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**Cancer patients' experiences of using mistletoe (*Viscum album*):  
A qualitative systematic review and synthesis**

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Keywords:	botanicals, cancer, systematic review, integrative med, qualitative research
Abstract:	<p><b>Objective</b> Systematic reviews of mistletoe therapy (MT) trials in cancer show promising results in improvement of patients' quality of life during chemotherapy and reduction of fatigue. However patients' experiences of side effects, the acceptability, tolerability and perceived benefits of MT have not been systematically reviewed. The aim of this study is to systematically review and synthesise the results of qualitative studies of cancer patients' experiences of using MT.</p> <p><b>Design</b> A systematic search was conducted in Medline, Embase, Psychlit, Cinahl and AMED to identify qualitative studies of MT. Articles were screened independently by two reviewers and critically appraised using the CASP tool. A thematic synthesis of the findings was carried out.</p> <p><b>Results</b> 173 papers were identified, 156 were excluded at initial screening. Seventeen papers were read in full, 14 of which were excluded. Three articles about patients' experiences of MT alongside conventional treatment were included in the synthesis, either as a mono-therapy (two articles) or as part of a package of anthroposophic treatment (one article). Patients reported demonstrable changes to their physical, emotional and psychosocial wellbeing following MT, and a reduction in chemo-therapy side-effects. Self-reported side-effects from MT were few, and the studies suggest good adherence to the therapy. Self-injection gave patients a sense of empowerment through involvement in their own treatment.</p> <p><b>Conclusions</b> A systematic search revealed a small number of qualitative studies of MT in cancer. These were effectively combined to provide a detailed overview of patients' experiences, to complement the developing evidence base from trials. Given the variation in context of MT delivery across the articles it is</p>

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	not possible to ascribe changes in patients' quality of life specifically to MT. The results of this review will help design outcome measures that more fully capture patients' experiences. It is essential to embed qualitative research of patients' experiences of MT and other CAM therapies within future trials.

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Cancer patients' experiences of using mistletoe (*Viscum album*):

A qualitative systematic review and synthesis

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**Abstract****Objective**

Systematic reviews of mistletoe therapy (MT) trials in cancer show promising results in improvement of patients' quality of life during chemotherapy and reduction of fatigue. However patients' experiences of side effects, the acceptability, tolerability and perceived benefits of MT have not been systematically reviewed. The aim of this study is to systematically review and synthesise the results of qualitative studies of cancer patients' experiences of using MT.

**Design**

A systematic search was conducted in Medline, Embase, Psychlit, Cinahl and AMED to identify qualitative studies of MT. Articles were screened independently by two reviewers and critically appraised using the CASP tool. A thematic synthesis of the findings was carried out.

**Results**

173 papers were identified, 156 were excluded at initial screening. Seventeen papers were read in full, 14 of which were excluded. Three articles about patients' experiences of MT alongside conventional treatment were included in the synthesis, either as a mono-therapy (two articles) or as part of a package of anthroposophic treatment (one article). Patients reported demonstrable changes to their physical, emotional and psycho-social wellbeing following MT, and a reduction in chemo-therapy side-effects. Self-reported side-effects from MT were few, and the studies suggest good adherence to the therapy. Self-injection gave patients a sense of empowerment through involvement in their own treatment.

**Conclusions**

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3 A systematic search revealed a small number of qualitative studies of MT in cancer. These  
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5 were effectively combined to provide a detailed overview of patients' experiences, to  
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7 complement the developing evidence base from trials. Given the variation in context of MT  
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## Introduction

Mistletoe has long been used in the treatment of a variety of acute and chronic conditions and has been used in the treatment of cancer since the 1920's.<sup>1</sup> It is given to patients either as the central component of a complex, broader treatment regimen in the practice of anthroposophic medicine,<sup>2</sup> mainly in Europe, or as a single herbal treatment agent outside the context of anthroposophic care. In the treatment of malignancies, it is most often used in conjunction with conventional treatments: surgery, radiotherapy and chemotherapy. It is given both prior to, concurrently and after these treatments, to reduce adverse reactions and improve quality of life.

A Cochrane review of mistletoe in oncology included 21 randomised controlled trials.<sup>3</sup> The recommendations of this review included replication of "two trials suggesting beneficial effects of mistletoe extracts on QoL of breast cancer patients during chemotherapy". A further systematic review of mistletoe therapy for cancer treatment which focused on QoL outcomes included 26 randomised controlled trials (RCTs) and 10 controlled trials.<sup>4</sup> The authors reported that the results of the RCTs showed improvement in QoL measures in 22 of the trials, three showed no differences and one did not report. In 2012, a systematic review was published focusing on the mistletoe preparation, Iscador®.<sup>5</sup> A random-effect meta-analysis of 13 controlled studies of which nine were RCTs estimated an overall short-term treatment standardised mean effect of 0.56 (95% CI 0.41, 0.71),  $p < 0.0001$  but emphasised that the methodological quality of studies was poor. There is some evidence that mistletoe might be particularly valuable in combating cancer fatigue, a debilitating side-effect of cancer and its treatment for which there are limited therapeutic strategies at present.<sup>6</sup>

A recent survey carried out in 11 European countries including the UK showed that 46% of women with breast cancer had used herbal medicine since diagnosis.<sup>7</sup> In the UK, overall complementary and alternative medicine (CAM) use by breast cancer patients was 38% but the proportion using herbal medicine is unknown. A recent qualitative meta-ethnography of

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2  
3 patient's experience of using CAM after a diagnosis of cancer showed that improving  
4 wellbeing and quality of life (QoL), dealing with symptoms and finding relief from the side  
5 effects of treatment were important motivating factors towards CAM use.<sup>8</sup>  
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10 In the light of the increasing interest by patients and health professionals for using CAM in  
11 supportive cancer care and the evidence from mistletoe trials, it is important to further  
12 explore the patients' experience of mistletoe therapy. One limitation of previous studies is  
13 the reliance on validated quality of life scales as outcome when the consensus regarding the  
14 definition of QoL for cancer is by no means established.<sup>6</sup> This highlights the need for  
15 qualitative studies to gauge the significance of the mistletoe treatment from the patient's  
16 point of view in terms of its benefit, acceptability and tolerability. Therefore, in this systematic  
17 review of qualitative studies, we aimed to articulate the experiences of cancer patients when  
18 using mistletoe. The review was guided by the research question 'what are cancer patients'  
19 views on and experiences of the use of mistletoe therapy (MT)?'  
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### 31 **Methods**

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34 The review had four stages: (1) scoping the topic, (2) systematic literature search, (3) critical  
35 appraisal, (4) synthesis of findings.  
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#### 38 *Scoping the topic*

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41 The SPIDER tool was used to scope the topic.<sup>9</sup> This tool comprises five items: **S**ample,  
42 **P**henomenon of **I**nterest, **D**esign, **E**valuation, **R**esearch type. Using this tool the inclusion  
43 and exclusion criteria were determined and in turn the search strategy written.  
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49 The inclusion criteria were: (i) studies of adult cancer patients regarding the use of  
50 anthroposophic mistletoe preparations by any administration route as a monotherapy or as  
51 part of a complex intervention (ii) studies of qualitative design such as focus groups,  
52 interviews and questionnaires with free text sections which describe views, experiences or  
53 opinions of cancer patients and health professionals; (iii) studies in all languages.  
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The exclusion criteria were: (i) studies of paediatric cancer patients (ii) studies of anthroposophic therapies that did not involve mistletoe; (iii) studies which included questionnaires concerning quality of life yielding quantitative data only.

#### *Systematic literature search*

The parent search strategy was devised and run in Medline & Medline in process (Figure 1). Modified search strategies based on this parent search were run in Embase, Psychlit, Cinahl and AMED from database inception until 21<sup>st</sup> November 2012. The search was up-dated to 17<sup>th</sup> April 2015 and no new articles were found that matched our inclusion criteria. The reference lists of papers that reached the full paper stage were screened for any extra studies. Authors that had at least three mistletoe publications in our search results were contacted in order to find out about any publications that we might have missed and to provide information on any current studies. Proceedings from mistletoe conferences were screened for extra studies at [www.mistelsymposium.de](http://www.mistelsymposium.de). The website [anthromed.org](http://anthromed.org) was also screened. This site includes past issues of the *Journal of Anthroposophical Medicine* from 1982-1999.

References from the searches were screened independently by two of the authors and then collated. Any disagreements or queries were resolved by a third author. The references were first screened by title and abstract and then those of interest were obtained as full papers and the second screening was conducted by reading the full text paper.

#### *Critical Appraisal*

Papers that met the inclusion criteria were assessed for quality using the CASP screening tool.<sup>10</sup>

#### *Synthesis*

Synthesis of qualitative studies involves a rigorous process of data extraction to identify the key concepts from each article.<sup>11</sup> There are many methods for synthesising qualitative

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3 research.<sup>12,13</sup> We used the approach of thematic synthesis to combine the studies.<sup>14</sup>

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5 Thematic synthesis has three stages: the coding of text line-by-line; the development of  
6  
7 descriptive themes and the generation of analytic themes. Descriptive themes are drawn  
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9 directly from the primary studies and analytic themes represent a stage of interpretation  
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11 whereby the reviewers 'go beyond' the primary studies and generate new interpretive  
12  
13 constructs. Two authors (ME and SB) independently extracted data from the included papers  
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15 using line-by-line coding to initially identify descriptive themes. These were drawn from  
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17 verbatim quotations from participants describing their views, accounts and interpretations of  
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19 their experiences of using MT, and from themes identified by the authors of the articles,  
20  
21 giving their views and interpretations of that data.  
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25 These data extraction sheets were compared between the two reviewers and consensus  
26  
27 reached. The descriptive themes were listed in an Excel spreadsheet and then synthesised  
28  
29 to develop analytic themes. These comprise the authors' interpretations of concepts  
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31 occurring across the articles. Table 3 lists the analytic themes and shows which descriptive  
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33 themes in each of the articles contributed to them.  
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## 37 **Results**

### 38 *Screening of articles*

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41 From the searches, 173 papers were identified and no additional papers were gained from  
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43 contacting authors. 156 were excluded at the title and abstract screening stage. The  
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45 remaining 17 papers were read in full and further screening took place. Three articles  
46  
47 relating to patients' experiences of mistletoe were included in the review.<sup>15-17</sup> (see PRISMA  
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49 diagram, Figure 2). One of these, written in German, was translated into English.<sup>15</sup>  
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### 53 *Critical Appraisal*

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3 The quality assessment of the included articles is summarised in Table 1. One paper relied  
4 on content analysis of interviews which can lack depth of interpretation.<sup>17</sup>Data for another  
5 article was drawn from a closed group undergoing psychotherapy who may not reflect the  
6 views of typical patients.<sup>15</sup> No authors reflected on the role of researcher-patient relationship.  
7  
8 However, despite these limitations, in line with other qualitative syntheses we were reluctant  
9 to exclude a paper on the basis of reporting quality alone as it might still be relevant to the  
10 synthesis. We evaluated each paper on the approach of Dixon-Woods et al.<sup>18</sup> Out of the  
11 three included articles, one could be classified as a 'Key Paper' in terms of its relevance to  
12 the overall research question despite some quality limitations and two were 'Satisfactory'. All  
13 three articles provided a rich resource of primary data for the purpose of synthesis.  
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#### 24 *Study descriptions*

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27 The three included articles varied in methodology and content. Study characteristics are  
28 given in Table 2. In the Konitzer study, MT was provided as a mono-therapy in general  
29 practice supported by regular group therapy sessions.<sup>15</sup> In the Arman et al. study, MT was  
30 embedded in an individually prescribed package of anthroposophic care at a specialist  
31 clinic.<sup>16</sup> This included '*natural remedies (herbs, plant extracts, essential oils, potentized*  
32 *natural substance)*'. This study included a mixed sample of patients some of whom were  
33 being treated for cancer and some for 'burn-out syndrome', but the data analysis did not  
34 distinguish between the two groups. In the Brandenberger et al study MT was given as an  
35 out-patient mono-therapy at a private integrative hospital.<sup>17</sup>  
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46 Mode of delivery of MT varied: one study used infusions,<sup>15</sup> one used sub-cutaneous  
47 injections,<sup>17</sup> one did not report methods of administration.<sup>16</sup> Data collection in two of the  
48 studies was by individual interview.<sup>16,17</sup> In the third, patients were asked to draw pictures of  
49 MT and talk about their experiences during an ongoing group therapy session.<sup>15</sup> All articles  
50 provided data on aspects of patients' experience of MT, reporting directly on perceived  
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3 changes in wellbeing<sup>16,17</sup> and in one article relating this symbolically to the nature of the  
4 mistletoe plant from which the extract is derived.<sup>15</sup>  
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### 8 *Overview*

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10 MT patients reported improvements to their physical, emotional and psycho-social wellbeing,  
11 and felt able to construct meaning from the experience of the disease and its treatment.  
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15 Six analytic themes were identified that encompassed all the relevant data in the articles and  
16 provided a synthesis across all three. Table 3 shows the concepts that emerged from each  
17 paper and contributed to the themes. It is not possible to distinguish the effects of MT from  
18 other aspects of the holistic package in the Arman et al.<sup>16</sup> However, patients' verbatim  
19 quotations were chosen where possible with specific reference to their experience of MT.  
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22 The themes were: 'Treating the inner and outer worlds', 'Moving from darkness into light',  
23 'Taking control and increasing personal autonomy', 'Tangible outcomes', 'Ambivalence about  
24 MT', 'Bridging the gap between conventional and integrative care'.  
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28 Verbatim quotations from the articles are used to illustrate the themes. Most quotations  
29 directly report the patients' words. Where the authors' words are quoted this is marked  
30 [authors].  
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### 33 **Treating the inner and outer worlds**

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35 The experience of receiving MT appears to be intimately connected to a sense of both the  
36 outer and inner worlds of the patient being nurtured and treated in a 'holistic' way. MT was  
37 perceived as an agent that works with body, mind and spirit. Treatment involved intense  
38 personal contact with health professionals in a relatively 'low-tech' environment so that  
39 patients felt they were fully '*seen*' by their carers. Staff provided holistic care and attention  
40 which was then mirrored by the patients who became more self-reflective, focussing on their  
41 inner needs as a precursor to growth and change.<sup>16</sup> This stimulated memories of childhood,  
42 like a return to '*mother's cradle*', a place where fear was diminished.<sup>15,16</sup> Patients felt able to  
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3 rest in a comfortable place, exemplified by one patient who physically lay down after each  
4 mistletoe injection.<sup>15</sup>  
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8 MT was perceived as a powerful positive force under-pinning many of the outcomes  
9 described by patients, as captured in one article with phrases such as '*mistletoe is a sincere*  
10 *agent*', '*like a small saviour out of the vicious circle*'.<sup>15</sup> The qualities of mistletoe in the wild  
11 were found to support its use as a treatment, and patients perceived MT to be redolent of  
12 healing energy: *the corresponding energy could only now be set free, so that I can finally*  
13 *come to my truth, to what I am*'.<sup>17</sup>  
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21 Patients described MT as providing a turning-point in their experience of disease and  
22 increasing their self-awareness: '*Patients were able to return to their own inner path,*  
23 *returning to their inner sources and discovery of basic values of their own lives*' [authors].<sup>16</sup>  
24  
25 Brandenberger refers to '*internal changes*' [authors] that helped patients to develop a greater  
26 sense of hope and ability to cope: '*Mistletoe therapy was adopted by the study patients*  
27 *mostly with a supportive aim and seemed to offer a platform for an integrative coping with*  
28 *the disease, which in itself is likely to have helped the cancer patients, inasmuch as it gave*  
29 *them hope and probably increased their motivation to deal with this devastating disease.*  
30 *During MT, the patients often perceived an improvement of QoL which was associated with*  
31 *a higher vitality and autonomy and translated into clear-cut personal achievements* [authors].  
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33 The interviewer noted that patients were more talkative, self-reflective and positive at second  
34 interview, following MT.  
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46 Life and vitality were seen as returning through a process that involved first of all patients  
47 allowing themselves to '*be sick*' [authors]<sup>16</sup> and letting the disease then become their  
48 '*teacher ... who shows me what is happening with me at each moment*'. The perceived  
49 transformative power of MT is emphasised by comments like '*I have experienced this myself*'  
50 as a way of vouching for the credibility of the patient's story.<sup>15</sup>  
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### Moving from darkness into light

The changing inner world of cancer patients receiving MT was conceptualised as moving from 'darkness' or a 'dreadful hole' into 'light'.<sup>15,16</sup> In both these papers MT is conceptualised as bright, warm, light, 'golden', a provider of energy akin to the sun. The experience was enhanced by injection as the mode of delivery, with patients describing a sense of the healing energy of mistletoe flowing into their body. Patients reported a reduction in 'dark thoughts' and fear, with a lightening in their mood state to an increased sense of 'joie de vivre'<sup>15</sup> or cheerfulness and an ability to see 'light at the end of the tunnel'.<sup>16</sup> This contrasted with a previous focus on 'duty' and 'survival'. The metaphor of 'lightness' encompassed their attitude to life more generally, 'not taking things as seriously as before.'<sup>17</sup> For some it led to improved personal relationships, an experience described as 'liberation'.<sup>17</sup> There was an effect on patients' attitude to life more generally: 'Yes this is a whole new phase for me, it's like I've become a brand new person afterwards, in a way.'<sup>16</sup> MT helped patients to make changes in their lives, convert ideas into actions and re-assess their priorities such as spending more time with their partner or setting limits to their professional life and reducing stress: *I now feel in terms of close relationships that I don't always have to be everywhere ... I can set boundaries for myself ... it's a relief.*<sup>17</sup>

### Taking control and increasing personal autonomy

The ritual of self-injection provided a sense of personal empowerment through active participation in the treatment process and gave patients a sense of control, particularly when conventional treatment ended. The injections functioned as a regular reminder of the disease and helped patients to become more accepting of its presence, also bringing them closer to family members: *In some cases, MT seemed to bring together family members, who until then had had different opinions on therapeutic choices or on disease perception, thereby fulfilling psychosocial functions ... it is likely that MT might have played a role in*

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3 *improving quality of life ... a chance to consider personal preferences, concepts and settings*  
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5 *to integrate the help of their loved ones' [authors].<sup>17</sup>*  
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8 Following MT, patients reported feeling less vulnerable and more assertive about getting  
9 their personal needs met, such as ensuring that their own daily rhythms and coping  
10 mechanisms being respected by health professionals and employers. Patients felt less  
11 constrained by conventional ways of behaving and were able to establish personal priorities  
12 and boundaries more clearly, leading to *'more genuine ways of living [authors].<sup>16</sup>* This  
13 improved sense of personal autonomy enabled patients to start new projects in their lives  
14 and reduce their experience of subjective stress.  
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### 22 **Tangible positive outcomes**

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26 Patients in all three articles reported tangible, potentially measurable, changes following MT  
27 in their physical and psychological wellbeing and a reduction in side effects of cancer and its  
28 treatment: *'The hair loss stopped! The side effects of the chemotherapy were less. I felt*  
29 *(feel) good!<sup>15</sup>* Some patients reported almost no side effects when undergoing  
30 chemotherapy and MT simultaneously and *'reported doing better after 3 months' of MT*  
31 *[authors].<sup>17</sup>*  
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39 Patients reported emerging from therapy with a *stronger vitality* 'new' view of life, with new  
40 priorities and *'tools for living a healthy life'* such as a good diet, the importance of rest and  
41 therapeutic exercises.<sup>16</sup> MT was seen as a *'health supporter'* leading to pain reduction, and  
42 less colds, suggesting improved immune function. Increased emotional stability, less  
43 depression and improved strength and energy led to new personal achievements and re-  
44 gaining of function: *'I got the mistletoe one I was quickly back on my legs again ... I can say,*  
45 *because I got nothing else [only mistletoe]. I really did feel it and I was in a terrible hole then,*  
46 *and I was absolutely not getting back up again and yet this has me completely back up.'<sup>15</sup>*  
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3 Patients gave example of tangible changes such as quitting a stressful job and accepting  
4 part-time employment, setting up a new horse stable, buying a computer in order to self-  
5 educate about cancer, chopping wood, booking tickets for travel and seeking information  
6 from other cancer sufferer: *'I don't fear anything – absolutely nothing; I don't have dark*  
7 *thoughts ... I feel fine and I have my projects ... and I have a new computer.'*<sup>17</sup>  
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### 14 15 16 **Ambivalence about MT**

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19 Decisions to use MT were mixed, sometimes driven by a lack of viable alternatives and a  
20 feeling that *'any therapy is better than none'*, particularly if conventional medicine had not  
21 helped and patients were hoping for improved disease outcome. Anthroposophic medicine,  
22 including MT was for some a mere *'snatching at straws'* and was challenging for those who  
23 had to *'overcome prejudice for another paradigm'* that lay outside conventional medicine.<sup>16,17</sup>  
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31 In the context of mostly positive feedback, some patients expressed uncertainty about  
32 whether changes they experienced could be attributed solely to MT, data which are  
33 unsurprising given the context of multi-modal treatments. In Brandenberger's article only  
34 three patients at interview attributed their improvements explicitly to MT. It was difficult to tell  
35 whether, for example, chemotherapy side-effects might have been worse without MT.  
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37 Patients undergoing chemotherapy and MT simultaneously reported having almost no side  
38 effects and doing better after the 3-month period of MT. This improvement could be  
39 attributable to MT, successful chemotherapy or diminishing side-effects over time. Accounts  
40 of negative experience of MT were rare. One patient reported a decrease in QoL during MT  
41 and died shortly after interview due to progression of the disease. Nevertheless, this patient  
42 reported that he still had hope and his spouse—who participated in the interview—felt *'that*  
43 *she and her husband had become closer to each other because of the process of choosing*  
44 *and doing MT together.'*<sup>17</sup>  
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3 Symbolic reference in the Konitzer article to the nature of the mistletoe plant illustrates this  
4 ambivalence. The parasitic plant can be likened to a cancer itself whilst it is also  
5 conceptualised as a bringer of light, energy and health. There were some reported side-  
6 effects of MT, such as redness and hardening at the injection site particularly following a  
7 high concentration or repeated injection at the same site. Local reactions such as these are  
8 expected with MT. One patient reported a systemic reaction: tiredness, fever, muscle aches,  
9 sleeplessness, and problems with concentration. However no patients in any of the three  
10 studies interrupted MT because of these reactions, although one patient reported feeling  
11 'relieved' when the treatment and the associated side-effects ended.  
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### 22 **Bridging the gap between conventional and integrative care**

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25 This theme is derived only from the Arman article but is relevant to the wider literature on  
26 integrative medicine. Arman points to a mutual scepticism between practitioners of  
27 conventional and anthroposophic health care, also evident amongst some patients,  
28 exemplified by one who expressed difficulty in 'opening up' to the idea of MT and  
29 'overcoming prejudices'. In this article, patients were seen as having to do the work of being  
30 'bridge-builders' between the two systems, carrying *'the burden and the risk which may*  
31 *cause stress'* [authors]: *'The gap implies a lack of knowledge and occasionally ignorance on*  
32 *both sides. Patients have to bridge the gap by themselves ... they feel like they are standing*  
33 *with one foot on each side'* [authors].  
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### 44 **Discussion**

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47 This systematic review has revealed a small number of qualitative studies of MT, which is in  
48 sharp contrast to the number of clinical and laboratory-based studies. The initial searches  
49 also revealed a total absence of studies investigating health professionals' attitudes to the  
50 use of MT, a key question for the transferability of MT to other clinical and international  
51 settings where it is not currently used.  
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3 This review does reveal a coherent narrative of patients' experience of MT despite diverse  
4 types of data drawn from the primary studies. All the articles were based in Northern Europe  
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6 and further studies may be needed of the appropriateness of MT in other in other contexts.  
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10 Although these three studies of the use of MT are a rich source of patient-centred  
11 information they are small-scale and exploratory. Synthesis of the findings gives added value  
12 by combining the insights gained in individual papers, and thereby gives a stronger  
13 indication of the likely impact of MT on patients. There was a multiplicity of ways in which MT  
14 was experienced and benefits were mediated via the symbolic nature of the mistletoe plant  
15 itself, the ritual of self-injection and the physiological impact of the therapy. It is not possible  
16 to clearly distinguish the effects of MT from other aspects of the holistic package in the  
17 Arman et al article.<sup>16</sup>  
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21 The data may reflect the particular context of MT delivery. Patients' descriptions of their  
22 experiences of MT in two of the articles were likely to have been influenced by the  
23 anthroposophic context of their treatment, in one case receiving a package of anthroposophic  
24 treatment<sup>16</sup> and in the other receiving group analytic therapy.<sup>15</sup> However in the  
25 Brandenberger et al article patients received MT in an integrative medicine setting where MT  
26 was combined with conventional rather than anthroposophic medicine. Significantly, all but  
27 two of the themes emerged from data across all three articles, suggesting a communality of  
28 experience.  
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32 There were many specific examples of a reduction in side-effects of chemotherapy and  
33 improvements in wellbeing such as improved mood and increased energy which are  
34 consistent with clinical trials and cohort studies. Patients' narratives went beyond the  
35 physical improvements into emotional and psycho-social benefits and the construction of  
36 meaning around their disease.  
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40 The fact that patients at interview were unwilling or unable to decisively ascribe these  
41 improvements to MT is not surprising given the multi-modal treatments that they were  
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3 receiving. However, despite some initial scepticism and some experience of side-effects, the  
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5 data suggest that patients' adherence to MT was impressive in these studies which  
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7 reinforces the importance that patients gave to the treatment. This review captures  
8  
9 important insights into changes that were meaningful for patients and underlines the  
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11 limitation of relying on quantitative measures of quality of life alone.  
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13  
14 The importance of MT as a means of gaining a sense of control is consistent with reports in  
15  
16 the literature on the use of complementary and alternative therapies in cancer.<sup>19</sup> Self-  
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18 injection enhances the experience of patient participation in their own treatment and  
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20 participation has been shown to improve mood and psychological coping and may impact on  
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22 survival.<sup>20</sup>  
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24  
25 One of the articles highlights the mutual professional scepticism across disciplinary  
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27 boundaries between conventional and integrative medicine, with patients feeling they have  
28  
29 to form a 'bridge'. Such institutional polarisation has previously been reported as a barrier for  
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31 patients in achieving a positive experience of complementary therapies in cancer care.<sup>4</sup> This  
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33 issue needs to be addressed through education for health care providers if MT use were to  
34  
35 be extended to clinical settings outside of central Europe.  
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### 38 **Limitations to the review**

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41 The focus of two of the articles was indirectly rather than directly relevant to the research  
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43 question, one reporting on symbolic understanding of mistletoe and the other on a package  
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45 of anthroposophic care, not just MT. Some of the data sources were 'non-standard', for  
46  
47 example material gathered from a therapy group, including the use of art therapy material.<sup>15</sup>  
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51 It is, difficult to separate the experience of MT from the context in which it was delivered. In  
52  
53 all three studies MT was part of a multi-modal approach to cancer treatment that included  
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55 conventional care and other, unspecified, complementary therapies.  
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3 The mode of delivery and dosage of mistletoe treatment were different in each of the  
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5 articles. The Arman study included a mixed sample of patients some of whom were being  
6  
7 treated for cancer and some for 'burn-out syndrome', but the data analysis did not  
8  
9 distinguish between the two groups.  
10

## 11 **Conclusions**

12  
13 The results of this review suggest that MT is well tolerated by patients who reported good  
14  
15 adherence to the therapy and articulated a range of important benefits in their physical and  
16  
17 psycho-social well-being. In line with patients' comments it is important to acknowledge that  
18  
19 we cannot necessarily ascribe the benefits directly to MT in the context of other therapies  
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21 being received, although references specifically to MT were frequent across articles.  
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25 Patients also welcomed active participation in treatment through self-injection.  
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29 Further good quality qualitative studies of MT need to be carried out and it is essential to  
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31 embed qualitative research of patients' experience within future trials of MT. A qualitative  
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33 approach to health professionals' views on MT would add an important dimension,  
34  
35 particularly within conventional care settings where anthroposophic medicine is not the  
36  
37 norm. A major goal for future research should be the disentangling of MT from the context of  
38  
39 delivery. Given the high prevalence of cancer, the expanding range of treatment options and  
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41 increased survivorship MT should be more widely assessed through well designed trials as a  
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43 potential adjunctive treatment in supportive cancer care, with high quality focussed  
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45 qualitative research as an essential element.  
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50  
51 **Author contributions:** ME, GF & AH were involved in the conception of the review. AH  
52  
53 lead on the written methods section and carried out the electronic searches. ME, SB & AH  
54  
55 screened the references. ME led the qualitative data extraction and drafted the results and  
56  
57 discussions. SB and ME completed the data extraction and synthesis. GF made a  
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substantial contribution to drafting the manuscript. All authors contributed to the final manuscript.

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Table 1: Summary of CASP quality assessment of included papers

Article	Was there a clear statement of the research aims?	Is a qualitative methodology appropriate?	Was the research design appropriate to address the aims of the research?	Was the recruitment strategy appropriate to the aims of the research?	Were the data collected in a way that addressed the research issue?	Has the relationship between researcher and participants been adequately considered?	Have ethical issues been taken into consideration?	Was the data analysis sufficiently rigorous?	Is there a clear statement of findings?	Is the research valuable?	Key Paper or Satisfactory Paper
Arman <i>et al</i> 2007 <sup>16</sup>	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	SAT
Brandenberger <i>et al</i> 2011 <sup>17</sup>	Y	Y	Y	Y	Y	N	Y	N	Y	Y	KP*
Konitzer <i>et al</i> 2001 <sup>15</sup>	Y	Y	Y	Y	Y	N	N	Y	Y	Y	SAT**

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Note: Y = Yes; N = No CT = Cannot tell

Source: Modified from Critical Appraisal Skills Programme (CASP) Public Health Resource Unit, England (2006)

NB: Final column uses Dixon-Woods appraisal criteria

\*KP: A Key paper is conceptually rich and could potentially make an important contribution to the synthesis

\*\*SAT: A Satisfactory Paper may provide less conceptual relevance to the synthesis

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Table 2: Study description table

Study	Aim	Setting	Theoretical approach	Methods	Sample, age and gender	Type of cancer	Types of therapy
Arman <i>et al</i>  2008 <sup>16</sup>  Sweden	1) To deepen understanding of what constitutes good care from a patient's perspective to alleviate patient suffering & identify clinical markers for this  2) To explore what in anthroposophic care is experienced as being beneficial or difficult	12-21 days spent as in-patient at anthroposophic clinic	Clinical application research, participatory and action research.	Narrative interviews in patients' homes 2-4 weeks after stay in the clinic	n= 16  Cancer n=9  Age range 50-72  Male (5) Female (4)  Burn-out syndrome n= 7  Age range 32-58  Male (4) Female (3)	Locally limited n=3  Recurrent n=6  Time since diagnosis 1-3 yrs.	An individually prescribed package of anthroposophic care, one element of which consisted of herbs and plants extracts including Iscador (mistletoe).  Mode of delivery of MT not stated  No reference to where and when patient received conventional treatment

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49	<b>Brandenberger</b>  <b>2011</b> <sup>17</sup>  Switzerland	What are patients' expectations & experiences of mistletoe therapy (MT) and its effects on quality of life	MT given to hospital out-patients at an integrative hospital	Mixed methods. exploratory, prospective, before/after cohort study using standard QoL questionnaires and interviews. Content and theory generating analysis.	Patient interviews at start of MT and 3 mths later in hospital or other location of patient's choice	n=17 (12 sets of repeat interviews included in the analysis) Wider cohort study (n=25) Mean age 62+/- 11.1 yrs Male (14) Female (11)	Wider cohort study: Colorectal n=7 Prostate n=4 Breast n=4 Lung n=3 Pancreatic n=3 Melanoma n=1 Renal n=1 Myeloma n=1 Multifocal basalioma n=1 Time since diagnosis: Ranged 1.5 months to >5 years	Sub-cutaneous injections of anthroposophic mistletoe preparations 2-3 times per week 'often performed by patient' Iscador (n=13), Abnoba viscum (n=11), Isorel (n=1).  Conventional treatment : Chemotherapy before n=9 (of which n=6 continued chemotherapy during MT) Radiotherapy before n=3 (of which n=2 during MT) Hormone therapy n=4 Other CAM therapies N=2 Psychotherapy n=1 No reference to whether conventional treatment and MT received at the same hospital
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<p><b>Konitzer</b>  <b>2001</b> <sup>15</sup>  Germany</p>	<p>To explore whether the term 'mistletoe' is associated with images of 'cancer' or a 'counter-agent against cancer' for those patients treated with it.</p>	<p>MT given in general practice over 1.5 years 1-3 x per week</p>	<p>Grounded theory. Linguistic data triangulated with pictures. Data triangulated with external theories on metaphor based in the work of Steiner, Seligman, Frazer.</p>	<p>Patients attending a weekly psychotherapy group session during MT were asked to draw pictures of their MT &amp; talk about their experiences</p>	<p>n=12 Mean age: 51.6 yrs (SD 3.65) Gender not stated</p>	<p>Breast cancer n=9 Uterine cancer n=2 Hypernephroma n=1  Time since diagnosis not stated</p>	<p>Infusions of mistletoe extracts: Isorel, Novipharm, Portsach  No reference to whether, where and when patient received conventional treatment</p>
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**Table 3: Development of analytic themes**A = Arman *et al* B= Brandenberger *et al* K= Konitzer *et al*

Analytic theme	Description	
Treating the inner and outer worlds	Patients described inner healing and increased self-awareness during MT, which was enhanced by positive interactions with health professionals	
	Home-coming	A
	Mirroring / being 'seen' by caregiver	A
	Intense personal contact with health professionals	B
	Absence of technology	A
	Return to mother's cradle	A
	Memories of childhood tastes	K
	Mistletoe is 'sincere'	K
	Comforting environment	A, K
	Holistic care	A
	Renewed hope and renewed opportunities	A
	New priorities	A, B
	Let the mask fall and be sick	A
	Changing relationship with disease	B
	Acceptance of the disease	B
	Disease as a teacher	B
	More positive attitude	B
Process past events	B	
Improved self-awareness	B, K	
Inner and outer atmospheres	A	
Stronger vitality	B	
Mistletoe as a 'saviour'	K	
Restitution narrative	K	
Moving from darkness into light	Patients graphically described their change in mood from dark to light following therapy, which is mirrored by imagery relating to	

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3		<b>the sun</b>	
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5			
6		Light at the end of the tunnel	A
7		Duty and survival to lightness	A
8			
9		MT associated with the sun	K
10			
11		Increased cheerfulness and joie de vivre	A, K
12			
13		Golden mistletoe	K
14			
15		Moving out of a 'dreadful hole'	K
16			
17	<b>Taking control and</b>		
18			
19	<b>increasing personal</b>	<b>MT injecting is seen to have ritual significance and the MT itself is</b>	
20			
21	<b>autonomy</b>	<b>redolent of healing energy</b>	
22			
23		Self-injection as a reminder of the disease	B
24		Self-injection as a small ritual	K
25			
26		More autonomy, less affected by others	B
27			
28		Free from conventions	B
29			
30		Distinguishing important and less important things	B
31			
32		Changing conditions of subjective stress	B
33			
34		Getting personal needs met	B
35		Drawing together family members	B
36			
37		Dealing with the disease better	A,B
38			
39		Active participation in multi-modal treatment	B
40			
41	<b>Tangible outcomes</b>	<b>External, potentially measurable, changes reported after MT</b>	
42			
43		Tools for living a healthy lifestyle	A
44			
45		New personal achievements	B
46			
47		Increased motivation to deal with disease	B
48			
49		Increased emotional stability	B
50			
51		Reduction in pain	B
52			
53		Less depression	B
54			
55		Reduction in frequency of colds	B
56			
57		Stronger vitality	B, K
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3		Converting ideas into actions	B
4		Cutting wood	B
5		Distinguishing important and less important things	B
6			
7			
8		Booking travel	B
9			
10		Starting new projects	B
11			
12		Increase in personal achievements	B
13			
14		On my legs again	K
15		Improve personal relationships	B
16			
17		Liberation in personal relationships	B
18			
19		Solving / limiting professional stress	B
20			
21		Bringing together family members	B
22			
23			
24		<b>Despite patients' commitment to MT uncertainty is expressed in</b>	
25	<b>Ambivalence about MT</b>	<b>relation to its uptake, its effectiveness and side-effects</b>	
26			
27		Overcoming prejudice for another paradigm	A
28			
29		Doubt about outcomes on disease and QoL	A, B
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31		Doubts about reduction of side-effects of radio-therapy	B
32			
33		Experience of side-effects of MT	B
34			
35		Mistletoe looks like cancer in the tree	K
36			
37		Decrease in QoL	B
38			
39	<b>Bridging the gap between</b>		
40	<b>conventional and</b>	<b>The perceived gap between conventional and integrative care is</b>	
41	<b>integrative care</b>	<b>problematised with patients having to function as a 'bridge'</b>	
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44		Contrasting environments of care	A
45			
46		Overcoming prejudice for another paradigm	A
47			
48		Patients as a 'bridge'	A
49			
50		Patients want more integration	A
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52		Patients taking 'burden' and 'risk'	A
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**Figure 1**

Parent search strategy run in Medline via Ovid

1. qualitative research.mp. or Qualitative Research/
2. questionnaires.mp. or Questionnaires/
3. focus groups.mp. or Focus Groups/
4. Interview/ or interviews.mp.
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6. mistletoe.mp. or Mistletoe/
7. Viscum album.mp. or Viscum album/
8. anthroposoph\*.mp. or Anthroposophy/
9. 6 or 7 or 8
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Figure 2

PRISMA diagram

