ORIGINAL ARTICLE

# Incidence of Basal Cell Carcinoma Multiplicity and Detailed Anatomic Distribution: Longitudinal Study of an Australian Population

Naomi M. Richmond-Sinclair[1,2], Nirmala Pandeya[1], Robert S. Ware[3], Rachel E. Neale[1], Gail M. Williams[3], Jolieke C. van der Pols[1] and Adèle C. Green[1]

A proportion of individuals are affected multiple times by basal cell carcinoma (BCC), but the rate and extent to which this occurs is unknown. We therefore prospectively estimated BCC incidence in a subtropical Australian population, focusing on the rate at which persons develop multiple primary BCCs and the precise anatomic sites of BCC occurrence. Between 1997 and 2006, 663 BCCs were confirmed in 301 of 1,337 participants in the population-based Nambour Skin Cancer Study. The incidence of persons affected multiple times by primary BCC was 705 per 100,000 person years compared to an incidence rate of people singly affected of 935 per 100,000 person years. Among the multiply and singly affected alike, site-specific BCC incidence rates were far highest on facial subsites, followed by upper limbs, trunk, and then lower limbs. We conclude that actual BCC tumor burden is much greater in the population than is apparent from normal incidence rates. Anatomic distribution of BCC is consistent with general levels of sun exposure across body sites.

*Journal of Investigative Dermatology* (2009) **129,** 323–328; doi:10.1038/jid.2008.234; published online 31 July 2008

## INTRODUCTION

Basal cell carcinoma (BCC) is the predominant skin cancer in Caucasian populations (Zedan *et al.*, 2001) and its treatment imposes a substantial economic burden (Mathers *et al.*, 1999; Joseph *et al.*, 2001). Because of its high frequency and low mortality, BCCs are not routinely registered (Green and MacLennan, 1989) and incidence estimates have largely come from *ad hoc* studies. The highest reported incidence rates are in Australia where 1–2 persons per 100 are affected by BCC each year (Staples *et al.*, 2006), an order of magnitude higher than corresponding estimates in Europe and North America (Bath-Hextall *et al.*, 2007; Karagas *et al.*, 1999).

The incidence of persons affected by BCC is likely to substantially underestimate the true incidence of this cancer due to the common occurrence of multiple primary tumors within individuals synchronously or at different times. In New Hampshire, USA, multiple BCCs occurred in 16% of affected patients in a 2-year period (Karagas *et al.*, 1999), whereas in a tropical Australian community, 26% of BCC patients were treated for multiple BCCs in a 3-year period (Raasch and Buettner, 2002), though whether these were diagnosed at the same or different times was unclear. To date the only detailed prospective study of BCC tumor incidence involved intensive skin examination surveys where there was evidence that more BCCs were being diagnosed due to increased surveillance (Valery *et al.*, 2004). Thus, the extent of the public health burden of routinely treated, multiple BCCs, remains unknown.

BCC incidence has a strong inverse relationship with latitude (Giles *et al.*, 1988); in general, chronically sun-exposed parts of the body develop a larger proportion of BCCs than those with less or infrequent exposure (Raasch *et al.*, 1998). Incidence has rarely been documented according to detailed anatomic subsites, and never in regard to multiplicity of BCC tumor occurrence.

Over the past decade we have closely monitored the occurrence of BCC, including multiple primary BCCs, in a subtropical Queensland community sample. We report here the results of this detailed longitudinal assessment of BCC incidence.

## RESULTS

### Study population

Of the 1,337 ongoing participants in the Nambour Skin Cancer Study on 1 January 1997, 1,244 (93%) had complete follow-up until 31 December 2006, 92 (7%) participants died during follow-up and one person withdrew from the study. At baseline in 1997, the mean age of this cohort was 54 years

[1]*Cancer and Population Studies Unit, Queensland Institute of Medical Research, Brisbane, Queensland, Australia;* [2]*School of Life Sciences and Institute of Health and Biomedical Innovation, Queensland University of Technology, Brisbane, Queensland, Australia and* [3]*School of Population Health, University of Queensland, Brisbane, Queensland, Australia*

*All work was conducted at the Queensland Institute of Medical Research.*

*Correspondence: Naomi M. Richmond-Sinclair, Cancer and Population Studies Unit, Queensland Institute of Medical Research, PO Royal Brisbane Hospital, Brisbane, Queensland 4029, Australia.*
*E-mail Naomi.Richmond@qimr.edu.au*

*Abbreviations: BCC, basal cell carcinoma; CI, confidence interval; pyar, person years at risk*

*Received 15 April 2008; revised 2 June 2008; accepted 15 June 2008; published online 31 July 2008*

and 56% were female (Table 1). Apart from a borderline difference ($P=0.05$) with regard to age distribution, the 1,337 participants in the present study were no different from the 1,621 participants who took part in a preceding skin cancer prevention trial (Table 1) and were representative of the original randomly selected Nambour Skin Cancer Study population (Green *et al.*, 1994). Among the 1,337 participants, 18% had a known history of BCC before 1997, and of these, 17% had experienced multiple primary BCCs.

**Table 1. Characteristics of participants of a skin cancer prevention trial 1992–1996 who were followed up and not followed up 1997–2006**

| Characteristic | Original 1992 community-based trial participants (*n*=1,621) | | |
|---|---|---|---|
| | Followed up (*n*=1,337) | Not followed up (*n*=284) | *P*-value |
| *Sex* | | | |
| Female | 749 (56%) | 162 (57%) | |
| Male | 588 (44%) | 122 (43%) | 0.75 |
| *Age at start of Nambour trial in 1992 (years)* | | | |
| 20–39 | 361 (27%) | 94 (33%) | |
| 40–59 | 650 (49%) | 117 (41%) | |
| 60+ | 326 (24%) | 73 (26%) | 0.05 |
| *Skin color* | | | |
| Fair | 739 (55%) | 156 (55%) | |
| Medium | 504 (38%) | 110(39%) | |
| Olive | 93 (7%) | 17 (6%) | 0.82 |
| *Occupational sun exposure* | | | |
| Mainly outdoors | 249 (19%) | 54 (19%) | |
| Both indoor and outdoor | 494 (37%) | 107 (38%) | |
| Mainly indoors | 593 (44%) | 122 (43%) | 0.93 |
| *Previous basal cell carcinoma (before 1997)* | | | |
| Yes | 234 (18%) | 38 (13%) | |
| No | 1,103 (82%) | 246 (87%) | 0.09 |

### Incidence estimates

During the 10-year period, 663 BCCs were diagnosed within the cohort: 394 primary tumors in 151 men and 269 tumors in 150 women (Table 2). The overall age-standardized incidence rate of BCC was 1,541 people affected per 100,000 person years at risk (pyar, 95% confidence interval (CI) 1,286–1,829), 1,813 per 100,000 pyar among men and 1,269 per 100,000 pyar among women. Incidence increased with age and was generally higher in men than women in each age group.

### Single BCC

Of those affected by BCC in the 10-year period, 162 (54%) persons developed one BCC only. Incidence of persons affected by a single BCC was 630 per 100,000 pyar in men under 40 years, rising to 2,614 per 100,000 pyar (95% CI 2,014–3,236) after age 60 years (Table 2). Incidence of women with only one BCC was very low before age 40 years (one person affected) but rose thereafter.

### Multiple BCCs

Among all those affected by BCC in the 10-year period, 46% (139 persons) developed multiple BCCs (range 2–28 BCCs). Of those multiply affected, 56% developed 3 or more, 26% 4 or more, and 17% developed 5 or more BCCs. The median time between BCCs decreased as a person developed successively more, but not in a proportionate manner. The median time between fourth and fifth BCCs (23 months) was less than half than that between first and second (57 months). A total of 41 people (29%) were diagnosed with two or more BCCs on the same date in the 10-year period.

The incidence of people affected by more than one BCC was 705 per 100,000 pyar (95% CI 539–905), 877 and 533 per 100,000 pyar in men and women, respectively (Table 2). For both sexes incidence of multiple BCCs increased steadily with age but was low before age 40 years. More men than women were affected by multiple BCCs.

### Anatomic distribution

Facial sites had by far the highest BCC incidence with peak rates seen on the nose (around 5.2 per 1,000 pyar), followed by forehead/temple, then cheek/perioral region, and then ears (Table 3). However, when unit surface area was accounted for, rank order noticeably altered. While nose maintained the highest rates (around 2,100 per 1,000 body units per year), followed by cheek/perioral region, then eyes, and then forehead/temple (Table 3). Surface-area-standardized incidence on the limbs was the next highest, then the trunk whose rate was 1/100th of that on the nose or cheek. Considering specific subsites, the upper arms and trunk had similar surface-area-standardized incidence rates. Anatomic distribution did not vary by sex or by number of BCCs treated in the 10-year period.

Incidence rates were compared among those assigned to regular sunscreen use (active intervention) and discretionary sunscreen use (control arm) during the preceding field trial and showed no material differences in person- or tumor-based incidence of BCC.

## DISCUSSION

We comprehensively analyzed the incidence rates and sites of occurrence of BCC in a subtropical Australian community over a 10-year period, with a focus on people affected by multiple BCCs. The incidence of people treated for new primary BCCs was 1.5% in 10 years, confirming the extraordinarily high incidence of BCC in white populations residing at low latitudes (Green *et al.*, 1996; Buettner and Raasch, 1998; Valery *et al.*, 2004) compared to European and North American populations living in temperate climates (Karagas *et al.*, 1999; Bath-Hextall *et al.*, 2007).

**Table 2. Age-specific incidence rates of basal cell carcinoma in Queensland, Australia, 1997–2006[1]**

| | All persons with BCC | | | Persons with single BCC | | | Persons with multiple BCC | | |
|---|---|---|---|---|---|---|---|---|---|
| | Number of persons | Person years | Incidence rate (95% CI) | Number of persons | Person years | Incidence rate (95% CI) | Number of persons | Person years | Incidence rate (95% CI) |
| *Male* | | | | | | | | | |
| *Age[2] (years)* | | | | | | | | | |
| 20–39 | 5 | 497 | 1,005 (210–1,982) | 3 | 476 | 630 (0–1,425) | 2 | 497 | 402 (0–1,062) |
| 40–59 | 46 | 2,575 | 1,786 (1,319–2,269) | 20 | 2,354 | 849 (509–1,218) | 26 | 2,575 | 1,010 (649–1,393) |
| 60+ | 100 | 2,531 | 3,950 (3,349–4,555) | 53 | 2,027 | 2,614 (2,014–3,236) | 47 | 2,531 | 1,856 (1,399–2,335) |
| Weighted average[3] | 151 | 5,604 | 1,813 (1,392–2,303) | 76 | 4,858 | 1,068 (729–1,475) | 75 | 5,604 | 877 (607–1,222) |
| *Female* | | | | | | | | | |
| *Age[2] (years)* | | | | | | | | | |
| 20–39 | 2 | 538 | 372 (0–947) | 1 | 530 | 189 (0–614) | 1 | 538 | 186 (0–623) |
| 40–59 | 61 | 3,515 | 1,736 (1,350–2,141) | 40 | 3,316 | 1,206 (863–1,569) | 21 | 3,515 | 597 (357–860) |
| 60+ | 87 | 3,209 | 2,711 (2,228–3,188) | 45 | 2,778 | 1,620 (1,184–2,060) | 42 | 3,209 | 1,309 (951–1,678) |
| Weighted average[3] | 150 | 7,261 | 1,269 (1,008–1,582) | 86 | 6,624 | 801 (602–1,047) | 64 | 7,261 | 533 (363–763) |
| Total[3] | 301 | 12,866 | 1,541 (1,286–1,829) | 162 | 11,482 | 935 (737–1,165) | 139 | 12,866 | 705 (539–905) |

BCC, basal cell carcinoma. CI, confidence interval.
[1]Incidence per 100,000 person years at risk.
[2]Age at the date of diagnosis.
[3]Age standardized to the standard world population (Ahmad *et al.*, 2001).

Nearly 50% of people routinely treated for BCC developed multiple primary BCCs during 10 years of observation. This is broadly consistent with previous observations that 43% of people affected by BCC developed a subsequent BCC within 4.5 years of active surveillance in the same population (Pandeya *et al.*, 2005) and those of a meta-analysis of seven independent studies, which showed the mean 3-year risk of BCC to be 44% after an initial diagnosis of BCC in North America (Marcil and Stern, 2000). Our estimate of over 700 persons per 100,000 person years affected by multiple BCCs is striking and gives some indication why treatment of BCC consumes a substantial proportion of annual health spending in Australia (Australian Institute of Health and Welfare (AIHW), 2005), North America (Chen *et al.*, 2001), and Europe (Morris *et al.*, 2005).

Our data indicate that the time between subsequent BCCs decreases with successive BCCs in an individual, which has implications for the clinical follow-up of BCC patients. Early detection and treatment of subsequent primary BCCs could be enhanced by encouraging regular personal skin inspection and professional skin examinations after an initial BCC diagnosis (Stern, 1999; Valery *et al.*, 2004).

We calculated the site-specific incidence of BCC standardized for the surface area of anatomic subsites. The standardization by unit surface area allowed the direct comparison of BCC tumor burden per unit area of skin taking into account large differences in surface area among body sites. We confirmed that the distribution of BCC across anatomic sites is consistent with level of sun exposure, in agreement with other studies (Franceschi *et al.*, 1996; Bastiaens *et al.*, 1998; Buettner and Raasch, 1998), though the actual site-specific rates per unit surface area are orders of magnitude higher in Australia than southern Europe (Franceschi *et al.*, 1996). Unlike our investigation, others have not examined anatomic subsites individually but rather have grouped sites based on their opportunity for sun-exposure. A study by Buettner and Raasch (1998) that included only single lesions per person reported BCC incidence was highest on the combined subsites of lip, orbit, nasolabial, ear, nose, and cheek. This agrees with our estimates but we have gone further showing the occurrence of BCC on the nose and cheek/perioral region to be the greatest. In addition, we have shown that anatomic subsite distribution of BCC is similar whether people are singly or multiply affected. The top five subsites (nose, cheek, eye area, forehead, and ears) correspond closely to the subsites that receive the greatest UV exposure (Diffey *et al.*, 1979), apart from the forehead which receives the second highest level of UV exposure (Diffey *et al.*, 1979) but had the fourth highest incidence of BCCs. This difference could be explained by the sun protection of the forehead offered by hair cover (which can decrease solar UV exposure by up to 80% (Green *et al.*, 2006)), or by caps or hats. Diffey *et al.* (1979) did not measure the mean UV exposure of the ears, however, it is likely the ears receive sun protection in a similar way to that of the forehead.

The anatomic site distribution of BCCs on nonfacial regions was less predictable and not as directly associated with general UV exposure. For example, the more highly sun-exposed hand

**Table 3. Site-specific and surface-area-standardized incidence rates for all persons affected by basal cell carcinoma in Queensland, Australia, 1997–2006[1,2,3]**

| Anatomical site | Number of tumors (%) | Incidence rate per 1,000 | Surface-area-standardized incidence rate per 1,000 |
|---|---|---|---|
| *Head and neck* | | | |
| *Overall* | *379 (57)* | *17.3* | *223.6* |
| Scalp | 5 | 0.2 | 6.3 |
| Forehead/temple | 61 | 3.0 | 426.6 |
| Ears | 38 | 1.8 | 366.5 |
| Eyes | 31 | 1.6 | 1,609.6 |
| Nose | 110 | 5.2 | 2,584.3 |
| Cheek/perioral | 64 | 2.8 | 2,122.6 |
| Chin/jaw | 14 | 0.6 | 121.2 |
| Neck | 47 | 1.7 | 72.7 |
| *Trunk* | | | |
| *Overall* | *111 (17)* | *4.7* | *20.8* |
| Back | 83 | 3.6 | 37.8 |
| Chest/abdomen | 27 | 1.1 | 19.2 |
| *Limbs* | | | |
| *Overall* | *172 (26)* | *7.9* | *13.9* |
| Arms | | | |
| *Overall* | *118 (18)* | *5.0* | *30.4* |
| Upper arm[4] | 63 | 2.8 | 35.6 |
| Lower arm | 36 | 1.4 | 23.2 |
| Hands | 9 | 0.3 | 13.4 |
| Legs | | | |
| *Overall* | *54 (8)* | *2.8* | *7.1* |
| Hip and upper leg | 4 | 0.2 | 0.9 |
| Lower leg | 45 | 2.5 | 17.7 |
| Feet | 2 | 0.06 | 0.9 |

Italic values provide overall estimates for anatomic regions.
[1]Surface-area-standardized and age-standardized per 1,000 body units per year.
[2]Anatomical site was unknown for one BCC and BCCs with unspecified subsites were excluded.
[3]Surface-area-standardized incidence rates may reach beyond 1,000 per 1,000 body units per year because people who have been affected by BCC more than once are included in the calculations.
[4]Calculations for the upper arm include the shoulder.

had a much lower proportion of BCCs compared to the forearm and upper arm, in agreement with previous reports (Pearl and Scott, 1986; Buettner and Raasch, 1998).

The strengths of this study were the longitudinal data collection and the community-based sample, with complete ascertainment of all confirmed BCCs in a 10-year period. Although complete records of participants' skin cancers were available from 1992, we purposely began observation for this incidence study in 1997 to avoid the unusually close dermatological surveillance participants received during the prevention trial (Valery *et al.*, 2004). Since the completion of the trial, we have investigated the long-term protective effect of sunscreen use against BCC and found no significant change in BCC incidence (Van der Pols *et al.*, 2006b). We furthermore showed that there was no impact of the sunscreen intervention on BCC tumor incidence measures in this follow-up study.

Present study participants were representative of the original community-based population with respect to sex, skin color, and frequency of outdoor occupations. However, there were a slightly higher proportion of people aged 40–59 years included in the current study which may explain why the participants were also somewhat more likely to have had a BCC before baseline compared to those who were not included (18 versus 13%, respectively). It is therefore possible that our incidence estimates are slightly inflated compared to those in the community at large, though this bias could not explain more than a small proportion of the very high magnitude of multiple BCC occurrences observed.

This report provides insight into the potential magnitude of the BCC tumor burden in Caucasian populations, especially those living or frequently holidaying in places of intense sun exposure. It is apparent that the actual BCC tumor burden is greater in a population than is apparent simply from incidence rates of BCC. There is not only the opportunity for early detection of BCC among people previously affected, but also the evidence about anatomic sites of BCC predilection can be translated directly into specific evidence-based health messages about sun protection. The prevention of BCC can be achieved by the avoidance of excessive UV exposure especially to the head and neck, and in particular, the nose.

## MATERIALS AND METHODS

### The Nambour Skin Cancer Study

Study participants were originally randomly selected in 1986 from the electoral register of all adult residents of the subtropical Queensland township of Nambour (latitude 26°S) for a baseline study of skin cancer (Green *et al.*, 1988). A total of 2,095 participants (70%) provided written informed consent to take part. They were representative of the community with regard to phenotypic and sun exposure skin cancer risk factors (Green *et al.*, 1988). Of these, 1,621 (77%) participated in a field trial to assess sunscreen application and β-carotene supplementation in skin cancer prevention (1992–1996). Detailed descriptions of the community sample, field trial, and its long-term outcomes are published (Green *et al.*, 1999; Van der Pols *et al.*, 2006a, b). Upon conclusion of the trial in 1996, participants were invited to take part in a follow-up study of skin cancer. Continuing participants consented to have subsequently diagnosed skin cancers notified to the investigators by regional Queensland Pathology Laboratories, allowing 100% ascertainment of all histologically confirmed BCCs. No participants were immunosuppressed or affected by Gorlin's syndrome. Long-term skin cancer follow-up continued to 31 December 2006. The Queensland Institute of Medical Research Ethics Committee provided ethical approval.

### Data collection

All BCCs were verified histologically. Investigators abstracted details of anatomic site from pathology reports. Because the same tumor may be histologically diagnosed twice, at initial biopsy/excision and again if reexcised, all records of apparently multiple BCCs diagnosed within a 6-month period in the same person and on the same anatomic site were crosschecked to identify duplicate reports. Recurrent BCCs diagnosed at the sites of earlier primary lesions were excluded. Information on skin cancer history before 1997 was based on skin cancers identified during skin examinations and surveys conducted among the participants between 1986 and 1996 (Green *et al*., 1988, 1994, 1996; Green and Battistutta, 1990), and on self-reports of any type of skin cancer before 1986 (Green *et al*., 1988) with histological verification of the subset of cancers reported in 1985–1986 (Green and Battistutta, 1990).

### Data analysis

All new BCCs that occurred among participants during 1997–2006 were included. Person- and tumor-based incidence rates of confirmed BCCs were calculated over the 10-year period 1 January 1997 to 31 December 2006, and were directly age-standardized to the standard world population (Ahmad *et al*., 2001). For person-based incidence rate calculation, the number of people with a histological BCC diagnosis was divided by the total number of pyar for the observation period and expressed per 100,000 pyar. Person years were counted until either date of death, date of withdrawal from the study, or the end date of observation, whichever came first. Calculations were carried out separately for persons with single and multiple BCCs treated during the 10-year study period. For calculation of site-specific incidence rates, the numbers of histologically confirmed tumors on each site were divided by the total number of pyar and rates were standardized for relative surface area (Pearl and Scott, 1986; Buettner and Raasch, 1998) and expressed per 1,000 body units, where each body unit is equivalent to the total surface area of the skin of a person. For example, the calculation of rates for the nose, age-standardized incidence rates were divided by 0.002 because the nose is an estimated 0.02% of the total body unit/surface area. These rates permit a direct comparison of the BCC incidence per unit area of skin on different anatomic sites. Median time interval between BCCs was estimated using PROC LIFETEST.

Confidence intervals were calculated using bias-corrected bootstrap methods (Efron and Tibshirani, 1993). We resampled from the original skewed distribution of cases 10,000 times with replacement. Statistical analyses were conducted using Stata version 9.1 (StataCorp, College Station, TX) and SAS version 9.1 (SAS Institute Inc., Cary, NC). $P<0.05$ was considered statistically significant.

## CONFLICT OF INTEREST

The authors state no conflict of interest.

## ACKNOWLEDGMENTS

We thank the Nambour Skin Cancer Study participants and their doctors who assisted in long-term monitoring of skin cancer. Our thanks are extended to Queensland Medical Laboratory and Sullivan Nicolaides Pathology for providing pathology reports for all study tumors. This project was supported by a grant from the National Health and Medical Research Council (Grant number 442976). Naomi Richmond-Sinclair was supported by a Smart State PhD Scholarship and an ANZ Trustees Medical Research in Queensland PhD Scholarship and Queensland Institute of Medical Research PhD Top-Up Scholarship. Rachel Neale was funded by a National Health and Medical Research Council (Aust) Sidney Sax Postdoctoral Fellowship.

## REFERENCES

Ahmad O, Boschi-Pinto C, Lopez A, Murray C, Lozano R, Inoue M (2001) *Age Standardization of Rates: A New WHO Standard*. World Health Organization: Geneva

Australian Institute of Health and Welfare (AIHW) (2005) *Health System Expenditures on Cancer and Other Neoplasms in Australia, 2000–01*. AIHW cat. no. HWE 29. Health and Welfare Expenditure Series No. 22. Australian Institute of Health and Welfare: Canberra

Bastiaens MT, Hoefnagel JJ, Bruijn JA, Westendorp RG, Vermeer BJ, Bouwes Bavinck JN (1998) Differences in age, site distribution, and sex between nodular and superficial basal cell carcinoma indicate different types of tumours. *J Invest Dermatol* 110:880–4

Bath-Hextall F, Leonardi-Bee J, Smith C, Meal A, Hubbard R (2007) Trends in incidence of skin basal cell carcinoma. Additional evidence from a UK primary care database study. *Int J Cancer* 121:2105–8

Buettner PG, Raasch BA (1998) Incidence rates of skin cancer in Townsville, Australia. *Int J Cancer* 78:587–93

Chen JG, Fleischer AB Jr, Smith ED, Kancler C, Goldman ND, Williford PM *et al*. (2001) Cost of nonmelanoma skin cancer treatment in the United States. *Dermatol Surg* 27:1035–8

Diffey BL, Tate TJ, Davis A (1979) Solar dosimetry of the face: the relationship of natural ultraviolet radiation exposure to basal cell carcinoma localisation. *Phys Med Biol* 24:931–9

Efron B, Tibshirani RJ (1993) *An Introduction to the Bootstrap*. Chapman & Hall: New York, NY, pp 178–201

Franceschi S, Levi F, Randimbison L, La Vecchia C (1996) Site distribution of different types of skin cancer: new aetiological clues. *Int J Cancer* 67:24–8

Giles GG, Marks R, Foley P (1988) Incidence of non-melanocytic skin cancer treated in Australia. *Br Med J (Clin Res Ed)* 296:13–7

Green A, Battistutta D (1990) Incidence and determinants of skin cancer in a high-risk Australian population. *Int J Cancer* 46:356–61

Green A, Battistutta D, Hart V, Leslie D, Marks G, Williams G *et al*. (1994) The nambour skin cancer and actinic eye disease prevention trial: design and baseline characteristics of participants. *Control Clin Trials* 15:512–22

Green A, Battistutta D, Hart V, Leslie D, Weedon D (1996) Skin cancer in a subtropical Australian population: incidence and lack of association with occupation. The Nambour Study Group. *Am J Epidemiol* 144:1034–40

Green A, Beardmore G, Hart V, Leslie D, Marks R, Staines D (1988) Skin cancer in a Queensland population. *J Am Acad Dermatol* 19:1045–52

Green A, MacLennan R (1989) Monitoring and surveillance of skin cancer. *Transact. Transact Menzies Found* 15:193–9

Green A, Williams G, Neale R, Hart V, Leslie D, Parsons P *et al*. (1999) Daily sunscreen application and betacarotene supplementation in prevention of basal-cell and squamous-cell carcinomas of the skin: a randomised controlled trial. *Lancet* 354:723–9

Green AC, Kimlin M, Siskind V, Whiteman DC (2006) Hypothesis: hair cover can protect against invasive melanoma on the head and neck (Australia). *Cancer Causes Control* 17:1263–6

Joseph AK, Mark TL, Mueller C (2001) The period prevalence and costs of treating nonmelanoma skin cancers in patients over 65 years of age covered by medicare. *Dermatol Surg* 27:955–9

Karagas MR, Greenberg ER, Spencer SK, Stukel TA, Mott LA (1999) Increase in incidence rates of basal cell and squamous cell skin cancer in New Hampshire, USA. New Hampshire Skin Cancer Study Ggroup. *Int J Cancer* 81:555–9

Marcil I, Stern RS (2000) Risk of developing a subsequent nonmelanoma skin cancer in patients with a history of nonmelanoma skin cancer: a critical review of the literature and meta-analysis. *Arch Dermatol* 136:1524–30

Mathers C, Vos T, Stevenson C (1999) *The Burden of Disease and Injury in Australia*. AIHW: Canberra

Morris S, Cox B, Bosanquet N (2005) *Cost of Skin Cancer in England*. Tanaka Business School, Imperial College of London: London, pp 1–19

Pandeya N, Purdie DM, Green A, Williams G (2005) Repeated occurrence of basal cell carcinoma of the skin and multifailure survival analysis: follow-up data from the Nambour Skin Cancer Prevention Trial. *Am J Epidemiol* 161:748–54

Pearl DK, Scott EL (1986) The anatomical distribution of skin cancers. *Int J Epidemiol* 15:502–6

Raasch B, Maclennan R, Wronski I, Robertson I (1998) Body site specific incidence of basal and squamous cell carcinoma in an exposed population, Townsville, Australia. *Mutat Res* 422:101–6

Raasch BA, Buettner PG (2002) Multiple nonmelanoma skin cancer in an exposed Australian population. *Int J Dermatol* 41:652–8

Staples MP, Elwood M, Burton RC, Williams JL, Marks R, Giles GG (2006) Non-melanoma skin cancer in Australia: the 2002 national survey and trends since 1985. *Med J Aust* 184:6–10

Stern RS (1999) The mysteries of geographic variability in nonmelanoma skin cancer incidence. *Arch Dermatol* 135:843–4

Valery PC, Neale R, Williams G, Pandeya N, Siller G, Green A (2004) The effect of skin examination surveys on the incidence of basal cell carcinoma in a Queensland community sample: a 10-year longitudinal study. *J Investig Dermatol Symp Proc* 9:148–51

Van der Pols JC, Williams GM, Neale RE, Clavarino A, Green AC (2006a) Long-term increase in sunscreen use in an Australian community after a skin cancer prevention trial. *Prev Med* 42:171–6

Van der Pols JC, Williams GM, Pandeya N, Logan V, Green AC (2006b) Prolonged prevention of squamous cell carcinoma of the skin by regular sunscreen use. *Cancer Epidemiol Biomarkers Prev* 15: 2546–2548

Zedan W, Robinson PA, Markham AF, High AS (2001) Expression of the Sonic Hedgehog receptor ''PATCHED'' in basal cell carcinomas and odontogenic keratocysts. *J Pathol* 194:473–7