UNIVERSITY OF COPENHAGEN
FACULTY OF HEALTH AND MEDICAL SCIENCES

Exam in Infectious Disease Epidemiology

SFOK09103U

Master of Public Health Science, elective course

December 11th 2017

(24-hour take-home exam)
The exam assignment consists of 5 pages inclusive the front page.

Exam guidelines:

The exam describes two cases followed by a total of nine questions. For Case 1 there is five questions and for Case 2 there is four questions. The assignment may consist of up to 5 pages (2400 strokes including spaces per page), totaling to 12000 strokes. Figures, tables and graphics can be included as appendices, and do not count in the total number of strokes.

Permitted aids:

The following aids are allowed (source: kurser.ku.dk):

All aids are allowed.

Practicalities

The assignment must be written in English, and handed in by December 12th 2017 at 10:00 AM.

Suggestions: This exam contains suggestive minimal answers for each of the questions. Other sound suggestions can be accepted.

Case 1: A recent report from WHO states that a new subtype of influenza (influenza-x) is emerging in Asia. The report states that influenza-x has potential to become endemic, including outside of Asia. The first analyses from WHO show that morbidity from influenza-x is similar to morbidity from the seasonal influenza occurring during winter in Denmark.

1. Propose possible surveillance setups for influenza-x in Denmark, and discuss associated advantages and disadvantages.

   E.g. use existing sentinel system for influenza-like illness with the Danish general practitioners, with additional questions regarding travel to Asia to compensate for poor specificity. Other sound suggestions including laboratory diagnostic based surveillance or hospital discharge registration are welcome.

2. Assuming that no extra resources are available, discuss how you prioritize the surveillance of influenza-x in the existing surveillance program in Denmark.

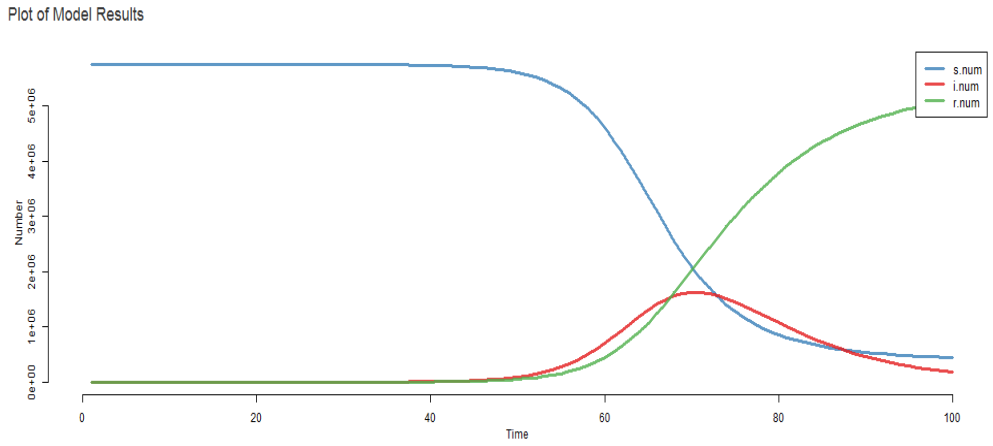
   Initially very high priority because of unknown natural history, great potential for spread and no available vaccination. With time, same high priority as other influenza types. Resources for initial increased priority of influenza-x can come from surveillance of e.g. SARS which is currently less of a problem.

3. Open R studio and copy and paste these lines into your Console, then hit 'Enter'.

   ```
   install.packages("shiny")
   install.packages("EpiModel")
   EpiModel::epiweb("dcm")
   ```

   Run a SIR-model with the below parameters and estimate how many of the 5,748,769 people in Denmark who would be infected with influenza-x at day 7 after influenza-x was first introduced in Denmark. Make a suitable graphical presentation, and suggest at which day the infection peaks.

   - People infected with influenza-x have a contact rate ('act rate' in R studio) of 6 per day
   - The attack rate ('transmission probability per act' in R studio) is 0.06
   - The recovery rate after infection with influenza-x is 0.125
   - The case-fatality ('Death rate (inf.)' in R studio) of influenza-x among the infected is 0.001



At day 7, four (4.07) people are infected. The infection peaks at day 70 with 1,625,616 infected.

4. Discuss the assumptions made in the above deterministic SIR-modeling.

   Homogeneous mixing: Infected likely stays at home, which may lead to overestimation.

   Large population: All Danes are included, so that's fine.

   Closed population: Births, deaths and traveling will occur, with possible underestimation of spread.

   Lifelong acquired immunity: It may be but virus mutates, which possibly leads to underestimation.

   No latent period: Unrealistic for most infections including influenza-x, which possibly leads to overestimation.

   Most model assumptions are violated. The overall effect of violations on the estimated speed with which influenza-x spread is not known.

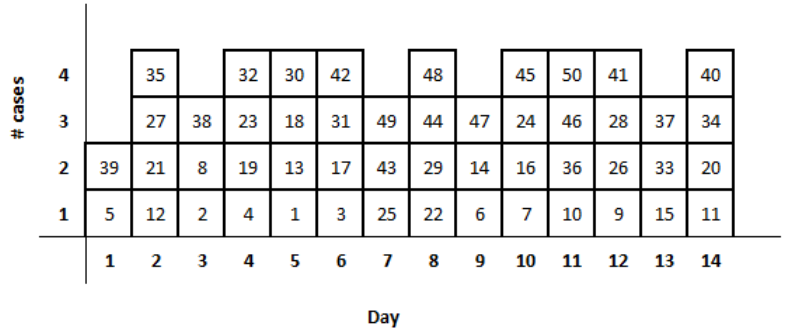
5. A vaccine against influenza-x is not yet available, but will be soon. Calculate R_0 for influenza-x and estimate the proportion of the Danish population who should be vaccinated against influenza-x in order for influenza-x never to take hold i.e. for each person to infect less than one other person.

   R_0 is the product of the risk of transmission per contact (β), the number of contacts (κ) and the duration of infectivity (D). Thus, $R_0 = \beta*\kappa*D \rightarrow R_0 = 0.06*6*(1/0.125) = 2.88$. On average, every infected case infects 2.88 other persons in the totally susceptible population. The proportion needed to vaccinate to obtain herd immunity is given by $1-1/R_0 = 1-1/2.88=0.65 = 65\%$

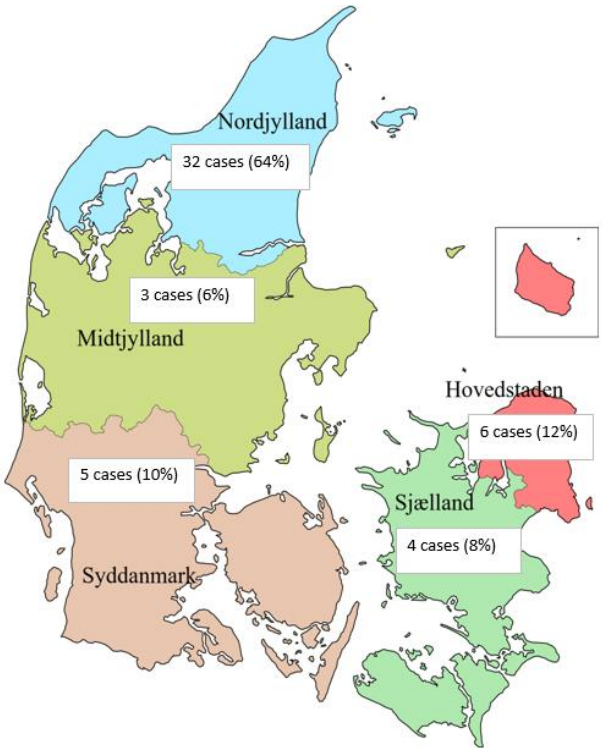
Case 2: 50 cases of severe vomiting and diarrhea are reported to SSI. Table 1 below shows the reported cases distributed on time, age, sex, and region. An Excel sheet containing the data in Table 1 is available for download at www.madskamper.dk/ide under the subheading 'Exam'. The vomiting and diarrhea is suspected to be caused by one or more food items. To investigate if certain food items may be causing the outbreak, a case-control study is set up. Fifty controls are matched to the 50 cases on age, sex and region. Cases and controls fill in a questionnaire regarding food items eaten. The results are shown in Table 2 below.

6. Make suitable presentations of the 50 cases shown in Table 1 distributed on time, region, age and sex, respectively. Which hints about the cause of disease do you obtain by your presentations?

Distribution of cases according to time



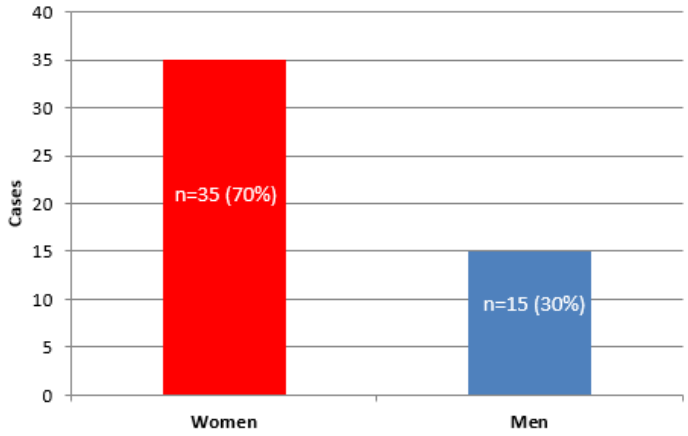
Distribution of cases according to region



Distribution of cases according to age

Age (years)	Cases
0-9	3
10-19	7
20-29	6
30-39	6
40-49	7
50-59	6
60-69	11
70+	4
Total	**50**

Distribution of cases according to sex



There are no apparent peaks in time, suggesting a propagated source. Nordjylland is hit hard, suggesting a local source. All age groups are hit, suggesting a common source. Women are hit hardest, suggesting a vegetable or fruit.

7. Based on the results shown in Table 2, calculate the odds ratio (OR) and belonging 95% confidence interval (95% CI) of exposure to each of the food items. Use controls as the reference group for each of the food items and report ORs and 95% CIs with 2 decimals.

Example of calculation for intake of pork.

	Cases	Controls
Exposed	16	18
Unexposed	34	32
Odds	0,47	0,56

OR	0,84					
95% CI						
	1 divided by	sqrt	multiply by 1.96	e raised	LCL	UCL
	0,17871732	0,42275	0,828589438	2,290086	0,37	1,92

Food item	**OR (95% CI)**
Pork	0.84 (0.37-1.92)
Raspberry	5.27 (1.08-25.78)
Lettuce	1.81 (0.80-4.08)
Grapes	0.78 (0.20-3.10)
Chicken	1.50 (0.68-3.10)

8. Interpret the ORs and belonging 95% confidence limits. If any, suggest which food item(s) caused the outbreak.

   Example of interpretation of OR (95% CI) for intake of pork: The odds of having eaten pork is 16% lower among cases than among controls. The difference is not statistically significant at a 95% level, however, because the confidence interval contains 1. Thus, eating pork had no effect on the odds of experiencing severe vomiting and diarrhea in the current study.

   Only raspberries were found to significantly increase the odds of disease, why raspberries are a plausible source. However, only 9 out of 50 cases reported having eaten raspberries, why further investigation is warranted.

9. Propose possible control measures and discuss associated advantages and disadvantages.

   Obtain stool samples from cases to identify infection. Obtain raspberry samples from cases or supermarkets if possible. Laboratory analysis of raspberries for presence of infection. If present, withdraw raspberries and stop further delivery. Examine production and locate problem before allowing further production. Communicate to public with instructions to throw out. Withdrawing products may seriously impact businesses, so beware of possible biases in your design, sample collection and analysis.

Table 1. Cases of vomiting and diarrhea reported to SSI. Distributed on time, age, sex, and region.

Case nr.	Day	Age (years)	Sex	Region
1	5	19	Male	Nordjylland
2	3	61	Female	Hovedstaden
3	6	70	Male	Nordjylland
4	4	46	Female	Nordjylland
5	1	44	Female	Nordjylland
6	9	39	Female	Nordjylland
7	10	52	Female	Sjælland
8	3	51	Male	Nordjylland
9	12	72	Female	Midtjylland
10	11	68	Female	Sjælland
11	14	65	Female	Nordjylland
12	2	17	Female	Hovedstaden
13	5	2	Male	Nordjylland
14	9	14	Female	Syddanmark
15	13	39	Male	Nordjylland
16	10	67	Female	Midtjylland
17	6	46	Female	Nordjylland
18	5	49	Female	Nordjylland
19	4	23	Male	Nordjylland
20	14	12	Female	Nordjylland
21	2	46	Female	Nordjylland
22	8	37	Female	Nordjylland
23	4	22	Female	Syddanmark
24	10	9	Female	Nordjylland
25	7	12	Male	Syddanmark
26	12	64	Female	Nordjylland
27	2	37	Male	Sjælland
28	12	68	Female	Nordjylland
29	8	21	Female	Nordjylland
30	5	57	Female	Hovedstaden
31	6	64	Female	Sjælland
32	4	53	Male	Nordjylland
33	13	28	Female	Nordjylland
34	14	46	Female	Nordjylland
35	2	58	Male	Syddanmark
36	11	61	Male	Nordjylland
37	13	57	Female	Hovedstaden
38	3	21	Male	Nordjylland
39	1	5	Male	Nordjylland
40	14	68	Female	Midtjylland
41	12	11	Male	Nordjylland
42	6	45	Female	Nordjylland
43	7	38	Female	Nordjylland
44	8	67	Female	Syddanmark
45	10	71	Female	Hovedstaden
46	11	27	Female	Nordjylland
47	9	16	Female	Nordjylland
48	8	74	Male	Nordjylland
49	7	39	Female	Hovedstaden
50	11	61	Female	Nordjylland

Table 2. Cases and controls according to food items eaten.

	Pork	Raspberry	Lettuce	Grapes	Chicken
Cases	16	9	34	4	29
Controls	18	2	27	5	24