

# SMOKING CESSATION BY NICOTINE TRANSDERMAL PATCH AND GUM: A REVIEW

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## Abstract

**Background:** World Health Organization recognizes smoking as a major public health issue all over the world. Nicotine replacement therapy (NRT) is to be considered as one of the best smoking cessation strategies so far. Most widely used NRT are nicotine gum and nicotine patches. The aim of this review is to determine the most effective and appropriate nicotine therapy for smoking cessation after making comparison between two most commonly used NRT, nicotine gum and nicotine transdermal patch.

**Method:** We systemically searched electronic databases including Medline, Scopus, PubMed, CINAHL, and Cochrane to review published literature in this area. Electronic searches were limited to smoking cessation, nicotine replacement therapy, nicotine gum, nicotine transdermal patch, and effectiveness. All placebo randomized controlled trials which investigated the effectiveness of NRT were eligible for this systematic review. Both male and female healthy participants who smoked more than 20-cigareetes per day were eligible for this systematic review with 20 to 65 years' age limit.

**Results:** A total of 975 articles were searched from above mentioned databases using the keywords. The number was dropped to 156 upon exclusion of repeated and irrelevant studies. Out of these 156 articles, 129 were excluded as titles or abstracts did not match eligibility criteria leaving 27 for this review. However, only 15 articles were included in this review following further screening, study population, intervention, or outcome of studies that did not met the selection criteria were excluded.

**Conclusion:** It was concluded that nicotine transdermal patch is more effective and more helpful as compared to nicotine gum in smoking cessation. In the light of result, it has also been recommended that nicotine transdermal patch must be used as a first priority in smoking cessation to achieve the target rather than nicotine gum.

**Keywords:** Smoking cessation, Nicotine replacement therapy, Nicotine gum, Nicotine transdermal patch, Effectiveness

## INTRODUCTION

According to World Health Organization (WHO) 0.1 billion people died in 20th century because of smoking addiction around the globe and if current trend remains the same, in 21st century ten times as many will die<sup>1</sup>. Due to smoking addiction 512, 000 people in USA and 655,000 in Europe died before 2007<sup>2</sup>. In UK, one of the major causes of mortality is cigarette smoking. According to National Health Service 106,000 smokers die every year in UK<sup>3</sup>. Due to smoking related diseases, hospital admission has been increased by 1.4

million in 2006/2007 in UK. Over all smoking cost £1.7 billion each year to NHS which is the major burden and needs to be reduced<sup>4</sup>. In cigarette, nicotine is the main element, which causes addiction, and this is same for other drugs<sup>5</sup>.

Recognizing this global issue, public health professionals have designed many smoking cessation strategies, which are helpful to decrease these number of deaths<sup>6</sup>. Many people around the world wants to quit smoking, like in western world, about 70% peoples people who

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smoke wants to stop smoking<sup>6</sup>. Nicotine replacement therapy (NRT) helps smokers to get rid of smoking and provides support with care<sup>7</sup>. Every year half of smokers try to stop smoking in United Kingdom but only 2-3% gets success. The reasons of low success rate are unplanned quit attempts and most appropriate NRT may not be used<sup>8</sup>.

Nicotine replacement therapies (NRT) are the most commonly used strategies for smoking cessation. Although there are various kinds of NRT available but nicotine, transdermal patch and nicotine gum are most popular and widely used for treatment. The main aim of this report is to make comparison in between these two NRT and make conclusion which intervention is most effective. Based on their usage, side effect, mode of action and availability, both NRT has diverse efficiency to help smokers to stop smoking.

Nicotine patch is available with or without NHS prescription (NHS 2008)<sup>3</sup>. On NHS, prescription smokers do not need to pay for it but without prescription the cost of patch is £15 per week (NHS Choices 2010). Two types of nicotine patch are available; 16-hour and 24-hour with three different doses 7mg, 14mg, and 21mg. Both kinds of patches release about 1mg of nicotine per hour<sup>9</sup>. In contrast to that, smokers can get nicotine gum without any cost and prescription (NHS Choices 2010). Research supports the effectiveness of nicotine gum. Furthermore, it is recognized as a first pharmacological

therapy for smoking cessation<sup>10</sup>. Nicotine gum is available in 2mg and 4mg doses<sup>11</sup>. It is supposed to be used on daily basis from one to six months without any discontinuation until and unless it causes any serious side effect, which is very unlikely. The dose of nicotine gum can be controlled by increasing or decreasing the number of pieces chewed per day<sup>12</sup>. In contrast to that, nicotine patch is adhesive, it smoothly sticks with the smoker's skin, and discharge fixed amount of nicotine into the body. Smokers just need to stick this adhesive patch with his body for a specific period of time<sup>9</sup>.

This research conducted on the strong basic hypothesis of evidence, which already published in previous researches. These researchers analyse the effectiveness of NRT. They recommend the patch as an easy to use, accessible, with fewer side effects and produce steady amount of nicotine. Therefore, researchers insisted that nicotine transdermal patch has more significant results than nicotine gum<sup>13,14</sup>. The present review is an attempt to find out the most effective intervention between nicotine transdermal patch and nicotine gum.

### METHODOLOGY

We systemically reviewed the published literature to identify studies regarding the effectiveness of NRT confined to the research topic. All published randomized controlled trial were selected for this research report. With the help of computerized indices

and databases a detailed search was carried out to locate all possible trials, which examined the comparison and effectiveness of NRTs. Electronic searches of databases including Medline, Scopus, PubMed, CIN AHL, and Cochrane for the literature published from January 2000 to Dec 2011. Boolean operators were used for searching of relevant articles. Keywords including Smoking cessation, Nicotine replacement therapy, Nicotine gum and Nicotine transdermal patch were used for literature review.

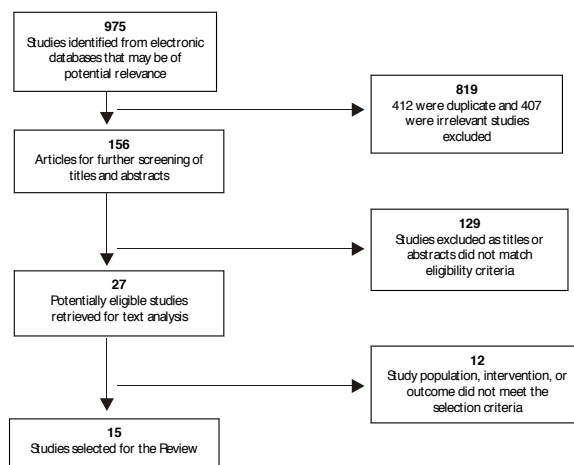
Initially, abstracts of all 80 articles were reviewed by two independent reviewers and were categorized into 'relevant', 'irrelevant' or 'unsure' groups. Full text articles were reviewed of all articles grouped into 'unsure' category to decide upon their relevancy for this review. The third reviewer was contacted in case where the two independent reviewers were not able to form consensus on inclusion or exclusion of an article or articles for this review. The inclusion criterion was limited to clinical trials published in English only. With the help of eligible criteria, most relevant and appropriate randomized controlled trials have been identified. Placebo-controlled randomized controlled trials of nicotine replacement therapies were included; which were available in full text publications. Trials which included any investigation of nicotine gum and transdermal patch (among smokers) were included. In addition, only those clinical trials were included in this review in which

participants smoked at least 10 sticks of cigarette per day. Both male and female participants were eligible with the age limit 20 to 65 years old. The primary outcome in the trials is was sustained reduction or smoking cessation at six months only. Trials were excluded involving smokers, who had chronic disease and the perceptions of health professional, effects of smoking on newborn babies, pregnant smokers, surgical and drug driven interventions. Above criteria are used to get the most appropriate and relevant papers. The quality of relevant literature has been assessed in the light of Cochrane Handbook for Systematic Reviews of Interventions. The Critical Appraisal Skills Programme (CASP) checklist for randomized controlled trial [17] was used to assess the internal validity and overall quality of the included studies.

### RESULTS

A total of 975 articles were searched from above mentioned databases using the keywords. The number was dropped to 156 upon exclusion of repeated and irrelevant studies. Out of these 156 articles, 129 were excluded as titles or abstracts did not match the eligibility criteria leaving 27 for this review. However, only 15 articles were included in this review following further screening, study population, intervention, or outcome of studies that did not met the selection criteria were excluded (Figure 1).

Figure 1. Flow diagram of study selection



Total number of participant in this research report was 8090. Out of 8090 participants, female participant was 3956. During investigation, it was found that treatment arm always gets favour over placebo in open studies because of no blinding<sup>15</sup>. In open studies participants

and researcher both knows what sort of treatment they are getting<sup>16</sup>. In contrast to that, blinding is the most vital factor in randomized control trials (RCT) and that is why RTC always brings the more acceptable and precise results<sup>15</sup>. Although it is much more difficult

process to keep participants and researcher blind at the same time but it is the art of RCT<sup>15</sup>. In this research report, most of the selected studies were double-blinded<sup>17, 18, 19, 20, 21, 22, 16, 14, 23, 24, 25</sup>.

**Table 1: Included Studies**

Comparison of nicotine gum (NG) versus placebo: outcome, smoking cessation or abstinence at 6 month					
Study	Study Design	Sample Size	Nicotine Gum	Placebo	Odds Ratio (OR)
Kinnunem <i>et al.</i> 2008	Double blind RCT	608	405	203	1.57
Herrera <i>et al.</i> 2007	Double blind RCT	154	76	78	3.26
Hughes <i>et al.</i> 2007	Double blind RCT	315	210	105	2.03
Killen <i>et al.</i> 2006	Double blind RCT	1217	600	617	1.23
Cooper <i>et al.</i> 2005	Double blind RCT	294	146	147	1.16
Hall <i>et al.</i> 2005	RCT	201	89	103	1.18
Wennike <i>et al.</i> 2003	Double blind RCT	411	205	206	3.13
Garvey <i>et al.</i> 2000	RCT	608	405	206	2.49
Comparison of nicotine patch (NP) versus placebo: outcome, smoking cessation or abstinence at 6 month					
Study	Study Design	Sample Size	Nicotine Patch	Placebo	Odds Ratio (OR)
Hays <i>et al.</i> 2009	Double blind RCT	958	636	322	2.38
Daughton <i>et al.</i> 2008	Double blind RCT	369	184	185	1.66
Paoletti <i>et al.</i> 2008	RCT	120	60	60	4.67
Stapleton <i>et al.</i> 2006	Double blind RCT	1200	800	400	2.14
Gourlay <i>et al.</i> 2005	RCT	629	315	314	1.25
Hurt <i>et al.</i> 2004	Double blind RCT	240	120	120	2.30
ICRF GPRG 2001	RCT	1686	842	844	1.48

**DISCUSSION**

This review was conducted to compare between nicotine gum and patch, the two most commonly available and frequently used NRT for smoking cessation. This research report was based upon the hypothesis that nicotine patch is the most effective treatment than nicotine gum. In the past published research reports, we found some evidence in favour of nicotine patch and the hypothesis of this research report was based on these evidences.

Most of the researches in the past included two outcome measures, continuous smoking cessation and the point prevalence at six and 12-month follow-up<sup>26</sup>. Outcome measure in

continuous smoking abstinence is more acceptable and provides more accurate result as compared to point prevalence<sup>27</sup>. This outcome was measure also suggested by many researchers, health professionals and health policy makers<sup>13</sup>. The reason behind this is that point prevalence provides data at the time when smokers stopped smoking, at least one week before bio-medical confirmation test<sup>13</sup>. Point prevalence could not provide the actual duration of smoking cessation<sup>28</sup>. In contrast to that in continuous smoking abstinence, smoker stopped smoking at the start of the trial and after six or 12 month it provided the accurate data that how many people did not smoke during that period of time<sup>27</sup>. Due to that reason, all those trials that provided data in point prevalence had

been excluded to get the more accurate result in this meta-analysis.

According to NICE (2008) smoking cessation rate would always get higher in those smokers who already are willing and provoked to get rid of smoking and seek help from behavioural support programme (NICE, 2008). In this review, most of the included smokers were already motivated and keen to stop smoking<sup>17, 22, 23, 25, 24, 29</sup> like participants in this review also confirmed the guide-lines provided by NICE (2008) for smoking cessation strategies. In one survey, it was found that smokers showed more curiosity in self-guided treatment programme rather than behavioural support. However, the results in both trials were not statistically significant and

both researchers were agreed at the end that behavioural support programme could be more helpful as compared to self-guided treatment plan<sup>18</sup>. Behavioural support programme not only provide the psychological support but also encourage people to stop smoking slowly and gradually<sup>23</sup>.

The number of participants who left the trial during the research before an end called dropout rate<sup>16</sup>. Drop-out rate have much more importance in any trial and accuracy of the result also depends upon this drop-out rate.<sup>16</sup> There could be a substantial bias if dropout rate exceeds more than normal value, which is 30%.<sup>30</sup> Out of 15 included trials in this review five trials have more than 30% drop-out rate which is also a draw-back of this report, these trials are.<sup>14, 23, 18, 22,</sup>

It has been observed that men respond NRT more positively as compared to women but most of the researcher did not raise this sensitive issue very well and ignored the gender differences. Most of the women quit smoking after pregnancy and peer pressure but at the same time, they were using NRT as well. Due to that, it is quite difficult to identify the impact of NRT on these women. Additional investigation is required after making the two groups of women, pregnant and non-pregnant. Dropout rate of women was much more as compared to men during the research. So many reasons have been identified like socio-economic condition, stress, time, traveling, as well as look after their kids. There is need to clarify all above points and to find out the effectiveness of NRT on these women.

Although all chosen countries in this report are well developed but still all of them, have their own cultural values. Effectiveness of NRT also influenced by family's values, weather, peer pressure and social conditions like some people smoke expensive cigarette due to status symbol and some smoke because of stress. After passing some period of time this bad habit become permanent and they all become addictive. Different countries have different GDP rate which also effect on smoking cessation rate so further research is required to discover these issues very well.

Randomized controlled trials is the only choice of methodology in all selected studies and the reason behind this, it is the only method which help to make comparison between two different treatment<sup>31</sup> and indicates which treatment would be the most effective but it is also one of the limitations. Various studies have been conducted on NRT's safety and effectiveness but in different methodology and the choice of study, here is Randomized Controlled Trials so there is a chance to missing some important data. Both male and female smokers with average range in between 20 to 65 years old has been included in this research report. Age restriction also limits the acceptability of this research report. It is well known truth that lot of smoker start smoking at under age and this is the vulnerable group<sup>5</sup>. Smoking is most popular in this age group and the researcher in this report excluded this group. Further search is required in which this age group must be include to make report more authenticate and more reliable.

## CONCLUSION

It was concluded that nicotine transdermal patch is more effective and more helpful as compared to nicotine gum in smoking cessation. Despite of this nicotine gum and patch both have the same function as others NRT. Both introduces small and safe amount of nicotine into the body. However, in the light of results, it has also been recommended that nicotine transdermal patch must be used as a priority in smoking cessation to achieve the target rather than nicotine gum.

## REFERENCES

1. Organization WH. History of the World Health Organization framework convention on tobacco control. 2009.
2. Tønnesen P. Smoking cessation: How compelling is the evidence? A review. *Health Policy*. 2009; 91:S15-S25.
3. Fuller E, Hawkins V. Smoking, drinking and drug use among young people in England in 2011: Health and Social Care Information Centre London; 2012.

4. Wang D, Connock M, Barton P, Fry-Smith A, Aveyard P, Moore D. 'Cut down to quit' with nicotine replacement therapies in smoking cessation: a systematic review of effectiveness and economic analysis. 2008.
5. Fagerström K. The epidemiology of smoking. *Drugs*. 2002; 62:1-9.
6. Commission CQ. The State of Health Care and Adult Social Care in England: Key themes and quality of services in 2009: The Stationery Office; 2010.
7. Niaura R, Goldstein MG, Abrams DB. Matching High-Dependence and Low-Dependence Smokers to Self-Help Treatment with or Without Nicotine Replacement. *Preventive Medicine*. 1994; 23:70-7.
8. Lamarche K. Review: varenicline, bupropion, and nicotine. 2009.
9. Hansen H. Textbook of lung cancer: CRC Press; 2008.
10. Fortmann SP, Killen JD, Telch MJ, Newman B. Minimal contact treatment for smoking cessation: A placebo controlled trial of nicotine polacrilex and self-directed relapse prevention: Initial results of the Stanford Stop Smoking Project. *Jama*. 1988; 260:1575-80.
11. Ries RK, Miller SC, Fiellin DA. Principles of addiction medicine: Lippincott Williams & Wilkins; 2009.
12. Thomas S. Smoking cessation part 2: nicotine replacement therapy. *Nursing Standard*. 2007; 22:44-7.
13. Ebbert JO, Post JA, Moyer TP, Dale LC, Schroeder DR, Hurt RD. Nicotine percentage replacement among smokeless tobacco users with nicotine patch. *Drug and alcohol dependence*. 2007; 89:223-6.
14. Hays JT, Croghan IT, Schroeder DR, Offord KP, Hurt RD, Wolter TD, et al. Over-the-counter nicotine patch therapy for smoking cessation: results from randomized, double-blind, placebo-controlled, and open label trials. *American Journal of Public Health*. 1999; 89:1701-7.

15. Schulz KF, Chalmers I, Hayes RJ, Altman DG. Empirical evidence of bias: dimensions of methodological quality associated with estimates of treatment effects in controlled trials. *Jama*. 1995; 273:408-12.
16. Daughton D, Susman J, Sitorius M, Belenky S, Millatmal T, Nowak R, et al. Transdermal nicotine therapy and primary care: importance of counseling, demographic, and participant selection factors on 1-year quit rates. *Archives of family medicine*. 1998; 7:425.
17. Garvey AJ, Kinnunen T, Nordstrom BL, Utman CH, Doherty K, Rosner B, et al. Effects of nicotine gum dose by level of nicotine dependence. *Nicotine & Tobacco Research*. 2000; 2:53-63.
18. Killen JD, Fortmann SP, Newman B, Varady A. Evaluation of a treatment approach combining nicotine gum with self-guided behavioral treatments for smoking relapse prevention. *J Consult Clin Psychol*. 1990; 58:85-92.
19. Herrera N, Franco R, Herrera L, Partidas A, Rolando R, Fagerström KO. Nicotine gum, 2 and 4 mg, for nicotine dependence: a double-blind placebo-controlled trial within a behavior modification support program. *Chest*. 1995; 108:447-51.
20. Hughes JR, Gust SW, Keenan RM, Fenwick JW, Healey ML. Nicotine vs placebo gum in general medical practice. *Jama*. 1989; 261:1300-5.
21. Kinnunen T, Korhonen T, Garvey AJ. Role of nicotine gum and pretreatment depressive symptoms in smoking cessation: twelve-month results of a randomized placebo controlled trial. *The International Journal of Psychiatry in Medicine*. 2008; 38:373-89.
22. Cooper TV, Klesges RC, DeBon MW, Zbikowski SM, Johnson KC, Clemens LH. A placebo controlled randomized trial of the effects of phenylpropanolamine and nicotine gum on cessation rates and postcessation weight gain in women. *Addictive behaviors*. 2005; 30:61-75.
23. Gourlay SG, Forbes A, Marriner T, Pethica D, McNeil JJ. Double blind trial of repeated treatment with transdermal nicotine for relapsed smokers. *Bmj*. 1995; 311:363-6.
24. Paoletti P, Fornai E, Maggiorelli F, Puntoni R, Viegi G, Carrozzi L, et al. Importance of baseline cotinine plasma values in smoking cessation: results from a double-blind study with nicotine patch. *European Respiratory Journal*. 1996; 9:643-51.
25. Stapleton JA, Russell MA, Feyerabend C, Wiseman SM, Gustavsson G, Sawe U, et al. Dose effects and predictors of outcome in a randomized trial of transdermal nicotine patches in general practice. *Addiction*. 1995; 90:31-42.
26. Moore D, Aveyard P, Connock M, Wang D, Fry-Smith A, Barton P. Effectiveness and safety of nicotine replacement therapy assisted reduction to stop smoking: systematic review and meta-analysis. *Bmj*. 2009; 338:b1024.
27. Stead LF, Perera R, Bullen C, Mant D, Hartmann-Boyce J, Cahill K, et al. Nicotine replacement therapy for smoking cessation. *The Cochrane Library*. 2012.
28. Fink A. *Conducting research literature reviews: from the Internet to paper*: Sage; 2005.
29. Hurt RD, Dale LC, Fredrickson PA, Caldwell CC, Lee GA, Offord KP, et al. Nicotine patch therapy for smoking cessation combined with physician advice and nurse follow-up: one-year outcome and percentage of nicotine replacement. *Jama*. 1994; 271:595-600.
30. Schuurmans MM, Diacon AH, Van Biljon X, Bolliger CT. Effect of pre-treatment with nicotine patch on withdrawal symptoms and abstinence rates in smokers subsequently quitting with the nicotine patch: a randomized controlled trial. *Addiction*. 2004; 99:634-40.
31. Solomon P, Cavanaugh MM, Draine J. *Randomized controlled trials: Design and implementation for community-based psychosocial interventions*: Oxford University Press; 2009.