

Clinical Rehabilitation 2010; **24**: 444–453

Factors associated with phantom limb pain: a 3½-year prospective study

Joline C Bosmans, **Jan HB Geertzen** Department of Rehabilitation Medicine and Graduate School for Health Research (SHARE), University Medical Centre Groningen, University of Groningen, **Wendy J Post** Department of Epidemiology, University Medical Centre Groningen, University of Groningen, **Cees P van der Schans** Hanze University, Applied Sciences, Research and Innovation group in Health Care and Nursing, Groningen and **Pieter U Dijkstra** Department of Rehabilitation Medicine and Graduate School for Health Research (SHARE), University Medical Centre Groningen, University of Groningen; Department of Oral and Maxillofacial Surgery, University Medical Centre Groningen, University of Groningen, The Netherlands

Received 6th August 2009; returned for revisions 24th November 2009; revised manuscript accepted 28th November 2009.

Objective: To analyse the prevalence of phantom (limb) pain over time and to analyse factors associated with phantom (limb) pain in a prospective cohort of amputees.

Design: A multicentre longitudinal study.

Patients: One hundred and thirty-four patients scheduled for amputation were included.

Methods: Patients filled in questionnaires before amputation, and postal questionnaires six months, 1½ years and 2½ years to a maximum of 3½ years after amputation. Preoperative assessment included patients' characteristics, date, side and level of, and reason for amputation. The follow-up questionnaires assessed the frequencies of the experienced phantom pain, prosthetic use and walking distance. The occurrence of phantom pain was defined as phantom pain a few times a day or more frequently.

Results: Pre- and postoperative questionnaires were available filled in by 85 amputees (33 females and 52 males). The percentage of lower limb amputees with phantom pain was the highest at six months after amputation, and of upper limb amputees at 1½ years. In general, more women than men experienced phantom pain. One and a half years and 2½ years after amputation the highest percentages of the lower limb amputees used their prosthesis more than 4 hours a day (66%), after that time this percentage decreased to 60%. The results of the two-level logistic regression analysis to predict phantom pain show that phantom pain was less frequently present in men (odds ratio (OR) = 0.12), in lower limb amputees (OR = 0.14) and that it decreased in due course (OR = 0.53 for 1 year).

Conclusion: Protective factors for phantom pain are: being male, having a lower limb amputation and the time elapsed since amputation.

Introduction

Phantom (limb) pain is a common problem after a limb amputation. The prevalence rate of phantom pain for all limb amputees varies considerably

Address for correspondence: JC Bosmans, Department of Rehabilitation Medicine–CB 40, University Medical Centre Groningen, University of Groningen, Hanzeplein, PO Box 30.001, 9700 RB Groningen, The Netherlands.
e-mail: j.c.bosmans@rev.umcg.nl

© The Author(s), 2010.

Reprints and permissions: <http://www.sagepub.co.uk/journalsPermissions.nav>

10.1177/0269215509360645

(41–85%).^{1–5} This wide range may be ascribed to differences in study populations, in the place of amputation (upper or lower limb), in the research design (prospective, retrospective or cross-sectional) and in the method of assessment (interview or questionnaire), to a lack of a clear definition of phantom pain, or it may be ascribed to differences in cut-off points for phantom pain.^{1,4,6–9} Generally, it is assumed that phantom pain decreases slightly over time. However, the prevalence rate remains more or less constant, but the duration and frequencies of phantom pain attacks decrease.^{4,5,7,10–13} Numerous factors have been associated with the development of phantom pain, including age, reason for amputation, pain prior to amputation, time elapsed since amputation, presence of phantom limb sensations or stump pain, dominance of the amputated upper limb and prosthetic use.^{1,3,4,8,10,12,14}

The association between phantom pain and prosthetic use is especially important from a rehabilitation perspective. With less frequent and less intense phantom pain and more prosthetic use amputees will regain as much independence in daily activities and mobility as possible and hence, will achieve a more successful functional outcome after amputation. The explanation of the association between phantom pain and prosthetic use, however, remains controversial and it is still unclear whether the experiencing of phantom pain is influenced by prosthetic use or vice versa.

The cause–effect relationship between the aforementioned risk factors and phantom pain remains unclear. Much of what is known up till now has been obtained from cross-sectional studies in which subjects were studied for several years after their amputation. Until now only few longitudinal studies have been published in which the different risk factors for developing phantom pain have been studied. Those studies, however, had relatively small population samples and the long-term follow-up seldom exceeded one year.^{10,12,15–18}

The aim of this study was to analyse the prevalence of phantom (limb) pain over time and to analyse factors associated with phantom (limb) pain, viz. age, sex, place of amputation (upper or lower limb), reason for amputation, level of amputation, time elapsed since amputation, prosthetic use and the ability to walk a certain distance

(abbreviation ‘walking distance’), in a prospective cohort of limb amputees.

Methods

Between 1 November 2003 and 1 May 2007, patients scheduled for a limb amputation because of either a peripheral vascular disease with or without diabetes mellitus, an ulcer, an infection, cancer, a trauma or a complex regional pain syndrome (CRPS I) were asked to participate in this prospective multicentre study on phantom limb pain. One university hospital and five general hospitals in the northern Netherlands participated in the study. The medical staff of the participating hospitals informed the primary investigator (JB) about potential participants. After being informed about the study by the medical staff and after having agreed to participate in the study, the patients were approached by the primary investigator and the study goals and study design were explained to them. Inclusion criteria were (1) age ≥ 18 years, (2) ability to read and write Dutch, and (3) an amputation level through the metacarpal or metatarsal phalangeal joints or more proximal. Patients were excluded if (1) they had had a previous ipsilateral amputation, (2) they showed signs of clinical dementia to such an extent that they could not be expected to fill in the questionnaires reliably, (3) they were too ill to be able to fill in the questionnaires or (4) the time interval between their amputation and inclusion exceeded five days.

After patients gave their written informed consent, they filled in questionnaires before or within five days (T_0) after amputation. Patients agreed to fill in follow-up questionnaires at the following intervals: six months (T_1), 1½ years (T_2), 2½ years (T_3) to a maximum of 3½ years (T_4) after amputation. To motivate amputees to continue participation during the follow-up, they were contacted by telephone (JB) before being sent the follow-up questionnaires. If amputees were still willing to participate, the questionnaires were posted to them, with a post-free self-addressed envelope. Amputees were asked to fill in the questionnaires regardless of the presence or absence of phantom pain, and regardless of whether they had a prosthesis or of their ability to walk.

Patients were asked to complete either the Groningen Questionnaire Problems after Leg Amputation (GQPLA)^{4,9,19} or, in case of an upper limb amputation, the Groningen Questionnaire Problems after Arm Amputation (GQPAA).³ To distinguish phantom pain from other phenomena, phantom limb pain was defined as any painful sensation perceived in the missing part of the limb after amputation.²⁰ Phantom limb sensations were defined as any non-painful sensation in the missing part of the limb, such as sensations of the missing part of the limb being in a certain position, of something touching, of warmth or cold, or of movements of the missing part of the limb. Stump pain was defined as any painful sensation in the stump, the remaining part of the limb.³

The preoperative assessment included patients' characteristics (date of birth, sex) and date, side and level of, and reason for amputation. The follow-up GQPLA assessed the frequencies of the experienced phantom limb pain (always, a few times an hour, a few times a day, a few times a week, a few times a month, a few times a year, never), having a prosthesis (yes/no), prosthetic use (time of use: ≥ 8 hours daily, 4–8 hours daily, < 4 hours daily, not daily but . . . days a week, never) and walking distance with the prosthesis (≥ 1 km, 500 m to < 1 km, 100 to < 500 m, < 100 m). The GQPAA asked the same questions, walking distance excepted, with a few added questions about the type of prosthesis (cosmetic, mechanical, myoelectrical).

The last follow-up date was 30 April 2008, meaning that the duration of the follow-up was not the same for all patients.

The study protocol was approved by the medical ethical committees of all hospitals participating.

Data entry

Before entering the data from the questionnaires, the medical information provided by patients was verified in the medical records and, if necessary, corrected.

The reason for amputation was categorized into peripheral vascular disease (with or without diabetes mellitus, an ulcer, an infection), cancer or trauma (trauma and/or CRPS I). Trauma and

CRPS I were grouped in one category for two reasons: because in most cases CRPS I was induced by trauma and to generate a group of patients with sufficient number of amputations. Lower limb amputations were categorized into distal (transtibial, ankle or foot), knee disarticulation or proximal (pelvis, hip or transfemoral). Upper limb amputations were categorized into distal (forearm or wrist) or proximal (forequarter, shoulder or upper arm); no elbow disarticulations were performed.

In case of a second amputation of the same extremity during the study period, the level of the last amputation was used for statistical analyses. In case of a bilateral lower limb amputation during the study period, the side of the first amputation was entered in the database. If the first amputation of the bilateral amputation was performed before the study was started, then the latest amputation was entered in the database. If an amputee died or dropped out during the follow-up, this was recorded.

The answers to the questions were entered in the database and checked for correct data entry. Data were processed anonymously.

Phantom pain was dichotomized as present in cases where an amputee suffered from phantom pain a few times a day or more frequently, and as absent in cases where phantom pain was experienced a few times a week or less frequently. Prosthetic use was dichotomized as prosthetic use ≥ 4 hours per day against prosthetic use < 4 hours per day. Walking distance (in case of a lower limb amputation) was dichotomized as walking distance ≥ 500 m against walking distance < 500 m.

Statistics

Statistical analyses were performed using SPSS version 16.0 for Windows (SPSS Inc., Chicago, IL, USA).

Differences in characteristics between included patients on the one hand and drop-out patients and excluded patients on the other were analysed using *t*-tests for independent samples and χ^2 tests as appropriate. A two-level logistic regression was performed in ML Win 2.02. Patients were the highest level, and time was the lowest level.

The dependent factor was presence of phantom pain and as possible predictors were entered age, sex, upper or lower limb amputation, reason for amputation, level of amputation, prosthetic use and walking distance. Categorical variables were entered as dummy variables. Random and fixed effects were taken into consideration. Independent variables remained in the regression equation when the beta-values were significant. P -values ≤ 0.05 were considered to be significant. Possible interactions between significant variables were explored. Data regarding amputees who filled in a pre-amputation questionnaire but who died or dropped out in the first six months after amputation were excluded from the analyses because no data on the occurrence of phantom pain were available.

Results

In total, 225 patients scheduled for a limb amputation were referred to this study. One hundred and thirty-four patients (120 lower limb and 14 upper limb amputations) fulfilled the inclusion criteria and filled in the first questionnaire (preoperative assessment). Seventy-five referred patients were excluded because they did not meet the inclusion criteria (one patient was younger than 18 years, 2 patients did not speak and read Dutch, 7 had had a previous ipsilateral amputation, 46 were too ill or had signs of a clinical dementia and 19 were referred more than five days after their amputation) or did not want to participate ($n=16$). Six months after amputation 37% (49 out of 134) amputees were lost to the follow-up because they died ($n=23$) or dropped out ($n=26$). Reasons for dropping out were 'being too ill or showing signs of dementia' ($n=12$), 'refusing to participate any longer' ($n=6$), 'non-responding' ($n=8$). Hence, 85 amputees filled in two or more questionnaires (a preoperative assessment and at least one postoperative assessment) (Figure 1), resulting in a total of 292 questionnaires available for analysis. One patient dropped out 1½ years after amputation because of 'unknown place of residence'.

Characteristics, reason for and level of amputation and the proportions of upper and lower limb amputees included and, on the other hand, of those

who were excluded and/or dropped out after inclusion (within six months after amputation) are summarized in Table 1. The amputees who were excluded and/or dropped out were significantly older ($P<0.001$) and underwent amputations because of peripheral vascular disease ($P=0.009$) significantly more often than those who were included in the analyses. No significant difference was found in sex and level of amputation between the amputees included in the analyses and those excluded from the analyses and/or drop-outs.

In total, 12 of the 14 patients with an upper limb amputation filled in two or more questionnaires (a preoperative assessment and at least one postoperative assessment). Table 2 shows the characteristics of the 73 lower limb and 12 upper limb amputees. None of the upper limb amputees had a brachial plexus injury.

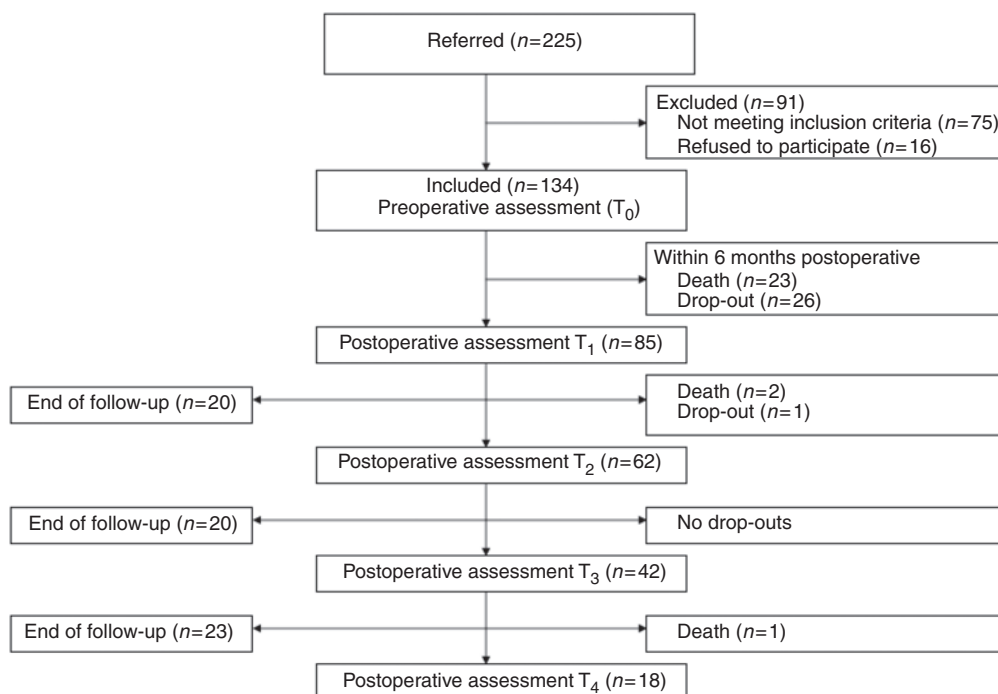
Table 3 shows that the percentages of lower limb amputees with phantom pain decreased in the course of time from 32% at six months after amputation to 27% (1½ years), 23% (2½ years) to 27% at 3½ years after amputation, respectively. In contrast, more upper limb amputees suffered phantom pain in the course of time, but the sample is small. As to prosthetic use, upper limb amputees rarely used their prosthesis ≥ 4 hours a day. One and a half years and 2½ years after amputation (T_2+T_3) the highest percentage of lower limb amputees used their prosthesis ≥ 4 hours a day (66%), but in the course of time this percentage decreased to 60%.

The proportions of limb amputees, female and male, who suffer from phantom pain over time are illustrated in Figure 2.

The results of the two-level regression analysis to predict phantom pain (a few times a day or more frequently against a few times a week or less frequently) are summarized in Table 4. Being male, having a lower limb amputation as well as the time elapsed since amputation, these factors all had a significant protective effect on the frequency of phantom pain.

Discussion

In this prospective study it appeared that the chance of having phantom (limb) pain was less

**Figure 1** Flow diagram of patients referred.**Table 1** Characteristics of all limb patients referred to the study

Referred (<i>n</i> = 225)	Included in the analyses	Drop-outs after inclusion + excluded from study	Significance of the difference between included in the analyses and drop-outs + excluded from study
<i>n</i> (%)	85 (38%)	140 (62%)	
Mean age at amputation, years	58.2 (SD 17.4)	67.1 (SD 16.0)	$P < 0.001$ 8.9 (95% CI 4.4–13.4) ^a $\chi^2 P = 0.861$
Patients			
Female	33 (39%)	56 (40%)	
Male	52 (61%)	84 (60%)	
Reason for amputation			$P < 0.001$
PVD	50 (59%)	113 (80%)	
Cancer	12 (14%)	15 (11%)	
Trauma	23 (27%)	12 (9%)	
Level of amputation			$\chi^2 P = 0.503$
Proximal	25 (29%)	51 (36%)	
KD	14 (17%)	18 (13%)	
Distal	46 (54%)	71 (51%)	
Amputation			$\chi^2 P < 0.001$
Upper limb	12 (14%)	2 (1%)	
Lower limb	73 (86%)	138 (99%)	
Bilateral amputation	4 (5%)	0 (0%)	

^aMean difference (95% confidence interval).

PVD, peripheral vascular disease; KD, knee disarticulation.

in men than in women, less in lower limb amputees than in upper limb amputees, and the chance of having phantom pain decreased over time. Other risk factors (e.g. age, reason for or level of amputation, prosthetic use and, in the case of lower limb amputees, walking distance) were not associated with having phantom pain.^{1,4,8,10}

Table 2 Characteristics of the 73 lower limb and 12 upper limb amputees included in the analyses

	Lower limb amputation (<i>n</i> = 73)	Upper limb amputation (<i>n</i> = 12)
Patients		
Female	26 (36%)	7 (58%)
Male	47 (64%)	5 (42%)
Mean age at amputation, years	59.8 (SD 16.5)	48.5 (SD 20.43)
Reason for amputation		
PVD	48 (66%)	2 (17%)
Cancer	11 (15%)	1 (8%)
Trauma	14 (19%)	9 (75%)
Level of amputation		
Proximal	20 (27%)	7 (58%)
KD	15 (21%)	
Distal	38 (52%)	5 (42%)

PVD, peripheral vascular disease; KD, knee disarticulation.

Differences between women and men in the way they perceive and experience pain, are well known.^{21–23} Women seem to be more willing to report pain whereas men under-report pain, women are more willing to seek health care than men, and the burden of pain and the frequency of pain attacks in women are greater.^{21,23} Biological as well as psychosocial differences have been found to explain sex differences in pain experience, such as differences in body size and skin thickness, hormonal differences and differences in nervous system organization. Furthermore, men and women seem to use different coping styles when in pain, which might explain the differences in pain sensitivity.^{22,23} These sex differences in pain experiences can also be expected in limb amputees. This expectation was not always confirmed in previous research on phantom pain.^{3,4,10,15,24} In contrast, other studies found that more females than males experienced phantom pain, or that women reported a higher phantom pain intensity than men, but no reason was given.^{25,26} Our finding that more women than men reported phantom pain might be related to differences in answering tendencies.

In the literature, the estimation of the prevalence rate of phantom pain for all limb amputees ranges considerably: between 41% and 85%.^{1–4} In general, upper limb amputees show a lower

Table 3 Description of the numbers and percentages (95% CI) of all amputees as well as a division into lower limb and upper limb amputation included in the analyses concerning phantom limb pain and prosthetic use at T₁ (six months), T₂ (1½ years), T₃ (2½ years) and T₄ (3½ years) after amputation, respectively

	T ₁	T ₂	T ₃	T ₄
<i>All amputees – available number (n)</i>	<i>n</i> = 85 ^a	<i>n</i> = 62 ^b	<i>n</i> = 42	<i>n</i> = 18
Phantom (limb) pain	29 (35%)	21 (35%)	12 (29%)	6 (33%)
95% CI	(25–45)	(24–48)	(17–44)	(16–56)
Prosthetic use ≥ 4h/day	37 (44%)	37 (60%)	23 (55%)	9 (50%)
95% CI	(23–46)	(47–71)	(40–69)	(29–71)
<i>Lower-limb amputees – available number (n)</i>	<i>n</i> = 73 ^a	<i>n</i> = 53 ^h	<i>n</i> = 35	<i>n</i> = 15
Phantom (limb) pain	23 (32%)	14 (27%)	8 (23%)	4 (27%)
95% CI	(22–43)	(17–41)	(12–39)	(11–52)
Prosthetic use ≥ 4h/day	36 (49%)	35 (66%)	23 (66%)	9 (60%)
95% CI	(38–61)	(53–77)	(49–79)	(36–80)
<i>Upper-limb amputees – available number (n)</i>	<i>n</i> = 12	<i>n</i> = 9	<i>n</i> = 1	<i>n</i> = 3
Phantom (limb) pain	6 (50%)	7 (78%)	4 (57%)	2 (67%)
95% CI	(25–75)	(45–94)	(25–84)	(21–94)
Prosthetic use ≥ 4h/day	1 (8%)	2 (22%)	0 (0%)	0 (0%)
95% CI	(1–35)	(6–55)	(0–35)	(0–56)

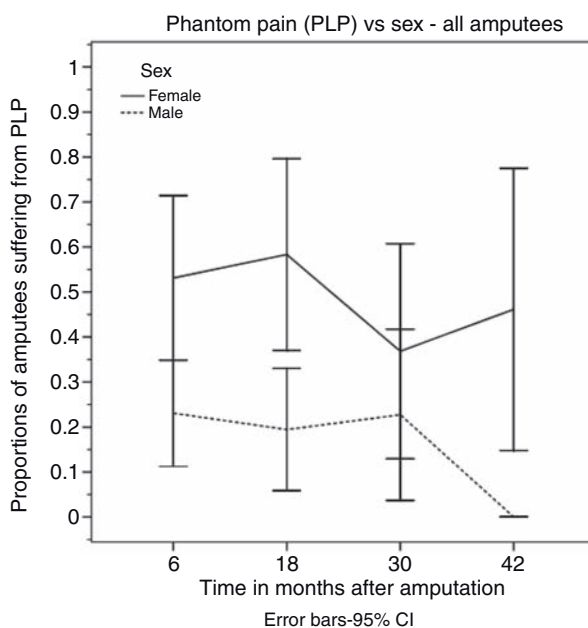


Figure 2 Proportions – with error bars – of reported phantom pain over time, categorized by sex.

Table 4 Results of the two-level regression analysis to predict phantom pain (a few times a day or more frequently against a few times a week or less frequently)

	β	SE β	OR	95% CI
Sex (0 = female, 1 = male)	-2.085	0.697	0.124	0.032 to 0.487
Extremity (0 = upper limb, 1 = lower limb)	-1.953	0.932	0.142	0.023 to 0.881
Time since amputation (years)	-0.645	0.218	0.525	0.342 to 0.804
Constant	2.808	1.002	16.577	2.326 to 118.146

β , regression coefficient; SE β , standard error of β ; OR, odds ratio; 95% CI, 95% confidence interval.

The results of the logistic regression analysis enable calculation of the chance rate (P) of having phantom pain. Using the following equation, $P = e^s / (1 + e^s)$, where e is 2.72 and s is the regression score. Filling in this equation for a female with a lower limb amputation who is now two years after amputation, results in the following chance rate:

$$P = e^{((-2.085 \times 0) + (-1.953 \times 1) + (-0.645 \times 2) + 2.808)} / (1 + e^{((-2.085 \times 0) + (-1.953 \times 1) + (-0.645 \times 2) + 2.808)}) = e^{-0.435} / (1 + e^{-0.435}) = 0.647 / (1 + 0.647) = 0.39.$$

Filling in this equation for a female with an upper limb amputation who is now six months after amputation, results in the following chance rate:

$$P = e^{((-2.085 \times 0) + (-1.953 \times 0) + (-0.645 \times 0.5) + 2.808)} / (1 + e^{((-2.085 \times 0) + (-1.953 \times 0) + (-0.645 \times 0.5) + 2.808)}) = e^{2.486} / (1 + e^{2.486}) = 12.0 / (1 + 12.0) = 0.92.$$

prevalence rate (41–59%, with one finding of 82% in 1982) than lower limb amputees (53–85%). Those rates are from cross-sectional studies in which the time elapsed since amputation varied

widely, from 3 to more than 15 years. In the only prospective study on upper limb amputees performed until now, the prevalence rates of phantom pain between the initial and the follow-up

session (within the first six months and 2–3 years after amputation) remained consistent (63%).²⁷

Few longitudinal studies on lower limb amputees assessed changes in prevalence rates of phantom pain over time. Jensen found a prevalence rate of 72% at eight days, 65% at six months and 59% at 2 years, while Nikolajsen found a rate of 68% at three months and of 73% at six months and it is said that the prevalence rate remains relatively constant over five years.^{10,12} Our findings, however, show that lower limb amputees have lower prevalence rates of phantom pain compared to the aforementioned studies (32% at six months, 26% at 1½ years, 23% at 2½ years and 27% at 3½ years, respectively).

A reason that our findings in prevalence rates differ from other studies may be the difference in cut-off points for phantom pain. In our study phantom pain was dichotomized as ‘present’ in cases where an amputee suffered from phantom pain a few times a day or more frequently, and as ‘absent’ in cases where phantom pain was experienced a few times a week or less frequently. Our assumption is that when patients were asked to fill in the questionnaire they remembered daily phantom pain better than those who suffered from phantom pain less frequently. So it was decided to choose the aforementioned cut-off points for phantom pain.⁹ For prosthesis use to have a relationship with phantom pain we considered that the prosthesis should be used a substantial amount of time per day. Therefore, our cut-off point for prosthetic use was chosen as ≥ 4 hours per day.

Similarly, for walking to have a relationship with phantom pain we considered that this activity should be performed a substantial amount of time per day. Therefore, our cut off-point for walking was ≥ 500 m. In addition, we considered that a walking distance of at least 500 m was needed to function independently indoors as well as outdoors (ability to walk from the parked car to a shop, to visit shops in the neighbourhood, recreational possibilities).¹⁹

Furthermore, a difference in prevalence rates of phantom pain between lower limb and upper limb amputees was found in our study, the upper limb amputees having much higher prevalence rates (50–78% in the course of time). It must be remembered that our sample of upper limb amputees is small, reflected in the wide 95%

confidence intervals. Despite the small number of upper limb amputees we found an upper limb amputation to be a significant factor associated with phantom pain. Our prevalence rates of phantom pain for upper limb amputees are higher than found by other researchers.^{3,27}

To explain phantom pain, several theories focusing on the peripheral and central nervous system have been developed.^{28–31} Insights into brain plasticity and functional magnetic resonance imaging (fMRI) suggest that phantom pain is a phenomenon related to cortical changes in the brain. At present, it is unknown whether the cortical reorganization is restricted to the hand and arm areas of the motor cortex or whether such reorganization may also be observed in the leg area of the motor cortex. It seems biologically reasonable to assume that a similar reorganization may occur in upper limb as well as in lower limb amputees. However, considering the much larger map of the hand and arm on the motor cortex (homunculus), it also seems reasonable to expect that the reorganization after an upper limb amputation will be much more pronounced than after a lower limb amputation. The influence of time on cortical reorganization, and so on phantom pain, is not known. Our findings show that, as the time since amputation elapsed, amputees reported phantom pain occurring less often.

As briefly stated in the introduction, the cause–effect relationship between the experience of phantom pain and prosthetic use remains controversial and it is not clear how these two phenomena influence each other. Until now, only one prospective study on upper limb amputees has been performed in which patients were asked after their prosthesis use and after phantom pain as well as phantom limb sensations, phantom limb awareness and stump pain.²⁷ In that study it was found that not phantom pain but phantom limb awareness may be influenced by the frequent use of a functional prosthesis. The study population, however, was small ($n=11$).²⁷ In our study, the relationship between phantom pain and prosthetic use was analysed and no association between phantom pain and prosthetic use was found.

The strength of our study is its prospective character, and that it has been performed on a substantial sample ($n=85$) with a follow-up to a maximum of 3½ years. In other prospective

studies the samples ranged from 21¹⁷ to 58¹⁰ patients and the drop-out rate ranged from 8%¹⁶ to 43%.³² In addition, only one study¹⁰ had a follow-up of two years with a drop-out rate of 41% of the original 58 patients, while in the other studies the follow-up did not exceed one year.^{12,15–18}

A limitation of this study is the selection bias through exclusion and drop-out within six months after amputation. The excluded and dropped-out patients were significantly older and underwent an amputation because of peripheral vascular disease more often than the included amputees. The phantom pain frequency of the excluded and dropped-out amputees who are still alive is unknown. The length of the follow-up was not the same for all patients; some patients dropped out from the study or died; for other patients the follow-up was limited to six months, 1½ or 2½ years because the study ended due to limited financial resources. In future, more prospective studies on upper limb and lower limb amputees are needed to examine the relationship between phantom pain and the different risk factors. Another limitation of this study is that the GQPLA and the GQPAA, the only available questionnaires in Dutch assessing phantom pain, have not been tested for reliability and validity. More research is needed to test the (Dutch) questionnaires for reliability and validity.

In conclusion, the results of our prospective study show that protective factors for phantom pain are: being male, having a lower limb amputation and the time elapsed since amputation.

Clinical messages

- More women than men experience phantom pain.
- More upper limb than lower limb amputees experience phantom pain.
- Phantom pain decreases over time.

Acknowledgements

We would like to thank all patients, surgeons and their secretaries, physiotherapists, rehabilitation physicians, ward doctors and all other persons from the seven participating hospitals for their active participation in this study. This study

was partially supported by grants from the OIM Foundation Assen, the Netherlands, and the Foundation Beatrixoord North Netherlands, Haren.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

References

- 1 Sherman RA, Sherman CJ, Parker L. Chronic phantom and stump pain among American veterans: results of a survey. *Pain* 1984; **18**: 83–95.
- 2 Kalauokalani DAK, Loeser JD. Phantom limb pain. In Crombie IK. ed. *Epidemiology of pain*, Seattle, IASP Press, 1999, 143–53.
- 3 Kooijman CM, Dijkstra PU, Geertzen JHB, Elzinga A, Schans van der CP. Phantom pain and phantom sensations in upper limb amputees. An epidemiological study. *Pain* 2000; **87**: 33–41.
- 4 Dijkstra PU, Geertzen JHB, Stewart R, Schans van der CP. Phantom pain and risk factors: a multivariate analysis. *J Pain Symptom Manage* 2002; **24**: 578–85.
- 5 Nikolajsen L, Jensen TS. Phantom limb. In McMahon SB, Koltzenburg M. eds. *Wall and Melzack's textbook of pain*, fifth edition. Edinburgh, Elsevier Churchill Livingstone, 2006, 961–71.
- 6 Pohjolainen T. A clinical evaluation of stumps in lower limb amputees. *Prosthet Orthot Int* 1991; **15**: 178–84.
- 7 Houghton AD, Nicholls G, Houghton AL, Saadah E, McColl L. Phantom pain: natural history and association with rehabilitation. *Ann R Coll Surg Engl* 1994; **76**: 22–25.
- 8 Wartan SW, Hamann W, Wedley JR, McColl I. Phantom pain and sensation among British veteran amputees. *Br J Anaesth* 1997; **78**: 652–59.
- 9 Borsje S, Bosmans JC, Schans van der CP, Geertzen JHB, Dijkstra PU. Phantom pain: a sensitivity analysis. *Disabil Rehabil* 2004; **26**: 905–10.
- 10 Jensen TS, Krebs B, Nielsen J, Rasmussen P. Immediate and long-term phantom limb pain in amputees: incidence, clinical characteristics and relationship to pre-amputation limb pain. *Pain* 1985; **21**: 267–78.
- 11 Melzack R. Phantom limbs. *Sci Am* 1992; **266**: 120–26.

- 12 Nikolajsen L, Ilkjaer S, Krøner K, Christensen JH, Jensen TS. The influence of pre-amputation pain on postamputation stump and phantom pain. *Pain* 1997; **72**: 393–405.
- 13 Raichle KA, Hanley MA, Molton I *et al.* Prosthesis use in persons with lower- and upper-limb amputation. *J Rehabil Res Dev* 2008; **45**: 961–72.
- 14 Lotze M, Grodd W, Birbaumer N, Erb M, Huse E, Flor H. Does use of a myoelectric prosthesis prevent cortical reorganization and phantom limb pain? *Nature Neurosci* 1999; **2**: 501–502.
- 15 Jensen TS, Krebs B, Nielsen J, Rasmussen P. Phantom limb, phantom pain and stump pain in amputees during the first 6 months following limb amputation. *Pain* 1983; **17**: 243–56.
- 16 Jahangiri M, Jayatunga AP, Bradley JW, Dark CH. Prevention of phantom pain after major lower limb amputation by epidural infusion of diamorphine, clonidine and bupivacaine. *Ann R Coll Surg Engl* 1994; **76**: 324–26.
- 17 Pinzur MS, Garla PG, Pluth T, Vrbos L. Continuous postoperative infusion of a regional anesthetic after an amputation of the lower extremity. A randomized clinical trial. *J Bone Joint Surg Am* 1996; **78**: 1501–505.
- 18 Lambert A, Dashfield A, Cosgrove C, Wilkins D, Walker A, Ashley S. Randomized prospective study comparing preoperative epidural and intraoperative perineural analgesia for the prevention of postoperative stump and phantom limb pain following major amputation. *Reg Anesth Pain Med* 2001; **26**: 316–21.
- 19 Geertzen JHB, Bosmans JC, Schans van der CP, Dijkstra PU. Claimed walking distance of lower limb amputees. *Disabil Rehabil* 2005; **27**: 101–104.
- 20 Merskey H, Bogduk N. *Classification of chronic pain: descriptions of chronic pain syndromes and definitions of pain terms*, second edition. Seattle, IASP Press, 1994.
- 21 Holdcroft A, Berkley KJ. Sex and gender differences in pain and its relief. In McMahon SB, Koltzenburg M. eds. *Wall and Melzack's textbook of pain*, fifth edition. Edinburgh, Elsevier Churchill Livingstone, 2006, 1181–97.
- 22 Derbyshire SWG. Gender, pain, and the brain. *Pain Clin updates* 2008; **16**: 1–4.
- 23 Keogh E, Denford S. Sex differences in perceptions of pain coping strategy usage. *Eur J Pain* 2008; **13**: 629–34.
- 24 Hirsh AT, Dillworth TM, Ehde DM, Jensen MP. Sex differences in pain and psychological functioning in persons with limb loss. *J Pain* 2010; **11**: 79–86.
- 25 Gallagher P, Allen D, Maclachlan M. Phantom limb pain and residual limb pain following lower limb amputation: a descriptive analysis. *Disabil Rehabil* 2001; **23**: 522–30.
- 26 Weiss SA, Lindell B. Phantom limb pain and etiology of amputation in unilateral lower extremity amputees. *J Pain Symptom Manage* 1996; **11**: 3–17.
- 27 Hunter JP, Katz J, Davis KD. Stability of phantom limb phenomena after upper limb amputation: a longitudinal study. *Neuroscience* 2008; **156**: 939–49.
- 28 Lotze M, Flor H, Grodd W, Larbig W, Birbaumer N. Phantom movements and pain. An fMRI study in upper limb amputees. *Brain* 2001; **124**: 2268–77.
- 29 Devor M. Response of nerves to injury in relation to neuropathic pain. In McMahon SB, Koltzenburg M. eds. *Wall and Melzack's textbook of pain*, fifth edition. Edinburgh, Elsevier Churchill Livingstone, 2006, 905–27.
- 30 Flor H, Nikolajsen L, Jensen TS. Phantom limb pain: a case of maladaptive CNS plasticity? *Nat Rev Neurosci* 2006; **7**: 873–81.
- 31 MacIver K, Lloyd DM, Kelly S, Roberts N, Nurmikko T. Phantom limb pain, cortical reorganization and the therapeutic effect of mental imagery. *Brain* 2008; **131**: 2181–91.
- 32 Nikolajsen L, Ilkjaer S, Christensen JH, Krøner K, Jensen TS. Randomised trial of epidural bupivacaine and morphine in prevention of stump and phantom pain in lower-limb amputation. *Lancet* 1997; **350**: 1353–57.