Diseases, Comorbidity, and Multimorbidity in Primary Care

Barbara Starfield, MD, MPH

Primary Care Course
(Based on Cape Town, South Africa, 2007;
and Barcelona, Spain, 2009)

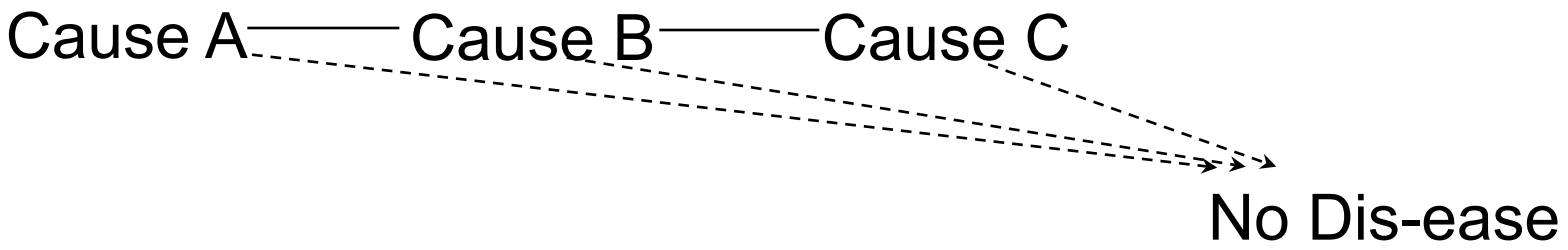
The purpose of this presentation is to explore the concepts of “disease” and “chronic disease” and to show why the current focus on specific diseases runs counter to improving health and, especially equity in health, and to show why a continuum of care (“primary care”) for all people and populations is more appropriate than care for targeted diseases.

Diseases

- are professional constructs
- can be and are artificially created to suit special interests; the sum of deaths attributed to diseases exceeds the number of deaths
- do not exist in isolation from other diseases and are, therefore, not an independent representation of illness
- are but one manifestation of ill health

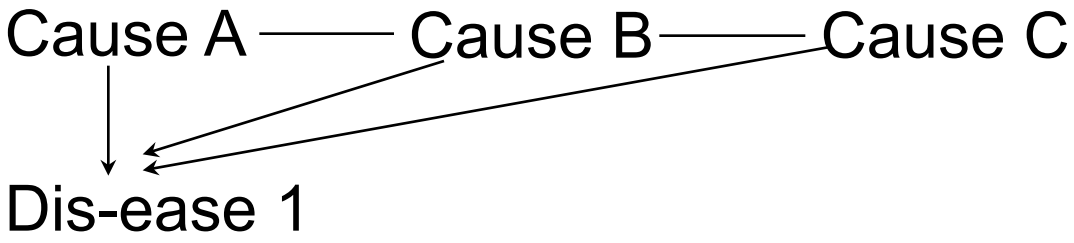
Sources: Chin. The AIDS Pandemic: the Collision of Epidemiology with Political Correctness. Radcliffe Publishing, 2007. De Maeseneer et al. Primary Health Care as a Strategy for Achieving Equitable Care: a Literature Review Commissioned by the Health Systems Knowledge Network. WHO Health Systems Knowledge Network, 2007. Available at: http://www.who.int/social_determinants/resources/csdh_media/primary_health_care_2007_en.pdf. Mangin et al, BMJ 2007; 335:285-7. Murray et al, BMJ 2004; 329:1096-1100. Tinetti & Fried, Am J Med 2004; 116:179-85. Walker et al, Lancet 2007; 369:956-963. Rosenberg, Milbank Q 2002;80:237-60. Moynihan & Henry, PLoS Med 2006;3:e191.

Penetrance



Pleiotropism

Etiologic Heterogeneity



Etiologic Heterogeneity

	# of different conventional risk factors
IHD	9
Stroke	7
Diabetes	6
Kidney disease	5
Arthritis	3
Osteoporosis	4
Lung cancer	1
Colorectal cancer	4
COPD	2
Asthma	2
Depression	5
Oral problems	3

Source: Australian Institute of Health and Welfare. Indicators for Chronic Diseases and Their Determinants, 2008. Canberra, Australia: AIHW, 2008.

Pleiotropism

# of specific diseases associated with selected risk factors	
Smoking	9
Physical activity	7
Alcohol	7
Nutrition	7
Obesity	7
Hypertension (?)	3
Dyslipidemia (?)	2
Impaired glucose tolerance (?)	1
Proteinuria (?)	1

Source: Australian Institute of Health and Welfare. Indicators for Chronic Diseases and Their Determinants, 2008. Canberra, Australia: AIHW, 2008.

Diseases Change over Time

- Biological phenomena change the environment around individuals. (Lewontin, 2010)
- The environment changes the manifestation of diseases. For example,

  Clostridium difficile is a different disease in 2010 than it was in 1995. During just one decade, mutations in the bacterium have transformed the organism from “a rare nosocomial infection to one that can spread rapidly in hospitals and has spilled out into the community. Now, infection of healthy individuals with few or no risk factors is not uncommon”, and rates are increasing. (JAMA 2010)

Sources: Lewontin, Not so natural selection. New York Review of Books, May 27, 2010. Voelker R. JAMA 2010;303:2017-9.

More than 60 studies found that standardized mortality rates across a range of serious mental disorders are 2-3 times greater than in the general population, with the majority of deaths attributed to medical illnesses. A growing list of risk factors for this excess are “unhealthy lifestyles, poor quality of medical care, poverty, biological mechanisms including dysregulation of the hypothalamic-pituitary-adrenal axis, and adverse metabolic consequences of psychotropic medications.”

Sources: Druss & Bornemann, JAMA 2010;303:1972-3.
Newcomer & Hennekens, JAMA 2007;298:1794-6.

- “The genetics of mental illness may really be the genetics of brain development, with different outcomes possible, depending on the biological and environmental context.”
- “Although many of the genes implicated (in the genesis of illness) are involved in brain development, copy number variants do not appear to be specific for illnesses in the current diagnostic scheme. Genetic variants do not map selectively onto current diagnostic categories … and the current diagnostic categories, based on clinical characteristics, do not seem to align well with findings from genetics and neuroscience.”
- “Although mental illnesses are more likely neurodevelopmental rather than neurodegenerative, the behavioral and cognitive manifestations … may be late stages of processes that start early in development …”; what may be required are novel interventions based on alternative plasticity or retuning circuitry rather than neurotransmitter pharmacology.
- IN OTHER WORDS, ILLNESSES ARE NOT DISCRETE ENTITIES; THEY RESULT FROM COMPLEX PROCESSES IN THE LIFE COURSE (INCLUDING FETAL). SIMILAR PHENOTYPES (DIAGNOSED “DISEASES”) HAVE DIFFERENT ETIOLOGIES (ETIOLOGIC HETEROGENEITY), REQUIRING DIFFERENT INTERVENTIONS.

Source: Insel & Wang, JAMA 2010;303:1970-1.

How “chronic” are chronic diseases?

Persistence of Diagnoses*

	Overall prevalence time 2	Prevalence among those having diagnosis in time 1	
Obesity	69	539	(x 7.8)
Asthma	70	628	(x 9.0)
Autoimmune disorder	18	641	(x 35.6)
Seizures	10	670	(x 67.0)

*per 1000, not adjusted for age

Starfield 09/07
D 5856 n

Persistence of Diagnoses*

	Overall prevalence time 2	Prevalence among those having diagnosis in time 1	
UTI	87	350	(x 4.0)
Hypertension	213	879	(x 4.1)
Headache	102	455	(x 4.5)
Lipoid disorders	144	720	(x 5.0)

*per 1000, not adjusted for age

Persistence of Diagnoses*

	Overall prevalence time 2	Prevalence among those having diagnosis in time 1	
URI	357	585	(x 1.6)
Pneumonia, non-bacterial	186	378	(x 2.0)
Sinusitis	231	525	(x 2.3)
Musculoskeletal s/s	190	461	(x 2.4)
Dermatitis, eczema	109	302	(x 2.8)
Abdominal pain	116	326	(x 2.8)
Otitis media	136	452	(x 3.3)

*per 1000, not adjusted for age

Not all chronic diseases are manifested year to year.

Acute diseases sometimes behave as if they were chronic, recurring year to year.

Only a minority of common chronic diseases or conditions are currently candidates for the vast majority of chronic disease management programs.

Acute and chronic conditions share a characteristic: inflammation.

There is more variability in disease manifestations and persistence within diseases than across diseases because:

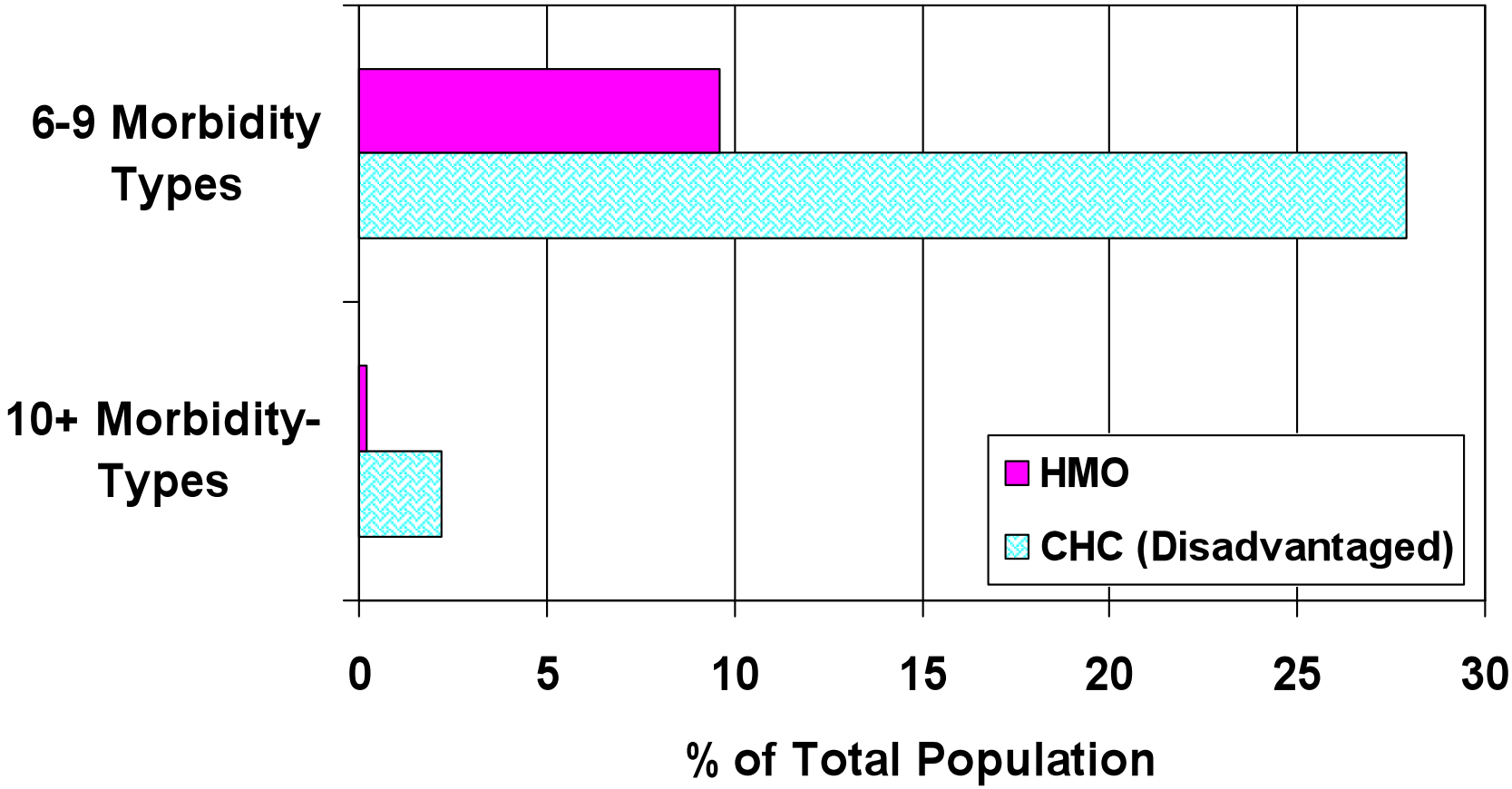
- diseases are not necessarily unique pathophysiological entities
- variability in diagnostic styles and practices
- presence of comorbidity

Co- and Multimorbidity (Morbidity Burden)

Comorbidity is the concurrent existence of one or more unrelated conditions in an individual with any given condition. Multimorbidity is the co-occurrence of biologically unrelated illnesses.

For convenience and by common terminology, we use comorbidity to represent both co- and multimorbidity.

Morbidity Burdens of Socially Disadvantaged and Socially Advantaged People



Source: ACG team, JHSPH

Starfield 09/07
CM 6336 n

The high frequency of

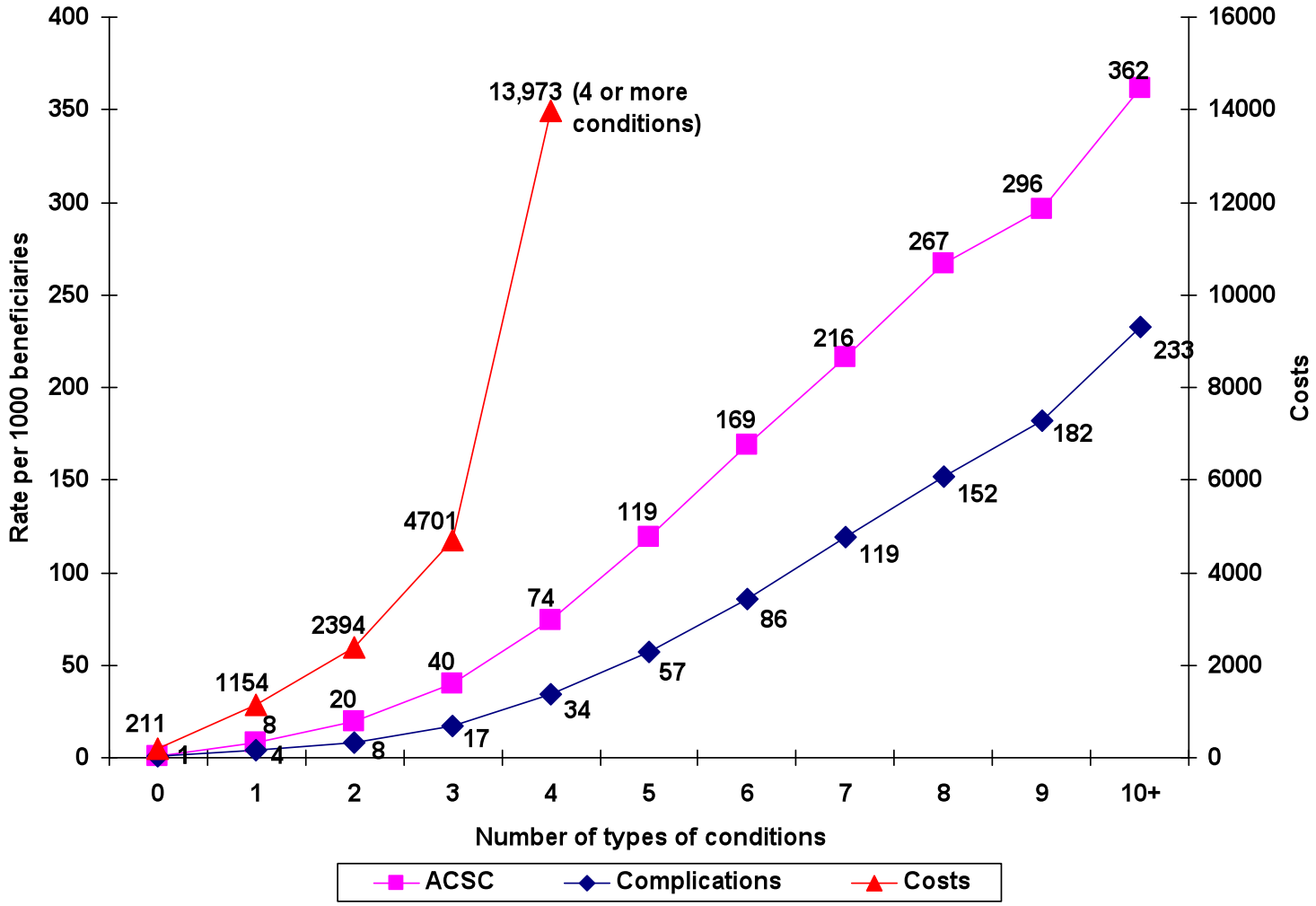
Comorbidity

Multimorbidity

Morbidity burden

makes it inappropriate to focus on single diseases

Comorbidity, Inpatient Hospitalization, Avoidable Events, and Costs*



Source: Wolff et al, Arch Intern Med 2002; 162:2269-76.

*ages 65+, chronic conditions only

Starfield 11/06
CM 5686 n

Expected Resource Use (Relative to Adult Population Average) by Level of Comorbidity, British Columbia, 1997-98

	None	Low	Medium	High	Very High
Acute conditions only	0.1	0.4	1.2	3.3	9.5
Chronic condition	0.2	0.5	1.3	3.5	9.8
High impact chronic condition	0.2	0.5	1.3	3.6	9.9

Thus, it is comorbidity, rather than presence or impact of chronic conditions, that generates resource use.

Source: Broemeling et al. Chronic Conditions and Co-morbidity among Residents of British Columbia. Vancouver, BC: University of British Columbia, 2005.

Starfield 09/07
CM 6622 n

As thresholds for diagnosing disease are lowered over time, the variability within “diseases” will increase even further, as will the prevalence of multiple simultaneous or sequential diseases.

Increase in Treated Prevalence: Selected Conditions, US, People with Private Insurance, 1987-2002

	Treated Prevalence Percentage Change, 1987-2002
Hyperlipidemia	437
(Heart disease	9)
Bone disorders	227
Upper GI problems	169
Cerebrovascular disease	161
Mental problems	136
Diabetes	64
Endocrine disorders	24
Hypertension	17
Bronchitis	13

Source: Thorp et al, Health Affairs 2005; W5:317-25, 2005.

Starfield 09/06
D 6838 n

Top Ten Health Conditions and Impact on Costs

	Medical and Rx costs	Lost productivity costs	Total costs
1	Other cancer	Fatigue	Back/neck pain
2	Back/neck pain	Depression	Depression
3	Coronary heart disease	Back/neck pain	Fatigue
4	Other chronic pain	Sleeping problem	Other chronic pain
5	High cholesterol	Other chronic pain	Sleeping problem
6	Gastroesophageal reflux disease	Arthritis	High cholesterol
7	Diabetes	Hypertension	Arthritis
8	Sleeping problem	Obesity	Hypertension
9	Hypertension	High cholesterol	Obesity
10	Arthritis	Anxiety	Anxiety

Source: Loeppke et al, J Occup Environ Med 2007; 49:712-21.

What is needed is person-focused care over time, NOT disease-focused care.

What Is the Appropriate Care Model?

- Primary care that meets primary care (not disease-specific) standards*
- Specialty referrals that are appropriate, i.e., evidence-based**
- Specialty care that meets specialty care standards**

*exist
**do not exist

When people (not diseases) are the focus of attention

- Outcomes are better
- Side effects are fewer
- Costs are lower
- Population health is greater

Source: Starfield et al, Health Aff 2005; W5:97-107.

PRIMARY HEALTH CARE “works” because it has definable system functions that provide the policy context for primary care.

PRIMARY CARE “works” because it has defined functions that include structural and process features of clinical health services that are known to improve outcomes of care.

- How valid/useful is the concept of chronic illness?
- Does it make sense to organize services around “chronic” illnesses?
- It is almost certain that morbidity, disability, and premature death are more likely in the presence of vulnerability to many types of illnesses. What are the implications for organization of health services?
- How can primary care and CCM be made complementary?

Is chronic care management pursuant to primary care or separate from it?

- Person-focused?
- Contributory to at least one of the four main features of primary care?

Is CCM part of primary care or separate from it?

- If the need for it is uncommon (as the data suggest), it is a referral function and not part of primary care.
- If the need for it is common, it is a way of enhancing some important and heretofore neglected element of care, possibly problem recognition.

Question: What critical process of care is served by CCM? Problem recognition? Follow-up and reassessment? If not, what?

Large medical groups that score higher in PRIMARY CARE ATTRIBUTES are more likely to score high on CHRONIC CARE MODEL elements. The primary care characteristics that are most related to the CCM score are

- COMPREHENSIVENESS of services (especially treatment of severe chronic illness and accepting financial risk for hospitalization)
- COORDINATION (problem list present in an electronic health record)

Source: Schmittdiel et al, Ann Fam Med 2006;4:117-23.

Implications of the Current Disease-Oriented Approach to Quality of Care and Payment for Performance

- Neglect of the problems of younger populations, especially children
- Neglect of quality of care and payment for performance in outpatient specialty care
- Failure to focus on inappropriate and unnecessary use
- Disease rather than person-focus
- Inadequate basis of evidence (non-generalizability to different populations; to people with multimorbidity; and to the influence of the way in which health services are delivered)

The management of the large percentage of people, especially the elderly, with high morbidity burdens should be returned to primary care, where care is person-focused, not disease-focused. Guidelines for the management of patients with multimorbidity are needed, in order to improve effectiveness of care, increase equity meeting health needs of socially-compromised populations, and reduce adverse events deriving from polypharmacy and other disease-specific interventions.

Any evaluation of enhancements to clinical primary care must consider the extent to which they better achieve the evidence-based primary care functions:

- First contact for new needs/problems
- Person (*not* disease) focused care (enhanced recognition of people's health problems)
- Breadth of services
- Coordination (enhanced problems/needs recognition over time)

Deaths may be attributed to chronic diseases, but people still get sick from acute diseases and acute exacerbations.

Any enhancement of primary care has to deal with this reality.

Modern medicine is largely atheoretical. With the exception of a few rare genetic conditions, we do not understand why some people have greater susceptibility to disease and, particularly why some people are more prone to multimorbidity than other people. On the other hand, some people seem to be more resilient to health problems. Why?

It appears that there may be only a few “types” of medical problems, based on most predominant etiology:

- Infectious
- External injury
- Developmental/physical abnormality
- Mendelian dominant genetic
- Autoimmune
- Cellular degradation/degeneration

Question: If this is true or even only partly true, is the International Classification of Diseases a useful schema for classifying health problems? Might there be one that lends itself better to understanding etiology for the purpose of more effective prevention and treatment?

Are diseases really discrete categorizations of pathology?

Everyone knows that cardiovascular disease is the leading cause of death, but what is it?

It is “hypertensive DISEASES, ischemic heart DISEASES, rheumatic fever, pulmonary heart disease and DISEASES of the pulmonary circulation, OTHER FORMS of heart disease, cerebrovascular DISEASES or stroke, DISEASES of veins, lymphatic vessels, and lymph nodes, OTHER AND UNSPECIFIED DISORDERS OF THE CIRCULATORY SYSTEM, AND congenital MALFORMATIONS, or birth defects of the circulatory system.”

What and for whom is there benefit from calling it a disease – or the leading cause of death?

Source: Mensah & Brown, Health Aff 2007; 26:38-48.

There appear to be many disorders included under the rubric of diabetes: insulin secretion; insulin transport; zinc-binding to insulin; and pancreatic islet beta cell development.

IS DIABETES A DISEASE? DOES IT MAKE SENSE TO ASSUME THAT GUIDELINES FOR THE IDENTIFICATION AND MANAGEMENT OF DIABETES APPLY TO ALL “DIABETICS”?

Source: Topol et al, JAMA 2007; 298:218-21.

If the association between obesity and diabetes is absent in people with low concentrations of persistent organic pollutants, and the association becomes stronger as the concentration of these pollutants rises, is obesity a risk factor for diabetes? Is diabetes a single disease?

Source: Jones et al, Lancet 2008; 371:287-8.

If a 90-year-old woman dies two months following hip fracture, did she die from an acute disease or a chronic disease?

What is the “cause of death” likely to be coded as?

If oral contraceptives are protective on epithelial and non-epithelial cervical cancer but not on mucinous cervical cancer, is cervical cancer a single disease?

Source: Franco & Duarte-Franco, Lancet 2008; 371:277-8.

COPD is a chronic systemic inflammatory syndrome with complex chronic comorbidities. Patients with COPD mainly die of non-respiratory disorders such as cardiovascular disease or cancer.

COPD is a heterogeneous disease process.

Although exacerbations of COPD, especially those defined as being infectious, are quite frequent, the number of randomized placebo-controlled trials of antibiotics is surprisingly small.

Sources: Fabbri & Rabe, Lancet 2007; 370:797-9. Calverley & Rennard, Lancet 2007; 370:774-85. Beasley et al, Lancet 2009;374:670-2.

When occurring in the same individual, BMI greater than 30, systolic blood pressure greater than 140, and blood cholesterol greater that 250 mg/dL are associated with a six-fold increased odds of Alzheimers disease.

What type of disease is Alzheimers? What is the disease?

Source: Michel et al, JAMA 2008; 299:688-90.

Hypothyroidism is three times more likely in women with rheumatoid arthritis than in the general population. Women with both conditions have a fourfold higher risk of cardiovascular disease than euthyroid women with arthritis, independent of conventional risk factors. Inflammation and autoimmunity are implicated in vulnerability to a wide variety of “chronic” diseases – and they may well be “acute”.

Source: Raterman et al, Ann Rheum Dis 2008; 67:229-32.

What Is a Chronic Disease?

Generally defined as persistence or recurrence, usually beyond one year

Chronic Disease: Expanded Definition

- Incurable
- Complex “causation”
- Multiple risk factors
- Long latency
- Prolonged course
- Associated with functional impairment or disability

Source: Australian Institute of Health and Welfare. Indicators for Chronic Diseases and Their Determinants, 2008. Canberra, Australia: AIHW, 2008.

Of all global deaths in 2005, 60% were said to be caused by chronic diseases, principally cardiovascular diseases (32%), cancers (13%), and chronic respiratory diseases (7%). Data such as these are used to argue that chronic diseases are of growing and epidemic importance as causes of death.

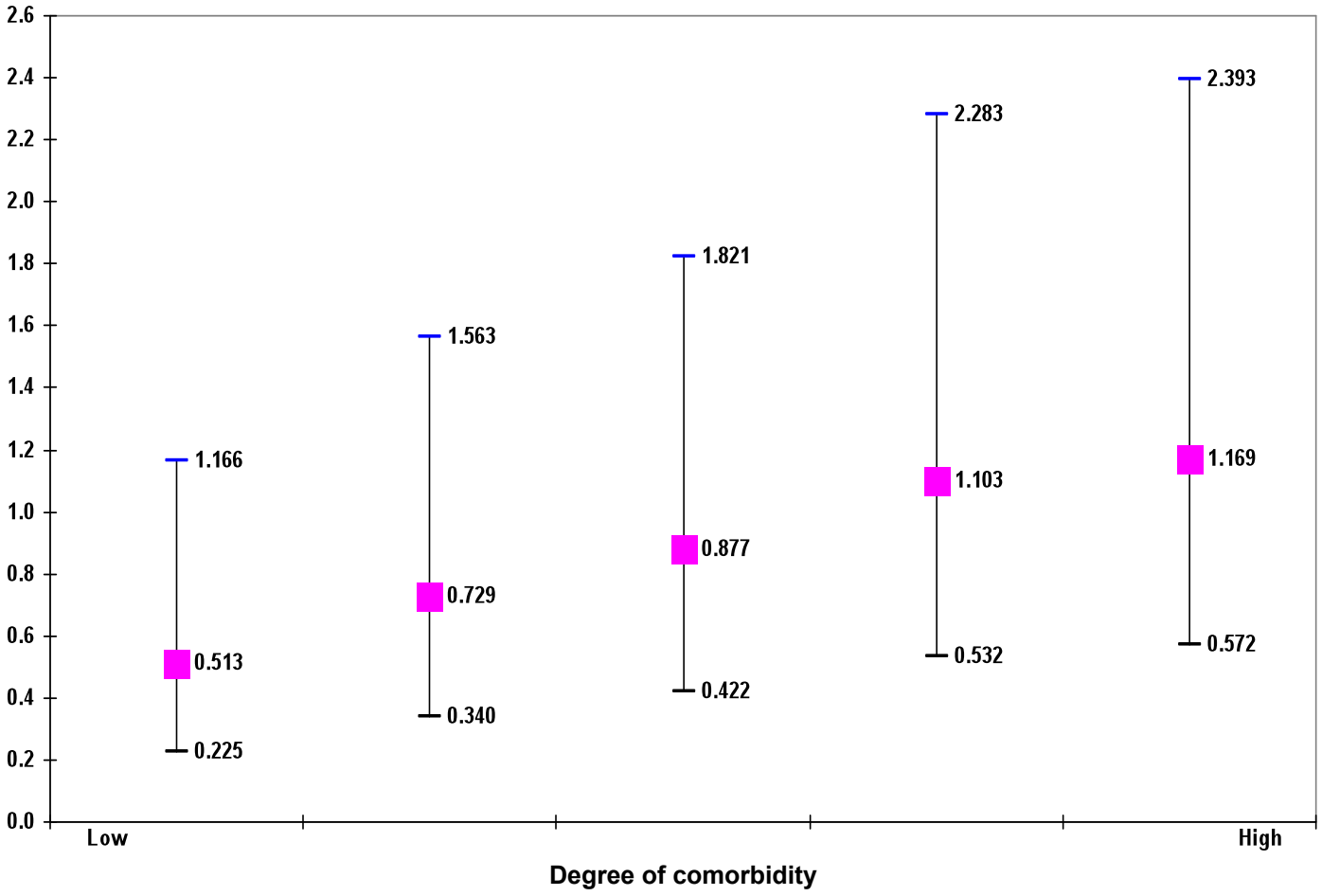
Question: What is the appropriate target for the percentage of deaths in the world that are attributable to chronic diseases? Isn't there a case to be made that perhaps ALL deaths should be due to chronic diseases, with acute illnesses falling towards zero percentage?

Source: Beaglehole et al, Lancet 2007; 370:2152-7.

The greater the morbidity burden, the greater the persistence of any given diagnosis.

That is, with high comorbidity, even acute diseases are more likely to persist.

Odds Ratios and Confidence Intervals for Persistence* by Degree of Comorbidity: Urinary Tract Infection



*controlled for age and sex

C Statistic .633

Starfield 09/07
D 5867 n