Teaching papers - Prognosis

Scholes, D., T. M. Hooton, et al. (2005). "**Risk factors associated with acute pyelonephritis in healthy women**." Ann Intern Med **142**(1): 20-27.

Type of Question: Prognosis **Beginner / Intermediate Case-control**.

Teaching Notes: Well-done case control study on a common condition. Transparent reporting of methods and results that show clear differences between the cases and controls makes this a very good case-control study to discuss, even for beginners. Good discussion points: As always with a case-control method, it is critical to get the learners to understand that a case control study begins with the identification of cases, who have already had the outcome. This is very clearly stated in this paper, as is the selection of controls. Another possible discussion point is the Managed Care setting (HMO in Seattle Washington). Could discuss a benefit of a managed care setting in which the databases are used to further understanding of risk factors for this very common problem.

Abstract: BACKGROUND: Although most cases of acute pyelonephritis occur in otherwise healthy women, data on risk factors for this condition are lacking. OBJECTIVE: To evaluate infection characteristics, incidence, and risk factors associated with acute pyelonephritis in a sample of women. DESIGN: Population-based case-control study. SETTING: Group Health Cooperative, a prepaid health plan in Washington. PARTICIPANTS: 788 nonpregnant women, 18 to 49 years of age. Case-patients (n = 242) were women with pyelonephritis who were identified from computerized databases. Controls were 546 similar-age women with no pyelonephritis diagnosis in the previous 5 years who were randomly selected from enrollment databases. Response rates for case-patients and controls were 73% and 64%, respectively. MEASUREMENTS: Characteristics of infection and potential risk factors for pyelonephritis, ascertained through computer-assisted telephone interview and computerized databases. RESULTS: 7% of case-patients were hospitalized. Escherichia coli was the infecting pathogen in 85% of cases. In multivariable models, factors associated with pyelonephritis risk were frequency of sexual intercourse in the previous 30 days (odds ratio, 5.6 [95% CI, 2.8 to 11.0] for > or =3 times per week), recent urinary tract infection (UTI) (odds ratio, 4.4 [CI, 2.8 to 7.1]), diabetes (odds ratio, 4.1 [CI, 1.6 to 10.9]), recent incontinence (odds ratio, 3.9 [CI. 2.6 to 5.9]), new sexual partner in the previous year (odds ratio, 2.2 [CI, 1.4 to 3.6]), recent spermicide use (odds ratio, 1.7 [CI, 1.1 to 2.8]), and UTI history in the participant's mother (odds ratio, 1.6 [CI, 1.1 to 2.5]). Risk factors for selected subgroups (patients < or = 30 years of age, patients > 30 years of age, patients with no UTI history, and inpatients) were also evaluated. LIMITATIONS: Potential recall bias, reliance on automated case definition criteria, and limited data on diabetes and incontinence variables. CONCLUSIONS: Few nonpregnant, community-dwelling women younger than 50 years of age with pyelonephritis are hospitalized. As with cystitis in reproductive-age women, sexual behaviors and patient and family history of UTI are associated with increased pyelonephritis risk. Diabetes and incontinence also seem to independently increase the risk for pyelonephritis.

Larson, E. B., M. F. Shadlen, et al. (2004). "**Survival after initial diagnosis of Alzheimer disease**." Ann Intern Med **140**(7): 501-509.

Type of Question: Prognosis **Beginner / Intermediate Prospective cohort**.

Teaching Notes: Important article that provides key information on survival in Alzheimer's disease. Good Discussion Points: Nicely illustrates the challenge of creating an inception cohort in a disease like dementia. Provides clear examples of survival analysis and Kaplan- Meier curves. Generates great discussion about how to apply (and not apply) this data to individual patients.

Abstract: BACKGROUND: Alzheimer disease is an increasingly common condition in older people. Knowledge of life expectancy after the diagnosis of Alzheimer disease and of associations of patient characteristics with survival may help planning for future care. OBJECTIVE: To investigate the course of Alzheimer disease after initial diagnosis and examine associations hypothesized to correlate with survival among community-dwelling patients with Alzheimer disease. DESIGN: Prospective observational study. SETTING: An Alzheimer disease patient registry from a base population of 23 000 persons age 60 years and older in the Group Health Cooperative, Seattle, Washington. PATIENTS: 521

newly recognized persons with Alzheimer disease enrolled from 1987 to 1996 in an Alzheimer disease patient registry. MEASUREMENTS: Baseline measurements included patient demographic features, Mini-Mental State Examination score, Blessed Dementia Rating Scale score, duration since reported onset of symptoms, associated symptoms, comorbid conditions, and selected signs. Survival was the outcome of interest. RESULTS: The median survival from initial diagnosis was 4.2 years for men and 5.7 years for women with Alzheimer disease. Men had poorer survival across all age groups compared with females. Survival was decreased in all age groups compared with the life expectancy of the U.S. population. Predictors of mortality based on proportional hazards models included a baseline Mini-Mental State Examination score of 17 or less, baseline Blessed Dementia Rating Scale score of 5.0 or greater, presence of frontal lobe release signs, presence of extrapyramidal signs, gait disturbance, history of falls, congestive heart failure, ischemic heart disease, and diabetes at baseline. LIMITATIONS: The base population, although typical of the surrounding Seattle community, may not be representative of other, more diverse populations. CONCLUSIONS: In this sample of community-dwelling elderly persons who received a diagnosis of Alzheimer disease, survival duration was shorter than predicted on the basis of U.S. population data, especially for persons with onset at relatively younger ages. Features significantly associated with reduced survival at diagnosis were increased severity of cognitive impairment, decreased functional level, history of falls, physical examination findings of frontal release signs, and abnormal gait. The variables most strongly associated with survival were measures of disease severity at the time of diagnosis. These results should be useful to patients and families experiencing Alzheimer disease, other caregivers, clinicians, and policymakers when planning for future care needs.

Salazar-Martinez, E., W. C. Willett, et al. (2004). "**Coffee consumption and risk for type 2 diabetes mellitus**." Ann Intern Med **140**(1): 1-8.

Type of Question: Prognosis

Beginner / Advanced Prospective cohort.

Teaching Notes: This is a sample packet. See the entire teaching package that is in this section. Strong methods for a pair of well published prospective cohort trials with long term follow up (the nurses health study and the health professions follow-up study). Great topic, as coffee consumption is applicable to most folks, regardless of specialty. Good discussion points: Great examples of how the groups are not equal at the start of the trials and how adjusted analyses attempt to control for those differences. In addition, surprising findings in that the study designers had expected the opposite finding. 'Surprise' findings always make for fun teaching papers.

Abstract: BACKGROUND: In small, short-term studies, acute administration of caffeine decreases insulin sensitivity and impairs glucose tolerance. OBJECTIVE: To examine the long-term relationship between consumption of coffee and other caffeinated beverages and incidence of type 2 diabetes mellitus. DESIGN: Prospective cohort study. SETTING: The Nurses' Health Study and Health Professionals' Follow-up Study. PARTICIPANTS: The authors followed 41 934 men from 1986 to 1998 and 84 276 women from 1980 to 1998. These participants did not have diabetes, cancer, or cardiovascular disease at baseline. MEASUREMENTS: Coffee consumption was assessed every 2 to 4 years through validated questionnaires. RESULTS: The authors documented 1333 new cases of type 2 diabetes in men and 4085 new cases in women. The authors found an inverse association between coffee intake and type 2 diabetes after adjustment for age, body mass index, and other risk factors. The multivariate relative risks for diabetes according to regular coffee consumption categories (0, <1, 1 to 3, 4 to 5, or > or =6 cups per day) in men were 1.00, 0.98, 0.93, 0.71, and 0.46 (95% CI, 0.26 to 0.82; P = 0.007 for trend), respectively. The corresponding multivariate relative risks in women were 1.00, 1.16, 0.99, 0.70, and 0.71 (CI, 0.56 to 0.89; P < 0.001 for trend), respectively. For decaffeinated coffee, the multivariate relative risks comparing persons who drank 4 cups or more per day with nondrinkers were 0.74 (CI, 0.48 to 1.12) for men and 0.85 (CI, 0.61 to 1.17) for women. Total caffeine intake from coffee and other sources was associated with a statistically significantly lower risk for diabetes in both men and women. CONCLUSIONS: These data suggest that long-term coffee consumption is associated with a statistically significantly lower risk for type 2 diabetes.

Sears, M. R., J. M. Greene, et al. (2003). "**A longitudinal, population-based, cohort study of childhood asthma followed to adulthood**." N Engl J Med **349**(15): 1414-1422.

Type of Question: Prognosis **Beginner / Advanced Prospective cohort**.

Teaching Notes: Well done prospective population based cohort. Good discussion points: Great for discussions of population selection for cohort studies and methodology for studies of prognosis. Tables and results are reasonably easy to read and understand for beginners.

Abstract: BACKGROUND: The outcome of childhood asthma in adults has been described in high-risk cohorts, but few population-based studies have reported the risk factors for persistence and relapse. METHODS: We assessed children born from April 1972 through March 1973 in Dunedin, New Zealand, repeatedly from 9 to 26 years of age with questionnaires, pulmonary-function tests, bronchial-challenge testing, and allergy testing. RESULTS: By the age of 26 years, 51.4 percent of 613 study members with complete respiratory data had reported wheezing at more than one assessment. Eighty-nine study members (14.5 percent) had wheezing that persisted from childhood to 26 years of age, whereas 168 (27.4 percent) had remission, but 76 (12.4 percent) subsequently relapsed by the age of 26. Sensitization to house dust mites predicted the persistence of wheezing (odds ratio, 2.41; P=0.001) and relapse (odds ratio, 2.18; P=0.01), as did airway hyperresponsiveness (odds ratio for persistence, 3.00; P<0.001; odds ratio for relapse, 3.03; P<0.001). Female sex predicted the persistence of wheezing (odds ratio, 1.71; P=0.03), as did smoking at the age of 21 years (odds ratio, 1.84; P=0.01). The earlier the age at onset, the greater the risk of relapse (odds ratio, 0.89 per year of increase in the age at onset; P<0.001). Pulmonary function was consistently lower in those with persistent wheezing than in those without persistent wheezing. CONCLUSIONS: In an unselected birth cohort, more than one in four children had wheezing that persisted from childhood to adulthood or that relapsed after remission. The factors predicting persistence or relapse were sensitization to house dust mites, airway hyperresponsiveness, female sex, smoking, and early age at onset. These findings, together with persistently low lung function, suggest that outcomes in adult asthma may be determined primarily in early childhood.

Hoberman, A., M. Charron, et al. (2003). "**Imaging studies after a first febrile urinary tract infection in young children**." N Engl J Med **348**(3): 195-202.

Type of Question: Prognosis **Beginner / Advanced Prospective cohort**.

Teaching Notes: Prospective cohort in children. This paper can be used to trigger discussion of prognosis as well as diagnosis.

Abstract: BACKGROUND: Guidelines from the American Academy of Pediatrics recommend obtaining a voiding cystourethrogram and a renal ultrasonogram for young children after a first urinary tract infection; renal scanning with technetium-99m-labeled dimercaptosuccinic acid has also been endorsed by other authorities. We investigated whether imaging studies altered management or improved outcomes in young children with a first febrile urinary tract infection. METHODS: In a prospective trial involving 309 children (1 to 24 months old), an ultrasonogram and an initial renal scan were obtained within 72 hours after diagnosis, contrast voiding cystourethrography was performed one month later, and renal scanning was repeated six months later. RESULTS: The ultrasonographic results were normal in 88 percent of the children (272 of 309); the identified abnormalities did not modify management. Acute pyelonephritis was diagnosed in 61 percent of the children (190 of 309). Thirty-nine percent of the children who underwent cystourethrography (117 of 302) had vesicoureteral reflux; 96 percent of these children (112 of 117) had grade I, II, or III vesicoureteral reflux. Repeated scans were obtained for 89 percent of the children (275 of 309); renal scarring was noted in 9.5 percent of these children (26 of 275). CONCLUSIONS: An ultrasonogram performed at the time of acute illness is of limited value. A voiding cystourethrogram for the identification of reflux is useful only if antimicrobial prophylaxis is effective in reducing reinfections and renal scarring. Renal scans obtained at presentation identify children with acute pyelonephritis, and scans obtained six months later identify those with renal scarring. The routine performance of urinalysis, urine culture, or both during subsequent febrile illnesses in all children with a previous febrile urinary tract infection will probably obviate the need to obtain either early or late scans.

Abramson, J. L., S. A. Williams, et al. (2001). "**Moderate alcohol consumption and risk of heart failure among older persons**." Jama **285**(15): 1971-1977.

Type of Question: Prognosis **Beginner / Advanced Propsective cohort**.

Teaching Notes: These two articles (see also Mukamal 2001) may be considered together (see sample case.) It is sometimes fun to compare and contrast two different articles about a similar prognosis topic. The populations studied through observational designs (in this case a cohort) are critical to how we understand and apply the information. Therefore, it is sometimes a good strategy to compare and contrast findings in studies done in different settings.In these two papers, there are many opportunities to discuss the impact of potential 'bias'; Try to consider why I chose these two papers- what about the two populations make for good comparison?? Note: either of these papers could also be looked at as a single paper.

Abstract: CONTEXT: Heavy consumption of alcohol can lead to heart failure, but the relationship between moderate alcohol consumption and risk of heart failure is largely unknown. OBJECTIVE: To determine whether moderate alcohol consumption predicts heart failure risk among older persons, independent of the association of moderate alcohol consumption with lower risk of myocardial infarction (MI). DESIGN: Prospective cohort study conducted from 1982 through 1996, with a maximum follow-up of 14 years. SETTING AND PARTICIPANTS: Population-based sample of 2235 noninstitutionalized elderly persons (mean age, 73.7 years; 41.2% male; 21.3% nonwhite) residing in New Haven, Conn, who were free of heart failure at baseline. Persons who reported alcohol consumption of more than 70 oz in the month prior to baseline were excluded. MAIN OUTCOME MEASURE: Time to first fatal or nonfatal heart failure event, according to the amount of alcohol consumed in the month prior to baseline. RESULTS: Increasing alcohol consumption in the moderate range was associated with decreasing heart failure rates. For persons consuming no alcohol (50.0%), 1 to 20 oz (40.2%), and 21 to 70 oz (9.8%) in the month prior to baseline, crude heart failure rates per 1000 years of follow-up were 16.1, 12.2, and 9.2, respectively. After adjustment for age, sex, race, education, angina, history of MI and diabetes, MI during follow-up, hypertension, pulse pressure, body mass index, and current smoking, the relative risks of heart failure for those consuming no alcohol, 1 to 20 oz, and 21 to 70 oz in the month prior to baseline were 1.00 (referent), 0.79 (95% confidence interval [CI], 0.60-1.02), and 0.53 (95% CI, 0.32-0.88) (P for trend =.02). CONCLUSIONS: Increasing levels of moderate alcohol consumption are associated with a decreasing risk of heart failure among older persons. This association is independent of a number of confounding factors and does not appear to be entirely mediated by a reduction in MI risk.

Mukamal, K. J., M. Maclure, et al. (2001). "**Prior alcohol consumption and mortality following acute myocardial infarction**." Jama **285**(15): 1965-1970.

Type of Question: Prognosis **Beginner / Intermediate Prospective cohort**.

Teaching Notes: These two articles (see also Abramson 2001) may be considered together (see sample case.) It is sometimes fun to compare and contrast two different articles about a similar prognosis topic. The populations studied through observational designs (in this case a cohort) are critical to how we understand and apply the information. Therefore, it is sometimes a good strategy to compare and contrast findings in studies done in different settings.In these two papers, there are many opportunities to discuss the impact of potential 'bias'; Try to consider why I chose these two papers- what about the two populations make for good comparison?? Note: either of these papers could also be looked at as a single paper.

Abstract: CONTEXT: Studies have found that individuals who consume 1 alcoholic drink every 1 to 2 days have a lower risk of a first acute myocardial infarction (AMI) than abstainers or heavy drinkers, but the effect of prior drinking on mortality after AMI is uncertain. OBJECTIVE: To determine the effect of prior alcohol consumption on long-term mortality among early survivors of AMI. DESIGN AND SETTING: Prospective inception cohort study conducted at 45 US community and tertiary care hospitals between August 1989 and September 1994, with a median follow-up of 3.8 years. PATIENTS: A total of 1913 adults hospitalized with AMI between 1989 and 1994. MAIN OUTCOME MEASURE: All-cause mortality, compared by self-reported average weekly consumption of beer, wine, and liquor during the year prior to AMI. RESULTS: Of the 1913 patients, 896 (47%) abstained from alcohol, 696 (36%) consumed less than 7 alcoholic drinks/wk, and 321 (17%) consumed 7 or more alcoholic drinks/wk. Compared with abstainers, patients who consumed less than 7 drinks/wk had a lower all-cause mortality rate (3.4 vs 6.3 deaths per

100 person-years; hazard ratio [HR], 0.55; 95% confidence interval [CI], 0.43-0.71) as did those who consumed 7 or more drinks/wk (2.4 vs 6.3 deaths per 100 person-years; HR, 0.38; 95% CI, 0.25-0.55; P<.001 for trend). After adjusting for propensity to drink and other potential confounders, increasing alcohol consumption remained predictive of lower mortality for less than 7 drinks/wk, with an adjusted HR of 0.79 (95% CI, 0.60-1.03), and for 7 or more drinks/wk, with an adjusted HR of 0.68 (95% CI, 0.45-1.05; P =.01 for trend). The association was similar for total and cardiovascular mortality, among both men and women, and among different types of alcoholic beverages. CONCLUSION: Self-reported moderate alcohol consumption in the year prior to AMI is associated with reduced mortality following infarction.

Helgason, S., G. Petursson, et al. (2000). "**Prevalence of postherpetic neuralgia after a first episode of herpes zoster: prospective study with long term follow up**." Bmj **321**(7264): 794-796.

Type of Question: Prognosis **Beginner Prospective cohort**.

Teaching Notes: Straightforward methods for a prospective cohort trial with long term follow up. Good discussion points: Can discuss Kaplan Meier plot, prevalence, odds ratios and confidence intervals

Abstract: OBJECTIVE: To estimate the frequency, duration, and clinical importance of postherpetic neuralgia after a single episode of herpes zoster. DESIGN: Prospective cohort study with long term follow up. SETTING: Primary health care in Iceland. PARTICIPANTS: 421 patients with a single episode of herpes zoster. MAIN OUTCOME MEASURES: Age and sex distribution of patients with herpes zoster, point prevalence of postherpetic neuralgia, and severity of pain at 1, 3, 6, and 12 months and up to 7.6 years after the outbreak of zoster. RESULTS: Among patients younger than 60 years, the risk of postherpetic neuralgia three months after the start of the zoster rash was 1.8% (95% confidence interval 0.59% to 4.18%) and pain was mild in all cases. In patients 60 years and older, the risk of postherpetic neuralgia increased but the pain was usually mild or moderate. After three months severe pain was recorded in two patients older than 60 years (1.7%, 2.14% to 6.15%). After 12 months no patient reported severe pain and 14 patients (3.3%) had mild or moderate pain. Seven of these became pain free within two to seven years, and five reported mild pain and one moderate pain after 7.6 years of follow up. Sex was not a predictor of postherpetic neuralgia. Possible immunomodulating comorbidity (such as malignancy, systemic steroid use, diabetes) was present in 17 patients. CONCLUSIONS: The probability of longstanding pain of clinical importance after herpes zoster is low in an unselected population of primary care patients essentially untreated with antiviral drugs.

Steinhauser, K. E., E. C. Clipp, et al. (2000). "**In search of a good death: observations of patients, families, and providers**." Ann Intern Med **132**(10): 825-832.

Type of Question: Prognosis **Beginner / Intermediate Qualitative / Focus groups and in-depth interviews**.

Teaching Notes: This is a sample package with a few suggested teaching scenarios to help think about and/ or teach about qualitative methodology.

Abstract: Despite a recent increase in the attention given to improving end-of-life care, our understanding of what constitutes a good death is surprisingly lacking. The purpose of this study was to gather descriptions of the components of a good death from patients, families, and providers through focus group discussions and in-depth interviews. Seventy-five participants-including physicians, nurses, social workers, chaplains, hospice volunteers, patients, and recently bereaved family members-were recruited from a university medical center, a Veterans Affairs medical center, and a community hospice. Participants identified six major components of a good death: pain and symptom management, clear decision making, preparation for death, completion, contributing to others, and affirmation of the whole person. The six themes are process-oriented attributes of a good death, and each has biomedical, psychological, social, and spiritual components. Physicians' discussions of a good death differed greatly from those of other groups. Physicians offered the most biomedical perspective, and patients, families, and other health care professionals defined a broad range of attributes integral to the quality of dying. Although there is no "right" way to die, these six themes may be used as a framework for understanding what participants tend to value at the end of life. Biomedical care is critical, but it is only a point of departure toward total end-of-life care. For patients and families, psychosocial and spiritual issues are as important as physiologic concerns.

Vento, S., T. Garofano, et al. (1998). "**Fulminant hepatitis associated with hepatitis A virus superinfection in patients with chronic hepatitis C**." N Engl J Med **338**(5): 286-290.

Type of Question: Prognosis **Beginner / Intermediate Prospective cohort**.

Teaching Notes: This is a sample packet. See the entire teaching package that is in this section. This is a cohort of patients followed through a GI clinic. Good example of a prospective cohort in a referral center.

Abstract: BACKGROUND: Hepatitis A virus (HAV) infection rarely causes fulminant hepatic failure in people with no underlying liver disease. There are limited data on the course of this infection in patients with chronic hepatitis B and chronic hepatitis C. METHODS: We prospectively followed, from June 1990 to July 1997, 595 adults with biochemical and histologic evidence of chronic hepatitis B (163 patients) or chronic hepatitis C (432 patients) who were seronegative for HAV antibodies. All were tested every four months for serum IgM and IgG antibodies to HAV. RESULTS: Twenty-seven patients acquired HAV superinfection, 10 of whom had chronic hepatitis B and 17 of whom had chronic hepatitis C. One of the patients with chronic hepatitis B, who also had cirrhosis, had marked cholestasis (peak serum bilirubin level, 28 mg per deciliter [479 micromol per liter]); the other nine had uncomplicated courses of hepatitis A. Fulminant hepatic failure developed in seven of the patients with chronic hepatitis C, all but one of whom died. The other 10 patients with chronic hepatitis C had uncomplicated courses of hepatitis A. CONCLUSIONS: Although most patients with chronic hepatitis B who acquired HAV infection had an uncomplicated course, patients with chronic hepatitis C had a substantial risk of fulminant hepatitis and death associated with HAV superinfection. Our data suggest that patients with chronic hepatitis C should be vaccinated against hepatitis A.

Fine, M. J., T. E. Auble, et al. (1997). "**A prediction rule to identify low-risk patients with community-acquired pneumonia**." N Engl J Med **336**(4): 243-250.

Type of Question: Prognosis **Advanced Clinical prediction rule**.

Teaching Notes: This is an example of a clinical prediction rule (a sum of factors used as a group to predict an outcome). This paper has a good example discussion of a derivation set (data used to develop the model to begin with) as compared with a validation set (once developed, different data is used to 'check' if the model makes sense.) This is a difficult paper for someone with more considerable experience looking for a challenge.

Abstract: BACKGROUND: There is considerable variability in rates of hospitalization of patients with community-acquired pneumonia, in part because of physicians' uncertainty in assessing the severity of illness at presentation. METHODS: From our analysis of data on 14,199 adult inpatients with community-acquired pneumonia, we derived a prediction rule that stratifies patients into five classes with respect to the risk of death within 30 days. The rule was validated with 1991 data on 38,039 inpatients and with data on 2287 inpatients and outpatients in the Pneumonia Patient Outcomes Research Team (PORT) cohort study. The prediction rule assigns points based on age and the presence of coexisting disease, abnormal physical findings (such as a respiratory rate of > or = 30 or a temperature of > or = 40 degrees C), and abnormal laboratory findings (such as a pH <7.35, a blood urea nitrogen concentration > or = 30 mg per deciliter [11 mmol per liter] or a sodium concentration <130 mmol per liter) at presentation. RESULTS: There were no significant differences in mortality in each of the five risk classes among the three cohorts. Mortality ranged from 0.1 to 0.4 percent for class I patients (P=0.22), from 0.6 to 0.7 percent for class II (P=0.67), and from 0.9 to 2.8 percent for class III (P=0.12). Among the 1575 patients in the three lowest risk classes in the Pneumonia PORT cohort, there were only seven deaths, of which only four were pneumonia-related. The risk class was significantly associated with the risk of subsequent hospitalization among those treated as outpatients and with the use of intensive care and the number of days in the hospital among inpatients. CONCLUSIONS: The prediction rule we describe accurately identifies the patients with community-acquired pneumonia who are at low risk for death and other adverse outcomes. This prediction rule may help physicians make more rational decisions about hospitalization for patients with pneumonia.

Barefoot, J. C. and M. Schroll (1996). "**Symptoms of depression, acute myocardial infarction, and total mortality in a community sample**." Circulation **93**(11): 1976-1980.

Type of Question: Prognosis **Beginner / Intermediate Prospective cohort**.

Teaching Notes: These two articles (see also Frasure-Smith 1993) may be considered together (see sample case.) It is sometimes fun to compare and contrast two different articles about a similar prognosis topic. The populations studied through observational designs (in this case a cohort) are critical to how we understand and apply the information. Therefore, it is sometimes a good strategy to compare and contrast findings in studies done in different settings. In these two papers, there are many opportunities to discuss the impact of potential 'bias'; Try to consider why I chose these two papers- what about the two populations make for good comparison?? Note: either of these papers could also be looked at as a single paper.

Abstract: BACKGROUND: Depression has been shown to adversely affect the prognosis of patients with established coronary artery disease, but there is comparatively little evidence to document the role of depression in the initial development of coronary disease. METHODS AND RESULTS: Study participants were 409 men and 321 women who were residents of Glostrup, Denmark, born in 1914. Physical and psychological examinations in 1964 and 1974 established their baseline risk factor and disease status and their level of depressive symptomatology. Initial myocardial infarction (MI) was observed in 122 participants, and there were 290 deaths during follow-up, which ended in 1991. A 2-SD difference in depression score was associated with relative risks of 1.71 (P = .005) for MI and 1.59 (P < .001) for deaths from all causes. These findings were unchanged after we controlled for risk factors and signs of disease at baseline. There were no sex differences in effect sizes. CONCLUSIONS: High levels of depressive symptomatology are associated with increased risks of MI and mortality. The graded relationships between depression scores and risk, long-lasting nature of the effect, and stability of the depression measured across time suggest that this risk factor is best viewed as a continuous variable that represents a chronic psychological characteristic rather than a discrete and episodic psychiatric condition.

Frasure-Smith, N., F. Lesperance, et al. (1993). "**Depression following myocardial infarction. Impact on 6-month survival**." Jama **270**(15): 1819-1825.

Type of Question: Prognosis **Beginner / Intermediate Prospective cohort**.

Teaching Notes: These two articles (see also Barefoot 1996) may be considered together (see sample case.) It is sometimes fun to compare and contrast two different articles about a similar prognosis topic. The populations studied through observational designs (in this case a cohort) are critical to how we understand and apply the information. Therefore, it is sometimes a good strategy to compare and contrast findings in studies done in different settings. In these two papers, there are many opportunities to discuss the impact of potential 'bias'; Try to consider why I chose these two papers- what about the two populations make for good comparison?? Note: either of these papers could also be looked at as a single paper.

Abstract: OBJECTIVE--To determine if the diagnosis of major depression in patients hospitalized following myocardial infarction (MI) would have an independent impact on cardiac mortality over the first 6 months after discharge. DESIGN--Prospective evaluation of the impact of depression assessed using a modified version of the National Institute of Mental Health Diagnostic Interview Schedule for major depressive episode. Cox proportional hazards regression was used to evaluate the independent impact of depression after control for significant clinical predictors in the data set. SETTING--A large, university-affiliated hospital specializing in cardiac care, located in Montreal, Quebec. PATIENTS--All consenting patients (N = 222) who met established criteria for MI between August 1991 and July 1992 and who survived to be discharged from the hospital. Patients were interviewed between 5 and 15 days following the MI and were followed up for 6 months. There were no age limits (range, 24 to 88 years; mean, 60 years). The sample was 78% male. PRIMARY OUTCOME MEASURE--Survival status at 6 months. RESULTS--By 6 months, 12 patients had died. All deaths were due to cardiac causes. Depression was a significant predictor of mortality (hazard ratio, 5.74; 95% confidence interval, 4.61 to 6.87; P = .0006). The impact of depression remained after control for left ventricular dysfunction (Killip class) and previous MI, the multivariate significant predictors of mortality in the data set (adjusted hazard ratio, 4.29; 95% confidence interval, 3.14 to 5.44; P = .013). CONCLUSION--Major depression in patients hospitalized following an MI is an independent risk factor for mortality at 6 months. Its impact is at least equivalent to

that of left ventricular dysfunction (Killip class) and history of previous MI. Additional study is needed to determine whether treatment of depression can influence post-MI survival and to assess possible underlying mechanisms.

Johnston, S. C., D. R. Gress, et al. (2000). "**Short-term prognosis after emergency department diagnosis of TIA**." Jama **284**(22): 2901-2906.

Type of Question: Prognosis **Beginner / Intermediate Cohort**.

Teaching Notes: Landmark study that changed thinking about otherwise 'uncomplicated' TIA's. Sound methodology. Good discussion points: An extra 'value added'-the authors assessed predictors of short term stroke and proposed a scoring system for the purpose of identifying a low-risk subgroup. This is the basis of a good entry level discussion of the difference between a validated prediction rule and the qualitative information embodied in identification of prognostic factors.

Abstract: CONTEXT: Management of patients with acute transient ischemic attack (TIA) varies widely, with some institutions admitting all patients and others proceeding with outpatient evaluations. Defining the short-term prognosis and risk factors for stroke after TIA may provide guidance in determining which patients need rapid evaluation. OBJECTIVE: To determine the short-term risk of stroke and other adverse events after emergency department (ED) diagnosis of TIA. DESIGN AND SETTING: Cohort study conducted from March 1997 through February 1998 in 16 hospitals in a health maintenance organization in northern California. Patients A total of 1707 patients (mean age, 72 years) identified by ED physicians as having presented with TIA. MAIN OUTCOME MEASURES: Risk of stroke during the 90 days after index TIA; other events, including death, recurrent TIA, and hospitalization for cardiovascular events. RESULTS: During the 90 days after index TIA, 180 patients (10.5%) returned to the ED with a stroke, 91 of which occurred in the first 2 days. Five factors were independently associated with stroke: age greater than 60 years (odds ratio [OR], 1.8; 95% confidence interval [CI], 1.1-2.7; P=.01), diabetes mellitus (OR, 2.0; 95% CI, 1.4-2.9; P<.001), symptom duration longer than 10 minutes (OR, 2.3; 95% CI, 1.3-4.2; P=.005), weakness (OR, 1.9; 95% CI, 1.4-2.6; P<.001), and speech impairment (OR, 1.5; 95% CI, 1.1-2.1; P=.01). Stroke or other adverse events occurred in 428 patients (25.1%) in the 90 days after the TIA and included 44 hospitalizations for cardiovascular events (2.6%), 45 deaths (2.6%), and 216 recurrent TIAs (12.7%). CONCLUSIONS: Our results indicate that the short-term risk of stroke and other adverse events among patients who present to an ED with a TIA is substantial. Characteristics of the patient and the TIA may be useful for identifying patients who may benefit from expeditious evaluation and treatment.

Rao, S. V., J. G. Jollis, et al. (2004). "**Relationship of blood transfusion and clinical outcomes in patients with acute coronary syndromes**." Jama **292**(13): 1555-1562.

Type of Question: Prognosis **Intermediate Cohort**.

Teaching Notes: Clinical data from multiple prospective randomized trials were pooled to create a cohort to study the relationship between blood transfusion in anemic patients with acute coronary syndromes and survival. A strength of this as a teaching paper is that one can discuss the fact that RCTs can provide much additional data in addition to the intervention initially studied. In addition, the results are interesting in that they suggest increased mortality associated with transfusion in some patients. This is counter to the common practice of transfusing to “a number threshold” rather than treating the patient. Good paper to combine with Hebert et al NEJM 1999;340:409-417

Abstract: CONTEXT: It is unclear if blood transfusion in anemic patients with acute coronary syndromes is associated with improved survival. OBJECTIVE: To determine the association between blood transfusion and mortality among patients with acute coronary syndromes who develop bleeding, anemia, or both during their hospital course. DESIGN, SETTING, AND PATIENTS: We analyzed 24,112 enrollees in 3 large international trials of patients with acute coronary syndromes (the GUSTO IIb, PURSUIT, and PARAGON B trials). Patients were grouped according to whether they received a blood transfusion during the hospitalization. The association between transfusion and outcome was assessed using Cox proportional hazards modeling that incorporated transfusion as a time-dependent covariate and the propensity to receive blood, and a landmark analysis. MAIN OUTCOME MEASURE: Thirty-day mortality. RESULTS: Of the patients included, 2401 (10.0%) underwent at least 1 blood transfusion during

their hospitalization. Patients who underwent transfusion were older and had more comorbid illness at presentation and also had a significantly higher unadjusted rate of 30-day death (8.00% vs 3.08%; P<.001), myocardial infarction (MI) (25.16% vs 8.16%; P<.001), and death/MI (29.24% vs 10.02%; P<.001) compared with patients who did not undergo transfusion. Using Cox proportional hazards modeling that incorporated transfusion as a time-dependent covariate, transfusion was associated with an increased hazard for 30-day death (adjusted hazard ratio [HR], 3.94; 95% confidence interval [CI], 3.26-4.75) and 30-day death/MI (HR, 2.92; 95% CI, 2.55-3.35). In the landmark analysis that included procedures and bleeding events, transfusion was associated with a trend toward increased mortality. The predicted probability of 30-day death was higher with transfusion at nadir hematocrit values above 25%. CONCLUSIONS: Blood transfusion in the setting of acute coronary syndromes is associated with higher mortality, and this relationship persists after adjustment for other predictive factors and timing of events. Given the limitations of post hoc analysis of clinical trials data, a randomized trial of transfusion strategies is warranted to resolve the disparity in results between our study and other observational studies. We suggest caution regarding the routine use of blood transfusion to maintain arbitrary hematocrit levels in stable patients with ischemic heart disease.

Chandratheva, A., Z. Mehta, et al. (2009). "**Population-based study of risk and predictors of stroke in the first few hours after a TIA**." Neurology **72**(22): 1941-1947.

Type of Question: Prognosis **Beginner Prospective Cohort**.

Teaching Notes: very nicely done, covers all the elements for critical appraisal of a prognosis paper

Abstract: BACKGROUND: Several recent guidelines recommend assessment of patients with TIA within 24 hours, but it is uncertain how many recurrent strokes occur within 24 hours. It is also unclear whether the ABCD2 risk score reliably identifies recurrences in the first few hours. METHODS: In a prospective, population-based incidence study of TIA and stroke with complete follow-up (Oxford Vascular Study), we determined the 6-, 12-, and 24-hour risks of recurrent stroke, defined as new neurologic symptoms of sudden onset after initial recovery. RESULTS: Of 1,247 first TIA or strokes, 35 had recurrent strokes within 24 hours, all in the same arterial territory. The initial event had recovered prior to the recurrent stroke (i.e., was a TIA) in 25 cases. The 6-, 12-, and 24-hour stroke risks after 488 first TIAs were 1.2% (95% confidence interval [CI]: 0.2-2.2), 2.1% (0.8-3.2), and 5.1% (3.1-7.1), with 42% of all strokes during the 30 days after a first TIA occurring within the first 24 hours. The 12- and 24-hour risks were strongly related to ABCD2 score ($p = 0.02$ and $p = 0.0003$). Sixteen (64%) of the 25 cases sought urgent medical attention prior to the recurrent stroke, but none received antiplatelet treatment acutely. CONCLUSION: That about half of all recurrent strokes during the 7 days after a TIA occur in the first 24 hours highlights the need for emergency assessment. That the ABCD2 score is reliable in the hyperacute phase shows that appropriately triaged emergency assessment and treatment are feasible.

Hasbun, R., J. Abrahams, et al. (2001). "**Computed tomography of the head before lumbar puncture in adults with suspected meningitis**." N Engl J Med **345**(24): 1727-1733.

Type of Question: Prognosis **Intermediate Prospective Cohort**.

Teaching Notes: Solid methodology, clearly reported. This prospective cohort study is an excellent example of how associations can be used in clinical decision making. Of note, you can also touch on principles of diagnosis/clinical decision rules (figure 5) when the authors test the diagnostic utility of combinations of baseline characteristics to predict normal or abnormal head CT.

Abstract: BACKGROUND: In adults with suspected meningitis clinicians routinely order computed tomography (CT) of the head before performing a lumbar puncture. METHODS: We prospectively studied 301 adults with suspected meningitis to determine whether clinical characteristics that were present before CT of the head was performed could be used to identify patients who were unlikely to have abnormalities on CT. The Modified National Institutes of Health Stroke Scale was used to identify neurologic abnormalities. RESULTS: Of the 301 patients with suspected meningitis, 235 (78 percent) underwent CT of the head before undergoing lumbar puncture. In 56 of the 235 patients (24 percent), the results of CT were abnormal; 11 patients (5 percent) had evidence of a mass effect. The clinical features at base line that were associated with an abnormal finding on CT of the head were an

age of at least 60 years, immunocompromise, a history of central nervous system disease, and a history of seizure within one week before presentation, as well as the following neurologic abnormalities: an abnormal level of consciousness, an inability to answer two consecutive questions correctly or to follow two consecutive commands, gaze palsy, abnormal visual fields, facial palsy, arm drift, leg drift, and abnormal language (e.g., aphasia). None of these features were present at base line in 96 of the 235 patients who underwent CT scanning of the head (41 percent). The CT scan was normal in 93 of these 96 patients, yielding a negative predictive value of 97 percent. Of the three misclassified patients, only one had a mild mass effect on CT, and all three subsequently underwent lumbar puncture, with no evidence of brain herniation one week later. CONCLUSIONS: In adults with suspected meningitis, clinical features can be used to identify those who are unlikely to have abnormal findings on CT of the head.

Gage, B. F., A. D. Waterman, et al. (2001). "**Validation of clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation**." JAMA **285**(22): 2864-2870.

Type of Question: Prognosis **Intermediate to Advanced Clinical prediction Rule**.

Teaching Notes: Useful prediction rule that utilizes data from multiple large studies to compare schemes for predicting risk of stroke in atrial fibrillation. While the methods may be difficult for less experienced learners, the applicability of this tool makes for compelling discussion. Also, a general understanding of clinical decision rules can be put forward.

Abstract: CONTEXT: Patients who have atrial fibrillation (AF) have an increased risk of stroke, but their absolute rate of stroke depends on age and comorbid conditions. OBJECTIVE: To assess the predictive value of classification schemes that estimate stroke risk in patients with AF. DESIGN, SETTING, AND PATIENTS: Two existing classification schemes were combined into a new stroke-risk scheme, the CHADS(2) index, and all 3 classification schemes were validated. The CHADS(2) was formed by assigning 1 point each for the presence of congestive heart failure, hypertension, age 75 years or older, and diabetes mellitus and by assigning 2 points for history of stroke or transient ischemic attack. Data from peer review organizations representing 7 states were used to assemble a National Registry of AF (NRAF) consisting of 1733 Medicare beneficiaries aged 65 to 95 years who had nonrheumatic AF and were not prescribed warfarin at hospital discharge. MAIN OUTCOME MEASURE: Hospitalization for ischemic stroke, determined by Medicare claims data. RESULTS: During 2121 patient-years of follow-up, 94 patients were readmitted to the hospital for ischemic stroke (stroke rate, 4.4 per 100 patient-years). As indicated by a c statistic greater than 0.5, the 2 existing classification schemes predicted stroke better than chance: c of 0.68 (95% confidence interval [CI], 0.65-0.71) for the scheme developed by the Atrial Fibrillation Investigators (AFI) and c of 0.74 (95% CI, 0.71-0.76) for the Stroke Prevention in Atrial Fibrillation (SPAF) III scheme. However, with a c statistic of 0.82 (95% CI, 0.80-0.84), the CHADS(2) index was the most accurate predictor of stroke. The stroke rate per 100 patient-years without antithrombotic therapy increased by a factor of 1.5 (95% CI, 1.3-1.7) for each 1-point increase in the CHADS(2) score: 1.9 (95% CI, 1.2-3.0) for a score of 0; 2.8 (95% CI, 2.0-3.8) for 1; 4.0 (95% CI, 3.1-5.1) for 2; 5.9 (95% CI, 4.6-7.3) for 3; 8.5 (95% CI, 6.3-11.1) for 4; 12.5 (95% CI, 8.2-17.5) for 5; and 18.2 (95% CI, 10.5-27.4) for 6. CONCLUSION: The 2 existing classification schemes and especially a new stroke risk index, CHADS(2), can quantify risk of stroke for patients who have AF and may aid in selection of antithrombotic therapy.

Wisnivesky, J. P., C. Henschke, et al. (2005). "**Prospective validation of a prediction model for isolating inpatients with suspected pulmonary tuberculosis**." Arch Intern Med **165**(4): 453-457.

Type of Question: Prognosis **Intermediate to Advanced Clinical Prediction Rule**.

Teaching Notes: Well done validation study of a clinical prediction rule for identification of patients at low risk for TB in order to inform decisions regarding respiratory isolation. Good paper for introducing the concept of clinical prediction rules and their utility.

Abstract: BACKGROUND: Current guidelines for the control of nosocomial transmission of tuberculosis (TB) recommend respiratory isolation for all patients with suspected TB. Application of these guidelines has resulted in many patients without TB being isolated on admission to the hospital, significantly increasing hospital costs. This study was conducted to prospectively validate a clinical

decision rule to predict the need for respiratory isolation in inpatients with suspected TB. METHODS: A cohort of 516 individuals, who presented to 2 New York City hospitals between January 16, 2001, and September 29, 2002, and who were isolated on admission for clinically suspected TB, were enrolled in the study. Face-to-face interviews were conducted to determine the presence of clinical variables associated with TB in the prediction model, including TB risk factors, clinical symptoms, and findings from physical examination and chest radiography. RESULTS: Of the 516 patients, 19 were found to have TB (prevalence, 3.7%; 95% confidence interval [CI], 2.2%-5.7%). The prediction rule had a sensitivity of 95% (95% CI, 74%-100%) and a specificity of 35% (95% CI, 31%-40%). Using a prevalence of TB of 3.7%, the positive predictive value was 9.6% and the negative predictive value was 99.7%. CONCLUSIONS: Among inpatients with suspected active pulmonary TB who are isolated on admission to the hospital, a prediction rule based on clinical and chest radiographic findings accurately identified patients at low risk for TB. Approximately one third of the unnecessary episodes of respiratory isolation could have been avoided had the prediction rule been applied. Future studies should assess the feasibility of implementing the rule in clinical practice.

Lim, W. S., M. M. van der Eerden, et al. (2003). "**Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study**." Thorax **58**(5): 377-382.

Type of Question: Prognosis **Intermediate to Advanced Clinical Prediction Rule**.

Teaching Notes: CURB-65 is an alternative to PORT scores for predicting severity of illness and to stratify groups by mortality risk. This is a well done, clearly reported study that enhances the original work done by Fine et al (Prediction rule to identify low-risk patients with community acquired pneumonia. NEJM: 1997:336:243-50).

Abstract: BACKGROUND: In the assessment of severity in community acquired pneumonia (CAP), the modified British Thoracic Society (mBTS) rule identifies patients with severe pneumonia but not patients who might be suitable for home management. A multicentre study was conducted to derive and validate a practical severity assessment model for stratifying adults hospitalised with CAP into different management groups. METHODS: Data from three prospective studies of CAP conducted in the UK, New Zealand, and the Netherlands were combined. A derivation cohort comprising 80% of the data was used to develop the model. Prognostic variables were identified using multiple logistic regression with 30 day mortality as the outcome measure. The final model was tested against the validation cohort. RESULTS: 1068 patients were studied (mean age 64 years, 51.5% male, 30 day mortality 9%). Age >/=65 years (OR 3.5, 95% CI 1.6 to 8.0) and albumin <30 g/dl (OR 4.7, 95% CI 2.5 to 8.7) were independently associated with mortality over and above the mBTS rule (OR 5.2, 95% CI 2.7 to 10). A six point score, one point for each of Confusion, Urea >7 mmol/l, Respiratory rate >/=30/min, low systolic(<90 mm Hg) or diastolic (</=60 mm Hg) Blood pressure), age >/=65 years (CURB-65 score) based on information available at initial hospital assessment, enabled patients to be stratified according to increasing risk of mortality: score 0, 0.7%; score 1, 3.2%; score 2, 3%; score 3, 17%; score 4, 41.5% and score 5, 57%. The validation cohort confirmed a similar pattern. CONCLUSIONS: A simple six point score based on confusion, urea, respiratory rate, blood pressure, and age can be used to stratify patients with CAP into different management groups.

Correll, C. U., P. Manu, et al. (2009). "**Cardiometabolic risk of second-generation antipsychotic medications during first-time use in children and adolescents**." JAMA **302**(16): 1765-1773.

Type of Question: Prognosis **Intermediate to Advanced Propsective Cohort**.

Teaching Notes: This cohort study examines the association of antipsychotic medications with weight gain and metabolic parameters in children and adolescents. As medication usage in children and adolescents continues to increase, the study of consequences of this use are increasingly important. This study can be used to discuss the relationship between prognosis (the distribution of outcomes over time) and harm. Learners may need to be guided to the correct critical appraisal sheet for a cohort study (prognosis sheet).

Abstract: CONTEXT: Cardiometabolic effects of second-generation antipsychotic medications are concerning but have not been sufficiently studied in pediatric and adolescent patients naive to

antipsychotic medication. OBJECTIVE: To study the association of second-generation antipsychotic medications with body composition and metabolic parameters in patients without prior antipsychotic medication exposure. DESIGN, SETTING, AND PATIENTS: Nonrandomized Second-Generation Antipsychotic Treatment Indications, Effectiveness and Tolerability in Youth (SATIETY) cohort study, conducted between December 2001 and September 2007 at semi-urban, tertiary care, academic inpatient and outpatient clinics in Queens, New York, with a catchment area of 4.5-million individuals. Of 505 youth aged 4 to 19 years with 1 week or less of antipsychotic medication exposure, 338 were enrolled (66.9%). Of these patients, 272 had at least 1 postbaseline assessment (80.5%), and 205 patients [corrected] completed the study (60.7%). Patients had mood spectrum (n = 130; 47.8%), schizophrenia spectrum (n = 82; 30.1%), and disruptive or aggressive behavior spectrum (n = 60; 22.1%) disorders. Fifteen patients who refused participation or were nonadherent served as a comparison group. INTERVENTION: Treatment with aripiprazole, olanzapine, quetiapine, or risperidone for 12 weeks. MAIN OUTCOME MEASURES: Weight gain and changes in lipid and metabolic parameters. RESULTS: After a median of 10.8 weeks (interquartile range, 10.5-11.2 weeks) of treatment, weight increased by 8.5 kg (95% confidence interval [CI], 7.4 to 9.7 kg) with olanzapine (n = 45), by 6.1 kg (95% CI, 4.9 to 7.2 kg) with quetiapine (n = 36), by 5.3 kg (95% CI, 4.8 to 5.9 kg) with risperidone (n = 135), and by 4.4 kg (95% CI, 3.7 to 5.2 kg) with aripiprazole (n = 41) compared with the minimal weight change of 0.2 kg (95% CI, -1.0 to 1.4 kg) in the untreated comparison group (n = 15). With olanzapine and quetiapine, respectively, mean levels increased significantly for total cholesterol (15.6 mg/dL [95% CI, 6.9 to 24.3 mg/dL] P < .001 and 9.1 mg/dL [95% CI, 0.4 to 17.7 mg/dL] P = .046), triglycerides (24.3 mg/dL [95% CI, 9.8 to 38.9 mg/dL] P = .002 and 37.0 mg/dL [95% CI, 10.1 to 63.8 mg/dL] P = .01), non-high-density lipoprotein (HDL) cholesterol (16.8 mg/dL [95% CI, 9.3 to 24.3 mg/dL] P < .001 and 9.9 mg/dL [95% CI, 1.4 to 18.4 mg/dL] P = .03), and ratio of triglycerides to HDL cholesterol (0.6 [95% CI, 0.2 to 0.9] P = .002 and (1.2 [95% CI, 0.4 to 2.0] P = .004). With risperidone, triglycerides increased significantly (mean level, 9.7 mg/dL [95% CI, 0.5 to 19.0 mg/dL]; P = .04). Metabolic baseline-to-end-point changes were not significant with aripiprazole or in the untreated comparison group. CONCLUSIONS: First-time second-generation antipsychotic medication use was associated with significant weight gain with each medication. Metabolic changes varied among the 4 antipsychotic medications.

Venditti, M., M. Falcone, et al. (2009). "**Outcomes of patients hospitalized with community-acquired, health care-associated, and hospital-acquired pneumonia**." Ann Intern Med **150**(1): 19-26.

Type of Question: Prognosis **Intermediate Prospective cohort**.

Teaching Notes: Good to teach prognosis

Abstract: BACKGROUND: Traditionally, pneumonia has been classified as either community- or hospital-acquired. Although only limited data are available, health care-associated pneumonia has been recently proposed as a new category of respiratory infection. "Health care-associated pneumonia" refers to pneumonia in patients who have recently been hospitalized, had hemodialysis, or received intravenous chemotherapy or reside in a nursing home or long-term care facility. OBJECTIVE: To ascertain the epidemiology and outcome of community-acquired, health care-associated, and hospital-acquired pneumonia in adults hospitalized in internal medicine wards. DESIGN: Multicenter, prospective observational study. SETTING: 55 hospitals in Italy comprising 1941 beds. PATIENTS: 362 patients hospitalized with pneumonia during two 1-week surveillance periods. MEASUREMENTS: Cases of radiologically and clinically assessed pneumonia were classified as community-acquired, health care-associated, or hospital-acquired and rates were compared. RESULTS: Of the 362 patients, 61.6% had community-acquired pneumonia, 24.9% had health care-associated pneumonia, and 13.5% had hospital-acquired pneumonia. Patients with health care-associated pneumonia had higher mean Sequential Organ Failure Assessment scores than did those with community-acquired pneumonia (3.0 vs. 2.0), were more frequently malnourished (11.1% vs. 4.5%, and had more frequent bilateral (34.4% vs. 19.7%) and multilobar (27.8% vs. 21.5%) involvement on a chest radiograph. Patients with health care-associated pneumonia also had higher fatality rates (17.8% [CI, 10.6% to 24.9%] vs. 6.7% [CI, 2.9% to 10.5%]) and longer mean hospital stay (18.7 days [CI, 15.9 to 21.5 days] vs. 14.7 days [CI, 13.4 to 15.9 days]). Logistic regression analysis revealed that depression of consciousness (odds ratio [OR], 3.2 [CI, 1.06 to 9.8]), leukopenia (OR, 6.2 [CI, 1.01 to 37.6]), and receipt of empirical antibiotic therapy not recommended by international guidelines (OR, 6.4 [CI, 2.3 to 17.6]) were independently associated with increased

intrahospital mortality. Limitations: The number of patients with health care-associated pneumonia was relatively small. Microbiological investigations were not always homogeneous. The study included only patients with pneumonia that required hospitalization; results may not apply to patients treated as outpatients. CONCLUSION: Health care-associated pneumonia should be considered a distinct subset of pneumonia associated with more severe disease, longer hospital stay, and higher mortality rates. Physicians should differentiate between patients with health care-associated pneumonia and those with community-acquired pneumonia and provide more appropriate initial antibiotic therapy.

El-Solh, A. A., C. Pietrantoni, et al. (2003). "**Microbiology of severe aspiration pneumonia in institutionalized elderly**." Am J Respir Crit Care Med **167**(12): 1650-1654.

Type of Question: Prognosis **Beginner cohort study**.

Teaching Notes: Prospective cohort study looking at etiology and also prognosis; Clear methods and descriptive distribution of microbiologic diagnoses; Also includes prognosis information including length of intubation, ICU stay and mortality

Abstract: We sought to investigate prospectively the microbial etiology and prognostic indicators of 95 institutionalized elders with severe aspiration pneumonia, and to investigate its relation to oral hygiene in using quantitative bronchial sampling. Data collection included demographic information, Activity of Daily Living, Plaque Index, antimicrobial therapy, and outcome. Out of the 67 pathogens identified, Gram-negative enteric bacilli were the predominant organisms isolated (49%), followed by anaerobic bacteria (16%), and Staphylococcus aureus (12%). The most commonly encountered anaerobes were Prevotella and Fusobacterium species. Aerobic Gram-negative bacilli were recovered in conjunction with 55% of anaerobic isolates. The Plaque Index did not differ significantly between the aerobic (2.2 +/- 0.4) and the anaerobic group (2.3 +/- 0.3). Functional status was the only determinant of the presence of anaerobic bacteria. Although seven cases with anaerobic isolates received initially inadequate antimicrobial therapy, six had effective clinical response. The crude mortality was 33% for the aerobic and 36% for the anaerobic group ($p = 0.9$). Stepwise multivariate analysis identified hypoalbuminemia ($p < 0.001$) and the burden of comorbid diseases ($p < 0.001$) as independent risk factors of poor outcome. In view of the rising resistance to antimicrobial agents, the importance of adding anaerobic coverage for aspiration pneumonia in institutionalized elders needs to be reexamined.

Condat, B., F. Pessione, et al. (2001). "**Current outcome of portal vein thrombosis in adults: risk and benefit of anticoagulant therapy**." Gastroenterology **120**(2): 490-497.

Type of Question: Prognosis **Intermediate - Advanced Cohort Study**.

Teaching Notes: Cohort study that records natural history and prognosis; Also tries to make inferences about interventions which is much more tricky, but in scenarios where there may not be RCT data.

Abstract: BACKGROUND & AIMS: The outcome of portal vein thrombosis in relation to associated prothrombotic states has not been evaluated. We assessed current outcome and predictors of bleeding and thrombotic events in a cohort of 136 adults with nonmalignant, noncirrhotic portal vein thrombosis, of whom 84 received anticoagulant therapy. METHODS: Multivariate Cox model analysis for event-free survival and analysis taking into account multiple events were used. RESULTS: Median follow-up was 46 months. The incidence rate of gastrointestinal bleeding was 12.5 (95% confidence interval [CI], 10-15) per 100 patient-years. Large varices were an independent predictor for bleeding. Anticoagulant therapy did not increase the risk or the severity of bleeding. The incidence rate of thrombotic events was 5.5 (95% CI, 3.8-7.2) per 100 patient-years. Underlying prothrombotic state and absence of anticoagulant therapy were independent predictors for thrombosis. In patients with underlying prothrombotic state, the incidence rates of splanchnic venous infarction were 0.82 and 5.2 per 100 patient-years in periods with and without anticoagulant therapy, respectively ($P = 0.01$). Two nonanticoagulated patients died of bleeding and thrombosis, respectively. CONCLUSIONS: In patients with portal vein thrombosis, the risk of thrombosis is currently as clinically significant as the risk of bleeding. The benefit-risk ratio favors anticoagulant therapy.