Tobacco use disorder

- Updated 2011 Mar 07 03:29:00 PM: varenicline appears effective for smoking cessation at 6–12 months and more effective than bupropion (Cochrane Database Syst Rev 2011 Feb 16) view update
- acupuncture may increase smoking cessation in short-term but not long-term compared to sham acupuncture (Cochrane Database Syst Rev 2011 Jan 19) view update
- community-based integrated intervention associated with less pulmonary functional decline, increased smoking cessation, and lower mortality in adults (BMJ 2010 Dec 1) view update

Related Summaries:

- Counseling for tobacco cessation
- Bupropion for smoking cessation
- Nicotine replacement therapy for smoking cessation
- Varenicline
- Smoking cessation strategies for hospitalized patients
- Physician Quality Reporting System 2011 Quality Measures

General Information (including ICD-9/-10 Codes)

Description:

- substance abuse disorder characterized by addiction to nicotine found in tobacco products

ICD-9 codes:

- 305.1 nondependent tobacco use disorder [used also for tobacco dependence]
- 649.0 tobacco use disorder complicating pregnancy, childbirth, or the puerperium

ICD-10 codes:

- F17 mental and behavioural disorders due to use of tobacco
    - F17.1 mental and behavioural disorders due to use of tobacco with harmful use
    - F17.2 mental and behavioural disorders due to use of tobacco with dependence syndrome
- P04.2 fetus and newborn affected by maternal use of tobacco
- Z50.8 care involving use of other rehabilitation procedures [tobacco rehabilitation]
- Z71.6 tobacco abuse counselling
- Z72.0 tobacco use
- Z81.2 family history of tobacco abuse
- Z86.4 personal history of psychoactive substance abuse

Incidence/Prevalence:

- global estimates of tobacco use
    - smoking estimated to cause 4.83 million premature deaths worldwide in 2000 (Lancet 2003 Sep 13;362(9387):847)
    - **17.3% students aged 13–15 years used tobacco products in past 30 days**
        - based on survey of nearly 750,000 students at almost 10,000 schools in > 130 countries
        - current tobacco use was highest in Americas (22.2%) and lowest in southeast Asia (12.9%) and western Pacific (11.4%) regions
        - current smoking reported in 8.9% overall, 17.5% in Americas, 17.9% in Europe, and < 10% in 4 other world regions
        - Reference – Lancet 2006 Mar 6;367(9512):749, also reported in MMWR Morb Mortal Wkly Rep 2006 May 26;55(20):553 full-text, summary can be found in Am Fam Physician 2006 Sep 15;74(6):1048
- prevalence in United States
    - smoking prevalence in United States adults
        - **current cigarette smoking in about 20% adults in United States in 2008**
            - 18.4% median prevalence of adult current smoking in 50 states and District of Columbia
                - smoking prevalence

        - 6.5% in United States Virgin Islands
        - 11.6% in Puerto Rico
        - 27.4% in Guam
    - Reference – MMWR Morb Mortal Wkly Rep 2009 Nov 13;58(44):1232 full-text
  - estimated 20.6% of adults in United States were current smokers in 2008
    - rate not significantly different from 2007
    - adults ≥ 25 years old with low educational attainment had highest prevalence of smoking
    - Reference – MMWR Morb Mortal Wkly Rep 2009 Nov 13;58(44):1227 full-text
- current cigarette smoking in 2007 ranged from 8.7%–31.1% in 50 states, District of Columbia, Guam, Puerto Rico, and United States Virgin Islands
  - only Utah and United States Virgin Islands met Healthy People 2010 target of adult smoking prevalence of 12%
  - Reference – MMWR Morb Mortal Wkly Rep 2009 Mar 13;58(9):221 full-text
  - estimated 19.8% of United States adults were current smokers in 2007
    - rate slightly decreased from 20.8% in 2006
    - current smoking rate higher in men than women (22.3% vs. 17.4%)
    - Reference – MMWR Morb Mortal Wkly Rep 2008 Nov 14;57(45):1221 full-text, correction can be found in MMWR Morb Mortal Wkly Rep 2008 Nov 28;57(47):1281
- estimates of current use in United States adults in previous years
  - estimated 20.2% of United States adults were current smokers in 2006; highest current smoking prevalence in Kentucky (28.6%) and lowest in Utah (9.8%); 25.3% median prevalence of current smoking in persons aged 18–35 years (MMWR Morb Mortal Wkly Rep 2007 Sep 28;56(38):993 full-text)

        - estimated 20.8% United States adults were current cigarette smokers in 2006 in another national study (MMWR Morb Mortal Wkly Rep 2007 Nov 9;56(44):1157 full-text)
        - estimated 20.9% of United States adults were current smokers in 2005, prevalence varied by race/ethnicity (32% American Indian/Alaskan Native patients, 21.9% non-Hispanic white patients, 21.5% non-Hispanic black patients, 16.2% Hispanic patients, 13.3% Asian patients) (MMWR Morb Mortal Wkly Rep 2006 Oct 27;55(42):1145 full-text)
        - estimated 20.9% of United States adults were current smokers in 2004 (MMWR Morb Mortal Wkly Rep 2005 Nov 11;54(44):1121 full-text)
        - estimated 21.6% of United States adults were current smokers in 2003 (MMWR Morb Mortal Wkly Rep 2005 May 27;54(20):509 full-text)
        - estimated 22.5% of United States adults were current smokers in 2002 (MMWR Morb Mortal Wkly Rep 2004 May 28;53(20):427 full-text)
        - estimated 22.8% of United States adults were current smokers in 2001 (MMWR Morb Mortal Wkly Rep 2003 Oct 10;52(40):953 full-text), correction can be found in MMWR Morb Mortal Wkly Rep 2003 Oct 24;52(42):1025
    - smoking prevalence in United States adolescents
    - **tobacco use within previous 30 days reported by 8.2% of middle school students and 23.9% of high school students in United States in 2009**
        - based on data from National Youth Tobacco Survey during 2000 to 2009
        - 22,679 students completed survey in 2009
        - declining trends in middle school and high school students from 2000 to 2009
            - current tobacco use
            - current cigarette use
            - cigarette smoking experimentation

        - overall prevalence rate stable from 2006 to 2009 for use of any tobacco
        - Reference – MMWR Morb Mortal Wkly Rep 2010 Aug 27;59(33):1063 full-text
        - **tobacco use within previous 30 days reported by 11.7% of middle school students and 28% of high school students in United States in 2004**
            - based on 2004 National Youth Tobacco Survey in 27,933 students
            - no significant changes from 2002
            - Reference – MMWR Morb Mortal Wkly Rep 2005 Apr 1;54(12):297 full-text
    - cigarette use in United States high school students
        - based on surveys 1991–2009 with sample sizes 10,904 to 16,410
        - prevalence of ever-tried smoking (even 1 or 2 puffs) decreased from 70.4% in 1999 to 50.3% in 2007 and 46.3% in 2009
        - prevalence of cigarette smoking in prior 30 days increased from 27.5% in 1991 to 36.4% in 1997 then decreased to 21.9% in 2003 and 19.5% in 2009
        - prevalence of current frequent cigarette use (smoking on at least 20 of prior 30 days) increased from 12.7% in 1991 to 16.8% in 1999 then decreased to 9.7% in 2003 and 7.3% in 2009
        - Reference – MMWR Morb Mortal Wkly Rep 2010 Jul 9;59(26):797 full-text
    - water-pipe use
        - waterpipe also called hookah or hubbly-bubbly (Pediatric Notes 2008 Jul 10;32(28):112); tobacco used in water-pipes also called nargile or shisha
        - **water-pipe used reported 2%-10% middle and high school students in Arizona**
            - based on 6,594 respondents to questionnaire administered to Arizona students in grades 6 through 12
            - prevalence of students reporting ever having smoked water pipe
                - overall 6.4%
                - middle school 2.1%

        - high school 10.3%
    - water-pipe reported to be third most common source of tobacco in middle and high school students
    - Reference – Pediatrics 2009 Feb;123(2):e282
- **water pipe use reported by 4%-11% middle and high school students in Florida**
    - based on data from 2007 Florida Youth Tobacco Survey
    - 4% middle school students and 11% high school students reported ever having used a water pipe
    - Reference – Am J Public Health 2009 Nov;99(11):2014
- **waterpipe tobacco smoking reported by 20% of students at one United States college campus**
    - based on cross-sectional Internet-based survey of first-year university students at Virginia Commonwealth University
    - 151 of 744 students (20%) reported waterpipe tobacco smoking within past 30 days
    - Reference – J Adolesc Health 2008 May;42(5):526

- smoking and pregnancy
    - 22.4% median prevalence of smoking in women of reproductive age in United States in 2006 (MMWR Morb Mortal Wkly Rep 2008 Aug 8;57(31):849 full-text)
    - 11.4% of women giving birth in United States in 2002 reported smoking during pregnancy (MMWR Morb Mortal Wkly Rep 2004 Oct 8;53(39):911 full-text)
    - **self-reporting of smoking during pregnancy appears to underestimate true smoking rate**
        - based on cross-sectional study of cotinine analysis of 3,475 samples from 21,029 pregnant women in Scotland
        - current smoking in 30% from cotinine measurement vs. 24% from self-reporting ($p < 0.001$)
        - Reference – BMJ 2009 Oct 29;339:b4347 full-text, commentary can be found in BMJ 2009 Dec 31;339:b5652
- **smoking-attributable mortality rates in 2000-2004 in United States**
    - smoking-attributable deaths were 269,655 deaths in males and 173,940 deaths in females

    - Reference – MMWR Morb Mortal Wkly Rep 2008 Nov 14;57(45):1226 full-text
    - state-specific smoking-attributable mortality rates can be found in MMWR Morb Mortal Wkly Rep 2009 Jan 23;58(2):29 full-text, correction can be found in MMWR Morb Mortal Wkly Rep 2009 Feb 6;58(4):91
- **smoking-attributable mortality rates decreased from 1987 to 2002 in United States**
    - smoking-attributable deaths were 402,000 in 1987 and 322,000 in 2002
    - in men aged ≥ 35 years smoking-attributable mortality accounted for
        - 24% of deaths in 1987 (556 deaths per 100,000 person-years)
        - 17% of deaths in 2002 (329 deaths per 100,000 person-years)
    - in women smoking-attributable mortality accounted for
        - 12% of deaths in 1987 (175 deaths per 100,000 person-years)
        - 9% of deaths in 2002 (122 deaths per 100,000 person-years)
    - Reference – Nicotine Tob Res 2007 Jul;9(7):781
    - prior estimates for number of deaths per year in United States attributable to smoking ranged from 400,000 (JAMA 2000 Aug 9;284(6):706, commentary can be found in JAMA 2000 Nov 8;284(18):2319) to 440,000 (MMWR Morb Mortal Wkly Rep 2002 Apr 12;51(14):300 full-text)
    - tobacco is the leading cause of death in the United States; tobacco caused 435,000 deaths in United States, or 18.1% of all United States deaths, in 2000 (JAMA 2004 Mar 10;291(10):1238), correction can be found in JAMA 2005 Jan 19;293(3):298, commentary can be found in JAMA 2004 Jun 23;291(24):2941, JAMA 2005 Jul 27;294(4):448
- **34.4% prevalence of childhood second-hand smoke exposure in the home**
    - based on retrospective analysis of nationally representative survey
    - 46,982 children aged 0-18 years in 2000-2004 were assessed
    - 34.4% prevalence of children living with ≥ 1 adult smoker
        - 49.4% of those below federal poverty level
        - 53.4% of those living in grandparents' homes
        - 33.3% of those living with parents vs. 46.2% living in homes of other adults
    - Reference – Pediatrics 2009 Apr;123(4):e559

- prevalence in Canada

    - 19% Canadians aged > 15 years reported smoking daily or occasionally in 2005 (CMAJ 2006 Aug 29;175(5):464)
    - 21% youths (grades 5–9) reported having experimented with tobacco products in Health Canada 2004–05 survey, 2% reported being smokers (compared with 7% in 1994) (CMAJ 2006 Oct 10;175(8):862)
    - 23% young adults reported to have used water-pipe in previous year
        - based on cohort study of 1,293 adults aged 18–24 years in Canada
        - 873 (68%) completed questionnaire
        - 23% reporting previous-year water-pipe use more likely to be older, male, not living with parents, and of higher income
        - Reference – Pediatrics 2010 Jun;125(6):1184
- in northeast England, estimated 33% of men and 26% of women > 16 years old are smokers in 2001 (BMJ 2005 Apr 2;330(7494):760)
- 37.7% prevalence of current smoking among adolescents in Denmark, including 16.5% daily and 21.2% occasional smokers; 21.7% ex-smokers and 40.6% never smokers; based on survey of 22,575 upper secondary school students in Denmark (Pediatrics 2003 May;111(5):e562 full-text)
- 42%–43% children aged 13–15 years in Philippines 2000–2003 reported ever smoking (even 1–2 puffs), 13% reported smoking first cigarette before age 10 years, based on survey of 11,630 children in 2000 and 7,478 children in 2003, rates of current smoking from 2000 to 2003 declined in boys (from 32.6% to 21.8%) and girls (from 12.9% to 8.8%) (MMWR Morb Mortal Wkly Rep 2005 Feb 4;54(4):94 full-text)
- self-reported smoking habits in students aged 13–15 years in Baghdad, Iraq in 2008
    - 12.9% had ever smoked shisha (water-pipe use)
    - 7.4% had ever smoked cigarettes
    - 6.3% currently smoked shisha
    - 3.2% currently smoked cigarettes
    - 13% of never smokers reported likely to initiate smoking within next year
    - Reference – MMWR Morb Mortal Wkly Rep 2009 Apr 3;58(12):305 full-text
- decrease in children aged 13–15 years reporting ever smoking in Panama 2002–2008

    - self-reported smoking in past 30 days decreased from 13.2% in 2000 to 4.3% in 2008
    - current use of tobacco products other than cigarettes decreased from 9.8% to 5.8%
    - Reference – MMWR Morb Mortal Wkly Rep 2009 Jan 9;57(53):1416
- tobacco use more common in sixth-graders than eighth-graders in India
    - study of 6,165 sixth-grade students and 5,477 eighth-grade students in 32 schools in Delhi and Chennai, India
    - ever use of tobacco reported by 24.8% sixth-graders and 9.3% eighth-graders
    - current use of tobacco reported by 6.7% sixth-graders and 2.9% eighth-graders
    - Reference – Lancet 2006 Feb 18;367(9510):589
- current tobacco use rate decreased in students aged 13–15 years in Sri Lanka from 4% in 1999 to 1.2% in 2007 (MMWR Morb Mortal Wkly Rep 2008 May 23;57(20):545 full-text)

Causes and Risk Factors

Pathogenesis:

- nicotine addiction can occur following single cigarette (J Fam Pract 2007 Dec;56(12):1017)
- review of why people smoke can be found in BMJ 2004 Jan 31;328(7434):277 full-text

Likely risk factors:

- smoking as adolescent greatly increases risk of smoking as adult (Health Psychol 1990;9(6):701)
- **tobacco advertising and promotion increases likelihood of initiation of smoking among adolescents**
    - based on Cochrane review
    - systematic review of 9 longitudinal studies with > 12,000 baseline nonsmokers
    - Reference – last updated 2003 May 13 (Cochrane Library 2003 Issue 4:CD003439)

- exposure to smoking in movies associated with increased risk of smoking in adolescents
    - **increased exposure to smoking in movies associated with increased risk of smoking initiation among adolescents in United States**
        - study of 3,547 children aged 10–14 years old who had never tried smoking on baseline survey
        - 50 movies sampled for number of smoking occurrences
        - 2,603 (73%) children had follow-up interview 13–26 months later
            - 259 (10%) had initiated smoking
            - stratified by exposure to movie smoking, 17% of highest quartile and 3% of lowest quartile initiated smoking
            - effect of movie smoking strongest in children with non-smoking parents
        - Reference – Lancet 2003 Jul 26;362(9380):281
    - **similar findings in cohort of 3,313 adolescents in Germany**
        - 503 (19%) had initiated smoking during follow up period
        - 28% initiation in highest quartile of exposure to movie smoking and 10% in lowest quartile
        - Reference – Pediatrics 2008 Jan;121(1):e108
    - **smoking in movies increases adolescents smoking**
        - based on review of 40 studies
        - Reference – Pediatrics 2005 Dec;116(6):1516
    - **extent of movie smoking exposure in young adolescents may predict established smoking in older adolescents and young adults**
        - based on prospective cohort study
        - 1,791 children aged 10–14 years at baseline had follow-up by survey 7–8 years later (mean age 18.7 years)
        - established smoking (defined as having smoked > 100 cigarettes) found in 6.6% with lowest quartile movie smoking exposure compared to
            - 10.8% in 2nd quartile (relative risk [RR] 1.53, $p < 0.05$)
            - 15.6% in 3rd quartile (RR 2.17, $p < 0.001$)
            - 21.8% in highest quartile (RR 2.88 $p < 0.001$)
        - Reference – Pediatrics 2009 Apr;123(4):e551
    - **positive and negative movie character types both associated with increased risk of smoking initiation in adolescents**

        - based on prospective cohort study
        - 6,522 adolescents aged 10–14 years assessed by telephone survey every 8 months for 24 months
        - hazard ratio for smoking initiation 4.42 for positive vs. 4.38 with negative movie character exposure
        - Reference – Pediatrics 2009 Jul;124(1):135
    - **early nicotine dependence symptoms associated with accelerated smoking habits**
        - based on prospective cohort study
        - 1,246 sixth-graders interviewed for symptoms of nicotine dependence and smoking frequency and followed for 4 years
        - 370 persons reported inhalation from a cigarette
            - 62% smoked ≥ 1 per month
            - 53% had dependence symptoms
            - 40% escalated to daily smoking
        - monthly smoking associated with development of dependence symptoms (hazard ratio [HR] 9.9, 95% CI 6.6–14.8)
        - any dependence symptom associated with increased risk of daily smoking (HR 6.81, 95% CI 4.4–10.5)
        - Reference – Pediatrics 2010 Jun;125(6):1127

Possible risk factors:

- **candy cigarette use in childhood appears associated with increased risk of smoking**
    - based on online survey of 25,887 adults in United States
    - 26.4% reported current smoking, 29.4% reported former smoking
    - candy cigarette use reported by 88% smokers (current and former) and 78% never-smokers ($p \leq 0.001$)
    - odds of smoking increased with increasing candy cigarette use
    - Reference – Prev Med 2007 Jul;45(1):26
- **common variant in nicotinic acetylcholine receptor gene cluster on chromosome 15q24 may be associated with smoking quantity and nicotine dependence**
    - based on genetic study
    - chromosome 15q24 variant associated with number of cigarettes smoked per day and nicotine dependence

    - Reference – Nature 2008 Apr 3;452(7187):638
    - chromosome 15q24 variant associated with increased risk of lung cancer (Nature 2008 Apr 3;452(7187):633)

Factors not associated with increased risk:

- **adolescent exposure to tobacco on Internet appears limited and does not appear to correlate with smoking status**
    - based on prospective cohort study
    - 346 adolescents aged 14–17 years consented to installation of Internet-tracking software on home computers and were monitored for 30 days
    - tobacco or smoking content on 0.72% of 1.2 million web pages viewed
    - no significant differences in exposure to tobacco or smoking content between smokers vs. nonsmokers
    - Reference – Pediatrics 2009 Aug;124(2):e180

Complications and Associated Conditions

Complications:

- chronic obstructive pulmonary disease (COPD)
    - cigarette smoking is primary risk factor (Proc Am Thorac Soc 2009 Dec;6(8):704 full-text)
    - regular cigar smoking associated with increased risk of COPD
        - based on prospective study of 17,774 men aged 30–85 years followed 22–31 years
        - Reference – N Engl J Med 1999 Jun 10;340(23):1773 full-text
- **smoking associated with shorter life expectancy**
    - on average, each cigarette smoked shortens lifespan by 11 minutes (BMJ 2000 Jan 1;320(7226):53)
    - smoking associated with increase in mortality similar to adding 5–10 years of age, based on United States 2004 data (J Natl Cancer Inst 2008 Jun 18;100(12):845)
    - at age 30 years, heavy smoking associated with 8.5 years less of life expectancy compared to never smoking (J Epidemiol Community Health 2004 Jul;58(7):604)

- lifelong smokers born in 1900–1930 have 10 years less of life than lifelong non-smokers, based on prospective cohort study of 34,439 British male doctors followed from 1951 to 2001 (BMJ 2004 Jun 26;328(7455):1519), editorial can be found in BMJ 2004 Jun 26;328(7455):1507, correction can be found in N Engl J Med 2010 Dec 2;363(23):2272
- **smoking in late adolescence may increase risk of mortality in adulthood**
  - based on records from Swedish military registry
  - 45,920 men (mean 18.7 years) were followed for 38 years
  - 2,897 men died
  - incidence of mortality in normal weight men 17/10,000 person years
  - risk of mortality (compared with normal weight men)
    - hazard ratio 1.33 (95% CI 1.15–1.53) in overweight men
    - hazard ratio 2.14 (95% CI 1.61–2.85) in obese men
    - hazard ratio 1.33 (95% CI 1.07–1.64) in extremely underweight (body mass index [BMI] < 17 40 kg/m^2) men
  - risk of mortality (compared with non-smokers)
    - hazard ratio 1.54 (95% CI 1.41–1.7) with light smoking at baseline
    - hazard ratio 2.11 (95% CI 1.92–2.31) with heavy smoking at baseline
  - relative excess risk with interaction of BMI and smoking status not significant in any stratum
  - Reference – BMJ 2009 Feb 24;338:b496 full-text
- **overall annual smoking-attributable mortality decreasing in adults ≥ 35 years old in United States**
  - based on data from Behavioral Risk Factor Surveillance System and death certificates
  - overall median annual smoking-attributable mortality rate in adults ≥ 35 years old
    - 288 per 100,000 population in 1996–1999
    - 263 per 100,000 population in 2000–2004
  - Oklahoma was only state to have increase in annual smoking-attributable mortality between 1996–1999 to 2000–2004 (increase of 26.9 deaths per 100,000 population)

        - Reference – MMWR Morb Mortal Wkly Rep 2009 Jan 23;58(2):29 full-text, correction can be found in MMWR Morb Mortal Wkly Rep 2009 Feb 6;58(4):91
    - **smoking considered major risk factor for mortality in China in 2005**
        - based on prospective cohort study of 169,871 Chinese adults ≥ 40 years old
        - 673,000 smoking-attributable deaths occurred (538,200 men, 134,800 women)
        - Reference – N Engl J Med 2009 Jan 8;360(2):150, commentary can be found in N Engl J Med 2009 Apr 30;360(18):1911
    - **smoking associated with 6-8 years reduced survival in India**
        - based on nationally representative case-control study in India with 74,123 cases (deaths) and 46,535 unmatched living controls
        - smoking more frequent in cases vs. controls
            - 9% vs. 4% in women
            - 51% vs. 32% in men
        - smoking associated with reduction in median survival
            - 8 years (99% CI 5-11 years) for women
            - 6 years (99% CI 5-7 years) for men
        - Reference – N Engl J Med 2008 Mar 13;358(11):1137, commentary can be found in N Engl J Med 2008 Jun 26;358(26):2842
    - **current and past smoking associated with increased mortality in women**
        - based on prospective cohort study
        - 104,519 women from Nurse's Health Study aged 30-55 years at baseline followed from 1980-2004
        - total mortality
            - never smokers 9.2%
            - past smokers 12.1%
            - current smokers 18.8%
        - smoking associated with significant increase in mortality due to
            - vascular disease
            - coronary heart disease
            - cerebrovascular disease
            - respiratory disease

        - COPD
        - lung cancer
        - colorectal cancer
        - all smoking-related cancers
    - Reference – JAMA 2008 May 7;299(17):2037
- **smoking 1-4 cigarettes/day associated with higher risk of mortality from all causes and from ischemic heart disease in men and women, and from lung cancer in women**
    - based on study of 42,722 men and women aged 39-49 years followed for about 17 years
    - Reference – Tob Control 2005 Oct;14(5):315
- **smoking increases mortality in middle age**
    - study of 24,505 women and 25,034 men aged 40-70 years in Norway
    - mortality for never-smokers vs. continuous heavy smokers (at least 20 cigarettes/day)
        - 9% vs. 26% women
        - 14% vs. 41% men
    - 1.4 years of life lost in women and 2.7 years in men attributed to continuous heavy smoking
    - Reference – Ann Intern Med 2006 Mar 21;144(6):381, editorial can be found in Ann Intern Med 2006 Mar 21;144(6):444
- **smoking in midlife has dose-dependent reduction in survival and health-related quality of life in old age**
    - based on prospective cohort with 1,658 men aged 40-55 years at baseline followed for 26 years
    - 37% were never smokers
    - 6.9% were current smokers at 26-year follow-up
    - survival at follow-up (estimated from figure, $p < 0.001$ for trend)
        - 55% for smokers of > 20 cigarettes/day
        - 68% for smokers of 11-20 cigarettes/day
        - 78% for smokers of 1-10 cigarettes/day
        - 84% for never smokers
    - higher number of daily cigarettes at baseline correlated with decreasing quality of life scores at follow-up for
        - general health

        - bodily pain
        - role limitations due to physical health
        - physical functioning
        - energy and vitality
    - Reference – Arch Intern Med 2008 Oct 13;168(18):1968, editorial can be found in Arch Intern Med 2008 Oct 13;168(18):1946
- **among most elderly, ever smoking associated with increased mortality from cancer and from respiratory diseases**
    - based on cohort of 56,167 Chinese persons > 65 years old in Hong Kong
    - Reference – J Am Geriatr Soc 2007 Dec;55(12):2090
- **smoking, but not oral contraceptives, increases overall mortality in women > 35 years old**
    - cohort study of 17,032 women aged 25–39 years followed for 26–32 years, 889 deaths occurred
    - oral contraceptives did not significantly affect overall mortality but were associated with
        - increased mortality from cervical cancer (rate ratio [RR] 7.2)
        - decreased mortality for uterine (RR 0.2) and ovarian (RR 0.4) cancers
        - among smokers increased mortality from ischemic heart disease
    - smoking increased overall mortality with RR 1.24 for smoking 1–14 cigarettes/day and RR 2.14 for smoking 15 or more cigarettes/day
    - Reference – Lancet 2003 Jul 19;362(9379):185, commentary can be found in Lancet 2003 Oct 11;362(9391):1241, summary can be found in Am Fam Physician 2004 Mar 1;69(5):1248
- **smoking increases mortality, especially from tuberculosis, in India**
    - based on large case–control study comparing 43,000 men who died from medical causes and 35,000 male controls
    - based on these results, smoking believed to be responsible for about 700,000 deaths per year in India
    - smoking–attributed increase in mortality rates

        - 2.1 for cancer
        - 1.8 for vascular disease
        - 4.5 for tuberculosis
    - Reference – Lancet 2003 Aug 16;362(9383):507, commentary can be found in Lancet 2003 Oct 11;362(9391):1243

- **cancer**
    - **smoking is the single largest population-attributable risk factor for cancer mortality worldwide**
        - comprehensive systematic review of population-attributable risk factors for cancer mortality
        - total 7,018,402 annual cancer deaths worldwide
        - 1,493,000 (21%) attributable to smoking
        - next most important risk factors were low fruit and vegetable intake (5% or 374,000 cancer deaths) and alcohol (5% or 351,000 cancer deaths)
        - Reference – Lancet 2005 Nov 19;366(9499):1784
    - **smoking associated with higher mortality from cancer for many cancer types**
        - prospective cohort of 34,439 male British doctors followed for 50 years from 1951 to 2001, cancer deaths recorded for 28 cancer types
        - 14 cancer types with increased mortality attributable to smoking include cancers of lung, esophagus, larynx, oropharynx/hypopharynx, bladder, unknown site, liver, oral cavity, pancreas, myeloid leukemia, nose/nasal sinuses, stomach, nasopharynx, and kidney
        - colorectal cancer also appears to have weak relationship with smoking
        - association of prostate cancer and smoking may be due to confounding factors
        - Reference – Br J Cancer 2005 Feb 14;92(3):426 full-text
    - **smoking associated with higher incidence of any cancer**
        - in adjusted analysis of 733,134 Korean men > 30 years old followed for 4 years

        - specific cancers with significant association with smoking included esophageal, lung, laryngeal, urinary bladder, gastric, oral and pharyngeal, pancreatic, and liver cancer
        - Reference – Cancer Detect Prev 2005;29(1):15
    - **smokeless tobacco use may increase cancer risk**
        - based on 2 systematic reviews of observational studies
        - systematic review of 11 epidemiologic studies evaluating cancer risk in smokeless tobacco users in United States and northern European countries
            - all studies were observational and risks were adjusted for smoking status
            - overall relative risks (RR) with any use of smokeless tobacco
                - oral cancer (RR 1.8, 95% CI 1.1–2.9) in 11 studies, results limited by heterogeneity
                - esophageal cancer (RR 1.6, 95% CI 1.1–2.3) in 5 studies
                - pancreatic cancer (RR 1.6, 95% CI 1.1–2.2) in 6 studies
                - lung cancer (RR 1.2, 95% CI 0.7–1.9) in 5 studies, results limited by heterogeneity
            - Reference – Lancet Oncol 2008 Jul;9(7):667
        - systematic review of 89 studies evaluating risk of smokeless tobacco use in North America and Scandinavian countries
            - overall relative risk (RR) with any use of smokeless tobacco
                - larynx cancer (RR 1.43, 95% CI 1.08–1.89) in 5 studies
                - oral cancer (RR 3.1, 95% CI 1.5–6.6) in 5 studies
                - prostate cancer (RR 1.2, 95% CI 1.03–1.4) in 5 United States studies
            - overall odds ratio (OR) with any use of smokeless tobacco
                - oral cancer (OR 2.38, 95% CI 1.87–3.04) in 5 case control studies before 1990

        - oral cancer (OR 1.36, 95% CI 1.04–1.77) in 9 case control studies dated after 1990
    - Reference – BMC Med 2009 Jul 29;7:36 full-text, commentary can be found in BMC Cancer 2009 Jul 29;9:256 full-text
- tobacco use associated with cardiovascular disease
    - **tobacco use associated with myocardial infarction worldwide**
        - case-control study in 52 countries (INTERHEART study) with 12,461 cases of acute myocardial infarction and 14,637 controls
        - current smokers had higher risk than never smokers (odds ratio 2.95, 95% CI 2.77–3.14), risk increased by 5.6% for each additional cigarette smoked
        - odds ratio with former smoking decreased to 1.87 (95% CI 1.55–2.24) at 3 years after quitting and to 1.22 (95% CI 1.09–1.37) after 20 years
        - all forms of tobacco exposure associated with increased risk
        - Reference – Lancet 2006 Aug 19;368(9536):647, editorial can be found in Lancet 2006 Aug 19;368(9536):621
    - **smoking associated with risk of cardiovascular disease in population with low cholesterol levels**
        - based on prospective cohort with 648,346 Korean men aged 30–64 years followed for 10 years
        - Reference – Stroke 2008 Mar;39(3):760
    - after coronary-artery bypass graft surgery, risk for myocardial infarction 5–15 years after surgery is 2.5 times higher for permanent smokers compared to quitters (29% vs. 17%) (Circulation 1996 Jan 1;93(1):42 full-text)
- **smokers may not recognize increased risk of heart disease or cancer**
    - survey of 3,031 persons including 737 current smokers and 868 former smokers
    - among current smokers, only 29% perceived they had increased risk of myocardial infarction and 40% perceived they had increased risk of cancer
    - Reference – JAMA 1999 Mar 17;281(11):1019 full-text, commentary can be found in JAMA 1999 Nov 10;282(18):1722
- **smoking associated with increased incidence of diabetes**

    - 906 United States adults free of diabetes followed for 5 years
    - incidence of diabetes 25% for current smokers and 14% for never smokers
    - Reference – Diabetes Care 2005 Oct;28(10):2501
- **short-term smoking history with light-to-moderate smoking associated with reduced physical and mental quality of life**
    - based on comparison of 77 smoking students with 97 never-smoking students
    - Reference – Chest 2004 Feb;125(2):425
- smoking associated with hot flashes
    - **current smoking and high body mass index each increase risk of hot flashes**
        - study of 1,087 women aged 40–60 years, 56% reported having hot flashes
        - current smoking increase risk for moderate to severe hot flashes (OR 1.9) and for daily hot flashes (OR 2.2)
        - risk was dose-dependent
        - former smokers did not have increased risk
        - high body mass index associated with increased risk for moderate to severe hot flashes (OR 2.1) and in women aged 40–50 years risk for any or daily hot flashes
        - Reference – Obstet Gynecol 2003 Feb;101(2):264 in ACOG News Release 2003 Jan 31
    - **current smoking associated with hot flushes**
        - based on cohort study of 628 menstruating women aged 45–54 years
        - Reference – Obstet Gynecol 2008 Nov;112(5):1037
- cognitive decline
    - **smoking associated with dementia and cognitive decline**
        - based on meta-analysis of 19 prospective studies
        - 26,374 participants followed for 2–30 years for dementia
        - 17,023 participants followed for 2–7 years to assess cognitive decline
        - mean age 74 years
        - comparing current smokers at baseline vs. never smokers

            - relative risk for incident Alzheimer's disease 1.79 (95% CI 1.43–2.23)
            - relative risk for incident vascular dementia 1.78 (95% CI 1.28–2.47)
            - relative risk for any dementia 1.27 (95% CI 1.02–1.6)
            - greater annual declines in Mini-Mental State Exam scores
        - comparing current smokers at baseline vs. former smokers
            - relative risk for incident Alzheimer's disease 1.7 (95% CI 1.25–2.31)
            - increased decline in cognitive abilities
            - no significant differences in risks of vascular dementia or any dementia
        - Reference – Am J Epidemiol 2007 Aug 15;166(4):367
        - current smoking associated with increased risk of dementia in 6,868 persons (≥ 55 years old) followed for mean 7.1 years (Neurology 2007 Sep 4;69(10):998)
    - **smoking associated with accelerated cognitive decline** in 2-year follow-up of 9,209 nondemented elderly persons (Neurology 2004 Mar 23;62(6):920)
    - **smoking associated with decreased memory performance** in analysis of 5,388 smokers and nonsmokers aged 35–55 years at baseline and followed for 20 years (Arch Intern Med 2008 Jun 9;168(11):1165)
- **cigarette smoking associated with increased risk of many bacterial and viral infections, especially invasive pneumococcal disease, influenza and tuberculosis**
    - based on review of epidemiologic studies
    - Reference – Arch Intern Med 2004 Nov 8;164(20):2206, commentary can be found in Am Fam Physician 2005 Mar 15;71(6):1184, Arch Intern Med 2005 Oct 10;165(18):2069, Arch Intern Med 2010 Feb 8;170(3):292
- **current smoking associated with erectile dysfunction**
    - based on cross-sectional study of 8,367 Australian men aged 16–59 years
    - Reference – Tob Control 2006 Apr;15(2):136
- **smokeless tobacco use appears to increase risk of cardiovascular mortality and myocardial infarction compared to non-use**, though lower risk than

smoking, but observational studies provide conflicting evidence (Arch Intern Med 2004 Sep 27;164(17):1845)

- tobacco use associated with increased risk of eye disease
    - **current smoking associated with age-related macular degeneration**
        - based on systematic review of 17 studies
        - 13 studies found statistically significant 2-3 times risk
        - Reference – Eye (Lond) 2005 Sep;19(9):935
    - tobacco use associated with increased risk for cataract
        - cigarette smoking
            - cigarette smoking increased risk from 57% to 64%-69% in follow-up of 660 people aged 52-80 years without baseline lens opacities (Arch Ophthalmol 1997 Sep;115(9):1113 in QuickScan Reviews in Fam Pract 1998 Apr;23(1):18)
            - cigarette smoking increased risk of cataract in 5-year prospective follow-up of adults aged 43-84 years (Ophthalmic Epidemiol 1999 Dec;6(4):247 in JAMA 2000 Feb 9;283(6):721)
        - tobacco use (especially smokeless tobacco) associated with cataract development in cohort of 3,924 patients in Southern India (Br J Ophthalmol 2006 Nov;90(11):1374 full-text)
- nicotine stomatitis (case presentation in J Fam Pract 2008 Jan;57(1):33)
- secondhand or environmental smoke exposure
    - **estimated worldwide mortality and disease burden attributable to secondhand smoke in 2004**
        - based on disease-specific relative risk estimates and area specific estimates of persons exposed to secondhand smoke in 192 countries during 2004
        - 47% of deaths from secondhand smoke occurred in women, 26% in men and 28% in children
        - mortality
            - 379,000 from ischemic heart disease
            - 165,000 from lower respiratory infection
            - 36,900 from asthma
            - 21,400 from lung cancer
        - disease burden included

        - respiratory infection in 5,939,000 children < 5 years old
        - ischemic heart disease in 2,836,000 adults
        - asthma in 1,246,000 adults
        - asthma in 651,000 children
    - Reference – Lancet 2011 Jan 8;377(9760):139, editorial can be found at Lancet 2010 Jan 8;377(9760):101
- **secondhand smoke at home associated with increased mortality from all causes and cardiovascular disease**
    - record linkage study of 668,262 adults aged 45–74 years participating in New Zealand census in 1981 or 1996 and nationality mortality records for up to 3 years after each census
    - lifelong nonsmokers living with smokers had increased risks for all-cause mortality
        - men had adjusted relative risk 1.17 in 1981 and 1.16 in 1996
        - women had adjusted relative risk 1.28 in 1996 cohort but not significant in 1981 cohort
    - lifelong nonsmokers living with smokers had increased risks for cardiovascular mortality
        - men had adjusted relative risk 1.19 in 1981 and 1.25 in 1996
        - women had adjusted relative risk 1.35 in 1996 cohort but not significant in 1981 cohort
    - association of passive smoking and death from respiratory disease and cerebrovascular disease found in men in 1996 cohort
    - no significant association of passive smoking and death from lung cancer
    - Reference – Am J Epidemiol 2007 Mar 1;165(5):530 in BMJ 2007 Apr 21;334(7598):841
- **environmental tobacco smoke exposure associated with increased mortality in Chinese women**
    - prospective cohort of 72,829 women in Shanghai, China who never smoked
    - exposure to tobacco smoke from husbands associated with increased all-cause mortality (hazard ratio 1.15, 95% CI

1.01–1.31) and cardiovascular mortality (hazard ratio 1.37, 95% CI 1.06–1.78)
        - exposure to tobacco smoke at work associated with lung cancer mortality (hazard ratio 1.79, 95% CI 1.09–2.93)
        - Reference – BMJ 2006 Aug 19;333(7564):376 full-text
    - **secondhand smoke exposure during pregnancy associated with increased risk of adverse perinatal outcomes**
        - based on systematic review of 76 studies evaluating effects of secondhand smoke on perinatal outcomes with 48,439 women exposed to secondhand smoke and 90,918 unexposed women
        - secondhand smoke exposure during pregnancy associated with
            - increased risk of congenital anomalies (odds ratio 1.17, 95% CI 1.03–1.34)
            - trend toward increased risk of low birthweight (< 2,500 gm) (risk ratio 1.16, 95% CI 0.99–1.36)
        - no differences in gestational duration of rates of preterm delivery
        - Reference – Acta Obstet Gynecol Scand 2010;89(4):423
    - **secondhand smoke exposure for infants living with any smoker who smokes within 3 meters of infant associated with increased risk of hospitalization**
        - compared with infants in smoke-free household
        - odds ratio 1.28 (95% CI 1.07–1.52) in prospective study in China of 8,327 newborns followed for 18 months
        - Reference – Arch Pediatr Adolesc Med 2004 Jul;158(7):687 in JAMA 2004 Oct 6;292(13):1534
    - **sleep problems associated with secondhand smoke exposure in children with asthma**
        - based on retrospective cohort study
        - 219 children aged 6–12 years with asthma and exposure to secondhand smoke from ≥ 5 cigarettes per day assessed for serum cotinine levels and sleep habits by caregiver questionnaire
        - increasing serum cotinine level associated with
            - overall sleep disturbance (p = 0.0002)
            - parasomnias (p = 0.002)

        - increased sleep-onset delay (p = 0.004)
        - sleep-disordered breathing (p = 0.02)
        - daytime sleepiness (p = 0.022)
    - Reference – Pediatrics 2010 Feb;125(2):e261
- **parental smoking associated with wheeze, asthma, bronchitis and nocturnal cough**
    - based on pooled analysis of 53,879 children from 12 cross-sectional studies
    - Reference – Tob Control 2006 Aug;15(4):294
- **smoking in the home associated with 5% increase in emergency department visits for respiratory conditions and 3% increase in hospitalization for respiratory conditions**
    - based on review of data from 2,759 children aged 0-4 years
    - Reference – Tob Control 2008 Feb;17(1):32
- **smoking outside still associated with second-hand smoke exposure**
    - based on study of hair samples from 327 children < 3 years old
    - Reference – Lancet 2002 May 11;359(9318):1673
- **high level of cotinine concentration from secondhand smoke may be associated with increased risk for cognitive impairment in nonsmokers**
    - based on cross-sectional study of 4,809 non-smoking adults ≥ 50 years old
    - odds ratios for cognitive impairment 1.44 (95% CI 1.07-1.94) for 0.8-13.5 ng/mL cotinine concentration (compared with lowest cotinine concentration [0-0.1 ng/mL])
    - Reference – BMJ 2009 Feb 12;338:b462 full-text, editorial can be found in BMJ 2009 Feb 12;338:a3070

Associated conditions:

- concomitant substance abuse
    - **smoking associated with alcohol misuse**
        - based on study of 42,374 United States adults
        - Reference – Arch Intern Med 2007 Apr 9;167(7):716
    - **water-pipe use associated with increased use of alcohol and other psychoactive drugs**
        - based on cohort study of 1,293 adults aged 18-24 years in Canada

        - 873 (68%) completed questionnaire
        - 23% reporting previous-year water-pipe use more likely to be older, male, not living with parents, and of higher income
        - water-pipe use associated with increased risk of psychoactive drug use ($p < 0.0001$) including
            - alcohol binge drinking (20% increased risk)
            - marijuana use (39% increased risk)
            - cigarette use (26% increased risk)
        - Reference – Pediatrics 2010 Jun;125(6):1184
    - see Counseling for tobacco cessation for information about counseling patients with co-occurring substance abuse
- **tobacco smoking associated with increased risk of tuberculosis**
    - based on systematic review of observational studies
    - 33 papers on tobacco smoking and tuberculosis, 5 papers on passive smoking and tuberculosis and 5 on indoor air pollution and tuberculosis
    - tobacco smoking, passive smoking and biomass fuel combustion associated with increased tuberculosis risk
    - Reference – PLoS Med 2007 Jan 16;4(1):e20 full-text
- **smoking associated with premature gray hair in men and women and premature balding in men**
    - based on study of 606 patients > 30 years old from a surgical outpatient clinic
    - based on predefined criteria, men who smoked had 1.9 times risk of baldness for age, and both men and women who smoked had 4.4 times more gray hair
    - Reference – BMJ 1996 Dec 21/28;313(7072):1616
- metabolic associations
    - **smoking associated with elevated LDL cholesterol** in study of 492 persons aged 26-66 years with hypercholesterolemia (Clin Exp Med 2002 Jul;2(2):83)
    - **cigarette use associated with decreased body mass index and height in adolescent boys**
        - based on observational study
        - 451 boys and 478 girls aged 12-13 years surveyed every 3 months for 5 years

        - prevalence of adolescents smoking ≥ 30 cigarettes/month on average
            - 7% boys and 14% girls during years 1–3
            - 9% boys and 18% girls during years 3–5
        - 100–cigarette/month increment in cigarette use in previous 2.5 years independently associated with lower body mass index (–0.4 kg/m^2) and shorter height (–0.7 cm) in boys
        - cigarette use not associated with height or adiposity in girls
        - Reference – Ann Epidemiol 2008 May;18(5):395
    - **adolescent smoke exposure associated with metabolic syndrome**
        - study of 2,273 United States adolescents aged 12–19 years
        - metabolic syndrome present in
            - 1.2% subjects unexposed to tobacco smoke
            - 5.4% those exposed to environmental tobacco smoke
            - 8.7% active smokers
        - among adolescents with body mass index > 85th percentile, metabolic syndrome present in
            - 5.6% subjects unexposed to tobacco smoke
            - 19.6% those exposed to environmental tobacco smoke
            - 23.6% active smokers
        - Reference – Circulation 2005 Aug 9;112(6):862
    - **cigarette smoking associated with metabolically adverse fat distribution profile**
        - cross–sectional study of 21,828 men and women aged 45–79 years in United Kingdom 1993–1997
        - despite lower body mass index in smokers compared to non–smokers, smokers had higher waist–hip ratio
        - Reference – Obes Res 2005 Aug;13(8):1466
- adolescent smoking associated with disruptive behavior disorders (oppositional defiant disorder, conduct disorder, attention–deficit/hyperactivity disorder), major depressive disorders, and drug and alcohol use disorders (J Am Acad Child Adolesc Psychiatry 2002 Nov;41(11):1294)
- **current daily smoking associated with subsequent occurrence of suicidal thoughts or attempts**
    - based on 10–year follow–up with adjusted odds ratio 1.82 (95% CI 1.22–2.69)

- Reference – Arch Gen Psychiatry 2005 Mar;62(3):328

History

Chief concern (CC):

- acknowledged smoking history

History of present illness (HPI):

- quantify duration of tobacco use
- quantify intensity of use (for example, cigarettes or packs per day)

Past medical history (PMH):

- history of depression predictive of major depression after smoking cessation, especially in patients with high levels of withdrawal symptoms (Am J Psychiatry 1997 Feb;154(2):263)

Social history (SH):

- ask about factors that would make it easier and factors that make it harder to quit
- ask about benefits and risks of smoking
- ask about benefits and risks of quitting
- ask about other substance use
- **for adolescents other factors beside transtheoretical model of change may be more useful to address**
  - based on questionnaire of 354 patients aged 12–21 years who reported past or current smoking
  - most important factors to assess may be
    - level of nicotine addiction
    - perceived stress
    - coping methods
  - Reference – Arch Pediatr Adolesc Med 2001 Apr;155(4):489 in Am Fam Physician 2001 Dec 1;64(11):1890

Review of systems (ROS):

- **depressive symptoms associated with difficulties maintaining abstinence from smoking**
    - nondepressed patients with history of major depression have increased risk of depression during smoking cessation
    - 3-month incidence of new major depression episodes during smoking cessation
        - 2% without history of depression
        - 17% with history of single depressive episode
        - 30% with history of recurrent depressive episodes
    - nicotine patch appears more effective than nicotine gum in these patients
    - Reference - Alternative Medicine Alert 1998 Jun;1(6):67

Physical

HEENT:

- dental staining

Lungs:

- cough
- wheeze

Extremities:

- staining of fingers

Diagnosis

Making the diagnosis:

- diagnosis based on any acknowledged current tobacco use (including smokeless tobacco) by patient

Testing to consider:

- none generally needed

- spirometry – informing patient of spirometric lung age increases smoking cessation rate at 12 months (level 1 [likely reliable] evidence)

Blood tests:

- **smokers have altered findings in complete blood count and lipid profiles**
    - based on cohort of 7,842 employees having annual check-up
        - 3,521 smokers
        - 2,694 non-smokers
    - male and female smokers had higher
        - hematocrit
        - leukocyte count
        - hemoglobin level
        - triglyceride level
    - male and female smokers had lower high-density lipoprotein cholesterol
    - male smokers had higher frequency of positive urinary occult blood
    - Reference – Intern Med 2006;45(18):1027 PDF
- continuous abstinence (biochemically confirmed) associated with rapid and sustained decreased in white blood cell count and absolute neutrophil count
    - based on cohort of 784 smokers participating in bupropion trial
    - Reference – Mayo Clin Proc 2005 Aug;80(8):1022

Other diagnostic testing:

- spirometry
    - **informing patient of spirometric lung age increases smoking cessation rate at 12 months (level 1 [likely reliable] evidence)**
        - based on randomized trial in England
        - 561 patients > 35 years old who smoked were randomized to receive spirometric lung function assessment results in terms of "lung age" (age of average healthy person performing similarly on spirometry) immediately vs. raw figure for forced expiratory volume at 1 second (FEV_1) (results provided in writing after 1 month)
        - all participants advised to quit and offered referral to local National Health Service smoking cessation services
        - follow-up completed in 89%

        - smoking cessation verified by salivary cotinine testing at 12 months
        - lung age calculation formula
            - for men lung age (in years) = (2.87 × height [in inches]) − (31.25 × observed FEV_1 [in liters]) − 39.375
            - for women lung age (in years) = (3.56 × height [in inches]) − (40 × observed FEV_1 [in liters]) − 77.28
        - comparing lung age vs. raw figure
            - smoking cessation in 13.6% vs. 6.4% (p = 0.005, NNT 14, 95% CI 9–46)
            - mean daily cigarette consumption 11.7 vs. 13.7 cigarettes (p = 0.03)
            - new diagnosis of chronic obstructive lung disease in 17% vs. 14% (statistical significance not stated)
        - Reference – Step2quit trial (BMJ 2008 Mar 15;336(7644):598 full-text), editorial can be found in BMJ 2008 Mar 15;336(7644):567, commentary can be found in BMJ 2008 May 10;336(7652):1034, ACP J Club 2008 Jul;149(1):5
    - **diagnosis of moderate to severe airflow limitation on spirometry testing associated with higher smoking cessation rates at 1 year**
        - based on cohort study in Poland
        - 659 patients participated in population spirometric screening for chronic obstructive pulmonary disease and smoking cessation advice, 558 invited to follow-up after 1 year
        - 368 (66%) of 558 smokers participated in follow-up, others assumed to still be smoking
        - smoking cessation rates were 16.5% with moderate to severe airflow limitation, 6.4% with mild airflow limitation and 8.4% with no airflow limitation
        - Reference – Chest 2003 Jun 6;123(6):1916 in Am Fam Physician 2004 Feb 1;69(3):637
- **limited evidence does not support use of biochemical markers to improve smoking cessation rates (level 2 [mid-level] evidence)**
    - based on Cochrane review of mostly low quality trials
    - systematic review of 11 randomized trials (12 interventions) evaluating use of exhaled carbon monoxide (3 trials), exhaled carbon monoxide and

spirometry (3 trials), spirometry alone (3 trials), genetic susceptibility (2 trials) or ultrasound of carotid and femoral arteries (1 trial) as additional components of smoking cessation intervention
    - 1 high quality trial described above
    - only 2 trials showed statistically significant increase in smoking cessation with treatment
        - spirometry with immediate feedback on "lung age" (13.6% vs. 6.4% in controls)
        - ultrasound with photographic demonstration of atherosclerotic plaques if present (17% vs. 6.3% in controls)
    - no significant differences in smoking cessation rate after at ≥ 6 months in other trials
    - Reference – Cochrane Database Syst Rev 2009 Apr 15;(2):CD004705
- **point of care test measuring salivary nicotine metabolites may increase smoking cessation rate (level 2 [mid-level] evidence)**
    - based on randomized trial without intention-to-treat analysis
    - 100 adult smokers at single general dental practice in London were given smoking cessation counseling, had point of care test measuring salivary nicotine metabolites, and were randomized to receive test results during baseline visit vs. at 8 week follow-up
    - outcomes for immediate test result group vs. delayed test result group
        - 23% vs. 7% quit smoking ($p < 0.039$, NNT 7)
        - 68% vs. 28% reduced overall tobacco use ($p < 0.001$, NNT 3)
    - 10 patients did not return for 8-week follow-up and were not included in analysis, outcomes in these 10 patients could potentially make findings no longer significant
    - Reference – BMJ 2005 Oct 29;331(7523):999 full-text, editorial can be found in BMJ 2005 Oct 29;331(7523):979

Prognosis

Prognosis:

Predictors of long-term abstinence:

- **smoking behavior on first day of quit attempt predicts long-term abstinence**

    - derivation sample of 159 patients and validation sample of 48 patients using 2 randomized nicotine replacement trials of smokers using > 1 pack/day and motivated to quit smoking
    - self-reported abstinence at 6 months verified by exhaled carbon monoxide < 8 parts per million
    - 24%-25% achieved abstinence at 6 months
    - quit date abstinence increased likelihood of 6 month abstinence, especially in low-nicotine-dependent smokers
    - smoking on the quit date may be an indication for postponing cessation attempt or increasing nicotine replacement dose
    - Reference - Arch Intern Med 1997 Feb 10;157(3):335 or in J Watch 1997 Mar 15;17(6);48); see also Br J Addict 1991;86;1119 in Drug Therapy Update 1997 Mar;10(3);11
- **refraining from tobacco products within first 2 weeks after quit attempt predicts long-term abstinence from smoking**
    - based on 2 randomized trials
    - Reference - J Fam Pract 2006 Sep;55(9):816
- **factors which predicted smoking abstinence at 7 weeks in bupropion trial were**
    - higher dose of bupropion (150-300 mg vs. 100 mg)
    - male sex
    - longest previous abstinent period < 24 hours or > 4 weeks
    - fewer cigarettes per day
    - Reference - Chest 2001 May;119(5):1357 full-text, summary can be found in Am Fam Physician 2002 Jan 1;65(1):109
- **unplanned quit attempts were 2.6 times more likely to result in at least 6 months of abstinence than planned quit attempts**
    - in cross-sectional survey of 918 smokers and 996 ex-smokers in England
    - Reference - BMJ 2006 Feb 25;332(7539):458 full-text
- **only 1 in 5 smokers quit after stroke**
    - prospective study of 511 patient who had first-ever stroke and survived 6 months
    - 198 (39%) were current smokers at time of stroke and only 43 (22%) gave up smoking within 6 months of stroke
    - Reference - Stroke 2002 Sep;33(9):2263

- **genotype for dopamine D2 receptor predicted efficacy of nicotine patch in women but not in men**
    - based on post-trial analysis of half the participants in a randomized trial
    - Reference – BMJ 2004 Apr 24;328(7446):989, editorial can be found in BMJ 2004 Apr 24;328(7446):965

Relapse rates:

- **relapse after smoking cessation common, even after 5 years**
    - cohort study of 487 patients with angina followed for 5 years
    - 395 reported to be non-smokers at baseline, of whom 21 (5%) subsequently reported smoking, 18 of whom had been ex-smokers
    - risk of resumption of smoking (these 21 patients) was 31% for patients who had quit smoking within < 1 year, 12% for patients who quit smoking 1-5 years prior and 5% for patients who quit smoking > 5 years prior
    - 92 reported to be smokers at baseline, 34 (37%) subsequently reported non-smoking
    - Reference – BMJ 2002 Apr 27;324(7344):1016 full-text
- **almost half of quitters relapsed at 8 years after nicotine patch trial**
    - 8-year follow-up of 1,532 out of 1,686 participants in randomized trial of nicotine patch
    - 153 quit smoking for 1 year in original trial, 70 (46%) had relapsed
    - among 1,472 who did not quit for 1 year in the trial, 116 (8%) were abstinent at follow-up
    - Reference – BMJ 2003 Jul 5;327(7405):28

Benefits of smoking cessation:

- **smoking cessation associated with significant reduction in mortality at 5 years compared to current smoking (level 2 [mid-level] evidence)**
    - based on prospective cohort study
    - 104,519 women from Nurse's Health Study aged 30-55 years at baseline followed from 1980-2004
    - mortality risk approaches risk associated with never smoking at ≥ 20 years after quitting
    - Reference – JAMA 2008 May 7;299(17):2037

- **smoking cessation associated with decreased risk of ischemic stroke, subarachnoid hemorrhage, and myocardial infarction (level 2 [mid-level] evidence)**
    - based on cohort study of 475,734 Korean men aged 30–58 years followed for 9 years
    - Reference – Stroke 2008 Sep;39(9):2432
- **smoking cessation associated with reduction in total mortality in patients with coronary heart disease (level 2 [mid-level] evidence)**
    - based on Cochrane review of observational studies
    - systematic review of 20 prospective cohort studies with 12,603 smokers followed at least 2 years
    - overall mortality rates 27.1% in patients who continued smoking vs. 18.4% in patients who stopped smoking (NNT 12)
    - Reference – systematic review last updated 2003 Nov 18 (Cochrane Library 2004 Issue 1:CD003041)
    - earlier version published in JAMA 2003 Jul 2;290(1):86, commentary can be found in JAMA 2003 Oct 1;290(13):1708, Bandolier 2003 Aug;114:4, Evidence-Based Medicine 2004 Jan-Feb;9(1):28
- **smoking cessation after myocardial infarction leads to recurrence risk equivalent to nonsmokers after 3 years**
    - based on study of 2,619 patients discharged from hospital after first myocardial infarction
    - Reference – Ann Intern Med 2002 Sep 17;137(6):494
- **smoking cessation associated with risk reduction of stroke (level 2 [mid-level] evidence)**
    - based on prospective cohort study of 7,735 men aged 40–59 years
    - mean follow-up 12.75 years
    - relative risk for stroke
        - 4.1 for current smokers
        - 1.9 for ex-smokers (excess risk for this group was primarily due to the contribution from heavy smokers)
        - 2.4 for primary pipe and cigar smokers
        - 3.2 for smokers who ceased cigarette smoking only to replace it with secondary pipe or cigar smoking
    - benefit of smoking cessation became apparent within 5 years of quitting

    - light smokers (< 20 cigarettes/day) who stopped smoking attained a stroke risk similar to those who had never smoked
    - hypertensive smokers had almost 20 times the risk of stroke
    - Reference – JAMA 1995 Jul 12;274(2):155
- **smoking cessation associated with improved survival across spectrum of pulmonary function**
    - based on cohort study of 1,582 men aged 40–59 years followed for 30 years
    - smoking cessation (compared to continued smoking) associated with improved median survival ranging from 6.3 years among third with poorest lung function to 7.65 years among third with best lung function
    - Reference – Thorax 2000 Sep;55(9):746 full-text
- **smoking cessation well into middle age still reduces risk for lung cancer substantially**
    - based on case-control study
    - Reference – BMJ 2000 Aug 5;321(7257):323, editorial can be found in BMJ 2000 Aug 5;321(7257):311

Additional information:

- **smoking cessation does not appear to cause increase in anxiety**
    - study of 101 subjects classified as nicotine dependent who attempted to stop smoking
    - abstinence verified by saliva cotinine 2 weeks before and 4 weeks after cessation
    - 70 of 101 subjects were able to stop without lapses
    - anxiety scores significantly decreased after 1 week
    - Reference – Am J Psychiatry 1997 Nov;154(11):1589
    - *DynaMed commentary* -- alternative interpretation could be that 31 patients with continued anxiogenic state were unable to quit
- **smoking cessation may be associated with increase or decrease in depressive symptoms**
    - study of 163 smokers during smoking cessation treatment who had history of major depressive disorder
    - 40% had increase in depressive symptoms (and were less likely to quit)
    - 47% had decrease in depressive symptoms
    - Reference – J Consult Clin Psychol 2002 Apr;70(2):356

- **smoking cessation and weight gain**
  - risk of weight gain highest during first 2 years after smoking cessation
  - sustained quitter gained average 5–6 kg (11–13 lb)
  - physical exercise, older age, higher baseline body mass index and lower rates of smoking reduce amount of weight gained after smoking cessation
  - evidence on permanence of expected weight gain conflicting
  - Reference – literature review in J Fam Pract 1998 Jun;46(6):460
  - **weight gain over 10-year period associated with smoking cessation was 4.4 kg (9.7 lb) for men and 5 kg (11 lb) for women**
    - based on surveys of 5,247 adults > 35 years old
    - Reference – N Engl J Med 1995 Nov 2;333(18):1165 in QuickScan Reviews in Fam Pract 1996 Apr:7
- cutting down on cigarette consumption
  - **cutting down amount of smoking not associated with reduced mortality**
    - prospective study of 24,959 men and 26,251 women aged 20–49 years screened twice 3–13 years apart and followed for about 28 years
    - sustained heavy smokers and smokers who reduced daily consumption by > 50% did not have statistically different risks for death from any cause, cardiovascular disease, ischemic heart disease, smoking-related cancer or lung cancer
    - Reference – Tob Control 2006 Dec;15(6):472
  - **smoking cessation, but not reduction in amount smoked, reduces risk for myocardial infarction**
    - based on study of almost 20,000 persons followed mean 14 years
    - Reference – J Epidemiol Community Health 2003 Jun;57(2):412
- **switching to chewing tobacco associated with higher mortality risk than smoking cessation**
  - based on cohort of 4,443 switchers and 111,952 abstainers followed for up to 20 years
  - all subjects were men
  - 44,374 men died
  - compared to smoking cessation, switching to chewing tobacco or snuff associated with increased risk for

        - overall mortality (hazard ratio 1.08, 95% CI 1.01–1.15)
        - lung cancer mortality (hazard ratio 1.46, 95% CI 1.24–1.73)
        - coronary heart disease mortality (hazard ratio 1.13, 95% CI 1–1.29)
        - stroke mortality (hazard ratio 1.24, 95% CI 1.01–1.53)
    - Reference – Tob Control 2007 Feb;16(1):22

Treatment

Treatment overview:

- treatment delivered by a variety of clinician types increases abstinence rates, so all clinicians should provide smoking cessation interventions (PHS Strength of Evidence A)
- more intensive interventions (that is, more sessions, longer sessions) are more effective than less intensive interventions and should be used whenever possible (PHS Strength of Evidence A)
- minimal interventions lasting < 3 minutes increase overall tobacco abstinence rates and should be offered to every tobacco user whether or not he or she is referred to intensive intervention (PHS Strength of Evidence A)
- 5–A method may be useful for screening and advising adult patients
    - **A**sk about tobacco use
    - **A**dvise to quit through clear personalized messages
    - **A**ssess willingness to quit
    - **A**ssist to quit
    - **A**rrange follow–up and support
- combination of counseling and medication is more effective than either alone and both should be offered (PHS Strength of Evidence A)
- counseling
    - all physicians should strongly advise every patient who smokes to quit because physician advice to quit smoking increases abstinence rates (PHS Strength of Evidence A)
    - counseling formats
        - smoking cessation interventions delivered using combinations of formats (proactive telephone counseling, group counseling, and individual counseling) increase abstinence rates and should be encouraged (PHS Strength of Evidence A)

        - consider self-help materials specific to patient's needs (both print and Web-based), to help people quit (PHS Strength of Evidence B)
    - smoking cessation interventions should provide both (PHS Strength of Evidence B)
        - practical counseling (such as recognizing situations that increase relapse risk and developing coping skills)
        - support and encouragement
- medications
    - effective medication should be offered unless contraindicated or for specific populations in which there is insufficient evidence for effectiveness (PHS Strength of evidence A)
    - nicotine replacement therapy (NRT) is effective for smoking cessation (level 1 [likely reliable] evidence)
    - bupropion (Zyban) (level 1 [likely reliable] evidence) and nortriptyline (generic, Pamelor) (level 2 [mid-level] evidence) each may improve smoking cessation rates, while selective serotonin reuptake inhibitors (SSRIs) are not effective (level 2 [mid-level] evidence)
    - varenicline (Chantix) may increase continuous abstinence rates and appears more effective than placebo, bupropion or transdermal nicotine (level 2 [mid-level] evidence)
    - bupropion may be more effective than nicotine replacement (level 2 [mid-level] evidence)
    - combination of bupropion plus nicotine replacement has inconsistent evidence
    - clonidine may be effective in promoting smoking cessation, but associated with high incidence of adverse effects (level 2 [mid-level] evidence)
- for smokers unwilling to quit, provide motivational interviewing (PHS Strength of Evidence B) which may improve quit rates (level 2 [mid-level] evidence)

United States Public Health Service (PHS) recommendations:

- tobacco dependence treatment is effective and should be delivered even if specialized assessments (for example, questionnaire, serum cotinine study, pulmonary function tests) are not used or available (PHS Strength of Evidence A)

- combination of counseling and medication is more effective than either alone and both should be offered (PHS Strength of Evidence A)
- all physicians should strongly advise every patient who smokes to quit because evidence shows that physician advice to quit smoking increases abstinence rates (PHS Strength of Evidence A)
- treatment delivered by a variety of clinician types increases abstinence rates, so all clinicians should provide smoking cessation interventions (PHS Strength of Evidence A)
- effective medication should be offered to most patients unless contraindicated (PHS Strength of evidence A)
- populations in which there is insufficient evidence for effectiveness include
    - pregnant women
    - smokeless tobacco users
    - adolescents
    - light smokers (< 10 cigarettes/day)
- medication options
    - effective medications (PHS Strength of Evidence A)
        - bupropion
        - nicotine gum (heavy smokers should be offered 4 mg rather than 2 mg gum [PHS Strength of evidence B])
        - nicotine inhaler
        - nicotine lozenge is effective (PHS Strength of Evidence B)
        - nicotine nasal spray
        - nicotine patch
        - varenicline
    - second-line medications (PHS Strength of Evidence A)
        - second-line medications are either not approved for tobacco dependence by FDA or associated with more concerns about side effects than first-line medications
        - second-line medications should be considered on a case-by base basis and used under physician's supervision
        - second-line options
            - clonidine
            - nortriptyline
    - combination therapies (PHS Strength of Evidence A)
        - nicotine patch and bupropion SR

        - nicotine patch and nicotine inhaler
        - nicotine patch for 14 weeks and another nicotine replacement therapy (for example, gum or spray)
    - over the counter nicotine patch therapy is effective (PHS Strength of Evidence B)
- counseling considerations
    - proactive telephone counseling, group counseling, and individual counseling formats are effective and should be used in smoking cessation interventions (PHS Strength of Evidence A)
    - smoking cessation interventions delivered in combinations of formats increase abstinence rates and should be encouraged (PHS Strength of Evidence A)
    - two particularly effective components that clinicians should use when counseling patients who are attempting to quit (PHS Strength of Evidence B)
        - practical counseling (such as recognizing situations that increase relapse risk and developing coping skills)
        - social support delivered as part of treatment
    - consider tailored self-help materials, both print and Web-based, to help people quit (PHS Strength of Evidence B)
- for smokers unwilling to quit, provide motivational interviewing (PHS Strength of Evidence B)
- Reference – DHHS 2008 May PDF or at National Guideline Clearinghouse 2008 May 12:12520[1]

Activity:

- **insufficient evidence regarding exercise-based interventions as adjunct to smoking cessation interventions**
    - based on Cochrane review
    - systematic review of 13 randomized trials evaluating exercise-based interventions to aid smoking cessation
    - only 1 of 13 trials found a benefit at 12-month follow up, but trials too small to exclude benefits
    - Reference – Cochrane Database Syst Rev 2008 Oct 8;(4):CD002295

- for trial which reported benefit -- **vigorous exercise may facilitate smoking cessation in women in cognitive-behavioral smoking cessation program** (level 2 [mid-level] evidence)
  - based on randomized trial with high dropout rate
  - 281 healthy, sedentary female smokers randomized to cognitive-behavioral smoking cessation program (12-sessions, group-based) with vigorous exercise (3 supervised sessions/week) vs. same program with equal staff contact time (3 supervised health education lectures/week)
  - abstinence from smoking based on self-report and verified by saliva cotinine level
  - follow-up rates 65%-69% at end of treatment, 47%-58% at 3 months, and 50%-56% at 12 months
  - comparing vigorous exercise vs. control
    - 16.4% vs. 8.2% continuous abstinence at 3 months (p = 0.03, NNT 13)
    - 11.9% vs. 5.4% continuous abstinence at 12 months (p = 0.05, NNT 16)
    - significantly increased functional capacity (estimated VO_2 peak 28 mL/kg/minute vs. 25 mL/kg/minute)
    - weight gain by end of treatment 5.4 kg (11.9 lb) vs. 3.05 kg (6.72 lb)
  - Reference - Commit to Quit study (Arch Intern Med 1999 Jun 14;159(11):1229)
- **exercise associated with reductions in cigarette cravings, withdrawal symptoms and smoking behavior for up to 50 minutes after exercise** (level 2 [mid-level] evidence)
  - based on systematic review without assessment of trial quality
  - systematic review of 14 studies evaluating effect of exercise on cigarette cravings, withdrawal symptoms or smoking behavior
  - 12 studies compared exercise vs. no exercise
    - 9 of 10 studies that looked at effects on craving reported significant reductions during and following exercise
    - 8 of 9 studies that compared effects on withdrawal symptoms reported significant difference in ≥ 2 withdrawal symptoms during and following exercise

        - 3 of 4 studies reported significant enhancement of mood and affect during and following exercise
        - 4 studies reported significant increase in time to smoking following exercise, with wide variation (57–188 minutes)
    - only 1 of 3 studies that compared effects of intensity of exercise on cravings reported significant difference
    - 2 studies reported contradictory results in response to cue-elicited cravings
    - Reference – Addiction 2007 Apr;102(4):534

Counseling:

- all clinicians should provide smoking cessation interventions (PHS Strength of Evidence A)
    - all physicians should strongly advise every patient who smokes to quit because evidence shows that physician advice to quit smoking increases abstinence rates (PHS Strength of Evidence A)
    - delivery of interventions by more than one type of clinician (for example, physician, nurse, pharmacist, oral health professional) is encouraged (PHS Strength of Evidence C)
    - brief advice from physician may have small effect on smoking cessation rates (level 2 [mid-level] evidence)
    - nursing advice and counseling may slightly increase smoking cessation rates (level 2 [mid-level] evidence)
- combining counseling and medication (PHS Strength of Evidence A)
    - combination of counseling and medication is more effective than either alone and both should be offered
    - many counseling sessions in combination with medication are more effective than fewer in promoting abstinence
- clinicians should try to meet ≥ 4 times with individuals quitting tobacco use (PHS Strength of Evidence A)
- using patient test results may support smoking cessation
    - informing patient of spirometric lung age increases smoking cessation rate at 12 months (level 1 [likely reliable] evidence)
    - sharing medical imaging results with patients might increase smoking cessation behaviors (level 2 [mid-level] evidence)
- counseling approaches

- more intensive interventions (that is, more sessions, longer sessions) are more effective than less intensive interventions and should be used whenever possible (PHS Strength of Evidence A); intensive behavioral interventions associated with increased smoking cessation (level 2 [mid-level] evidence)
- smoking cessation interventions delivered using combinations of formats (proactive telephone counseling, group counseling, and individual counseling) increase abstinence rates and should be encouraged (PHS Strength of Evidence A)
- smoking cessation interventions should provide both (PHS Strength of Evidence B)
  - practical counseling (such as recognizing situations that increase relapse risk and developing coping skills)
  - support and encouragement
- face-to-face individual smoking cessation counseling may help patients quit (level 2 [mid-level] evidence)
- motivational interviewing appears to modestly increase smoking cessation compared with usual care or brief advice (level 2 [mid-level] evidence
- consider tailored self-help materials (both print and Web-based) which appear effective in helping people quit (PHS Strength of Evidence B)
  - self-help materials associated with small benefit over no materials but may not offer additional benefit when used in conjunction with personal interaction or nicotine replacement therapy (level 2 [mid-level] evidence)
  - individualized self-help materials appear more effective than untailored self-help materials (level 2 [mid-level] evidence)
- group therapy may be more effective than self-help programs (level 2 [mid-level] evidence)
- telephone counseling may help smokers interested in quitting (level 2 [mid-level] evidence)
- web- and computer-based smoking cessation programs may be effective for adults (level 2 [mid-level] evidence)

- in adolescents
  - some counseling approaches may have modest efficacy for promoting cessation in adolescent smokers (level 2 [mid-level] evidence)

    - motivational interviewing may reduce rates of tobacco use in teenagers (level 2 [mid-level] evidence)
- for smokeless tobacco users, behavioral interventions including telephone counselling or oral exam may increase abstinence rates (level 2 [mid-level] evidence)
- for smokers unwilling to quit, provide motivational interviewing (PHS Strength of Evidence B) which may improve quit rates (level 2 [mid-level] evidence)

- see Counseling for tobacco cessation for details
- facts which may be useful for brief counseling
    - on average, each cigarette smoked shortens lifespan by 11 minutes (BMJ 2000 Jan 1;320(7226):53)
    - smoking associated with increase in mortality similar to adding 5–10 years of age, based on United States 2004 data (J Natl Cancer Inst 2008 Jun 18;100(12):845)
    - smoking associated with higher mortality from cancer for many cancer types (Br J Cancer 2005 Feb 14;92(3):426 full-text)
    - secondhand smoke at home associated with increased mortality from all causes and cardiovascular disease (Am J Epidemiol 2007 Mar 1;165(5):530)

Medications:

- medications with efficacy for smoking cessation include
    - nicotine as gum, inhaler, lozenge, nasal spray or patch
    - bupropion
    - nortriptyline
    - varenicline
- combining counseling and medication (PHS Strength of Evidence A)[1]
    - combination of counseling and medication is more effective than either alone and both should be offered
    - many counseling sessions in combination with medication are more effective than fewer in promoting abstinence
- **numerous medications may be effective for smoking cessation (level 2 [mid-level] evidence)**
    - based on systematic review without assessment of trial quality and with indirect comparisons

- 69 randomized placebo-controlled trials with 32,098 patients were reviewed to compare effectiveness of smoking cessation medications either indirectly or directly
- inclusion criteria included biochemical verification of smoking cessation, and application of counseling, if provided, across all treatment arms
- smoking cessation defined as either 6 or 12 months continuous abstinence from expected quit date or from last follow-up depending on study
- treatments associated with smoking cessation vs. placebo
    - varenicline 25.59% vs. 14.81% (adjusted odds ratio [OR] 2.55, 95% CI 1.99-3.24, NNT 10) in 13 trials with 3,395 patients
    - bupropion 19.74% vs. 10.86% (adjusted OR 2.12, 95% CI 1.76-2.56, NNT 12) in 16 trials with 6,653 patients
    - nicotine replacement therapies
        - nicotine tablet 17.27% vs. 9.45% (adjusted OR 2.06, 95% CI 1.47-2.87, NNT 13) in 6 trials with 2,306 patients
        - nicotine inhaler 17.14% vs. 9.05% (adjusted OR 2.18, 95% CI 1.38-3.45, NNT 13) in 4 trials with 976 patients
        - nicotine patch 13.29% vs. 7.47% (adjusted OR 1.88 95% CI 1.6-2.22, NNT 18) in 30 trials with 12,431 patients
        - nicotine gum 18.95% vs, 13.98% (adjusted OR 1.65, 95% CI 1.37-2.01, NNT 21) in 22 trials with 5,104 patients
        - nicotine nasal spray 23.88% vs. 11.84% (adjusted OR 2.37, 95% CI 1.57-3.6, NNT 9) in 4 trials with 887 patients
- varenicline not clearly more effective than bupropion in direct comparison
- smoking cessation with varenicline 22.23% vs. 20.45% with bupropion (OR 1.4, 95% CI 0.75-2.66) in meta-analysis of 5 trials with 1,870 patients
- Reference – (CMAJ 2008 Jul 15;179(2):135 full-text), correction can be found in CMAJ 2008 Oct 7;179(8):802 full-text, editorial can be found in CMAJ 2008 Jul 15;179(2):123 full-text, commentary can be found in CMAJ 2008 Nov 4;179(10):1037 full-text

Nicotine replacement therapy (NRT):

- nicotine replacement therapy (NRT) is effective for smoking cessation (level 1 [likely reliable] evidence)
    - effective forms of NRT include gum, transdermal patch, sublingual tablet/lozenge, oral inhaler and nasal spray
    - various types of nicotine replacement products appear equally effective for achieving short-term abstinence (level 2 [mid-level] evidence)
- nicotine replacement therapy for reduction in cigarette consumption may increase smoking cessation rates (level 2 [mid-level] evidence)
- nicotine patch therapy prior to quitting smoking may increase smoking abstinence rates (level 2 [mid-level] evidence)
- insufficient evidence to support nicotine replacement therapy in adolescents
- combination of NRT approaches
    - addition of nicotine nasal spray for 1 year to use of nicotine patch for 5 months improves abstinence rates (level 1 [likely reliable] evidence)
    - nicotine patch plus nicotine lozenge increases 6-month quit rate (level 1 [likely reliable] evidence)
    - addition of nicotine patch to nicotine inhaler may improve short-term quit rates (level 2 [mid-level] evidence)
- comparative efficacy with other medications
    - bupropion may be more effective than nicotine replacement (level 2 [mid-level] evidence)
    - varenicline may increase continuous abstinence rates more than transdermal nicotine (level 2 [mid-level] evidence)
- combination of bupropion plus nicotine replacement has inconsistent evidence
    - combination bupropion plus nicotine inhaler may be more effective than either monotherapy, bupropion appears more effective than nicotine inhaler (level 2 [mid-level] evidence)
    - addition of bupropion for 7 weeks appears no more effective than placebo in patients taking nicotine replacement therapy and counseling (level 2 [mid-level] evidence)
- safety
    - nicotine replacement therapy does not appear to acutely increase risk of myocardial infarction, stroke or death (level 2 [mid-level] evidence)
    - nicotine replacement therapy appears safe in patients with cardiac disease (level 2 [mid-level] evidence)

    - nicotine replacement therapy associated with increased mortality in critically ill patients (level 2 [mid-level] evidence)
- see Nicotine replacement therapy for smoking cessation for details

Antidepressants:

- **bupropion (level 1 [likely reliable] evidence) and nortriptyline (level 2 [mid-level] evidence) each may improve smoking cessation rates, while selective serotonin reuptake inhibitors (SSRIs) do not appear effective (level 2 [mid-level] evidence)**
    - based on Cochrane review of trials with variable quality
    - systematic review of 66 randomized trials evaluating antidepressants for smoking cessation with ≥ 6 months follow-up
    - 52% of trials had unclear allocation concealment; high losses to follow-up in many trials
    - significantly increased rate of smoking cessation with
        - bupropion as sole pharmacotherapy compared with placebo (risk ratio [RR] 1.69, 95% CI 1.53-1.85, NNT 13-21 for control event rate 9%) in analysis of 36 trials with 11,140 patients
        - nortriptyline as sole pharmacotherapy compared with placebo (RR 2.34, 95% CI 1.61-3.41, NNT 4-17 for control event rate 10%) in analysis of 6 trials with 975 patients
        - restricting inclusion in bupropion vs. placebo meta-analysis to trials with adequate allocation concealment did not change results
    - addition of bupropion (6 trials) or nortriptyline (3 trials) to nicotine patch had conflicting results
    - no significant difference in cessation rates
        - comparing bupropion vs. nortriptyline in analysis of 3 trials
        - in placebo-controlled of SSRIs (4 trials of fluoxetine, 1 trial of sertraline or 1 trial of paroxetine)
        - in placebo-controlled trials of moclobemide (1 trial), selegiline (3 trials) or venlafaxine (1 trial)
    - extended bupropion after cessation not shown to prevent relapse in 3 trials
    - Reference – Cochrane Database Syst Rev 2009 Oct 7;(4):CD000031; commentary on earlier version can be found in Evidence-Based

Medicine 2004 Jan-Feb;9(1):15, Am Fam Physician 2005 Jan 1;71(1):67, ACP J Club 2005 May-Jun;142(3):67

- bupropion for smoking cessation
  - bupropion is antidepressant available generically or as Aplenzin, Budeprion XL, Wellbutrin, Wellbutrin XL, Zyban
  - extended-release bupropion (Zyban) FDA approved for smoking cessation, alone or in combination with nicotine replacement therapy
  - dosing
    - start 1-2 weeks before smoking cessation
    - initially 150 mg daily for first 3 days
    - continue 150 mg twice daily for 7-12 weeks
    - discontinue if no progress after 7 weeks of therapy
    - bupropion sustained-release 150 mg twice daily appears more effective than 150 mg once daily (level 2 [mid-level] evidence)
  - bupropion (level 1 [likely reliable] evidence) and nortriptyline (level 2 [mid-level] evidence) each may improve smoking cessation rates, while selective serotonin reuptake inhibitors (SSRIs) not do appear effective (level 2 [mid-level] evidence)
  - bupropion appears effective for smoking cessation in various populations
    - healthy adults (level 2 [mid-level] evidence)
    - African Americans (level 1 [likely reliable] evidence)
    - indigenous New Zealand population (level 2 [mid-level] evidence)
    - adolescents during treatment, but may not have long-term effect (level 2 [mid-level] evidence)
    - patients with chronic obstructive pulmonary disease (COPD) (level 2 [mid-level] evidence)
    - smokers previously treated with bupropion sustained-release (level 2 [mid-level] evidence)
  - bupropion may be more effective than nicotine replacement (level 2 [mid-level] evidence)
  - combination of bupropion plus nicotine replacement has inconsistent evidence

        - combination bupropion plus nicotine inhaler may be more effective than either monotherapy, bupropion appears more effective than nicotine inhaler (level 2 [mid-level] evidence)
        - addition of bupropion for 7 weeks appears NO more effective than placebo in patients taking nicotine replacement therapy and counseling (level 2 [mid-level] evidence)
    - continued bupropion for 45 weeks in patients who quit smoking after bupropion for 7 weeks reduces rates of return to smoking during treatment and for up to 6 months after treatment, but may not affect rates at 1 year after treatment cessation (level 2 [mid-level] evidence)
    - cautions
        - observe patients starting bupropion for clinical worsening, suicidality or unusual behavior changes
        - additional serious adverse effects include seizures, unmasking of bipolar disorder, hypersensitivity reactions, hypertension, drug interactions
        - common adverse effects include agitation, dry mouth, insomnia, headache, nausea, vomiting, constipation, tremor
        - Pregnancy Category B
    - see Bupropion for smoking cessation for details
- nortriptyline (Pamelor) may be effective for smoking cessation
    - nortriptyline dosing strategies used in trials for smoking cessation
        - 25 mg once daily started 1–2 weeks prior to quit date
        - increased after 4 days to 50 mg once daily
        - increased after another 4 days to 75 mg once daily
        - after 6–8 weeks of therapy taper over 1–2 weeks before discontinuation
    - **nortriptyline may improve short-term cessation rates (level 2 [mid-level] evidence)**
        - based on randomized trial with allocation concealment not stated
        - 214 patients aged 18–70 years who smoked 10 or more cigarettes per day and were without current major depression randomized to nortriptyline (started at 25 mg nightly 10 days prior to quit day and titrated to 75 mg/day or maximal tolerated

dose, further adjusted based on serum levels, tapered to 50 mg/day at 8 weeks) vs. placebo
        - behavioral intervention consisted of 2 group sessions and 12 individual follow-up visits
        - comparing nortriptyline vs. placebo
            - biochemically confirmed cessation rate at 6 months 14% vs. 3% (p=0.03, NNT 9)
            - significant reduction in several withdrawal symptoms including anxiety/tension, anger/irritability, difficulty concentrating, restlessness and impatience by day 8 after quit day in nortriptyline group
            - frequent adverse effects included dry mouth (64%) and taste disturbance (20%)
        - blinding not completely effective as many patients and investigators guessed allocation
        - Reference – Arch Intern Med 1998 Oct 12;158(18):2035 full-text, commentary can be found in Arch Intern Med 1999 Jun 14;159(11):1257
    - **nortriptyline may promote smoking cessation in depressed and non-depressed patients (level 2 [mid-level] evidence)**
        - based on randomized trial with low adherence rate
        - 199 cigarette smokers (33% with history of depression, those with depression within 3 months excluded) randomized to 2 concurrent interventions
            - nortriptyline for 12 weeks vs. placebo
            - cognitive-behavioral therapy vs. control
        - 24% of patients did not complete treatment
        - biologically verified abstinence from cigarettes measured up to 64 weeks
        - mood measured up to 8 days after smoking quit date (quit date 5 weeks into treatment)
        - nortriptyline alleviated negative affect occurring after smoking cessation
        - comparing nortriptyline vs. placebo
            - continuous abstinence in 24% vs. 12% (p = 0.02, NNT 13)

            - nortriptyline produced higher abstinence rates than placebo independent of history of major depressive disorder
        - history of depression associated with significantly lower cessation rates, but group receiving cognitive behavior therapy and placebo had 29% cessation rate vs. 20% cessation rate in parallel treatment group without history of depression (not significant)
        - Reference – Arch Gen Psychiatry 1998 Aug;55(8):683 full-text, editorial can be found in Arch Gen Psychiatry 1998 Aug;55(8);692
    - **nortriptyline may increase smoking cessation rates (level 2 [mid-level] evidence)**
        - based on randomized trial with allocation concealment not stated
        - 144 patients randomized to nortriptyline 75 mg/day vs. placebo for 6 weeks
        - all patients had behavioral group orientation for 5 weeks
        - cessation rates 56% with nortriptyline vs. 23% with placebo ($p > 0.001$, NNT 3)
        - Reference – Chest 2002 Aug;122(2):403 full-text, commentary can be found in J Fam Pract 2002 Dec;51(12):1008, commentary can be found in Am Fam Physician 2003 Jan 1;67(1):184
    - **addition of nortriptyline for 8 weeks to nicotine replacement may not be more effective than nicotine replacement alone for smoking cessation (level 2 [mid-level] evidence)**
        - based on randomized trial with wide confidence intervals
        - 901 participants ≥ 18 years old who smoked ≥ 10 cigarettes/day and attended a United Kingdom National Health Service stop smoking service were treated with nicotine replacement (of own choice) and behavioral support and randomized to nortriptyline vs. placebo and followed for 12 months
        - nortriptyline started 1–2 weeks before quit day with initial dose 25 mg daily for 3 days, then 50 mg/day for 4 days, then to 75 mg/day for 6 weeks (reduced if not tolerated), then tapered over 1 week

        - persons excluded if taking other antidepressant
        - comparing nortriptyline vs. placebo
            - participants taking both allocated treatment and nicotine replacement
                - 79% vs. 75% on quit day
                - 58.9% vs. 55.6% at 4 weeks
            - prolonged abstinence in
                - 16.2% vs. 12.1% at 6 months (not significant, 95% CI −0.4% to +8.7%)
                - 11% vs. 8.8% at 12 months (not significant, 95% CI −1.7% to +6.1%)
            - no differences in withdrawal symptoms or urges to smoke
        - nortriptyline group had significantly lower depression and anxiety scores at quit day but differences negligible at 4 weeks
        - nortriptyline group had higher ratings of dry mouth and constipation
        - Reference – BMJ 2008 May 31:336(7655);1223 full-text, editorial can be found in BMJ 2008 May 31;336(7655):1200
    - **addition of nortriptyline to nicotine patch may improve smoking cessation rate (level 2 [mid-level] evidence)**
        - based on randomized trial with allocation concealment not stated
        - 158 Veterans Affairs medical center smokers aged 18–65 years were treated with transdermal nicotine 8 weeks and randomized to nortriptyline vs. placebo until 12 weeks after quit day
            - nortriptyline 25 mg started 14 days before quit day
            - titrated by 25 mg/day every 4 days up to 75 mg/day as tolerated
            - tapered for final 2 weeks
        - patients were not depressed, but all patients had behavioral intervention with 12 brief, individual visits
        - comparing nortriptyline vs. placebo
            - biochemically confirmed cessation rates 23% vs. 10% (p = 0.052, NNT 8) at 6 months
            - withdrawal symptom scores 1.51 vs. 1.37 (not significant)

        - significant side effects of nortriptyline included dry mouth (38% vs. 8%, p = 0.001, NNH 3) and sedation (20% vs. 3%, p = 0.001, NNH 5)
    - Reference – Arch Intern Med 2004 Nov 8;164(20):2229 full-text
- **addition of sertraline (Zoloft) to intensive cessation counseling may reduce irritability and withdrawal symptoms but may not improve smoking cessation rates in patients with major depression (level 2 [mid-level] evidence)**
    - based on randomized trial with high dropout rate
    - 134 smokers with history of major depression underwent 1-week placebo run-in then were randomized to sertraline vs. placebo for 9 weeks followed by 9-day drug taper then 6-month drug-free follow-up
    - all patients received intensive cessation counseling over 9 visits
    - 25% of patients dropped out before their expected quit date
    - sertraline reduced total withdrawal symptoms, irritability, anxiety, craving, and restlessness compared to placebo
    - comparing sertraline vs. placebo
        - abstinence rates at 6 months 11.8% vs. 16.7% (not significant)
        - withdrawal symptoms scores 4.75 vs. 9.38 (p = 0.003) in subgroup analysis of 81 patients 1 week after quit date
    - higher than expected abstinence rates may be related to intensive counseling
    - Reference – Am J Psychiatry 2002 Oct;159(10):1731 full-text

Nicotine partial agonists:

- **varenicline appears effective for smoking cessation at 6-12 months and more effective than bupropion (level 2 [mid-level] evidence)**
    - based on Cochrane review with high dropout rates
    - systematic review of 16 randomized trials evaluating nicotine receptor partial agonists (varenicline or cytisine) with minimum 6-month follow-up in > 10,300 adults (6,892 used varenicline)
    - varenicline compared to placebo
        - varenicline associated with increased continuous abstinence
            - using standard dose 1 mg twice daily in analysis of 10 trials with 4,443 adults at ≥ 24 weeks
                - risk ratio (RR) 2.31 (95% CI 2.01-2.66)

            - NNT 6–9 assuming 11% abstinence in placebo group
        - using lower or variable doses in analysis of 4 trials with 1,272 adults at ≥ 24 weeks
            - RR 2.09 (95% CI 1.56–2.78)
            - NNT 6–18 assuming 10% abstinence in placebo group
        - as maintenance therapy with standard dose (1 mg twice daily) in 1 trial with 377 adults at 52 weeks
            - 35% varenicline vs. 7% placebo ($p < 0.00001$, NNT 4)
    - standard dose varenicline associated with increased continuous abstinence compared to low dose varenicline in analysis of 3 trials with 1,083 adults at 52 weeks ($p = 0.051$)
    - varenicline compared to bupropion in analysis of 3 trials with 1,622 adults at 52 weeks
        - varenicline associated with increased continuous abstinence
            - RR 1.52 (95% CI 1.22–1.88)
            - NNT 8–33 assuming 14% abstinence in bupropion group
    - no significant difference varenicline compared to nicotine replacement therapy for point prevalence abstinence in analysis of 2 trials with 778 adults at 24 weeks
    - adverse events include
        - nausea (mild-to-moderate) in analysis of 11 trials with 4,782 adults
            - RR 3.19 (95% CI 2.78–3.67)
            - NNH 4–6 assuming 10% nausea in placebo group
        - insomnia in analysis of 10 trials with 4,472 adults
            - RR 1.55 (95% CI 1.33–1.82)
            - NNH 12–30 assuming 10% insomnia in placebo group
        - abnormal dreams in analysis of 8 trials with 3,827 adults
            - RR 3.04 (95% CI 2.35–3.94)
            - NNH 9–19 assuming 4% abnormal dreams in placebo group
        - headache in analysis of 9 trials with 4,155 adults
            - RR 1.18 (95% CI 1.01–1.39)

        - NNH 23–876 assuming 11% headache in placebo group
    - 1 placebo-controlled trial with 1,214 adults reported increased self-reported abstinence with cytisine at 2 year follow-up
    - Reference – Cochrane Database Syst Rev 2011 Feb 16;(2):CD006103

- varenicline tartrate (Chantix)
    - varenicline tartrate (Chantix) FDA approved for smoking cessation
    - varenicline is nicotinic receptor partial agonist which reduces withdrawal symptoms and blocks nicotine effects from smoking
    - varenicline may be associated with serious neuropsychiatric symptoms, including changes in behavior, agitation, depressed mood, suicidal ideation, and attempted and completed suicide
    - varenicline may increase continuous abstinence rates and appears more effective than placebo, bupropion or transdermal nicotine (level 2 [mid-level] evidence)
    - varenicline increases continuous abstinence rates in patients with cardiovascular disease (level 1 [likely reliable] evidence)
    - start 1 week before target quit date
    - dosing orally after eating with full glass of water
        - 0.5 mg once daily for 3 days
        - 0.5 mg twice daily for days 4–7
        - 1 mg twice daily for 11 weeks
        - additional 12 weeks approved for patients with successful smoking cessation
        - maximum dose 0.5 mg twice daily if severe renal impairment (creatinine clearance < 30 mL/minute), maximum dose 0.5 mg once daily on hemodialysis
    - most common adverse effects in clinical trials were nausea (30%–40% patients), headache, vomiting, flatulence, insomnia, abnormal dreams, and dysgeusia
    - Pregnancy Category C
    - see Varenicline for details
- **cytisine (a nicotinic receptor agonist) may be effective for smoking cessation (level 2 [mid-level] evidence)**
    - based on systematic review with mostly low-quality trials

- systematic review of 10 studies reporting effects of cytisine on smoking cessation with 4,404 treated smokers and 3,518 controls
- only 4 studies were controlled, of which only 3 placebo-controlled, only 2 were double-blind, and only 1 was randomized
- 9 studies used Bulgarian drug Tabex (cytisine 1.5 mg per tablet), 1 Russian study used buccal films containing cytisine 1.5 mg, or cytisine 0.75 mg plus anabasine 0.75 mg
- cessation rates often reported based on mailed surveys rather than confirmed quit rates
- quit rates comparing cytisine vs. control in controlled studies
  - in randomized double-blind trial of 520 patients
    - 3-4 week quit rate 41.2% vs. 31.1% ($p = 0.02$, NNT 10)
    - 3 month quit rate 27.2% vs. 21.1% (not significant)
  - in double-blind trial of 1,214 patients
    - 4-6 week quit rate 65.1% vs. 40.5% ($p < 0.001$, NNT 4)
    - 6 month quit rate 30.5% vs. 16% ($p < 0.001$, NNT 7) in double-blind placebo-controlled trial in 1,214 patients
    - 2 year quit rate 20.9% vs. 13% ($p < 0.001$, NNT 13) in double-blind placebo-controlled trial in 1,214 patients
  - 3 week quit rate 70.1% vs. 53% ($p < 0.001$, NNT 6) in trial using autogenic training as control in 620 patients
- adverse effects slightly more common than placebo were weight gain, headache and heartburn
- Reference – Arch Intern Med 2006 Aug 14-28;166(15):1553 full-text, editorial can be found in Arch Intern Med 2006 Aug 14-28;166(15):1547

Rimonabant – WITHDRAWN from market:

- rimonabant (Acomplia, Zimulti, Riobant, Slimona, Rimoslim) is a selective type 1 cannabinoid receptor antagonist
- rimonabant withdrawn from market in Europe and not approved in United States (see Weight loss medications withdrawn from market)
- **rimonabant may improve smoking cessation and relapse prevention rates (level 2 [mid-level] evidence)**
  - based on Cochrane review of trials with unclear allocation concealment
  - systematic review of 3 randomized trials of rimonabant in adult smokers

        - 2 trials with 1,567 smokers evaluated rimonabant for 10 weeks for smoking cessation (STRATUS-EU, STRATUS-US)
        - 1 trial with 1,661 quitters evaluated rimonabant for 10 weeks for relapse prevention (STRATUS-WW)
    - none of the trials reported methods of randomization or allocation concealment
    - some data inconsistent across unpublished reports used for meta-analysis
    - 30%-40% treatment non-completion rates reported in STRATUS-US and STRATUS-EU
    - comparing rimonabant 20 mg vs. placebo for cessation in 2 trials with 1,049 patients
        - continuous abstinence during 50 weeks follow-up in 16.5% vs. 10.9% (p = 0.01, NNT 18)
        - continuous abstinence during last 4 weeks of treatment in 26.1% vs. 17.9% (p = 0.001, NNT 13)
    - comparing rimonabant 20 mg vs. 5 mg for cessation in 2 trials with 1,046 patients
        - continuous abstinence during 50 weeks follow-up in 16.5% vs. 12.2% (p = 0.05, NNT 24)
        - continuous abstinence during last 4 weeks of treatment in 26.1% vs. 19.9% (p = 0.02, NNT 16) but limited by heterogeneity (p = 0.02)
    - comparing rimonabant 5 mg vs. placebo for cessation in 2 trials with 1,039 patients
        - prolonged abstinence at 50 weeks in 12.2% vs. 10.9% (not significant)
        - continuous abstinence during last 4 weeks of treatment in 19.9% vs. 17.9% (not significant)
    - comparing different doses of rimonabant vs. placebo for relapse prevention at 52 weeks
        - relapse in 41.5% with rimonabant 20 mg vs. 32.2% with placebo in analysis of 682 patients (p = 0.01, NNT 11)
        - relapse in 41.8% with rimonabant 5 mg vs. 32.2% with placebo in analysis of 677 patients (p = 0.01, NNT 11)
    - adverse events included nausea and upper respiratory tract infections

- rimonabant 20 mg associated with less weight gain with smoking cessation than 5 mg or placebo
- Reference – systematic review last updated 2007 Aug 6 (Cochrane Library 2007 Issue 4:CD005353)

Other agents:

- **clonidine may be effective in promoting smoking cessation, but associated with high incidence of adverse effects (level 2 [mid-level] evidence)**
  - based on Cochrane review of trials with unclear allocation concealment
  - systematic review of 6 randomized placebo-controlled trials with 776 patients evaluating clonidine (3 oral, 3 transdermal) for smoking cessation at ≥ 12 weeks after end of treatment
  - all trials had unclear allocation concealment
  - smoking cessation in 24.9% with clonidine vs. 14.4% with placebo (p = 0.001, NNT 10), but only 1 individual trial had statistically significant results
  - clonidine associated with high incidence of dose-dependent side effects, especially dry mouth and sedation
  - Reference – Cochrane Database Syst Rev 2008 Oct 8;(4):CD000058, commentary on earlier version can be found in ACP J Club 2005 Jan-Feb;142(1):12
- **addition of mecamylamine (nicotine antagonist) to nicotine may be more effective than nicotine alone in promoting smoking cessation (level 2 [mid-level] evidence)**
  - based on Cochrane review with limited evidence
  - systematic review of 2 randomized trials evaluating mecamylamine alone or in combination with nicotine replacement therapy for promoting smoking cessation in 128 adults
  - in trial of 48 adults, 1-year abstinence rate 37.5% in mecamylamine plus nicotine patch group vs. 4.2% with nicotine patch alone (p = 0.004, NNT 3)
  - in trial of 80 adults randomized to mecamylamine capsules and/or nicotine patch vs. no drug for 4 weeks prior to cessation (all patients given nicotine and mecamylamine for 6 weeks after scheduled quit date) highest abstinence rate in mecamylamine plus nicotine pretreatment group (40% vs. 15% with nicotine alone vs. 20% with

mecamylamine alone or no drug at 6 months) but results not statistically significant
    - Reference – Cochrane Database Syst Rev 2011 Jan 19;(1):CD001009
    - *DynaMed commentary* –– mecamyline (Inversine) manufacture discontinued in 2009 (Targacept 2009 Jun 4 PDF)
- **selegiline 10 mg/day has inconsistent evidence in promoting smoking cessation**
    - based on 1 randomized trial with allocation concealment not stated and 1 small randomized trial
    - 101 adults with nicotine dependence randomized to selegiline hydrochloride 5 mg twice daily vs. placebo for 8 weeks and followed for 6 months
        - all patients received brief smoking cessation counseling
        - 7-day point prevalence of smoking cessation comparing selegiline vs. placebo
            - 16% vs. 20% at end of treatment (not significant)
            - 12% vs. 16% at 6-month follow-up (not significant but trial not powered for this outcome)
        - Reference – Drug Alcohol Depend 2010 Mar 1;107(2-3):188
    - 40 patients with nicotine dependence randomized to selegiline hydrochloride 5 mg vs. placebo orally twice daily for 8 weeks
        - comparing selegiline vs. placebo on smoking cessation
            - 7-day point prevalence at 8 weeks 45% vs. 15% ($p < 0.05$, NNT 4)
            - 7-day point prevalence at 6-month follow-up 20% vs. 5% (not significant)
        - Reference – Biol Psychiatry 2003 Jan 15;53(2):136
- **insufficient evidence regarding opioid antagonists (such as naltrexone) for smoking cessation**
    - based on Cochrane review
    - systematic review of randomized trials evaluating opioid antagonists for smoking cessation and reporting on abstinence of ≥ 6 months
    - 4 naltrexone trials with 582 adults met inclusion criteria
    - no significant effect of naltrexone on long-term abstinence but wide confidence intervals compatible with both clinically significant benefit and possible negative effects

- no trials of naloxone or buprenorphine reported long term follow-up
- Reference – Cochrane Database Syst Rev 2009 Oct 7;(4):CD003086
- **naltrexone 100 mg/day may increase smoking cessation rates with nicotine patch (level 2 [mid-level] evidence)**
    - 400 cigarette smokers in Connecticut who smoked 20 or more cigarettes daily for at least 1 year and had at least 1 previous quit attempt were treated with transdermal nicotine patches (NicoDerm CQ) 21 mg for 6 weeks starting on quit date and randomized to placebo or naltrexone hydrochloride 25, 50 or 100 mg/day
    - naltrexone was titrated as 12.5 mg for 1 day, 25 mg for 1 day, 50 mg for 2 days, then 100 mg/day up to target dose
    - naltrexone started about 4 hours after nicotine patch placement on second day, then taken with patch placement on subsequent days
    - all patients had counseling with nurse for 45 minutes for first session then weekly for 15-minute sessions
    - study was blinded but pharmacist who assigned patients not blinded to assignment (unclear allocation concealment)
    - 295 (74%) completed treatment, 385 (96%) included in analysis
    - outcomes
        - number of cigarettes smoked increased over 6 weeks in all groups except 100 mg group which remained low ($p = 0.04$)
        - no significant differences in 7-day point prevalences at 3, 6 or 12 months
        - no significant naltrexone effect on prolonged abstinence in last 4 weeks at 1 year
        - among treatment completers (74%) at 1 year, continuous abstinence more likely with naltrexone 100 mg vs. placebo (71.6% vs. 48%, $p = 0.004$, NNT 5)
    - Reference – Arch Intern Med 2006 Mar 27;166(6):667
- **no randomized trials with ≥ 6 month follow-up identified evaluating lobeline (a botanical derivative) for smoking cessation**
    - based on Cochrane review
    - Reference – Cochrane Database Syst Rev 2009 Apr 15;(2):CD000124

- topiramate may improve smoking cessation rates in some subgroups of patients
    - **topiramate may improve smoking cessation rates in patients with alcohol dependence (level 2 [mid-level] evidence)**
        - based on subgroup analysis of randomized trial with high dropout rate
        - 150 patients with alcohol dependence randomized to topiramate (25 mg daily titrated to 150 mg twice daily) vs. placebo for 12 weeks in addition to weekly standardized medication compliance management
        - only 103 patients completed the study
        - in subgroup analysis of 94 smokers in this trial, 16.7% topiramate vs. 6.9% placebo smokers had confirmed smoking abstinence at 12 weeks
        - Reference – Arch Intern Med 2005 Jul 25;165(14):1600
        - *DynaMed commentary* –– unclear how analysis accounts for 37% study dropout rate
    - **effects of topiramate on smoking cessation rates unclear**
        - based on randomized trial with inadequate statistical power to rule out clinically significant benefits
        - 38 men and 49 women who smoked > 10 cigarettes/day and were motivated to quit smoking were randomized to topiramate vs. placebo
            - topiramate titrated up to 200 mg/day in divided doses for 6 weeks then maintained for 5 weeks
            - both groups had brief counseling
        - no significant differences between groups in confirmed abstinence rates during weeks 8–11
        - in subgroup analysis, trend toward increased quit rate in men with topiramate vs. placebo (37.5% vs. 13.6%, p = 0.098)
        - topiramate associated with higher trial discontinuation rate due to adverse events (23% vs. 2%, NNH 4)
        - Reference – Addiction 2008 Apr;103(4):687
- **insufficient evidence to evaluate silver acetate (gum, lozenge, spray) for smoking cessation**
    - based on Cochrane review

    - systematic review of randomized trials evaluating silver acetate for smoking cessation with ≥ 6 months follow-up
    - 2 placebo-controlled trials met inclusion criteria; no significant difference in quit rates but wide confidence intervals cannot rule out positive or negative effect
    - lack of effect of silver acetate may reflect poor compliance with treatment designed to create unpleasant stimulus to smoking
    - Reference – Cochrane Database Syst Rev 2009 Apr 15;(2):CD000191
- **anxiolytics may not be effective for smoking cessation (level 2 [mid-level] evidence)**
    - based on Cochrane review with wide confidence intervals
    - systematic review of randomized trials comparing anxiolytics vs. placebo or alternative therapy for smoking cessation
    - interventions included diazepam (1 trial), meprobamate (1 trial), metoprolol (1 trial), oxprenolol (1 trial), and buspirone (2 trials)
    - no interventions significantly effective for smoking cessation but wide confidence intervals cannot rule out possible benefit
    - Reference – Cochrane Database Syst Rev 2010 Jan 20;(1):CD002849
- **nicotine vaccines**
    - nicotine vaccines produce antibodies that bind nicotine
    - nicotine vaccines appear safe and well tolerated in early trials, but immunological response rate variable and duration of effect unclear
    - 9 nicotine vaccines have been tested in animals and 3 vaccines are in clinical trials
        - TA-NIC which links nicotine to recombinant cholera toxin B
        - NicQb which uses bacteriophage Qb
        - NicVAX which uses recombinant exoprotein A
    - Reference – Canadian Agency for Drugs and Technologies in Health (CADTH) Health Technology Assessment 2007 Sep PDF
    - nicotine vaccine (NicQb) not associated with continuous abstinence in phase II randomized trial with 341 patients, but large effect noted in subgroup with high antibody levels (PLoS ONE 2008 Jun 25;3(6):e2547 full-text)
- **no randomized trials found evaluating Nicobrevin (quinine, menthyl valerate, camphor and eucalyptus oil) for smoking cessation with ≥ 6 months follow-up**
    - based on Cochrane review

    - Reference – Cochrane Database Syst Rev 2009 Apr 15;(2):CD005990
- **St. John's wort does not appear to promote smoking cessation (level 2 [mid-level] evidence)**
    - based on randomized trial with inadequate statistical power
    - 143 patients who smoke were randomized to 1 of 4 treatments
        - St. John's wort 900 mg daily plus placebo
        - chromium 400 mcg daily plus placebo
        - St. John's wort 900 mg plus chromium 400 mcg daily
        - double placebo
    - treatment started 2 weeks before quit date and continued for 14 weeks
    - patients followed for 6 months
    - prolonged abstinence from smoking at 4 weeks in 8.5% with St. John's wort vs. 12.5% with placebo (not significant)
    - effect of chromium on weight gain after cessation unclear due to insufficient rate of abstinence at 6 months
    - Reference – Drug Alcohol Depend 2009 Jun 1;102(1–3):116

Costs:

- costs of 30 days' treatment in United States dollars
    - bupropion sustained release
        - available in 50, 100, 150 and 200 mg tablets; dosing 150 mg twice daily
        - generic $164.40, Wellbutrin SR $210.00, Zyban 150 mg $211.20
        - Zyban FDA approved for smoking cessation, Wellbutrin SR not FDA approved for smoking cessation
    - nicotine replacement products – all FDA approved for treatment of tobacco dependence
        - nicotine oral inhaler (Nicotrol Inhaler) 10-mg cartridges (delivers 4 mg), 4–16 cartridges/day, $178.08 for 168 cartridges
        - nicotine nasal spray (Nicotrol NS) 0.5 mg/spray (10-mL bottle holds 200 sprays), 8–40 doses/day (2 sprays/dose), $178.00 for four 10-mL bottles
        - nicotine polacrilex gum – available without a prescription
            - 2 mg or 4 mg/piece, 8–24 pieces/day
            - generic $64.80, Nicorette $96.00
        - nicotine polacrilex lozenge – available without a prescription

        - 2 mg or 4 mg/lozenge, 8–20 lozenges/day
        - generic $122.40, Commit $124.80
    - nicotine transdermal – available without a prescription
        - 7 mg, 14 mg or 21 mg/24 hour patch
        - generic $76.50, NicoDerm CQ $103.20
- varenicline (Chantix) 0.5 and 1 mg tablets; dosing 1 mg twice daily, $129.60
- second-line medications (not FDA approved for smoking cessation)
    - clonidine
        - orally available as 0.1, 0.2 or 0.3 mg tablets; dosing 0.2 or 0.3 mg twice daily, generic $15.60, Catapres $113.40
        - transdermally as 0.1, 0.2 or 0.3 mg/day patches; dosing 1 patch/week, Catapres TTS $163.68
    - nortriptyline 10, 25, 50 or 75 mg capsules; dosing 25 mg 3–4 times daily, generic $61.20
- Reference – Treat Guidel Med Lett 2008 Sep;6(73):61 TOC

Other management:

Reduced nicotine content cigarettes:

- **0.05 mg nicotine cigarette associated with increased rate of smoking cessation at 6 weeks compared with 0.3 mg nicotine cigarette (level 2 [mid-level] evidence)**
    - based on randomized trial with high dropout rate
    - 165 community-dwelling smokers randomized to 0.05 mg nicotine cigarettes vs. 0.3 mg nicotine cigarettes vs. 4 mg nicotine lozenges for 6 weeks
    - 58% completed 6-week follow-up
    - biochemically verified abstinence 47.2% for 0.05 mg nicotine cigarette group vs.
        - 23.1% for 0.3 mg nicotine cigarette group (p = 0.04)
        - 36.7% for nicotine lozenge group (not significant)
    - Reference – Addiction 2010 Feb;105(2):343, editorial can be found in Addiction 2010 Feb;105(2):356

Smoking cessation strategies for hospitalized patients:

- counseling interventions that include hospital contact and at least 1 month of follow-up contact are effective in promoting smoking cessation in hospitalized patients (level 1 [likely reliable] evidence)
- behavior modification counseling plus pharmacotherapy for 12 weeks may increase smoking cessation rates and reduce mortality in hospitalized smokers (level 2 [mid-level] evidence)
- psychosocial interventions may be effective for smoking cessation in patients with coronary artery disease (level 2 [mid-level] evidence)
- single session interventions lasting 20–30 minutes delivered within routine care during hospitalization NOT likely to influence highly dependent smokers
- insufficient evidence to evaluate benefit of adding nicotine replacement therapy or bupropion to counseling interventions in hospitalized smokers

- see Smoking cessation strategies for hospitalized patients for details

Perioperative smoking cessation:

- **intensive preoperative smoking cessation interventions reduce risk of postoperative complications (level 1 [likely reliable] evidence)**
    - based on systematic review
    - systematic review of 9 randomized trials (11 publications) of smoking cessation interventions in 1,194 patients with planned surgery
    - postoperative complications evaluated included
        - events causing additional treatment or investigation
        - prolonged hospital stay
        - unscheduled postoperative checkups
        - wound complications
    - intensive smoking cessation interventions evaluated in 2 trials (237 patients)
        - intensive interventions included
            - weekly counseling (4 weeks in 1 trial, 6–8 weeks in 1 trial)
            - nicotine replacement therapy
        - surgeries included
            - hip or knee alloplasty
            - laparoscopic cholecystectomy
            - hernia

        - both trials met all quality criteria
        - in pooled analysis of these 2 trials (210 patients) postoperative complications occurred in 19% intervention vs. 46% control patients ($p < 0.05$, NNT 4)
    - interventions in other trials (less intensive interventions) included bupropion or nicotine replacement therapy and/or limited short-term counseling
        - surgeries included cardiovascular, ophthalmological, urological, gynecological, and non-cardiac elective
        - in pooled analysis of 4 of these trials reporting postoperative complications (342 patients) postoperative complications occurred in 11% intervention vs. 16% control patients (not significant)
    - Reference – Br J Surg 2009 May;96(5):451
    - similar results in Cochrane review of 8 randomized trials (including 7 of these trials) (Reference – Cochrane Database Syst Rev 2010 Sep 08;(9):CD002294)
- **perioperative smoking cessation associated with reduced risk for postoperative complications (level 2 [mid-level] evidence)**
    - based on randomized trial without adequate statistical power
    - 117 patients aged 18–79 years having elective abdominal or orthopedic surgery who smoked > 2 cigarettes daily were randomized to smoking cessation program vs. standard care and followed for 30 days after surgery
    - smoking cessation program included weekly individual counseling and nicotine replacement 4 weeks before and 4 weeks after surgery
    - 87% follow-up rate at 30 days
    - overall complication rate was 21% for smoking cessation group vs. 41% for standard care ($p = 0.03$, NNT 5) in intention-to-treat analysis
    - Reference – Ann Surg 2008 Nov;248(5):739
- **postoperative smoking cessation program may decrease complications after acute fracture surgery (level 2 [mid-level] evidence)**
    - based on randomized trial without attention control
    - 105 patients who smoked and had fracture of lower or upper extremity needing acute surgical treatment were randomized to smoking

cessation program for 6 weeks vs. no additional support and followed for 12 weeks
    - complications included infections, skin breakdown, neurological complications, deep vein thrombosis and pulmonary embolus
    - comparing smoking intervention vs. no intervention
        - postoperative complications in 20% vs. 38% (p = 0.048, NNT 6)
        - most common complication was superficial wound infection in 8% vs. 20% (not significant)
    - Reference – J Bone Joint Surg Am 2010 Jun;92(6):1335

Aversion techniques:

- **insufficient evidence to determine efficacy of rapid smoking; other aversion treatments appear ineffective for smoking cessation (level 2 [mid-level] evidence)**
    - based on Cochrane review of mostly low-quality trials
    - systematic review of 25 randomized trials including 12 trials of rapid smoking and 9 trials of other aversion treatments
    - rapid smoking protocol in most trials was puffing cigarette every 6–10 seconds for 3 minutes, consumption of 3 cigarettes or inability to continue; then repeating 2–3 times in one session; 3–10 sessions of rapid smoking over 1–4 weeks
    - rapid smoking increased rate of abstinence at long-term follow-up in analysis of 12 trials with 536 patients
        - odds ratio 2.01, 95% CI 1.36–2.95, NNT 5–18 assuming 22% cessation rate in controls
        - most trials had serious methodological flaws and funnel plot suggests publication bias
        - only 1 trial used biochemical validation of smoking cessation and did not find significant results
    - dose-response relationship between level of aversive stimulation and abstinence at long-term follow-up had borderline statistical significance (odds ratio 1.67, 95% CI 0.99–2.81) in analysis of 10 trials with 326 patients
    - other aversive therapies not shown to be effective (odds ratio 1.15, 95% CI 0.73–1.82) in analysis of 9 trials with 475 patients
    - Reference – Cochrane Database Syst Rev 2010 Jan 20;(1):CD000546

Inpatient (residential) treatment:

- **inpatient (residential) treatment may be more effective than outpatient treatment for nicotine dependence (level 2 [mid-level] evidence)**
    - based on cohort study
    - comparing 146 patients treated in a Mayo Clinic residential nicotine dependence program vs. 292 matched patients who had an outpatient nicotine dependence consultation by a trained counselor
        - 6-month abstinence rates 45% vs. 26% ($p < 0.001$, NNT 6)
        - 12-month abstinence rates 45% vs. 23% ($p < 0.001$, NNT 5)
    - Reference – Mayo Clin Proc 2001 Feb;76(2):124, editorial can be found in Mayo Clin Proc 2001 Feb;76(2):121
    - *DynaMed commentary* -- differences in motivational levels were not measured and could easily account for differences in outcomes because voluntary hospital admission would require significant motivation

Acupuncture:

- **acupuncture may increase smoking cessation in short-term but not long-term compared to sham acupuncture (level 2 [mid-level] evidence)**
    - based on Cochrane review with poor reporting of methodology
    - systematic review of 33 randomized trials evaluating acupuncture, acupressure, laser therapy and electrostimulation for smoking cessation
    - many included trials did not report or had unclear method of randomization, baseline characteristics or allocation concealment
    - comparing acupuncture to sham acupuncture
        - acupuncture more effective for smoking cessation in short-term in analysis of 12 trials (14 comparisons) with 2,206 patients
            - risk ratio 1.18 (95% CI 1.03-1.34)
            - NNT 11-127 assuming 26% smoking cessation in sham group
            - results limited by significant heterogeneity
        - no significant difference in smoking cessation in long-term in analysis of 7 trials with 1,662 patients

- acupuncture less effective for smoking cessation in both short- and long-term compared to nicotine replacement therapy in analyses of 2 trials with 914 patients
- no significant difference in smoking cessation comparing acupuncture to psychological interventions in both short- and long-term in analyses of 3 trials with 396 patients
- electrostimulation results reported in transcranial stimulation section below
- insufficient evidence to evaluate acupressure or laser therapy for smoking cessation
- Reference – Cochrane Database Syst Rev 2011 Jan 19;(1):CD000009

- **acupuncture appears no more effective than sham acupuncture for smoking cessation (level 2 [mid-level] evidence)**
  - based on review of 39 systematic reviews (BMC Complement Altern Med 2001;1:3 full-text), summary can be found in NHS CRD Effective Health Care bulletin 2001 Nov;7(2) PDF
  - based on meta-analysis of 15 poor quality trials (Br J Gen Pract 1990 Sep;40(338):379 PDF)
- **electroacupuncture may not reduce tobacco use or nicotine withdrawal symptoms ((level 2 [mid-level] evidence))**
  - based on randomized trial with high dropout rate
  - 76 adults who wanted to stop smoking randomized to 100 hertz electroacupuncture with needles inserted into appropriate point in each ear vs. sham control procedure over mastoid bone with interventions given on days 1, 3 and 7 of smoking cessation
  - 32% dropout/withdrawal rate
  - no significant difference in mean reduction of nicotine withdrawal symptom scores in daily diary from day 1 to day 14
  - objectively confirmed tobacco abstinence on day 14 in 39% vs. 42% (not significant)
  - Reference – Arch Intern Med 1998 Nov 9;158(20):2251 full-text, commentary can be found in Arch Intern Med 1999 Jun 14;159(11):1256

Transcranial stimulation:

- **electrostimulation may not be effective for smoking cessation (level 2 [mid-level] evidence)**
    - based on Cochrane review of trials with poor reporting of methodology
    - systematic review of 33 randomized trials evaluating acupuncture, acupressure, laser therapy and electrostimulation for smoking cessation
    - included trials did not report or had unclear method of randomization or baseline characteristics
    - 5 trials compared electrostimulation to sham electrostimulation
        - no significant difference in smoking cessation in short-term in analysis of 4 trials with 462 patients
        - no significant difference in smoking cessation in long-term in analysis of 2 trials with 405 patients
    - Reference – Cochrane Database Syst Rev 2011 Jan 19;(1):CD000009

- **repeated transcranial magnetic stimulation may reduce short-term cigarette consumption and craving (level 2 [mid-level] evidence)**
    - based on small randomized trial
    - 52 healthy chronic smokers randomized to sham vs. real repeated transcranial magnetic stimulation (rTMS) of left dorsolateral prefrontal cortex (10 sessions daily for 10 days)
    - real rTMS associated at day 10 with
        - reduced nicotine consumption (by cotinine-to-creatinine ratio) ($p < 0.02$)
        - reduced self-reported cigarette consumption ($p < 0.0001$)
        - reduced nicotine dependence scores ($p < 0.0001$)
    - similar findings in subgroups observing smoking-related or neutral pictures prior to daily rTMS
    - high drop-out rate prevented analysis of month-long maintenance phase
    - Reference – Addiction 2009 Apr;104(4):653
- **transcranial direct current stimulation may reduce tobacco cravings (level 3 [lacking direct] evidence)**
    - based on small randomized crossover trial without clinical outcomes
    - 24 smokers randomized to sham vs. active transcranial direct current stimulation of the left and right dorsolateral prefrontal cortex

- smoking craving cues included cigarette manipulation and smoking video exposure
- transcranial direct current stimulation reduced craving with ($p = 0.005$) and without ($p = 0.007$) smoking-craving cues
- smoking cessation rates not reported
- Reference – J Clin Psychiatry 2008 Jan;69(1):32

Hypnotherapy:

- **hypnotherapy may not improve 6-month quit rates compared to other interventions or no intervention (level 2 [mid-level] evidence)**
  - based on Cochrane review limited by clinical heterogeneity
  - systematic review of 11 randomized trials evaluating hypnotherapy for smoking cessation in approximately 1,120 patients
  - heterogeneity of control interventions limited analyses; overall metaanalysis not performed
  - no significant difference in outcomes comparing hypnosis of varying durations vs. attention, advice, fenfluramine, placebo drug, rapid smoking or psychological treatment
  - hypnotherapy increased 12-month point prevalence cessation rate compared to wait list in 1 trial with 20 patients
  - insufficient evidence to compare hypnotherapy to counselling
  - Reference – Cochrane Database Syst Rev 2010 Oct 6;(10):CD001008

- hypnotizability reportedly associated with success in maintaining tobacco abstinence for 2 years in 23% of smokers
  - based on cohort of 226 participants in smoking cessation program who were referred to one session of hypnosis
  - Reference – Am J Psychiatry 1993 Jul;150(7):1090
- practical review of medical applications of hypnosis can be found in Aust Fam Physician 1994 Sep;23(9):1744

Switching type of tobacco use:

- arguments for and against advocating snus and other smokeless tobacco as nicotine replacements for cigarettes can be found in BMJ 2008 Feb 16;336(7640):358 and BMJ 2008 Feb 16;336(7640):359

- for cigarette smokers unable to quit, switching to pipes or cigars may reduce risk of smoking-associated diseases by about 50% (BMJ 1997 Jun 28;314(7098):1860 in QuickScan Reviews in Fam Pract 1998 Jan;22(10):20), commentary can be found in BMJ 1998 Mar 14;316(7134):862

Reduced smoking prior to quitting:

- **reducing smoking prior to quit date and abrupt quitting appear similarly effective for smoking cessation (level 2 [mid-level] evidence)**
    - based on Cochrane review of trials with methodologic limitations
    - systematic review of 10 randomized trials of smoking cessation interventions that included at least 1 condition in which participants reduced smoking prior to quit date and at least 1 condition in which participants quit abruptly
    - 3,760 participants
    - interventions included
        - pharmacotherapy in 3 trials
        - behavioral support in 6 trials
        - self-help therapy in 5 trials
    - methodologic limitations included
        - unclear allocation concealment
        - lack of blinding
        - lack of intention-to-treat analysis
    - no significant differences in abstinence rates comparing reduced smoking vs. abrupt quitting in analysis of
        - all trials
        - trials with pharmacotherapy interventions
        - trials with behavioral support
        - trials with self-help therapy
    - Reference – Cochrane Database Syst Rev 2010 Mar 17;(1):CD008033

School-based curricula:

- **school-based curriculum may be effective for motivated adolescents (level 2 [mid-level] evidence)**
    - based on randomized trial without attention control

    - 74 high school students interested in quitting smoking were randomized to classroom-based smoking cessation curriculum designed for adolescents (8 sessions over 6 weeks) vs. informational pamphlet on how to quit smoking with classroom curriculum provided 3 months later
    - participants attended mean 4.4 sessions
    - comparing intervention group vs. control
        - smoke-free at end of curriculum 59% vs. 17% ($p < 0.001$, NNT 24)
        - smoke-free 4 weeks later 52% vs. 20% ($p = 0.01$, NNT 3)
    - Reference – Pediatrics 2001 Apr;107(4):E50 full-text
- **reformatting of school-based smoking cessation programs into shorter, more numerous sessions does not appear to have significant benefit (level 2 [mid-level] evidence)**
    - based on randomized trial with high loss to follow-up
    - 407 adolescents (mean age 16 years) interested in smoking cessation were randomized to reformatted vs. standard Not on Tobacco (NOT) or Kickin' Butts programs
    - follow-up in 62%
    - reformatted vs. standard protocols
        - 15 lunch sessions of 25-30 minutes each vs. 8 sessions of 50 minutes each for Kickin' Butts program
        - 20 lunch sessions of 25-30 minutes each vs. 10 sessions of 50-minutes each for NOT program
    - quit rate with reformatted vs. standard protocol
        - no significant differences for Kickin' Butts program
        - 28% vs. 15% at 1 month after end of program by self-report for NOT program ($p < 0.05$) (no significant difference by cotinine-confirmed quit rates)
        - no differences in self reported or saliva cotinine-confirmed quit rates for either program at end of program or at 3, 6 and 12 month follow-up
    - Reference – Pediatrics 2009 Aug;124(2):e187

Incentives and Competitions:

- **incentives and competitions do not appear to increase long-term cessation rates (level 2 [mid-level] evidence)**
    - based on Cochrane review limited by heterogeneity

    - systematic review of 17 randomized and controlled trials evaluating competitions and incentives for smoking cessation
    - comparing competitions and incentives vs. control
        - competitions and incentives associated with higher cessation rates at 6 months ($p = 0.042$), but results may be limited by heterogeneity ($p = 0.09$)
        - no significant differences as 12, 18 or 24 months, but results at 12 months may be limited by heterogeneity ($p = 0.02$)
    - rewarding participation may improve recruitment rates, but no clear differences in cessation rates
    - Reference – Cochrane Database Syst Rev 2008 Jul 16;(3):CD004307
- **quit and win contests may increase reported quit rates but results subject to high levels of deception and unlikely to have substantial impact at population level**
    - based on Cochrane review
    - systematic review of 5 randomized or controlled trials evaluating quit and win contests for smoking cessation
    - Reference – Cochrane Library 2005 Issue 2:CD004986
- **company-sponsored financial incentives associated with increased short and long-term quit rates (level 2 [mid-level] evidence)**
    - based on randomized trial without blinding
    - 878 employees of 1 company in United States randomized to information about smoking-cessation programs plus financial incentives (≤ $750) vs. information about smoking-cessation programs only
    - employees followed for 12 months (or 18 months if confirmed negative result within first 12 months)
    - smoking cessation confirmed by cotinine test
    - comparing financial incentives vs. information only
        - smoking cessation within 6 months of enrollment in 20.9% vs. 11.8% ($p < 0.001$, NNT 11)
        - smoking cessation at 9 or 12 months in 14.7% vs. 5% ($p < 0.001$, NNT 11)
        - smoking cessation at 15 or 18 months in 9.4% vs. 3.6% ($p < 0.001$, NNT 18)
        - enrollment in smoking-cessation program in 15.4% vs. 5.4% ($p < 0.001$, NNT 10)

        - completion of smoking-cessation program in 10.8% vs. 2.5% ($p < 0.001$, NNT 12)
    - Reference – N Engl J Med 2009 Feb 12;360(7):699 full-text

Work-based approaches:

- **workplace interventions focused on individual smokers may reduce smoking (level 2 [mid-level] evidence)**
    - based on Cochrane review of trials with allocation concealment not stated
    - systematic review of 51 randomized or quasi-randomized trials evaluating 53 workplace interventions to promote smoking cessation
    - only 6 trials reported allocation concealment
    - 37 trials focused on individual workers, 16 trials applied to the workplace as a whole
    - interventions with strong evidence for benefit were those directed towards individual smokers
        - individual counseling
        - group counseling
        - nicotine replacement therapy
    - smoking cessation in 10.9% with individual behavioral therapy vs. 7.4% in controls in analysis of 11 trials with 2,271 participants ($p = 0.00029$, NNT 29)
    - self-help interventions were less effective
    - interventions which do not clearly help smokers quit at work
        - workplace-level environmental support (4 trials with 1,111 participants)
        - social support
        - competitions
        - incentives (4 trials with 1,050 participants)
    - competitions and incentives may increase uptake of other interventions
    - Reference – Cochrane Database Syst Rev 2008 Oct 8;(4):CD003440

Population-based approaches:

- **health care financing systems that fully support smoking cessation treatments may modestly improve smoking cessation rates (level 2 [mid-level] evidence)**

- based on Cochrane review of trials with methodologic limitations
- systematic review of 9 randomized trials and controlled studies evaluating financial benefit interventions to smokers and/or their healthcare providers
- limitations included unclear or adequate allocation concealment, follow-up rate 80%, and possible differences in baseline characteristics
- in patient-focused trials, full financial coverage significantly improved outcomes compared with no coverage
  - abstinence in 9.5% vs. 5.6% in analysis of 4 trials with 2,760 participants (NNT 26)
  - quit attempts in 35.6% vs. 30.5% in analysis of 3 trials with 2,540 participants (NNT 20)
  - increased utilization of nicotine replacement therapy, bupropion, or behavioral interventions
- no significant effect on abstinence rates
  - comparing full vs. partial financial coverage
  - comparing partial vs. no financial coverage
  - in 2 trials with interventions directed at healthcare providers
- cost per additional quitter ranged from $260 to $1,453, comparing full vs. partial or no financial benefit
- Reference – Cochrane Database Syst Rev 2009 Apr 15;(2):CD004305

- **comprehensive tobacco control programs which include mass media campaigns may be effective in changing smoking behavior in adults, but intensity and duration of campaigns may influence effectiveness (level 2 [mid-level] evidence)**
  - based on Cochrane review limited by heterogeneity
  - systematic review of 11 controlled trials evaluating mass media interventions in communities, regions or states to encourage smokers to quit (target audience was adults at least 25 years old who regularly smoked cigarettes)
  - mass media defined as channels of communication such as television, radio, newspapers, billboards, posters, leaflets or booklets intended to reach large numbers of people, not dependent on person-to-person contact

- statewide tobacco control campaigns in California and Massachusetts associated with decreased smoking prevalence compared to rest of United States
- studies differed in design, settings, duration, content and intensity of intervention, length of follow-up, methods of evaluation, and definitions and measures of smoking behavior used
- 1 state-wide tobacco control program (Massachusetts) showed positive results up to 8 years after the campaign, but another state-wide program (California) showed positive results only during period of adequate funding and implementation
- 6 of 9 studies conducted in communities or regions showed some positive effects on smoking behavior and at least 1 significant change in smoking prevalence
- Reference – systematic review last updated 2007 Nov 12 (Cochrane Library 2008 Issue 1:CD004704)

Treatment of non-cigarette tobacco use:

- **insufficient evidence to guide medication selection for cessation of smokeless tobacco use**
  - based on systematic review with limited description of methodology
  - 4 randomized trials evaluated nicotine patch and had conflicting results
  - 2 randomized trials evaluated nicotine gum and had conflicting results
  - 2 randomized trials evaluated bupropion, significantly increased quit rates at 7 weeks in 1 trial but differences at 12 weeks not statistically significant in either trial
  - no published evidence found for varenicline
  - Reference – J Fam Pract 2008 Apr;57(4):238
- **no trials of smoking cessation interventions for waterpipe smokers identified**
  - based on Cochrane review
  - no randomized, quasi-randomized or cluster-randomized trials of smoking cessation interventions for waterpipe smokers identified
  - Reference – systematic review last updated 2007 Aug 9 (Cochrane Library 2007 Issue 4:CD005549)

Follow-up:

Follow-up visits:

- clinicians should try to meet ≥ 4 times with individuals quitting tobacco use (PHS Strength of Evidence A)[1]
- all patients who receive a tobacco dependence intervention should be assessed for abstinence at completion of treatment and during subsequent contacts (PHS Strength of Evidence C)[1]
    - abstinent patients should have their quitting success acknowledged, and clinician should offer to assist patient with problems associated with quitting
    - patients who have relapsed should be assessed to determine whether they are willing to make another quit attempt

Relapse prevention:

- self-monitoring (for example, cigarette use diary) increases preventive behaviors and may increase success rate (Patient Educ Couns 1997 Nov;32(3):157 in Evidence-Based Medicine 1998 May/Jun;3(3):85)
- **insufficient evidence to support any specific behavioral intervention for relapse prevention in smokers who have successfully quit, but extended varenicline treatment may reduce relapse (level 2 [mid-level] evidence)**
    - based on Cochrane review with differential loss to follow-up in varenicline trial
    - systematic review of 54 randomized or quasi-randomized trials evaluating relapse prevention interventions in persons already abstaining from smoking with minimum 6 months follow-up
    - no significant differences between behavioral interventions and control in 36 trials that randomized persons who already quit or 18 trials that randomized persons prior to quit date
    - extended treatment with varenicline significantly reduced relapse rate in 1 trial
    - nicotine gum significantly reduced relapse rate by 12 months in analysis of 2 trials with 2,261 participants ($p = 0.014$, NNT 25), period of unassisted abstinence before trial entry considered short in both these trials

- 2 trials of nicotine replacement (gum in 1 trial, inhaler in 1 trial) did not find significant long-term effect in 553 patients with abstinence following cessation therapy
- extended treatment with bupropion associated with nonsignificant trend toward reduced relapse in analysis of 5 trials with 1,587 participants (p = 0.064)
- Reference – Cochrane Database Syst Rev 2009 Jan 21;(1):CD003999, earlier version also published in Arch Intern Med 2006 Apr 24;166(8):828

Relapse intervention:

- patients who have relapsed should be assessed for willingness for another quit attempt (PHS Strength of Evidence C)[1]
- **repeated cycles of pharmacotherapy associated with quitting following treatment failure (level 2 [mid-level] evidence)**
  - based on cohort of 726 smokers who were offered up to 4 courses of smoking cessation pharmacotherapy over 2 years
  - Reference – Arch Intern Med 2009 Nov 9;169(20):1928

Weight gain:

- **smoking cessation and weight gain**
  - risk of weight gain highest during first 2 years after smoking cessation
  - sustained quitter gained average 5–6 kg (11–13 lb)
  - physical exercise, older age, higher baseline body mass index and lower rates of smoking reduce amount of weight gained after smoking cessation
  - evidence on permanence of expected weight gain conflicting
  - Reference – literature review in J Fam Pract 1998 Jun;46(6):460
  - **weight gain over 10-year period associated with smoking cessation was 4.4 kg (9.7 lb) for men and 5 kg (11 lb) for women**
    - based on surveys of 5,247 adults > 35 years old
    - Reference – N Engl J Med 1995 Nov 2;333(18):1165 in QuickScan Reviews in Fam Pract 1996 Apr:7
- **insufficient evidence to support or refute specific interventions for preventing weight gain after smoking cessation**

- based on Cochrane review
- systematic review of trials evaluating smoking cessation and post-cessation weight gain
- pharmacologic interventions aimed at reducing post-cessation weight gain associated with significant reduction in weight gain at end of treatment, but no evidence of maintenance of treatment effect seen at 6 or 12 months
    - dexfenfluramine had mean difference −2.5 kg (95% CI −2.98 kg to −2.02 kg) in 1 trial with 33 patients
    - phenylpropanolamine had weighted mean difference (WMD) −0.5 kg (95% CI −0.8 kg to −0.2 kg) in analysis of 3 trials with 112 patients
    - fluoxetine (30 mg or 60 mg daily) associated with reduced weight gain at end of treatment compared to placebo in 1 trial with 119 patients (mean difference −1.3 kg, 95% CI −1.91 kg to −0.69 kg)
    - fluoxetine had mean difference −0.8 kg (95% CI −1.27 kg to −0.33 kg) in 1 trial with 25 patients
    - bupropion 300 mg/day associated with reduced weight gain at end of treatment compared to placebo in analysis of 6 trials with 774 patients (WMD −1.11 kg, 95% CI −1.57 kg to −0.76 kg)
        - no evidence that the weight reducing effect of bupropion was dose-dependent
        - effect of bupropion at 1 year was smaller and confidence intervals included no effect (−0.38 kg [−2.001 kg to 1.24 kg])
    - nicotine replacement therapy
        - nicotine replacement therapy associated with attenuation of post-cessation weight gain at end of treatment (−0.45 kg, 95% CI −0.7 kg to −0.2 kg)
        - no evidence that effect differed for different forms of nicotine replacement therapy
        - results no longer significant at 12 months
    - naltrexone had mean difference −0.76 kg (95% CI −1.51 kg to −0.01 kg) in 1 trial with 157 patients
    - varenicline

        - no evidence that varenicline significantly reduced post-cessation weight gain at end of treatment in analysis of 6 trials with 1,092 patients
        - no follow-up data currently available
        - varenicline associated with more weight gain than bupropion in analysis of 3 trials with 598 patients
        - no significant differences in weight gain comparing varenicline vs. nicotine replacement therapy in 1 trial with 319 patients
      - no relevant data on effect of rimonabant on weight gain
    - lifestyle interventions
      - individualized programs associated with reduced weight gain at end of treatment and at 12 months (WMD −2.58 kg, 95% CI −5.11 kg to −0.05 kg), with no effect on abstinence
      - very low calorie diets associated with improved abstinence and reduced weight gain at end of treatment and at 12 months (WMD −1.3 kg, 95% CI −3.49 kg to 0.89 kg at 12 months)
      - cognitive behavioral therapy (CBT) associated with improved abstinence and reduced weight gain at end of treatment and at 12 months (WMD −5.2 kg, 95% CI −9.28 kg to −1.12 kg at 12 months)
      - weight control advice associated with possible reduction in abstinence, but not associated with reduction in weight gain
      - exercise interventions did not reduce post-cessation weight gain at end of treatment, but evidence for significant effect seen at 12 months (−2.1 kg, 95% CI −3.78 kg to −0.36 kg)
    - Reference – Cochrane Database Syst Rev 2009 Jan 21;(1):CD006219
- addition of weight-control program modestly increased long-term rate of smoking cessation, although weight reduction not achieved in trial of 287 women (BMJ 1999 Aug 21;319(7208):490 full-text)

Other concerns after smoking cessation:

- **cold symptoms and mouth ulcers may occur in first week or two after smoking cessation**
    - study of 174 patients who smoked at least 10 cigarettes/day for 3 years and attended 6-week smoking cessation treatment program

    - 127 (73%) were abstinent at 1 week
    - among these 127 quitters at 1 week
        - 100 (79%) developed new cough
        - 25 (20%) developed sneeze (while 7 [6%] lost a sore throat)
        - 25 (20%) developed new sore throat (while 12 [9%] lost a sore throat)
        - 17 (13.4%) developed new mouth ulcers (while 1 [0.8%] lost an ulcer)
    - Reference – Tob Control 2003 Mar;12(1):86 PDF
- **smokers with history of major depression are at significant risk for recurrence of depression after smoking cessation**
    - 100 smokers with history of major depression were randomized to sertraline vs. placebo for 11 weeks for smoking cessation, results from this trial not reported
    - 76 patients were followed 6 months after end of trial
    - 13 (31%) of 42 abstainers and 2 (6%) of 34 smokers had symptoms of major depression during follow-up
    - Reference – Lancet 2001 Jun 16;357(9272):1929, editorial can be found in Lancet 2001 Jun 16;357(9272):1900, commentary can be found in Lancet 2001 Sep 22;358(9286):1011, summary can be found in Am Fam Physician 2002 Jan 15;65(2):313

Prevention and Screening

- see below for Screening

Prevention:

Family based approaches:

- **family-based programs may prevent adolescent smoking (level 2 [mid-level] evidence)**
    - based on Cochrane review with mixed results
    - systematic review of 20 randomized trials of family interventions to prevent tobacco use in children (aged 5–12 years) or adolescents (aged 13–18 years)
        - 6 trials had minimal risk of bias

        - 9 trials had risk of bias in 1 or more areas
        - 5 trials had risks of bias in design and execution limiting reliability of conclusions
    - evaluating 15 trials with lower risk of bias
        - comparing family intervention vs. control, 4 of 9 trials had significant positive effects and 1 trial showed significant negative effects
        - comparing family intervention vs. school intervention in 1 of 5 trials had significant positive effect
        - none of 6 trials comparing incremental effects of family plus school program vs. school program alone had significant positive effects
        - no effect comparing family tobacco intervention vs. family non-tobacco safety intervention
    - in 2 trials that did not have a specific tobacco intervention
        - general risk reduction intervention given to parent and teen associated with less smoking than intervention given to teen only in 1 trial
        - interventions to reduce alcohol use associated with less smoking than control in 1 trial
    - Reference – systematic review last updated 2006 Nov 10 (Cochrane Library 2007 Issue 1:CD004493)
- **parental disapproval of smoking may be effective (level 2 [mid-level] evidence)**
    - based on cross-sectional and longitudinal study of about 700 children per year over 3 years
    - adolescents who perceive that both parents would respond negatively and be upset by their smoking are less likely to smoke
    - Reference – Pediatrics 2001 Dec;108(6):1256
- **parental monitoring intervention may reduce substance use when added to adolescent risk-reduction intervention (level 2 [mid-level] evidence)**
    - based on randomized trial without adequate attention control
    - 817 African American youth aged 13-16 years in 35 low-income, urban sites participated in Focus On Kids (8-session, small group risk-reduction intervention)

- youth and parents randomized to no additional treatment vs. ImPACT (1 session for parents and youth with videotape and discussion, then parental monitoring, half of the ImPACT group also had 4 Focus On Kids booster sessions)
- comparing youth who had risk-reduction intervention without vs. with ImPACT over 2 years
  - mean number of days suspended 1.17 vs. 0.65
  - 9.6% vs. 4.1% carried bat as a weapon
  - 22.7% vs. 12.5% smoked cigarettes
  - 26.8% vs. 18.3% used marijuana
  - 5.6% vs. 1.4% used other illicit drugs
- Reference – Arch Pediatr Adolesc Med 2004 Oct;158(10):947 full-text

- **increased frequency of family meals (≥ 5 per week) may decrease substance use among female adolescents (level 2 [mid-level] evidence)**
  - based on retrospective longitudinal cohort study with high dropout rate
  - 806 adolescents in public schools completed surveys at mean age 12.7 years and at mean age 17 years
  - ≥ 5 family meals/week associated with reduced
    - cigarette smoking (odds ratio [OR] 0.47, CI 0.29–0.75)
    - alcohol use (OR 0.49, CI 0.29–0.83)
    - marijuana use (OR 0.49, CI 0.26–0.93)
  - no significant association with any substance use among males
  - Reference –J Adolesc Health 2008 Aug;43(2):151
- **increased frequency of family meals associated with decreased substance use and depressive symptoms in teenagers (level 2 [mid-level] evidence)**
  - based on cross-sectional survey
  - 4,734 teenagers (mean age 15 years) in 31 public schools in Minneapolis/St. Paul area surveyed
  - about 25% reported eating 7 or meals per week with their family
  - > 33% reported eating < 3 meals per week with their family
  - increased family meal frequency associated with decreasing rates of substance abuse (tobacco, marijuana and alcohol), depressive symptoms, suicidal ideation and suicidal attempts, and increasing grade-point average

    - Reference – Arch Pediatr Adolesc Med 2004 Aug;158(8):792 in QuickScan Reviews in Fam Pract 2005 Jan 31;30(8):1, summary can be found in Am Fam Physician 2005 Mar 15;71(6):1192
- **positive family management practices may reduce escalation to daily smoking in adolescents (level 2 [mid-level] evidence)**
    - based on subgroup analysis of prospective cohort study
    - 270 adolescents reporting no daily cigarette smoking in 7th grade and smoking by 8th grade were assessed by survey for daily smoking in 12th grade
    - progression to daily smoking significantly associated with
        - antisocial behavior
        - parental smoking
        - peer smoking
    - parental use of positive family management practices (appropriate use of consequences for and monitoring of child's behavior) significantly associated with decreased risk of progression to daily smoking
    - Reference – Pediatrics 2009 Sep;124(3):888
- **supporting smoking parents to provide antismoking socialization of children can reduce children's initiation of smoking (level 2 [mid-level] evidence)**
    - based on randomized trial without adequate attention control
    - 873 parents–offspring pairs in which parents were current smokers and child was in third grade and had not tried smoking were randomized to intervention vs. control
    - intervention group received 5 printed activity guides, parenting tip sheets, child newsletters and incentives over 3 months, then booster activity guide 1 year later; control group received fact sheets about smoking
    - 776 children (89%) evaluated at 3 years (sixth grade)
    - 12% intervention children vs. 19% control children reported initiation of smoking (first instance of puffing on a cigarette) ($p < 0.001$, NNT 15)
    - Reference – Arch Pediatr Adolesc Med 2006 Jan;160(1):56

Enforcement of minor purchase laws:

- **active enforcement and multicomponent educational strategies may decrease illegal sales of tobacco to minors but may not lead to achievement of sustained compliance (level 2 [mid-level] evidence)**

- based on Cochrane review without statistical analysis
- systematic review of 14 controlled trials and 21 uncontrolled studies evaluating interventions to deter shopkeepers from selling tobacco to minors
- interventions included education about legal requirements, notification of results of compliance checks, warning of enforcement, and implementation of enforcement by police or health officials
- most trials assessed retailer compliance by use of test purchasers
- active enforcement and/or multicomponent educational strategies more effective in reducing illegal sales than providing information to retailers
- no strategy achieved complete, sustained compliance
- little effect of intervention on youth perceptions of access to tobacco products or prevalence of youth smoking in 3 controlled trials
- Reference – Cochrane Database Syst Rev 2008 Jul 16;(3):CD001497

- **interventions to prevent ability of teenagers to purchase cigarettes do not appear associated with prevalence of youth smoking (level 2 [mid-level] evidence)**
  - based on systematic review of cross-sectional studies
  - systematic review of 9 studies found no correlation between level of merchant compliance and prevalence of youth smoking
  - Reference – Pediatrics 2002 Jun;109(6):1088 full-text

School-based interventions:

- **limited evidence that school-based programs are effective for preventing smoking**
  - based on Cochrane review
  - systematic review of 94 randomized trials of behavioral interventions in schools to prevent smoking initiation in children aged 5-18 years
    - 23 trials of high quality
  - social influence interventions evaluated in 13 high quality trials
    - 9 trials reported some positive effects on smoking prevalence, 4 did not show significant effects
    - the most rigorous study, the Hutchinson Smoking Prevention Project, found no long-term effect on smoking behavior of an intensive 8-year program with 65 lessons

    - results inconclusive in trials evaluating
        - information giving (1 higher quality trial)
        - teaching social competence (2 higher quality trials)
        - combined social influences and social competence interventions (3 higher quality trials)
    - Reference – systematic review last updated 2006 Apr 20 (Cochrane Library 2006 Issue 3:CD001293)
- **school-based tobacco use prevention programs appear effective for short-term reduction in smoking prevalence**
    - based on systematic review
    - Reference – Prev Med 2008 Apr;46(4):289
- **peer-led school-based intervention may be effective for adolescent smoking prevention after 1 year but less effective after 2 years (level 2 [mid-level] evidence)**
    - based on cluster-randomized trial without intention-to-treat analysis
    - 59 schools in England and Wales randomized to peer-led intervention (5,372 students) vs. usual smoking education (5,358 students) for students aged 12–13 years
    - for peer-led intervention, influential students were trained to provide information to other students about effects of smoking and benefits of not smoking in informal conversations
    - comparing peer-led intervention vs. usual smoking education
        - weekly smoking in 12.49% vs. 15.13% at 1 year follow-up (adjusted odds ratio 0.77, p = 0.043)
        - weekly smoking in 18.95% vs. 21.74% at 2 year follow-up (adjusted odds ratio 0.85, p = 0.067)
    - Reference – ASSIST trial (Lancet 2008 May 10;371(9624):1595), editorial can be found in Lancet 2008 May 10;371(9624):1556

Media-based interventions:

- **conflicting evidence exists that mass media can be effective in preventing uptake of smoking in young people (level 2 [mid-level] evidence)**
    - based on Cochrane review
    - systematic review of 7 randomized and other trials evaluating the effect of mass media on the uptake of smoking in young people

    - 3 of 7 trials showed benefit of mass media in preventing uptake of smoking by pre-teens and adolescents and 4 had no effect reported
    - Reference - Cochrane Database Syst Rev 2010 Dec 08;(12):CD001006

- 11.6% decrease in smoking prevalence among men and 15.2% decrease among Hispanics reported in New York City in 2002-2006 following extensive city and state anti-tobacco media campaigns (MMWR Morb Mortal Wkly Rep 2007 Jun 22;56(24):604 full-text)
- **tobacco-control messages emphasizing dangers of secondhand smoke to smokers and nonsmokers reduce social acceptability of smoking**
    - based on previously secret tobacco-industry marketing documents
    - Reference - JAMA 2002 Jun 12;287(22):2983
- Centers for Disease Control and Prevention and United States Preventive Services Task Force report on strategies for reducing exposure to environmental tobacco smoke, increasing tobacco-use cessation, and reducing initiation in communities and health-care systems can be found in Am J Prev Med 2001 Feb;20(2 Suppl):10

Community-based interventions:

- **limited evidence supports effectiveness of community interventions in helping prevent smoking in young people**
    - based on Cochrane review
    - Reference - systematic review of 17 trials last updated 2002 Sep 24 (Cochrane Library 2003 Issue 1:CD001291)
- **community interventions to reduce smoking prevalence in adults have limited effect**
    - based on Cochrane review
    - Reference - systematic review of 32 trials last updated 2002 Jan 15 (Cochrane Library 2002 Issue 3:CD001745)
- **community-based integrated intervention associated with less pulmonary functional decline, increased smoking cessation, and lower mortality in adults (level 2 [mid-level] evidence)**
    - based on cluster-randomized trial with baseline differences
    - 872 patients aged 40-89 years classified as healthy, high-risk for COPD or with COPD randomized by community (in Guangdong, China) to integrated intervention vs. usual care from 2002-2007

        - intervention included systematic health education, treatment and rehabilitation
        - intervention increased in intensity for patients at high risk of or with current COPD to include personalized lifestyle counseling
    - history of occupational dust/gas/fumes at baseline in 34% with intervention vs. 57% with control ($p < 0.001$)
    - integrated intervention associated with lower annual rate of decline in
        - forced expiratory volume in 1 second (FEV_1) ($p < 0.05$)
        - forced vital capacity (FVC) ($p = 0.029$)
    - no significant difference in rate of decline of FEV_1 or FVC in subgroup of 101 patients with COPD
    - comparing integrated intervention vs. standard care
        - smoking cessation in 21% vs. 8% ($p < 0.004$, NNT 8)
        - all-cause mortality 1% vs. 3% ($p < 0.009$, NNT 50)
    - no significant difference in incidence of COPD or death from COPD
    - Reference – BMJ 2010 Dec 1;341:c6387 full-text
    - *DynaMed commentary* -- cement factory in intervention community was relocated in 2005 resulting in decreased outdoor air pollution
- **Drug Abuse Resistance Education (DARE) appears ineffective in preventing use of alcohol, tobacco or illicit drugs (level 2 [mid-level] evidence)**
    - based on systematic review without quality assessment of trials
    - meta-analysis of 11 published controlled trials found no significant effect of DARE program in preventing alcohol, tobacco or illicit drug use in school-aged youth
    - Reference – Am J Public Health 2004 Jun;94(6):1027 full-text
- **DARE Plus program in seventh grade may reduce drug use in eighth grade boys**
    - based on randomized trial
    - 24 schools randomized to Drug Abuse Resistance Education (DARE) vs. DARE Plus vs. delayed program control (DARE Plus activities included youth-led extracurricular activities and community adult action teams)
    - 6,237 seventh-grade students evaluated at end of eighth grade
    - no significant differences in self-reported tobacco, alcohol and multidrug use and victimization between DARE and control groups

    - DARE Plus associated with reduced self-reported tobacco, alcohol and multidrug use and victimization among boys but no significant differences in outcomes among girls
    - Reference – Arch Pediatr Adolesc Med 2003 Feb;157(2):178 full-text, summary can be found in Am Fam Physician 2003 Aug 1;68(3):550
- **limited evidence regarding interventions for prevention of drug use by young people delivered in non-school settings**
    - based on Cochrane review
    - systematic review of 17 studies
    - motivational interviewing and some family interventions may have some benefit
    - Reference – systematic review of 17 studies last updated 2005 Nov 2 (Cochrane Library 2006 Issue 1:CD005030)

Smoking restrictions:

- **comprehensive, multicomponent approaches to implement policies banning smoking within institutions may reduce smoking within public places (level 2 [mid-level] evidence)**
    - based on withdrawn Cochrane review of 11 before and after studies
    - Reference – systematic review last updated 2000 Apr 27 (Cochrane Library 2000 Issue 3:CD001294)
    - *DynaMed commentary* -- Cochrane review withdrawn 2008 Issue 3 because it has been updated by new review (CD005992)
- **smoke-free workplaces may improve quit rates and reduce cigarette consumption (level 2 [mid-level] evidence)**
    - based on systematic review and meta-analysis of 26 studies
    - totally smoke-free workplaces reduced prevalence of smoking by 3.8% (95% CI 2.8%-4.7%) and reduced number of cigarettes/day among smokers by 3.1 (95% CI 2.4-3.8)
    - Reference – BMJ 2002 Jul 27;325(7357):188, editorial can be found in BMJ 2002 Jul 27;325(7357):174
- **restrictions on smoking at home, public places and school all associated with reduced teenage smoking (level 2 [mid-level] evidence)**
    - based on survey of 17,287 high school students

    - Reference – BMJ 2000 Aug 5;321(7257):333, correction can be found in BMJ 2000 Sep 9;321(7261):623, editorial can be found in BMJ 2000 Aug 5;321(7257):310
- **smoke-free household and workplace restrictions associated with reduced smoking in adolescents (level 2 [mid-level] evidence)**
    - based on surveys of 17,185 adolescents
    - Reference – JAMA 2000 Aug 9;284(6):717
- arguments for and against smoking ban in outside public spaces can be found in BMJ 2008 Dec 11;337:a2806, BMJ 2008 Dec 11;337:a2804

Screening:

- all patients should be asked if they use tobacco and should have tobacco use documented on regular basis (PHS Strength of Evidence A)[1]
- United States Preventive Services Task Force (USPSTF) recommendations in adults
    - all clinicians should ask adult patients about tobacco use and provide tobacco cessation intervention (USPSTF Grade A)
    - all clinicians should ask all pregnant women if they use tobacco and should provide augmented pregnancy-tailored counseling (USPSTF Grade A)
    - 5-A strategy
        - Ask about tobacco use
        - Advise to quit through clear personalized messages
        - Assess willingness to quit
        - Assist to quit
        - Arrange follow-up and support
    - Reference – Ann Intern Med 2009 Apr 21;150(8):551 full-text
- insufficient evidence to recommend for or against routine screening for tobacco use in children or adolescents (USPSTF 2003 Nov)
- clinic screening systems (for example, including tobacco use status in vital signs or use of reminder systems) significantly increase rates of clinician intervention (PHS Strength of Evidence A)[1]

▶ Quality Improvement

Physician Quality Reporting System 2011 Quality Measures:

- 226. Preventive Care and Screening: Tobacco Use: Screening and Cessation Intervention
    - Percentage of patients ≥ 18 years old who were screened for tobacco use ≥ 1 times within 24 months AND who received cessation counseling intervention if identified as a tobacco user
- see Physician Quality Reporting System 2011 Quality Measures for additional information

▼References including Reviews and Guidelines

General references used:

- 1. Fiore MC, Jaen CR, Baker TB, et al; U.S. Department of Health and Human Services, Public Health Service. Clinical practice guideline: Treating tobacco use and dependence: 2008 update. DHHS 2008 May PDF or at National Guideline Clearinghouse 2008 May 12:12520, endorsed by American Academy of Pediatrics (Pediatrics 2008 Aug;122(2):471 PDF)
    - Public Health Service guideline panel Strength of Evidence ratings
        - Strength of Evidence A – multiple well-designed randomized clinical trials, directly relevant to the recommendation, yielded a consistent pattern of findings
        - Strength of Evidence B – some evidence from randomized clinical trials supported the recommendation, but the scientific support was not optima
        - Strength of Evidence C – reserved for important clinical situations in which Panel achieved consensus on recommendation in the absence of relevant randomized controlled trials

MEDLINE search:

- to search MEDLINE for (Tobacco use disorder) with targeted search (Clinical Queries), click therapy, diagnosis or prognosis

Reviews:

- review of realistic approaches to counseling in office setting can be found in Am Fam Physician 2009 Feb 15;79(4):277

- review can be found in CMAJ 2007 Nov 20;177(11):1373 full-text, correction can be found in CMAJ 2008 Mar 11;178(6):732
- review of assessing dependence and motivation to stop smoking can be found in BMJ 2004 Feb 7;328(7435):338
- review can be found in N Engl J Med 2002 Feb 14;346(7):506, commentary can be found in N Engl J Med 2002 Jul 25;347(4):294
- National Institutes of Health (NIH) Consensus Conference 2006 Jun 12-14 on tobacco use can be found in NIH Consens State Sci Statements 2006 Jun 12-14;23(3):1 or at National Guideline Clearinghouse 2009 Mar 23:11828 or in Ann Intern Med 2006 Dec 5;145(11):839, supporting systematic review in AHRQ Evidence Report on Tobacco Use: Prevention, Cessation and Control 2006 Jun:140 or in Ann Intern Med 2006 Dec 5;145(11):845
- review of tobacco addiction can be found in Lancet 2008 Jun 14;371(9629):2027, editorial can be found in Lancet 2008 Jun 14;371(9629):1976, commentary can be found in Lancet 2008 Oct 4;372(9645):1217
- review of management of smokers can be found in JAMA 2005 Jul 27;294(4):482, commentary can be found in JAMA 2005 Nov 16;294(19):2434
- review of treatment of tobacco dependence can be found in Mayo Clin Proc 2008 Apr;83(4):479
- review of smoking cessation tactics can be found in J Fam Pract 2007 Oct;56(10):817
- review of evidence based approach to managing smoking cessation in primary care can be found in Aust Fam Physician 2008 Jan-Feb;37(1-2):10
- systematic review of smoking cessation pharmacotherapy can be found in BMC Public Health 2006 Dec 11;6:300 full-text
- evidence-based review of pharmacotherapy can be found in J Am Board Fam Pract 2002 Nov-Dec;15(6):489 PDF
- brief "What you should do" review on smoking cessation can be found in BMJ 2008 Jan 26;336(7637):217
- review of interventions to facilitate smoking cessation can be found in Am Fam Physician 2006 Jul 15;74(2):262, commentary can be found in Am Fam Physician 2007 Apr 15;75(8):1151 full-text
- review of smoking cessation can be found in BMJ 2007 Jul 7;335(7609):37, commentary can be found in BMJ 2007 Jul 21;335(7611):112

- review of brief advice and behavioral support can be found in BMJ 2004 Feb 14;328(7436):397
- review of cessation of smokeless tobacco use can be found in J Fam Pract 2008 Apr;57(4):238
- review of smoking cessation for prevention and treatment of chronic obstructive pulmonary disease can be found in BMJ 2006 Jun 3;332(7553):1324
- review of youth tobacco use can be found in Pediatrics 2006 Sep;118(3):e890
- review of reducing tobacco use in adolescents can be found in Am Fam Physician 2008 Feb 15;77(4):483
- review of nicotine replacement therapy can be found in BMJ 2004 Feb 21;328(7437):454, correction can be found in BMJ 2004 Mar 20;328(7441):686
- review of cessation interventions in routine health care can be found in BMJ 2004 Mar 13;328(7440):631
- review of parental tobacco control (interventions in child health care setting) can be found in Pediatrics 2005 Mar;115(3):750
- review of smoking cessation in pregnancy and postpartum relapse prevention can be found in J Am Board Fam Pract 2004 Jul-Aug;17(4):264 full-text

Guidelines:

- see also Substance use disorders for general substance use guidelines

United States guidelines:

- United States Public Health Service clinical practice guideline for treating tobacco use and dependence can be found at DHHS 2008 May PDF or at National Guideline Clearinghouse 2008 May 12:12520, endorsed by American Academy of Pediatrics (AAP)
- United States Preventive Services Task Force guidelines for counseling and interventions to prevent tobacco use and tobacco-caused disease in adults and pregnant women can be found in Ann Intern Med 2009 Apr 21;150(8):551 full-text
- Surgeon General report on biology and behavioral basis for smoking-attributable disease can be found at Office of Surgeon General 2010 Dec
- American Academy of Pediatrics (AAP) guidelines

    - AAP policy statement on tobacco use: a pediatric disease can be found in Pediatrics 2009 Nov;124(5):1474
    - AAP technical report on secondhand and prenatal tobacco smoke exposure can be found in Pediatrics 2009 Nov;124(5):e1017
    - AAP technical report on tobacco as a substance of abuse can be found in Pediatrics 2009 Nov;124(5):e1045
- Institute for Clinical Systems Improvement (ICSI) guideline on primary prevention of chronic disease risk factors can be found at ICSI 2010 May PDF or at National Guideline Clearinghouse 2010 Dec 27:23859
- Michigan Quality Improvement Consortium (MQIC) guideline on tobacco control can be found at National Guideline Clearinghouse 2010 Apr 26:15338
- American College of Obstetricians and Gynecologists (ACOG) Committee Opinion 471 on smoking cessation during pregnancy can be found in Obstet Gynecol 2010 Nov;116(5):1241, commentary can be found in ACOG News Release 2010 Oct 21
- New York State Department of Health guidelines on smoking cessation in HIV-infected patients can be found at National Guideline Clearinghouse 2008 Jun 23:12564
- American Diabetes Association (ADA) policy statement on smoking and diabetes can be found in Diabetes Care 2004 Jan;27(suppl 1):S74
- Substance Abuse and Mental Health Services Administration (SAMHSA) guideline on physical detoxification services for withdrawal from specific substances can be found at National Guideline Clearinghouse 2006 Aug 7:9118
- American Academy of Pediatric Dentistry policy on tobacco use 2003 PDF

Canadian guidelines:

- Registered Nurses Association of Ontario (RNAO) guideline on integrating smoking cessation into daily nursing practice can be found at National Guideline Clearinghouse 2008 Mar 24:11503
    - TobaccoFreeNurses provides free guide for nurses and students nurses to help smokers quit (AHRQ Research Activities 2005 May;297:27)

United Kingdom guidelines:

- National Institute for Health and Clinical Excellence (NICE) public health intervention guidance on smoking cessation services can be found at NICE 2008 Feb:PH10 or at National Guideline Clearinghouse 2008 Jul 7:12286
- NICE public health guidance on interventions and referral for smoking cessation in primary care and other settings can be found at NICE 2006 Mar:PH1 or at National Guideline Clearinghouse 2007 Feb 26:9740
- NICE public health guidance on preventing uptake of smoking by children and young people can be found at NICE 2008 Jul:PH14
- NICE public health guidance on school–based interventions to prevent smoking can be found at NICE 2010 Feb:PH23
- NICE public health guidance on workplace smoking can be found at NICE 2007 Apr:PH15 or at National Guideline Clearinghouse 2009 Mar 30:13254

Guideline grading systems used:

- United States Preventive Services Task Force (USPSTF) grades of recommendation
    - Grade A – USPSTF recommends the service with high certainty of substantial net benefit
    - Grade B – USPSTF recommends the service with high certainty of moderate net benefit or moderate certainty of moderate to substantial net benefit
    - Grade C – USPSTF recommends against routinely providing the service with at least moderate certainty that net benefit is small, but in individual patients considerations may support providing the service
    - Grade D – USPSTF recommends against providing the service with moderate to high certainty of no net benefit or harms outweighing benefits
    - Grade I – insufficient evidence to assess balance of benefits and harms
    - Reference – USPSTF Grade Definitions

- United States Preventive Services Task Force (USPSTF) grades of recommendations (prior to May 2007)
    - Grade A – USPSTF strongly recommends that clinicians provide the service to eligible patients, based on good evidence that the service improves important health outcomes and that benefits substantially outweigh harms

- Grade B – USPSTF recommends that clinicians provide the service to eligible patients, based on at least fair evidence that the service improves important health outcomes and that benefits outweigh harms
- Grade C – USPSTF makes no recommendation for or against routinely providing the service, based on at least fair evidence that the service can improve health outcomes but the balance of benefits and harms is too close to justify a general recommendation
- Grade D – USPSTF recommends against routinely providing the service to asymptomatic patients, based on at least fair evidence that the service is ineffective or that harms outweigh benefits
- Grade I – USPSTF concludes that the evidence is insufficient to recommend for or against routinely providing the service
- Reference – USPSTF Grade Definitions

▸Patient Information

Patient information:

- support from Smokefree.gov
- consumer booklet on how tobacco smoke causes disease from surgeon general can be found at CDC 2010 Dec
- online support for smoking cessation in United Kingdom can be found at Smokefree from NHS
- handout on "Do I want to quit?" can be found in Am Fam Physician 2002 Nov 1;66(9):1747
- handout on quitting smoking can be found in Am Fam Physician 2002 Mar 15;65(6):1117
- handout on tobacco use in adolescents can be found in Am Fam Physician 2008 Feb 15;77(4):491
- handout that provides assessment of readiness to quit and identification of smoking triggers can be found in Am Fam Physician 2000 Aug 1;62(3):591
- handout on cessation of smokeless tobacco can be found in Am Fam Physician 2000 Sep 15;62(6):1427
- handout on smoking cessation in recovering alcoholics from American Academy of Family Physicians or in Am Fam Physician 2000 Mar 15;61(6):1895
- comprehensive Web site which offers free services of reminder E-mails and other interactive methods to assist smoking cessation can be found at QuitNet

- handout on tips to help you quit smoking can be found in Am Fam Physician 2006 Jul 15;74(2):276
- support materials for tobacco prevention and cessation from American Academy of Family Physicians

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