



Key Questions

- How well does our current assessment of risk/benefit of drugs work?
- Can we improve this system?
- If so how?

The Benefits – During the last 50 years Pharmaceutical / Device Advances Have Significantly Impacted Health and Survival

Disease	Disease Before Treatment	Pharmaceutical/Device Advances	The Impact
Coronary Heart Disease	1979 345 deaths/100,000 pop. ¹	1980s – 1990s <ul style="list-style-type: none"> ACE inhibitors Beta blockers Thrombolytics/Stents Anti-platelet Tx ICDs 	2002 171 deaths/100,000 pop. ¹ 50% Reduction
Stroke	1960 178 deaths/100,000 pop. ¹	Treatment of hypertension <ul style="list-style-type: none"> Diuretics ACE inhibitors Beta blockers Calcium channel blockers 	2002 56 deaths/100,000 pop. ¹ 70% Reduction
HIV/AIDS	1997 6,647 deaths / 100,000 HIV/AIDS patients. ²	Mid-1990s <ul style="list-style-type: none"> Nucleoside Reverse Transcriptase Inhibitors Non-Nucleoside Reverse Transcriptase Inhibitors Protease Inhibitors 	2003 1,620 deaths / 100,000 HIV/AIDS patients. ² 75% Reduction
Measles	1963 3-4 million U.S. cases (~500,000 reported) ³	1963 <ul style="list-style-type: none"> Measles vaccine 	2000 86 confirmed cases in the U.S. ³
Chronic myelogenous leukemia	1997 50% survival post-diagnosis at 18 months ⁴	2001 <ul style="list-style-type: none"> Kinase inhibitors 	2004 3 year survival rate estimated at ~94% ⁴

1. <http://www.cdc.gov/nchs/hus.htm> Trend tables and Chartbook Tables in Excel format (ftp) Table 29.xls file

2. HIV/AIDS Surveillance Report Vol. 7, No. 2 Table 27 (Persons reported to be living with HIV infection and with AIDS, 1995), HIV/AIDS Surveillance Report Vol. 9, No. 2 Table 33 (Persons reported to be living with HIV infection and with AIDS, 1997), A Glance at the HIV/AIDS Epidemic <http://www.cdc.gov/hiv/PUBS/Facts/At-A-Glance.htm>, Update: Trends in AIDS Incidence, Deaths, and Prevalence -- United States, 1996 www.cdc.gov/mmwr/preview/mmwrhtml/00046531.htm, ICD Code: 042.9 AIDS and HIV Infection

3. CDC www.cdc.gov/nip/diseases/measles/history.htm CDC Measles, Mumps and Rubella Vaccine, MMWR V51:9;pp190.-13 million doses = annual need for MMR vaccine in the U.S.

<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5033a5.htm> CDC. Summary of notifiable diseases, United States, 2000. MMWR 2000:49(no. 53) Wood DL, Brunel PA, Clinical Microbiology Reviews Apr 1995 pp.260-267 <http://cmr.asm.org/cgi/reprint/8/2/260.pdf>

4. <http://www.emedicine.com/med/topic371.htm>, Hematology 2002;pp.111-135, JAMA. 2004;291:1238-1245; http://seer.cancer.gov/statfacts/html/cm1l_print.html 1995-2001 5 yr survival rate 39%

* All websites accessed week of Jan 16-22 2006

The Benefits and The Risks – During the last 50 years Pharmaceutical/ Device Advances Have Significantly Impacted Health and Survival

Disease	Disease Before Treatment	Pharmaceutical/Device Advances	Positive Impact	Risks – Negative Impact
Coronary Heart Disease	1979 345 deaths/100,000 pop. ¹	1980s – 1990s <ul style="list-style-type: none"> ACE inhibitors Beta blockers Thrombolytics/Stents Anti-platelet Tx ICDs 	2002 171 deaths/100,000 pop. ¹ 50% Reduction	Thrombolytics 1% risk of intracranial hemorrhage ⁶ Angioplasty with or without stents 0.4% MI 0.5%-1.4% mortality ⁷
Stroke	1960 178 deaths/100,000 pop. ¹	Treatment of hypertension <ul style="list-style-type: none"> Diuretics ACE inhibitors Beta blockers Calcium channel blockers 	2002 56 deaths/100,000 pop. ¹ 70% Reduction	Diuretics <10% Hypokalemia, hypotension, <1% serious allergic responses ¹⁴ ACE Inhibitors - hypotension, acute renal failure, hyperkalemia ¹⁵
HIV/AIDS	1997 6,647 deaths / 100,000 HIV/AIDS patients. ²	Mid-1990s <ul style="list-style-type: none"> Nucleoside Reverse Transcriptase Inhibitors Non-Nucleoside Reverse Transcriptase Inhibitors Protease Inhibitors 	2003 1,620 deaths / 100,000 HIV/AIDS patients. ² 75% Reduction	GI symptoms, metabolic abnormalities, malaise ⁵
Measles	1963 3-4 million U.S. cases (~500,000 reported) ³	1963 <ul style="list-style-type: none"> Measles vaccine 	2000 86 confirmed cases in the U.S. ³	2/1 million doses Pneumonia, 1/1 million doses Encephalitis, 5/1 million doses Anaphalaxis (none fatal) ⁸
Chronic myelogenous leukemia	1997 50% survival post-diagnosis at 18 months ⁴	2001 <ul style="list-style-type: none"> Kinase inhibitors 	2004 3 year survival rate estimated at ~94% ⁴	GI symptoms, myalgia ⁹

1. <http://www.cdc.gov/nchs/hsus.htm> Trend tables and Chartbook Tables in Excel format (ftp) Table 29 xls file

2. HIV/AIDS Surveillance Report Vol. 7, No. 2 Table 27 (Persons reported to be living with HIV infection and with AIDS, 1995), HIV/AIDS Surveillance Report Vol. 9, No. 2 Table 33 (Persons reported to be living with HIV infection and with AIDS, 1997), A Glance at the HIV/AIDS Epidemic <http://www.cdc.gov/hiv/PUBS/Facts/At-A-Glance.htm>, Update: Trends in AIDS Incidence, Deaths, and Prevalence -- United States, 1996

3. CDC www.cdc.gov/mmwr/preview/mmwrhtml/00046531.htm, ICD Code: 042.9 AIDS and HIV Infection

4. CDC www.cdc.gov/nip/diseases/measles/history.htm, CDC Measles, Mumps and Rubella Vaccine, MMWR V51:9:pp190.-13 million doses = annual need for MMR vaccine in the U.S. <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5033a5.htm>, CDC. Summary of notifiable diseases, United States, 2000. MMWR 2000;49(no. 53) Wood DL, Brunel PA. Clinical Microbiology Reviews Apr 1995 pp.260-267 <http://cmr.asm.org/cgi/reprint/8/2/260.pdf>

5. <http://www.emedicine.com/med/topic371.htm>, Hematology 2002;pp.111-135, JAMA. 2004;291:1238-1245; http://seer.cancer.gov/statfacts/html/cmyl_print.html, 1995-2001 5 yr survival rate 39%

6. http://www.hivandhepatitis.com/hiv_and_aids/hiv_treat.htm

7. Lancet 1999 Aug 28;354(9180):716-22, Circulation 1997 Jun 3;95(11):2508-16

8. J Am Coll Cardio 2002 Apr 3;39(7):1096-103, Am J Cordio 2001 Sept;88(5):497-503

9. Patja A, Davidkin I, Kurki T, Kallio MJ, Valle M, Peltola H. Serious adverse events after measles-mumps-rubella vaccination during a fourteen-year prospective follow-up. Pediatr Infect Dis J 2000; 19:1127-34. <http://www.aafp.org/afp/20021201/2113.html>

10. <http://www.fda.gov/cder/drug/infopage/gleevec/ga.htm>

11. JAMA 2003 289:2560 The JNC 7 Report <http://jama.ama-assn.org/cgi/content/full/289/19/2560>

12. Am Heart J 1996; 131:350

13. Am Heart J 1996; 131:350

14. Am Heart J 1996; 131:350

15. Am Heart J 1996; 131:350

* All websites accessed week of Jan 16-22 2006

The Value of a Drug Always Involves a Balance of Risk and Benefit

Statins

1,000,000 people on statin treatment per year *

Benefits

Prevent:

>3,000 deaths
>4,000 nonfatal MIs
>10,000 CV events

Risks

AEs:

40 Rhabdomyolysis leading to:
6 Renal Failures
1 Death

Driving

1,000,000 licensed drivers in U.S. **

Benefits

Personal,
Efficient,
Affordable,
Reliable, Fast
Transportation

Risks

221 Fatalities/year

Minimized via regulations, incl. drivers licenses, seat belts, car seats, airbags, ABS, public awareness programs, etc.

* Continuing Medical Implementation, <http://www.cvtoolbox.com>, 4S trial – Lancet 1994; 344: 1383-89, CARE trial – NEJM 335:1001-1009, LIPID trial NEJM 339:1349-1357, HPS trial – Lancet vol360:9326, Pravacol label, Lipitor label, Zocor label Ward MM. Factors predictive of acute renal failure in rhabdomyolysis. *Arch Intern Med* 1988;148:1553-7 Sauret J, Marinides G, Wang, G Rhabdomyolysis. *AFP* 2002;65(5):907-912, PD Thompson et al. Statin-associated myopathy. *JAMA* 2003 289: 1681-90, DJ Graham et al. Incidence of hospitalized rhabdomyolysis in patients treated with lipid-lowering drugs. *JAMA* 2004 292: 2582-2590 ** NHTSA <http://www-fars.nhtsa.dot.gov/>

Key Questions

- Should we develop standardized methods to assess risk/benefit ratios for drugs?
- Should we use quantitative approaches for comparing risk/benefit ratios of drugs?
- How do we set the appropriate risk/benefit ratio for a particular drug at a particular time and enable it to change over time?
- How do we follow up on safety signals seen in early drug development?
- How do we better communicate these results to patients and physicians?

