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ORIGINAL ARTICLE

Network geometry shows evidence sequestration for medical vs. surgical practices: treatments for basal cell carcinoma

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Abstract

Objectives: Basal cell carcinoma (BCC) is the most common cancer with 2 million treatments per year with little evidence-based guidelines for treatment. There are three classes of interventions (surgical, destructive, and topical) for BCC, and this study aimed to determine whether there are preferences or avoidances in comparisons of different types of treatments for BCC in randomized controlled trials (RCTs).

Study Design and Setting: PubMed, Cochrane Central Registry of Clinical Trials, and ClinicalTrials.Gov were used to identify eligible published and registered ongoing RCTs.

Results: Fifty-five trials (42 published and 13 registered trials) were identified. Only one unpublished registered trial compared a topical vs. a surgical intervention, and only one trial compared a topical vs. a destructive intervention. Conversely, 44 of the 55 trials compared interventions within the same treatment class and 9 of 55 trials compared surgical vs. destructive interventions. In most trials, selection of same-class comparators was not necessitated by the type of BCC lesions (nonaggressive superficial or nodular vs. aggressive, infiltrative, morpheic BCCs, $P = 0.155$) or their location (face vs. nonfacial, $P = 0.137$).

Conclusion: This is the first time that an evaluation of network geometry is applied to address issues of comparisons between different families of interventions that belong to different specialties and practices (medical vs. surgical). Previous evaluations of homophily have addressed different families of interventions, in which all interventions are medical (drugs) and performed in the same health-care settings. The noncommunicating bodies of evidence between medical and surgical interventions that we document highlight a problem of unnecessary sequestration of the evidence and the corresponding health-care practices.

Keywords: Basal cell carcinoma; Homophily; Treatment; Randomized controlled trials; Network, Comparative effectiveness

1. Introduction

Having a strong evidence base is critical to make the best clinical decisions. Numerous randomized controlled trials and meta-analyses are conducted to strengthen the evidence base for treatment decisions; however, examining the totality of the evidence is also crucial. The evaluation of trial networks is one way to achieve this [1,2]. A trial network illustrates the amount of evidence available and the types of comparisons performed between different treatments for a specific disease. Evaluation of such networks can inform in particular whether certain drugs or treatments are compared more frequently or avoided. This is essential in assessing the evidence base of treatments for diseases with multiple treatment modalities.

Basal cell carcinoma (BCC) is the most common malignancy in humans, and many treatment options are available [3–5]. Because BCCs are rarely invasive or metastasize (0.0028–0.55%) [3,6–8], BCCs are often successfully treated with one of three major treatment classes: surgical (ie, excision, Moh's micrographic surgery), destructive (curettage, cryosurgery), and topical (imiquimod, 5-fluoruracil cream) [3]. Each of the three treatment classes has a greater than 80% cure rate for most BCCs; however, there are significant differences in their approach (invasive vs. conservative), potential adverse events (eg, scarring, infection, and bruising) [3,9], and costs [10]. BCC is approximately the fourth most costly cancer of the Medicare population [11], and because

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What is new?

Key findings

- Most trials of basal cell carcinoma (BCC) compare interventions within the same class (ie, surgery vs. other surgical treatments) and most commonly even the same intervention against itself in different doses or formulation. The selection of same-class comparators was not necessitated by the histologic type or the tumor location.

What this adds to what was known?

- Despite 55 trials, there is a dearth of comparative evidence on conservative vs. invasive treatments for BCC. This is the first time that a network geometry was applied to demonstrate the noncommunicating bodies of evidence between different families of interventions (medical vs. surgical) for the same disease.

What is the implication and what should change now?

- The treatment of BCC is estimated to cost more than $1 billion in the United States alone, and thus, randomized clinical trials are needed to compare different treatment classes as each varies in cost and patient access.

Caucasians have a 30% lifetime risk of developing a BCC [5,6], the treatment of BCCs is a major health-care burden. Moreover, in many countries, different interventions may be performed by different specialists. In particular, Moh's micrographic surgery is done by a specialized set of surgeons, whereas surgical excision is done by many practitioners, and destructive or topical treatments have an even wider range of practicing dermatologists who use them.

When several treatment options exist for the same disease, a strong evidence base requires multiple randomized comparisons between treatments within and across different classes of treatment [12]. In the case of BCC, there are different types of BCCs (eg, less aggressive—such as nodular and superficial BCCs—and aggressive—such as infiltrative, morpheaform, sclerosing, and micronodular histologic variants), and these tumors can occur in different locations and have different clinical outcomes [6]. Thus, it is critical to know the relative merits of different treatment options for different types of tumor presentations.

In this study, our research goal was to survey the available randomized controlled trials (RCTs) on treatments of BCC to evaluate whether there is sufficient randomized evidence to guide the clinical decisions between different classes of treatments for BCC. To achieve this goal, we used methods that evaluate the geometry of the networks of the comparisons involved in RCTs to understand what treatments have been compared and determine if there is homophily, when treatment interventions are compared against other interventions of the same class, but not with interventions of a different class, in these trials [1,12].

This is the first time that an evaluation of network geometry is applied to address issues of comparisons between different families of interventions that belong to different specialties and practices (medical vs. surgical). Previous evaluations of homophily have addressed different families of interventions in which all interventions are medical (drugs) and performed in the same health-care settings [12]. The noncommunicating bodies of evidence that we document between medical and surgical interventions highlight a problem of unnecessary sequestration of the evidence and the corresponding health-care practices.

2. Methods

2.1. Data sources and search strategies

RCTs evaluating different classes of treatments (surgical, destructive, and topical) [3] for BCC were considered eligible. Only trials with full texts in English were included. Reviews, nonrandomized studies, and trials related to prevention of BCC were excluded.

We searched PubMed (last search in September 2012) using search term "basal cell" and randomized controlled trial as the type of publication. We also searched the Cochrane Central Registry of Clinical Trials and the references of previous reviews on BCC for any missed trials. Furthermore, the ClinicalTrials.gov database was also searched with the terms "randomized, basal cell carcinoma, skin" to identify ongoing or recently completed randomized trials that compared different treatment modalities for BCC. The consideration of both published and registered trials aimed to address whether the geometry might be different in the published evidence alone.

From each eligible trial, information on the publication year, types of treatments compared, type of BCC (less aggressive: nodular BCC, superficial BCC; or aggressive: recurrent BCC, or infiltrative, morpheaform, sclerosing, and micronodular BCC), location of tumors, and sample size (actual or intended, if ongoing) was collected.

2.2. Construction of networks and homophily testing

Networks of trial comparisons were drawn using each intervention as a node and with links between the nodes representing the presence of trials comparing the two linked interventions. The thickness of the connections between the nodes is drawn proportional to the number of trial comparisons [13]. Whenever a trial compares the same intervention given at different dosing, formulation, timing, or schedule, this is drawn as an autoloop around the node of that intervention. The thickness of the autoloops is proportional to the number of such trial comparisons.