariate. Risk, intervention status and their interaction were included as fixed factors. The analysis was performed using SPSS version 11.0.

Ethics

Approval for the study was obtained from the Joint Ethics Committee of Aberdeen University and Grampian Health Board, and the research ethics committees of Bro Taf and Iechyd Morgannwg health authorities.

Confidentiality was maintained by using a unique study identification number for each participant in all data collection procedures. Computer files were password protected and only a limited number of research staff could gain access. The master file linking individual-identifying details with their unique numbers was held in a secure file accessible only by the principal investigator and the research fellow.

Chapter 9

Nurse counsellor intervention: results

Patient data

Recruitment

Full details of the recruitment are given in *Figures 22* and *23*. These flowcharts follow the Consolidated Standards of Reporting Trials (CONSORT) guidelines, and show the numbers of patients randomly assigned to each arm, treated and completing the study.

Grampian

In total, 517 referred patients were considered for recruitment to the trial. Of these, 28 did not meet inclusion criteria, 99 did not respond to the letter of invitation and 48 refused participation. Of the remaining 342 patients who consented and were randomised (227 intervention, 115 control), 289 returned a baseline questionnaire and attended the clinic (193 intervention, 96 control). In total, 17 did not receive the allocated management. Five women were allocated to the control arm but seen in the intervention arm, because of administrative errors (two women) and joint family appointments (three women). Twelve women allocated to the intervention arm were seen in the control arm, because of administrative errors (four women), a joint family appointment (one woman) or a decision by the head of service (seven women). For these latter women, this was to avoid an unacceptably long waiting time arising from unexpected extended sick leave by the nurse counsellor responsible for intervention patients (four women), and for three patients, it was based on clinical factors that came to light following randomisation, and which indicated the need for a consultant geneticist appointment.

The mean time from referral to the date of the first offered appointment fell from 19.0 weeks at the beginning of the trial to 11.8 weeks at the end. Apart from the second 6-month period of the study, when women randomised to the intervention arm waited a mean of 2.7 weeks longer than the control group, this waiting time was similar across the groups.

For women randomised to the intervention arm, the number of appointments attended before they were discharged ranged between one and four, with 149 out of 193 (77%) attending for one counselling appointment. Thirty-eight (20%) attended for two appointments, and five (3.6%) and one (0.5%) attended three and four appointments, respectively. For women randomised to the control arm, 81 out of 96 (84%) did so only once, with 13 (13.5%) attending two appointments and two (2%) attending for three appointments before being discharged.

Wales

In total, 464 patients were considered for recruitment to the trial. Of these, six did not meet the inclusion criteria, 59 did not respond to the invitation letter and 26 refused to participate. Of the remaining 373 patients who consented and were randomised (247 intervention, 126 control), 297 returned a baseline questionnaire and attended clinic (197 intervention, 100 control). Six did not receive the allocated management where women randomised to the intervention arm were seen in the control arm, four as part of a family appointment and two because of administrative errors. In both intervention and control arms of the trial, all women attended for one appointment before being discharged or referred on.

The mean time from referral to date of first offered appointment fell from 30.2 weeks at the beginning of the trial (reflecting a high referral demand for a previously unavailable service) to 17.9 weeks at the end. In the middle 12 months of the trial, this time was on average 6.5 weeks shorter for women allocated to the intervention group compared with the control group; otherwise the waiting times were similar for the two arms.

Data are presented for women who returned a baseline questionnaire and attended the clinic. *Table 10* summarises response rates throughout the trials. Follow-up 1 (FU1) data were collected following the counselling episode (i.e. after risk status had been established and communicated to the patient, and before further management). Follow-up 2 (FU2) data were collected 6 months later. Slightly higher response rates were observed in the Grampian than in the Wales trial, and in intervention than control groups.

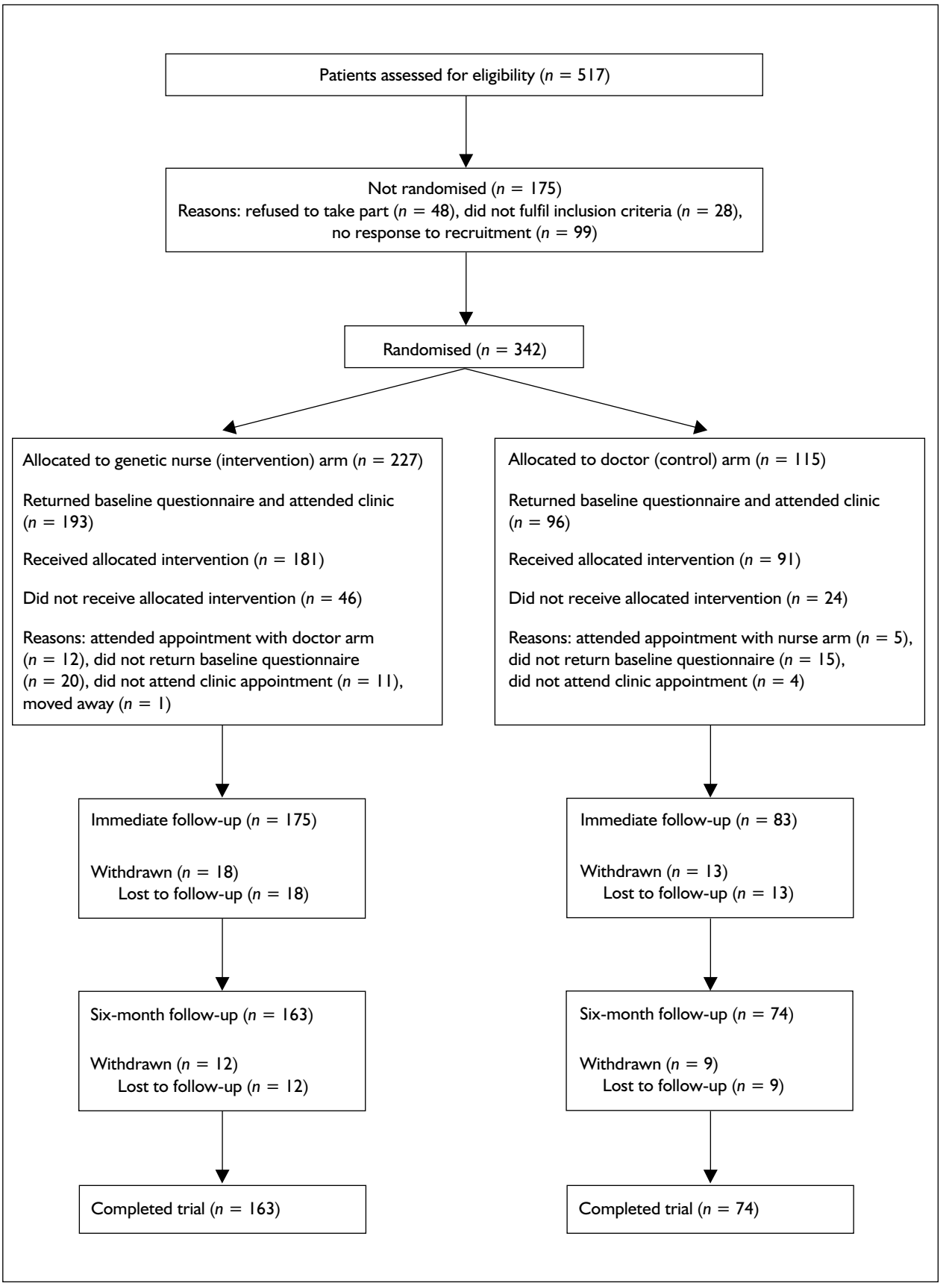

FIGURE 22 *CONSORT diagram for Grampian (progress of patients through the trial)*

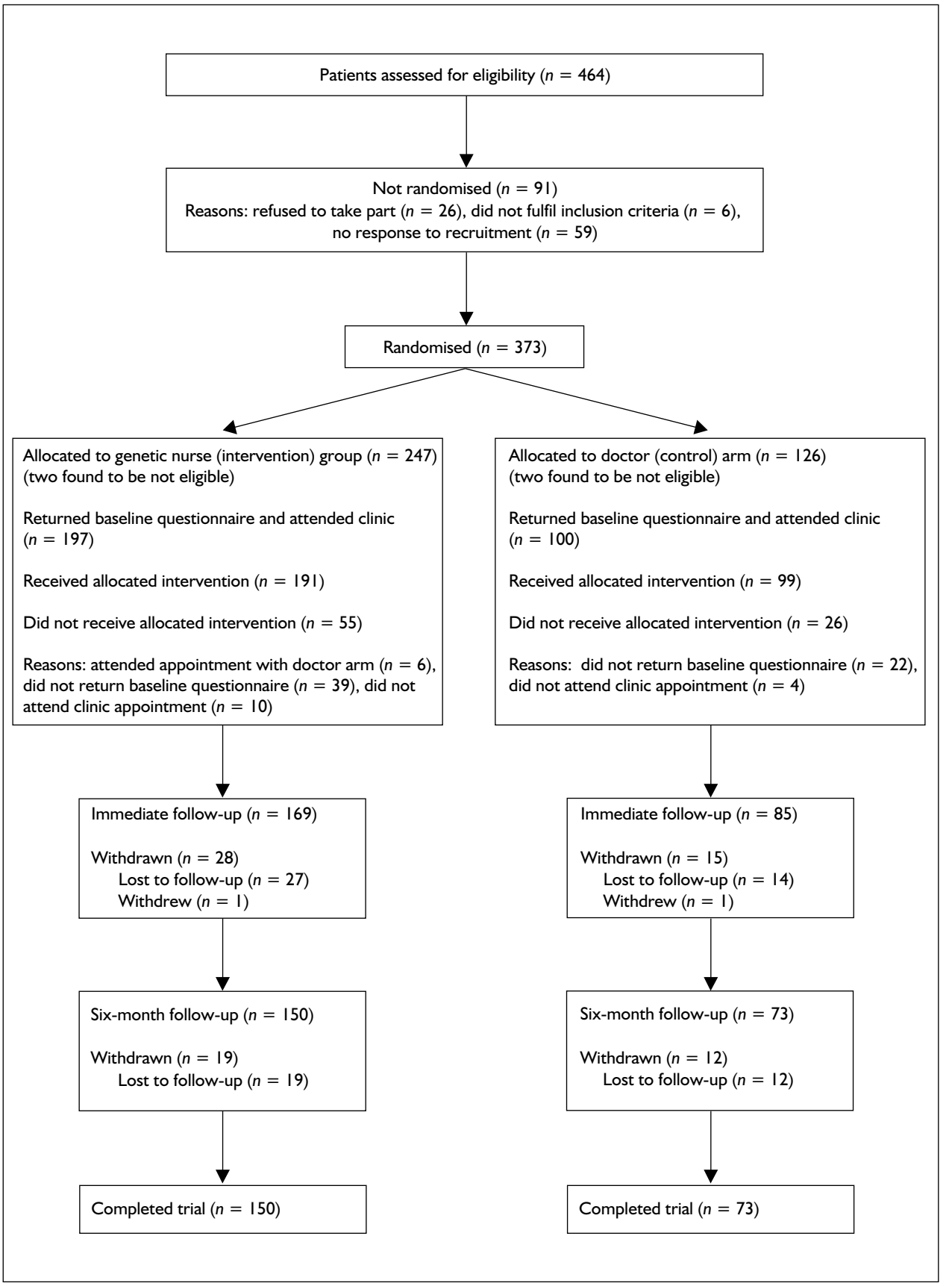

FIGURE 23 *CONSORT diagram for Wales (progress of patients through the trial)*

TABLE 10 *Questionnaire response rates,* n *(%)*

		Intervention	Control	Overall
Grampian	Baseline	193	96	289
	FU1	175 (90.7)	83 (86.5)	258 (89.3)
	FU2	163 (84.5)	74 (77.1)	237 (82.0)
Wales	Baseline	197	100	297
	FU1	169 (85.8)	85 (85.0)	254 (85.5)
	FU2	150 (76.1)	73 (73.0)	223 (75.1)

TABLE 11 *Baseline demographic variables*

	Grampian		Wales	
	Intervention (*n* = 193)	Control (*n* = 96)	Intervention (*n* = 197)	Control (*n* = 100)
Age (years), mean (SD)	40.7 (10.3)	41.4 (9.4)	39.8 (10.2)	39.0 (9.3)
Married/cohabiting, *n* (%)	151 (78.2)	74 (77.9)	161 (81.7)	84 (84)
With children, *n* (%)	157 (81.3)	73 (76.0)	157 (79.7)	73 (73.0)
Postsecondary education, *n* (%)	76 (39.4)	43 (44.8)	73 (37.1)	42 (42.0)
Referral source, *n* (%):				
GP	133 (68.9)	63 (65.6)	117 (59.4)	56 (56.0)
Breast surgeon	35 (18.1)	19 (19.8)	73 (37.1)	42 (42.0)
Breast screening clinic	17 (8.8)	10 (10.4)	–	–
Other	8 (4.1)	4 (4.2)	7 (3.5)	2 (2.0)

TABLE 12 *Baseline scores of primary outcome variables, mean (SD)*

Variable	Grampian		Wales	
	Intervention (*n* = 193)	Control (*n* = 96)	Intervention (*n* = 197)	Control (*n* = 100)
STAI[a]	37.3 (13.6)	36.5 (12.8)	40.9 (15.1)	40.0 (14.5)
HADS anxiety[a]	6.7 (4.3)	6.4 (4.5)	8.1 (4.7)	7.4 (4.2)
HADS depression[b]	3.9 (3.7)	3.4 (3.4)	4.5 (3.7)	4.2 (3.8)
SF-36 role–emotional[c]	80.5 (34.6)	82. 6 (33.4)	74.4 (38.7)	71.0 (40.6)
SF-36 mental health[c]	71.0 (18.2)	73.6 (17.7)	67.3 (18.8)	68.4 (19.3)

[a] Higher score indicates greater level of anxiety.
[b] Higher score indicates greater level of depression.
[c] Higher score indicates better health state.

Demographic characteristics are presented in *Table 11*. The intervention and control groups were similar in terms of most demographic characteristics, with only a small difference in the proportions having children. Over 98% of respondents described themselves as 'white'. In Grampian, about 10% of participants were referred directly from a breast screening clinic, whereas in Wales, more women were referred by a breast surgeon.

The baseline scores for the outcomes of primary interest, shown in *Table 12*, suggest small but consistent differences between the Grampian and Wales study populations, but generally comparable scores between intervention and control groups within each population.

Adjustment for baseline scores is made in analysis of between-group differences in outcomes in intervention and control groups at follow-up.

TABLE 13 *Participants' self-reported risk at baseline,* n *(%)*

Personal breast cancer risk perception		Grampian		Wales	
		Intervention (n = 181)[a]	Control (n = 91)[a]	Intervention (n = 179)[b]	Control (n = 90)[b]
High		40 (22.1)	15 (16.5)	55 (30.7)	27 (30.0)
	'Inevitable'	2 (1.1)	1 (1.1)	15 (8.4)	6 (6.7)
	'Much more than the average woman'	38 (21.0)	14 (15.4)	40 (22.3)	21 (23.3)
Moderate	'More than the average woman'	90 (49.7)	50 (54.9)	94 (52.5)	49 (54.4)
Low		51 (28.2)	26 (28.6)	30 (16.8)	14 (15.5)
	'Same as the average woman'	49 (27.1)	24 (26.4)	29 (16.2)	12 (13.3)
	'Less than the average woman'	2 (1.1)	1 (1.1)	1 (0.6)	2 (2.2)
	'Much less than the average woman'	0	1 (1.1)	0	0

[a] Excludes eight participants already affected by breast cancer (seven intervention, one control).
[b] Excludes 13 participants already affected by breast cancer (ten intervention, three control).

TABLE 14 *Baseline expectations of genetic counselling;* n *(%) agreeing/strongly agreeing with selected statements*

Statement: "I want …"	Grampian		Wales	
	Intervention (n = 192)	Control (n = 95)	Intervention (n = 196)	Control (n = 97)
'to be given accurate information about the causes of breast cancer'	184 (95.9)	93 (97.9)	193 (98.5)	95 (98)
'to be given the exact risk of getting breast cancer myself'	178 (92.7)	83 (87.4)	176 (89.8)	85 (87.6)
'information about preventing breast cancer'	186 (96.9)	94 (99)	193 (99)	95 (98)
'information about genetic tests to determine my risk of breast cancer more accurately'	181 (94.3)	89 (93.7)	183 (93.8)	87 (89.7)

Table 13 shows the participants' self-reported perceptions of risk at baseline. Participants were able to select one of six categories to represent their own perceptions. When participants already affected by breast cancer are excluded, the intervention and control groups in each location showed similar perceptions. In Grampian, just over 70% of women perceived themselves to be at higher than average risk of breast cancer, and in Wales, over 80%.

Table 14 summarises participants' expectations of genetic counselling at baseline, before their first appointment. Almost all participants agreed or strongly agreed with the statements provided, with few differences between groups or between locations.

Follow-up data

STAI

Table 15 summarises the primary outcome, anxiety, as measured using the six-item short form of the state scale of the STAI. As described in Chapter 8, a difference of ±4 units is taken to indicate 'equivalence' at the originally defined level and ±10 units to indicate 'likely equivalence'. If any of the confidence intervals overlapped by ±10 units, equivalence was uncertain. All adjusted point estimates for the differences between control and intervention groups were less than 4 units. The 95% confidence intervals indicated likely equivalence for this outcome at both follow-up points for both trials, except at the first follow-up point in Grampian, where they indicated equivalence.

HADS anxiety and depression

Table 16 presents the HADS data on anxiety and depression. As described in the Methods section, a priori equivalence limits of up to ±0.33 of a standard deviation between groups is taken to indicate equivalence. Based on baseline data collected in both centres, equivalence limits were defined as ±1.4 (Grampian) and ±1.5 (Wales) for

TABLE 15 *Short-form STAI anxiety score, mean (SD)*

Measure	Grampian			Wales		
	Intervention	Control	Difference (95% CI)[a]	Intervention	Control	Difference (95% CI)[a]
STAI						
Baseline	37.3 (13.6)	36.5 (12.8)		40.9 (15.1)	40.0 (14.5)	
FU1	36.4 (14.0)	34.4 (14.0)	0.8 (–2.1 to 3.7)	38.1 (14.9)	38.9 (15.6)	–1.5 (–4.5 to 1.5)
FU2	36.0 (13.5)	32.1 (11.7)	2.9 (–0.2 to 5.9)	38.9 (14.9)	38.1 (14.1)	0.6 (–2.9 to 4.1)

[a] Adjusted for baseline.

TABLE 16 *HADS anxiety and depression scores, mean (SD)*

Measure	Grampian			Wales		
	Intervention	Control	Difference (95% CI)[a]	Intervention	Control	Difference (95% CI)[a]
HADS anxiety						
Baseline	6.7 (4.3)	6.4 (4.5)		8.1 (4.7)	7.4 (4.2)	
FU1	6.3 (4.3)	5.5 (3.9)	0.5 (–0.4 to 1.3)	7.0 (4.9)	7.1 (4.8)	–0.4 (–1.3 to 0.5)
FU2	6.2 (4.4)	5.5 (3.7)	0.1 (–0.7 to 1.0)	7.4 (4.7)	6.4 (4.1)	0.5 (–0.6 to 1.5)
HADS depression						
Baseline	3.9 (3.7)	3.4 (3.4)		4.5 (3.7)	4.2 (3.8)	
FU1	3.5 (3.6)	2.9 (2.8)	0.3 (–0.4 to 1.0)	4.0 (3.8)	4.0 (3.8)	–0.2 (–1.0 to 0.5)
FU2	3.42 (3.6)	2.76 (2.9)	0.3 (–0.5 to 1.0)	4.5 (4.1)	3.9 (3.8)	0.6 (–0.4 to 1.5)

[a] Adjusted for baseline.

TABLE 17 *SF-36 scores (role–emotional and mental health domains), mean (SD)*

Measure	Grampian			Wales		
	Intervention	Control	Difference (95% CI)[a]	Intervention	Control	Difference (95% CI)[a]
Role–emotional						
Baseline	80.5 (34.6)	82. 6 (33.4)		74.4 (38.7)	71.0 (40.6)	
FU1	81.6 (35.2)	82.5 (33.2)	1.9 (–6.3 to 10.1)	74.8 (39.5)	71.5 (40.0)	2.9 (–6.9 to 12.7)
FU2	80.3 (35.9)	86.0 (30.7)	–2.5 (–11.0 to 5.9)	74.9 (38.7)	73.1 (42.2)	0.5 (–9.4 to 10.5)
Mental health						
Baseline	71.0 (18.2)	73.6 (17.7)		67.3 (18.8)	68.4 (19.3)	
FU1	72.2 (18.6)	74.4 (17.7)	0.6 (–2.9 to 4.1)	68.8 (20.5)	68.0 (21.3)	1.3 (–2.7 to 5.2)
FU2	72.3 (18.4)	77.4 (14.9)	–2.7 (–6.5 to 1.2)	67.1 (21.1)	67.4 (21.1)	0.3 (–4.2 to 4.8)

[a] Adjusted for baseline.

anxiety and ±1.2 (both centres) for depression. These are close to the smallest possible difference in score for an individual, which is ±1 point. The results of all these analyses are consistent with equivalence.

SF-36 role–emotional and mental health domains

Table 17 summarises the observed differences in the remaining primary outcomes, SF-36 role–emotional and mental health domains. For each of these, zero represents the worst possible

TABLE 18 *SF-36 scores, mean (SD)*

Measure	Grampian			Wales		
	Intervention	Control	Difference (95% CI)[a]	Intervention	Control	Difference (95% CI)[a]
Physical functioning						
Baseline	88.9 (18.6)	85.4 (21.8)		83.5 (21.8)	88.9 (18.3)	
FU1	88.2 (19.1)	88.6 (18.7)	–0.5 (–3.3 to 2.2)	84.9 (20.9)	88.0 (22.5)	0.3 (–3.7 to 4.3)
FU2	87.9 (18.5)	86.4 (21.3)	0.2 (–2.3 to 2.7)	84.6 (21.3)	88.6 (20.1)	–0.5 (–5.5 to 4.5)
Social functioning						
Baseline	84.0 (23.4)	84.6 (22.1)		77.7 (24.4)	79.8 (26.2)	
FU1	83.4 (23.9)	85.2 (21.2)	–0.6 (–5.7 to 4.5)	78.9 (24.8)	79.9 (25.4)	0.3 (–4.9 to 5.4)
FU2	84.7 (21.8)	87.2 (23.2)	–1.0 (–6.4 to 4.4)	78.0 (26.9)	80.1 (26.4)	–1.0 (–7.6 to 5.5)
Role–physical						
Baseline	87.1 (29.0)	86.1 (31.3)		81.6 (33.5)	84.9 (30.9)	
FU1	86.8 (30.2)	85.1 (32.6)	5.1 (–1.6 to 11.8)[b]	77.4 (37.7)	82.7 (33.4)	–3.9 (–11.4 to 3.6)
FU2	86.0 (30.9)	87.1 (30.3)	1.3 (–6.1 to 8.7)	77.5 (37.9)	74.0 (38.7)	5.5 (–4.3 to 15.4)
Vitality						
Baseline	58.6 (21.3)	58.5 (23.3)		53.6 (21.1)	54.9 (21.3)	
FU1	60.8 (21.7)	61.7 (19.4)	0.5 (–3.7 to 4.7)	57.1 (22.3)	55.7 (20.3)	2.0 (–2.3 to 6.3)
FU2	61.6 (20.7)	63.9 (19.0)	–1.4 (–5.7 to 2.9)	55.3 (22.5)	58.3 (21.1)	–1.8 (–7.0 to 3.4)
Bodily pain						
Baseline	76.3 (23.9)	76.6 (25.1)		72.3 (25.4)	75.5 (25.0)	
FU1	78.6 (24.7)	77.4 (24.4)	2.3 (–2.4 to 7.1)	75.8 (24.6)	75.8 (26.0)	–0.2 (–5.3 to 4.9)
FU2	78.2 (24.5)	76.1 (23.8)	1.7 (–3.8 to 7.2)	74.9 (24.9)	75.2 (19.4)	–0.2 (–6.8 to 6.4)
General health						
Baseline	73.5 (19.8)	73.4 (18.9)		66.0 (20.6)	71.2 (20.0)	
FU1	75.2 (20.7)	74.9 (18.4)	0.8 (–2.5 to 4.0)	67.9 (21.4)	69.9 (20.7)	1.0 (–2.4 to 4.3)
FU2	75.0 (18.6)	73.7 (18.5)	1.7 (–2.0 to 5.4)	68.6 (21.5)	72.5 (19.4)	–0.03 (–3.9 to 3.8)

[a] Adjusted for baseline.
[b] Larger than expected difference owing to baseline imbalance of responders at FU1.

and 100 the best possible health state. The equivalence limits, set at ±0.33 of a standard deviation derived from the baseline measurements, were set at ±11.4 and ±13.1 for the role–emotional score, and ±6.0 and ±6.3 for the mental health scale, for Grampian and Wales, respectively. The data suggest equivalence in both of these outcomes, in both trials, at both follow-up points, with the exception of the mental health score at the second follow-up point in the Grampian trial, which indicated that equivalence was uncertain.

SF-36 other domains and overall health status

Table 18 shows the other health status outcomes and overall health status, as assessed by the SF-36. For any given domain, zero represents the worst possible and 100 the best possible health state. Scores were generally high, the lowest being observed for the vitality domain in both trials. On average, higher scores were observed in all domains in the Grampian data than in the Wales data. In general, observed between-group differences at baseline were small. At both follow-up points, only small differences were observed between groups in both trials. The largest differences in the Grampian data were observed for the role–physical and bodily pain domains at first follow-up. For the Wales data, the largest differences were observed for the role–physical domain at both follow-up points. In general, however, the mean scores were relatively stable over time within each domain and group, and all confidence intervals were consistent, with no between-group differences in any measure at either follow-up point.

Statistical note: normal assumption versus bootstrapped confidence intervals

Although the distributions of the outcome measures were generally skewed, a parametric approach has been presented. To test the robustness of the parametric analyses presented, bootstrap estimates were also calculated. Bootstrap confidence intervals (bias-corrected) were computed for regression coefficients in the linear regression (data not shown). These indicated that the linear regressions conducted on the data were robust to the departures from normality exhibited in the data.

Knowledge of risk after counselling

Knowledge of risk after counselling was assessed by level of agreement with a set of statements, and the results are presented in *Figures 24–28.* The 'appropriate' response for each statement depends partly on the particular advice given during genetic counselling, and this was not assessed for individual women. However, current evidence about breast cancer risk factors in general is presented to all patients during counselling, and for most participants such advice would apply. Responses consistent with this advice would be expected to cluster around the 'disagree/strongly disagree' categories for the risk factors stress, having one close relative with breast cancer and minor injury, and 'disagree/strongly disagree/not sure' for the other two.

At baseline, only small between-group differences were observed for each statement, and response patterns were generally similar for Grampian and Wales. Generally small between-group differences were observed for all knowledge variables postintervention in both trials. Two general patterns were observed: for some statements, the responses were fairly stable between baseline, first and second follow-up (stress and minor injury, *Figures 24* and *28*), whereas for others, at the first follow-up a shift was observed towards responses consistent with the advice given, with reversal towards preintervention levels by the second follow-up (most obviously for a close relative with cancer, *Figure 25)*.

Risk

Table 19 summarises women's perceptions of their own risk of breast cancer at baseline. Within each trial, women in each arm were equally likely to perceive themselves at elevated (higher than population) risk, although Wales participants overall were more likely to view themselves as elevated risk than Grampian participants. Within the group perceiving themselves at elevated risk in the Grampian trial, more intervention than control group women considered themselves to be at highest risk.

The lifetime risk of breast cancer for participants, allocated after the counselling episode at the cancer genetics clinic, is shown in *Table 20*. In the Grampian trial, women in the intervention group were significantly more likely than those in the control group to be judged as at elevated (higher than population) risk, whereas the converse was observed for the Wales trial (although only just statistically significant).

An important outcome of counselling is an accurate perception of real risk. This was assessed by comparing the perceptions of women after counselling with their actual risk. Women whose perceptions matched the assessed risk were considered 'concordant' and those whose did not, 'non-concordant'.

Table 21 shows slight, non-significant, baseline differences between intervention and control groups in both trials. Concordance was similar between the groups at follow-up, with no statistically significant differences detected at the 5% significance level. Equivalence limits were not specified a priori, so it cannot be stated that concordance was equivalent between the groups. At least one-third of study women continued to have risk perceptions non-concordant with assessed risk.

Acceptability to patients

Figures 29–31 suggest that the majority of women had their expectations met regarding the type of information that they wanted on breast cancer causes and risks. Few differences were observed between intervention and control groups in each trial. *Figure 32* shows data relating specifically to information about genetic tests. Although the clear majority of women still agreed or strongly agreed that they had been given the kind of information they wanted, the proportion (around 87–93%) was lower than for the other questions. Clear differences were apparent in responses from Grampian trial participants, but not from Wales participants, Grampian intervention participants apparently being more likely to agree or strongly agree than control participants.

Figures 33–39 summarise women's satisfaction with the processes of care. High levels of satisfaction were observed across all questions asked, for both trials. No differences were detected between intervention and control groups in either trial.

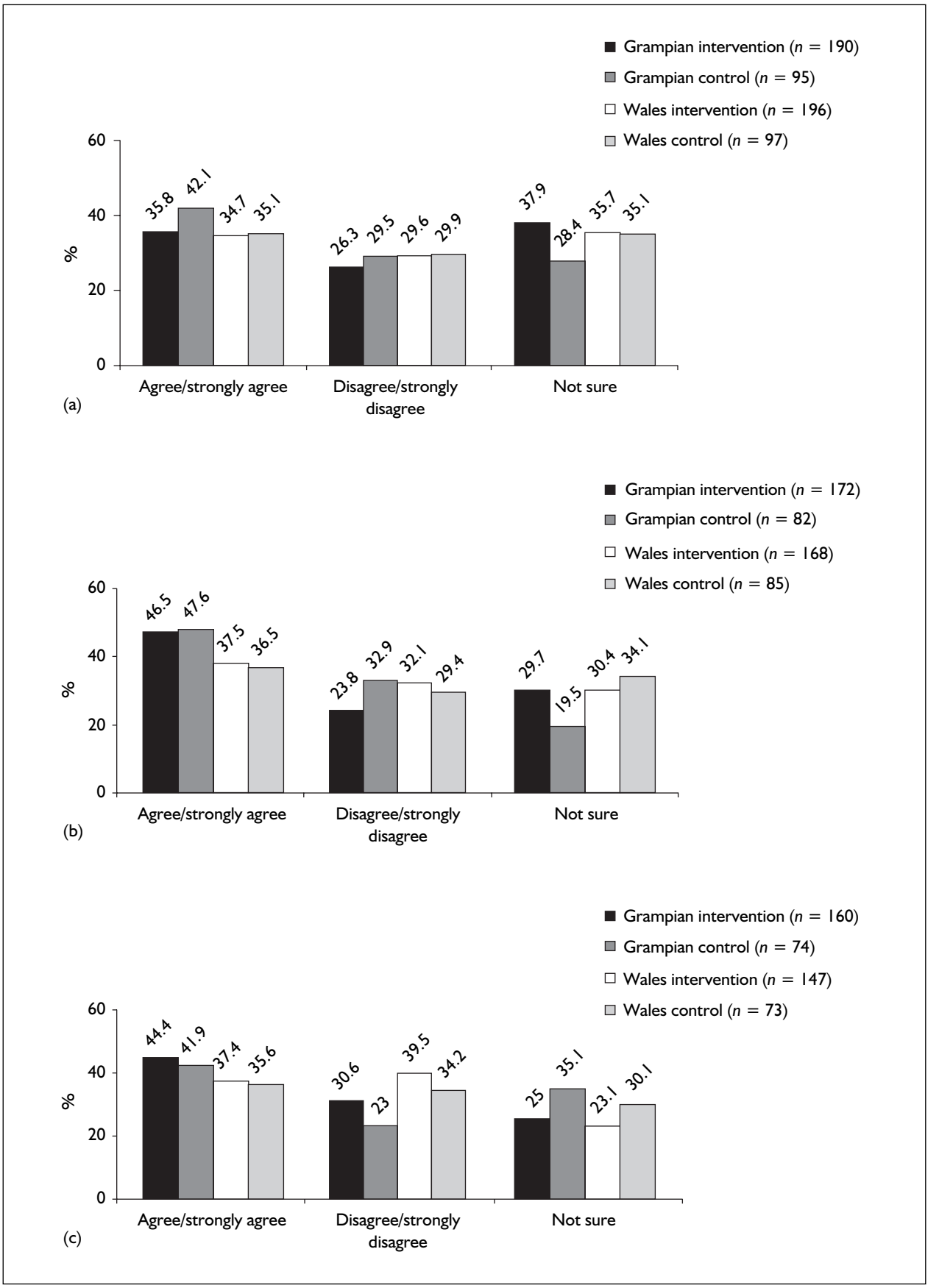

FIGURE 24 *Responses to the statement: 'Stress is a major cause of breast cancer'. (a) Baseline; (b) FU1; (c) FU2. Intervention vs control: (b)* p = *0.14 (Grampian),* p = *0.82 (Wales); (c)* p = *0.22 (Grampian),* p = *0.51 (Wales) (χ^2 test).*

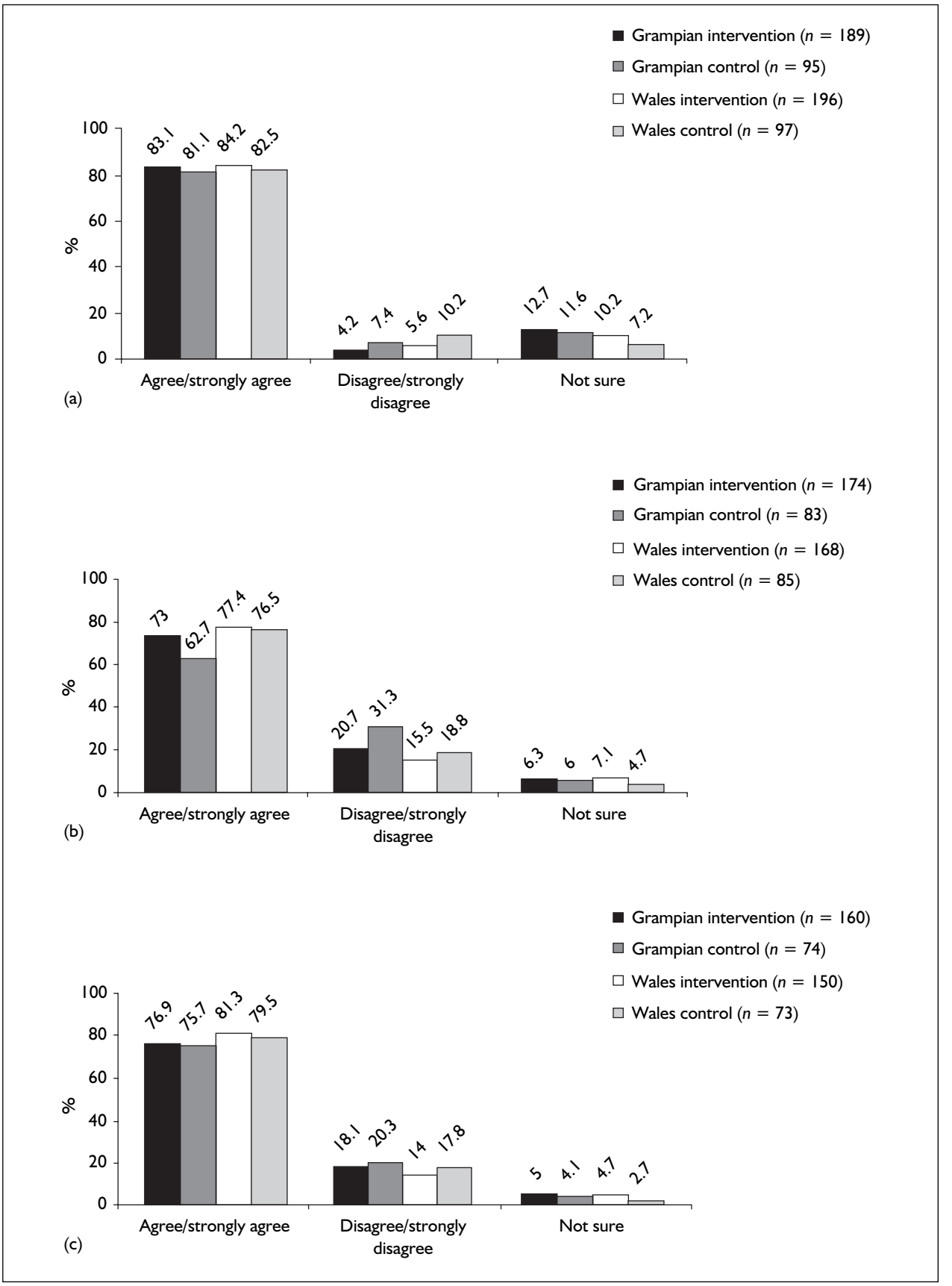

FIGURE 25 *Responses to the statement: 'Having one close relative with breast cancer always increases your risk considerably'. (a) Baseline; (b) FU1; (c) FU2. Intervention vs control: (b)* p = *0.17 (Grampian),* p = *0.63 (Wales); (c)* p = *0.89 (Grampian),* p = *0.63 (Wales) (χ^2 test).*

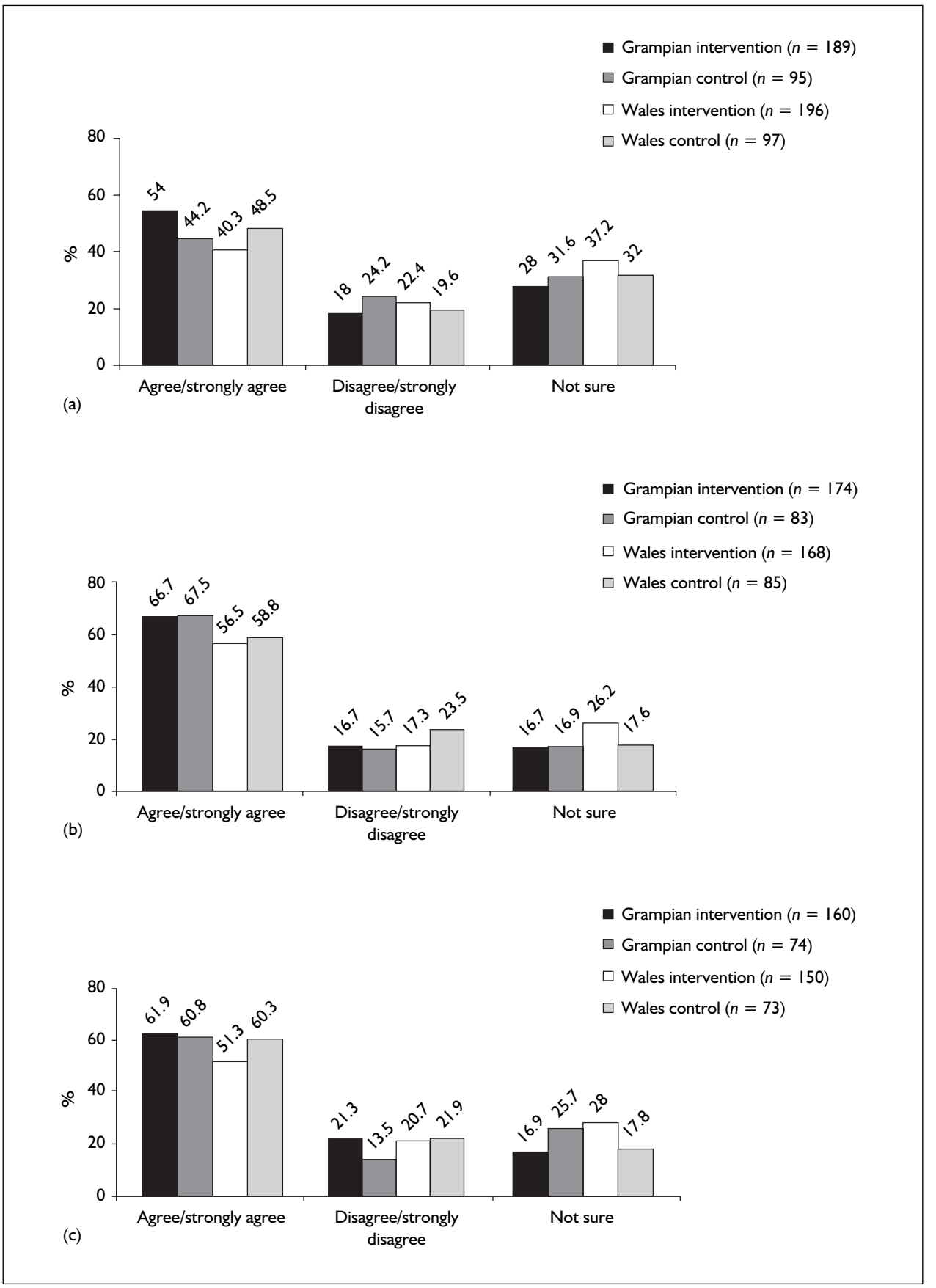

FIGURE 26 *Responses to the statement: 'A healthy diet can prevent breast cancer'. (a) Baseline; (b) FU1; (c) FU2. Intervention vs control: (b)* p = *0.98 (Grampian),* p = *0.23 (Wales); (c)* p = *0.16 (Grampian),* p = *0.24 (Wales) (χ^2 test).*

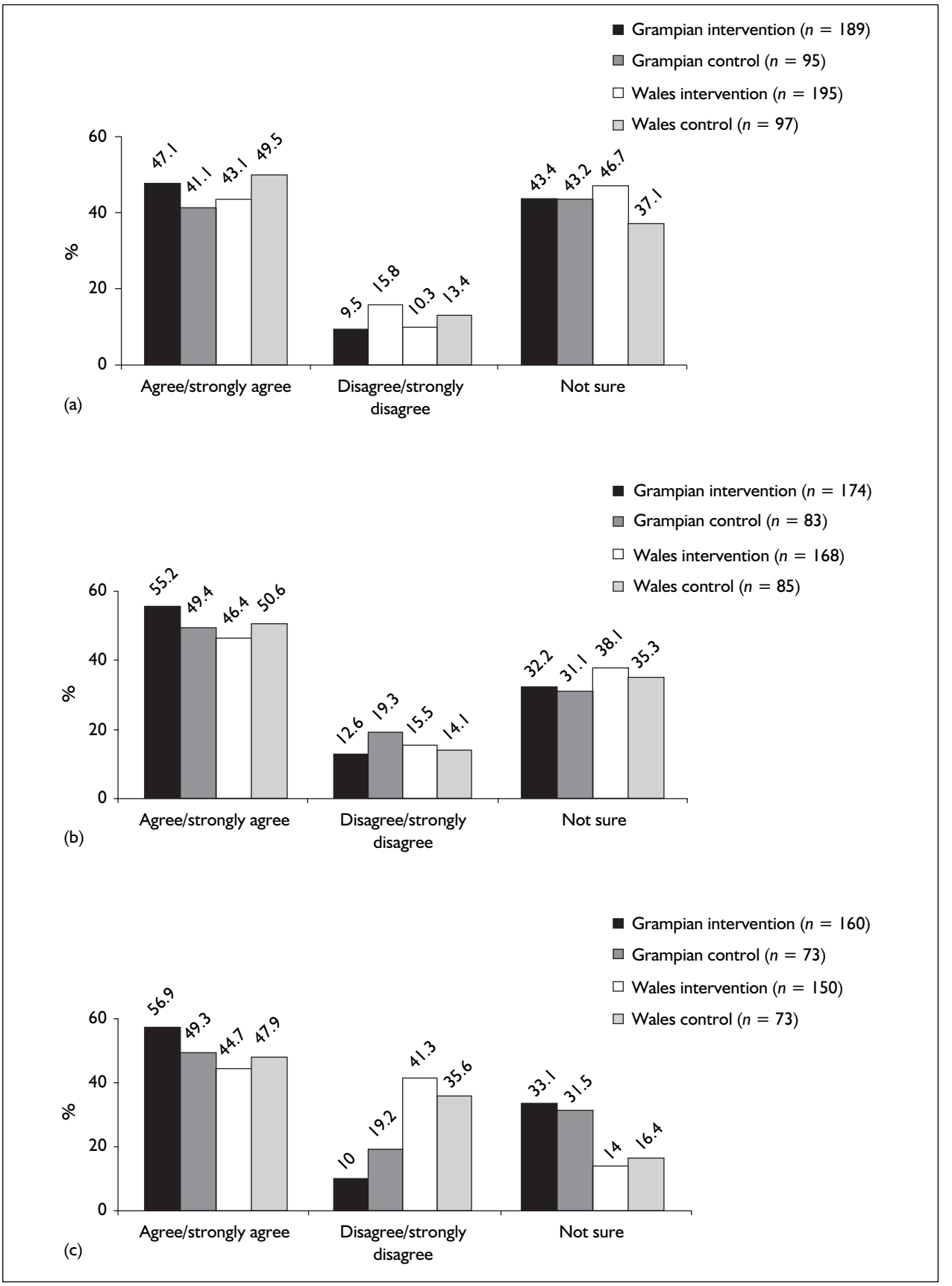

FIGURE 27 *Responses to the statement: 'Oral contraceptives can significantly increase the risk of breast cancer'. (a) Baseline; (b) FU1; (c) FU2. Intervention vs control: (b)* p = *0.36 (Grampian),* p = *0.82 (Wales); (c)* p = *0.15 (Grampian),* p = *0.70 (Wales) (χ^2 test).*

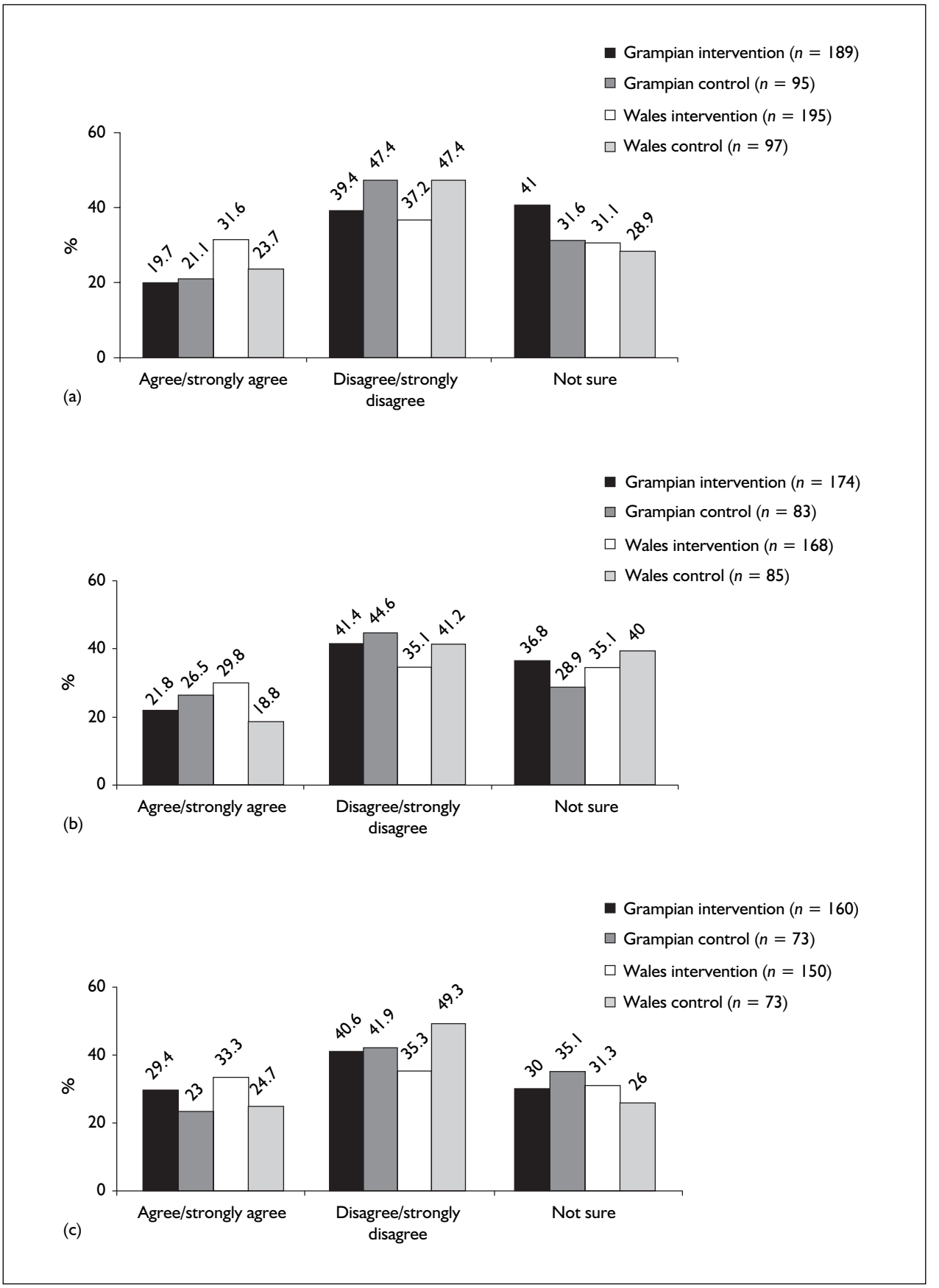

FIGURE 28 *Responses to the statement: 'Minor injury to the breast can cause breast cancer'. (a) Baseline; (b) FU1; (c) FU2. Intervention vs control: (b)* p = *0.43 (Grampian),* p = *0.17 (Wales); (c)* p = *0.55 (Grampian),* p = *0.13 (Wales) (χ^2 test).*

TABLE 19 *Baseline risk perception,* n *(%)*

	Grampian		Wales	
	Intervention (*n* = 181)	**Control (*n* = 91)**	**Intervention (*n* = 179)**	**Control (*n* = 90)**
Low	51 (28.2)	26 (28.6)	30 (16.8)	14 (15.5)
Elevated	130 (71.8)	65 (71.4)	149 (83.2)	76 (84.4)
High	40 (22.1)	15 (15.5)	55 (30.7)	27 (30.0)
Moderate	90 (49.7)	50 (54.9)	94 (52.5)	49 (54.4)

TABLE 20 *Final risk assessed at clinic,* n *(%)*

	Grampian			Wales		
Measure	**Intervention (*n* = 191)[a]**	**Control (*n* = 95)[b]**	**RR (95% CI)**	**Intervention (*n* = 197)[c]**	**Control (*n* = 100)[d]**	**RR (95% CI)**
Low	19 (9.9)	21 (22.1)	1.0	52 (26.4)	16 (16.0)	1.0
Elevated	172 (90.0)	74 (77.9)	1.16	145 (73.6)	84 (84.0)	0.88
High	55 (28.8)	25 (26.3)	(1.03 to 1.30)	57 (28.9)	32 (32.0)	(0.78 to 0.99)
Moderate	117 (61.3)	49 (51.6)		88 (44.7)	52 (52.0)	

Patients previously affected by breast cancer are included.
[a] Four elevated, one low.
[b] One elevated.
[c] Four elevated, six low.
[d] Three elevated.

TABLE 21 *Concordance of perceived and actual risk at follow-up,* n *(%)*

	Grampian			Wales		
Concordant	**Intervention**	**Control**	**RR**	**Intervention**	**Control**	**RR**
Baseline	(*n* = 181)	(*n* = 91)	(95% CI)	(*n* = 179)	(*n* = 90)	(95% CI)
No	100 (55.2)	52 (57.1)	1.0	95 (53.1)	37 (41.1)	1.0
Yes	81 (44.7)	39 (42.9)	1.04 (0.78 to 1.39)	84 (46.9)	53 (58.9)	0.80 (0.63 to 1.00)
FU1	(*n* = 162)	(*n* = 78)		(*n* = 145)	(*n* = 79)	
No	82 (50.6)	34 (43.6)	1.0	55 (37.9)	31 (39.2)	1.0
Yes	80 (49.4)	44 (56.4)	0.87 (0.68 to 1.12)	90 (62.1)	48 (60.8)	1.02 (0.82 to 1.27)
FU2	(*n* = 148)	(*n* = 73)		(*n* = 129)	(*n* = 66)	
No	74 (50.0)	39 (53.4)	1.0	56 (43.4)	30 (45.5)	1.0
Yes	74 (50.0)	34 (46.6)	1.07 (0.80 to 1.44)	73 (56.6)	36 (54.5)	1.04 (0.79 to 1.35)

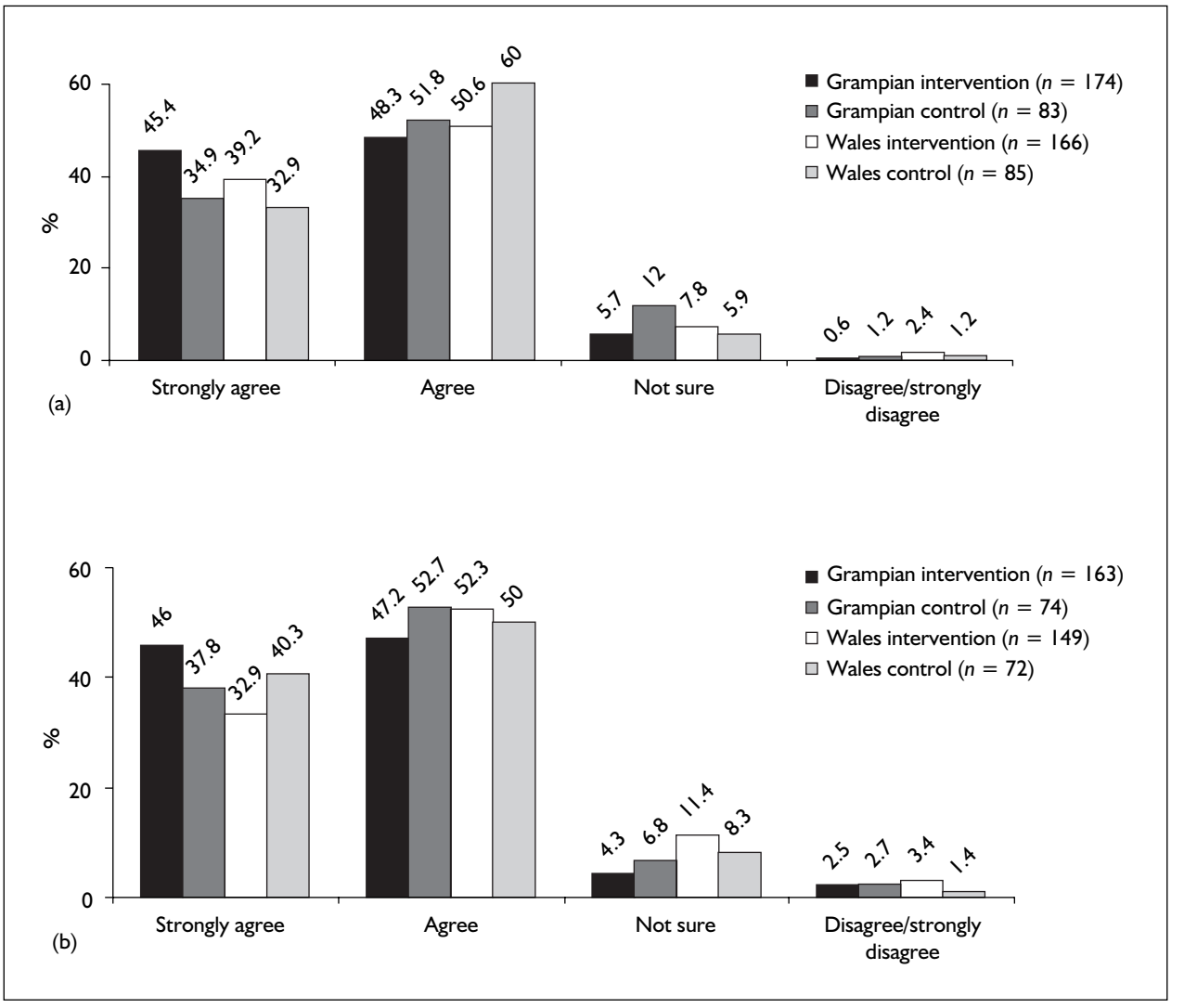

FIGURE 29 *Responses to the statement: 'I was given the kind of information I wanted about the causes of breast cancer'. (a) FU1; (b) FU2. Intervention vs control: (a)* p = *0.04 (Grampian),* p = *0.84 (Wales); (b)* p = *0.25 (Grampian),* p = *0.17 (Wales) (χ^2 test for trend).*

General practitioner outcomes

Seventy-four and 87 GPs in Grampian and Wales, respectively, referred at least one patient who was subsequently recruited to the trial, randomised to the intervention arm and participated (i.e. returned baseline questionnaire and/or attended her appointment). Of these, 68 (92%) in Grampian and 75 (86%) in Wales responded to the follow-up survey. *Figure 40* shows that over 80% of Grampian respondents and almost 70% of Wales respondents could not tell whether their patient had been seen in the intervention or control arm of the trial. Most of those who could distinguish one from the other offered favourable comments on the intervention (*Table 22*).

Almost all respondents (100% and 98.7% in Grampian and Wales, respectively) reported that they would be happy for future referred patients to be seen at the clinic by the genetic nurse counsellor. Overall, 62 (91%) Grampian and 67 (89%) Wales GP respondents reported that they were 'satisfied' or 'very satisfied' with the service provided by their regional cancer genetics centre (*Figure 41*). The main themes arising from an invitation to comment on any aspect of cancer genetics are summarised in *Table 23*. The most frequent comments related to patient satisfaction, concerns about nurse counsellor training, guidelines/protocols and communication.

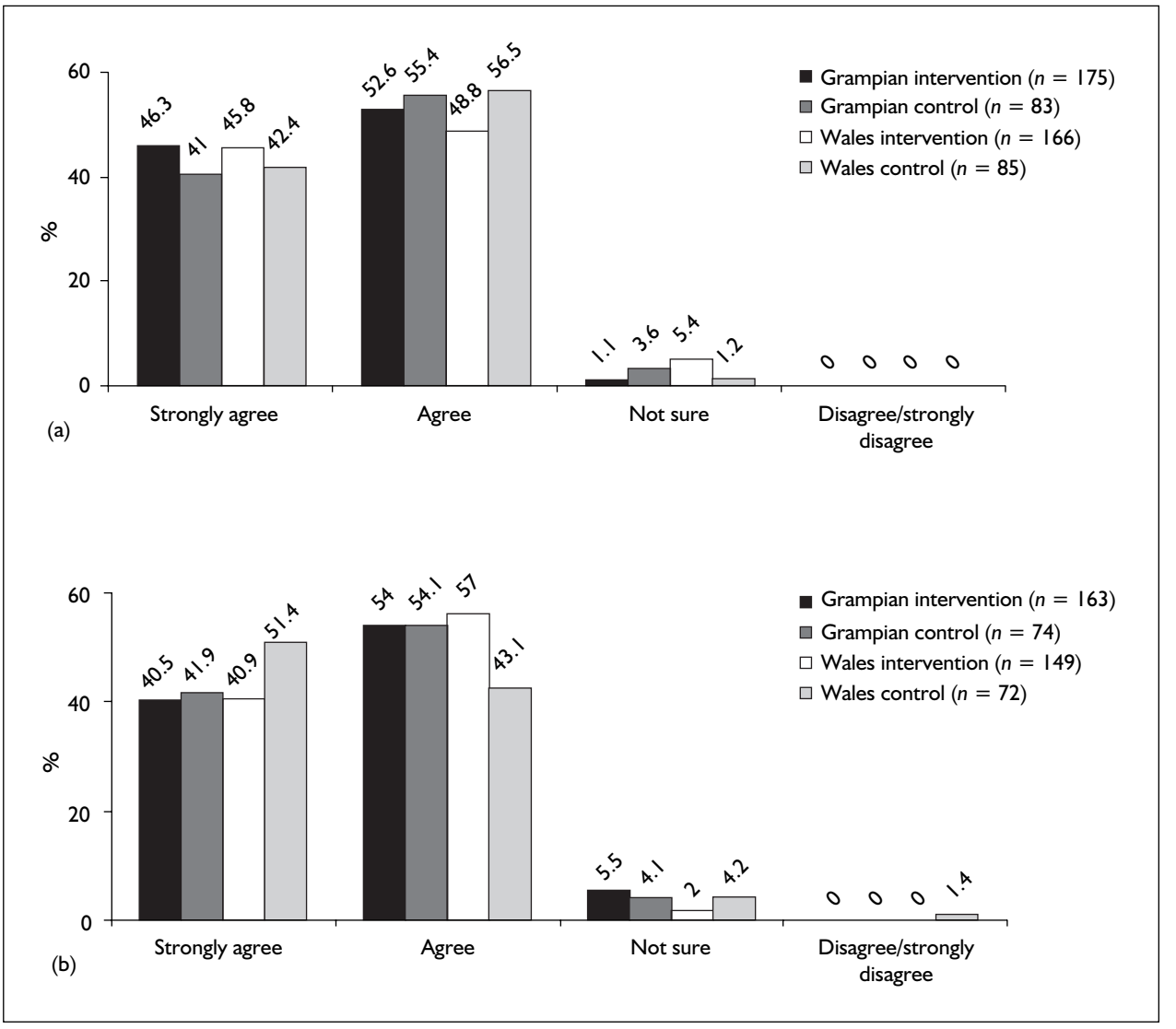

FIGURE 30 *Responses to the statement: 'I was given the kind of information I could understand about my risk of getting breast cancer'. (a) FU1; (b) FU2. Intervention vs control: (a)* p = *0.27 (Grampian),* p = *0.91 (Wales); (b)* p = *0.72 (Grampian),* p = *0.50 (Wales) (χ^2 test for trend).*

Planned subgroup analyses

Subgroup analysis by participants' perceived risk at baseline was conducted. Three subgroups were identified: those who perceived themselves to be at low risk, moderate risk or high risk at baseline (*Tables 24–27*). Although the analysis was preplanned, the study was not adequately powered for this subgroup analysis, and therefore the results should be interpreted with caution. In the Grampian trial, no tests for interaction achieved statistical significance and the mean values (adjusted for baseline) did not indicate any pattern of a differential effect of the intervention in the three subgroups. In Wales a possible differential effect of the intervention across the three subgroups was apparent. The data suggest that in women perceiving themselves to be at high risk, anxiety levels were lower in the intervention group following counselling. The analysis was by ITT, so this difference cannot be explained by those high-risk patients randomised to the intervention (nurse counsellor) group being seen in the control (clinical geneticist) group.

Comparison ITT and PP analyses for primary outcomes

The full results of the PP analysis are reported in Appendix 6, including CONSORT flowcharts

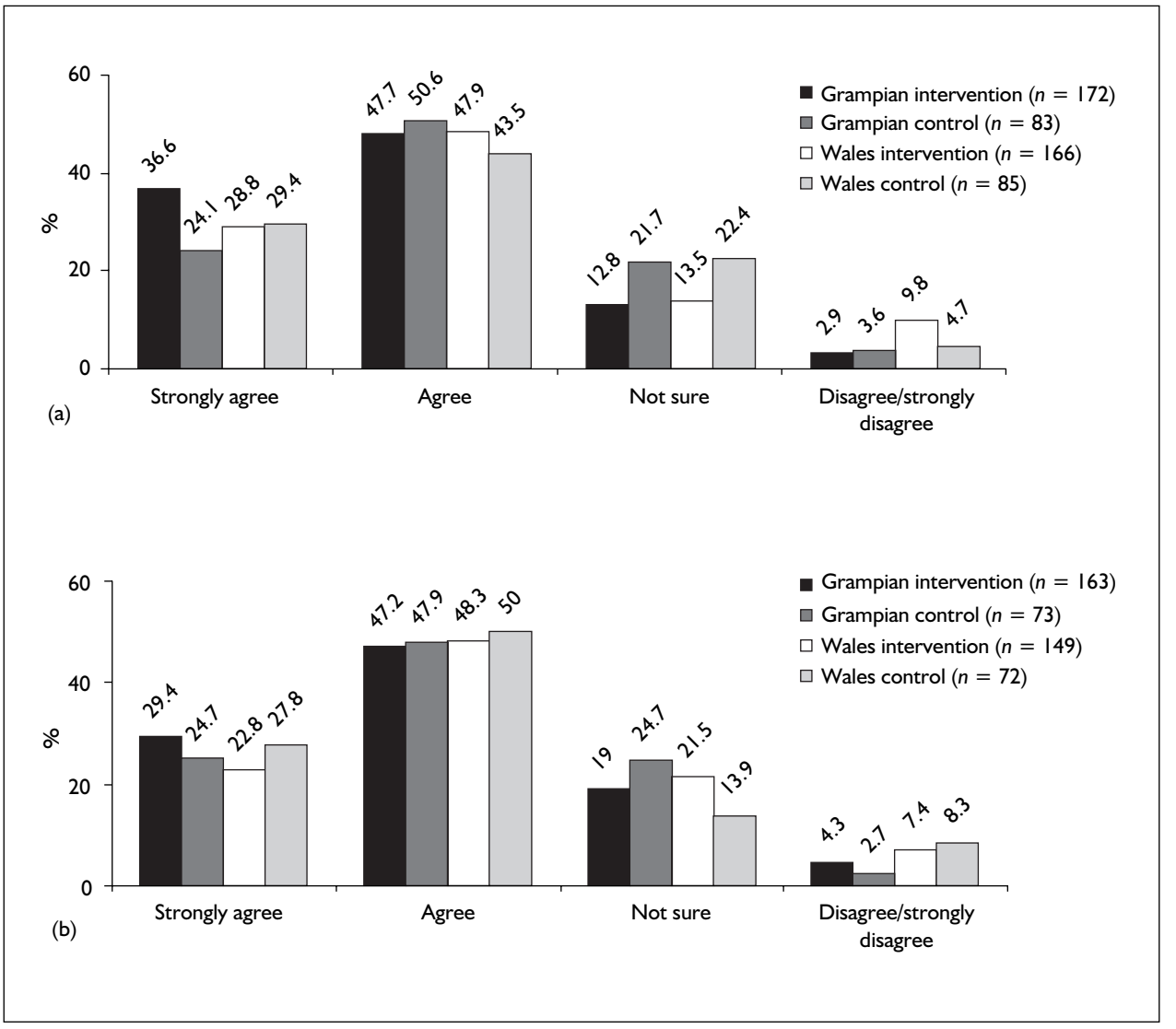

FIGURE 31 *Responses to the statement: 'I was given the kind of information I wanted about reducing my chances of getting breast cancer'. (a) FU1; (b) FU2. Intervention vs control: (a)* p = *0.03 (Grampian),* p = *0.87 (Wales); (b)* p = *0.52 (Grampian),* p = *0.39 (Wales) (χ^2 test for trend).*

showing the process of patients through the trial. *Table 28* compares the data from the ITT and PP (as-treated) analyses for the primary trial outcomes. Very few differences are observed between the analyses and, taken overall, they support the conclusion of equivalence between intervention and control as judged by the primary outcomes.

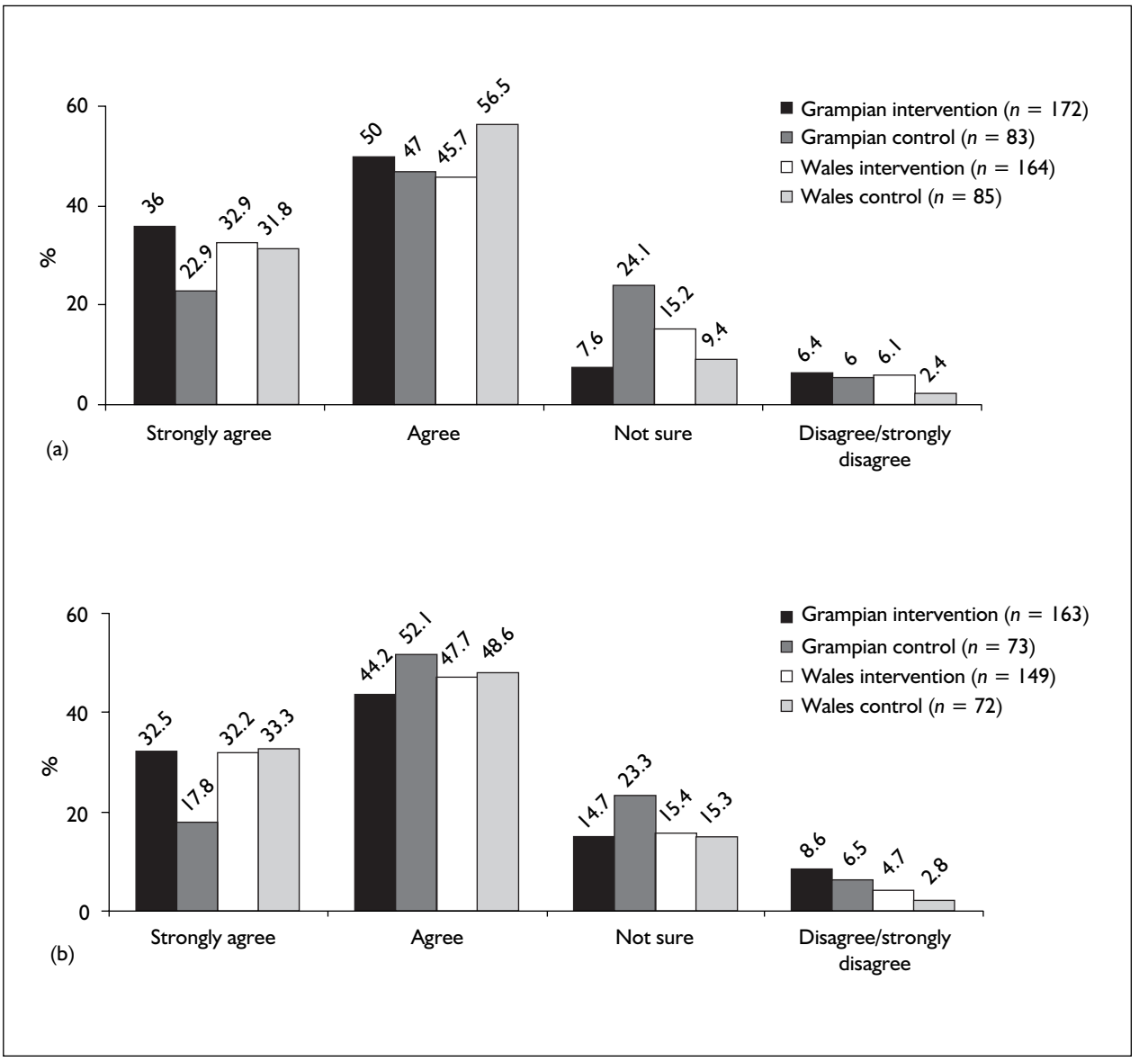

FIGURE 32 *Responses to the statement: 'I was given the kind of information I wanted about genetic tests for estimating my risk of breast cancer'. (a) FU1; (b) FU2. Intervention vs control: (a)* p = *0.009 (Grampian),* p = *0.26 (Wales); (b)* p = *0.11 (Grampian),* p = *0.66 (Wales) (χ^2 test for trend).*

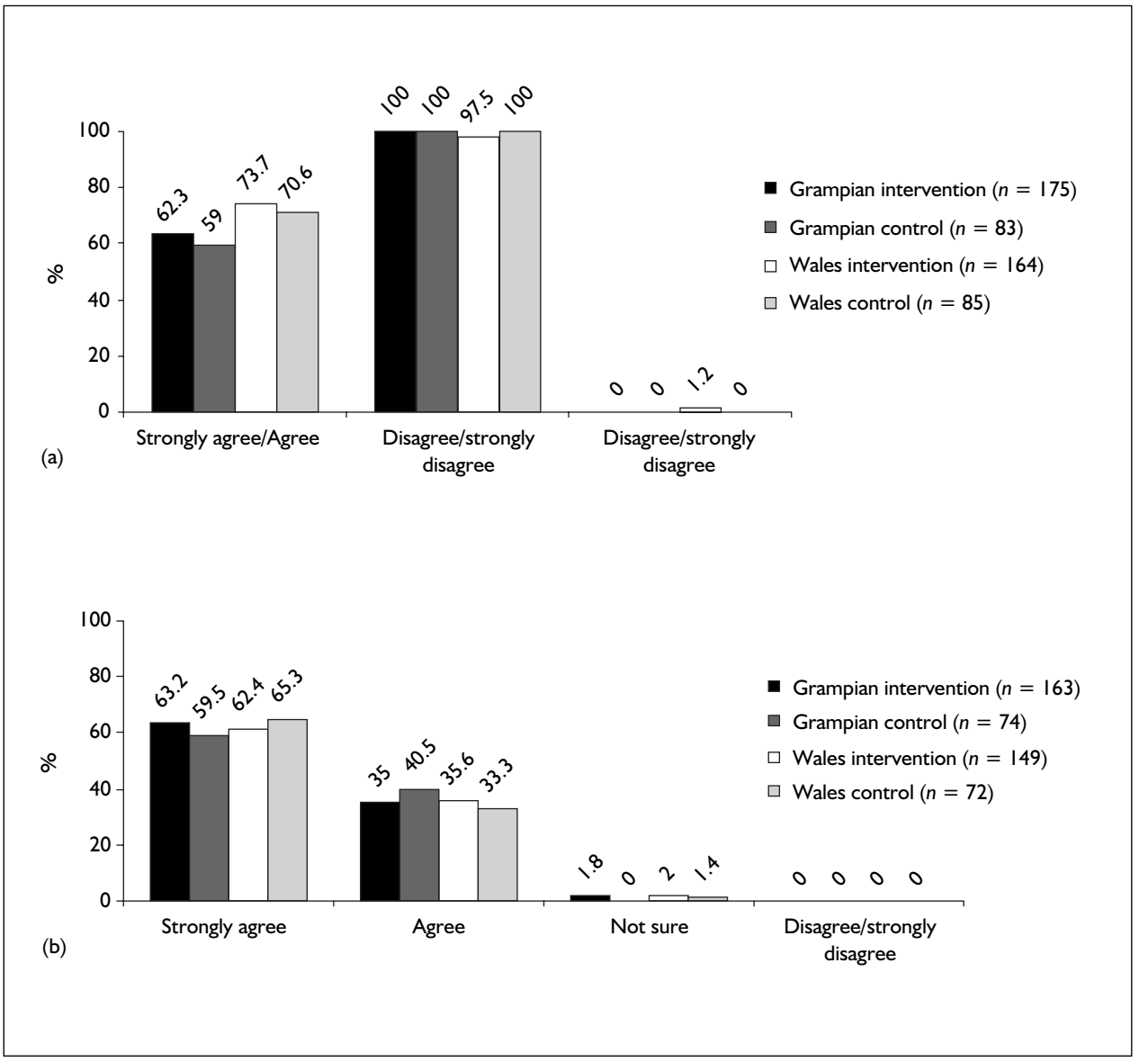

FIGURE 33 *Responses to the statement: 'The doctor/nurse listened to what I had to say'. (a) FU1; (b) FU2. Intervention vs control: (a)* p = *0.062 (Grampian),* p = *0.94 (Wales); (b)* p = *0.79 (Grampian),* p = *0.64 (Wales) (χ^2 test for trend).*

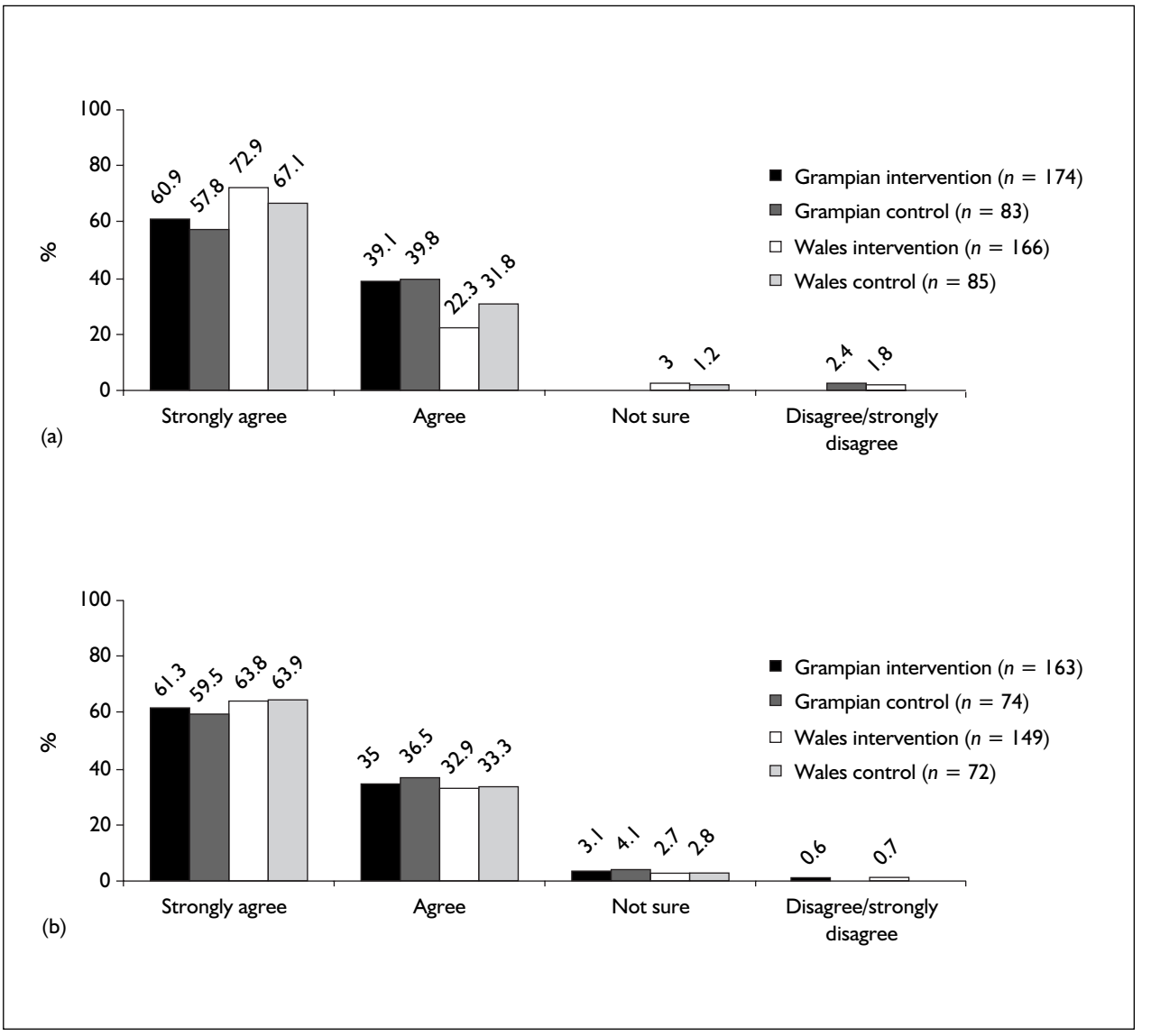

FIGURE 34 *Responses to the statement: 'The doctor/nurse took my concerns seriously'. (a) FU1; (b) FU2. Intervention vs control: (a)* p = *0.10 (Grampian),* p = *0.96 (Wales); (b)* p = *0.84 (Grampian),* p = *0.87 (Wales) (χ^2 test for trend).*

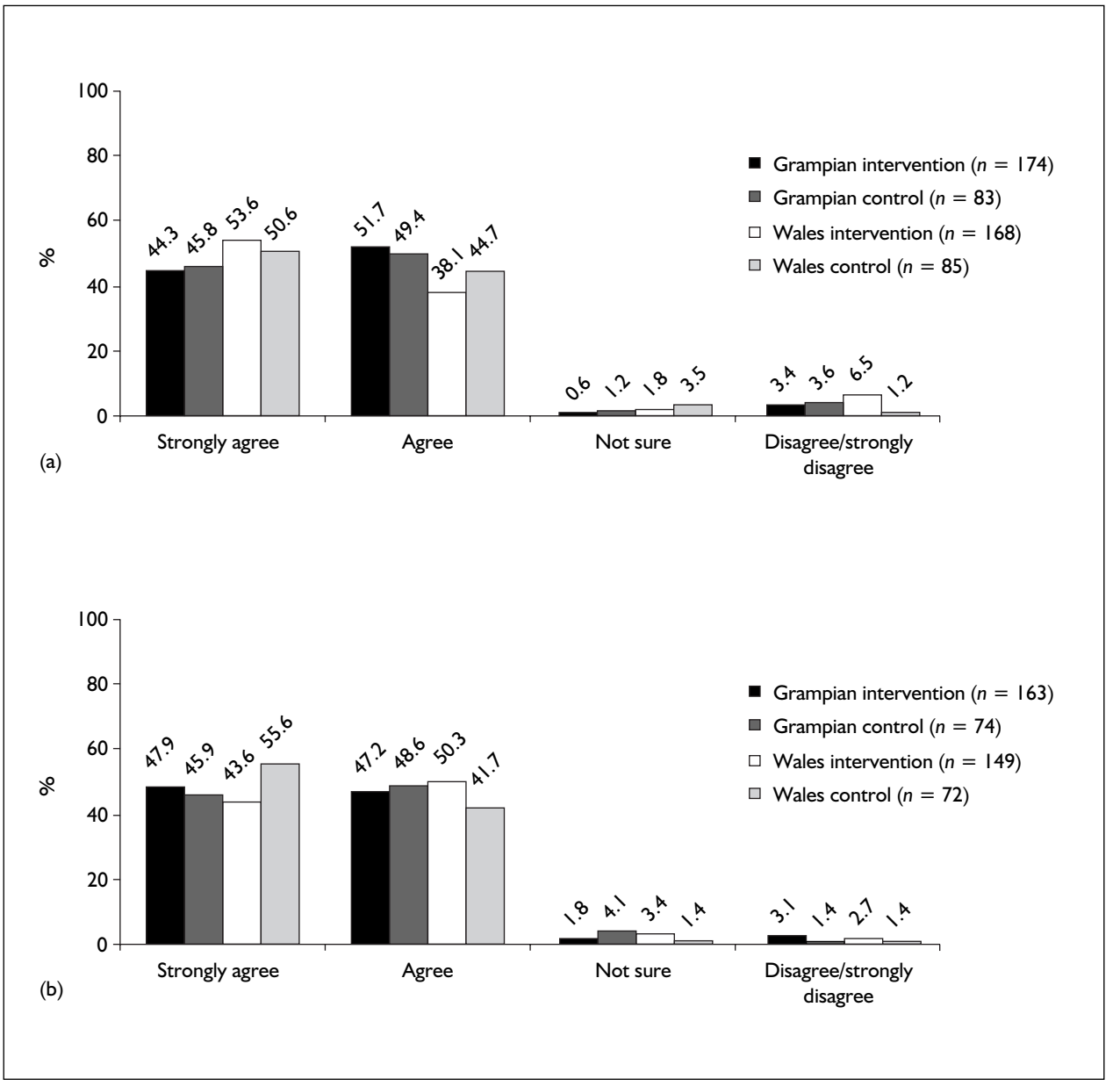

FIGURE 35 *Responses to the statement: 'I am satisfied with the time I had to wait until my first appointment with the doctor/nurse'. (a) FU1; (b) FU2. Intervention vs control: (a)* p = *0.95 (Grampian),* p = *0.55 (Wales); (b)* p = *0.83 (Grampian),* p = *0.08 (Wales) (χ^2 test for trend).*

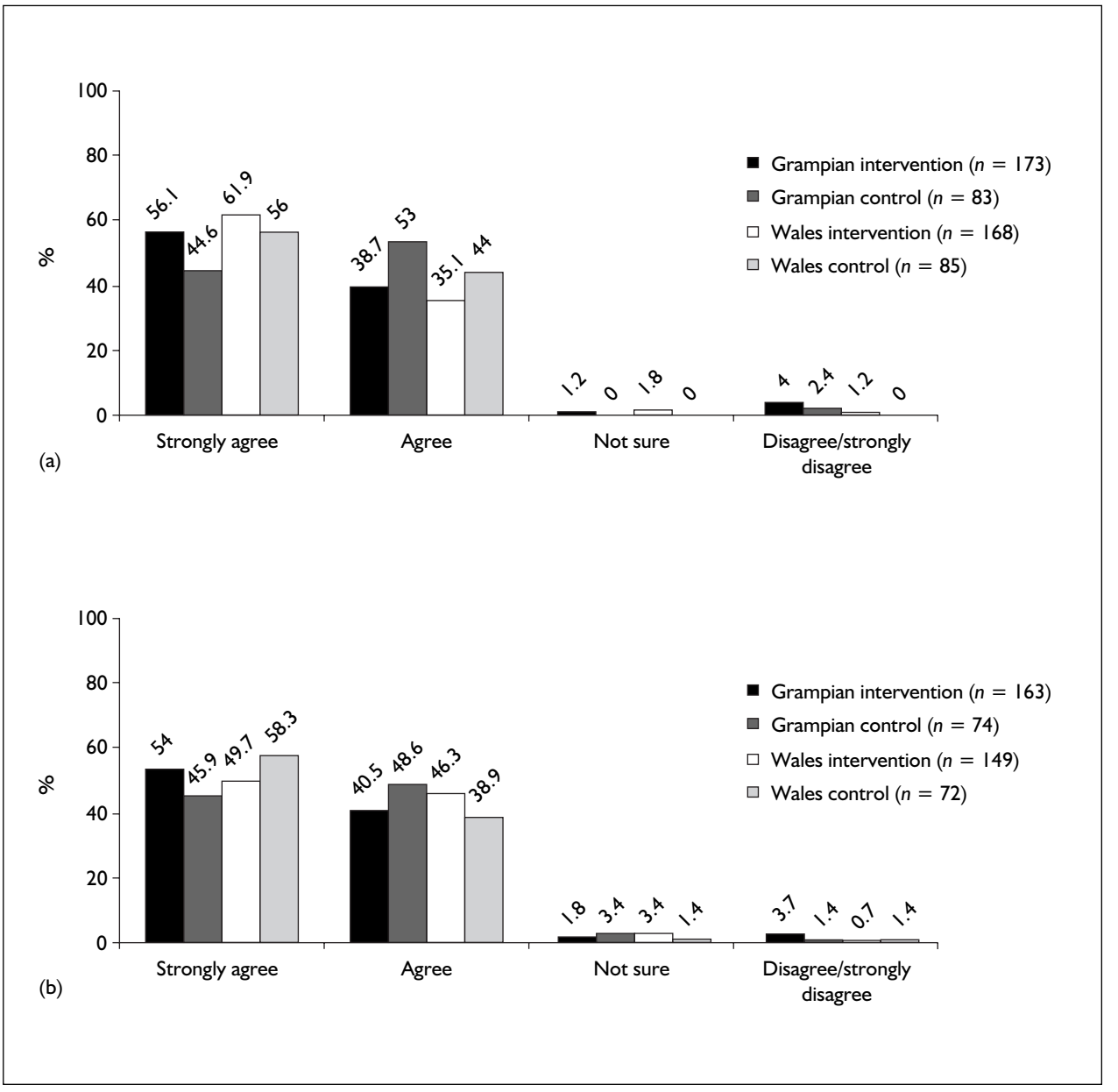

FIGURE 36 *Responses to the statement: 'I am satisfied with the length of time I had to wait in the waiting area before my appointment'. (a) FU1; (b) FU2. Intervention vs control: (a)* p = *0.44 (Grampian),* p = *0.81 (Wales); (b)* p = *0.56 (Grampian),* p = *0.29 (Wales) (χ^2 test for trend).*

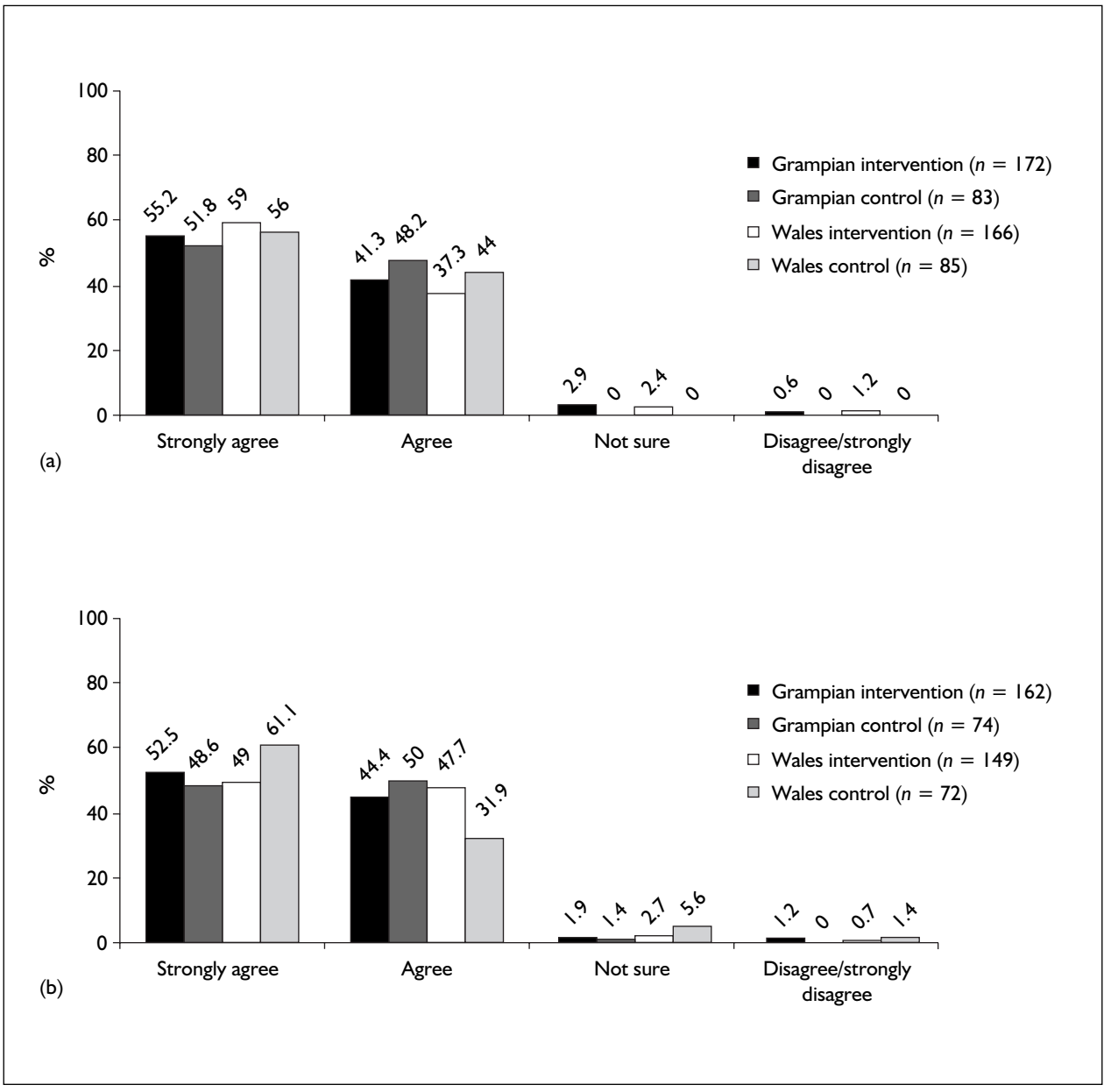

FIGURE 37 *Responses to the statement: 'I am satisfied with the way that other staff dealt with me (e.g. the secretary, nurses running the clinic)'. (a) FU1; (b) FU2. Intervention vs control: (a)* p = *0.93 (Grampian),* p = *0.82 (Wales); (b)* p = *0.92 (Grampian),* p = *0.38 (Wales) (χ^2 test for trend).*

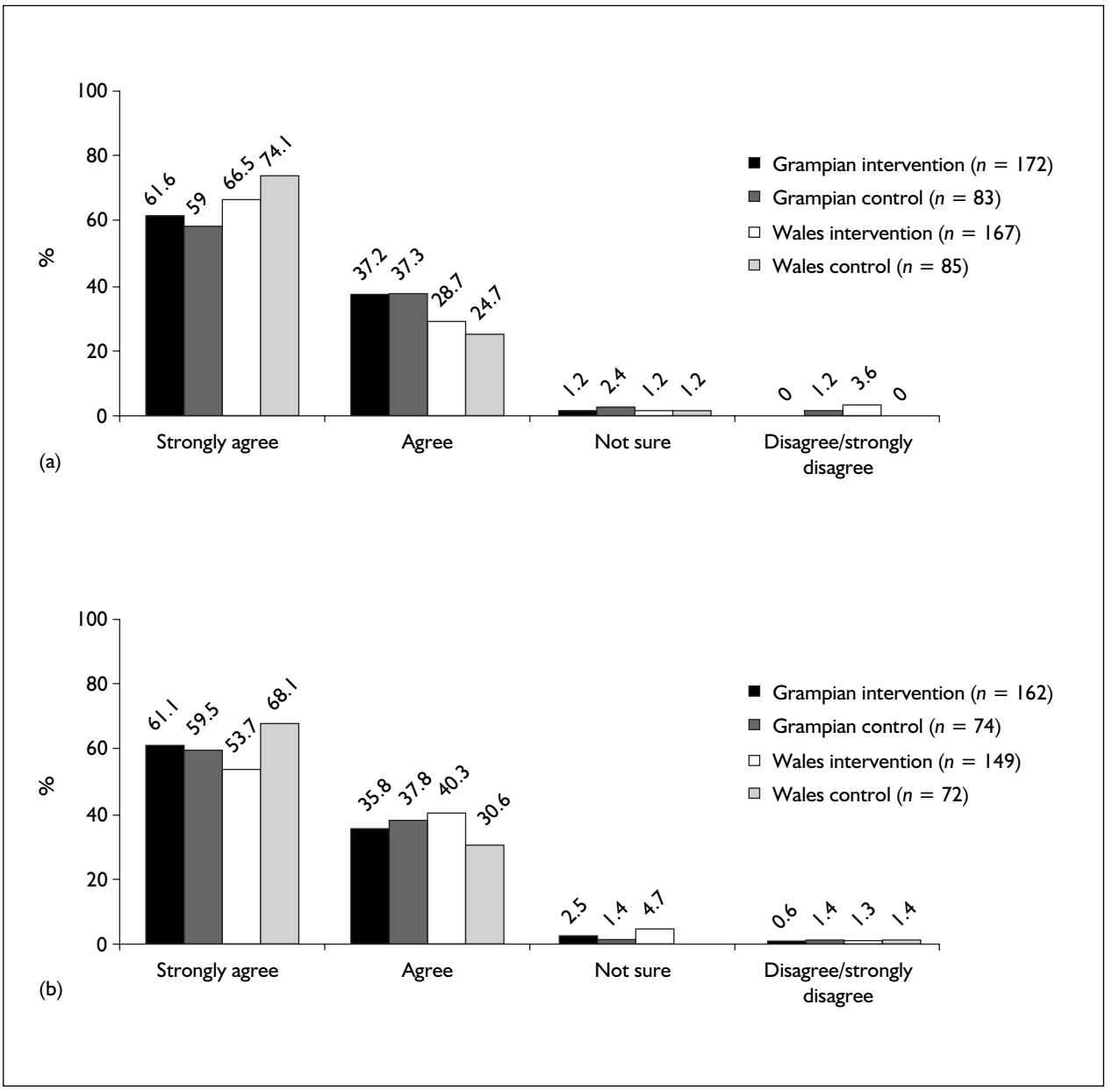

FIGURE 38 *Responses to the statement: 'Overall, the consultation was helpful'. (a) FU1; (b) FU2. Intervention vs control: (a)* p = *0.39 (Grampian),* p = *0.08 (Wales); (b)* p = *0.81 (Grampian),* p = *0.04 (Wales) (χ^2 test for trend).*

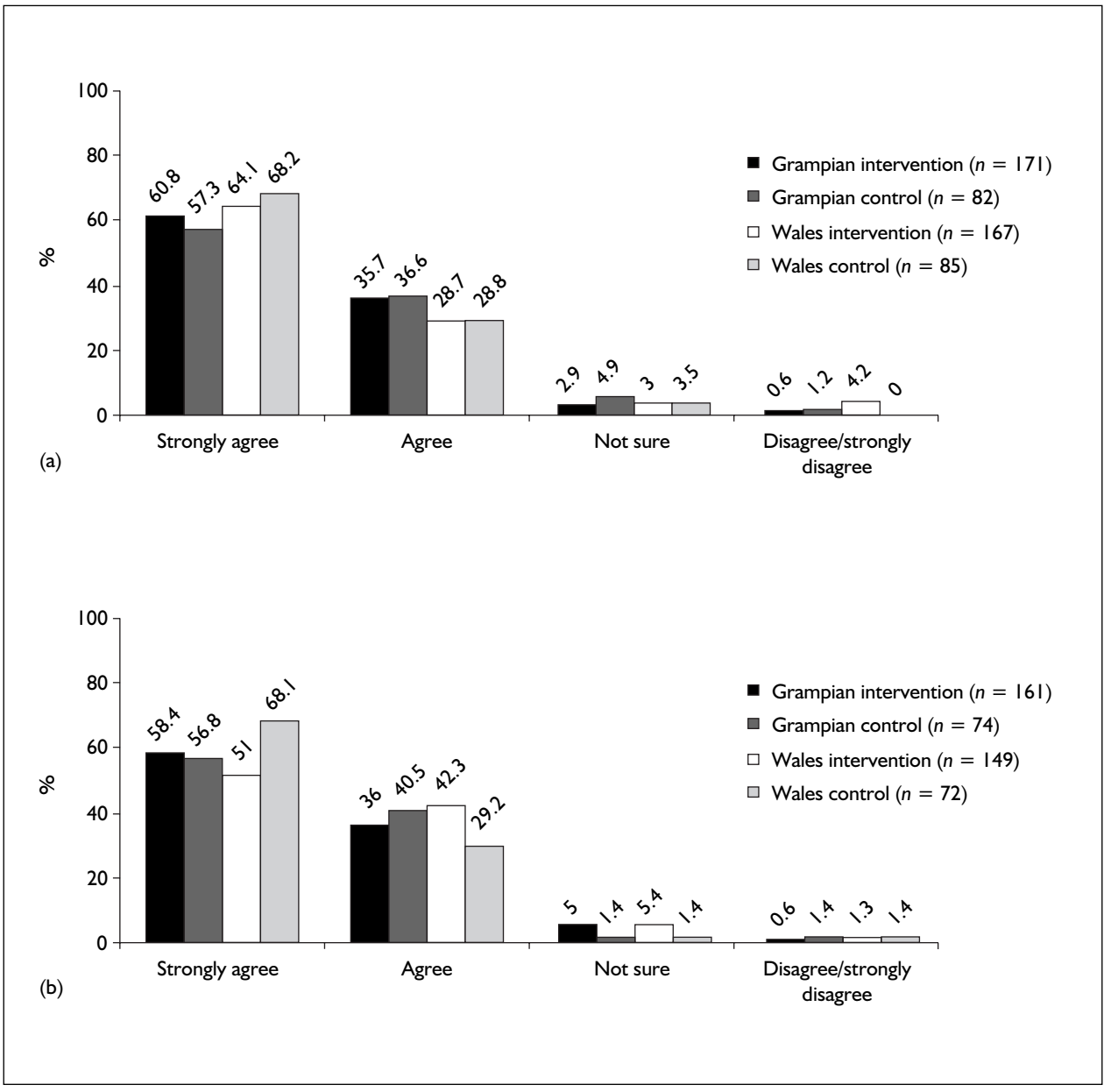

FIGURE 39 *Responses to the statement: 'Overall, I am satisfied with the consultation'. (a) FU1; (b) FU2. Intervention vs control: (a)* p = *0.41 (Grampian),* p = *0.19 (Wales); (b)* p = *0.95 (Grampian),* p = *0.024 (Wales) (χ^2 test for trend).*

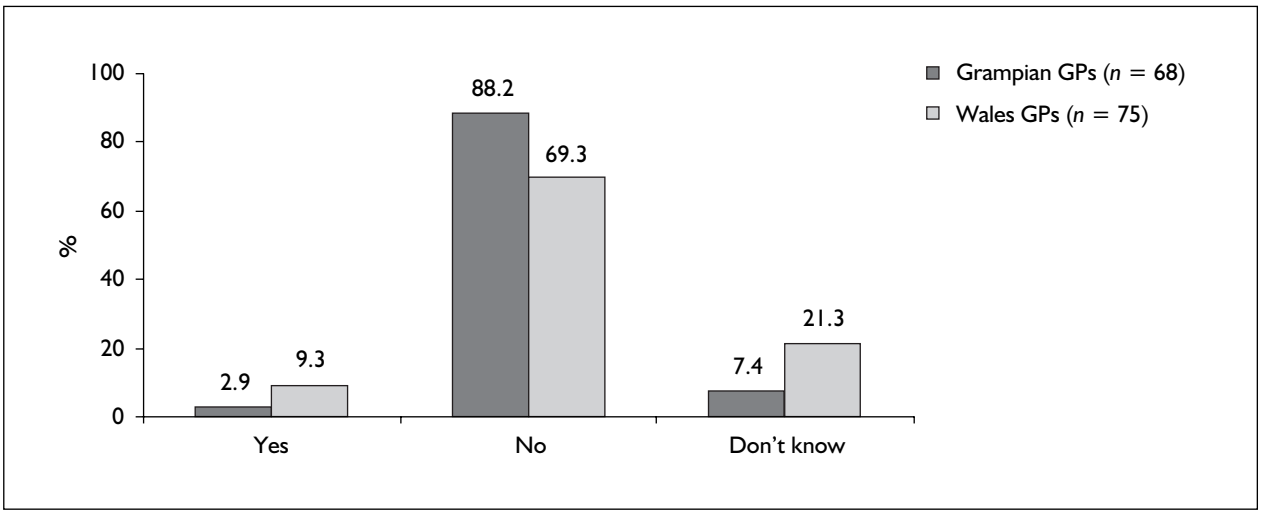

FIGURE 40 *Responses to the question: 'Did you notice any difference from the usual service provided by the Medical Genetics Department for your patient who was seen by the nurse specialist as part of the ARC study?'*

TABLE 22 *Open comments from GPs regarding differences between intervention and control*[a]

Theme	Summary of comments
Waiting times	Extra consultation required after initial nurse counsellor assessment Perception of shorter waiting time for appointment
Communication	Letters from nurse counsellors thorough, easy to understand
Patient satisfaction	Patients better informed, more relaxed, more satisfied, happier

[a] Full verbatim comments are listed in Appendix 5.

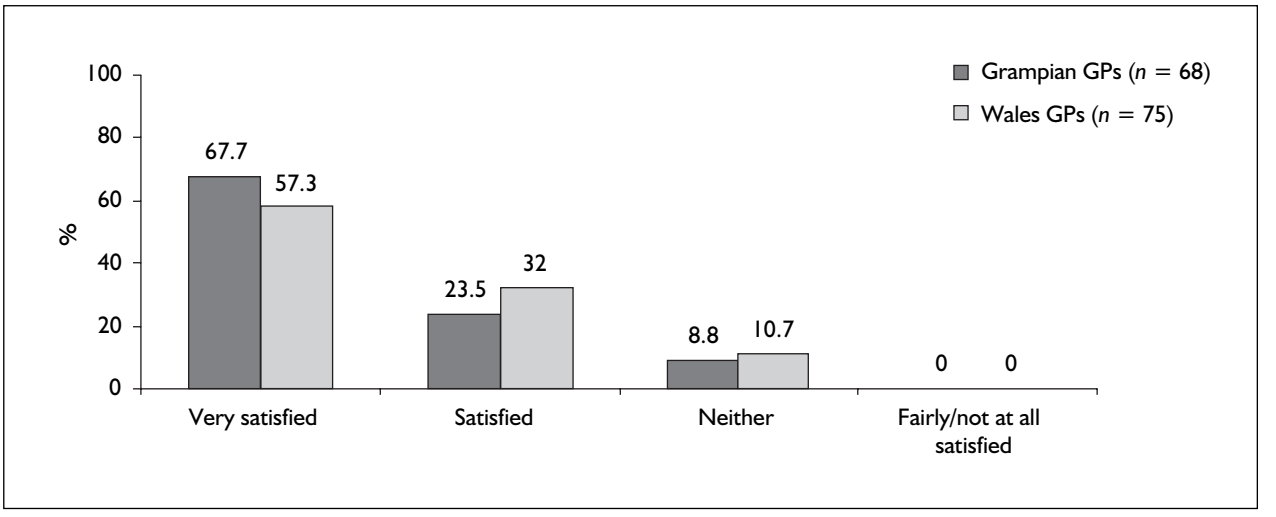

FIGURE 41 *Responses to the question: 'Overall, how would you rate your satisfaction with the service provided by the Medical Genetics Department?'*

TABLE 23 *Open comments from GPs*[a]

Theme	Summary of comments
Perception of patient satisfaction	Active, positive patient feedback Patient gets more information from nurse counsellor
Guidelines and training	So long as adequate training and working to protocols, should be no problem GPs would benefit from clear referral guidelines Nurse counsellors better trained than GPs
Communication	Letters clear, authoritative, easy to understand Letters to both patient and GP appreciated
Waiting times and relationship with clinic	Service has a good case for more resources Service approachable and user-friendly Service efficient and appropriate

[a] Full verbatim comments are listed in Appendix 5.

TABLE 24 *Demographic characteristics by perceived risk status at baseline for Grampian*

	Grampian[a]					
	Low		Moderate		High	
Characteristic	Intervention	Control	Intervention	Control	Intervention	Control
No. of patients, *n* (%)	51 (28.2)	26 (28.6)	90 (49.7)	50 (54.9)	40 (22.1)	15 (16.5)
Age (years), mean (SD)	45.7 (8.4)	44.7 (10.3)	40.0 (8.8)	40.0 (8.7)	34.5 (10.9)	39.1 (9.1)
Married/cohabiting, *n* (%)	39 (84.3)	21 (84.6)	74 (82.2)	36 (72.0)	39 (75.0)	13 (86.7)
With children, *n* (%)	46 (90.2)	20 (76.9)	74 (82.2)	37 (74.0)	28 (70.0)	13 (86.7)
Postsecondary education, *n* (%)	14 (27.5)	11 (42.3)	44 (48.9)	23 (46.0)	10 (25.0)	7 (46.7)

[a] Excludes eight participants already affected by breast cancer (seven intervention, one control).

TABLE 25 *Demographic characteristics by perceived risk status at baseline for Wales*

	Wales[a]					
	Low		Moderate		High	
Characteristic	Intervention	Control	Intervention	Control	Intervention	Control
No. of patients, *n* (%)	30 (16.8)	14 (15.6)	94 (52.5)	49 (54.4)	55 (30.7)	27 (30.0)
Age (years), mean (SD)	42.6 (10.4)	43.8 (8.9)	39.2 (9.7)	38.5 (9.3)	37.1 (9.9)	37.6 (8.9)
Married/cohabiting, *n* (%)	27 (90)	13 (92.9)	76 (80.9)	41 (83.8)	40 (72.7)	20 (74.1)
With children, *n* (%)	29 (96.7)	12 (85.7)	71 (75.5)	38 (77.6)	43 (78.2)	18 (66.7)
Postsecondary education, *n* (%)	8 (26.7)	4 (28.6)	40 (42.6)	26 (53.1)	22 (40.0)	10 (37.0)

[a] Excludes 13 participants already affected by breast cancer (10 intervention, three control).

TABLE 26 *Psychological characteristics by perceived risk status at baseline for Grampian, mean[a] (SD)*

Measure	Grampian						
	Low		Moderate		High		
	Intervention (n = 51)[b]	Control (n = 26)[b]	Intervention (n = 90)[b]	Control (n = 50)[b]	Intervention (n = 40)[b]	Control (n = 15)[b]	p-Value[c]
STAI							
Baseline	36.3	34.7	37.8	37.5	39.5	40.4	
FU1	36.5	34.2	36.9	35.4	34.8	39.4	0.28
FU2	35.5	33.4	36.1	32.2	36.2	35.9	0.66
HADS anxiety							
Baseline	6.0	5.3	6.4	6.2	8.6	9.6	
FU1	6.1	6.0	6.5	5.7	5.5	5.7	0.60
FU2	5.9	6.3	6.2	5.7	5.4	6.2	0.45
SF-36							
Role–emotional							
Baseline	80.0	92.3	80.7	82.3	75.2	64.4	
FU1	85.8	80.6	82.1	78.9	83.1	86.9	0.78
FU2	79.2	74.7	83.7	88.9	78.0	81.4	0.62[d]
Mental health							
Baseline	71.7	79.2	72.4	71.5	64.5	65.3	
FU1	73.0	73.3	72.5	71.6	74.2	71.6	0.87
FU2	72.0	73.5	73.3	76.0	73.6	74.4	0.93

[a] FU1 and FU2 means are estimated from ANCOVA evaluated at mean baseline value.
[b] Number who completed baseline questionnaire.
[c] p-Values relate to interaction term in the ANCOVA model.
[d] Heterogeneity of variances: Levene's test, $p < 0.05$.

TABLE 27 *Psychological characteristics by perceived risk status at baseline for Wales, mean[a] (SD)*

Measure	Wales						
	Low		Moderate		High		
	Intervention (n = 30)[b]	Control (n = 14)[b]	Intervention (n = 94)[b]	Control (n = 49)[b]	Intervention (n = 55)[b]	Control (n = 27)[b]	p-Value[c]
STAI							
Baseline	39.5	35.5	38.3	38.1	44.2	45.7	
FU1	35.3	41.8	38.4	36.4	38.1	42.3	0.08
FU2	42.0	42.5	37.7	34.1	38.4	45.1	0.05
HADS anxiety							
Baseline	7.3	6.6	7.5	6.7	9.3	8.8	
FU1	7.0	7.5	6.8	6.4	7.1	8.7	0.20[d]
FU2	8.3	5.8	7.1	6.2	7.3	8.4	0.10
SF-36							
Role–emotional							
Baseline	82.7	66.7	78.9	75.5	71.0	61.3	
FU1	67.5	71.2	78.1	84.3	75.0	55.7	0.08[d]
FU2	73.7	66.4	81.4	88.7	66.5	57.0	0.31[d]
Mental health							
Baseline	67.5	65.1	70.1	71.7	63.4	61.3	
FU1	70.4	71.8	67.8	71.4	69.9	59.2	0.11
FU2	63.6	67.3	68.8	72.8	65.6	56.3	0.04[d]

[a] FU1 and FU2 means are estimated from ANCOVA evaluated at mean baseline value.
[b] Number who completed baseline questionnaire.
[c] p-Values relate to interaction term in the ANCOVA model.
[d] Heterogeneity of variances: Levene's test, $p < 0.05$.

TABLE 28 *Comparison of ITT and PP analyses*

Outcome	Equivalence limit	Trial		ITT analysis		PP analysis	
				95% CI[a]	Equivalence	95% CI[a]	Equivalence
STAI	±4.0	Grampian	FU1	–2.1 to 3.7	'Yes'	–3.6 to 2.2	'Yes'
			FU2	–0.2 to 5.9	'Likely'	–1.0 to 4.9	'Likely'
	±4.0	Wales	FU1	–4.5 to 1.5	'Likely'	–4.0 to 2.0	'Yes'
			FU2	–2.9 to 4.1	'Likely'	–3.5 to 3.4	'Yes'
HADS anxiety	±1.4	Grampian	FU1	–0.4 to 1.3	'Yes'	–0.6 to 1.0	'Yes'
			FU2	–0.7 to 1.0	'Yes'	–0.9 to 0.8	'Yes'
	±1.5	Wales	FU1	–1.3 to 0.5	'Yes'	–1.2 to 0.6	'Yes'
			FU2	–0.6 to 1.5	'Yes'	–0.3 to 1.7	'Uncertain'
HADS depression	±1.2	Grampian	FU1	–0.4 to1.0	'Yes'	–0.6 to 0.8	'Yes'
			FU2	–0.5 to1.0	'Yes'	–0.7 to 0.7	'Yes'
	±1.2	Wales	FU1	–1.0 to 0.5	'Yes'	–0.6 to 0.9	'Yes'
			FU2	–0.4 to 1.5	'Uncertain'	–0.2 to 1.7	'Uncertain'
SF36 role–emotional	±11.4	Grampian	FU1	–6.3 to 10.1	'Yes'	–3.1 to 13.0	'Uncertain'
			FU2	–11.0 to 5.9	'Yes'	–9.3 to 7.3	'Yes'
	±13.1	Wales	FU1	–6.9 to 12.7	'Yes'	–10.1 to 9.3	'Yes'
			FU2	–9.4 to 10.5	'Yes'	–12.3 to 7.4	'Yes'
SF36 mental health	±6.0	Grampian	FU1	–2.9 to 4.1	'Yes'	–2.3 to 4.5	'Yes'
			FU2	–6.5 to 1.2	'Uncertain'	–5.4 to 2.2	'Yes'
	±6.3	Wales	FU1	–2.7 to 5.2	'Yes'	–3.0 to 4.8	'Yes'
			FU2	–4.2 to 4.8	'Yes'	–5.4 to 3.4	'Yes'

[a] Adjusted for baseline.

Chapter 10

Nurse counsellor trial: economic evaluation

Introduction

The overall approach taken for the economic evaluation of the nurse counsellor trial was a cost-minimisation analysis (CMA). CMA aims to identify the lower cost alternative if an evaluation of two interventions reveals no difference in effects.[45] This approach was considered appropriate[105] in the context of the nurse counsellor trial, which was designed as an equivalence trial and appeared to demonstrate equivalence in effect between the two interventions. The main aim of the economic evaluation was, therefore, to produce a 'cost per counselling episode' per person allocated to each policy. A societal perspective was adopted, taking into account costs incurred by both the health service and patients.[106] Marginal costing was performed to provide information on the cost of an extra counselling appointment.

Methods

NHS unit costs

Four categories of NHS resource use were examined: staff, consumables, room and equipment. It was assumed that breast cancer genetic counselling consumed a similar level of resources to other forms of genetic counselling. From discussions with clinical staff, this appeared an appropriate assumption. Structured information on the use of health service resources was collected using questionnaires, and then local unit costs were applied to the resource information.

Staff

Staff costs were calculated by estimating the amount of time staff devoted to various activities associated with genetic counselling, classified here as 'direct' and 'indirect' counselling appointment time. Direct counselling time included the time spent with the patient during the outpatient clinic appointment. In the absence of time-allocation diaries, staff estimated that they allocated approximately 1 hour per patient during these clinic appointments. An additional hour was required for preparation work such as creating pedigrees, obtaining further family history information and letter writing or dictating. Indirect counselling appointment time largely comprised meetings, such as weekly clinic meetings, during which all genetics patients (not solely trial patients) were discussed; the annual throughput of patients in the genetics services was therefore used as a denominator in each centre. In both study centres, the nurse counsellor was required to meet a consultant geneticist to discuss patient cases and determine the need for any further counselling and/or management recommendations. This weekly time (30 minutes in Grampian and 1.5 hours in Wales) was added to the intervention arm. In the control arm in Grampian, three specialist registrars each met with a consultant geneticist for 20 minutes per month to discuss patient cases; in the Wales control arm the clinical assistant met with the consultant geneticist for approximately 1–2 hours each month.

Staff costs were valued using local unit costs where readily available, and national rates otherwise.[48] The midpoint of the salary scale for each grade of staff was used to reflect a 'replacement' aspect, and employer's on-costs (National Insurance and Superannuation) at 13% were included.

Consumables

Consumables such as paper, envelopes, printer toner and postage were measured by estimating the required amount of correspondence required for a typical patient. Local unit costs were then applied to the consumable resources required for a counselling appointment.

Rooms and equipment

For room and equipment costs it was assumed that both the intervention and control groups used a similar level of resources. Room costs included the capital cost of using the building and overheads in the outpatients department. Owing to difficulty interpreting building costs in Wales, Grampian costs were used as a proxy in the analysis for Wales. The size of the floor space used for counselling was first established and a local unit cost was then applied for an actual new hospital building in Grampian. An EAC was then calculated, automatically incorporating both the depreciation and opportunity cost aspects of the capital item, with the opportunity cost of capital

reflected in the discount rate.[45] A 6% discount rate was used for the EAC, as specified in the guidelines for conducting health technology assessments,[46] over a 50-year lifespan. Overheads are those costs shared by the entire hospital, such as heating, lighting and cleaning. Overheads were calculated by measuring the amount of time for which a consulting room was required and combining it with floor space, then this was valued using Grampian hospital finance data.

Equipment costs were included for networked computers (based on manufacturer's guidance), with an EAC performed at a 6% discount rate, over a 5-year lifespan, with additional maintenance costs for computing services included.

Cost per counselling episode

Once the unit cost per single counselling appointment had been estimated, the number of appointments for each patient during their counselling episode was derived from the trial database. This included appointments for patients who attended and those who failed to attend without cancellation. The latter group were included if they had already attended one appointment and missed the second, as the clinician or nurse would be waiting in the outpatients department and not easily able to perform alternative activities during this time. Therefore, these missed appointments, where the patient failed to attend, were assigned the same unit cost as derived above. The unit cost for a single appointment was multiplied by the number of appointments in each arm of the trial to examine whether there was any difference in the total cost of counselling care between the two groups. In Wales, all trial patients were only seen once, and thus the cost per counselling episode was fixed for all patients. In Grampian, where the number of appointments varied, the mean costs per counselling episode were compared across intervention and control groups using an independent *t*-test and the 95% confidence interval for the mean difference is presented.

Sensitivity analysis

Because assumptions had to be made about certain costs, and because the nurse counsellor intervention was new to both centres, a sensitivity analysis was performed on the health service cost data. This examined the effects of changing several assumptions, such as the grades of staff, the length of consultations, the amount of consultant supervision required by the nurse counsellors, and the discount rate and lifespan of equipment items.

Patient costs

A section on patient costs was included in the first follow-up questionnaire relating to patient clinic visits. It covered travel costs, the amount of time away from usual activities and what these activities were, and whether or not the women were accompanied to the clinic. Travel costs were valued using the average cost per mile suggested by the Automobile Association.[107] Patient time costs were valued according to national average wage rates, with time away from paid work being valued at £8.43 per hour for women.[47] Socio-economic questions on income level and number of adults and children in the household were also included.

Results

NHS costs

The unit cost results for the health service costing are presented in *Table 29*. All costs are presented in Sterling (£) for the year 2001. Staff costs include nursing and/or medical staff, and administrative staff. A more detailed breakdown of these staff costs is provided in *Tables 38* and *39* in Appendix 7.

The mean costs per counselling appointment were very similar for the control arms in both trials. For Grampian, the difference in marginal costs per single counselling appointment was £15.66 higher in the control than in the intervention arm; in Wales, the difference in marginal cost per counselling appointment was £10.89 higher in the intervention than in the control arm. Differences between the intervention and control arms across the two centres were determined entirely by staff costs, as other categories of cost were similar across the trial arms. Medical staff costs were different in the two control arms because the Grampian service employed doctors at higher grades (a combination of specialist registrar, staff grade and consultant) than the Wales service (a clinical assistant, supervised by a consultant). However, these differences were offset by the higher secretarial and administrative support costs in Wales than in Grampian. The difference in intervention arm costs, per counselling appointment, is accounted for by the difference in consultant supervision time for the nurse counsellor (30 minutes per week in Grampian and 1.5 hours in Wales).

Table 30 presents the total costs per counselling episode for each patient, which incorporate the actual number of appointments in the

TABLE 29 *Health service unit costs per counselling appointment*

	Grampian			Wales		
	Mean cost per appointment (£)		Difference in marginal costs (£)	Mean cost per appointment (£)		Difference in marginal costs (£)
	Intervention	Control		Intervention	Control	
Staff	63.26	78.92	–15.66	90.55	79.66	+10.89
Consumables	2.11	2.11	0	2.42	2.42	0
Rooms	26.59	26.59	0	26.59	26.59	0
Equipment	2.12	2.12	0	2.47	2.47	0
Total	94.08	109.74	–15.66	122.03	111.14	+10.89

TABLE 30 *Comparison of total costs per counselling episode*

Group	Grampian		Wales		
	Mean no. of randomised appointments	Mean total cost per patient (£)	Mean no. of randomised appointments	Mean total cost per patient (£)	Total cost difference (£) (Grampian – Wales)
Intervention	1.26 (range 1–4)	118.94	1	122.03	3.09
Control	1.18 (range 1–3)	129.17	1	111.14	18.03
Total cost difference (intervention – control)		–10.23		+10.89	

intervention and control groups. The mean cost per counselling episode in Grampian was £118.94 in the intervention group and £129.17 in the control group, a difference of £10.23 (95% CI –£1.69 to 22.15). The cost per counselling episode was higher for Grampian patients than per appointment, but not for Wales, as all patients were given one appointment only. Overall, the cost per counselling episode in the intervention arm was £3.09 lower in Grampian than in Wales, and the control arm was £18.03 higher in Grampian than in Wales.

Sensitivity analysis

The sensitivity analysis performed on the NHS unit costs indicated that the costs were sensitive to certain factors in both Grampian and Wales, and across each trial arm. These factors included the grades of staff in control and intervention arms, the level of supervision required for the nurse specialists and the length of outpatient counselling appointments, but not the choice of discount rate or lifespan of equipment items. The main results of the sensitivity analysis are discussed below. Further information and tabulated results for the sensitivity analysis can be found in *Tables 40–51* in Appendix 8.

Grades of medical staff

In Grampian, the control arm was particularly sensitive to changes in the grades of clinical staff providing counselling. Compared with other genetics services in the UK, Aberdeen employs doctors in relatively high grades. For example, if the consultant geneticists and associate specialists were covered by more of the other grades providing the counselling in Grampian, staff grades and specialist registrars, the unit cost per counselling episode would be reduced by £13.05 to £96.69 per patient. In contrast, Wales employed clinicians in lower grades (mainly a clinical assistant, sometimes a specialist registrar, with no direct consultant geneticist input for the first appointment). If Wales were to use consultant geneticists and increased specialist registrar time, this would increase the total unit costs for a counselling appointment in the control group to £118.47, a difference of £7.33.

Both centres employed a grade H nurse in the intervention arm. If a nurse of lesser grade were employed, it would reduce the cost of the counselling appointment, but additional supervision time might be required. However, this would be unlikely to alter total costs substantially.

Supervision required

In Wales, the nurse spent up to 1.5 hours per week with a consultant geneticist. It is likely that this time would be reduced as a nurse counsellor gains more experience (a learning effect). If the time were reduced to 30 minutes per week, similar to the supervision time in the Grampian trial, the total unit cost would be reduced by £17.06 to £104.97 per counselling appointment (compared with the estimate of £111.14 in the control group).

Length of consultation

The average length of time for a counselling appointment in both Grampian and Wales was 1 hour per patient. However, if a patient presented with a complicated history or clinical picture, this might increase the length of the consultation. In Grampian, increasing the consultation to 1.5 hours would increase the total cost per appointment in the intervention group by £30.06 to £124.14, and in the control group by £40.23 to £149.97 (difference £25.83). A similar adjustment in Wales would lead to an increase of £30.89 to £152.92 in the intervention group and £38.24 to £149.38 in the control group (difference £3.54). Conversely, if consultation times were shortened, for instance to 45 minutes, the total cost per appointment in Grampian would drop by £15.03 to £79.05 in the intervention group, and by £19.67 to £90.07 in the control group (difference £11.02). For Wales, the figures would fall by £15.44 to £106.59 (intervention group) and by £19.12 to £92.02 (control group).

Overall, the results of the sensitivity analysis highlight that there are several areas where changes in the total cost per appointment, and hence per episode, could occur. However, the length of a consultation is largely dependent on the patients and histories. Although it may be possible to alter the grades of clinical staff, this may affect other aspects of care or even patient outcomes, and these issues were not addressed in this study.

Patient costs

A response rate of 88% (255/289) was achieved for completed questionnaires in the Grampian trial and 85% (251/297) in the Wales trial for the patient cost component of the follow-up questionnaire.

Tables 52–54 in Appendix 9 present the results of the travel cost, time away from usual activity and socio-economic questions. In both centres the main mode of transport to a genetic counselling appointment was private car, 220/255 (87%) in Grampian and 225/251 (90%) in Wales. For those who travelled by car the average travel cost for a one-way journey was £23.70 and £14.81 in Grampian and Wales, respectively. The main form of usual activity was paid work, with the average time taken away from work being 226 minutes in Grampian and 227 minutes in Wales. For these women this led to a cost of £31.77 and £31.91 in Grampian and Wales respectively. With respect to socio-economic information, 112 out of 237 (47%) in Grampian and 99 out of 235 (42%) in Wales were in the highest specified income bracket.

Overall, while the patient cost results were fairly similar across the two study centres, the area where there was an obvious difference was the distance travelled to the genetics clinic (*Table 52*, Appendix 9). Grampian patients tended to travel longer distances (23.7 miles compared with 14.8 miles), therefore incurring higher travel costs.

Chapter 11

Nurse counsellor trial: discussion

This study has demonstrated that, in the field of breast cancer genetic counselling, genetic nurse counsellors can provide care of equivalent effectiveness to clinical geneticists, when working under similar constraints. The similar findings in the two separate trials support the generalisability of the findings, and the economic evaluation suggests that a nurse counsellor-led service can be a cost-effective alternative to a doctor-led service.

There is no reason to think that the study was prone to serious bias. The trial groups were generated by random allocation and were well balanced in both centres in relation to the primary outcome. The only variable with a notable imbalance was in the final assessed risk, which was essentially a baseline variable. The intervention arm in Grampian had a higher proportion of participants at elevated genetic risk compared with the control arm, the opposite being observed in Wales. However, the rates of non-response to questionnaires were similar in the trial groups, there was no indication of differential dropouts from the groups, and there was no associated differential in anxiety scores at baseline or follow-up.

Some women allocated to the nurse counsellor group actually saw a geneticist. There was concern that this might reduce the differences in the care received in the two groups and hence make an 'equivalence' result more likely. For this reason analysis based on actual person seen (PP analysis) was considered and performed. However, some of those allocated to the nurse counsellor group who actually saw a geneticist did so because they were thought to be at high risk. These cases would be likely to make a PP analysis suggest equivalence; for this reason the primary analysis was based on the ITT principle. In the event, the two approaches gave essentially similar results, both suggesting equivalence within the prestated boundaries.

The design of the evaluation overcame many of the limitations observed in other published evaluations of nurse practitioners and specialists. For example, it was ensured that the nurse counsellors worked under the same conditions as the doctors in the control arms, in terms of the time they had available to see patients, their waiting times and the resources available to them.[108] Longer consulting times by nurses compared with doctors have been observed in several trials, and some argue that this may be an important reason for higher levels of patient satisfaction with nurse practitioners.[108] In contrast, the nurse counsellors in the trials reported here were allocated the same amount of clinic time for the same number of patients as the geneticists. It has also been observed previously that nurse practitioners order more investigations on average than doctors, which would reduce cost-effectiveness if such investigations were unnecessary. However, in this study, nurse counsellors followed the same management guidelines as their medical counterparts[38] and their clinical decisions were regularly reviewed by the consultant in charge of the service. In only a few cases were risk assessments altered as a result of this review, and few changes were made to management plans. Some of these cases may reflect differences of opinion rather than errors. However, no data were collected comparing doctors' assessments, which would have allowed the extent of this to have been evaluated.

The trials were powered to test the equivalence of the intervention and control policies, and the equivalence limits were specified a priori. The authors are therefore confident that the results indicate equivalence between the policies, rather than a type II statistical error (i.e. failure to reject a null hypothesis of no difference). The equivalence limits for the primary outcome (STAI) were set at a very strict level, and in reality they probably represent a smaller difference than would normally be considered clinically significant between two clinicians considered equally competent.

By conducting two separate trials, rather than a two-centre trial, the researchers could allow flexibility in the way the intervention and control arms were implemented, while maintaining the key comparison of interest, assessment by a nurse counsellor compared with a geneticist. A broad range of outcome measures appropriate to cancer genetic counselling was chosen to try to maximise the chances (within reason) of detecting specific

differences between the intervention and control arms. The main focus was on anxiety, the reduction of which is regarded by many as a key counselling objective.[109,110] Anxiety was assessed using the STAI, which has been used extensively in applied psychology research and appears to be a reliable and sensitive measure, focusing on the cognitive component of anxiety. The short form is quicker to complete than the original 20-item state scale, and minimises potential bias towards respondents who find reading easy. The short version is reported to produce results comparable with the full state scale[87] and has been used in genetic counselling research.[89,90,92–94,111] The study also used the HADS, which was developed specifically for use in hospital outpatient populations and designed to detect clinically significant anxiety and depression. It also appears to be sufficiently sensitive to detect non-pathological alterations in anxiety and depression, and has been used in surveys of non-hospital populations as well as outpatient populations.[112]

Acceptably high response rates to the baseline and follow-up surveys were obtained and the stability of the outcomes could be assessed over a 6-month period following the counselling episode. A high proportion of eligible patients was recruited into both trials, suggesting that the study populations were representative of the target populations, all women referred for breast cancer genetic counselling in the two areas. Small baseline differences between the two trial populations were evident, which may reflect differences in the populations from which they were drawn. Comparative data on the general population are available only for SF-36 scores. For a general Aberdeen population, mean scores of 75 (role–emotional domain) and 73.7 (mental health domain) were obtained by Garratt and colleagues;[96] equivalent scores of 71.6 and 71.5 for a West Glamorgan population, from which a large proportion of participants in the Wales trial was drawn, were published by Lyons and colleagues.[113] When these are compared with the baseline data (reported in *Table 12*), it appears that both study populations were slightly more anxious than the underlying populations, but the between-trial differences were similar to the background between-population differences. A slightly lower proportion of the Wales participants was assigned elevated genetic risk after assessment than the Grampian participants, which may reflect differences in the relative maturity of the two services, or in professional or patient knowledge or expectations.

At the time this study was conceived and designed, there were few published controlled trials of substituting nurse specialists or practitioners for a traditional doctor's role.[83] However, there is now an emerging body of research evidence on the relative effectiveness of nurses in specialist roles compared with doctors in both primary-care[108,114–117] and secondary-care settings.[118–121] Most studies have found that nurses working within guidelines appear to provide care that is equal to that provided by doctors, with comparable health outcomes. Similarly, patient satisfaction was found to be high, and in some trials it has been suggested that patients were more satisfied with care provided by a nurse practitioner.[108] This may also be explained by nurse practitioners' longer consultation times and the tendency to order more investigations than doctors, both of which are associated with higher levels of patient satisfaction.[114]

To date, only one other formal evaluation of nurse counsellors in cancer genetics has been published,[122–125] with mixed findings. A cluster randomised trial compared the performance of a community clinic for initial risk assessment and counselling, run by specialist genetic nurses, with the standard regional service, which involved a genetics nurse specialist and consultant geneticist. The two models appeared generally comparable in terms of psychological outcomes[123] and patient satisfaction,[125] although the trial was not designed or analysed as an equivalence study. The GPs involved appeared positively disposed towards their patients being seen by specialist genetics nurses, although the standard service was preferred over the community clinic.[124] It is not possible to draw direct conclusions regarding the relative effectiveness of nurse counsellors compared with clinical geneticists from this study, as they were compared in different clinical settings and were not evaluated head to head.

This evaluation was not designed to assess the effectiveness of genetic counselling for breast cancer genetic risk as an intervention in itself. However, taken at face value, the findings suggest that expected improvements over baseline in anxiety, general health status, understanding of risk factors and accuracy of risk perception were not observed following counselling in any of the groups. While this is consistent with the limited evidence base in breast cancer genetic counselling,[91] formal evaluation requires rigorous comparison of genetic counselling with appropriate control interventions.

Economics

Given the increased demand for genetic counselling, healthcare decision-makers will undoubtedly strive to maximise the cost-effectiveness of the services they provide. To determine the factors influencing the cost-effectiveness of breast cancer genetic counselling services, it is useful to compare the way in which the services were organised in the two trial locations. As well as being relevant to decision-makers in Wales and Grampian, it provides insight relevant to others planning how best to introduce a new genetics service for breast cancer, or to expand an existing service.

Given that equivalence was found in the outcomes component of the trial, the health service costs were the main factor determining the relative cost-effectiveness in both the intervention and control arms. In terms of the nurse intervention, the cost of nurse supervision in Wales drove the unit cost difference of £27.95 compared with the intervention arm in Grampian. To improve the cost-effectiveness in this location, Wales could have employed a more experienced nurse counsellor as Grampian had chosen to do, which could have reduced the time required for consultant supervision, and hence staff costs.

Alternatively, if a nurse of a lesser grade were employed, it would reduce the cost of the counselling appointment, but additional supervision time might be required. In Wales, the nurse spent up to 1.5 hours per week with a consultant geneticist. It is likely that this time would be reduced as a nurse counsellor gained more experience (a learning effect). If the time were reduced to 30 minutes per week, similar to the supervision time in the Grampian trial, the total unit cost would be reduced by £17.06 per counselling appointment.

With respect to the intervention arm in Grampian, although this location achieved a lower unit cost than Wales, it is not necessarily the case that this location was more efficient overall because Grampian employed more expensive medical staff than Wales. For instance, the cost per hour for a consultant in Grampian was £73.54 compared with a specialist registrar at £36.60 per counselling appointment, almost a two-fold difference. If Grampian attempted to improve its cost-effectiveness, then an important consideration would be the more frequent use of lower grade doctors. The relative cost-effectiveness of the intervention arm is therefore influenced by the experience of the nurse counsellor and the grades of clinical staff providing counselling.

For the control arm, while the staff costs appear similar across the two locations, in Grampian, the control arm was particularly sensitive to changes in the grades of clinical staff providing counselling. Again, the issue of Grampian employing doctors at relatively high grades is important. Grampian could potentially adopt the policy seen in Wales of using lower grade clinicians for first appointments. In Wales, there was no direct consultant geneticist input for the first appointment, freeing the consultant to perform other activities and focus on follow-up appointments for patients considered as possibly higher risk. In Grampian, if the consultant geneticist and associate specialist activities were undertaken by more junior grades of staff, such as staff grades and specialist registrars, the unit cost per counselling episode could be reduced by £13.05 per patient. The relative cost-effectiveness of the control arm is therefore influenced largely by grades of clinical staff.

In terms of the implications of this study for those involved in planning breast cancer genetics services, there are four key factors to consider.

Current staff skill mix

It is crucial to determine the current skill mix of staff. If nurse counsellors are to be employed, then decision-makers need to take into account, among other things, the grade (and therefore salary cost) of the doctor whom a nurse counsellor may be replacing, relative training costs, and the relative scarcity of appropriately qualified nurses and doctors in the healthcare job market.

Experience of nurse counsellors

For a new service, the employment of genetic counsellors with as much experience as possible could be helpful. Although this may imply employing a nurse higher within the H grade scale or on a higher scale entirely, this cost could be offset by the reduction in required supervision time. If a decision is made not to employ more experienced nursing staff, then planners need to factor into their budget the necessary skill mix required. For instance, are there enough whole-time equivalent doctors with capacity to supervise genetic nurse counsellors?

Clinical staff grades

The evidence from this study suggests that the use of lower grade clinical staff could potentially improve the cost-effectiveness of the geneticist counselling, as long as there was no reduction in effectiveness.

Other types of genetics counsellor

Finally, there are other types of counsellors such as non-clinical and non-nursing counsellors. Although these were not considered in this evaluation, future research should collect data on the costs and effects of alternative types of counsellors in order to comment on their cost-effectiveness relative to clinical and nurse counsellors.

Generalisability

Consideration should be given to the extent to which the findings can be transferred to other settings, such as other types of genetic clinic. As genetic services in the UK are organised on a regional basis,[2,11] the hospital settings for the present trials are generally similar to those across the country. The authors have maximised the ability of decision-makers in other locations to make use of the data by reporting resource use and costs separately. In addition, there were differences in the characteristics of the two populations and, particularly, the organisation of the two cancer genetics clinics (reflected in part in the control arms of the trials). However, the findings cannot necessarily be extrapolated directly to genetic counselling for other conditions, particularly in other areas of genetics such as prenatal testing or counselling couples about reproductive risks. Furthermore, the study observed the effect of only three nurses in total (one in Grampian, two in Wales), so it cannot be concluded with certainty that the effects observed were those of the policy of recruiting a nurse counsellor, rather than the skills and personalities of the individuals themselves. This is a major limitation[126] of this study and other published studies.[120,127,128] However, the two concurrent trials do address this issue to some extent. In a trial of nurse practitioners in ten general practices, the finding of a wide variation in mean patient satisfaction scores across the clinicians (doctors and nurses) underlines the influence of the individual practitioner,[116] and is a key issue that must be addressed in future similar trials.

Future research directions

Given the concerns about the generalisablity of the findings in this trial, it would be reassuring if further evaluation were conducted in other settings involving larger numbers of nurse counsellors. There are likely to be alternative models for how nurse counsellors may provide a risk assessment service.

When this trial was conceived, the intention was for the nurse counsellors not only to substitute for geneticists in the regional clinic setting, but also to run outreach clinics in peripheral hospitals or large health centres. As the trials progressed, however, it became clear that this would be difficult to arrange in both trial locations because of organisational factors specific to each area. Indeed, doing so would fundamentally detract from the pragmatic approach that the researchers wished to take. The concept of genetic counsellors working in liaison or outreach settings has been proposed by a number of authors.[2,5,9,14,129] An evaluation of such a model, compared with the traditional service in south-east Scotland, suggested no difference in patient psychological outcomes[123] and no clear preference amongst patients or GPs for one configuration over the other.[125] The community-based intervention was associated with higher GP referral rates, but no improvement in GP confidence.[124] Further work is required to determine which elements, if any, of an outreach model are likely to lead to which kinds of benefit, and the likely sustainability of different potential configurations of outreach services.

Given the pressure on genetics services, particularly in relation to other late-onset disorders (e.g. other cancers, neurodegenerative diseases, haemochromatosis), it is likely that the role for nurse counsellors will be extended to other groups of patients. These developments should be formally evaluated before their widespread introduction.

Chapter 12

Overall conclusions

The studies reported here evaluated two approaches aimed at meeting the increasing demand for breast cancer genetic counselling in a cost-effective way, one a primary-care intervention and the other based in regional genetics clinics. The interventions were designed and implemented with the intention that they should be potentially sustainable if shown to be effective. This meant that they needed to be informed by a realistic understanding of service needs, clinicians and GPs had to be involved in their development and implementation, and a wide range of outcomes and costs should be assessed to provide as full as possible an evaluation.

The primary-care intervention, an on-demand computer decision support system, was developed over a lengthy period with the input of target users, and was implemented by a combination of passive and active dissemination strategies. It could not be concluded from the evaluation that it was effective in improving GP confidence, and the study had insufficient statistical power to determine whether or not it influenced GP referral patterns or patient outcomes. Around one-third of intervention practices sent at least one partner to attend the education session, which is in keeping with other studies where this has been used as a dissemination strategy. However, only one-fifth of all intervention GPs reported that they were aware that their practice had received the software, and less than 10% reported ever having used it. The study had insufficient statistical power to determine whether or not it was effective in improving the confidence of those GPs who reported using it. This experience confirms the poor effectiveness of passive dissemination strategies. It also suggests that a more active strategy, the accompanying educational session, is not necessarily effective at the level of a general practice, and that targeting individual practitioners may be necessary to improve uptake of the intervention.

The published literature on GPs and genetics suggests an enthusiasm for computer-based systems to help them to make patient management decisions. Computer-based guidelines were identified by a large proportion of respondents to a preintervention GP survey as a potentially attractive intervention to assist them with breast cancer genetics. Apart from the intervention reported here, the authors are aware of only one other similar computer system in the UK; it has been shown to be effective in promoting appropriate GP management decisions in cancer genetics, but was evaluated using a selected group of participants and simulated patients under highly controlled circumstances, and not in the field. The present evaluation demonstrates that one cannot assume that apparently positive views expressed in surveys, or demonstration of efficacy in artificial conditions, are sufficient to ensure that such systems are used, even when they are developed in a careful manner to meet the needs of the specific target audience. Barriers to the use of computer support systems in genetics may be the resources required for active dissemination strategies, the changing evidence base in genetics, which may require relatively frequent software upgrading, and the scepticism of some practitioners about the balance of harms and benefits to individual patients of focusing on genetic explanations for disease, especially when there are few effective interventions to alter natural history for the majority of those at risk.

Campbell and colleagues[58] describe a framework to guide the development and evaluation of complex health interventions. They suggest that data from quantitative and qualitative studies should be used to inform the development of interventions such as this one in an iterative way. The findings here underscore the importance of building up a detailed understanding of those attributes of the intervention most likely to lead to the desired improvements in genetics in primary care. For example, the widespread attention currently being given to the growing number of applications of handheld computers [personal digital assistants (PDAs)] in medical practice[130] suggests that these may prove more attractive to GPs than the more cumbersome desktop systems used in the study reported here. However, despite their ease of use, PDAs would be only part of a system of clinical decision-making, and would therefore require thoughtful development and rigorous evaluation.

The findings of the nurse counsellor evaluation suggest that, under certain circumstances, this may be a cost-effective policy for meeting demand for breast cancer genetic counselling. Two similar trials, conducted in settings where there were differences in health service organisation, historical development of genetic services, available resources and patient populations, indicated that a wide range of outcomes was equivalent in patients counselled by nurses or doctors. The economic analysis underlines the importance of examining the whole picture when judging the relative worth of an intervention. In the NHS context, the costs of a nurse counsellor are mainly determined by his or her salary, but are also influenced by the level of consultant supervision required, which is itself dependent on the grade and experience of the individual. Decision-makers need to take into account, among other things, the grade (and therefore salary cost) of the doctor whom a nurse counsellor may be replacing, relative training costs, and the relative scarcity of appropriately qualified nurses and doctors in the healthcare job market.

The findings of this study are consistent with a growing body of literature on the acceptability and effectiveness of experienced or advanced nurses substituting for doctors in particular clinical situations. An outstanding question left unanswered from many of these studies has been whether greater levels of patient satisfaction with nurse care could be explained by the longer time that nurses spent with patients, or higher levels of test ordering, compared with doctors. This study was able to demonstrate equivalence in patient satisfaction when nurse counsellors were working under the same constraints as doctors.

Taken together, the present findings suggest that there are fundamental challenges remaining in the field of genetics in primary care. Simple interventions to disseminate or implement guidelines are unlikely to prove effective by themselves, and the added effectiveness of active implementation strategies remains to be clarified. In terms of meeting demand for genetic counselling, this study provides evidence that nurse counsellors may be a cost-effective alternative to medical geneticists, in the context of a specialist service working to clear risk assessment and management guidelines.

Recommendations for future research

Computer support system

Future evaluations must identify and address barriers to use in practice. Research should clarify whether the failure of GPs to use such systems is related to the computer system itself (including how well it addresses GPs' needs, its integration into practice routines, and the frequency or infrequency with which it is required) or the effectiveness of dissemination strategies promoting awareness and use.

The framework described by Campbell and colleagues[58] could be used to guide the development and evaluation of the intervention. Research is needed into the attributes of the intervention most likely to lead to improvements in genetics in primary care (e.g. the use of PDAs).

Assessment by nurse counsellors

Replication of this study in other settings would provide reassurance of generalisability. Other models of nurse-based assessment, such as in outreach clinics, should be evaluated. In addition, given the pressure on genetics services, particularly in relation to other late-onset disorders (e.g. other cancers, neurodegenerative diseases, haemochromatosis), it is likely that the role for nurse counsellors will be extended to other groups of patients. These developments should be formally evaluated before their widespread introduction.

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Contribution of authors

Brenda Wilson (Associate Professor of Epidemiology and Community Medicine) was involved in the conception and design of the study, development and implementation of both interventions, overall coordination of the three trials and interpretation of the analysis, and led the writing of the report.

Nicola Torrance (Research Fellow, Public Health) was the research fellow on the project, and contributed to the development and implementation of both interventions, coordinated recruitment, data collection, statistical analysis and interpretation of the analysis, and contributed to writing the report.

Jill Mollison (Senior Lecturer in Medical Statistics) contributed to the design of the study, development and implementation of both interventions, statistical analysis, interpretation of the analysis and writing of the report.

Sarah Wordsworth (Research Fellow, Health Economics) conducted the economic evaluation, was involved in interpretation of the analysis and contributed to drafting the report.

Jonathon Gray (Consultant in Medical Genetics) was involved in the conception and design of the study, was the clinical lead in the Wales trial, contributed to the development and implementation of the nurse counsellor intervention and the interpretation of the analysis, and commented on the report.

Neva Haites (Professor Medical Genetics) was involved in the conception of the study, was the clinical lead in the North East Scotland trials, contributed to the development and implementation of both interventions, and commented on the report.

Adrian Grant (Director, Health Services Research Unit) was involved in the conception of the study, and developing the design and application, contributed to the interpretation of analysis and commented on the report.

Marion Campbell (Programme Director, Health Services Research Unit) contributed to the conduct of the study and interpretation of the analysis and commented on the report.

Zosia Miedzybrodzka (Senior Lecturer in Clinical Genetics) was involved in clinical aspects of the overall study, contributed to the development and implementation of both interventions, and interpretation of the analysis, and commented on the report.

Angus Clarke (Professor in Clinical Genetics) was involved in the conception and design of the study, and development of the nurse counsellor intervention, and commented on the report.

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Alison Douglas (General Practitioner) contributed to the study from the perspective of general practice in the development of the primary care intervention and commented on the report.

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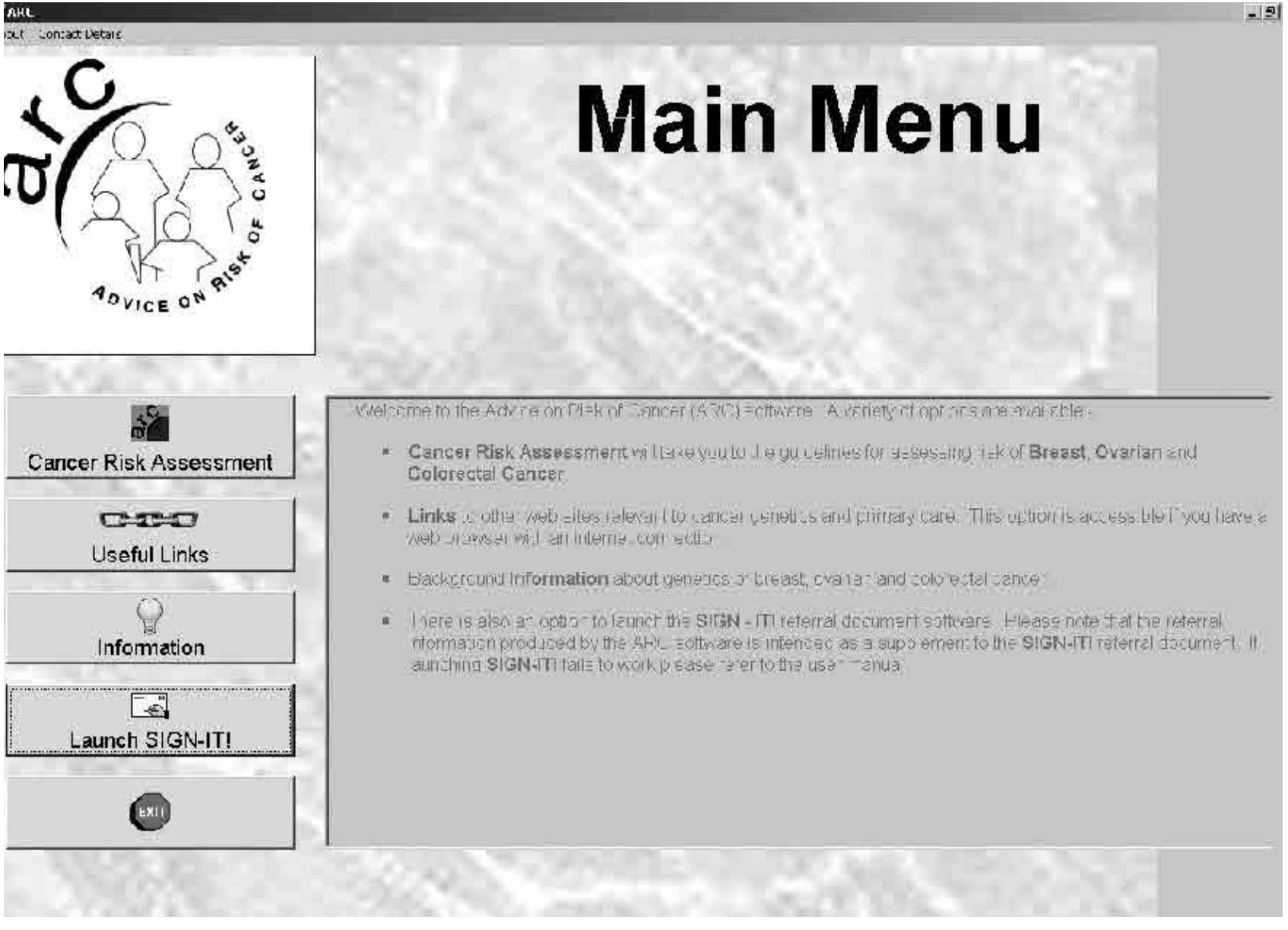
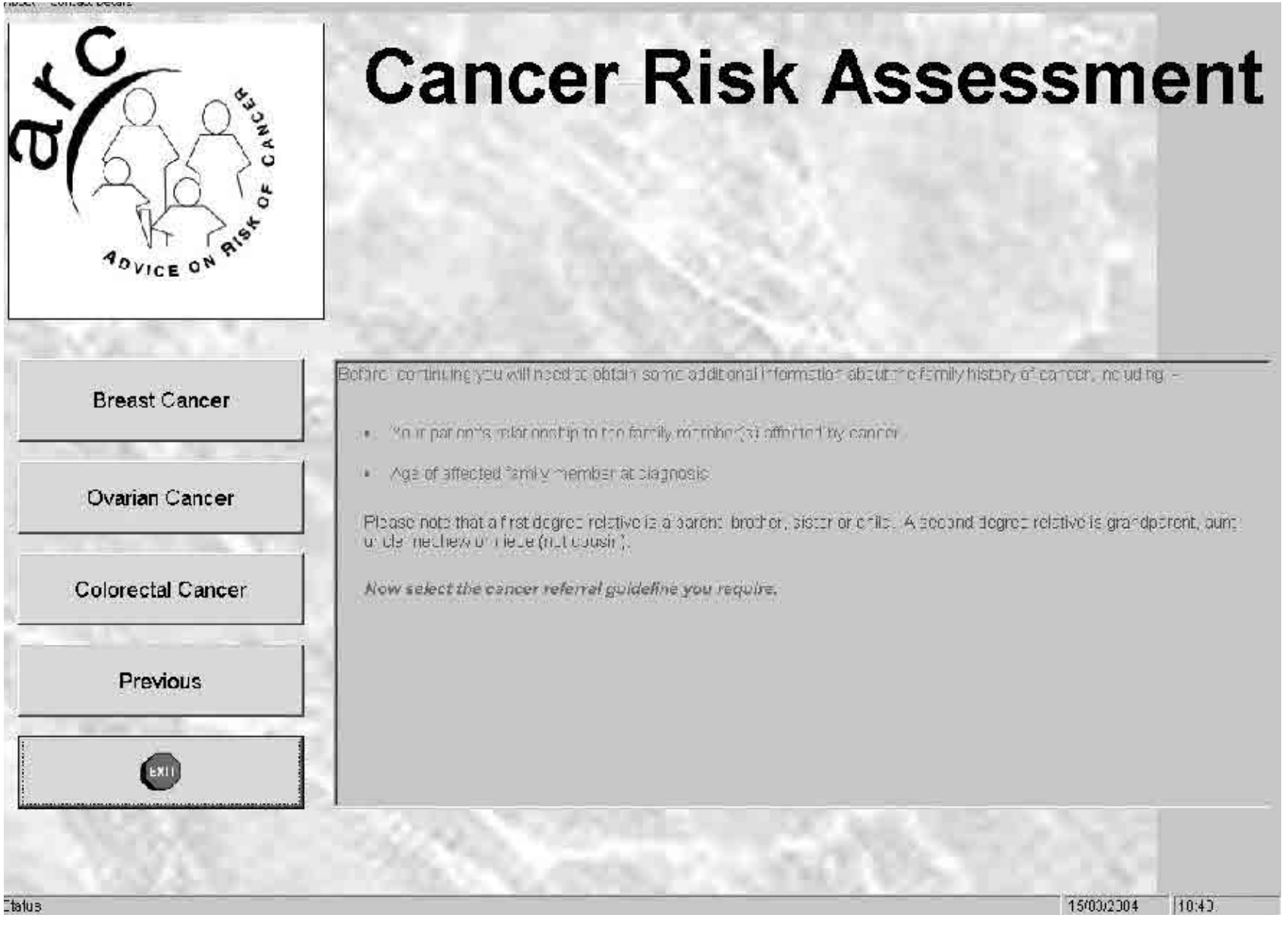
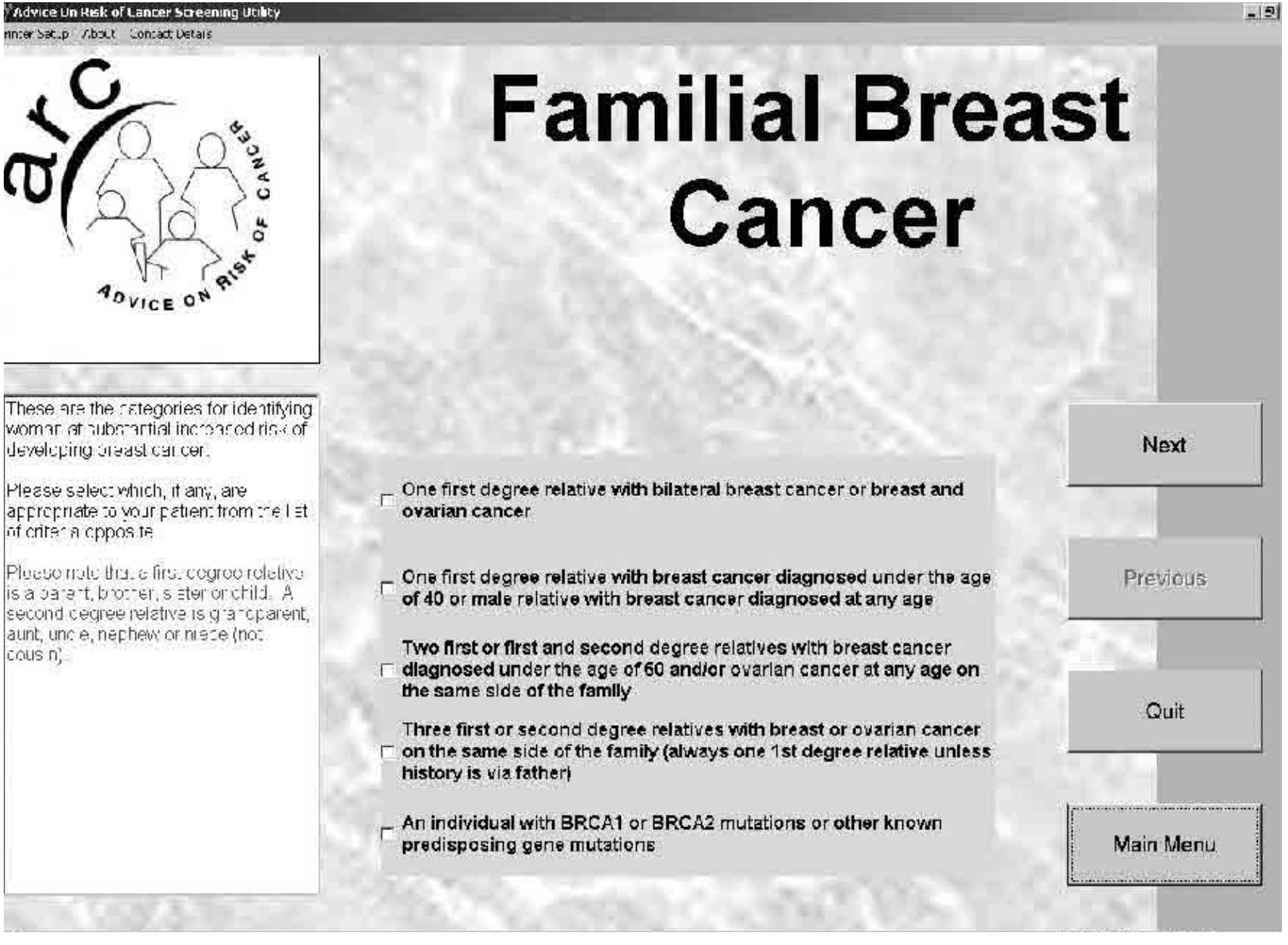
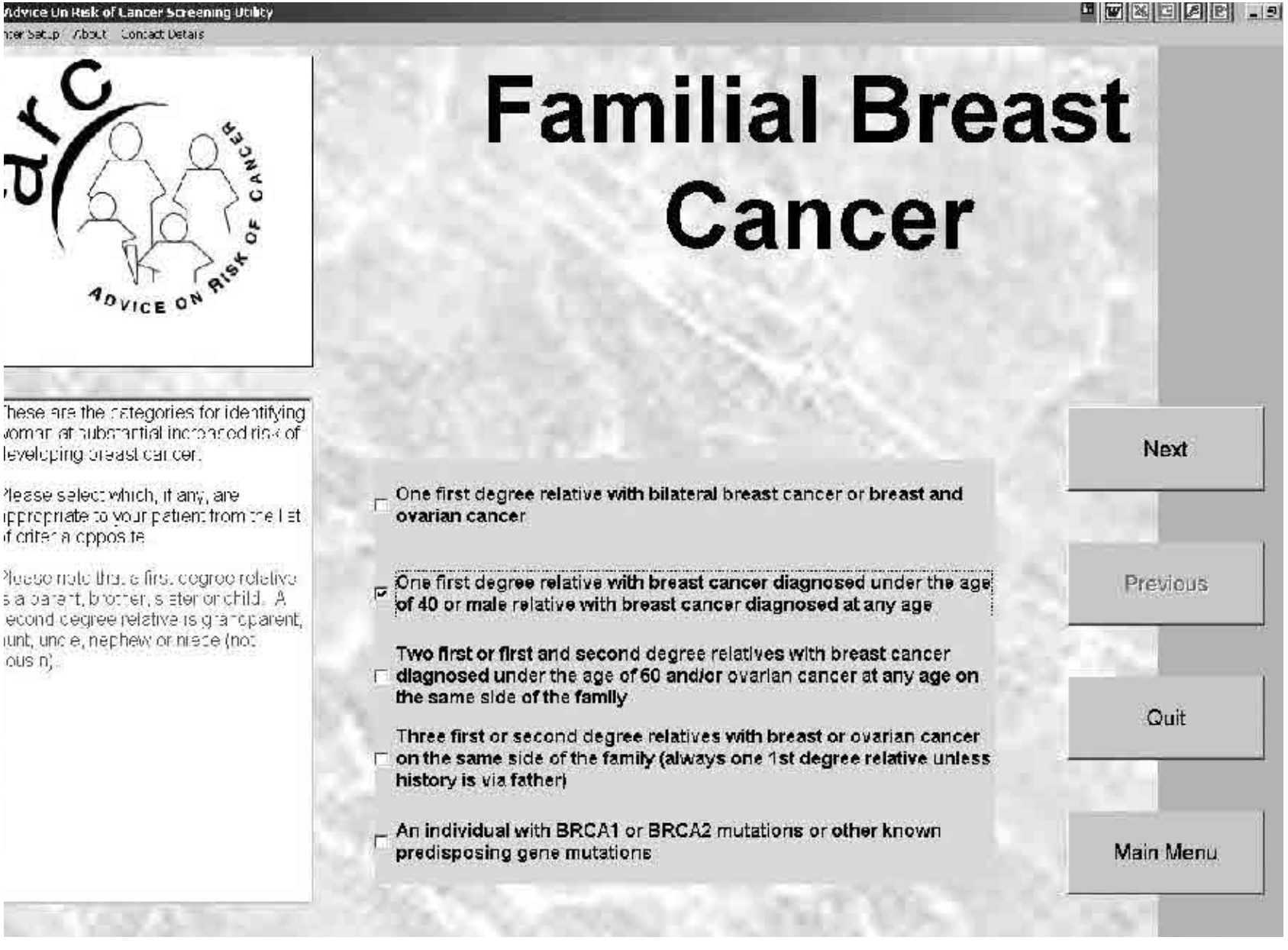
Appendix 1

Primary care trial: screenshots of software


ARC
Contact Details
ADVICE ON RISK OF CANCER
Main Menu
Cancer Risk Assessment
Useful Links
Information
Launch SIGN-IT!
EXIT
Welcome to the Advice on Risk of Cancer (ARC) software. A variety of options are available:
Cancer Risk Assessment will take you to the guidelines for assessing risk of Breast, Ovarian and Colorectal Cancer.
Links to other web sites relevant to cancer genetics and primary care. This option is accessible if you have a web browser and an internet connection.
Background Information about genetics of breast, ovarian and colorectal cancer.
There is also an option to launch the SIGN - IT! referral document software. Please note that the referral information produced by the ARC software is intended as a supplement to the SIGN-IT! referral document. If launching SIGN-IT! fails to work please refer to the user manual.




Advice On Risk of Cancer Screening Utility
About
Contact Details
arc
ADVICE ON RISK OF CANCER
Familial Breast Cancer
These are the categories for identifying women at substantial increased risk of developing breast cancer.
Please select which, if any, are appropriate to your patient from the list of criteria opposite.
Please note that a first degree relative is a parent, brother, sister or child. A second degree relative is grandparent, aunt, uncle, nephew or niece (not cousin).
One first degree relative with bilateral breast cancer or breast and ovarian cancer
One first degree relative with breast cancer diagnosed under the age of 40 or male relative with breast cancer diagnosed at any age
Two first or first and second degree relatives with breast cancer diagnosed under the age of 60 and/or ovarian cancer at any age on the same side of the family
Three first or second degree relatives with breast or ovarian cancer on the same side of the family (always one 1st degree relative unless history is via father)
An individual with BRCA1 or BRCA2 mutations or other known predisposing gene mutations
Next
Previous
Quit
Main Menu


Advice On Risk of Cancer Screening Utility
About
Contact Details
ADVICE ON RISK OF CANCER
Familial Breast Cancer
These are the categories for identifying women at substantial increased risk of developing breast cancer.
Please select which, if any, are appropriate to your patient from the list of criteria opposite.
Please note that a first degree relative is a parent, brother, sister or child. A second degree relative is grandparent, aunt, uncle, nephew or niece (not cousin).
One first degree relative with bilateral breast cancer or breast and ovarian cancer
One first degree relative with breast cancer diagnosed under the age of 40 or male relative with breast cancer diagnosed at any age
Two first or first and second degree relatives with breast cancer diagnosed under the age of 60 and/or ovarian cancer at any age on the same side of the family
Three first or second degree relatives with breast or ovarian cancer on the same side of the family (always one 1st degree relative unless history is via father)
An individual with BRCA1 or BRCA2 mutations or other known predisposing gene mutations
Next
Previous
Quit
Main Menu

Appendix 2

Primary care and nurse counsellor intervention trial: patient risk perception, understanding and clinic expectations

PATIENT QUESTIONNAIRE

The chance of the average woman getting breast cancer is 1 in 12. In your opinion, would you say your chances of getting breast cancer are –

Tick (✓) ONE box

- Inevitable ☐ (I will definitely get breast cancer)
- Much more than the average woman ☐ (say, between 1 in 2 and 1 in 5)
- More than the average woman ☐ (say, between 1 in 5 and 1 in 12)
- Same as the average woman ☐ (1 in 12)
- Less than the average woman ☐ (say, between 1 in 12 and 1 in 50)
- Much less than the average woman ☐ (say, between 1 in 50 and 1 in 100)

Please try to answer all of the following questions by putting a tick in the box that most closely represents your opinion:

Tick (✓) ONE box for each question

	Strongly Disagree	**Disagree**	**Agree**	**Strongly Agree**	**Not Sure**
a) Stress is a major cause of breast cancer	☐	☐	☐	☐	☐
b) Having one close relative (mother/sister) with breast cancer always increases your risk considerably	☐	☐	☐	☐	☐
c) A healthy diet can prevent breast cancer	☐	☐	☐	☐	☐
d) Oral contraceptives (the pill) can significantly increase the risk of breast cancer	☐	☐	☐	☐	☐
e) Minor injury (for example, a bump or bang) to the breast can cause breast cancer	☐	☐	☐	☐	☐

f) Overall, in your opinion, what is the single most important cause of breast cancer?

Please answer all of the following questions by putting a tick in the box that most closely represents your opinion:

Tick (✓) ONE box for each question

	Strongly Disagree	Disagree	Agree	Strongly Agree	Not Sure
a) I want to be given accurate information about the causes of breast cancer	☐	☐	☐	☐	☐
b) I want to be given the exact risk of getting breast cancer myself	☐	☐	☐	☐	☐
c) I want information about preventing breast cancer	☐	☐	☐	☐	☐
d) I want information about genetic tests to determine my risk of breast cancer more accurately	☐	☐	☐	☐	☐
e) Have you any further expectations or concerns about the clinic?	☐	☐	☐	☐	☐

Appendix 3

Nurse counsellor intervention: patient satisfaction questionnaire

GENETICS CLINIC

The following set of statements are about your visit to the Genetic Clinic. Please indicate whether or not you agree with the statements by putting a tick (✓) in the appropriate box. There are no 'right' or 'wrong' answers, your real opinions and feelings are what we want to find out.

Tick (✓) one box for each question

19. I was given the kind of information –	**Strongly Agree**	**Agree**	**Not Sure**	**Disagree**	**Strongly Disagree**
a) I wanted about the causes of breast cancer	☐	☐	☐	☐	☐
b) I could understand about my risk of getting breast cancer	☐	☐	☐	☐	☐
c) I wanted about reducing my chances of getting breast cancer	☐	☐	☐	☐	☐
d) I wanted about genetic tests for estimating my breast cancer risk more accurately	☐	☐	☐	☐	☐

20. The doctor/nurse –	**Strongly Agree**	**Agree**	**Not Sure**	**Disagree**	**Strongly Disagree**
a) listened to what I had to say	☐	☐	☐	☐	☐
b) took my concerns seriously	☐	☐	☐	☐	☐

21. I am satisfied with the –	**Strongly Agree**	**Agree**	**Not Sure**	**Disagree**	**Strongly Disagree**
a) time I had to wait until my first appointment with the doctor/nurse	☐	☐	☐	☐	☐
b) length of time I had to wait in the waiting area before my appointment	☐	☐	☐	☐	☐
c) way that other staff dealt with me (e.g. the secretary, nurses running the clinic)	☐	☐	☐	☐	☐

22. Overall –	**Strongly Agree**	**Agree**	**Not Sure**	**Disagree**	**Strongly Disagree**
a) The consultation was helpful	☐	☐	☐	☐	☐
b) I am satisfied with the consultation	☐	☐	☐	☐	☐

Appendix 4

Nurse counsellor intervention: GP acceptability questionnaire

1. Did you notice any difference from the usual service provided by the Medical Genetics Department for your patient who was seen by a **Nurse Specialist** as part of the ARC study?

   Yes ☐ No ☐ Don't know ☐

   If **Yes**, could you explain what those differences were?

   _____

   _____

   _____

2. Would you be happy for your patients who are concerned about a family history of breast cancer to be seen at the Genetic Clinic by a Nurse Specialist in the future?

   Yes ☐ No ☐ Don't know ☐

   Please indicate your reasons below

   _____

   _____

   _____

3. Overall, how would you rate your satisfaction with the service provided by the Medical Genetics Department?

Very satisfied	Fairly satisfied	Neither satisfied nor dissatisfied	Fairly dissatisfied	Not at all satisfied
☐	☐	☐	☐	☐

4. Do you have any comments you would like to add?

   _____

   _____

   _____

Appendix 5

Nurse counsellor intervention: GP acceptability questionnaire; verbatim comments

GP VERBATIM COMMENTS

1. Did you notice any difference from the usual service provided by the Medical Genetics Department for your patient who was seen by a **Nurse Specialist** as part of the ARC study?

YES. Letters were less technical and easier to understand
2 consultations as opposed to 1
Seemed to be much shorter wait for appointment
Seems to be more thorough regarding the risk factors although I have not seen a letter from a Clinical Geneticist
I have no other recent referrals with which to compare
Seen sooner
Patient better informed therefore more relaxed
Patients seemed more satisfied with explanations and discussion ensuing. Felt happier leaving the session than going in
Have hardly used the service therefore little to compare
Patient more informed and relaxed, not worried much

2. Would you be happy for your patients who are concerned about a family history of breast cancer to be seen at the Genetic Clinic by a Nurse Specialist in the future?

Advice given by specialist nurse working to guidelines is very satisfactory in the first instance
With appropriate training and following agreed protocols this should be perfectly OK and may help to speed up the process
Patients happy with service
Service appears to be efficient and appropriate
Advice was clear, authoritative and, I am confident, accurate
Trained nursing staff will usually inform patients as well if not better than doctors
Feedback from patient was positive

As long as the work has been assessed and is correct for the women – seeing a nurse may be preferable

With appropriate training obviously

Haven't noticed any difference in service. No reason why nurse-led service following protocols shouldn't work as well

Because same standard of letter received as for geneticist and I presume if a geneticist's opinion is needed, nurse would ask for it

Fast access. Good counselling

Very adequate assessment and it presumably speeds your response. Patient seemed very content

Presumably she is fully trained etc!!

Even though I quote the same figures sometimes patients can be reassured by the hospital surroundings

Reassurance to patients, risk assessment, if increased risk, may need earlier mammography/US therefore early detection rate

Thorough approach. Well presented info in letter to patient and GP (but feel need consultant-led service)

If they are working to protocols/current evidence I see no reason why the advice should differ from that given by a Dr

Provided the patient is seen by a geneticist at one stage

Good service. Comprehensive reply letters

No change in high quality of service provided by genetics unit

Quick appointment, expertise

Expertise and knowledge base

Can't see a problem with an adequately trained nurse specialist counselling patients – may well be better at it!

Good feedback from patient

More information and advice leads to improved compliance and care. GPs have difficulty with information needs of these patients

As long as appropriately trained and good availability

If appropriately qualified

?faster service

Specifically trained in assessing risk. GPs currently have no training

Patient gets more information and are happy to be seen by specialist nurse

4. Do you have any comments you would like to add?

Keep going!

Feedback from patients is very positive

My experience of your service is limited but the concept is excellent and seems very well managed

Patient made a point of coming to tell me how helpful the service had been

I think the service is excellent. Patients often comment how clear the information is that they are given and it's easy to understand

Main difficulty (as ever) = waiting times and hopefully this initiative will improve access to service

I have found the published guidelines in Wales to be particularly useful

Direct access to refer cases to Nurse Specialist is desirable

Relatively quick access is important and availability of telephone advice/follow up appointments to support and clarify concerns, etc. Written report to patient – as given – also essential

Patient seen within 4 months – less than anticipated

Necessary service for patients – advice & support

Postgraduate education for local GPs would be welcome. I only currently refer if patient requests referral specifically. Wary of interpretation of results by insurance companies, etc. Not keen on requesting inappropriate advice from your department. Once results are in GP notes they have to be disclosed

Good work. Carry on

Very comprehensive letter. Nicely laid out and clear. I am sure that patients will greatly appreciate that it is addressed directly to them

Would wish further information on effects of enhanced screening and decision support software or support used. Could these be rolled out to primary care? What is potential for BRCA1 &2 screening?

The nursing role has to be extended to meet general patient demand/expectation – it can't all be done by expensive scarce doctors

Should I address referrals to Genetics re breast cancer to the nurse counsellor?

Patient seemed surprised initially and this particular patient felt she might be shortchanged. However she seemed entirely satisfied after the event

All practices would benefit from clear guidelines on who best to refer

Too little experience truly to comment. The concept is a good one, however!

Waiting list – but not unique!

In recent years there has been a growing awareness in both patients and doctors of the genetic predisposition to some diseases such as cancer. The increased knowledge and technology in determining risk assessment too, I'm sure will lead to ever increasing demand in this field and I would support extra resources being allocated to clinical genetics department

Well done! Good use of skilled staff

Obviously as demand increases waiting times increase which can affect attendance at clinics

Overall happy as service very approachable and user friendly

I am very satisfied with the promptness of the patient receiving a questionnaire

All patients have been very pleased with the advice/reassurance/follow-up from the clinic

Very helpful that copy of letter to patient is sent to GP so GP knows what info has been provided

Appendix 6

Nurse counsellor intervention: per-protocol analysis; primary outcomes

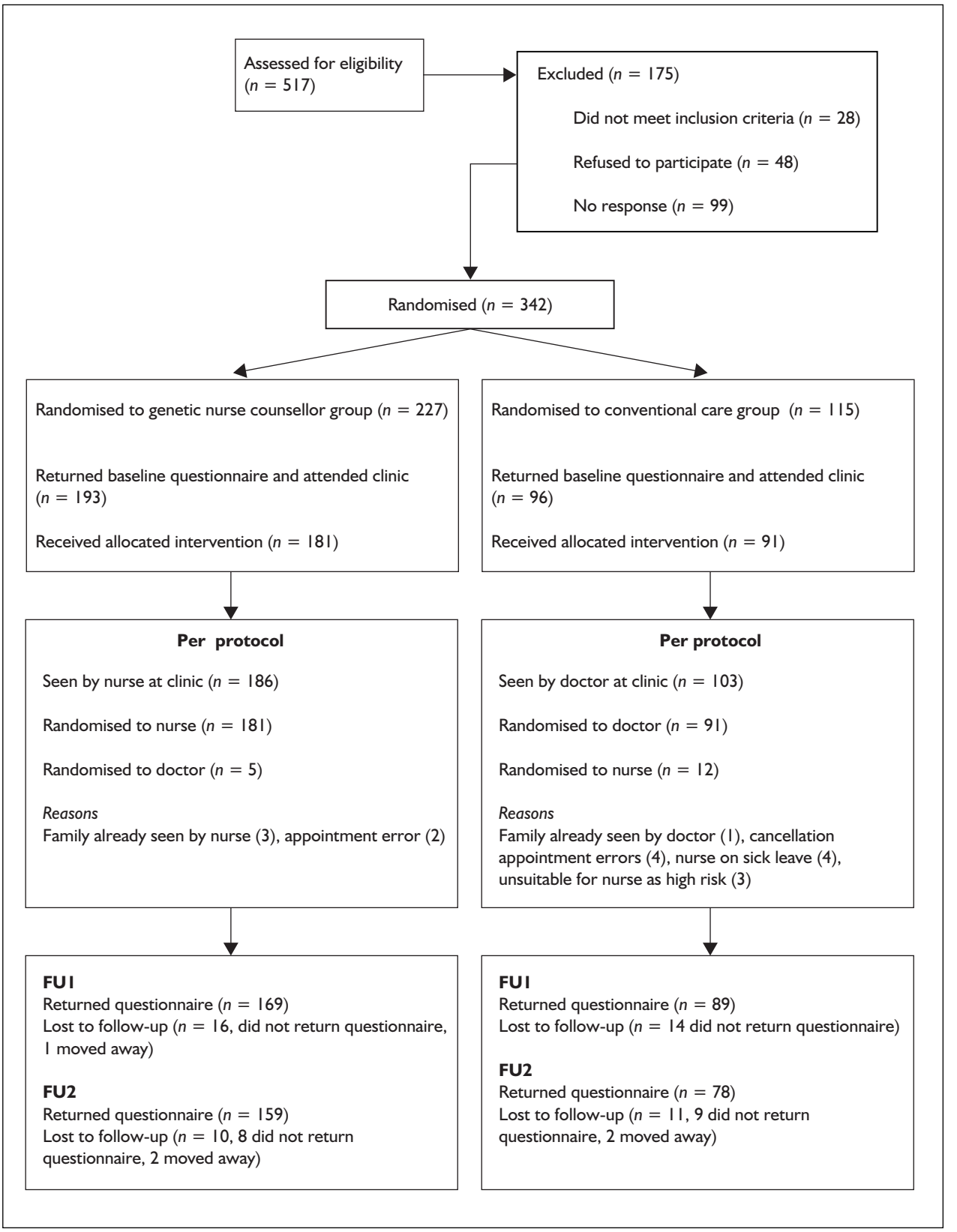


FIGURE 42 *CONSORT diagram for Grampian per protocol (progress of patients through the trial)*

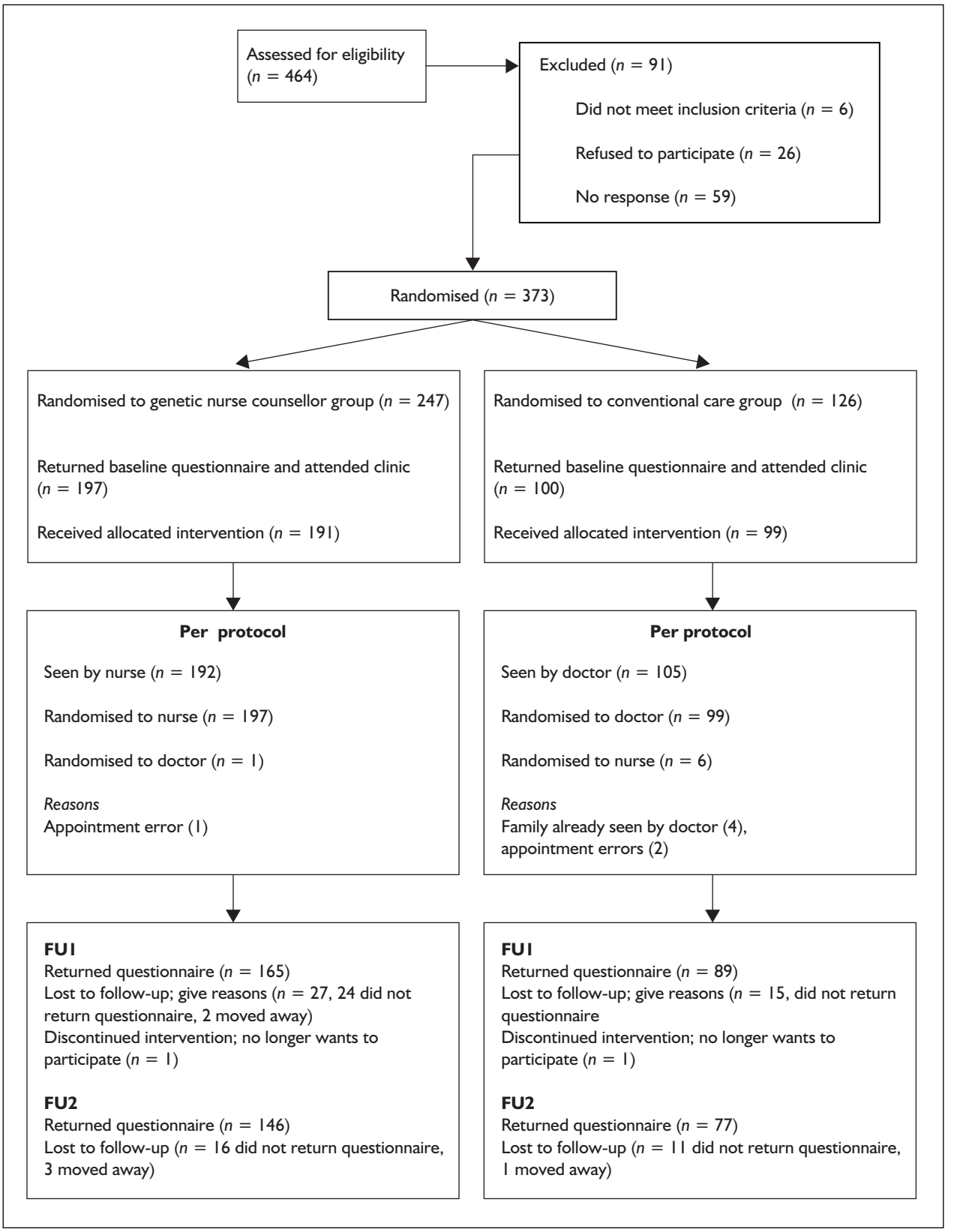


FIGURE 43 *CONSORT diagram for Wales per protocol (progress of patients through the trial)*

TABLE 31 *PP analysis: baseline demographic characteristics*

	Grampian		Wales	
	Intervention (*n* = 186)	**Control (*n* = 103)**	**Intervention (*n* = 192)**	**Control (*n* = 105)**
Age (years), mean (SD)	41.4 (9.4)	40.7 (10.3)	40.1 (10.1)	38.6 (9.5)
Married/cohabiting, *n* (%)	149 (80.1)	82 (79.6)	159 (82.8)	86 (81.9)
With children, *n* (%)	148 (79.6)	82 (79.6)	157 (81.8)	79 (75.2)
Postsecondary education, *n* (%)	75 (40.3)	44 (42.7)	70 (36.5)	45 (42.9)
Referral source				
GP	131 (70.4)	65 (63.1)	113 (58.9)	60 (57.1)
Breast surgeon	31 (16.7)	23 (22.3)	73 (38.0)	42 (40.0)
Breast screening	16 (8.6)	11 (10.7)	–	–
Other	8 (4.2)	4 (3.9)	6 (3.1)	3 (2.9)

TABLE 32 *PP analysis: baseline scores of primary outcome variables, mean (SD)*

	Grampian		Wales	
	Intervention (*n* = 186)	**Control (*n* = 103)**	**Intervention (*n* = 192)**	**Control (*n* = 105)**
STAI	37.1 (13.2)	36.9 (13.6)	41.3 (14.9)	39.3 (14.8)
HADS anxiety score	6.6 (4.2)	6.6 (4.6)	8.1 (4.8)	7.4 (4.1)
HADS depression score	3.8 (3.5)	3.6 (3.9)	4.6 (3.7)	4.1 (3.8)
SF-36 role–emotional	81.8 (33.8)	80.2 (35.0)	74.7 (38.3)	70.5 (41.1)
SF-36 mental health	71.5 (17.7)	72.6 (19.1)	67.1 (18.8)	68.6 (19.3)

TABLE 33 *PP analysis: short-form STAI score, mean (SD)*

	Grampian			Wales		
Measure	**Intervention (*n* = 186)**	**Control (*n* = 103)**	**Difference (95% CI)[a]**	**Intervention (*n* = 192)**	**Control (*n* = 105)**	**Difference (95% CI)[a]**
STAI						
Baseline	37.1 (13.2)	36.9 (13.6)		41.3 (14.9)	39.3 (14.8)	
FU1	35.7 (13.3)	35.9 (14.1)	–0.7 (–3.6 to 2.2)	38.5 (15.0)	38.2 (15.4)	–1.0 (–4.0 to 2.0)
FU2	35.6 (13.1)	33.1 (12.8)	1.9 (–1.0 to 4.9)	38.2 (14.8)	38.9 (14.6)	–0.1 (–3.5 to 3.4)

[a] Adjusted for baseline.

TABLE 34 *PP analysis: HADS anxiety and depression scores, mean (SD)*

	Grampian			Wales		
Measure	**Intervention (*n* = 186)**	**Control (*n* = 103)**	**Difference (95% CI)[a]**	**Intervention (*n* = 192)**	**Control (*n* = 105)**	**Difference (95% CI)[a]**
HADS anxiety						
Baseline	6.6 (4.2)	6.6 (4.6)		8.1 (4.8)	7.4 (4.1)	
FU1	6.1 (4.2)	5.8 (4.1)	0.2 (–0.6 to +1.0)	7.1 (4.9)	7.0 (4.7)	–0.3 (–1.2 to 0.6)
FU2	6.1 (4.4)	5.8 (3.8)	–0.04 (–0.9 to +0.8)	7.5 (4.8)	6.2 (4.1)	0.7 (–0.3 to 1.7)
HADS depression						
Baseline	3.8 (3.5)	3.6 (3.9)		4.6 (3.7)	4.1 (3.8)	
FU1	3.4 (3.5)	3.1 (3.2)	0.1 (–0.6 to 0.8)	4.0 (3.8)	3.9 (3.8)	–0.1 (–0.6 to 0.9)
FU2	3.3 (3.2)	3.1 (3.8)	–0.01 (–0.7 to 0.7)	4.6 (4.1)	3.8 (3.8)	0.7 (–0.2 to 1.7)

[a] Adjusted for baseline.

TABLE 35 *PP analysis: SF-36 scores (role–emotional and mental health domains), mean (SD)*

Measure	Grampian			Wales		
	Intervention (*n* = 186)	**Control (*n* = 103)**	**Difference (95% CI)[a]**	**Intervention (*n* = 192)**	**Control (*n* = 105)**	**Difference (95% CI)[a]**
SF-36 role–emotional						
Baseline	81.8 (33.8)	80.2 (35.0)		74.7 (38.3)	70.5 (41.1)	
FU1	83.1 (34.4)	79.6 (34.8)	5.0 (–3.1 to 13.0)	74.0 (39.8)	73.2 (39.7)	–0.4 (–10.1 to 9.3)
FU2	81.2 (35.4)	83.8 (32.6)	–1.0 (–9.3 to 7.3)	74.3 (39.0)	74.5 (41.5)	–2.5 (–12.3 to 7.4)
SF-36 mental health						
Baseline	71.5 (17.7)	72.6 (19.1)		67.1 (18.8)	68.6 (19.3)	
FU1	72.8 (18.1)	73.1 (18.9)	1.1 (–2.3 to 4.5)	68.7 (20.7)	68.3 (21.0)	0.9 (–3.0, to –4.8)
FU2	73.0 (17.4)	75.7 (17.9)	–1.6 (–5.4 to 2.2)	66.5 (21.1)	68.4 (21.0)	–1.0 (–5.4 to 3.4)

[a] Adjusted for baseline.

TABLE 36 *PP analysis: baseline risk perception,* n *(%)*

Personal breast cancer risk perception		Grampian		Wales	
		Intervention (*n* = 174)[a]	**Control (*n* = 98)[a]**	**Intervention (*n* = 174)[b]**	**Control (*n* = 95)[b]**
High		38 (21.8)	17 (17.3)	53 (30.5)	29 (30.5)
	'Inevitable'	2 (1.1)	1 (1.1)	15 (8.6)	6 (6.3)
	'Much more than the average woman'	36 (20.7)	16 (16.3)	38 (21.8)	23 (24.2)
Moderate	'More than the average woman'	87 (50.0)	53 (54.1)	90 (51.7)	53 (55.8)
Low		49 (28.2)	26 (26.5)	30 (17.2)	13 (13.7)
	'Same as the average woman'	47 (27.0)	24 (24.5)	29 (16.7)	11 (11.6)
	'Less than the average woman'	2 (1.1)	1 (1.0)	1 (0.6)	2 (2.1)
	'Much less than the average woman'	0	1 (1.0)	0	0

[a] Excludes eight participants already affected by breast cancer (seven intervention, one control).
[b] Excludes 13 participants already affected by breast cancer (ten intervention, three control).

TABLE 37 *Per-protocol analysis: final risk assessed at clinic,* n *(%)*

Measure	Grampian			Wales		
	Intervention (*n* = 185)[a]	**Control (*n* = 102)[b]**	**RR (95% CI)**	**Intervention (*n* = 192)[c]**	**Control (*n* = 105)[d]**	**RR (95% CI)**
Low	17 (9.2)	23 (22.5)	1.0	53 (27.6)	16 (15.2)	1.0
Elevated	168 (90.8)	79 (77.5)	1.17	139 (72.4)	89 (84.8)	0.85
High	55 (29.7)	25 (24.5)	(1.05 to 1.31)	55 (28.6)	34 (32.4)	(0.76 to 0.96)
Moderate	113 (61.1)	54 (52.9)		84 (43.8)	55 (52.4)	

Patients previously affected by breast cancer are included.
[a] Four elevated, one low.
[b] One elevated.
[c] Four elevated, six low.
[d] Three elevated.

Appendix 7

Nurse counsellor intervention: breakdown of staff costs

TABLE 38 *Breakdown of staff costs in Grampian*

Grade	Midpoint annual salary[a] (£)	Cost for appointment[b] (£)
Intervention group		
Nurse counsellor (NHS grade H)	28,908	33.52
Supervision		6.38
Meetings		9.50
Control group[c]		
Consultant	65,126	73.54
Associate specialist	46,519	50.56
Staff grade	37,799	41.08
Specialist registrar	33,681	36.60
Supervision		9.50
Meetings		3.46
Both groups		
Support staff	12,917	11.56
Clerical officer (NHS grade 3) and secretary (NHS grade 3)		
Nurse (NHS grade A) at outpatient reception	11,585	2.30

[a] Includes National Insurance and Superannuation.
[b] Includes 1 hour for outpatient appointment and 1 hour preparation time.
[c] The mean average cost for an appointment for the control group was an average of all the medical staff, weighted according to how many patients each group saw. This mean average was £52.10 per appointment.

TABLE 39 *Breakdown of staff costs in Wales*

Grade	Midpoint annual salary[a] (£)	Cost for appointment[b] (£)
Intervention group		
Nurse counsellor (NHS grade H)	30,338	35.18
Supervision		26.59
Meetings		8.96
Control group[c]		
Clinical assistant	40,793	44.34
Supervision		5.54
Meetings		8.96
Both groups		
Support staff	13,428	18.52
Nurse (NHS grade A) at outpatient reception	11,585	2.30

[a] Includes National Insurance and Superannuation.
[b] Includes 1 hour for outpatient appointment and 1 hour preparation time.
[c] Based on hourly reported rate of £22.17, 40 hours per week × 46 weeks.

Appendix 8

Nurse counsellor intervention: sensitivity analysis (NHS costs)

Grampian: intervention group

TABLE 40 *Nurse counsellor supervision time*

Supervision time	Total unit cost per appointment (£)	Difference in total unit cost per appointment (£)
30 minutes per week (baseline)	94.08	
15 minutes per week	90.89	–3.19
60 minutes per week	97.27	+6.38

TABLE 41 *Length of counselling appointment*

Time	Total unit cost per appointment (£)	Difference in total unit cost per appointment (£)
1 hour (baseline)	94.08	
1.5 hours	124.14	+30.06
45 minutes	79.05	–15.03

TABLE 42 *Nurse counsellor grade*

NSH grade[a]	Total unit cost per appointment (£)	Difference in total unit cost per appointment (£)
H (baseline)	94.08	
I	97.58	+3.50
G	90.66	–3.42

[a] The cost for the general staff meetings is also altered to incorporate the new nurse grade. Supervision time is left unchanged.

Grampian: control group

TABLE 43 *Medical staff grade*

NSH grades	Total unit cost per appointment (£)	Difference in total unit cost per appointment (£)
Mix of grades (baseline)[a]	109.74	
No consultant geneticists or associated specialists[b]	96.69	–13.05

[a] Consultants, associate specialists, staff grade and specialist registrar.
[b] Staff grade and specialist registrar only.

TABLE 44 *Nurse counsellor NHS grade*

NSH grade[a]	Total unit cost per appointment (£)	Difference in total unit cost per appointment (£)
H (baseline)	109.74	
I	125.51	+15.77
G	118.63	–8.89

[a] The cost for the general staff meetings is also altered to incorporate the new grade. Supervision time is left unchanged.

TABLE 45 *Preparation time for outpatient counselling appointment*

Preparation[a]	Total unit cost per appointment (£)	Difference in total unit cost per appointment (£)
Medical staff (baseline)	109.74	
Nurse counsellor	100.45	–9.29

[a] Preparation time of approximately 1 hour per patient includes preparing patient histories. Medical staff then undertakes the actual appointments, following preparation.

TABLE 46 *Length of counselling appointment*

Time[a]	Total unit cost per appointment (£)	Difference in total unit cost per appointment (£)
1 hour (baseline)	109.74	
1.5 hours	149.97	+40.23
45 minutes	90.07	–19.67

[a] Adjustments to room and staff costs.

Wales: intervention group

TABLE 47 *Nurse counsellor supervision*

Supervision time	Total unit cost per appointment (£)	Difference in total unit cost per appointment (£)
1.5 hours per week (baseline)	122.03	
1 hour per week	113.50	–8.53
0.5 hours per week	104.97	–17.06

TABLE 48 *Length of counselling appointment*

Time per appointment[a]	Total unit cost per appointment (£)	Difference in total unit cost per appointment (£)
1 hour (baseline)	122.03	
1.5 hours	152.92	+30.89
45 minutes	106.59	–15.44

[a] Adjustments to room and staff costs.

Wales: control group

TABLE 49 *Medical staff grade*

Grades	Total unit cost per appointment (£)	Difference in total unit cost per appointment (£)
Clinical assistant only (baseline)	111.14	
Mix of consultant geneticist, senior registrar and clinical assistant[a]	118.47	+7.33

[a] Equal split of time for the three grades of staff. Only supervision time for the clinical assistant is included here.

TABLE 50 *Clinical assistant supervision time*

Supervision time	Total unit cost per appointment (£)	Difference in total unit cost per appointment (£)
15–30 minutes per week (baseline)	111.14	
30 minutes per month	108.37	–2.77
2 hours per month	116.68	+5.54

TABLE 51 *Length of counselling appointment*

Time per appointment[a]	Total unit cost per appointment (£)	Difference in total unit cost per appointment (£)
1 hour (baseline)	111.14	
1.5 hours	149.38	+38.24
45 minutes	92.02	−19.12

[a] Adjustments to room and staff costs.

Appendix 9

Nurse counsellor intervention: patient time and travel costs

TABLE 52 *Travel costs*

One-way travel costs	**Grampian (*n* = 255)**	**Wales (*n* = 251)**
Mode of travel, *n* (%)	(*n* = 255)	(*n* = 251)
Private car	220 (86.3)	225 (89.6)
Bus	23 (9.0)	17 (6.8)
Other	12 (4.7)	9 (3.6)
Travel time (minutes), mean (SD)	(*n* = 254) 47.34 (35.64)	(*n* = 251) 35.66 (20.15)
Distance travelled (miles), mean (SD)	(*n* = 216) 23.70 (21.71)	(*n* = 208) 14.81 (15.0)
Cost of travel (£ Sterling), mean (95% CI)	(*n* = 216)	(*n* = 208)
Car	£12.06 (10.57 to 13.55)	£7.55 (6.85 to 8.26)
Bus/other	(*n* = 26) £3.73 (2.11 to 5.35)	(*n* = 24) £2.99 (1.96 to 4.02)

TABLE 53 *Time away from usual activity for counselling appointment*

Time away	**Grampian (*n* = 255)**	**Wales (*n* = 251)**
Usual activity, *n* (%)	(*n* = 255)	(*n* = 249)
Paid work	134 (52.5)	144 (57.8)
Housework	89 (34.9)	78 (31.3)
Other	32 (12.5)	27 (10.8)
Missing		2
Time away from work (minutes), mean (SD)	226.15 (139.27)	227.11 (149.04)
Cost of time away from work (£ Sterling) mean (95% CI)	(*n* = 130) £31.77 (28.38 to 35.17)	(*n* = 135) £31.91 (28.34 to 35.47)
Accompanied to counselling appointment, *n* (%)	83 (32.5)	140 (55.8)

TABLE 54 *Socio-economic information*

Socio-economic information	**Grampian (*n* = 255)**	**Wales (*n* = 251)**
Annual household income (£ Sterling), *n* (%)	(*n* = 237)	(*n* = 235)
≤ 15 000	58 (24.5)	62 (26.4)
15,001–25,000	67 (28.3)	74 (31.5)
≥ 25,001	112 (47.3)	99 (42.1)
Missing	18	16
Number of adults in household, *n* (%)	(*n* = 253)	(*n* = 244)
1	38 (15.0)	28 (11.5)
2	162 (64.0)	173 (70.9)
3	33 (13.0)	29 (11.9)
4	20 (7.9)	12 (4.9)
5	–	2 (0.8)
Missing	2	7
Number of children under 16, *n* (%)	(*n* = 247)	(*n* = 243)
0	127 (51.4)	108 (44.4)
1	42 (17.0)	50 (20.6)
2	58 (23.5)	66 (27.2)
3	19 (7.7)	13 (5.3)
4	1 (0.4)	5 (2.1)
6		1 (0.4)
Missing	8	8

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Feedback

The HTA Programme and the authors would like to know your views about this report.

The Correspondence Page on the HTA website (http://www.ncchta.org) is a convenient way to publish your comments. If you prefer, you can send your comments to the address below, telling us whether you would like us to transfer them to the website.

We look forward to hearing from you.

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