COPD 2010

Opportunity from Science

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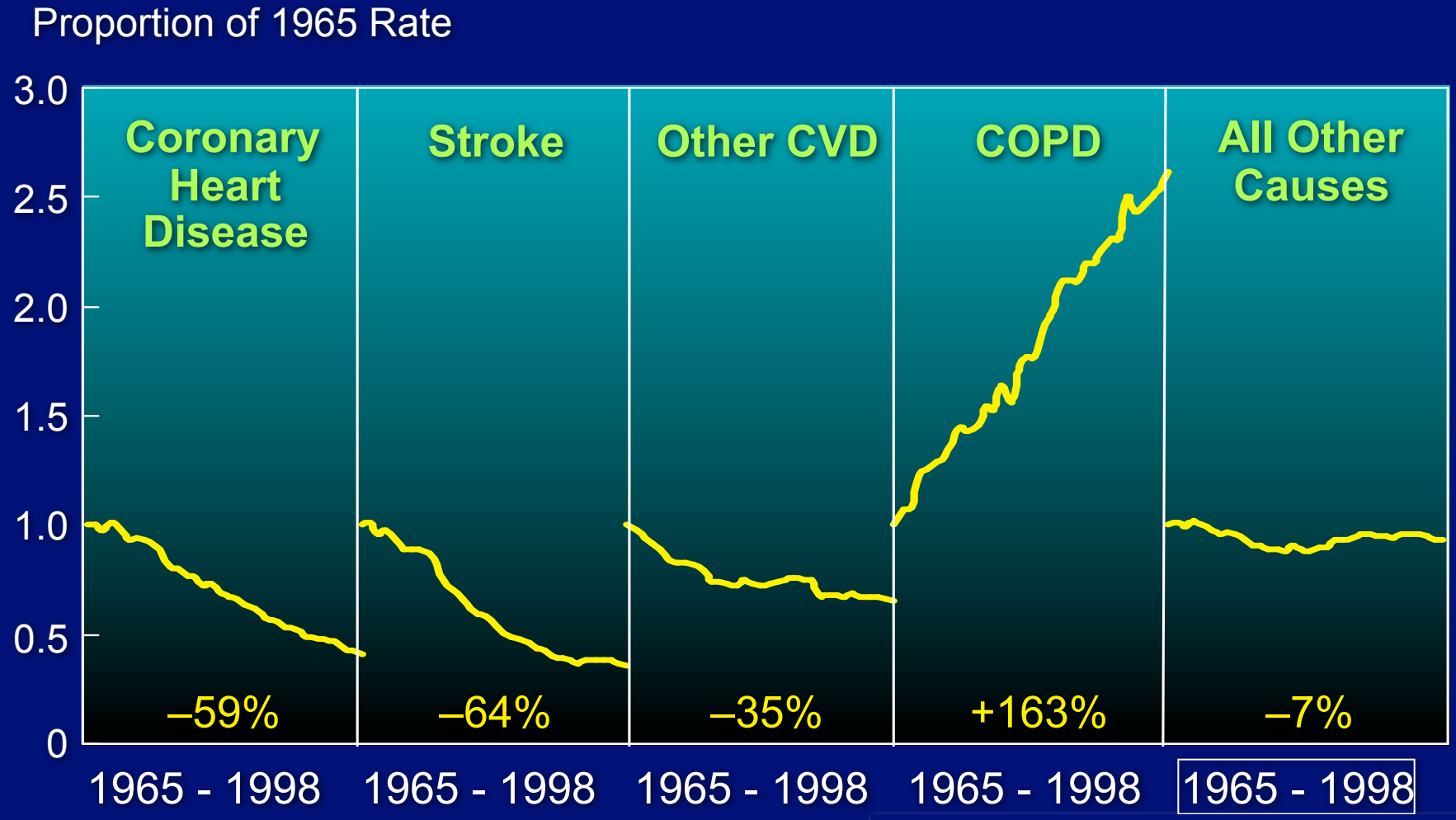
Burden of COPD

Burden of COPD

- Proportion of population with disease
- Effect of disease on affected individuals
- Costs to society incurred

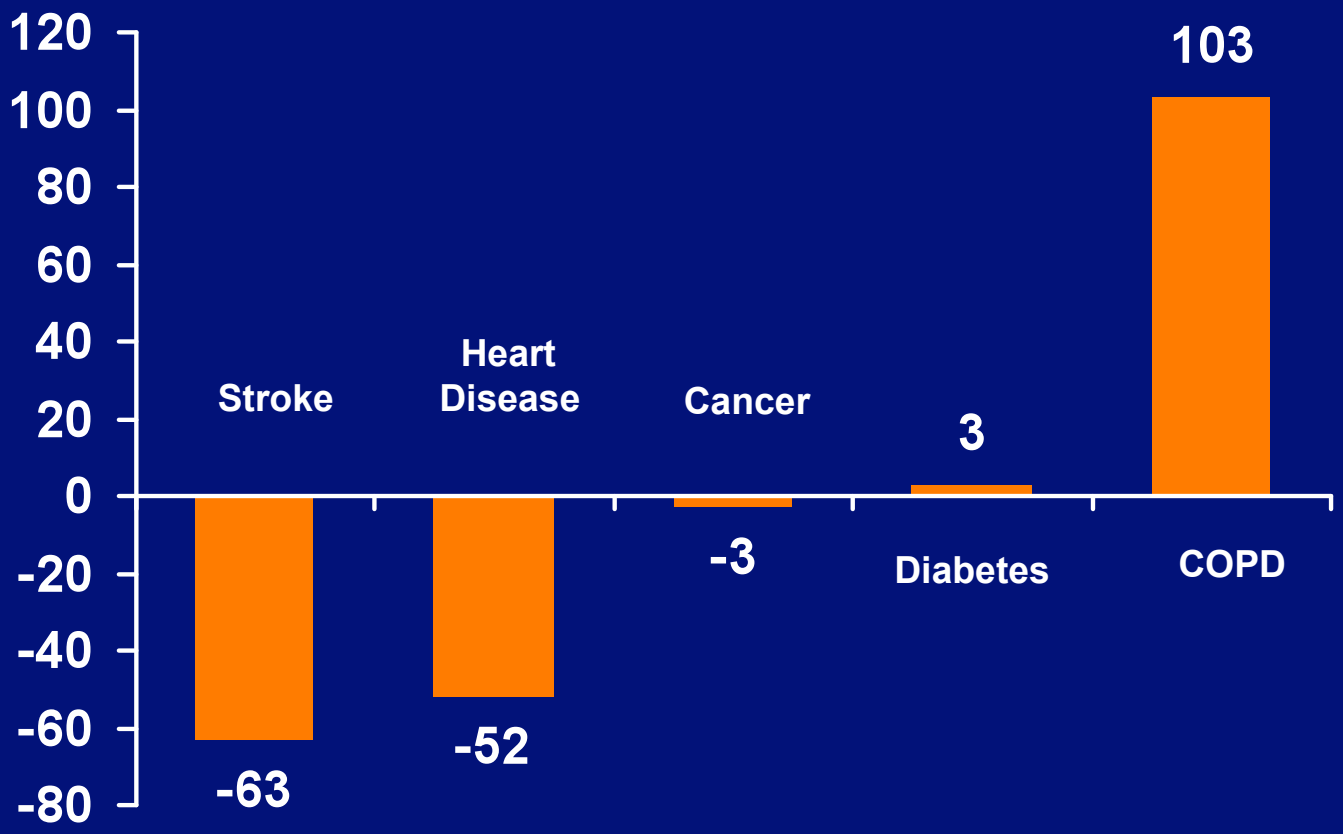
Percent Change in Age-Adjusted Death Rates, U.S., 1965-1998



Source: NHLBI/NIH/DHHS

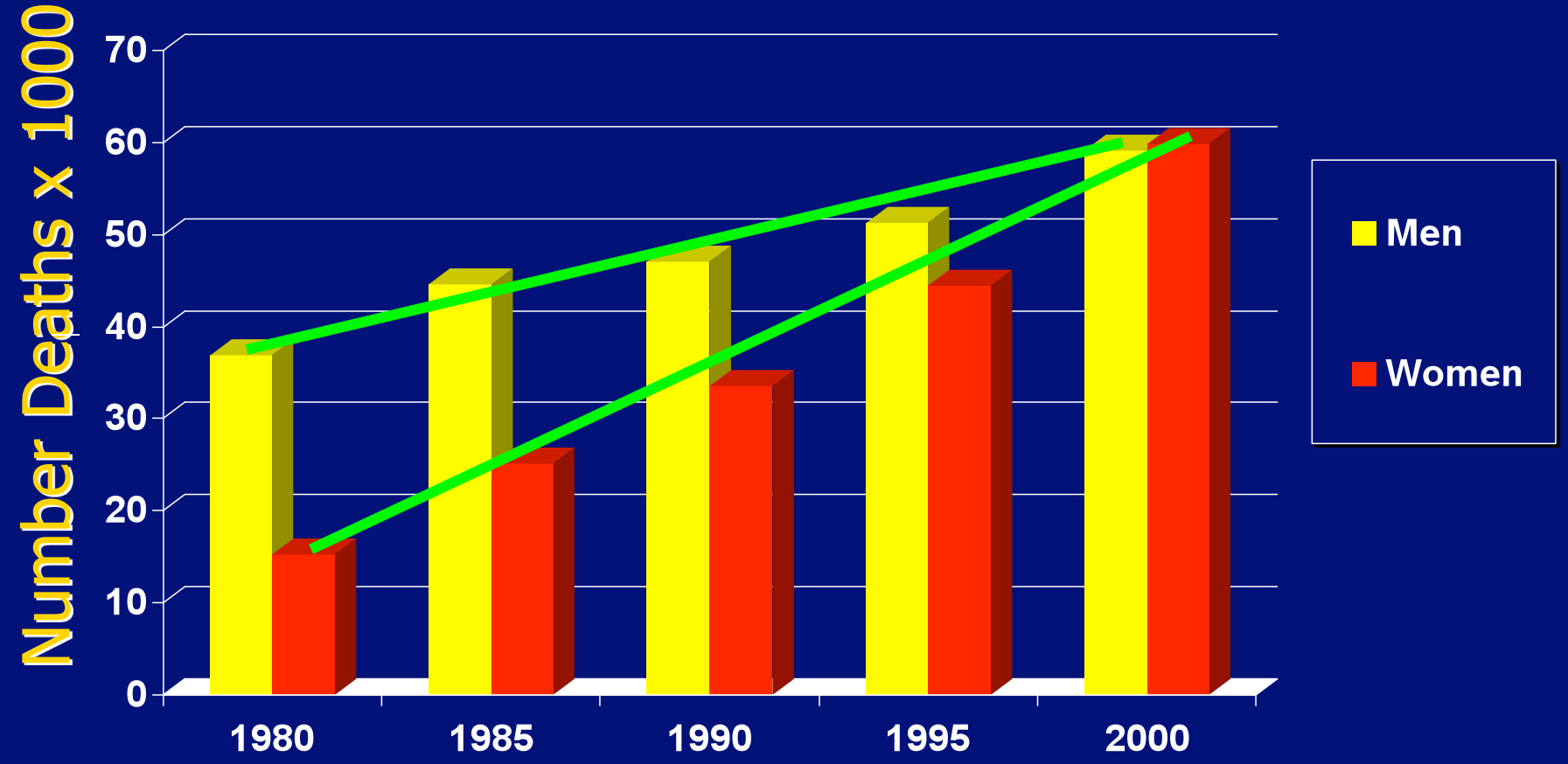
Major Causes of Death

% Change in Age-Adjusted Death Rate in USA, from 1970 to 2002 (%)



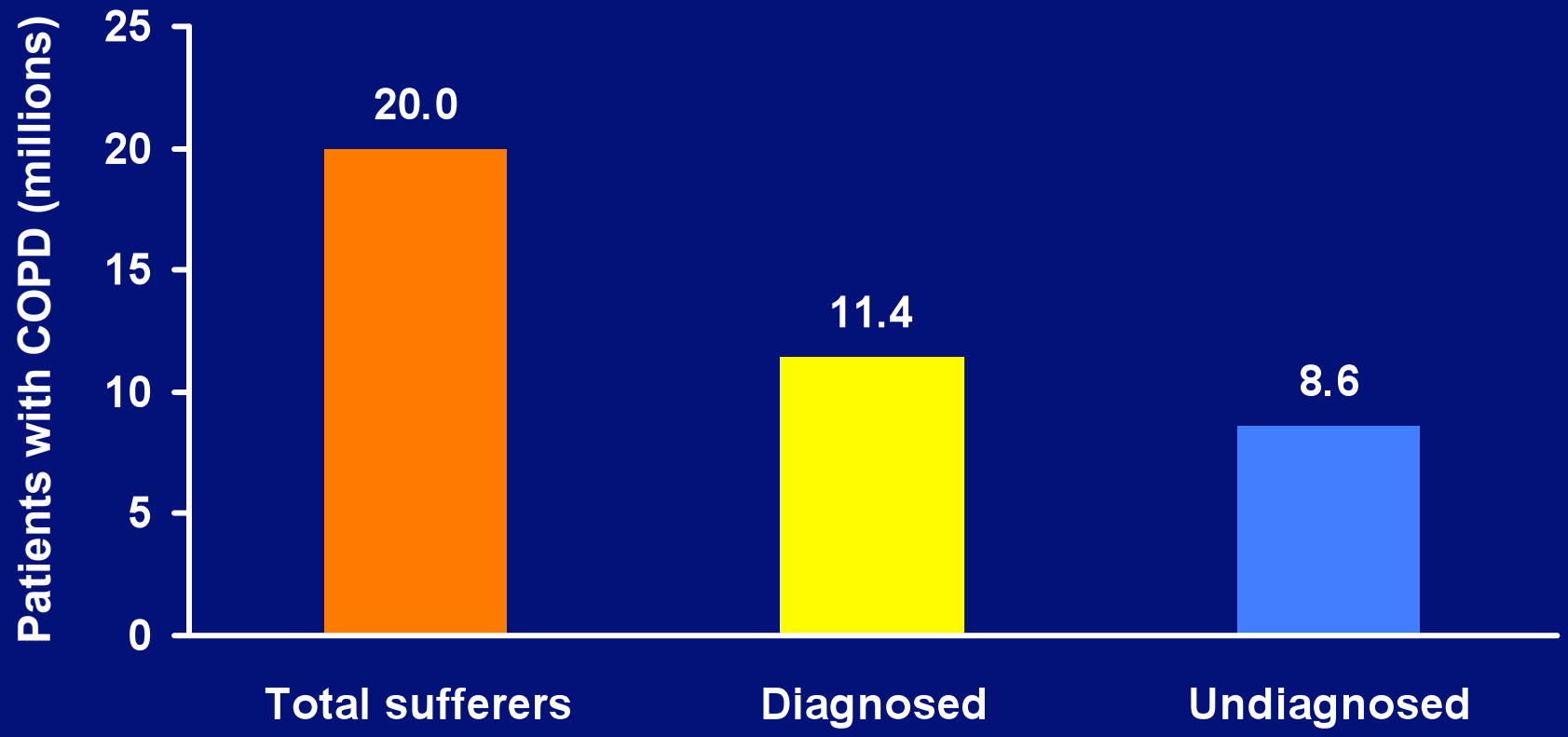
Jemal A, et al. *JAMA*. 2005;294:1255-1259.

COPD Mortality by Gender
U.S. 1980-2000



Source: US Centers for Disease Control and Prevention, 2002

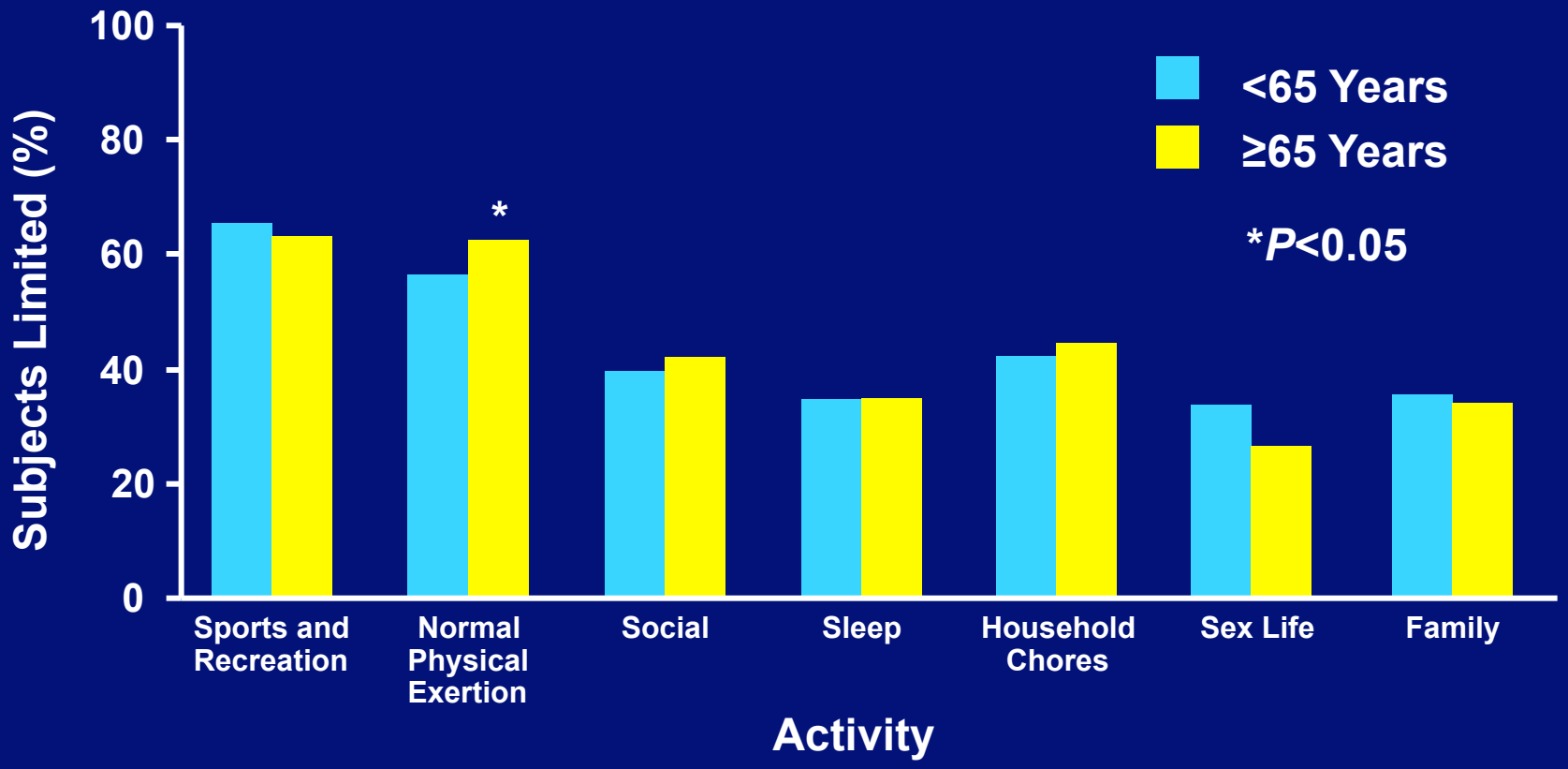
Americans with COPD



Of patients diagnosed, ~35% are not being treated with prescription medicines

Mannino DM et al. *MMWR*. 2002;51(SS-6):1–16.
NHANES III, NHIS, 2002, SDI, 2005.

COPD Limits Daily Activities for Patients Regardless of Age

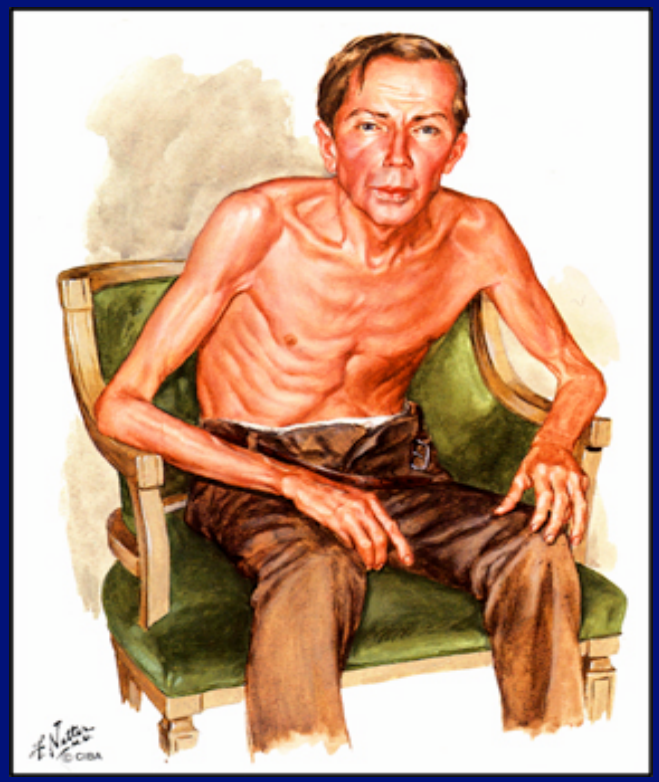


ADVAIR has not been shown to impact these endpoints.

P17. How much do you feel your respiratory condition limits what you can do in each of the following areas? n=3,265

Rennard S, et al. *Eur Respir J.* 2002;20:799-805.

Classic Representations of Patients with COPD



Emphysema

Chronic Bronchitis

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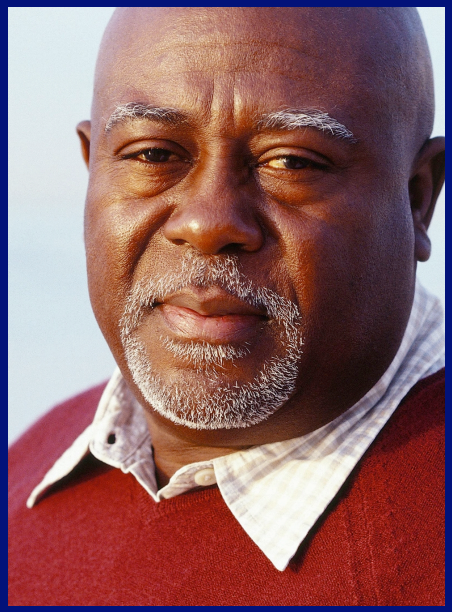
The Changing Face of COPD



- 55-year-old male
- FEV_1 55% predicted
- Current smoker
- Productive cough in the morning
- No longer can walk up stairs

- 48-year-old female
- FEV_1 60% predicted
- 20 pack-year history of smoking
- Increased shortness of breath when gardening

Risk Factors for COPD

- Smoking
- Occupational and environmental exposures
- Genetic factors
- Increased airway responsiveness

Complications of COPD

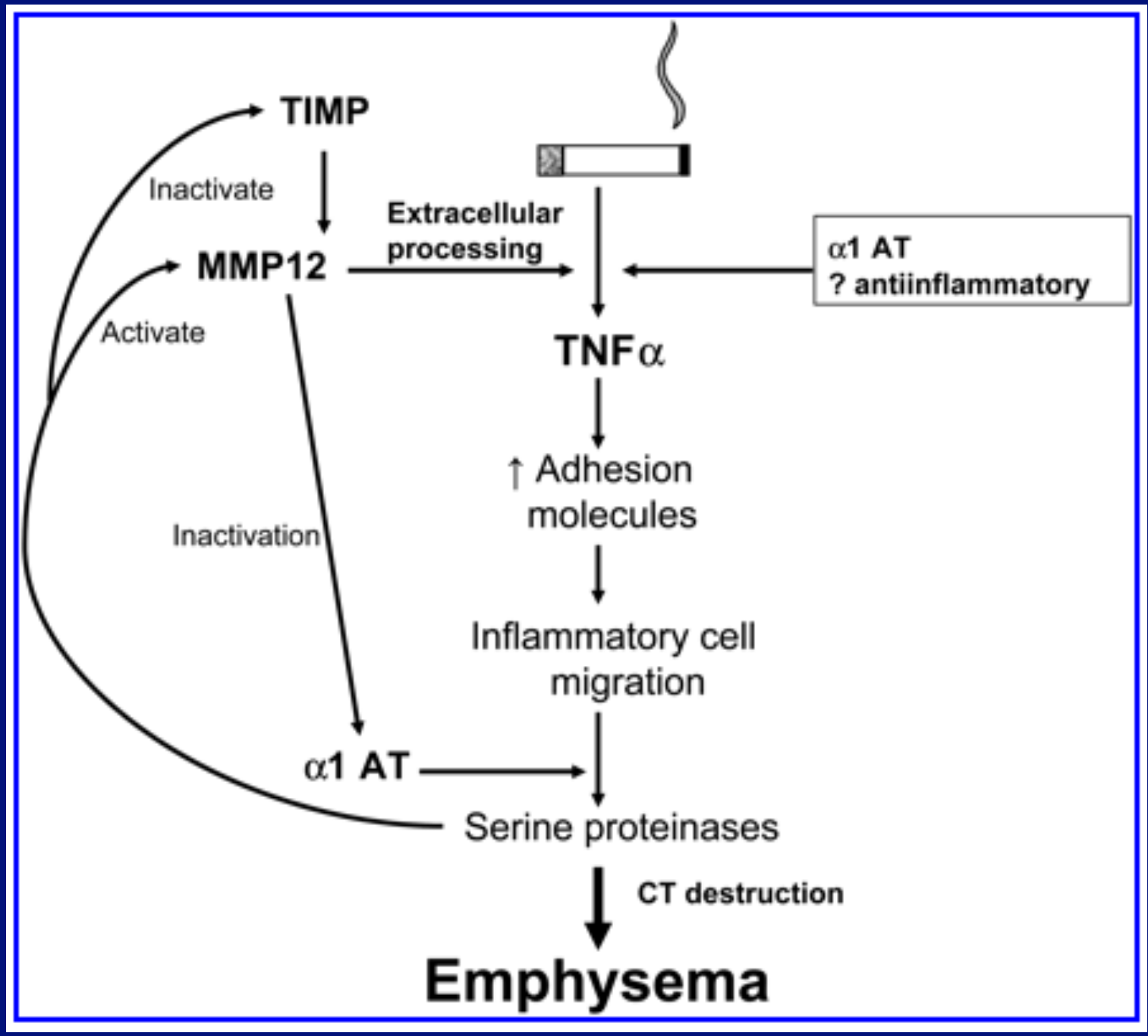
- Chronic illnesses associated
  - Cardiovascular disease
  - Depression
  - Osteoporosis
  - Lung cancer

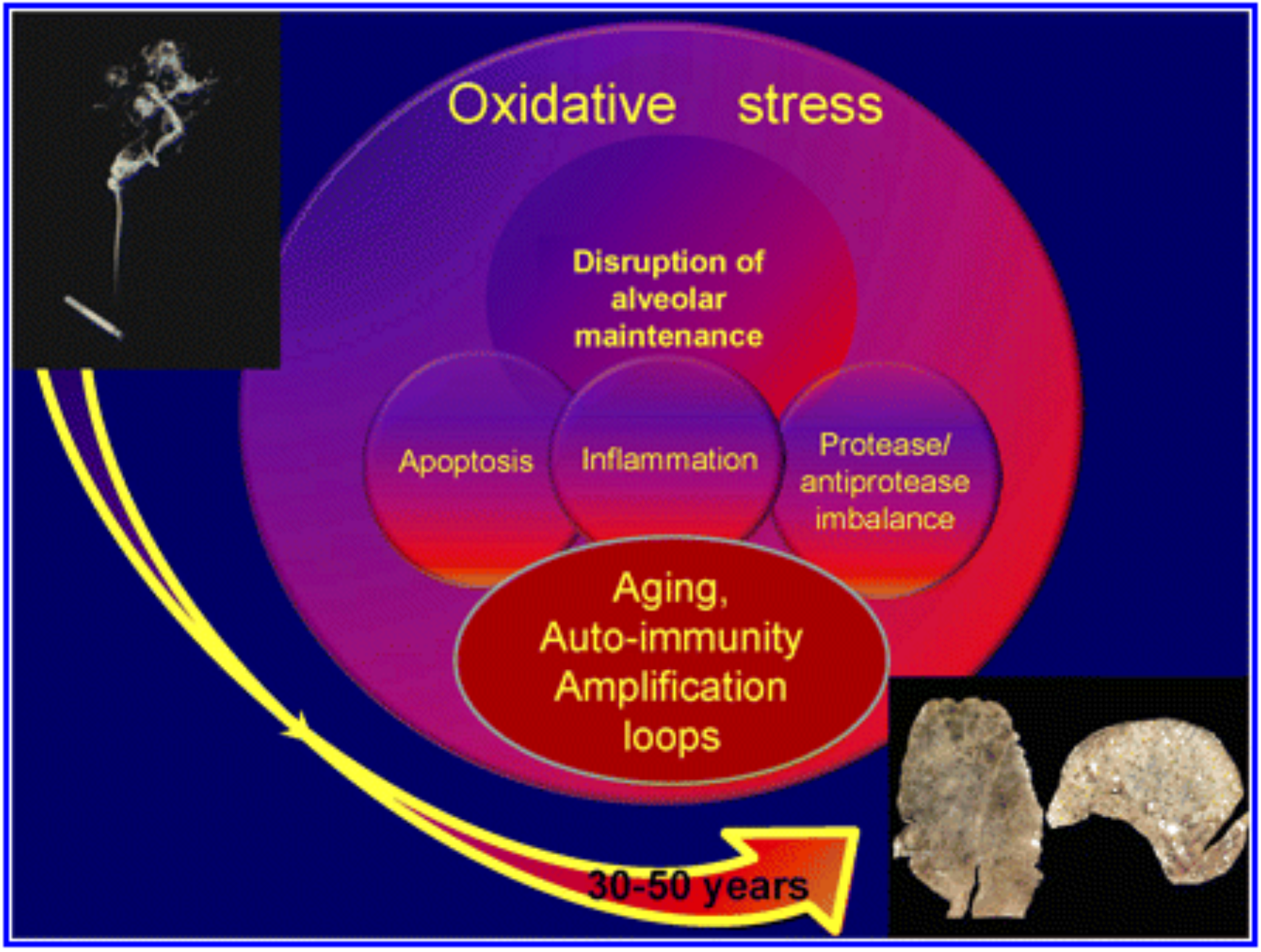
COPD

- Opportunities

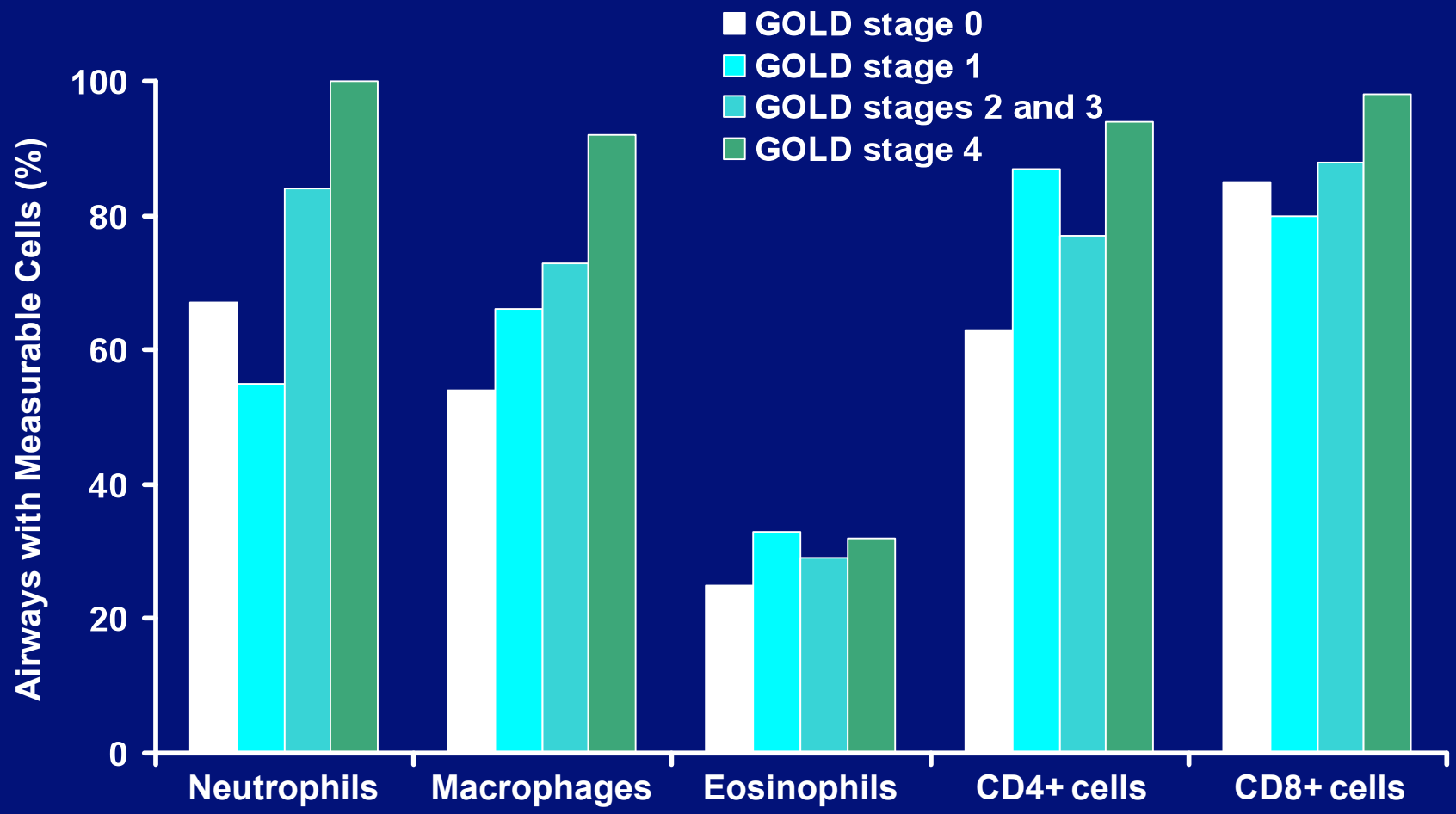
- Advocacy

Pathophysiology and Molecular Mechanisms


TIMP
Inactivate
MMP12
Activate
Extracellular processing
α1 AT
? antiinflammatory
TNFα
↑ Adhesion molecules
Inactivation
Inflammatory cell migration
α1 AT
Serine proteinases
CT destruction
Emphysema


Oxidative stress
Disruption of alveolar maintenance
Apoptosis
Inflammation
Protease/ antiprotease imbalance
Aging, Auto-immunity Amplification loops
30-50 years

Inflammation in COPD Occurs Even in the Early Stages



Adapted from Hogg JC, et al. *N Engl J Med*. 2004;350:2645-2653.

COPD

- Opportunities

- Advocacy

Risk Factors for COPD
Latest Research

Passive Smoking Exposure and Risk of COPD Among Adults in China: the Guangzhou Biobank Cohort Study

P Yin, CQ Jiang, KK Cheng, TH Lam , KH Lam, MR Miller, WS Zhang, BH Thomas, P Adab

Lancet 2007;370:751-757

COPD

Yin et al, Lancet 2007

- n = 15,379 never smokers
- Guangzhou Cohort study
- Age > 50 yrs
- Women 88%
- Measurement of passive smoking
  - Questionnaire
  - Childhood, adulthood (work, home)
- Outcomes
  - Chronic respiratory symptoms
  - COPD (FEV1/FVC < .70)

COPD

Yin et al, Lancet 2007

- Association with COPD (n=6497)
  - Cumulative passive smoke exposure during adulthood
  - Highest category of passive smoking
    - > 5 yr
    - 40 hrs/wk total exposure
    - COPD risk 1.48 O.R. (CI 1.18-1.85)

COPD

- Opportunities

- Advocacy

Occupational Exposures and the Risk of COPD: dusty trades revisited

PD Blanc, C Iribarren, L Trupin, G Earnest,
PP Katz, J Balmes, S Sidney , MD Eisner

Thorax 2009;64:6-12

Occupational Exposures

Blanc et al, Thorax 2009

- N = 1302 with COPD; 302 without COPD
- Occupational exposure
  - Reported exposure to vapor, dust, gas, fumes (longest held job)
  - Job exposure matrix (longest held job) probability
    - Low
    - Intermediate
    - High

Occupational Exposures

Blanc et al, Thorax 2009

- Reported VGDF exposure
  - Double odds of COPD (OR 2.13)
- JEM exposure
  - Greater risk of COPD (OR 2.33)
- Cigarette smoking + exposure history
  - Greatly increased risk of COPD
    - Smoking and VGDF OR 14
    - Smoking only OR 6.7
    - VGDF OR 2.0

Occupational Exposures

Blanc et al, Thorax 2009

- Clinical Implications
  - Both smoking and occupational exposure are strong risk factors for developing COPD
  - Elimination of one, but not the other, will not be fully effective in preventing COPD

COPD

- Opportunities

- Advocacy

Occupational Exposures and COPD: an Ecological Analysis of International Data

PD Blanc, AM Menezes, E Plana, DM Mannino, PC Hallal, Toren K, MD Eisner, JP Zock

Eur Respir J 2009;33:298-304

Occupational Exposure

Blanc et al, Eur Respir J 2009

- Gold stage II or greater
- Prevalence of COPD, occupational exposure, and ever smoking
- Every 10% increase in occupational exposure prevalence, prevalence of COPD increased by 0.8%
- Every 10% increase in proportion of ever smoking population, prevalence of COPD increased by 1.3%

COPD

- Opportunities

- Advocacy

COPD
Disease Progression

COPD Progression and Long Term Outcomes

- UPLIFT Study
  - 5993 patients (moderate, severe COPD)
  - 4 years
  - Tiotropium v. placebo
  - Tiotropium group
    - Increased baseline FEV1 (47-65 ml)
    - No slowing of rate of decline after day 30
    - Improved secondary outcomes
      - HRQL
      - COPD exacerbations
      - Hospitalizations
      - Respiratory failure

COPD Progression and Long Term Outcomes

- TORCH Study
  - Moderate, severe COPD
  - Salmeterol, fluticasone (SFC, SAL, FP, placebo)
  - Rate of lung function decline
    - SFC -39 ml/yr
    - SAL -42 ml/yr
    - FP -42 ml/yr
    - Placebo -55 ml/yr

COPD Progression and Long Term Outcomes

- Mucolytic Therapy
  - Carbocisteine v. placebo
  - n = 709
  - Gold stage II-III
  - Exacerbation rate
    - Reduced by 25% (1.35 to 1.01)
  - HRQL
    - Overall SGRQ, symptom subscale scores

COPD

- Opportunities

- Advocacy

COPD
Global Needs Assessment

COPD
Global Needs Assessment

- Preventable
- Under-diagnosed
- Treatable

COPD
Global Needs Assessment

- Preventable

COPD

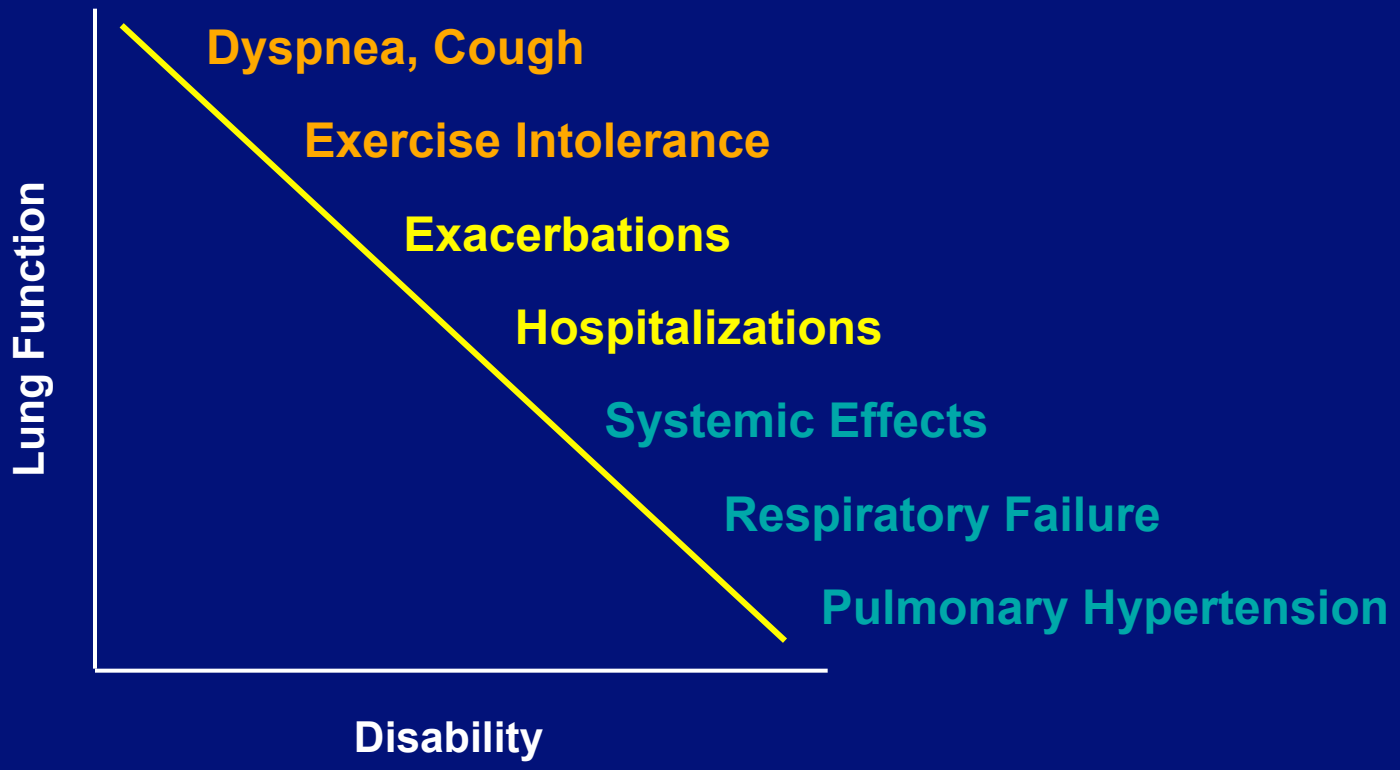
- Opportunities

- Advocacy

COPD
Global Needs Assessment

- Under-diagnosed

Challenges to Diagnosing COPD Early

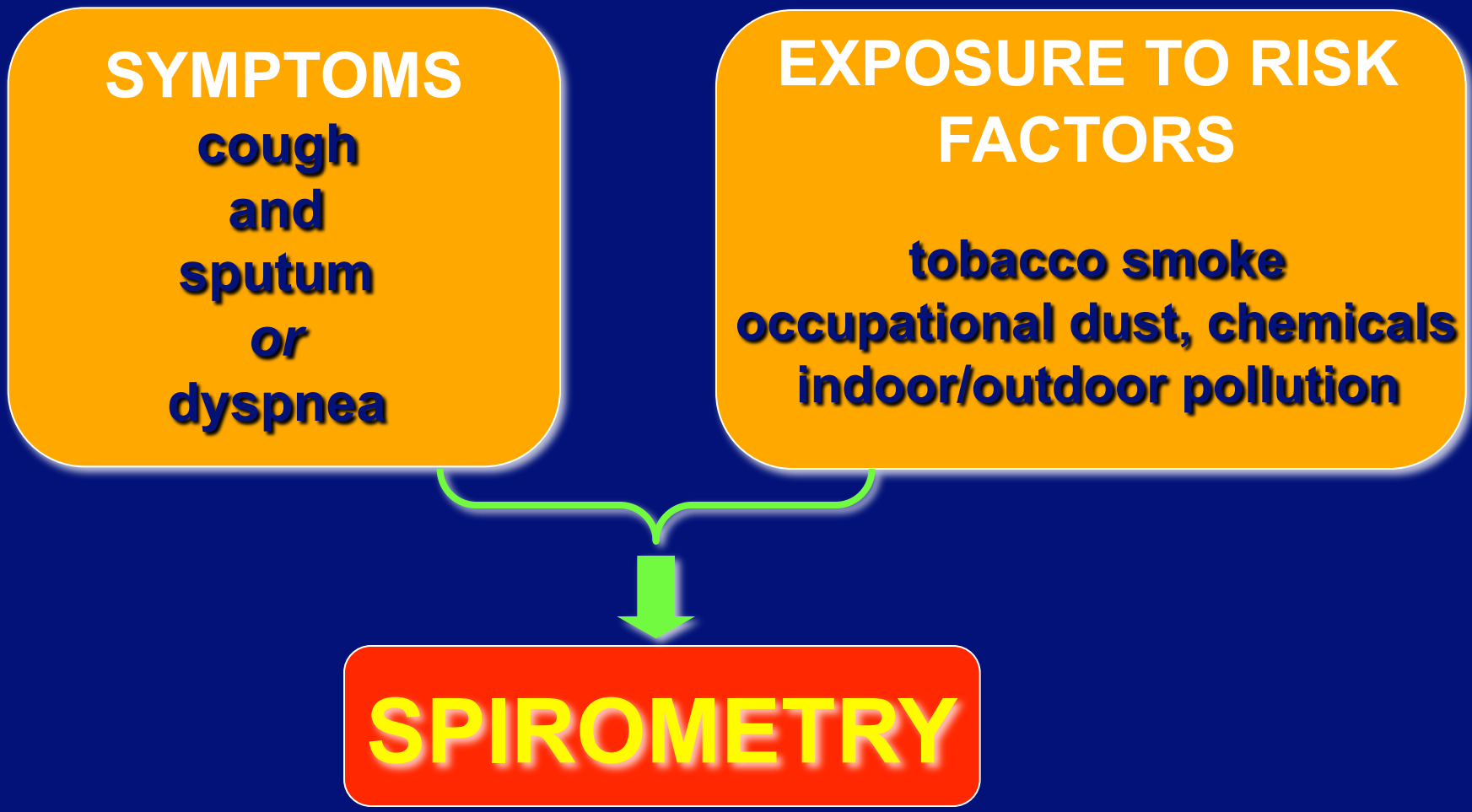


Adapted from Fletcher C and Peto R. *Br Med J*. 1977;i:1645-1648.

COPD
Global Needs Assessment

- Under-diagnosed
  - Few symptoms early
  - Slowly progressive
  - Unrecognized
  - Mistaken identity

Diagnosis of COPD



SPIROMETRY

- Detect occult disease
- Stage COPD
- Guide therapy
- Predict
  - Quality of life
  - Exacerbations
  - Survival

COPD Underdiagnosis

Buist et al, Lancet 2007

- BOLD study (n=1258)
- Questionnaire, spirometry
- FEV1/FVC < 0.70 (n=304)
  - Never smokers 108
  - Physician diagnosis 35 (11.5%)
  - Correct diagnosis
    - 70-80 y.o. 20%
    - Other ages 10%

COPD Underdiagnosis

Buist et al, Lancet 2007

- Presence of respiratory symptoms
  - Doubled probability of COPD diagnosis
- Non-respiratory comorbidities
- Asymptomatic patients with no respiratory comorbidities
  - Likely to be undiagnosed and untreated

COPD
Never Smokers

- NHANES III (1998-1994) (n=16084)
  - Petty, Chest 2000
  - Airway obstruction prevalence 9%
  - Never smokers
    - mild COPD 5%
    - moderate/severe 2%
- BOLD
  - Never smokers
    - Moderate/severe 5.5%

Prevalence, Severity, and Underdiagnosis of COPD in the Primary Care Setting

Bednarek et al, Thorax 2008

- n = 1960 (87%)
- Spirometry 92% met ATS criteria
- Airflow limitation
  - Pre BD 211 (11%)
  - Post BD 183 (9%)
    - Mild 31%
    - Moderate 51%
    - Severe 15%
    - Very severe 3%

Knowledge and Use of Office Spirometry by PCPs

Kaminsky et al, Respir Care 2005

- Spirometry use
- Perceptions
- N = 57 PCP offices
  - 29 (51%) responded
  - 66% owned own spirometer
  - 21/29 participated in workshop

Knowledge and Use of Office Spirometry by PCPs

Kaminsky et al, Respir Care 2005

- Survey
  - Local practice of office spirometry
  - Barriers to performance
  - General knowledge
- Educational program
  - 60 minute educational workshops

Knowledge and Use of Office Spirometry by PCPs

Kaminsky et al, Respir Care 2005

- Not performing spirometry
  - Uncertainty about impact 41%
  - MD, staff unfamiliarity 38%
  - Lack of training 34%
- Increase in performance (3 mo) 59%
  - Barriers
    - MD, staff unfamiliarity 22%
    - Uncertain about results 22%
    - Time 22%
    - Reimbursement 22%

COPD

- Opportunities

- Advocacy

COPD
Global Needs Assessment

- Treatable

COPD
Global Needs Assessment

- Drug therapy
  - Guidelines
  - Combination therapy
  - Optimal therapy

COPD
Global Needs Assessment

- Non pharmacologic therapy
  - Oxygen
    - Improved survival
    - Improved QOL
  - Rehabilitation
    - Improved exercise capacity
    - Reduced dyspnea
    - Improved HRQL
    - Reduced health care utilization
    - Reduced anxiety, depression

Pulmonary Rehabilitation Following Exacerbations of COPD

M Puhan, M Scharplatz, T Troosters,
EH Walters, J Steurer.

Cochrane Database of Systematic Reviews 2009

Issue 1. Art. No.: CD 005305.

Rehab Following Exacerbations

Puhan, Cochrane Database 2009

- Randomized clinical trials of any duration
- COPD exacerbation
- Included pulmonary rehabilitation v. control
- Calculated pooled odds ratio

Rehab Following Exacerbations

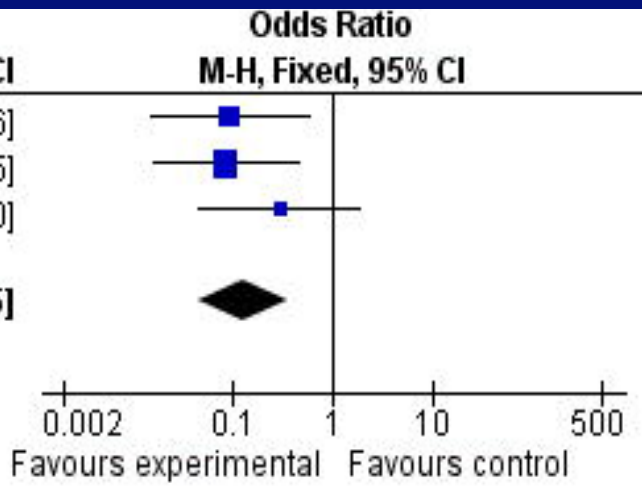
Puhan, Cochrane Database 2009

- 6 trials
- Effects of pulmonary rehabilitation
  - Reduced hospital admissions
  - Number needed to treat
  - Mortality
  - Health related quality of life
  - Improved exercise capacity

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Behnke 2000	3	14	9	12	34.0%	0.09 [0.01, 0.56]
Man 2004	2	20	12	21	47.1%	0.08 [0.02, 0.45]
Murphy 2005	2	13	5	13	18.9%	0.29 [0.04, 1.90]
Total (95% CI)		**47**		**46**	**100.0%**	**0.13 [0.04, 0.35]**
Total events	7		26			

Heterogeneity: Chi² = 1.11, df = 2 (P = 0.57); I² = 0%

Test for overall effect: Z = 3.98 (P < 0.0001)

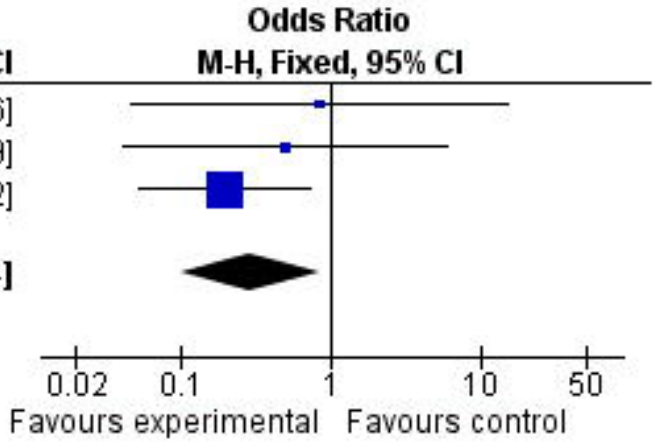


Puhan et al, Cochrane Database
2009

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Behnke 2000	1	14	1	12	7.8%	0.85 [0.05, 15.16]
Man 2004	1	20	2	21	14.4%	0.50 [0.04, 5.99]
Troosters 2000	6	24	12	19	77.9%	0.19 [0.05, 0.72]
Total (95% CI)		**58**		**52**	**100.0%**	**0.29 [0.10, 0.84]**
Total events	8		15			

Heterogeneity: Chi² = 1.07, df = 2 (P = 0.59); I² = 0%

Test for overall effect: Z = 2.29 (P = 0.02)



Forest plot of comparison: 1 Rehabilitation versus control, outcome: 1.2 Mortality.

Puhan et al, Cochrane Database
2009

A Specific Home Care Program Improves the Survival of Patients with COPD Receiving Long Term Oxygen Therapy

M Rizzi, M Grassi, M Pecis, A Andreoli,
AE Taurino, M Sergi, F Fanfulla

Arch Phys Med Rehabil
2009;90:395-401

Home Care and COPD

Rizzi et al Arch Phys Med Rehabil 2009

- Objectives
  - To analyze the influence of a home care program on outcomes of patients with COPD receiving LTOT in comparison with outcomes of patients receiving standard care

Home Care and COPD

Rizzi et al Arch Phys Med Rehabil 2009

- Methods
  - 2 parallel cohorts (HC v. SC)
  - University hospital
  - 10 year follow-up
  - Enrollment
    - COPD diagnosis
    - On LTOT for one year
    - At least one exacerbation
    - Optimal pharmacologic therapy

Home Care and COPD

Rizzi et al Arch Phys Med Rehabil 2009

- Methods
  - Comorbidity by Charlson index
  - Home care
    - Planned outpatient visits, evaluations
    - Home care evaluations
    - Rehabilitation program
    - MDs, respiratory nurses, rehab therapists
  - Standard care
  - Patients chose the cohort

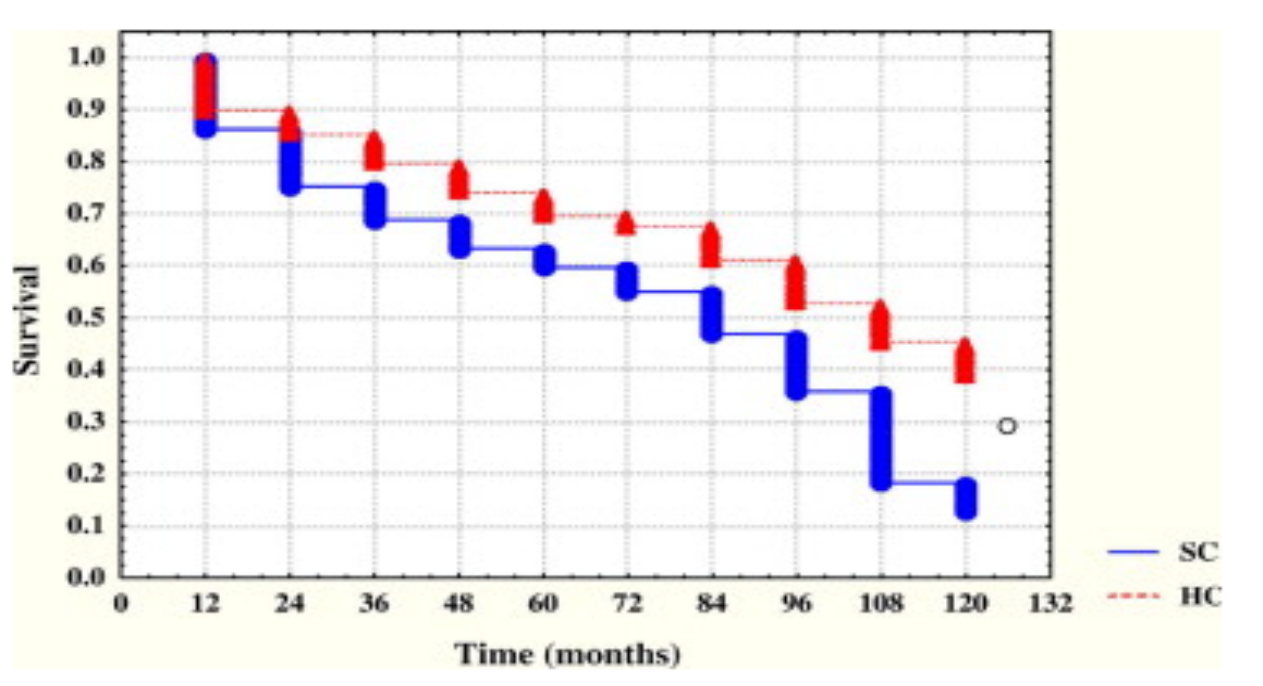
Home Care and COPD

Rizzi et al Arch Phys Med Rehabil 2009

- Methods
  - Prescriptions of home ventilation
  - ED visits
  - Hospital admissions (days, numbers)
  - Causes of death

Survival Curves

Home Care v. Standard Care



Rizzi et al, APMR 2009

Home Care and COPD

Rizzi et al Arch Phys Med Rehabil 2009

- Discussion
  - Increased survival rate (HC group)
    - Reduced exacerbations
    - Fewer ICU admissions
    - Stabilized of lung function
    - Decreased need for home ventilation
    - Improved physiologic status (e.g. BMI,MIP, P_aCO_2)

COPD

- Opportunities

- Advocacy

KNOWLEDGE
Gaps

COPD
Knowledge Gaps

- Nihilistic attitude
- Under-diagnosis
- Mistaken identity
- Lack of guideline awareness
- Lack of guideline implementation
- Patient avoidance of care

COPD
Knowledge Gaps (Patient)

- Patient care barriers
  - Lack of knowledge
  - Low MD supervision
  - Insufficient resources
  - Smokers avoid medical care
  - Low awareness of symptoms
  - Non-adherence

Living with COPD: A Survey of Patient's Knowledge and Attitudes

P Hernandez, M Balter, J Bourbeau,
R Hodder

Respir Med 2009;103:1004-1012

Patient's Knowledge and Attitudes

Hernandez Respir Med 2009

- Objectives
  - To determine whether Canadians with COPD are properly educated and supported
  - To recommend solutions to any care gaps identified

Patient's Knowledge and Attitudes

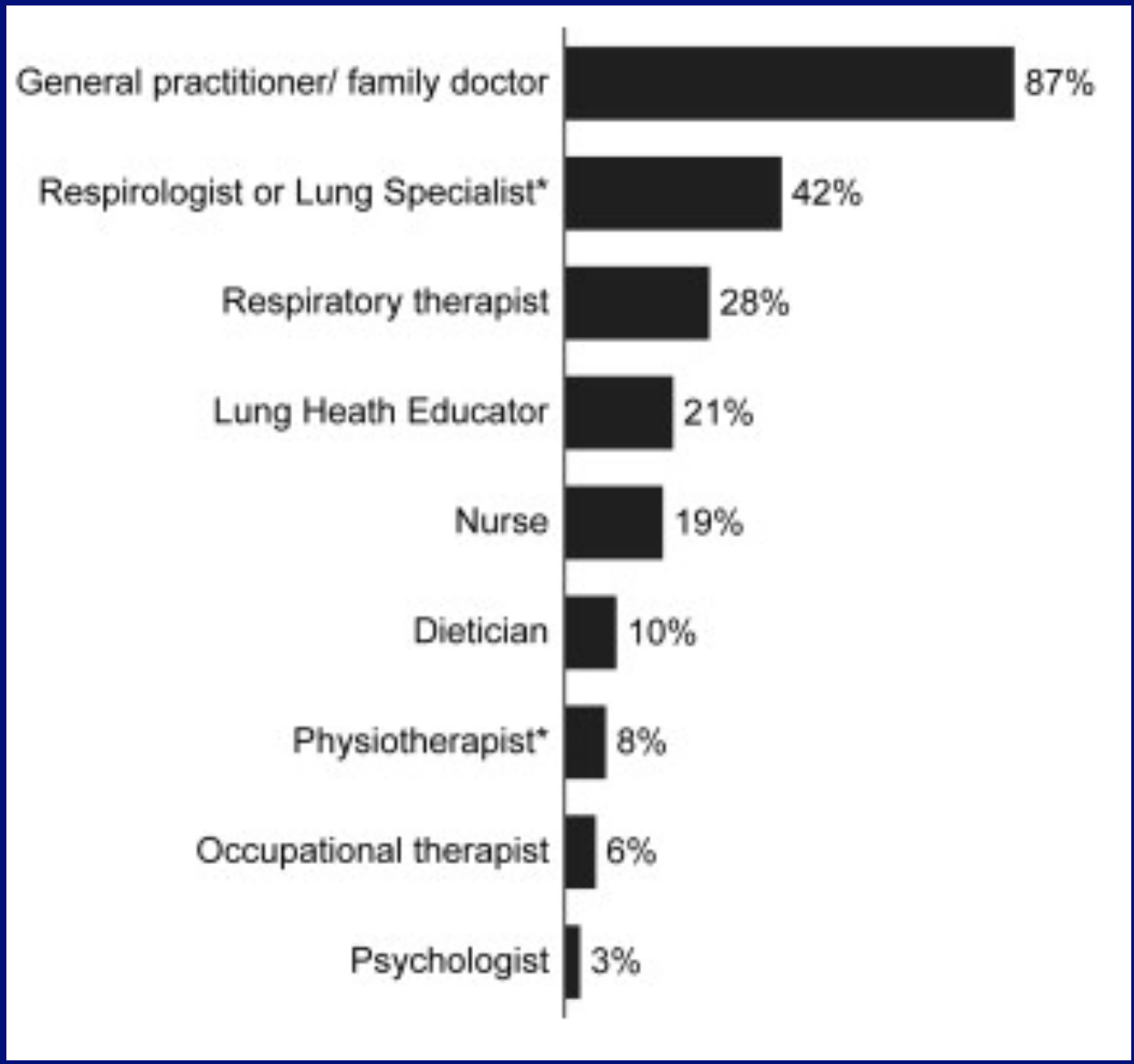
Hernandez Respir Med 2009

- Methods
  - 389 Canadians
  - Telephone survey (35 minutes)
  - Over age 40
  - COPD diagnosis
  - Current or former smokers
  - Severity (MRC score)
  - 2006-2007

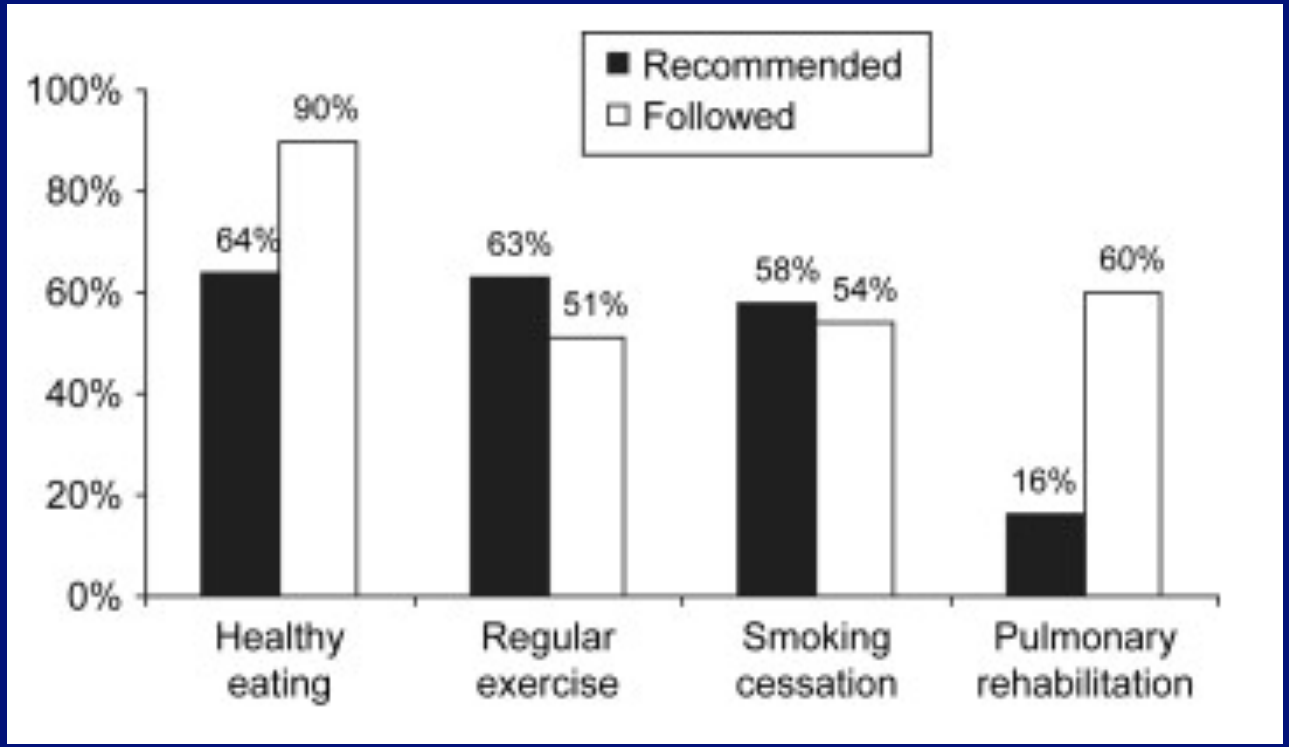
Patient's Knowledge and Attitudes

Hernandez Respir Med 2009

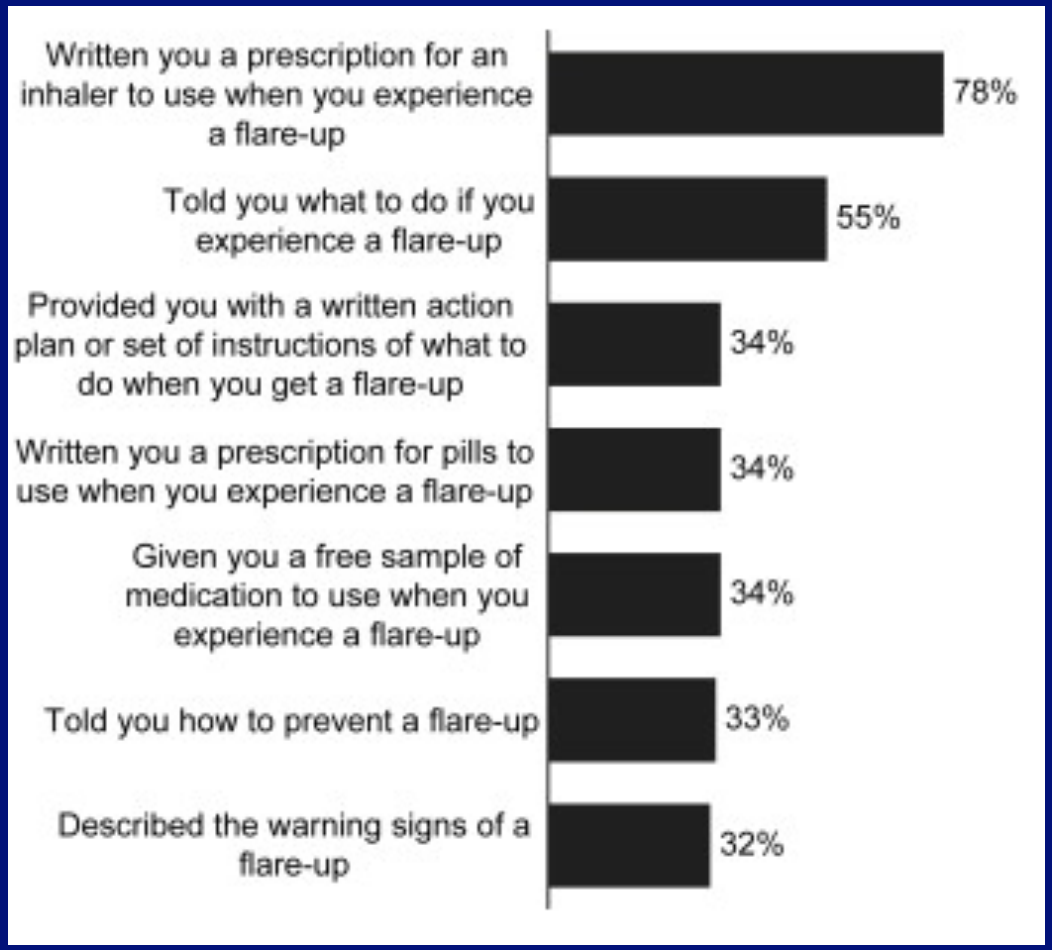
- Methods
  - Main healthcare provider- family physician
  - Information solicited
    - Understanding of disease impact on life
    - Current medications, perceived effectiveness
    - Healthcare providers seen over last year
    - Routine management, care actions
    - Demographic details
    - Knowledge gained since diagnosis
    - Flare-ups (treatment, advice)



Hernandez et al, Respir Med 2009



Hernandez et al, Respir Med 2009



Hernandez et al, Respir Med 2009

Patient's Knowledge and Attitudes

Hernandez Respir Med 2009

- Results
  - Most had spirometry done at diagnosis
  - Discordant pattern of medication use
  - Rehab rarely recommended

Patient's Knowledge and Attitudes

Hernandez Respir Med 2009

- Results
  - Written action plan
    - 34%
  - Instructions for exacerbation preventions
    - 33%

Patient's Knowledge and Attitudes

Hernandez Respir Med 2009

- Conclusions
  - Symptom burden and psychosocial impact of living with COPD is substantial
  - Significant gaps in patient knowledge
    - Management of COPD
    - Little contact with lung health educators

Patient's Knowledge and Attitudes

Hernandez Respir Med 2009

- Clinical Implications
  - Significant gaps in knowledge underlie the importance of education and instruction for patients with COPD
  - Greater need for such education is necessary

COPD

- Opportunities

- Advocacy

COPD
Care Gaps

- Care Barriers
  - General care
  - Exacerbation care
  - Hospital care

COPD Stakeholders

- Patient
- Family
- Physicians
- Insurance
- Society

COPD

- Opportunities

- Advocacy

"It's a Boy!"

— and his life expectancy is brighter, and longer by 15 years — thanks to medicine's "men in white."

Cold figures . . . with a warm, wonderful significance. This table based on figures from several leading insurance companies tells in seven lines as much as a five-foot shelf of volumes on the amazing strides modern medical science has made in protecting and prolonging life.

AVERAGE LIFE EXPECTANCY IN U.S.—1900-1943

YEAR	MEN	WOMEN
1900-02	48	51
1901-10	49	52
1909-11	50	53
1920-29	57	60
1930-39	60	64
1939-41	62	67
1943	63	68

According to a recent Nationwide survey:

According to a recent Nationwide survey:

MORE DOCTORS SMOKE CAMELS THAN ANY OTHER CIGARETTE!

THAT's the significant showing made when three leading, independent research organizations put this question to 113,597 physicians in the United States: "What cigarette do you smoke?"

Figures were checked and re-checked!

And more doctors named Camel as their smoke than any other cigarette!

Doctors, like all of us, smoke for pleasure. Camel's rich, full flavor appeals to their taste...Camel's cool mildness registers with their throats...just as with millions of smokers the world over!

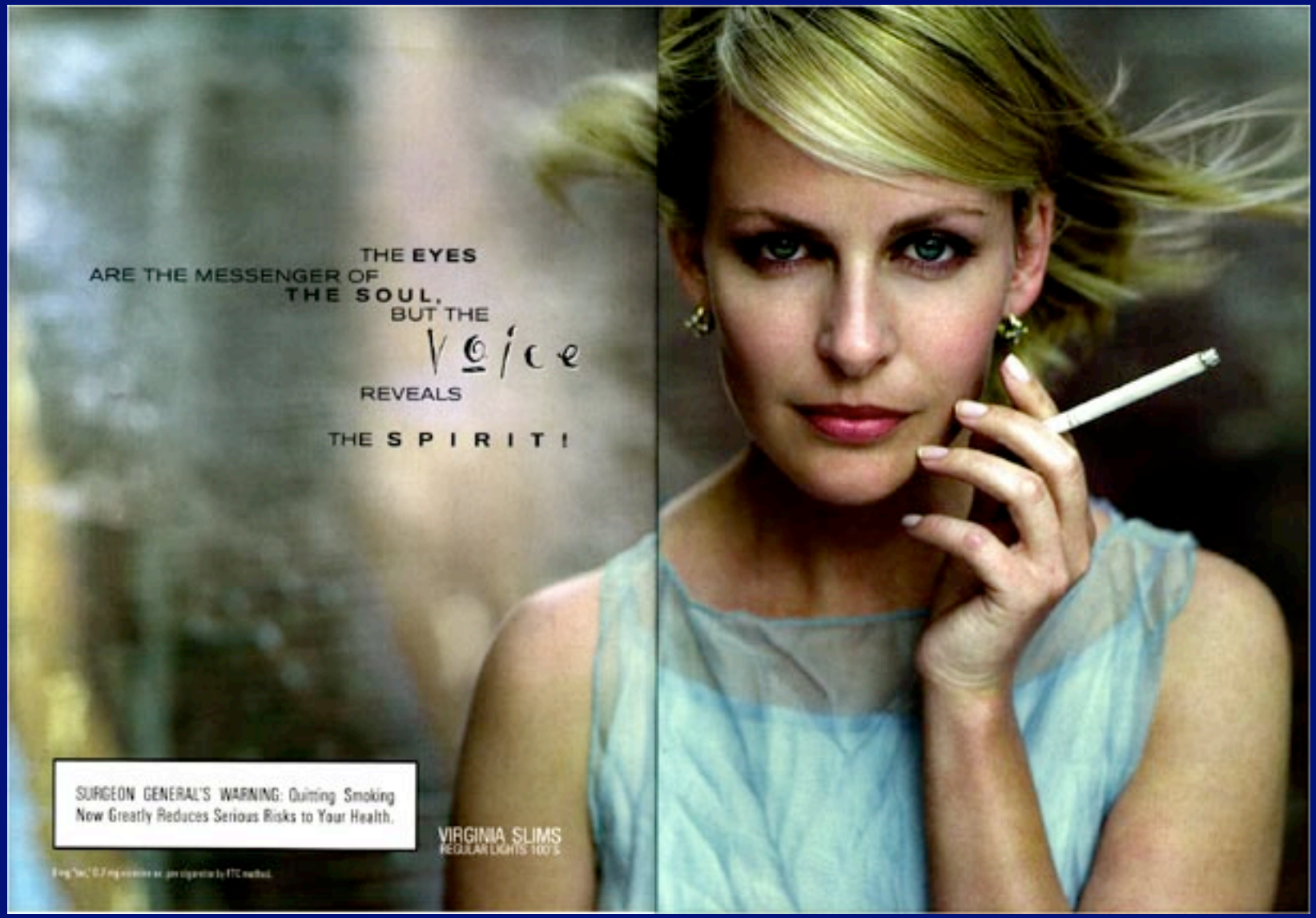
The "T-Zone"—T for Taste and T for Throat

The best proving ground . . . the most critical "laboratory"... for a cigarette is your own taste and throat. Your taste is the place to "test" the rich, full flavor of Camel's costlier tobaccos. Your throat will tell you most conclusively how Camel's cool mildness agrees with it.

CAMELS *Costlier Tobaccos*

R. J. Reynolds Tobacco Company, Winston-Salem, N. C.

Hey!
Emphysema
Can Kill You!
See Your Doctor
For a Breathing Test
Test Your Lungs...
Know Your Numbers
HANOVER Hospital
A MEMBER OF HANOVER HEALTHCARE PLUS NETWORK


THE EYES
ARE THE MESSENGER OF
THE SOUL,
BUT THE
Voice
REVEALS
THE SPIRIT!
SURGEON GENERAL'S WARNING: Quitting Smoking Now Greatly Reduces Serious Risks to Your Health.
VIRGINIA SLIMS
REGULAR LIGHTS 100's