Year : 2012

Predictors of Weight Change in Sedentary Smokers Receiving a Standard Smoking Cessation Intervention

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THESE

préparée sous la direction du Professeur Jacques Cornuz

et présentée à la Faculté de biologie et de médecine de
l'Université de Lausanne pour l'obtention du grade de

DOCTEUR EN MEDECINE

par

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Médecin diplômé de la Confédération Suisse
Originaire de Bursins (Vaud)

Lausanne

2012

FACTEURS PRÉDICTIFS DE L'ÉVOLUTION DU POIDS CHEZ DES FUMEURS SÉDENTAIRES RECEVANT UNE INTERVENTION STANDARD D'AIDE À L'ARRÊT DE LA CIGARETTE

L'arrêt de la cigarette est généralement associé à une prise de poids. Celle-ci peut menacer la motivation des fumeurs à s'engager dans un processus d'arrêt du tabac et constitue un motif de rechute. L'ordre de grandeur et la cinétique de la prise de poids liée à une tentative d'arrêt chez les fumeurs pris en charge selon les recommandations cliniques actuelles est peu décrite dans la littérature médicale.

Le but de cette étude était de quantifier cette prise de poids, d'en déterminer la cinétique ainsi que les facteurs qui l'influencent, chez des fumeurs sédentaires bénéficiant d'une intervention d'aide à l'arrêt du tabac individualisée, composée de conseils individuels et d'une substitution nicotinique associant plusieurs modes d'administration.

Nous avons analysé des données récoltées durant un essai clinique randomisé contrôlé au cours duquel était étudié l'impact d'une activité physique modérée sur les taux d'arrêt du tabac après un an chez des fumeurs sédentaires. Nous avons modélisé l'évolution du poids de l'ensemble des participants au cours du temps, selon la technique statistique des « modèles mixtes longitudinaux ». En séparant les périodes d'abstinence de la cigarette de celles de rechute et de l'utilisation reportée de substituts nicotiniques. Cette approche nous a permis de prendre en compte chaque participant à l'étude, par opposition à un modèle plus simple qui séparerait les sujets abstinents de ceux qui rechutent à n'importe quel moment de la période de suivi. Nous avons également ajusté ces modèles pour l'âge, le sexe, le niveau de dépendance à la nicotine et le niveau de formation des participants.

Parmi l'ensemble des participants, nous avons noté une augmentation du poids durant les trois premiers mois de l'intervention, suivie d'une stabilisation. Au total, la prise de poids moyenne s'est élevée à 3.3 kg pour les femmes et 3.9 kg pour les hommes. Durant les périodes d'abstinence, les caractéristiques suivantes étaient associées à la prise de poids : sexe masculin et forte dépendance nicotinique. Un âge supérieur à 43 ans était associé à une prise de poids également durant les périodes de rechute. Nous avons observé une tendance, non statistiquement significative, vers une réduction de la prise des poids avec l'utilisation de substituts nicotiniques.

Notre étude apporte de nouvelles données sur l'évolution du poids chez les fumeurs sédentaires qui bénéficient d'une intervention d'aide à l'arrêt du tabac. Ils prennent donc du poids, de manière modérée et limitée aux premiers mois. Parmi eux, les hommes, les individus les plus dépendants à la nicotine et les plus âgés doivent s'attendre à une prise de poids supérieure à la moyenne.

Original Investigation

Predictors of Weight Change in Sedentary Smokers Receiving a Standard Smoking Cessation Intervention

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Received October 26, 2011; accepted August 27, 2012

Abstract

Introduction: Quitting smoking is associated with weight gain, which may threaten motivation to engage or sustain a quit attempt. The pattern of weight gained by smokers treated according to smoking cessation guidelines has been poorly described. We aimed to determine the weight gained after smoking cessation and its predictors, by smokers receiving individual counseling and nicotine replacement therapies for smoking cessation.

Methods: We performed an ancillary analysis of a randomized controlled trial assessing moderate physical activity as an aid for smoking cessation in addition to standard treatment in sedentary adult smokers. We used mixed longitudinal models to describe the evolution of weight over time, thus allowing us to take every participant into account. We also fitted a model to assess the effect of smoking status and reported use of nicotine replacement therapy at each time point. We adjusted for intervention group, sex, age, nicotine dependence, and education.

Results: In the whole cohort, weight increased in the first 3 months, and stabilized afterwards. Mean 1-year weight gain was 3.3 kg for women and 3.9 kg for men (p = .002). Higher nicotine dependence and male sex were associated with more weight gained during abstinence. Age over median was associated with continuing weight gain during relapse. There was a nonsignificant trend toward slower weight gain with use of nicotine replacement therapies.

Conclusion: Sedentary smokers receiving a standard smoking cessation intervention experience a moderate weight gain, limited to the first 3 months. Older age, male sex, and higher nicotine dependence are predictors of weight gain.

Introduction

Smoking cessation is generally followed by weight gain (Filozof, Fernández Pinilla, & Fernández-Cruz, 2004; Klesges, Meyers, Klesges, & La Vasque, 1989). Hypotheses for this postcessation weight gain involve both increased energy intake and decreased energy expenditure, which might occur by a combination of changes in food preferences, increased food intake as a substitute for cigarette, and suppression of the stimulating effect of nicotine on metabolic rate (Filozof et al., 2004).

Concern about weight gain may put smokers off a quit attempt (Klesges et al., 1989). Weight gain after quitting is one of the main causes of relapse (Pisinger and Jorgensen, 2007).

Nicotine replacement therapy (NRT) and some other drugs helping smokers quit may limit weight gain, at least during the course of the treatment (Farley, Hajek, Lycett, & Aveyard, 2012). Many studies evaluated weight gain in quitters treated by either oral (Doherty, Militello, Kinnunen, & Garvey, 1996; Ferguson, Shiffman, Rohay, Gitchell, & Garvey, 2010; Nides et al., 1994; Nordstrom, Kinnunen, Utman, & Garvey, 1999; O'Hara et al., 1998) or transcutaneous (Cropsey et al., 2010; Dale et al., 1998; Lycett, Munafò, Johnstone, Murphy, & Aveyard, 2011; Ussher, West, McEwen, Taylor, & Steptoe, 2003) NRT. Some of these studies have suggested an inverse dose–response relationship between NRT and weight gain (Dale et al., 1998; Doherty et al., 1996; Ferguson et al., 2010; Nides et al., 1994; Nordstrom et al., 1999). However, to our knowledge, no previous study evaluated weight gained by smokers treated with a combination of NRTs, whereas international guidelines for smoking cessation currently recommend a combination of smoking cessation agents (Fiore et al., 2008).

Although the amount of weight gained while quitting smoking has been well studied (Filozof et al., 2004; Klesges et al.,

doi:10.1093/ntr/nts217

1989), few studies have described the pattern of this weight gain in the short term (<1 year), using more than one time point during that time (Cropsey et al., 2010; Doherty et al., 1996). It could, however, have a strong clinical importance, as weight gain is a common reason to relapse, as stated earlier (Pisinger & Jorgensen, 2007).

Available data about gender-related differences in weight gain is conflicting (Chinn et al., 2005; Doherty et al., 1996; Nides et al., 1994; O'Hara et al., 1998; Williamson et al., 1991). Many studies in the field assess single gender cohorts (Cropsey et al., 2010; Munafò, Tilling, & Ben-Shlomo, 2009; Swan & Carmelli, 1995).

We aimed to determine the pattern and amount of weight change among sedentary adult smokers who participated in a randomized controlled clinical trial (RCT) assessing moderate physical activity (PA) as an aid for smoking cessation in addition to standard treatment (Bize et al., 2010). We also aimed to identify predictors of this weight gain, among baseline characteristics of the participants. Since there has been no difference in any outcomes between the groups, data of the two groups have been merged and we propose here an ancillary analysis by using a 1-year prospective cohort study design.

Additionally, we aimed at determining the effect on weight of abstinence from smoking, as opposed to relapse. In order to do that, we considered abstinence as a characteristic that could vary with time in each participant, from visit to visit. This was supported by the behavior observed in the participants, as most proved not to be continuously abstinent, but rather to maintain periods of abstinence, separated by one or several periods of relapse.

Methods

Participants

We analyzed data of a RCT assessing the effect of a program of moderate PA as an aid for smoking cessation, when added to a standard care for smoking cessation including counseling and combination NRT, provided in an urban primary care setting. We recruited sedentary smokers willing to quit smoking. Among other criteria, they had to be classified as insufficiently active based on the Swiss HEPA Survey 1999 instrument (Mäder, Martin, Schutz, & Marti, 2006; Martin, Jimmy, & Marti, 2001) and currently smoking ≥10 cigarettes/day regularly for ≥3 years. The full inclusion and exclusion criteria, as well as the study design and intervention, are described in details elsewhere (Bize et al., 2010). Of the 481 subjects, which met inclusion criteria in the primary RCT study, we excluded 4 individuals considered here as "outliers" in the weight variable (more than 120 kg at the baseline visit and/or a weight variation of more than 30 kg between the baseline and the last visit).

Smoking Cessation Program

All participants attended a 9-week program with a weekly 15-min individual smoking cessation intervention, combining counseling, and prescription of free NRTs (16-hr transdermal patches and/or 2 mg gum, 1 mg lozenge, or 10 mg inhaler). This program was based on the international and Swiss clinical guidelines for smoking cessation (Cornuz et al., 2002; Fiore et al., 2008).

Participants enrolled in the intervention group attended a 9-week weekly 60-min moderate-intensity PA group program (Suisse, 2008), mainly brisk walking and slow jogging (Borg, 1998). They were encouraged to practice at least an additional 30-min session of moderate-intensity PA four times per week by their own. Participants enrolled in the control group attended a weekly 60-min health education program during 9 weeks to ensure equal contact conditions.

For this ancillary analysis, we chose to consider all participants to the RCT as a cohort, by pooling the data of both groups and controlling our analyses for the group of randomization to avoid creating a bias in the process.

Data Collection

Participants were weighted wearing underwear and socks only to the nearest 0.1 kg. Their height was measured to the nearest 0.5 cm. Body mass index (BMI) was computed using the formula: weight (kg)/height^2 (cm). After the participant's quit date, we considered as abstinents the participants who declared not having smoked, validated by carbon monoxide (CO) concentration in exhaled air below 10 ppm, as measured with a Micro Smokerlyser® (Bedfont). Participants with a CO concentration ≥10 ppm or reporting smoking were considered as relapsers.

Continuous abstinence was defined as being classified as abstinent to all previous visits.

Weight, smoking status, and NRT use were recorded at each visit. Visits were scheduled every week during the PA/health education program and at 10 weeks, 6-, and 12-month follow-up. The median (interquartile range) of the duration of the program (difference between time of the last program visit and the time of the baseline visit) were 14.3 (12.9 – 15.9) weeks. The median (interquartile range) of the 6-month follow-up (difference between time of the 6-month follow-up visit and the time of the baseline visit) were 30.6 (28.6 – 32.3) weeks. The median (interquartile range) of the follow-up (difference between time of the 1-year follow-up visit and the time of the baseline visit) were 57.9 (55.7 – 60.3) weeks.

We recorded each participant's reported number of cigarettes per day (CPD) at baseline as a measure of nicotine dependence and number of years of education as a measure of socio-economic level.

Statistical Analyses

Firstly, we performed a comparison between the median duration of abstinence of the control and the intervention group, using the nonparametric Wilcoxon test. We also compared smoking cessation rates in the two groups, with a z test, and the mean weight changes among the continuous abstinent of the two groups, using the Student's t-test.

Secondly, after merging data of the control and the intervention groups to create a 1-year prospective cohort, we used longitudinal models in order to estimate a mean weight trajectory, taking into account the interindividual variability (Pinheiro & Bates, 2000; Raudenbush & Bryk, 2002). Longitudinal models are methods of choice for analyzing data with repeated measures for each participant (Cnaan, Laird, & Slasor, 1997; Gibbons, Hedeker,

& DuToit, 2010). These models can deal with unbalanced data due to missing values. They also allow to consider the time in a continuous scale, which is especially useful when measures are not equally spaced for the different subjects (Petkova & Teresi, 2002). Namely, a polynomial longitudinal model was fitted over the entire follow-up period and a linear longitudinal model over the duration of the program. Both models were adjusted for sex in order to investigate the possibility of a sex-specific weight dynamic after smoking cessation. All participants were included in this analysis.

Thirdly, a piecewise linear longitudinal model was used to test the effect of smoking status on weight gain during the duration of the program (Lange, 1992; Naumova, Must, & Laird, 2001). To take into account the states of "abstinence" and "relapse," the model was estimated on the 417 participants who stopped smoking at least once (87% of total), and the starting time of the model was set at the *first quit date* of each participant. The first quit date was defined as the mid-date between the last visit in the "smoking" status and the first visit in the status of "abstinent"; relapse dates and higher order quit dates were defined in the same way, as the midpoint of two consecutive visits involving a change of status ("abstinent" to "relapse," or "relapse" to "abstinent"). Using quit, relapse, and possibly requit dates, we could calculate at each visit the total time spent in the "abstinence" and "relapse" status, and thus give a separate estimate of the time effect for abstinence and relapse periods. We adjusted this analysis for the following baseline characteristics: baseline weight, sex, age (above vs. under the median), reported CPD at baseline (above vs. under the median), number of years of education, and intervention group of the RCT. Of these, only covariates significantly ($p < .05$) associated with weight levels and/or dynamics were kept.

To test the influence of NRT use on weight gain, we estimated a second piecewise longitudinal model, with different time slopes for abstinence periods with and without NRT use. We carried this analysis over the duration of the program and included the 382 participants who practically used NRT (80% of study population).

We used the Stata/IC statistical software (v 11.0, StataCorp LP) for baseline data description and the R system for statistical computation and graphics for all longitudinal models (v 2.11.1, http://www.r-project.org/, function "lme," library "nlme").

Results

The study population included 477 participants, 252 in the control group and 225 in the intervention group. Baseline characteristics of participants are described in Table 1. During the follow-up, participants showed a median duration of abstinence of 12.2 weeks, with an interquartile range of 4.0–51.6 weeks. In the control group, the median abstinence was of 13.8 (4.5 – 52.4) weeks, while in the intervention group it was of 11.4 (3.4 – 52.1) weeks (p of the difference = .96). Of the 477 participants, 132 (27.7%) were continuous abstinent (CO-verified) for the duration of the follow-up, 72 and 60 in the control and intervention groups, respectively. As already underlined in the main analysis of these data (Bize et al., 2010), the rates of smoking cessation were not significantly different in the two randomization groups: 28.6% and 26.7% in the control and intervention group, respectively (p of the difference = .64). A comparison between the mean weight change for control and intervention group among continuous abstinent at the end of the treatment, at 6 and 12 months is reported in Table 2. The difference in mean weight change for the control and intervention groups was not significant at any time ($p = .31$ at the end of the program; $p = .95$ at 6 months; $p = .11$ at 12 months).

Since the intervention group did not show any effect on the abstinence duration, the cessation rates, and the weight change during the follow-up, we could collapse the two groups. Applying a polynomial longitudinal model to the unique 1-year prospective cohort resulting from the collapse, we found that weight increased during the intervention and stabilized afterwards. The latter stabilization is reflected by the significant quadratic and cubic fit ($p < .001$ for square and cubic coefficients). We also found a significant interaction between sex and time, attesting a different evolution of weight over the entire follow-up for men and women. Based on the model, the mean weight gain from baseline to 1-year follow-up was 3.3 kg for women and 3.9 for men (p of the difference = .002) (Figure 1). By restricting the model to the duration of the program, we found a significant linear increase of the mean weight ($p < .0001$), with a different slope for both sexes. Women showed a mean weight increase of 0.138 kg/week, while the mean increase for men was of 0.176 kg/week (p-value of the difference <.0001).

Table 1. Baseline Characteristics of Participants ($N = 477$)

Characteristics		
Age, mean (*SD*), years	42.4	(9.7)
Men, No (%)	269	(56)
Weight, mean (*SD*), kg	71.9	(13.9)
BMI, mean (*SD*), kg/m^2	24.4	(3.8)
No of years of education, mean (*SD*)	12.5*	(1.9)
No of cigarettes per day, mean (*SD*)	26.7	(10.0)
Age when started smoking, mean (*SD*), years	17.3	(3.2)
No of years smoked, mean (*SD*)	25.1	(9.4)
Fagerström score, mean (*SD*)	5.4	(2.2)

Note: number; *SD*: standard deviation; BMI: body mass index.
*Data available for $N = 458$ (96%).

Table 2. Mean (*SD*) Weight Change (kg) Among Continuous Abstinent at the End of the Program, at 6 Months, and at 12 Months Visit

	Control group			Intervention group			p of the difference*
	Mean	(*SD*)	*N*	Mean	(*SD*)	*N*	
End of the program	2.4	(2.5)	113	2.8	(2.5)	101	.31
6 months	4.2	(3.1)	86	4.3	(3.4)	70	.95
12 months	6.2	(3.8)	72	5.2	(3.6)	60	.11

*Student's *t*-test.

In order to introduce information about the individual smoking status at each visit, we restricted the analysis to the duration of the program. As shown by the models above, this is the period of linear increase of weight, while in the second part of follow-up a stabilization occurs. Using a piecewise linear longitudinal model, we could give a separate estimate of the weight change during abstinence and relapse episodes of the intervention time. According to the model, weight increased on average by 0.186 kg/week ($p < .001$) during periods of abstinence, and by 0.035 kg/week ($p = .098$) during periods of relapse (p-value of the difference <.001). The model was then adjusted for potential determinants of weight gain (Figure 2). The adjusted model showed a significant effect of sex and the number of CPD at baseline on weight gain during abstinence periods and a significant effect of age on weight gain during relapse periods. During abstinence periods, the estimated mean weight gain was 0.139 kg/week ($p < .001$) among women smoking ≤25 CPD (median CPD at baseline), and 0.173 kg/week for men smoking ≤25 CPD at baseline (p value of the difference = .01). An additional average weight gain of 0.072 kg/week ($p < .001$) was estimated for participants (men and women) smoking >25 CPD at baseline. During periods of relapse, participants aged >43 years (median age at baseline) gained 0.082 kg/week ($p = .005$), while weight gain of younger participants was not significantly different from zero. For instance, a man older than 43 years, smoking more than 25 CPD at baseline, and being abstinent during 8 weeks, was predicted to gain 2.5 kg at the median duration of the program (14.3 weeks). A woman younger than 43 years, smoking less than 25 CPD at baseline, and having the same smoking/abstinence behavior during the program was predicted to gain 1.1 kg (Figure 2). If the two described profiles were abstinent for the *entire* duration of 14.3 weeks, the predicted weight gain would be of 3.5 and 2.0 kg, respectively.

In order to confirm the above findings about the lack of effect of the randomization group (control and intervention) on the weight change over the duration of the program (Table 2), we tested this variable as a covariate of the model: no significant effect on weight gain was found for randomization group, neither during abstinence nor during relapse.

In addition, baseline weight had no significant effect on the weight evolution with time. Adjustment for the number of years of education, as a proxy for socio-economic level, did not change the results.

When further separating periods of abstinence with and without NRT use, average weight gain was 0.181 kg/week during abstinence with NRT use and 0.201 kg/week during abstinence without NRT use (p-value of the difference = .4).

Discussion

We found that sedentary smokers receiving individual smoking cessation counseling and NRTs gained weight within the first 3 months after quitting, with a stabilization afterwards. Our

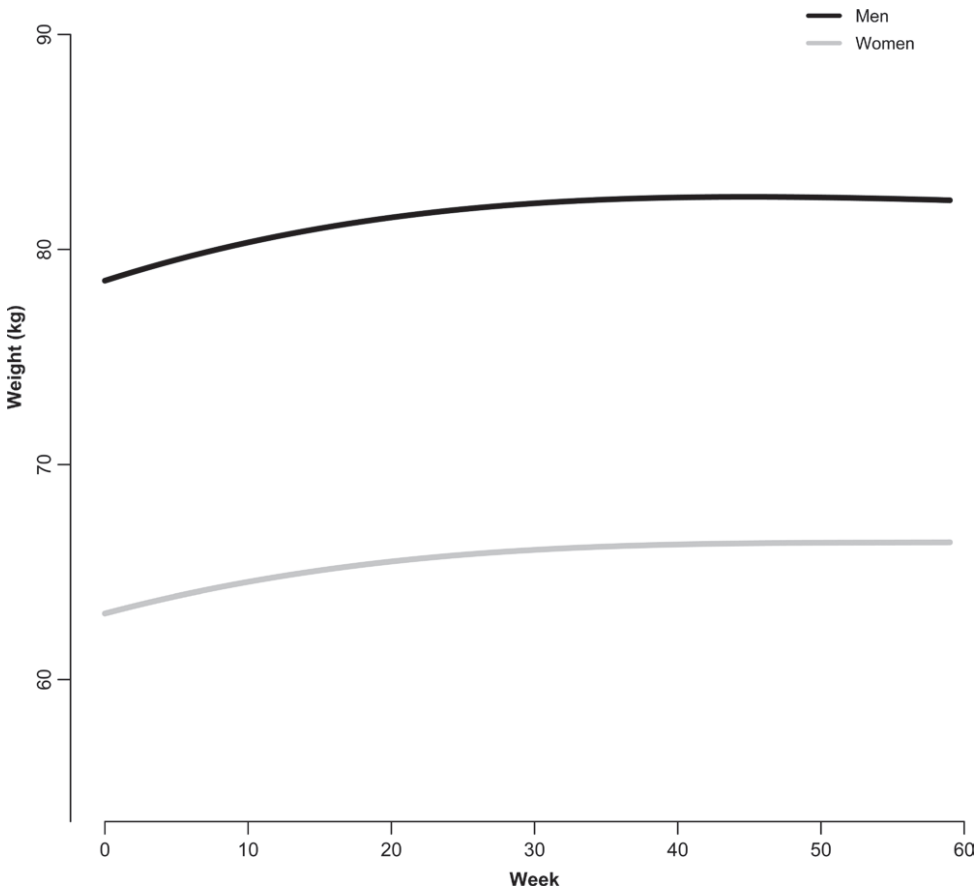

Figure 1. Mean weight trajectories according to the longitudinal model across the entire follow-up time ($N = 477$ participants).

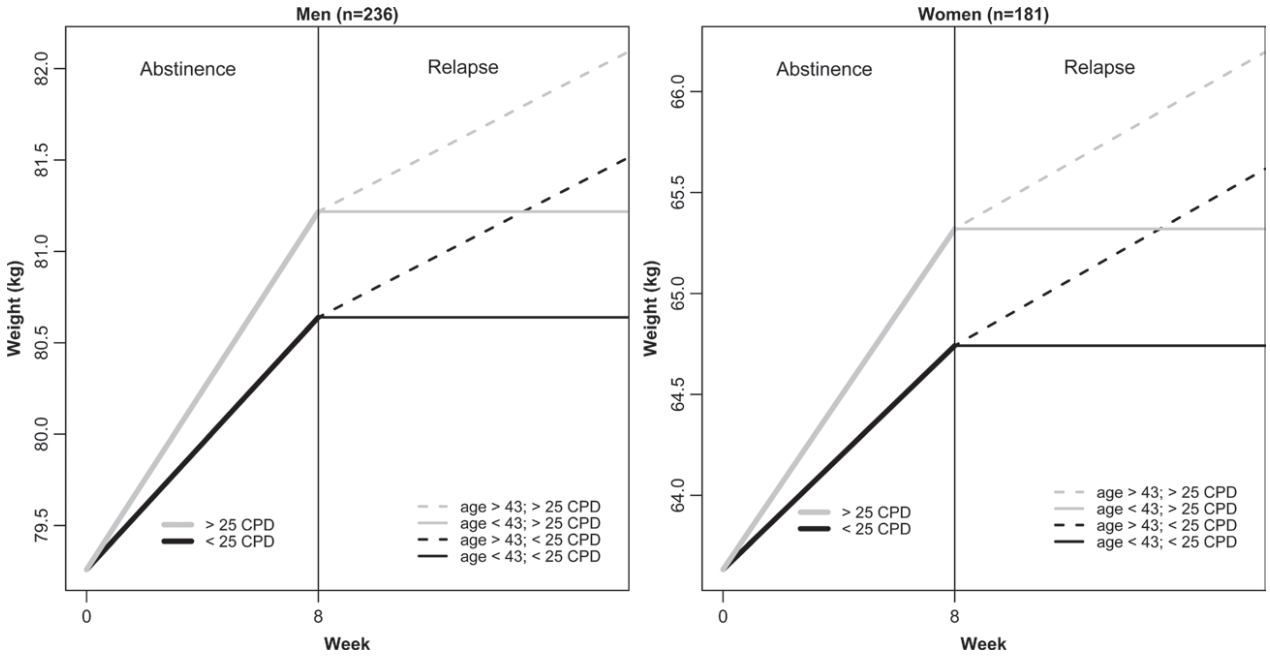

Figure 2. Mean weight trajectories based on the adjusted piecewise longitudinal model for a subject relapsing after 8 weeks of abstinence according to sex, age (dichotomized at the median age of 43 years), and number of cigarettes smoked at baseline (dichotomized at the median number of 25 CPD). The model is estimated on the 417 participants who stopped smoking at least once.

model showed that the mean weight gain was 3.3 kg for women and 3.9 kg for men at 1-year follow-up. In the first few weeks, men consistently put on weight faster than women, and similar findings were found for high nicotine–dependent smokers compared to low nicotine–dependent smokers. Conversely, no differences in weight gain were found in participants receiving a moderate PA intervention compared to those who did not, and a nonsignificant trend toward less weight gain in those who reported using NRT was also found.

Our findings about the amount and pattern of weight gain are consistent with the existing literature (Cropsey et al., 2010; Filozof et al., 2004; Klesges et al., 1989, 1997; Moffatt & Owens, 1991).

Many studies about postcessation weight gain did not compare both sexes (Cropsey et al., 2010; Munafò et al., 2009; Swan & Carmelli, 1995). We show a greater weight gain in men than women over 1 year after quitting. This is reflected by a faster weight gain in men during the first 3 months, which we show to sum up the whole weight gain over the studied period. Literature data about gender differences in weight are currently conflicting, as some prospective studies support our finding of a greater weight gain in men (Chinn et al., 2005; Doherty et al., 1996), whereas other show the opposite (O'Hara et al., 1998; Williamson et al., 1991) or no significant difference (Nides et al., 1994).

NRT has been shown to slow weight gain (Farley et al., 2012), but it is unclear whether it actually reduces weight gain on the long term. A nonsignificant trend toward less weight gain was found in our participants reporting NRT use. The amount of weight gained by quitters treated by combination NRT was comparable to the weight gained by quitters treated by a single NRT as reported in the literature (Cropsey et al., 2010; Dale et al., 1998; Doherty et al., 1996; Ferguson et al., 2010; Lycett et al., 2011; Nides et al., 1994; Nordstrom et al., 1999; O'Hara et al., 1998; Ussher et al., 2003). To our view, a dose–response relationship between NRT and weight gain is difficult to demonstrate, because of issues on therapeutic adherence assessment, differences of bioavailability of modes of administration, and wide range of nicotine doses self-administered by smokers (Benowitz, 2008; Berlin et al., 2011; Le Houezec, 2003).

There is a well-known link between weight issues and nicotine dependence (Chiolero, Faeh, Paccaud, & Cornuz, 2008; Chiolero, Jacot-Sadowski, Faeh, Paccaud, & Cornuz, 2007). In agreement with previous studies (Williamson et al., 1991), our data show that higher CPD before quitting is linked with a larger weight gain in the first weeks after quitting smoking.

Some studies have shown that quitters who relapse lose the weight they gained while attempting to quit (Lycett et al., 2011; O'Hara et al., 1998). In our study, older smokers conversely kept putting on weight in case of a relapse. This age-related inertia in weight gain points toward a mechanism of weight gain, which possibly lasts longer in older people. However, our data does not seem appropriate to identify the latter mechanism.

The lack of benefit of PA practice has been attributed to its moderate intensity, which is probably insufficient to compensate for the energy unbalance after quitting. We were not able to account for individual levels of PA, due to issues in measuring it reliably (Shephard & Aoyagi, 2011; van Poppel, Chinapaw, Mokkink, van Mechelen, & Terwee, 2010; Warren et al., 2010). As the measure of PA is of particular interest in weight gain, this is one of the major limitations to our study. More research is needed in this important area.

Most studies about weight gain after smoking cessation have compared those who manage to quit with those who do not. However, quitters and continuing smokers may differ by

unmeasured differences. For instance, smokers and ex-smokers have different food habits (Morabia & Wynder, 1990). Also, more quitters than relapsers remain in follow-up during RCTs about smoking cessation (West, Hajek, Stead, & Stapleton, 2005). Moreover, weight gain is a frequent cause of relapse (Pisinger & Jorgensen, 2007). This results in a possible systematic error in the estimation of weight gain after smoking cessation. We sought to avoid this potential caveat by analyzing our data through a longitudinal model, despite its added complexity. Indeed, this model considers the individual trajectory of weight change of each participant. Thus, it enabled us to take into account the weight change of every participant, as opposed to a more simple comparison of weight at baseline and at the end of the study that looks only at those who succeed in quitting or only at those who complete the whole follow-up. Besides, mixed longitudinal models are the method of choice for analyzing longitudinal data (Gibbons et al., 2010).

Our study has several other strengths. Our data were collected prospectively and for a large number of participants, both men and women. Smoking status and weight were assessed by objective measures, following international standard outcome criteria for smoking cessation trials (West et al., 2005). The participants attended a program based on international guidelines for smoking cessation. In particular, they were offered a combination of both oral and transcutaneous NRT, as currently recommended by the international guidelines for smoking cessation (Fiore et al., 2008). Although some of them also benefited from a moderate PA intervention, this was accounted for in the analyses. This makes the participants to our study very similar to patients seen in a smoking cessation clinic, thus improving the external validity of our results.

We recruited smokers interested in quitting smoking, to participate in a trial focusing on a lifestyle intervention. They may well be on overall more concerned by their health and alimentation than smokers generally are. This is a built-in limitation to the external validity, common to studies recruiting smokers prospectively, which no statistical model can account for.

In conclusion, sedentary smokers receiving individual counseling and combination NRT experienced a moderate weight gain occurring during the first 3 months following quitting. Besides smoking abstinence itself, we found that male sex and higher cigarettes consumption are predictors of a larger weight gain after quitting smoking.

Funding

The Department of Ambulatory Care and Community Medicine of the University of Lausanne, Switzerland, supported the study.

Declaration of Interests

None declared.

Acknowledgments

The authors thank Ms. Sylvie Payot (Department of Ambulatory Care and Community Medicine, University of Lausanne, Switzerland) for her help in managing the data, as well as Prof. Luc Tappy (Department of Physiology, University of Lausanne, Switzerland) for his valuable comments in the early planning of the analysis.

References

Benowitz, N. L. (2008). Clinical pharmacology of nicotine: Implications for understanding, preventing, and treating tobacco addiction. *Clinical Pharmacology and Therapeutics*, *83*, 531–541. doi:10.1038/clpt.2008.3

Berlin, I., Jacob, N., Coudert, M., Perriot, J., Schultz, L., & Rodon, N. (2011). Adjustment of nicotine replacement therapies according to saliva cotinine concentration: The ADONIS* trial—A randomized study in smokers with medical comorbidities. *Addiction (Abingdon, England)*, *106*, 833–843. doi:10.1111/j.1360-0443.2010.03306.x

Bize, R., Willi, C., Chiolero, A., Stoianov, R., Payot, S., Locatelli, I. Cornuz, J. (2010). Participation in a population-based physical activity programme as an aid for smoking cessation: A randomised trial. *Tobacco Control*, *19*, 488–494. doi:10.1136/tc.2009.030288

Borg, G. (1998). *Borg's perceived exertion and pain scales*. Champaign, IL: Human Kinetics.

Chinn, S., Jarvis, D., Melotti, R., Luczynska, C., Ackermann-Liebrich, U., Antó, J. M., Cerveri, I., de Marco, R., Gislason, T., Heinrich, J., Janson, C., Künzli, N., Leynaert, B., Neukirch, F., Schouten, J., Sunyer, J., Svanes, C., Vermeire, P., Wjst, M., Burney, P. (2005). Smoking cessation, lung function, and weight gain: A follow-up study. *Lancet*, *365*, 1629–1635; discussion 1600-1. doi:10.1016/S0140-6736(05)66511-7

Chiolero, A., Faeh, D., Paccaud, F., & Cornuz, J. (2008). Consequences of smoking for body weight, body fat distribution, and insulin resistance. *The American Journal of Clinical Nutrition*, *87*, 801–809. Retrieved from http://www.ajcn.org/content/87/4/801.full

Chiolero, A., Jacot-Sadowski, I., Faeh, D., Paccaud, F., & Cornuz, J. (2007). Association of cigarettes smoked daily with obesity in a general adult population. *Obesity (Silver Spring, Md.)*, *15*, 1311–1318. doi:10.1038/oby.2007.153

Cnaan, A., Laird, N. M., & Slasor, P. (1997). Using the general linear mixed model to analyse unbalanced repeated measures and longitudinal data. *Statistics in Medicine*, *16*, 2349–2380. doi:10.1002/(SICI)1097-0258(19971030)16:20<2349::AID-SIM667>3.0.CO;2-E

Cornuz, J., Humair, J.-P., Seematter, L., Stoianov, R., van Melle, G., Stalder, H., & Pécoud, A. (2002). Efficacy of resident training in smoking cessation: A randomized, controlled trial of a program based on application of behavioral theory and practice with standardized patients. *Annals of Internal Medicine*, *136*, 429–437. Retrieved from http://www.annals.org/content/136/6/429.full.pdf+html

Cropsey, K. L., McClure, L. A., Jackson, D. O., Villalobos, G. C., Weaver, M. F., & Stitzer, M. L. (2010). The impact of quitting smoking on weight among women prisoners participating in

a smoking cessation intervention. *American Journal of Public Health*, *100*, 1442–1448. doi:10.2105/AJPH.2009.172783

Dale, L. C., Schroeder, D. R., Wolter, T. D., Croghan, I. T., Hurt, R. D., & Offord, K. P. (1998). Weight change after smoking cessation using variable doses of transdermal nicotine replacement. *Journal of General Internal Medicine*, *13*, 9–15. Retrieved from http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1496892&tool=pmcentrez&rendertype=abstract

Doherty, K., Militello, F. S., Kinnunen, T., & Garvey, A. J. (1996). Nicotine gum dose and weight gain after smoking cessation. *Journal of Consulting and Clinical Psychology*, *64*, 799–807. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/8803371

Farley, A. C., Hajek, P., Lycett, D., & Aveyard, P. (2012). Interventions for preventing weight gain after smoking cessation. *Cochrane Database of Systematic Reviews (Online)*, *1*, CD006219. doi:10.1002/14651858.CD006219.pub3

Ferguson, S. G., Shiffman, S., Rohay, J. M., Gitchell, J. G., & Garvey, A. J. (2010). Effect of compliance with nicotine gum dosing on weight gained during a quit attempt. *Addiction (Abingdon, England)*. doi:10.1111/j.1360-0443.2010.03244.x

Filozof, C., Fernández Pinilla, M. C., & Fernández-Cruz, A. (2004). Smoking cessation and weight gain. *Obesity Reviews: An Official Journal of the International Association for the Study of Obesity*, *5*, 95–103. doi:10.1111/j.1467-789X.2004.00131.x

Fiore, M., Jaén, C., Baker, T., Bailey, W., Bennett, G., Benowitz, N., Christiansen, B., Connell, M., Curry, S. J., Dorfman, S. F., Fraser, D., Froelicher, E. S., Goldstein, M. G., Hasselblad, V., Healton, C. G., Heishman, S., Henderson, P. N., Heyman, R. B., Husten, C., Koh, H. K., Kottke, T. E., Lando, H. A., Leitzke, C., Mecklenburg, R. E., Mermelstein, R. J., Morgan, G., Mullen, P. D., Murray, E. W., Orleans, C. T., Piper, M. E., Robinson, L., Stitzer, M. L., Theobald, W., Tommasello, A. C., Villejo, L., Wewers, M. E., Williams, C. (2008). A clinical practice guideline for treating tobacco use and dependence: 2008 update. A U.S. Public Health Service report. *American Journal of Preventive Medicine*, *35*, 158–176. doi:10.1016/j.amepre.2008.04.009

Gibbons, R. D., Hedeker, D., & DuToit, S. (2010). Advances in analysis of longitudinal data. *Annual Review of Clinical Psychology*, *6*, 79–107. doi:10.1146/annurev.clinpsy.032408.153550

Klesges, R. C., Meyers, A. W., Klesges, L. M., & La Vasque, M. E. (1989). Smoking, body weight, and their effects on smoking behavior: A comprehensive review of the literature. *Psychological Bulletin*, *106*, 204–230. doi:10.1037//0033-2909.106.2.204

Klesges, R. C., Winders, S. E., Meyers, A. W., Eck, L. H., Ward, K. D., Hultquist, C. M., Ray, J. W., Shadish, W. R. (1997). How much weight gain occurs following smoking cessation? A comparison of weight gain using both continuous and point prevalence abstinence. *Journal of Consulting and Clinical Psychology*, *65*, 286–291. doi:10.1037//0022-006X.65.2.286

Lange, N. (1992). Graphs and stochastic relaxation for hierarchical Bayes modelling. *Statistics in Medicine*, *11*, 2001–2016. doi:10.1002/sim.4780111417

Le Houezec, J. (2003). Role of nicotine pharmacokinetics in nicotine addiction and nicotine replacement therapy: A review. *The International Journal of Tuberculosis and Lung Disease : The Official Journal of the International Union Against Tuberculosis and Lung Disease*, *7*, 811–819. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12971663

Lycett, D., Munafò, M., Johnstone, E., Murphy, M., & Aveyard, P. (2011). Associations between weight change over 8 years and baseline body mass index in a cohort of continuing and quitting smokers. *Addiction (Abingdon, England)*, *106*, 188–196. doi:10.1111/j.1360-0443.2010.03136.x

Mäder, U., Martin, B. W., Schutz, Y., & Marti, B. (2006). Validity of four short physical activity questionnaires in middle-aged persons. *Medicine and Science in Sports and Exercise*, *38*, 1255–1266. doi:10.1249/01.mss.0000227310.18902.28

Martin, B. W., Jimmy, G., & Marti, B. (2001). Promotion of exercise among the physically inactive: A challenge also in Switzerland. *Therapeutische Umschau. Revue thérapeutique*, *58*, 196–201. doi:10.1024/0040-5930.58.4.196

Moffatt, R. J., & Owens, S. G. (1991). Cessation from cigarette smoking: Changes in body weight, body composition, resting metabolism, and energy consumption. *Metabolism: Clinical and Experimental*, *40*, 465–470. doi:10.1016/0026-0495(91)90225-L

Morabia, A., & Wynder, E. L. (1990). Dietary habits of smokers, people who never smoked, and exsmokers. *The American Journal of Clinical Nutrition*, *52*, 933–937. Retrieved from http://www.ajcn.org/content/52/5/933.long

Munafò, M. R., Tilling, K., & Ben-Shlomo, Y. (2009). Smoking status and body mass index: A longitudinal study. *Nicotine & Tobacco Research: Official Journal of the Society for Research on Nicotine and Tobacco*, *11*, 765–771. doi:10.1093/ntr/ntp062

Naumova, E. N., Must, A., & Laird, N. M. (2001). Tutorial in Biostatistics: Evaluating the impact of "critical periods" in longitudinal studies of growth using piecewise mixed effects models. *International Journal of Epidemiology*, *30*, 1332–1341. doi:10.1093/ije/30.6.1332

Nides, M., Rand, C., Dolce, J., Murray, R., O'Hara, P., Voelker, H., & Connett, J. (1994). Weight gain as a function of smoking cessation and 2-mg nicotine gum use among middle-aged smokers with mild lung impairment in the first 2 years of the Lung Health Study. *Health Psychology : Official Journal of the Division of Health Psychology, American Psychological Association*, *13*, 354–361. doi:10.1037/0278-6133.13.4.354

Nordstrom, B. L., Kinnunen, T., Utman, C. H., & Garvey, A. J. (1999). Long-term effects of nicotine gum on weight gain after smoking cessation. *Nicotine & Tobacco Research : Official Journal of the Society for Research on Nicotine and Tobacco*, *1*, 259–268. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/11072423

O'Hara, P., Connett, J. E., Lee, W. W., Nides, M., Murray, R., & Wise, R. (1998). Early and late weight gain following smoking cessation in the Lung Health Study. *American Journal of*

Epidemiology, *148*, 821–830. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/9801011

Petkova, E., & Teresi, J. (2002). Some statistical issues in the analyses of data from longitudinal studies of elderly chronic care populations. *Psychosomatic Medicine*, *64*, 531–547. Retrieved from http://www.psychosomaticmedicine.org/content/64/3/531.long

Pinheiro, J. C., & Bates, D. M. (2000). *Mixed-effects models in Sand S-PLUS*. New York: Springer. doi:10.1007/978-1-4419-0318-1

Pisinger, C., & Jorgensen, T. (2007). Weight concerns and smoking in a general population: The Inter99 study. *Preventive Medicine*, *44*, 283–289. doi:10.1016/j.ypmed.2006.11.014

Raudenbush, S. W., & Bryk, A. S. (2002). *Hierarchical linear models: Applications and data analysis methods* (p. 485). Thousand Oaks, CA: Sage Publications.

Shephard, R. J., & Aoyagi, Y. (2011). Measurement of human energy expenditure, with particular reference to field studies: An historical perspective. *European Journal of Applied Physiology*. doi:10.1007/s00421-011-2268-6

Suisse. (2008). Allez Hop! Retrieved July 29, 2008, from http://www.allezhop.ch/

Swan, G. E., & Carmelli, D. (1995). Characteristics associated with excessive weight gain after smoking cessation in men. *American Journal of Public Health*, *85*, 73–77. Retrieved from http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1615288&tool=pmcentrez&rendertype=abstract

Ussher, M., West, R., McEwen, A., Taylor, A., & Steptoe, A. (2003). Efficacy of exercise counselling as an aid for smoking cessation: A randomized controlled trial. *Addiction (Abingdon, England)*, *98*, 523–532. doi:10.1046/j.1360-0443.2003.00346.x

van Poppel, M. N. M., Chinapaw, M. J. M., Mokkink, L. B., van Mechelen, W., & Terwee, C. B. (2010). Physical activity questionnaires for adults: A systematic review of measurement properties. *Sports Medicine (Auckland, N.Z.)*, *40*, 565–600. doi:10.2165/11531930-000000000-00000

Warren, J. M., Ekelund, U., Besson, H., Mezzani, A., Geladas, N., & Vanhees, L. (2010). Assessment of physical activity—A review of methodologies with reference to epidemiological research: A report of the exercise physiology section of the European Association of Cardiovascular Prevention and Rehabilitation. *European Journal of Cardiovascular Prevention and Rehabilitation: Official Journal of the European Society of Cardiology, Working Groups on Epidemiology & Prevention and Cardiac Rehabilitation and Exercise Physiology*, *17*, 127–139. doi:10.1097/HJR.0b013e32832ed875

West, R., Hajek, P., Stead, L., & Stapleton, J. (2005). Outcome criteria in smoking cessation trials: Proposal for a common standard. *Addiction (Abingdon, England)*, *100*, 299–303. doi:10.1111/j.1360-0443.2004.00995.x

Williamson, D. F., Madans, J., Anda, R. F., Kleinman, J. C., Giovino, G. A., & Byers, T. (1991). Smoking cessation and severity of weight gain in a national cohort. *The New England Journal of Medicine*, *324*, 739–745. doi:10.1056/NEJM199103143241106