NEW ZEALAND INSTITUTE FOR THE STUDY OF COMPETITION AND REGULATION INC.

The Power of Persuasion: Can Advertising Help You Quit Smoking?

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The Power of Persuasion
(famous quotes)

- "Advertisements contain the only truth to be relied on in a newspaper."
  Thomas Jefferson

- "Advertising is a racket … its contribution to humanity is exactly minus zero." F. Scott Fitzgerald

Advertising Pharmaceuticals

- Direct-to-consumer (DTC) advertising of Rx drugs is currently legal in only 2 countries
  - New Zealand
  - the U.S.
- DTC is controversial
  - Report to the New Zealand Ministry of Health (2003) recommends “That the New Zealand government introduce regulations and/ or legislation to prohibit the advertising of prescription medicines directly to the public, through print and broadcast media or any other means.”

DTC Controversies, *cont.*

- Europe
  - July 2001: European Commission proposal to partially lift DTC ban
  - October 2002: European Parliament rejects by a vote of 494 to 42 the EC proposals
  - Opponent said that Europe was at a crossroads and had to decide if it wants to go down the 'slippery slope' towards hard-sell drug advertising as seen in the U.S.
- U.S.
  - "The great majority of DTC ads are for very expensive me-too drugs that require a lot of pushing because there is no good reason to think they are any better than drugs already on the market." Angell, The Truth About Drug Companies: How They Deceive Us and What to Do About It (2005, p. 124)

Case Study: Advertising Smoking Cessation Products

- Smoking cessation is a major public health objective
- Pharmaceutical companies might be able to make profits and promote public health
- Lessons for regulating DTC advertising
  - In the U.S.
  - In New Zealand

Outline

- Background on smoking cessation
- Studies of the effects of advertising
  - Completed study of magazine advertising (published in June 2007 *Journal of Political Economy*)
  - In progress study of TV advertising
- Completed study of impact of U.S. regulations on advertising (published in 2007 *Journal of Regulatory Economics*)
- Directions for future work on N.Z.

BACKGROUND ON SMOKING CESSATION

Smoking Cessation & Public Health

- Smoking cessation is an important part of tobacco control
  - "Quitting smoking now greatly reduces serious risks to your health." – U.S. Surgeon General's warning label
  - *Healthy People 2010* objective to cut U.S. smoking prevalence almost in half (to 12%) can not be met without large increases in smoking cessation rates (Mendez and Warner 2000)
- New Zealand
  - 23% New Zealanders smoke; 46% Maori smoke
  - "Clearing the Smoke: A 5 Year Plan for Tobacco Control in New Zealand 2004 – 2009"
  - New Zealand Health Strategy

Advances in Smoking Cessation

- Long History of Ineffective/unpleasant Methods
  - April 1862 Harper's Weekly advertises product to those wanting to have their "craving for tobacco cured."
  - By 1956 more than 26 products and remedies nationally advertised including "Beat-Nic", "Tobak-O-Stop", and "Kwit-Smoke"
  - Other methods also used.
    - **Rapid smoking**: smokers inhale deeply from a cigarette about every six seconds until they become nauseated.
    - **Aversion therapy**: "In one study, as the subject puffed a cigarette the investigator fired a .22-caliber rifle 50 times from 2 feet behind the subject's head twice a week for 5 weeks. In 4 weeks the subject reduced his smoking from 18 to 14 cigarettes daily and in the final week to 10 cigarettes daily. The investigator claimed the experiment a success." (Schwartz 1969)

Advances in Smoking Cessation,

cont.

	Quit Rates	Odds ratio (95% C.I.)
Zyban (n=2)	30.5%	2.1 (1.5,3.0)
Nicotine nasal spray (n=3)	30.5	2.7 (1.8, 4.1)
Nortriptyline (n=2)	30.1	3.2 (1.8, 5.7)
Clonidine (n=5)	25.6	2.1 (1.4, 3.2)
Nicotine gum (n=13)	23.7	1.5 (1.3, 1.8)
Nicotine inhaler (n=4)	22.8	2.5 (1.7, 3.6)
Rapid smoking (n=19)	19.9	2.0 (1.1, 3.5)
Nicotine patch (n=27)	17.7	1.9 (1.7, 2.2)
MD advice to quit, alone (n=7)	10.2	1.3 (1.1,1.6)
Acupuncture (n=5)	8.3	1.1 (0.7, 1.6)
Annual quit rate (1990)	**5%**	

(n= number of clinical trials)

Smoking Cessation Guidelines

- New Zealand & U.S. published guidelines state that there is strong evidence for
  - Nicotine replacement therapies
  - Buproprion
  - Nortriptyline
  - Varenicline
- (PHARMAC only subsidizes the nicotine replacement therapies)

Advertising & Smoking Cessation

- Advertising of smoking cessation products similar to public service anti-smoking campaigns

- 1996 Great American Smokeout, sponsored by the American Cancer Society, in collaboration with a manufacturer of nicotine medications
  - Estimates suggest paid advertisements from the campaign reached 122 million adults (Burton et al. 1997)

- Producer advertising has been shown to be an important source of health information that leads to changes in consumption of dietary fiber and fat (Ippolito and Mathios 1990, 1995)

- A growing body of evidence on the impact of DTC advertising on consumer demand for pharmaceutical products (Bradford and Kleit's review, *The Elgar Companion to Health Economics*, 2006)

STUDIES OF THE EFFECTS OF ADVERTISING

Data Overview

- Collected data on magazine DTC ads
- Purchased TNS data on TV DTC ads, 1996 – 2004
  - For each ad, know: product advertised, and the time, national network or local station, and program on which it aired
- Individual-level data from Simmons NCS, 1997-2004
  - Demographics, smoking
  - Detailed information on what magazines they read
  - Detailed information on TV-watching habits
- Merge DTC ads that appeared in magazines the respondent reports regularly reading
- Merge TV ads that appeared over the last year during programs or dayparts the respondent reports regularly watching

Table 1 SCADS Magazine Advertising Pages of Smoking Cessation products, Cigarettes and Tobacco products and Anti-smoking Public Service Announcements 1994-2002

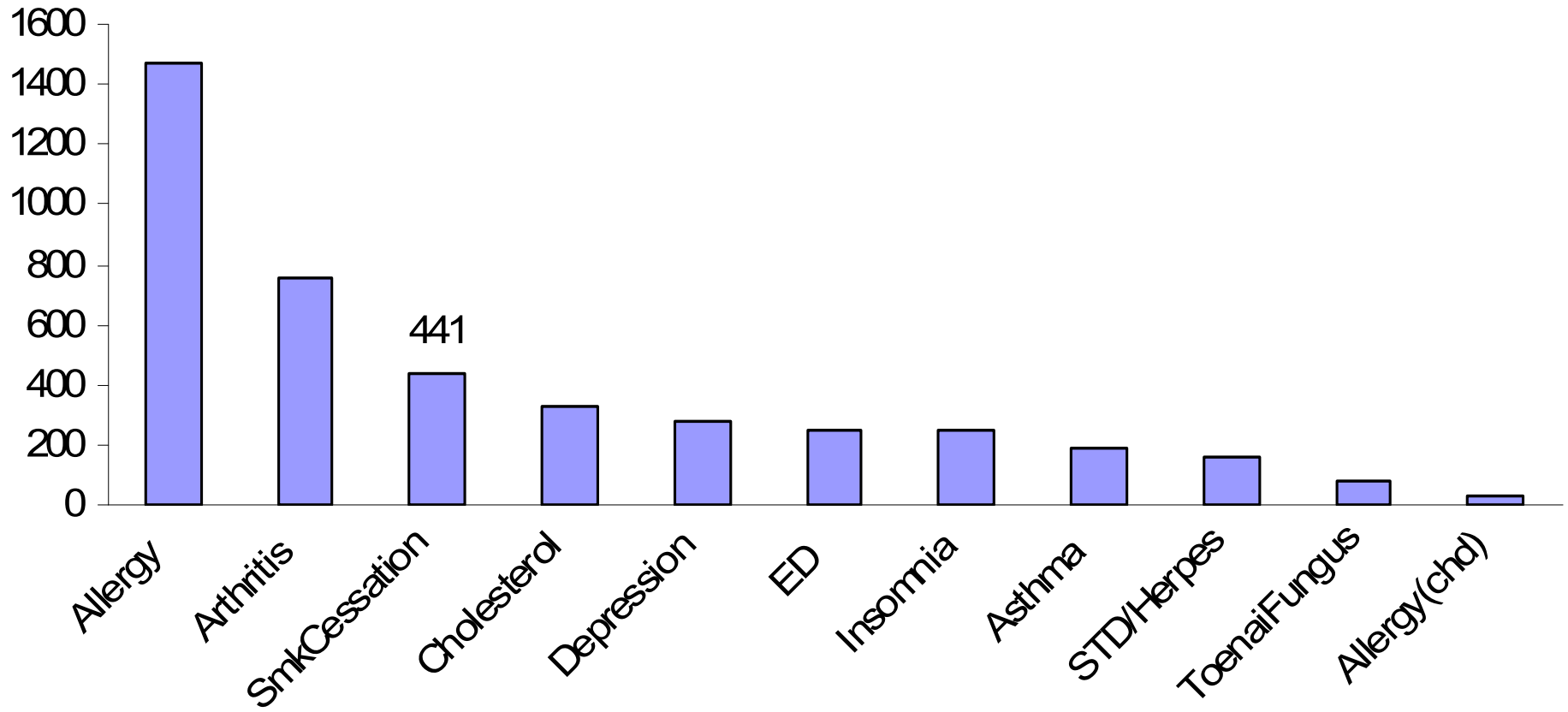
Magazine	Cessation	Cigarettes	PSA
Better Homes and Gardens	53	327	11
Black Enterprise	0	69	3
Business Week	5	6	4
Cosmopolitan	28	764	2
Ebony	26	307	5
Essence	2	310	5
Family Circle	13	284	11
Glamour	10	591	8
Good Housekeeping	13	0	1
Jet	14	477	1
McCall's/Rosie	0	295	0
Money	4	49	0
National Geographic	6	0	0
Newsweek	44	173	6
People	110	1352	18
Playboy	12	1160	2
Reader's Digest	63	0	2
Rollingstone	18	1030	3
Seventeen	0	0	11
Sports Illustrated	63	1354	9
TV Guide	72	804	17
Time	91	442	35
US News & World Report	30	97	2
Woman's Day	26	446	5
Vogue	0	454	0
Total	704	10790	161

Source: SCADS data archive


Better Home and Garden
Easy-living
Garden splendor
BLACK ENTERPRISE
Hammerin' Hank Aaron
BusinessWeek
WHY MATH WILL ROCK YOUR WORLD
COSMOPOLITAN
Total body REHAB
EBONY
The new Black FATHER
THE REAL REASON YOU CAN'T STOP
Family Circle
15 Meals in 15 Minutes
Supermarket Savings
Feeling Tired?
GLAMOUR
Look & feel like the sexiest woman in the room
Good Housekeeping
Great Grilled Dinners
Save on Everything!
JET
A YEAR AFTER KATRINA Spike Lee UNCOVERS WHAT REALLY HAPPENED
JAMA
McCall's
Mature Maturity
A movie's lasting magic
Money
Everything You Always Needed to Know About Money*
NATIONAL GEOGRAPHIC
The NEW ENGLAND JOURNAL of MEDICINE
Newsweek
South Park!
People
WWE'S CANDYLICIOUS CHALLENGER
PLAYBOY
CANDICE MICHELLE
Reader's Digest
How Doctors Gamble With Your Life
Rolling Stone
seventeen
hair issue!
SPIN
TOO BRUTAL OR THE FUTURE?
Ultimate Fighting
TIME
Reborn In the USA
TV GUIDE
AMERICAN IDOL!
U.S.News & WORLD REPORT
America's Best COLLEGES
VOGUE
45 Best Dressed Girls of Summer
KEIRA KNIGHTLEY
Woman's Day
Brad's rage stuns Jennifer

Measure of Exposure to TV Ads

ads seen in past 12 months



Source: NCS 2000-2004, N=80,615

Quit Attempt & Successful Quit by Quintile of Magazine Ads Exposure

Exposure Quintile	Exposure	% Quit Attempt	%Successful Quit
Q1(0-.75)	0.1	41.6	9.6
Q2 (.76-4.12)	2.3	45.6	9.8
Q3 (4.13-0.29)	7.2	44.0	9.8
Q4 (10.3-8.99)	14.4	44.8	9.5
Q5 (19 +)	29.9	49.3	10.3

Quit Attempt & Successful Quit by Quintile of TV Ads Exposure

Quintile	Exposure range	Mean exposure	% Quit attempt	% Successful quit
1	(0-134)	58.9	40.3	8.9
2	(134-285)	206.8	43.0	9.5
3	(285-475)	375.7	45.4	10.1
4	(475-797)	617.4	46.7	11.3
5	(797+)	1339.6	47.9	10.9

N = 27,743 smokers

Econometric Model

$Y_i^* = \gamma_0 + \gamma_1 AdExp_i + Z\,\gamma_2 + \varepsilon_i$

Y_i^* = smoking behaviors (quit, attempt, product)

$AdExp_i$ = person i's exposure of person to cessation ads

Z = control variables (exposure to other smoking-related ads, magazine-reading and TV-watching habits, socio-economic characteristics, survey wave dummies)

Estimation Issues: Exposure Endogeneity

- Producers target advertising → exposure varies systematically with observable characteristics
  - Problematic if producers observe characteristics the econometrician can't: error term will be correlated with measures of ad exposure
  - Common (unresolved) problem: Emery et al. (2003), Wakefield et al. (2003) and Iizuka and Jin (2005)
- Consumers select magazines, TV shows → exposure varies systematically with unobservable characteristics shared with other readers
  - Problematic if unobservables determine smoking behavior

Identification Strategy, part I

- Control for socio-economic characteristics used to target advertising
  - We literally observe what producers observe
  - Simmons NCS website's promotion materials state that their data are used by every major marketing firm and advertising agency in U.S.
- Uses variation in exposure within demographic groups to identify the effect of exposure on smoking cessation.

Identification Strategy, part II

- Exploit alternative sources of identifying variation
- In study of effect of magazine ads
  - Within-category variation because one person reads *Time*, another reads *Newsweek,* etc.
  - Within-magazine variation due to reading intensity
  - For more discussion, see June 2007 *JPE*
- In study of TV ads
  - Within-daypart variation because people watch different prime time shows, etc.

Regression Results for Magazine Ads

Quit Attempts		
Cessation ad exposure	0.0022***	(0.0006)
Successful Quits		
Cessation ad exposure	0.0008**	(0.0003)
Product Use		
Cessation ad exposure	0.0008**	(0.0004)
Cold Turkey		
Cessation ad exposure	0.0014***	(0.0005)

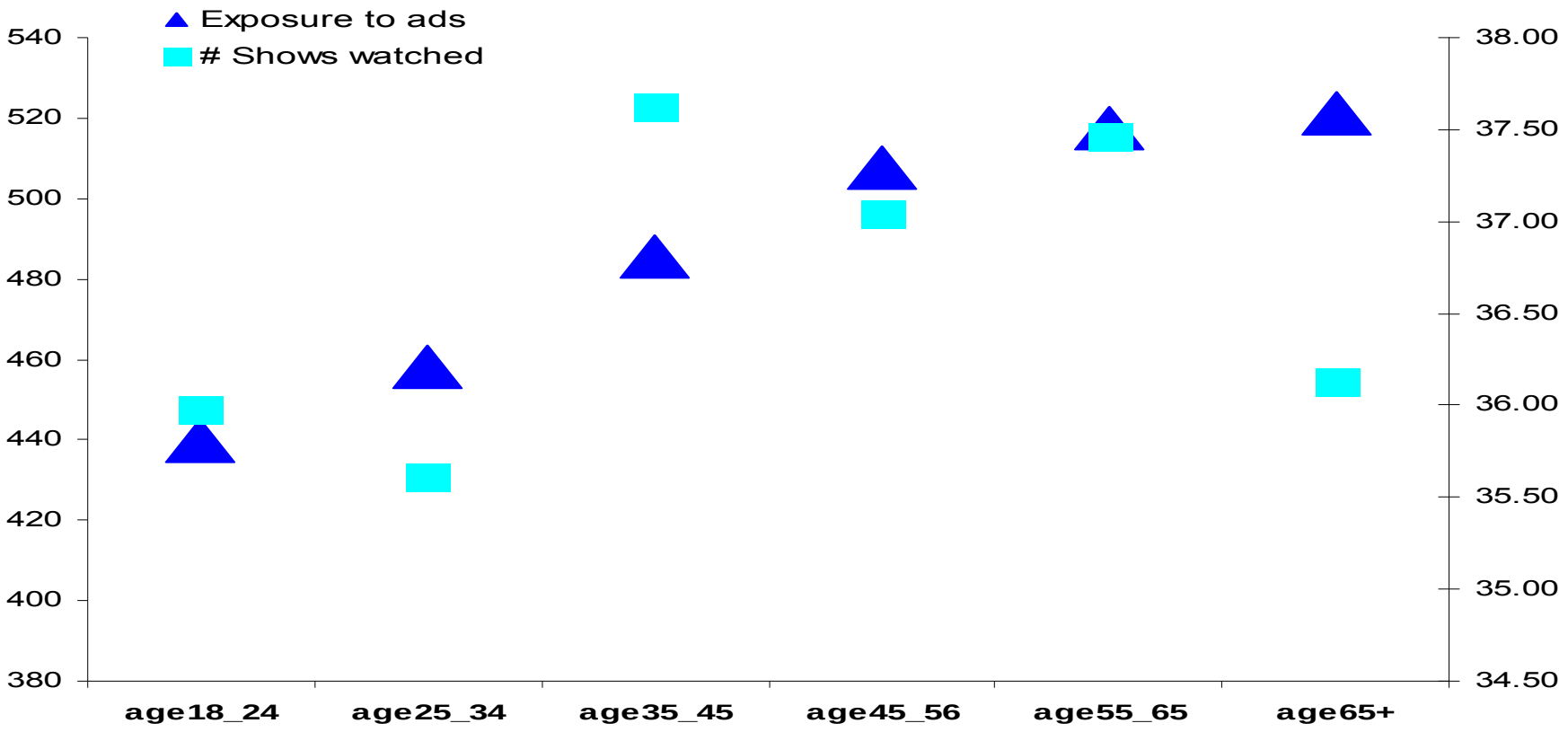
Notes: Results from Stata, probit coefficients and standard errors. All models control for exposure to other smoking-related ads, individual demographics, general magazine reading, TV habits, etc.

Regression results for TV ads

	Quit attempt	Successful quit
TV Ads (per 100 ads)	0.261* (0.143)	0. 155* (0.087)

* P<.10

Cessation Ads Seen Closely Match # TV Shows Seen



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Effects of Cessation Ads Exposure
Placebo Tests

	Quit attempt		Successful quit	
Cessation ads (per 100)	0.164	0.289*	0.147	0.184**
Anti-depression ads (per 100)	0.449***	0.493**	0.039	0.079
Children's Allergy ads (per 100)	-0.420	0.110	-.429	-0.093

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Effects of DTC advertising

- We think we have robust evidence that magazine ads increase smoking cessation
  - For complete discussion, see June 2007 *Journal of Political Economy*
- We are not yet sure about our evidence that TV ads increase smoking cessation
  - This project is very much “work in progress”

Discussion: Private Returns to Magazine Ads

- Suppose industry increased expenditures by $2.6 million (10%): this would imply an increase of Mean Ad Exposure of 2.1 advertisements
- Model implies increase cessation attempts by .45 percentage points (from a baseline of 45 percent of attempters)
- 50 million smokers would imply 225,000 new quit attempts with about 80,000 using a product.
- If a typical user spends $35 implies increase in sales of $2.8 million
  - Maybe some future return from the attempts w/out products – stages of change

Discussion: Public Health Returns to Magazine Ads

- Increase in Ad Expenditure increases exposure by the same 2.1 advertisements↑
- Model implies successful cessation would increase by .16 percentage points.
- With 50 million smokers would increase successful quits by 80,000.

IMPACT OF U.S. REGULATIONS ON DTC ADVERTISING

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U.S. Regulations on DTC Advertising

- FDA regulates DTC advertising of Rx
- FTC regulates DTC advertising of drugs that are available over-the-counter (OTC)
- Difference between FDA, FTC → easier (less costly) to advertising when product becomes available OTC

"I know I should quit. Don't tell me why, tell me how."

You don't need lectures, you need help. Well, now there's a revolutionary product that can actually help relieve the body's craving for nicotine, when used as part of a comprehensive behavioral smoking-cessation program.

Nicoderm is a small, thin 24-hour patch that goes on your upper body and delivers a continuous flow of nicotine through your skin. Nicoderm has been clinically proven to help relieve the withdrawal symptoms that usually come with quitting.

As part of your smoking-cessation program, your doctor can provide a free Nicoderm Committed Quitter's book containing strategies for outwitting – and outlasting – your habit.

The Nicoderm patch is available only with a prescription. Why not ask your doctor about it? After just 10 weeks of Nicoderm therapy you could be on your way to a new nonsmoking life-style.

Nicoderm should be used as part of a comprehensive behavioral smoking-cessation program. Nicoderm should not be used for more than 3 months. If you are pregnant or nursing, you should discuss other ways to stop smoking with your doctor. Because Nicoderm, like cigarettes, contains nicotine, it could harm your baby. Marion Merrell Dow does not recommend use of Nicoderm in pregnant women.

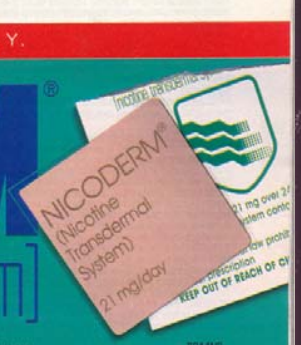
If you have cardiovascular disease, discuss other ways to stop smoking with your doctor. If you are taking any prescription medicines or are under a doctor's care for any condition, you should discuss the potential risk of using Nicoderm with your doctor.

There may be other risks associated with the use of Nicoderm. **Ask Your Doctor About the Nicoderm Patch.**

NOW IN PLENTIFUL SUPPLY.

NICODERM®

[nicotine transdermal system]



NIDAJ411/AB765 © 1992, Marion Merrell Dow Inc. Please see brief summary of prescribing information on an adjacent page. 8914N2

Brief Summary of
Prescribing Information as of January 1992

NICODERM®
(nicotine transdermal system)

Systemic delivery of 21, 14, or 7 mg/day over 24 hours

Caution: Federal law prohibits dispensing without prescription.

DESCRIPTION

NICODERM is a transdermal system that provides systemic delivery of nicotine for 24 hours following its application to intact skin.

The NICODERM system is a multilayered rectangular film containing nicotine as the active agent. For the three doses the composition per unit area is identical. Proceeding from the visible surface toward the surface attached to the skin are (1) an occlusive backing (polyethylene/aluminum/polyester/ethylene-vinyl acetate copolymer); (2) a drug reservoir containing nicotine (in an ethylene-vinyl acetate copolymer matrix); (3) a rate-controlling membrane (polyethylene); (4) a polyisobutylene adhesive; and (5) a protective liner that covers the adhesive layer and must be removed before application to the skin.

INDICATIONS AND USAGE

NICODERM treatment is indicated as an aid to smoking cessation for the relief of nicotine withdrawal symptoms. NICODERM treatment should be used as part of a comprehensive behavioral smoking-cessation program.

The use of NICODERM systems for longer than 3 months has not been studied.

CONTRAINDICATIONS

Use of NICODERM systems is contraindicated in patients with hypersensitivity or allergy to nicotine or to any of the components of the therapeutic system.

WARNINGS

Nicotine from any source can be toxic and addictive. Smoking causes lung cancer, heart disease, and emphysema and may adversely affect the fetus and the pregnant woman. For any smoker, with or without concomitant disease or pregnancy, the risk of nicotine replacement in a smoking-cessation program should be weighed against the hazard of continued smoking while using NICODERM systems and the likelihood of achieving cessation of smoking without nicotine replacement.

Pregnancy Warning

Tobacco smoke, which has been shown to be harmful to the fetus, contains nicotine, hydrogen cyanide, and carbon monoxide. Nicotine has been shown in animal studies to cause fetal harm. It is therefore presumed that NICODERM systems can cause fetal harm when administered to a pregnant woman. The effect of nicotine delivery by NICODERM systems has not been examined in pregnancy (see PRECAUTIONS).

Therefore pregnant smokers should be encouraged to attempt cessation using educational and behavioral interventions before using pharmacological approaches. If NICODERM systems are used during pregnancy, or if the patient becomes pregnant while using NICODERM systems, the patient should be apprised of the potential hazard to the fetus.

Safety Note Concerning Children

The amounts of nicotine that are tolerated by adult smokers can produce symptoms of poisoning and could prove fatal if the NICODERM system is applied or ingested by children or pets. Used 21 mg/day systems contain about 75% (83 mg) of their initial drug content. Therefore, patients should be cautioned to keep both the used and unused NICODERM systems out of the reach of children and pets.

PRECAUTIONS

The patient should be urged to stop smoking completely when initiating NICODERM therapy (see DOSAGE AND ADMINISTRATION). Patients should be informed that if they continue to smoke while using NICODERM systems, they may experience adverse effects due to peak nicotine levels higher than those experienced from smoking alone. If there is a clinically significant increase in cardiovascular or other effects attributable to nicotine, the NICODERM dose should be reduced or NICODERM treatment discontinued (see WARNINGS). Physicians should anticipate that concomitant medications may need dosage adjustment (see Drug Interactions).

The use of NICODERM systems beyond 3 months by patients who stop smoking should be discouraged, because the chronic consumption of nicotine by any route can be harmful and addicting.

Allergic Reactions

In a 6-week, open-label, dermal irritation and sensitization study of NICODERM systems, 7 of 230 patients exhibited definite erythema at 24 hours after application. Upon rechallenge, 4 patients exhibited mild to moderate contact allergy. Patients with contact sensitization should be cautioned that a serious reaction could occur from exposure to other nicotine-containing products or smoking. In the efficacy trials, erythema following system removal was typically seen in about 14% of patients, some edema in 3%, and dropouts due to skin reactions occurred in 2% of patients.

Patients should be instructed to promptly discontinue the use of NICODERM systems and contact their physicians, if they experience severe or persistent local skin reactions (eg, severe erythema, pruritus, or edema) at the site of application or a generalized skin reaction (eg, urticaria, hives, or generalized rash).

Patients using NICODERM therapy concurrently with other transdermal products may exhibit local reactions at both application sites. Reactions were seen in 2 of 7 patients using concomitant Estraderm® (estradiol transdermal system) in clinical trials. In such patients, use of one or both systems may have to be discontinued.

Skin Disease

NICODERM systems are usually well tolerated by patients with normal skin, but may be irritating for patients with some skin disorders (atopic or eczematous dermatitis).

Cardiovascular or Peripheral Vascular Diseases

The risks of nicotine replacement in patients with certain cardiovascular and peripheral vascular diseases should be weighed against the benefits of including nicotine replacement in a smoking-cessation program for them. Specifically, patients with coronary heart disease (history of myocardial infarction and/or angina pectoris), serious cardiac arrhythmias, or vasospastic diseases (Buerger's disease, Prinzmetal's variant angina) should be carefully screened and evaluated before nicotine replacement is prescribed.

Tachycardia occurring in association with the use of NICODERM therapy was reported occasionally. If serious cardiovascular symptoms occur with the use of NICODERM therapy, it should be discontinued.

NICODERM therapy was as well tolerated as placebo in a controlled trial in patients with coronary artery disease (see CLINICAL STUDIES). One patient on NICODERM 21mg/day, two on NICODERM 14 mg/day, and eight on placebo discontinued treatment due to adverse events.

NICODERM therapy did not affect angina frequency or the appearance of arrhythmias on Holter monitoring in these patients.

NICODERM therapy generally should not be used in patients during the immediate post-myocardial infarction period, patients with serious arrhythmias, and patients with severe or worsening angina pectoris.

Renal or Hepatic Insufficiency

The pharmacokinetics of nicotine have not been studied in the elderly or in patients with renal or hepatic impairment. However, given that nicotine is extensively metabolized and that its total system clearance is dependent on liver blood flow, some influence of hepatic impairment on drug kinetics (reduced clearance) should be anticipated. Only severe renal impairment would be expected to affect the clearance of nicotine or its metabolites from the circulation (see Pharmacokinetics).

Endocrine Diseases

NICODERM therapy should be used with caution in patients with hyperthyroidism, pheochromocytoma, or insulin-dependent diabetes, since nicotine causes the release of catecholamines by the adrenal medulla.

Peptic Ulcer Disease

Nicotine delays healing in peptic ulcer disease; therefore, NICODERM therapy should be used with caution in patients with active peptic ulcers and only when the benefits of including nicotine replacement in a smoking-cessation program outweigh the risks.

Accelerated Hypertension

Nicotine therapy constitutes a risk factor for development of malignant hypertension in patients with accelerated hypertension, therefore, NICODERM therapy should be used with caution in these patients and only when the benefits of including nicotine replacement in a smoking-cessation program outweigh the risks.

Information for Patient

A patient instruction booklet is included in the package of NICODERM systems dispensed to the patient. The instruction sheet contains important information and instructions on how to properly use and dispose of NICODERM systems. Patients should be encouraged to ask questions of the physician and pharmacist. Patients must be advised to keep both used and unused systems out of the reach of children and pets.

Drug Interactions

Smoking cessation, with or without nicotine replacement, may alter the pharmacokinetics of certain concomitant medications

May Require a Decrease in Dose at Cessation of Smoking	Possible Mechanism
acetaminophen, caffeine, imipramine, oxazepam, pentazocine, propranolol, theophylline	Disinduction of hepatic enzymes on smoking cessation.
insulin	Increase in subcutaneous insulin absorption with smoking cessation.
adrenergic antagonists (eg, prazosin, labetalol)	Decrease in circulating catecholamines with smoking cessation.
May Require an Increase in Dose at Cessation of Smoking	**Possible Mechanism**
adrenergic agonists (eg, isoproterenol, phenylephrine)	Decrease in circulating catecholamines with smoking cessation.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Nicotine itself does not appear to be a carcinogen in laboratory animals. However, nicotine and its metabolites increased the incidences of tumors in the cheek pouches of hamsters and forestomach of F344 rats, respectively, when given in combination with tumor initiators. One study, which could not be replicated, suggested that cotinine, the primary metabolite of nicotine, may cause lymphoreticular sarcoma in the large intestine in rats.

Nicotine and cotinine were not mutagenic in the Ames *Salmonella* test. Nicotine induced repairable DNA damage in an *E. coli* test system. Nicotine was shown to be genotoxic in a test system using Chinese hamster ovary cells. In rats and rabbits, implantation can be delayed or inhibited by a reduction in DNA synthesis that appears to be caused by nicotine. Studies have shown a decrease in litter size in rats treated with nicotine during gestation.

Pregnancy

Pregnancy Category D (see WARNINGS).

The harmful effects of cigarette smoking on maternal and fetal health are clearly established. These include low birth weight, increased risk of spontaneous abortion, and increased perinatal mortality. The specific effects of NICODERM therapy on fetal development are unknown. Therefore pregnant smokers should be encouraged to attempt cessation using educational and behavioral interventions before using pharmacological approaches.

Spontaneous abortion during nicotine replacement therapy has been reported; as with smoking, nicotine as a contributing factor cannot be excluded.

NICODERM therapy should be used during pregnancy only if the likelihood of smoking cessation justifies the potential risk of use of nicotine replacement by the patient who may continue to smoke.

Teratogenicity

Animal Studies: Nicotine was shown to produce skeletal abnormalities in the offspring of mice when given doses toxic to the dams (25 mg/kg IP or SC).

Human Studies: Nicotine teratogenicity has not been studied in humans except as a component of cigarette smoke (each cigarette smoked delivers about 1 mg of nicotine). It has not been possible to conclude whether cigarette smoking is teratogenic to humans.

Other Effects

Animal Studies: A nicotine bolus (up to 2 mg/kg) to pregnant rhesus monkeys caused acidosis, hypercarbia, and hypotension (fetal and maternal concentrations were about 20 times those achieved after smoking 1 cigarette in 5 minutes). Fetal breathing movements were reduced in the fetal lamb after intravenous injection of 0.25 mg/kg nicotine to the ewe (equivalent to smoking 1 cigarette every 20 seconds for 5 minutes). Uterine blood flow was reduced about 30% after infusion of 0.1 mg/kg/min nicotine for 20 minutes to pregnant rhesus monkeys (equivalent to smoking about 6 cigarettes every minute for 20 minutes).

Human Experience: Cigarette smoking during pregnancy is associated with an increased risk of spontaneous abortion, low birth weight infants, and perinatal mortality. Nicotine and carbon monoxide are considered the most likely mediators of these outcomes. The effect of cigarette smoking on fetal cardiovascular parameters has been studied near term. Cigarettes increased fetal aortic blood flow and heart rate and decreased uterine blood flow and fetal breathing movements. NICODERM therapy has not been studied in pregnant humans.

Labor and Delivery

The NICODERM system is not recommended to be left on during labor and delivery. The effects of nicotine on a mother or the fetus during labor are unknown.

Use in Nursing Mothers

Caution should be exercised when NICODERM therapy is administered to nursing women. The safety of NICODERM therapy in nursing infants has not been examined. Nicotine passes freely into breast milk; the milk to plasma ratio averages 2.9. Nicotine is absorbed orally. An infant has the ability to clear nicotine by hepatic first-pass clearance; however, the efficiency of removal is probably lowest at birth. The nicotine concentrations in milk can be expected to be lower with NICODERM therapy, when used as directed, than with cigarette smoking, as maternal plasma nicotine concentrations are generally reduced with nicotine replacement. The risk of exposure of the infant to nicotine from NICODERM therapy should be weighed against the risks associated with the infant's exposure to nicotine from continued smoking by the mother (passive smoke exposure and contamination of breast milk with other components of tobacco smoke) and from NICODERM therapy alone or in combination with continued smoking.

Pediatric Use

NICODERM therapy is not recommended for use in children, because the safety and effectiveness of NICODERM therapy in children and adolescents who smoke have not been evaluated.

Geriatric Use

Fifty-six patients over the age of 60 participated in clinical trials of NICODERM therapy. NICODERM therapy appeared to be as effective in this age group as in younger smokers. However, asthenia, various body aches, and dizziness occurred slightly more often in patients over 60 years of age.

ADVERSE REACTIONS

Assessment of adverse events in the 1,131 patients who participated in controlled clinical trials is complicated by the occurrence of GI and CNS effects of nicotine withdrawal as well as nicotine excess. The actual incidences of both are confounded by concurrent smoking by many of the patients. When reporting adverse events during the trials, the investigators did not attempt to identify the cause of the symptom.

Topical Adverse Events

The most common adverse event associated with topical nicotine is a short-lived erythema, pruritus, and/or burning at the application site, which was seen at least once in 47% of patients on the NICODERM system in the clinical trials. Local erythema after system removal was noted at least once in 14% of patients and local edema in 3%. Erythema generally resolved within 24 hours. Cutaneous hypersensitivity (contact sensitization) occurred in 2% of patients on NICODERM systems (see PRECAUTIONS, Allergic Reactions).

Probably Causally Related

The following adverse events were reported more frequently in NICODERM-treated patients than in placebo-treated patients or exhibited a dose response in clinical trials.

Digestive System: Diarrhea*, dyspepsia*
Mouth/Tooth Disorders: Dry mouth†
Musculoskeletal System: Arthralgia†, myalgia*
Nervous System: Abnormal dreams*, insomnia (23%), nervousness*
Skin and Appendages: Sweating†

Frequencies for 21 mg/day system
* Reported in 3% to 9% of patients
† Reported in 1% to 3% of patients
Unmarked if reported in <1% of patients

Causal Relationship UNKNOWN

Adverse events reported in NICODERM- and placebo-treated patients at about the same frequency in clinical trials are listed below. The clinical significance of the association between NICODERM systems and these events is unknown, but they are reported as alerting information for the clinician.

Body as a Whole: Asthenia*, back pain*, chest pain†, pain*
Digestive System: Abdominal pain†, constipation*, nausea*, vomiting†
Nervous System: Dizziness*, headache (29%), paresthesia†
Respiratory System: Cough increased*, pharyngitis*, sinusitis†
Skin and Appendages: Rash*
Special Senses: Taste perversion*
Urogenital System: Dysmenorrhea*

Frequencies for 21 mg/day systems
* Reported in 3% to 9% of patients
† Reported in 1% to 3% of patients
Unmarked if reported in <1% of patients

DRUG ABUSE AND DEPENDENCE/TREATMENT OF OVERDOSE

For further information, please see Full Prescribing Information

Manufactured by
ALZA Corporation
Palo Alto, CA 94304 for
Marion Merrell Dow Inc.
Kansas City, MO 64114

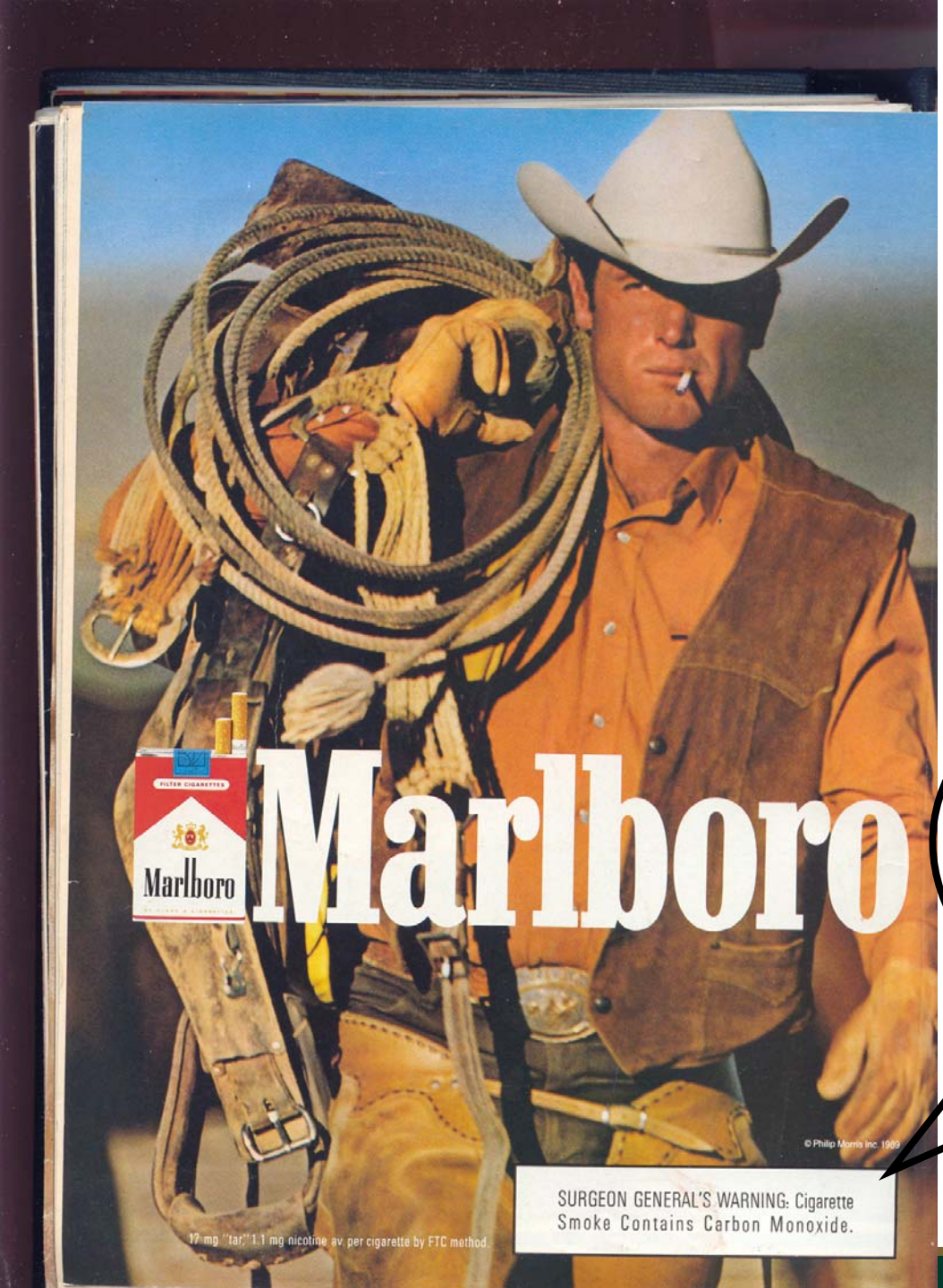
Prescribing Information as of January 1992

nidb0192c

MARION MERRELL DOW INC.
PRESCRIPTION PRODUCTS DIVISION
KANSAS CITY, MO 64114

NIDAJ411/AB765 6914N2

Nicoderm Print Advertisement 1992



Surgeon General's Warning

NEW ZEALAND INSTITUTE FOR THE STUDY OF COMPETITION AND REGULATION INC.

Lessons for regulating DTC advertising in the U.S.

- More ads could improve public health
- Less regulation
  - In JRE study, we estimate that if FDA had allowed all products to be sold OTC instead of Rx, smoking cessation ads in magazines would have increased by 80%
  - Simply moving each product OTC one year earlier would have increased ads by 9%
  - 1997 regulatory change → expenditures on TV ads sharply ↑
- More competition
  - Large 'introduction effect': advertise during new product launch
  - 'Wasteful competition' = advertising for market share → profits dissipated but public health benefits
  - We find evidence of inverted U-shape: advertising maximized at 4-5 products

IMPACT OF NEW ZEALAND REGULATIONS ON DTC ADVERTISING

NEW ZEALAND INSTITUTE FOR THE STUDY OF COMPETITION AND REGULATION INC.

Regulatory Options Under Consideration (as of 2006)

- Option 1: allow DTC advertising to continue, with more stringent regulation including mandatory pre-approval of advertisements and stronger penalties for non-compliant advertisements

- Option 2: allow DTC advertising but with stricter requirements than specified by Therapeutic Products Advertising Code, possibly including more explicit generic warning statements and prohibiting advertising new products for a set period

- Option 3: ban direct-to-consumer advertising of specific prescription products. Disease-state advertisements designed to raise awareness about medical conditions without mentioning specific medicines would be allowed but regulated.

- Source: Ministry of Health (2006). *Direct-to-Consumer Advertising of Prescription Medicines in New Zealand: Consultation document* Wellington: Ministry of Health.

Profit-maximizing DTC Advertising

- In the U.S.: 1997 FDA regulatory change "allows" DTC ads on TV; spending from $1 b. in 1995 to $4.2 b. in 2005
- "Drugs that are advertised to consumers are predominantly new drugs used to treat chronic conditions."
- Of the 20 most-advertised drugs in 2005:
  - 10 were introduced in 2000 or later
  - 17 of the 20 advertising campaigns began within a year after FDA approval
- Source for this slide, and the next two slides: Donohue et al., *N Engl J. Med,* August 16, 2007

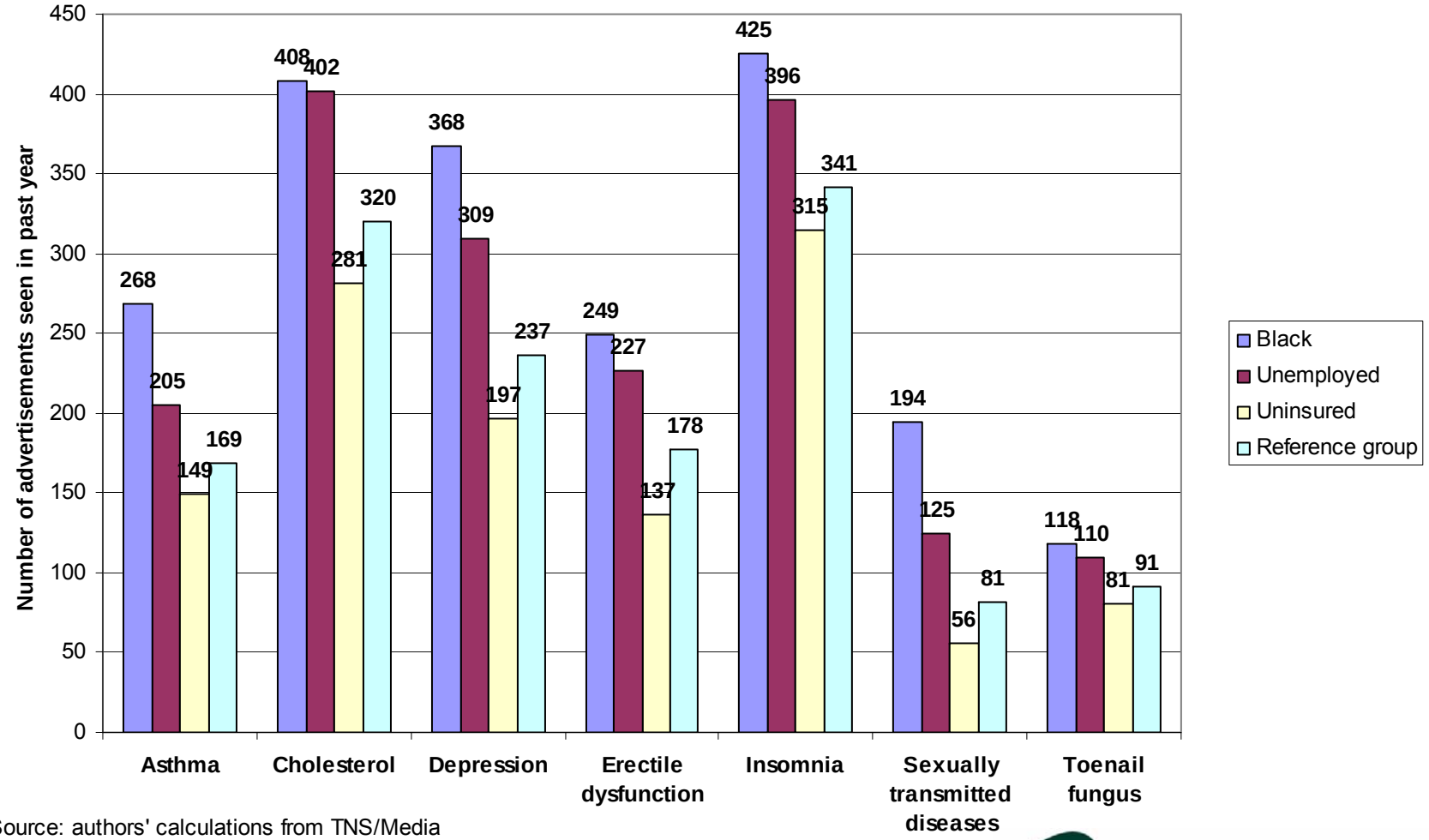
Table 1. Annual Spending on Direct-to-Consumer Advertising and Promotion to Health Professionals, 1996–2005.*

Variable	Annual Spending									
	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
Direct-to-consumer advertising										
Total spending (millions of $)	985	1,301	1,578	2,166	2,798	2,954	2,864	3,478	4,160	4,237
Percentage of sales	1.2	1.5	1.6	1.8	2.1	2.0	1.9	2.2	2.5	2.6
Professional promotion										
Total spending (millions of $)										
Detailing	3,747	4,093	4,861	5,064	5,447	6,055	6,731	7,364	7,585	6,777
Journal advertising	571	621	597	551	549	469	474	476	516	429
Percentage of sales	5.4	5.4	5.6	4.7	4.6	4.5	4.8	5.0	4.9	4.4
Free samples										
Total retail value (millions of $)	6,104	7,358	7,910	8,476	9,021	11,539	12,928	14,362	16,404	18,438
Percentage of sales	7.6	8.4	8.1	7.1	6.9	8.0	8.6	9.1	9.9	11.2
Total promotion										
Total spending (millions of $)	11,407	13,373	14,946	16,257	17,815	21,018	22,997	25,680	28,664	29,881
Percentage of sales	14.2	15.3	15.3	13.7	13.6	14.6	15.2	16.3	17.2	18.2

Table 3. Top 20 Pharmaceutical Products in Terms of Spending on Direct-to-Consumer Advertising in 2005.*

Drug	Company	Therapeutic Category	Spending†	FDA Approval Date‡	Year That Campaign Started§
			millions of dollars		
Nexium (esomeprazole)	AstraZeneca	Proton-pump inhibitor	224	Feb. 2000	2001
Lunesta (eszopiclone)	Sepracor	Hypnotic–sedative	214	Dec. 2004	2005
Vytorin (ezetimibe–simvastatin)	Merck/Schering-Plough	Cholesterol absorption blocker–HMG-CoA reductase inhibitor	155	July 2004	2004
Crestor (rosuvastatin)	AstraZeneca	HMG-CoA reductase inhibitor	144	Aug. 2003	2004
Advair (fluticasone and salmeterol)	GlaxoSmithKline	Corticosteroid–β-adrenergic–receptor agonist	137	Aug. 2000	2001
Nasonex (mometasone)	Schering-Plough	Corticosteroid	124	Dec. 1997	1998
Flonase (fluticasone)	GlaxoSmithKline	Corticosteroid	111	Oct. 1994	1995
Lamisil (terbinafine)	Novartis	Allylamine antifungal	110	May 1996	1997
Plavix (clopidogrel)	Bristol-Myers Squibb/Sanofi	Platelet-aggregation antagonist	110	Nov. 1997	2001
Cialis (tadalafil)	Lilly ICOS	PDE5 inhibitor	110	Nov. 2003	2004
Wellbutrin XL (bupropion)	GlaxoSmithKline	Dopamine reuptake inhibitor–SNRI	108	Aug. 2003	2004
Singulair (montelukast)	Merck	Leukotriene D4–receptor antagonist	105	Feb. 1998	1998
Lipitor (atorvastatin)	Pfizer	HMG-CoA reductase inhibitor	93	Dec. 1996	1998
Ambien (zolpidem)	Sanofi-Aventis	Hypnotic–sedative	88	Sept. 2005	2005
Humira (adalimumab)	Abbott	Monoclonal antibody	88	Dec. 2002	2003
Imitrex (sumatriptan)	GlaxoSmithKline	Vascular 5-HT1–receptor agonist	82	Aug. 1997	1998
Viagra (sildenafil)	Pfizer	PDE5 inhibitor	80	March 1998	1998
Neulasta (pegfilgrastim)	Amgen	G-CSF analogue	74	Jan. 2002	2002
Valtrex (valacyclovir)	GlaxoSmithKline	DNA polymerase inhibitor	72	June 1995	1996
Prevacid (lansoprazole)	TAP	Proton-pump inhibitor	71	May 1995	2000

Figure 2B
Predicted exposure to TV advertisements for medications to treat other conditions



Source: authors' calculations from TNS/Media Intelligence advertisements and NCS data

Table 2. New Zealand 2001 advertising spend (at rate card) for four pharmaceuticals marketed directly to consumers

Product	Formulations	Press	Magazine	TV	Radio	Total
Flixotide®	11		$117,980	$1,711,824		$1,829,804
Lamisil®	2		$145,385	$618,836		$764,221
Losec®	4	$15,052	$145,785	$809,610	$109,834	$1,080,281
Oxis®	2		$143,793	$1,099,337		$1,243,130

SOURCE: PHARMAC [12]

How are the incentives for DTC advertising different in N.Z.?

- PHARMAC subsidies
- High demand for subsidized products → high returns from advertising
  - Increase public sector costs
- But …

  Subsidized products tend to be older, less expensive (more cost-effective) →

  Advertise un-subsidized competing products to increase profits

My Ideas

- In process of purchasing data on DTC advertising expenditures in New Zealand
  - "Analgesics, remedies, medicines"
  - Annual expenditures 1995 – 2007, plus Jan- May 2008
  - per advertiser
  - per product/brand
  - per media type
- Describe patterns
- Econometric analysis: explore impact of PHARMAC subsidies of different products

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  - ISCR

ISCR NEW ZEALAND INSTITUTE FOR THE STUDY OF COMPETITION AND REGULATION INC.