Exercises diagnostic testing

1) Exercise on Down syndrome

2) elearning

http://www.vphibern.ch/e_epi/EN/

3)

Evidence base of clinical diagnosis
The architecture of diagnostic research
D L Sackett, R B Haynes

BMJ 2002; 324:539-41

Example:

Assessment of the value of the plasma concentration of B-type natriuretic peptide (BNP) in the diagnosis of left ventricular dysfunction in humans.

3.a)

Investigators at a British university hospital measured concentrations of a BNP precursor in non-systematic („convenience“) samples from normal controls and from patients who had various combinations of hypertension, ventricular hypertrophy and left ventricular dysfunction.

If you had access to the raw data which statistical test could be used (just think, no need to use R)?

Table 1.

	Patients known to have disorder	Normal controls
Median (range) concentration of BNP precursor (pg/ml)	493.5 (248.9-909.0)	129.4 (53.6-159.7)

What would be your conclusion from the information given in the table?

How would you describe the research question or hypothesis of this study at the end of the introduction?

3.b)

A second group of investigators at a Belgian university hospital measured BNP concentrations in normal controls and in three groups of patients with coronary artery disease and varying degrees of left ventricular dysfunction. Among the analyses they performed was a simple plot of individual BNP results, which generated the results shown in table 2 by picking the cut-off point that best distinguished patients with severe left ventricular dysfunction from normal controls.

Table 2.

	Patients known to have target disorder	Normal controls
High BNP concentration	39	2
Normal BNP concentration	1	25

Use R and calculate (with 95 % CI) the test characteristics, predictive values, likelihood ratios and diagnostic odds ratio.

What is your conclusion now (compare to your answer in 3.a)?

How would you describe the research question of this Belgian study?

3.c)

Another UK group of clinical investigators reported having invited general practitioners in their area „to refer patients with suspected heart failure to our clinic“. These referred patients (n=126) underwent independent, blind BNP measurements and echocardiography (used as a gold standard to diagnose left ventricular dysfunction).

Table 3.

	Patients with LVD on echocardiography	Patients with normal results on echocardiography
Concentration of BNP:		
High (>17.9 pg/ml)	35	57
Normal (<18 pg/ml)	5	29
Prevalence (pretest probability) of LVD	40/126=32%	

Calculate (with 95 % CI) the test characteristics, predictive values, likelihood ratios and diagnostic odds ratio.

What is your conclusion now (compared to your previous answers)?

How would you describe the research question of this UK study?

4) Kappa

Calculate the corresponding kappa values (inter-rater reliability) for two diagnosticians (A, B)

Table 1)

	Diagnostician A	
Diagnostician B	+	-
+	85	5
-	5	5

Table 2)

	Diagnostician A	
Diagnostician B	+	-
+	45	5
-	5	45

Calculate also the overall agreement for both tables.

What are your conclusions when you compare the kappa values for table 1 and 2?

5) ROC curves

Two data sets with OD values from four serological assays (p45, FL74, EPK211 and p15E) to detect antibodies against feline leukemia virus (FeLV). The "gold standard" used here is the PCR "Provirus". One data set is based on a study from experimentally infected cats ("ROC_exp.csv"), the other data set originates from a field study ("ROC_field.csv").

The data have been modified and are a subset from this paper:

Detection of Antibodies to the Feline Leukemia Virus (FeLV) Transmembrane Protein p15E: an Alternative Approach for Serological FeLV Detection Based on Antibodies to p15E

Eva Boenzli, Maik Hadorn, Sonja Hartnack, Jon Huder, Regina Hofmann-Lehmann and Hans Lutz
J. Clin. Microbiol. 2014, 52(6):2046. DOI: 10.1128/JCM.02584-13.

Please choose at least one of the three serological assays (p45, FL74 or EPK211) from the experimental and the field data set and

a) Download the pROC package
b) Plot a ROC curve for this serological assay and p15E
c) Provide AUC for this serological assay and p15E
d) Please compare at least one of the other two serological assays (p45 or FL74 or EPK211) against p15E. Do they significantly differ?
e) Do the experimental and the field data set differ? Could you explain this?

If you would like to do more….

f) Provide pAUC for sensitivities and specificities above 90% and appropriate plots.

If you would like to do more stuff:

Have a look on the pROC website http://web.expasy.org/pROC/

or check the reference manual http://cran.r-project.org/web/packages/pROC/pROC.pdf

6) STARD guidelines

Read the paper and discuss in group if the paper is compliant with all items of the STARD guidelines.