

Question 1 (30%)

In this exercise, you are going to use the template **GDM_template**.

Read all the information in the template (all sheets) carefully.

Currently, in Norway, pregnant women are recommended to screen for gestational diabetes mellitus (GDM) between pregnancy weeks 24 and 28. The Norwegian health authorities are considering whether to change the screening guidelines and have requested a health economic analysis.

You are appointed by the health authorities to evaluate the cost-effectiveness of two candidate screening strategies, in addition to a no screening alternative:

- Current guidelines, involving screening with the oral glucose tolerance test (“OGTT”)
- Screening with the glucose challenge test (“GCT”)

As only one of these strategies can be adopted, all three alternatives should be compared simultaneously (so-called competing choice problem).

You are told that the health authorities currently apply a cost-effectiveness threshold of NOK 400,000 per QALY.

Answer the following questions and provide an explanation based on the results of your analysis:

- Using deterministic analysis, estimate the expected costs and quality-adjusted life-years associated with each strategy, and calculate incremental cost-effectiveness ratios (ICERs). Interpret the findings and provide a recommendation for the health authorities.

Solution:

Results					
Strategy	Cost	Incr Costs	QALY	Incr QALY	ICER
No screening	kr 490		0,920		
GCT	kr 1 895	kr 1 405	0,932	0,0123	kr 114 063
OGTT	kr 2 382	kr 487	0,933	0,0008	kr 611 696

GCT would be preferred given the threshold.

- Based on your discussions with clinical experts, you realize that GDM prevalence in Norway ranges from 4% to 11%. Accordingly, conduct a 1-way sensitivity analysis

(comparing only the two screening strategies) using this prevalence range and interpret your findings.

p_GDM	ICER (OGTT vs GCT)
4,0 %	4 397 500
4,5 %	2 175 155
5,0 %	1 443 088
5,5 %	1 078 667
6,0 %	860 528
6,5 %	715 315
7,0 %	611 696
7,5 %	534 038
8,0 %	473 672
8,5 %	425 400
9,0 %	385 919
9,5 %	353 027
10,0 %	325 203
10,5 %	301 358
11,0 %	280 697

OGTT is preferred when prevalence is 9% or higher. + interpretation

- c) As part of your literature review to inform the sensitivity of GCT and OGTT, you identified a range of different sensitivity values for each of the diagnostic tests. Specifically, the sensitivity of GCT varied from 74% to 88%, while OGTT varied from 80% to 94%. To investigate further, you should conduct a 2-way sensitivity analysis (comparing only the two screening strategies) where you explore the impact of the range of sensitivity values identified in the literature. Interpret your findings.

Solution:

		sens of GCT							
	611 696	0,74	0,76	0,78	0,8	0,82	0,84	0,86	0,88
sens of OGTT	0,80	5 133 958	(2 691 522)	(1 072 457)	(672 043)	(490 605)	(387 086)	(320 164)	(273 348)
	0,82	1 304 468	5 133 958	(2 691 522)	(1 072 457)	(672 043)	(490 605)	(387 086)	(320 164)
	0,84	744 055	1 304 468	5 133 958	(2 691 522)	(1 072 457)	(672 043)	(490 605)	(387 086)
	0,86	518 932	744 055	1 304 468	5 133 958	(2 691 522)	(1 072 457)	(672 043)	(490 605)
	0,88	397 484	518 932	744 055	1 304 468	5 133 958	(2 691 522)	(1 072 457)	(672 043)
	0,90	321 497	397 484	518 932	744 055	1 304 468	5 133 958	(2 691 522)	(1 072 457)
	0,92	269 471	321 497	397 484	518 932	744 055	1 304 468	5 133 958	(2 691 522)
	0,94	231 615	269 471	321 497	397 484	518 932	744 055	1 304 468	5 133 958

+ interpretation

For both b and c, we expect an interpretation of findings and how the different components influenced ICER (prevalence and sensitivity). If the candidate had different findings, this did not influence the evaluation here.

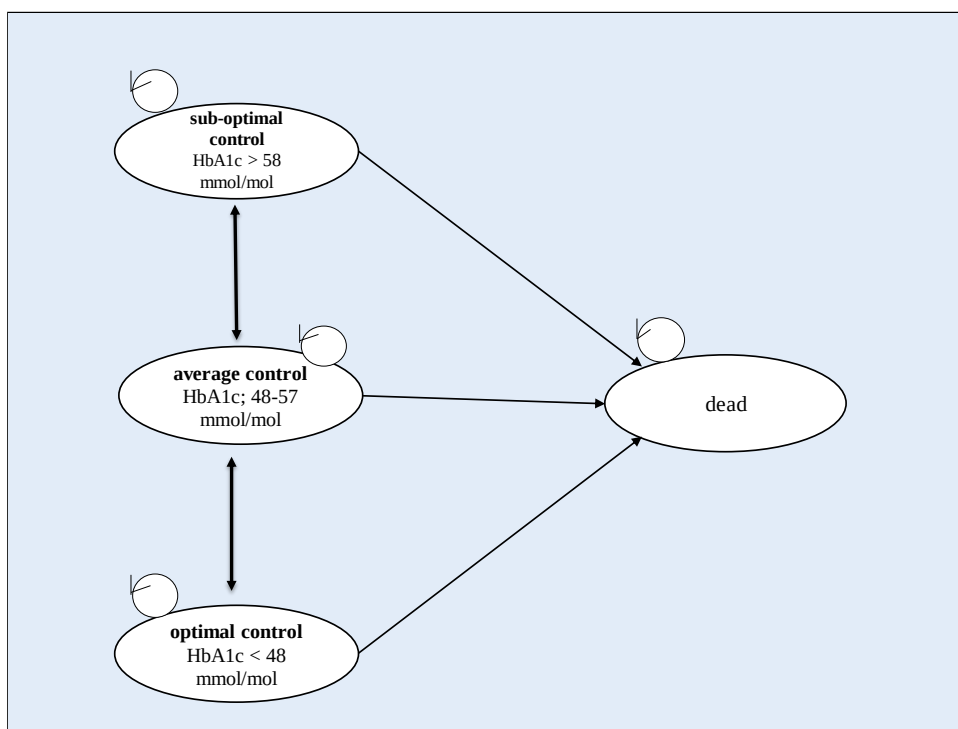
Question 2 (40%)

In this exercise, you are going to use the **DHM-deterministic_template**.

Read all the information in the template (all sheets) carefully.

In this task you are going to evaluate the cost-effectiveness of implementing digital home monitoring for patients with diabetes type 2.

Based on your conversations with clinical experts, you decide to model the disease using four health states, reflecting glycemic control: Sub-optimal control, average control, optimal control, and death. Sub-optimal control reflects a health state with the worst glycemic control. Diabetes type 2 is a chronic condition, and patients' health and glycemic control fluctuate over time, and can worsen or improve. *This means that individuals can move back and forth between better or worse health states, such as between sub-optimal and average, and between average and optimal.* Individuals can transition at annual cycles between the health states as depicted in the model schematic below (and included in the Excel template).



Only patients with sub-optimal control are eligible for DHM. Therefore, all individuals start in the sub-optimal control health state. In the DHM strategy, you can assume that patients receive DHM throughout their life. DHM improves the probability of progressing from sub-optimal to average control, and from average to optimal control.

The relevant time horizon for your analysis is 25 years.

Model outcomes include quality-adjusted life-years (QALYs) and costs.

You adopt a healthcare analytic perspective in the main analysis but will explore a scenario where you include patients' time and travel costs associated with receiving healthcare (often referred to as an extended healthcare perspective). You can assume that patients only experience time and travel costs associated with GP visits (there are no time and travel costs for receiving medications or digital home monitoring).

- a) Estimate the general practitioner (GP) costs for diabetes type 2 patients according to health state, with and without time and travel costs:
 - Sub-optimal control: 4 GP visits per year
 - Average control: 2 GP visits per year
 - Optimal control: 1 GP visit per year

The GP cost per visit is NOK850. The total time and travel cost associated with each visit is NOK250.

Without time and travel:

- Sub-optimal control: NOK 3400
- Average control: NOK 1700
- Optimal control: NOK 850

With time and travel:

- Sub-optimal control: NOK 4400 (NOK1000 is the time/travel)
- Average control: NOK 2200 (NOK500 is the time/travel)
- Optimal control: NOK 1100 (NOK250 is the time/travel)

- b) Using deterministic analysis, estimate the discounted expected costs, QALYs and ICER. Given a cost-effectiveness threshold of NOK690,000, what is your recommendations when using a healthcare perspective? What is your recommendation when using an extended healthcare perspective?

Discounted half-cycled corrected results - HEALTHCARE PERSPECTIVE

Strategy	Cost	QALY
Standard care		10,9
Drug	kr 43 758	
GP	kr 33 432	
Time and travel		
AE (only used in question 2i)	kr -	
Total	kr 77 190	
Digital home monitoring		11,2
Drug	kr 41 393	
GP	kr 29 023	
Time and travel		
DHM follow-up	kr 229 971	
AE (only used in question 2i)		
Total	kr 300 386	
Increment	kr 223 196	0,3
ICER		Incremental cost/QALY
		kr 693 359

DHM not cost-effective in a healthcare perspective

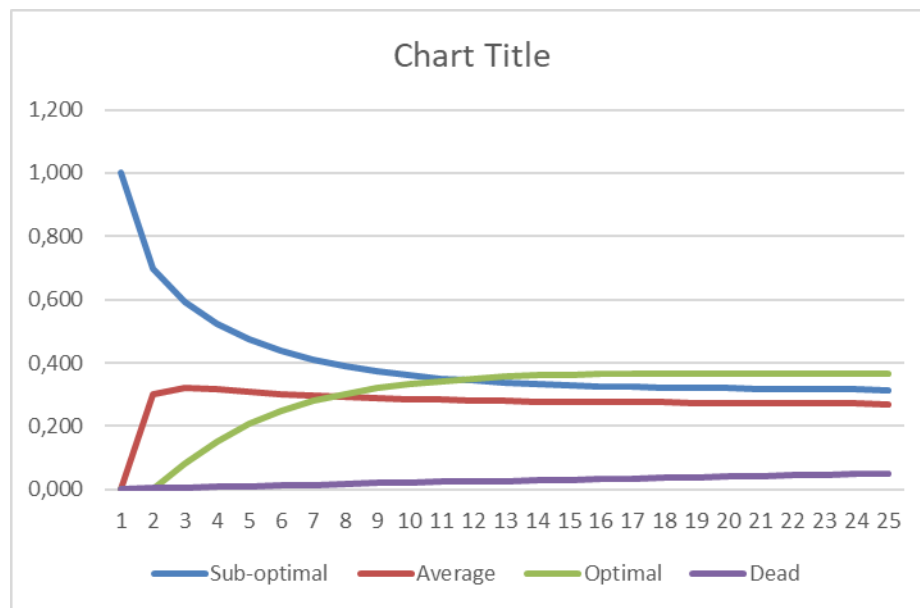
Discounted half-cycled corrected results - EXTENDED HEALTHCARE PERSPECTIVE

Strategy	Cost	QALY
Standard care		10,9
Drug	kr 43 758	
GP	kr 33 432	
Time and travel	kr 9 833	
AE (only used in question 2i)	kr -	
Total	kr 87 023	
Digital home monitoring		11,2
Drug	kr 41 393	
GP	kr 29 023	
Time and travel	kr 8 536	
DHM follow-up	kr 229 971	
AE (only used in question 2i)	kr -	
Total	kr 308 923	
Increment	kr 221 899	0,3
ICER		Incremental cost/QALY
		kr 689 330

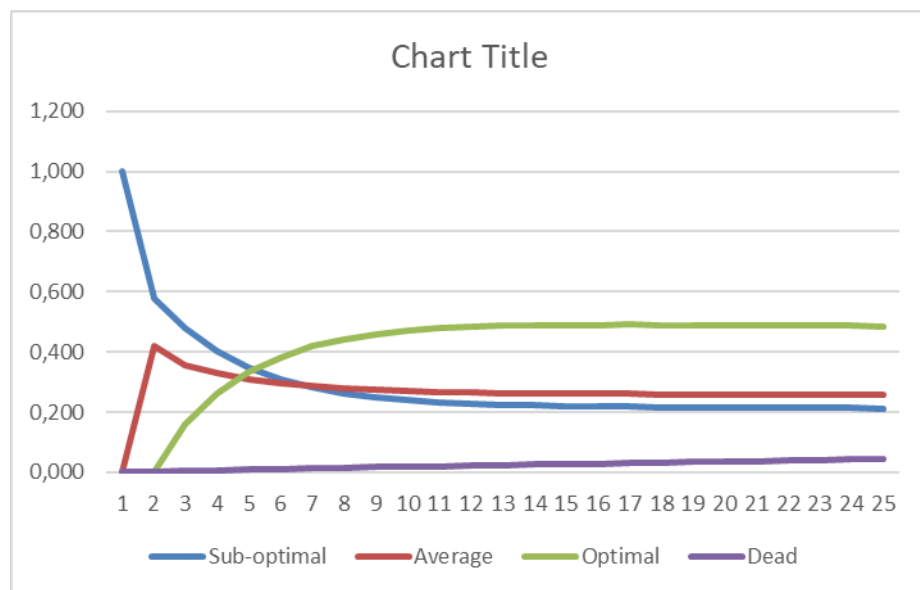
DHM is cost-effective in an extended healthcare perspective

- c) Plot the Markov traces for each treatment alternative and describe and compare the Markov traces.

Standard care:



DHM:



A description and comparison of the traces is expected.

- d) Conduct a deterministic scenario analysis where patients receive DHM for 10 years instead of 25 years. Assume that the treatment effect lasts until end of cycle 14. Calculate the incremental costs, incremental QALYs and the ICER. Interpret your findings and provide a recommendation using a healthcare perspective.

Discounted half-cycled corrected results		
Strategy	Cost	QALY
Standard care		10,9
Drug	kr 43 758	
GP	kr 33 432	
Time and travel		
AE (only used in question 2i)	kr -	
Total	kr 77 190	
Digital home monitoring		11,1
Drug	kr 41 852	
GP	kr 29 857	
Time and travel		
DHM follow-up	kr 119 289	
AE (only used in question 2i)		
Total	kr 190 998	
Increment	kr 113 807	0,3
ICER		Incremental cost/QALY kr 434 039

DHM is cost-effective.

- e) Going back to your model version in question b) and conduct a scenario analysis where you add adverse events in terms of hospitalizations and run a deterministic analysis. Calculate the incremental costs, incremental QALYs and the ICER. What is your interpretation?

Discounted half-cycled corrected results - HEALTHCARE PERSPECTIVE		
Strategy	Cost	QALY
Standard care		10,9
Drug	kr 43 758	
GP	kr 33 432	
Time and travel		
AE (only used in question 2e)	kr 33 670	
Total	kr 110 860	
Digital home monitoring		11,2
Drug	kr 41 393	
GP	kr 29 023	
Time and travel		
DHM follow-up	kr 229 971	
AE (only used in question 2e)	kr 28 822	
Total	kr 329 209	
Increment	kr 218 349	0,3
ICER		Incremental cost/QALY kr 674 371

DHM is cost-effective.

Question 3 (20%)

In this question, you are going to use the **DiabetesType2_template**. This is a modified version of the model used in question 2, where the patient population is still diabetes type 2 patients. However, the intervention is now a new medication regime (called “Medication X”) instead of digital home monitoring, compared to a standard medication regime (standard care). All parameters have been changed, and the model structure is simplified, so you should not compare the results in this model with the results in question 2.

The model is prepared with deterministic values, and you should prepare the model to run probabilistic analysis by assigning appropriate distributions. State your assumptions.

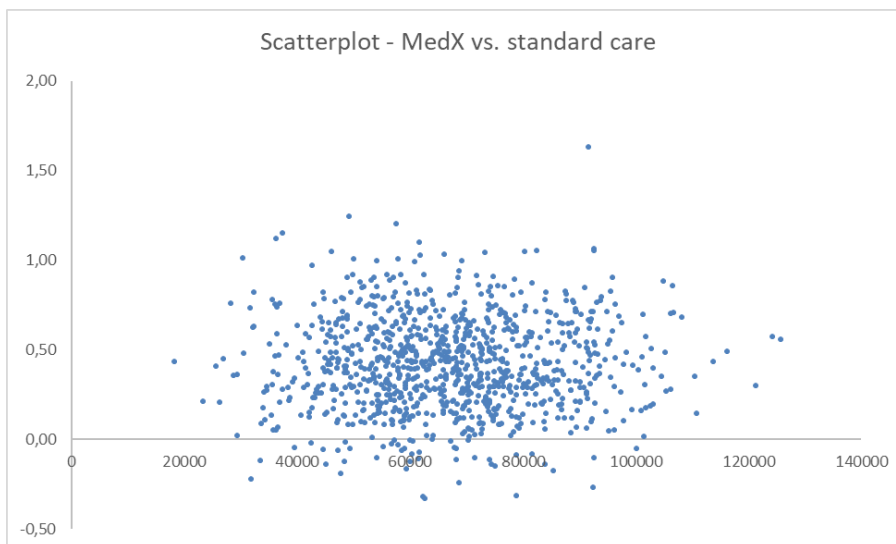
- a) Run a probabilistic analysis using 1000 trials and estimate the ICER based on the probabilistic results. Create a cost-effectiveness scatterplot, CEAC and CEAF. Interpret the findings. *Remember to set cell E4 in the parameter sheet to 1 to prepare for probabilistic analysis. A macro code is provided in the grey box below.*

Justify choice of probability distribution for the different type of parameters.

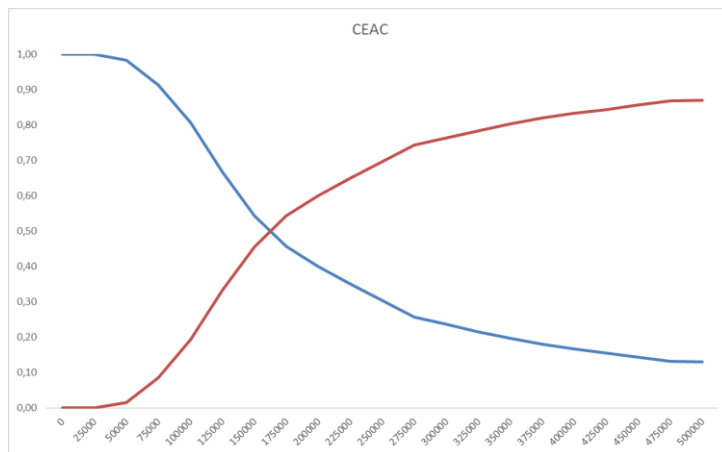
Higher score to those who were able to run macro for themselves. Those who ran the macro will have slightly different results than the solution file.

ICER based on average incr. costs and QALYs = 160 408

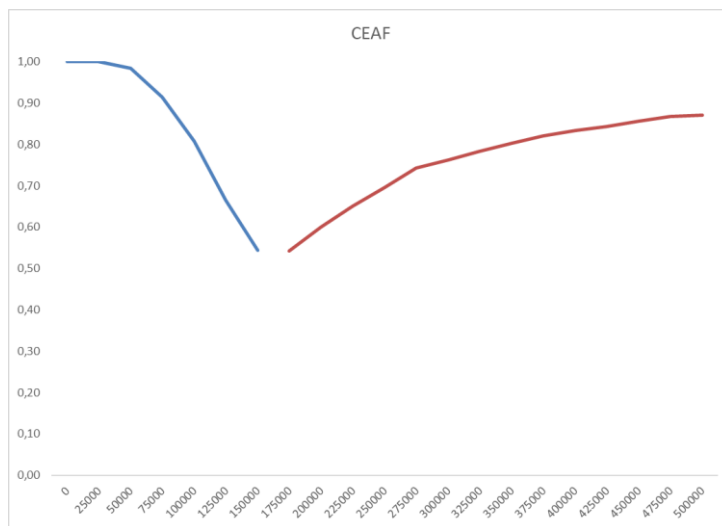
Scatterplot + interpretation



CEAC + interpretation



CEAF + interpretation



- b) Given a threshold of NOK200,000 per QALY gained, what is the probability that MedX is cost-effective compared to standard care?

MedX has a 60% probability of being cost-effective at a threshold of NOK200,000.

Macro code for running probabilistic analysis

```
Sub PSA()
' Simulation PSA
'
'
Application.DisplayStatusBar = True
Index = 0
Trials = 1000
Do
Sheets("PSA").Select
Range("B10:H10").Select
Selection.Copy
```

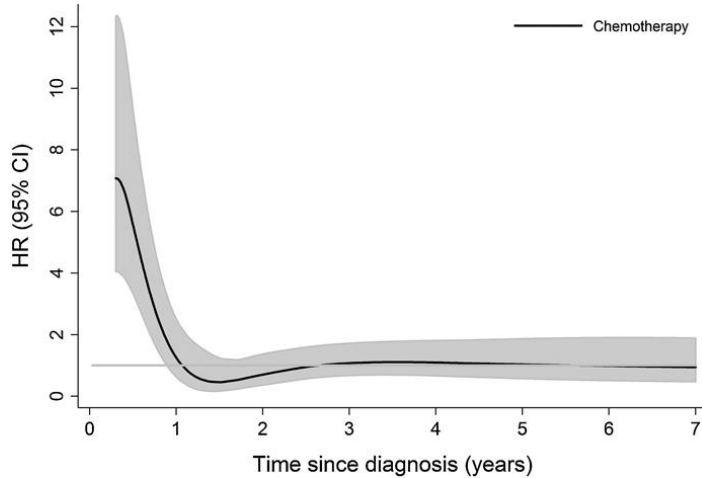
```
Range("B11:H11").Select
ActiveCell.Offset(Index, 0).Range("A1").Select
Selection.PasteSpecial Paste:=xlPasteValues, Operation:=xlNone, SkipBlanks _
:=False, Transpose:=False
Application.CutCopyMode = False

Index = Index + 1
Loop While Index < Trials

End Sub
```

Question 4 (10%)

a) Look at the hazard plot below. Briefly explain the figure (4-6 sentences)



Define hazard, describe axes, describe how the hazard varies over time.

b) Based on the figure in a), which of the following distributions could you exclude and why: exponential, Weibull and lognormal?

Need to at least state you can exclude the Exponential – constant hazard over time

c) Assume that you have fitted the following models to survival data from a different study than the one in question a).

- Exponential
- Weibull
- Lognormal
- Gompertz

You get the following AIC and BIC values for each model:

Modell	AIC	BIC
Exponential	210.0	215.0
Weibull	205.5	210.5
Lognormal	207.0	211.0
Gompertz	206.0	212.0

Explain what AIC and BIC represents, and how it can be used to evaluate and compare models. Based on the AIC and BIC values in the table above, which model would you recommend, and why?

Weibull – lowest AIC and BIC values