

Postpartum dysgalactia Patogenese og diagnose

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KØBENHAVNS UNIVERSITET



Baggrund

Postpartum dysgalactia syndrome (PDS)

- Årsag?
- Diagnose?

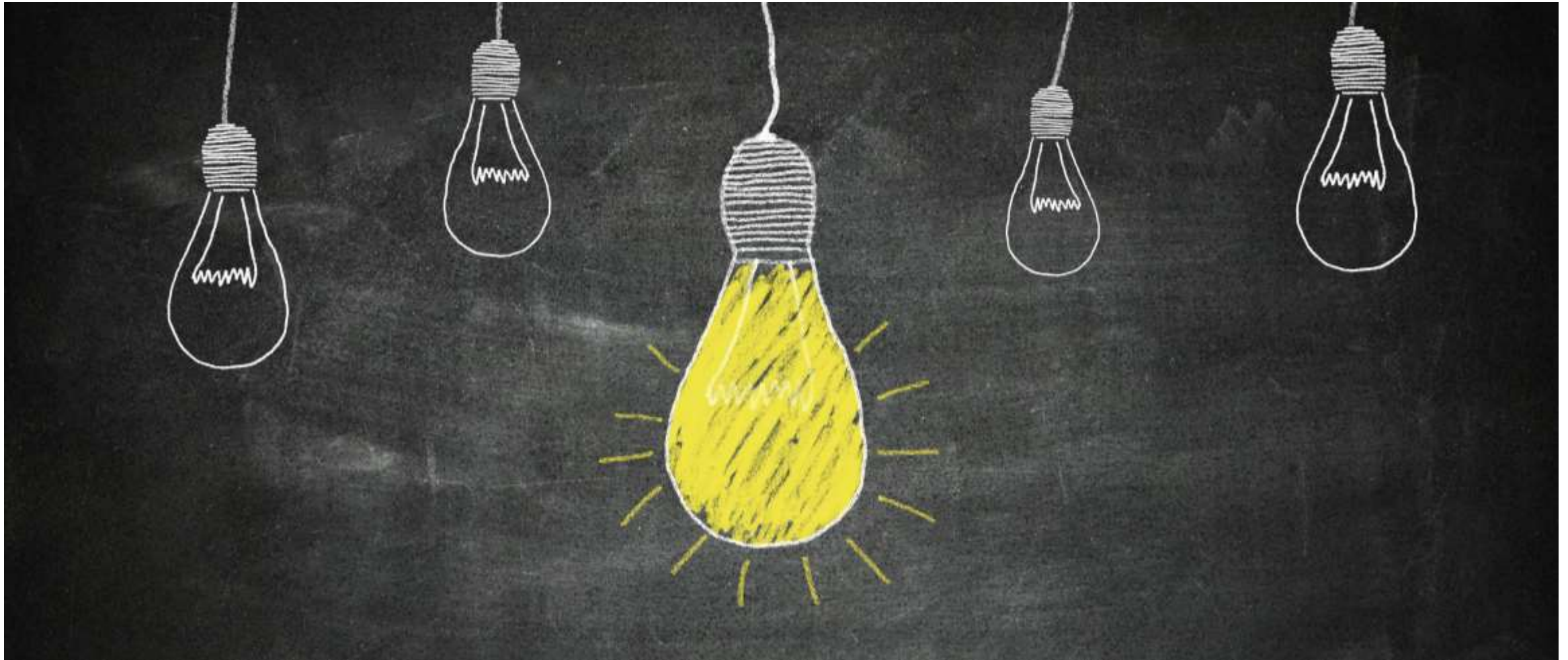
- 12% behandlinger i EU
6,1% 10,8% 15,3% 34%...

Stor effekt på pattegrise

- Sult
- Sygdom
- Død



En tanke...



Formål

Diagnose

- Bedre
- Tidligere

Patogenesen



Metode



Metode

- Marts – November 2014
- Case – Kohorte



Metode

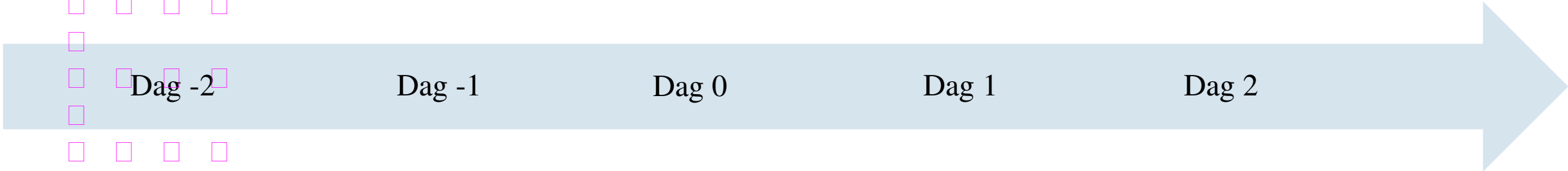
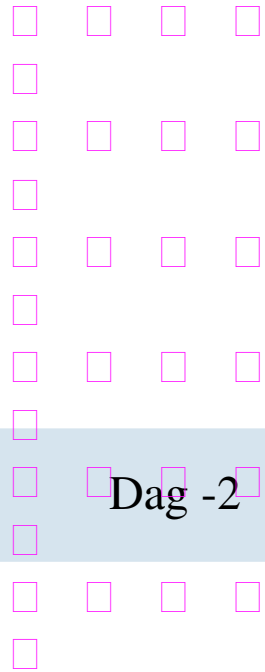
PDS+ so

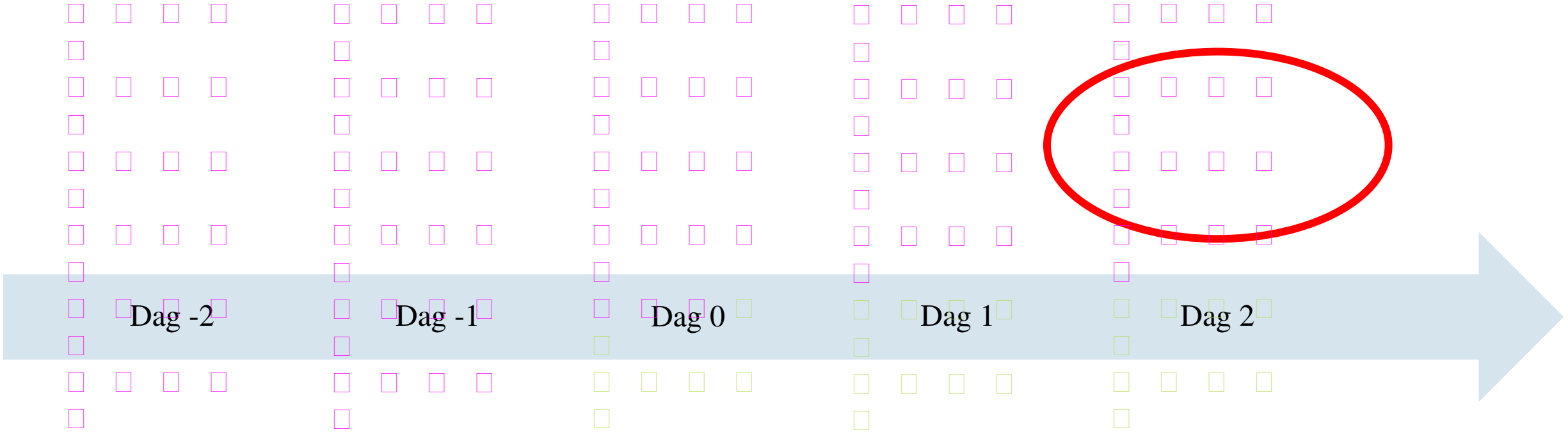
$\geq 39.5^{\circ}\text{C}$

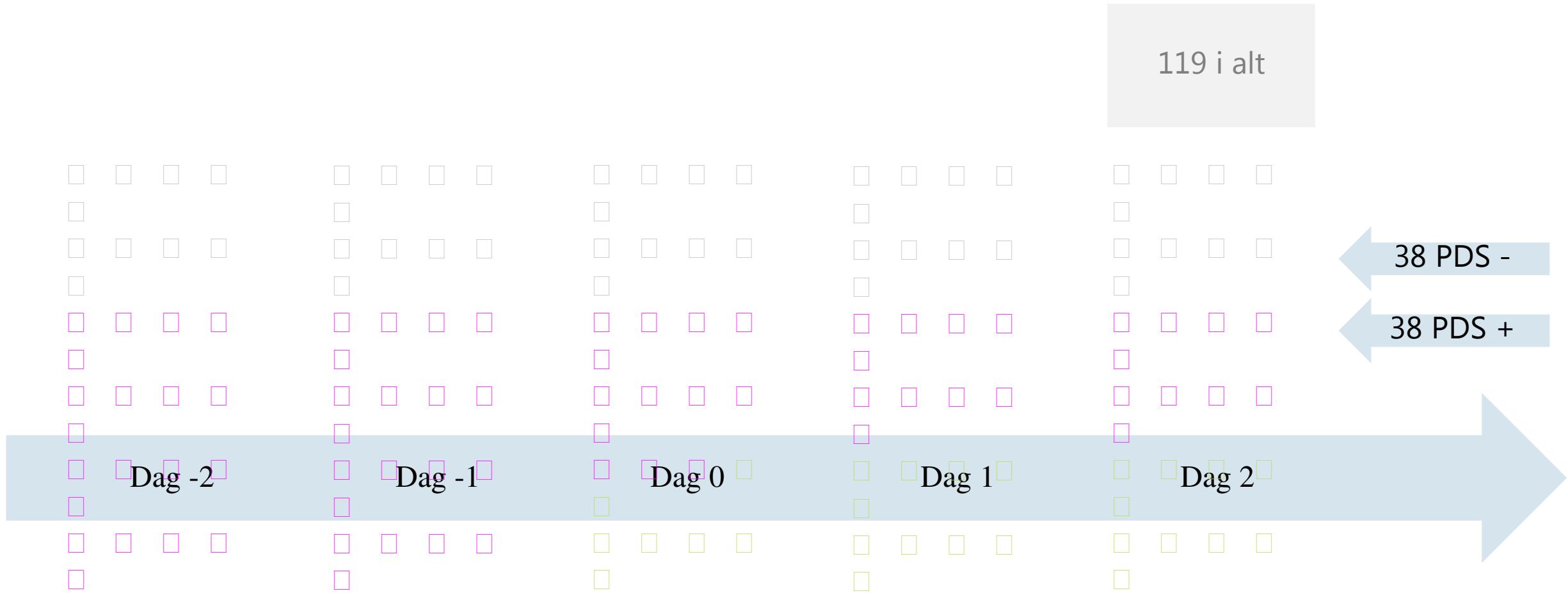
Foder i krybben efter 30 min.

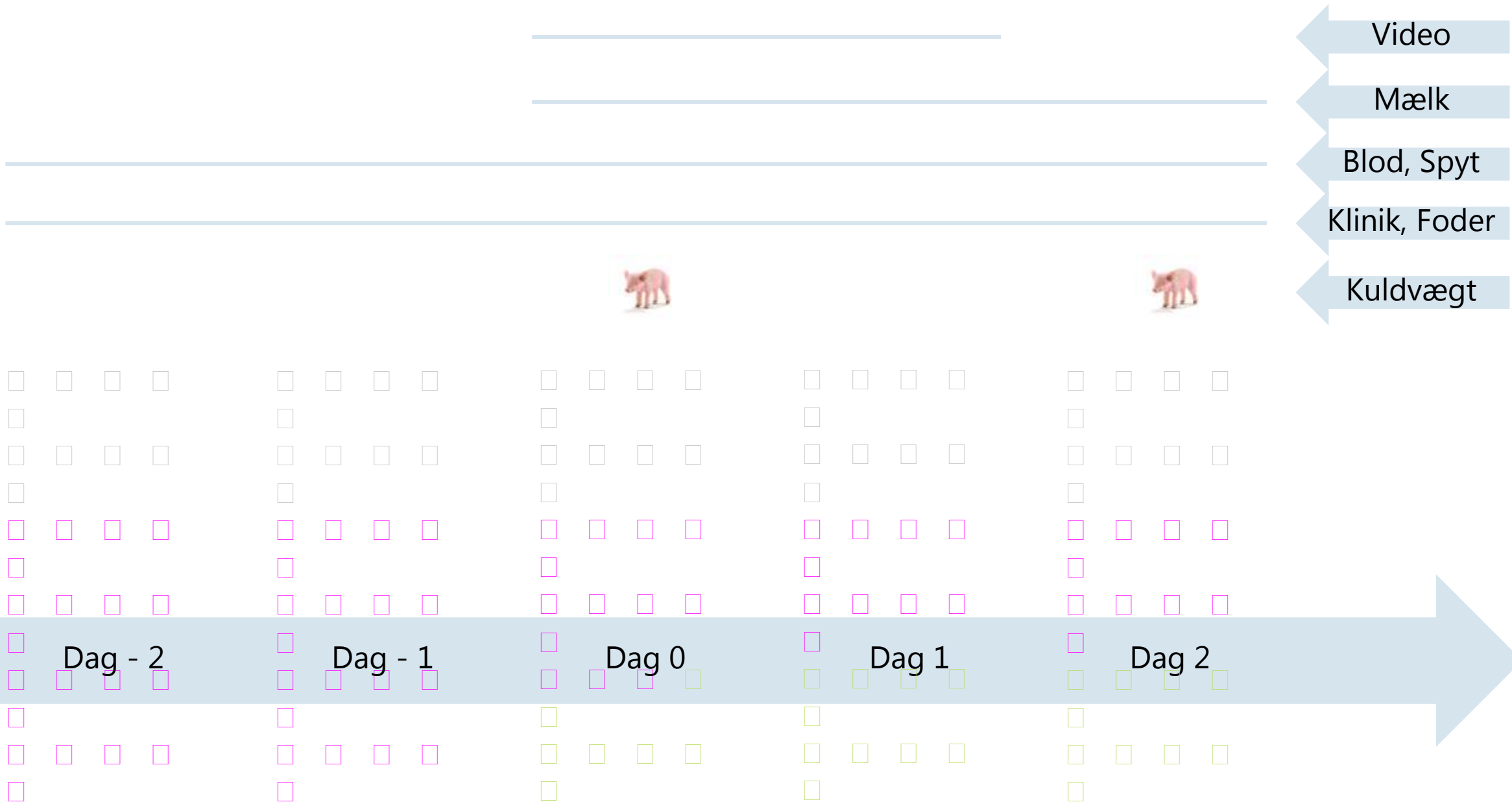
Betændelse i yver

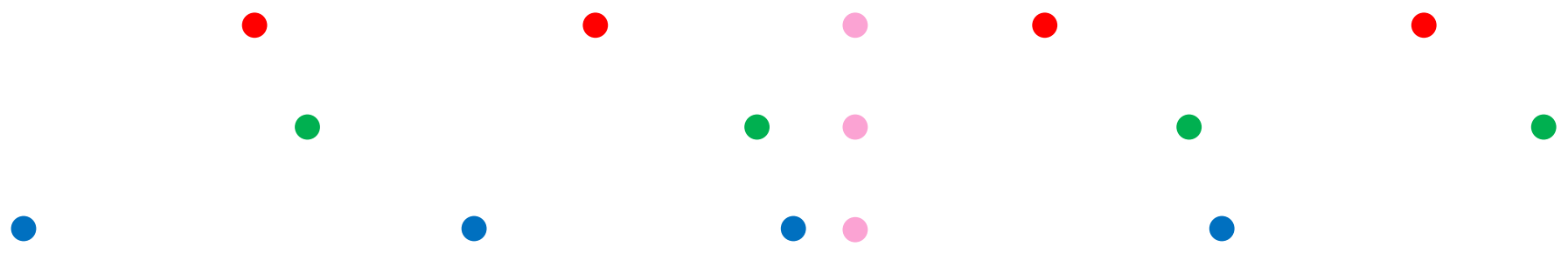
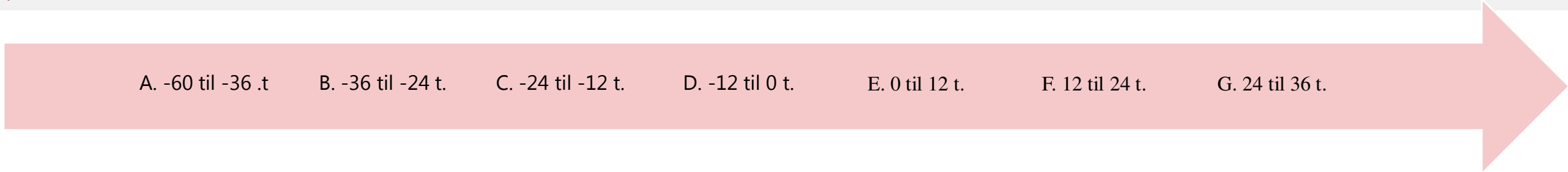












- Fødsel af første gris
- Test tidspunkt for so X
- Test tidspunkt for so Y
- Testtidspunkt for so Z

Eksempel: Fiktive test tidspunkter i relation til fødsel af første grise ved tidspunktet 0





Spytprøve - Fastende



Glukose test - Fastende



Sukker





Klinisk undersøgelse



Blodprøver - Halsvenen



Blodprøver - Yvervene

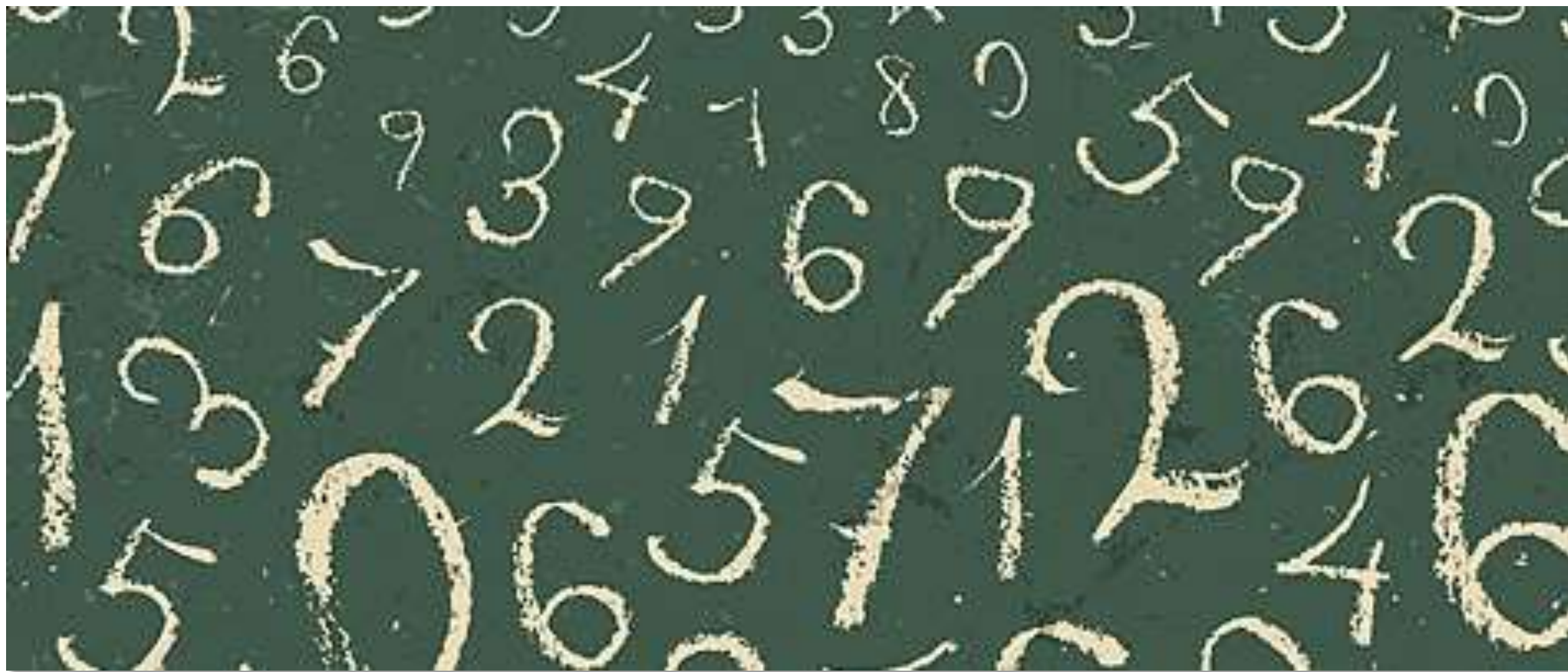


Mælkeprøver

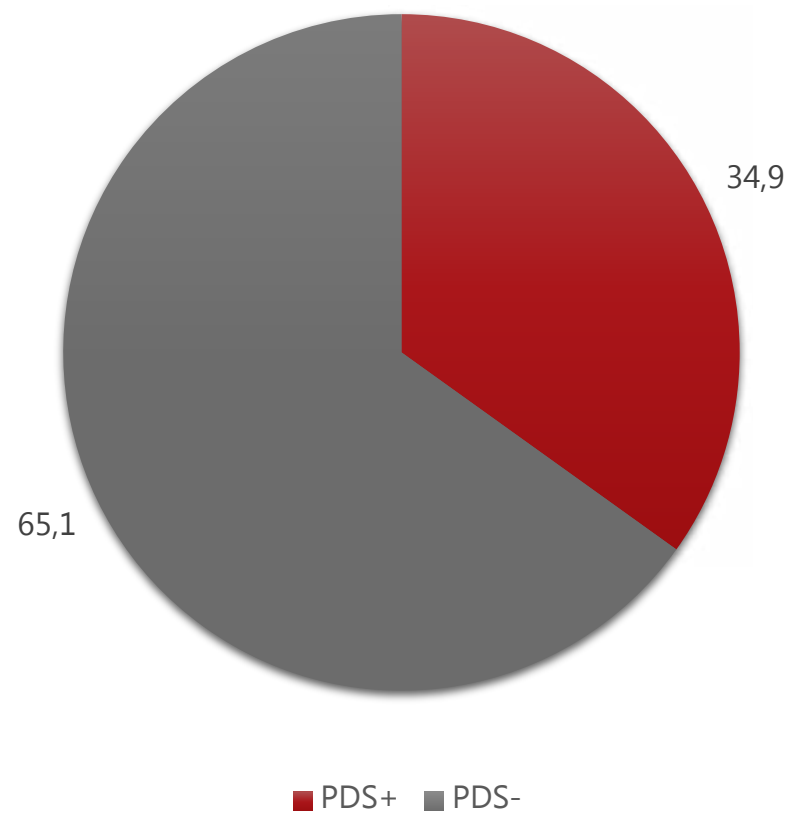


Bakterier

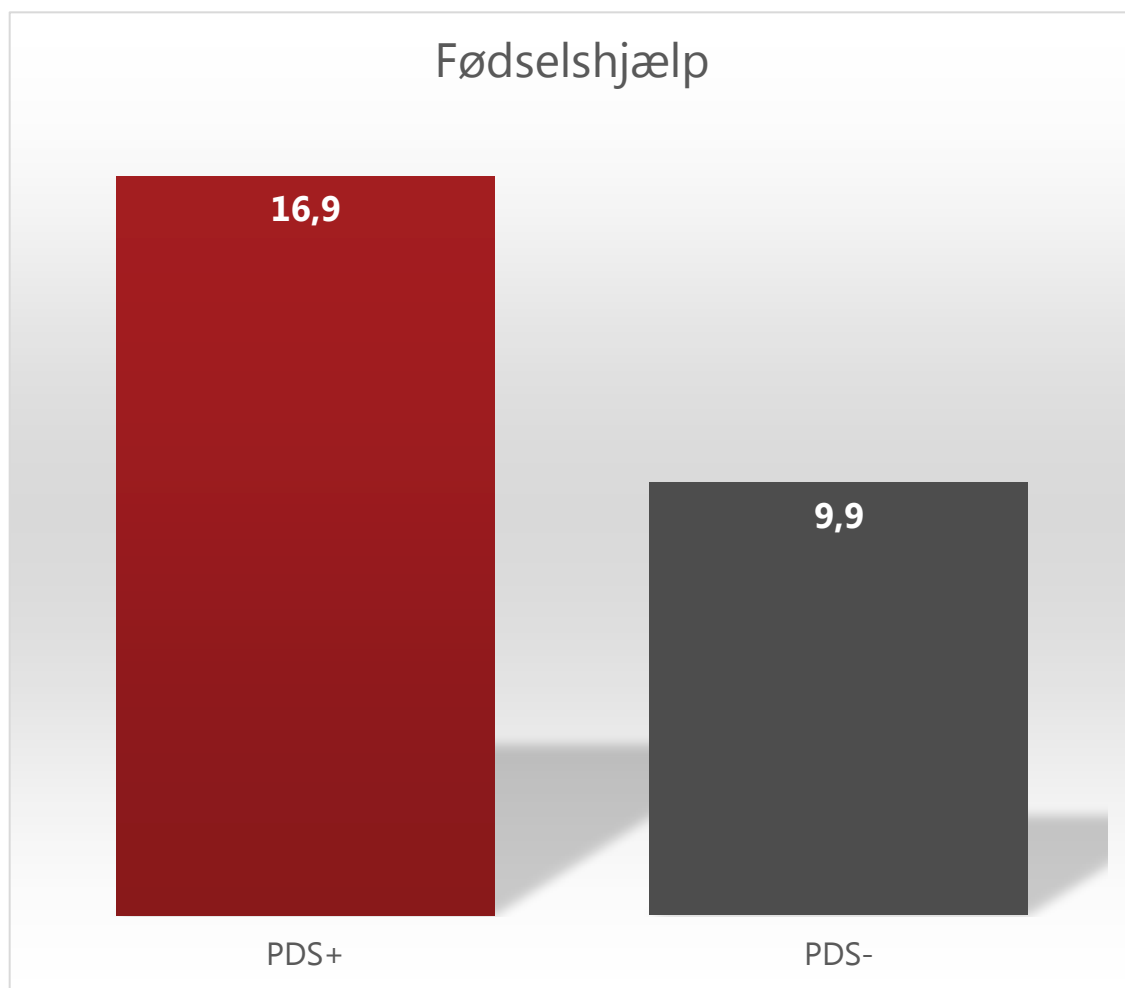
Resultater



Resultater - Forekomst



Resultater - Fødselshjælp



Resultater - Tidspunkt

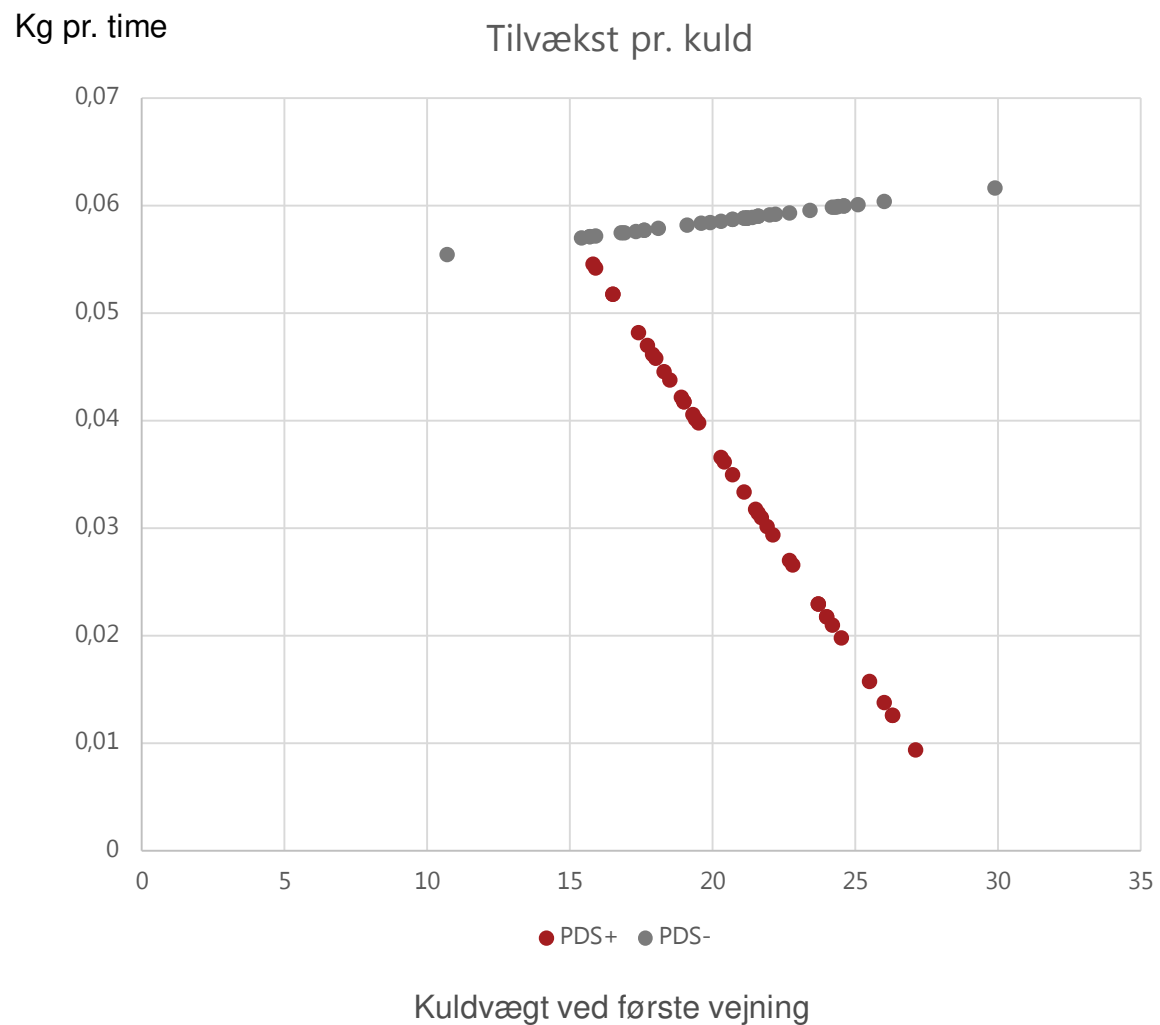
Gennemsnits længde for observation af sygdom

→ 1115,3 min. (18,6 t.)

- Tidligste: 360 min. (6 t.)
- Seneste: 1609 min. (26,8 t.)



Resultater - Kuldtilvækst



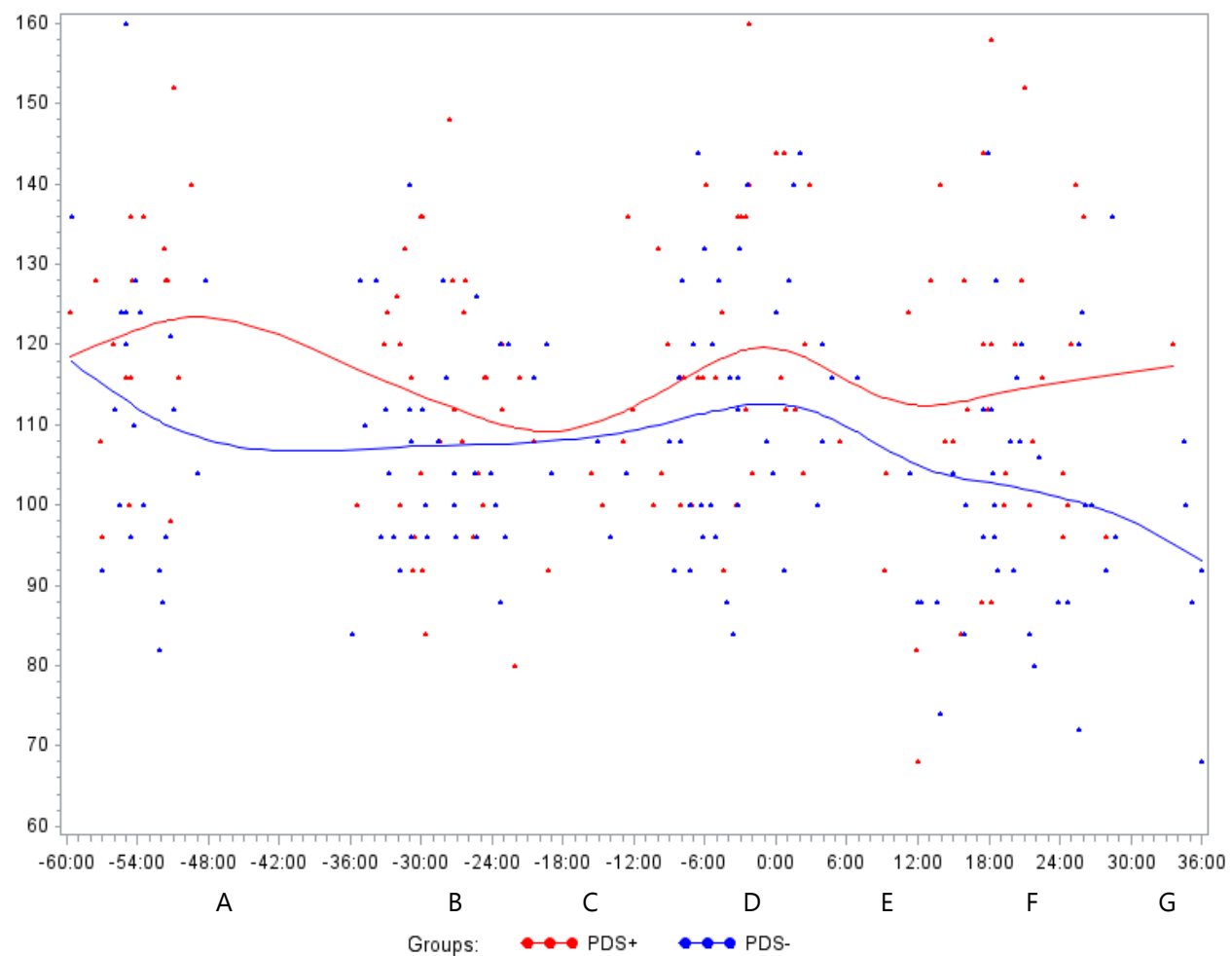
Klinisk undersøgelse af søer



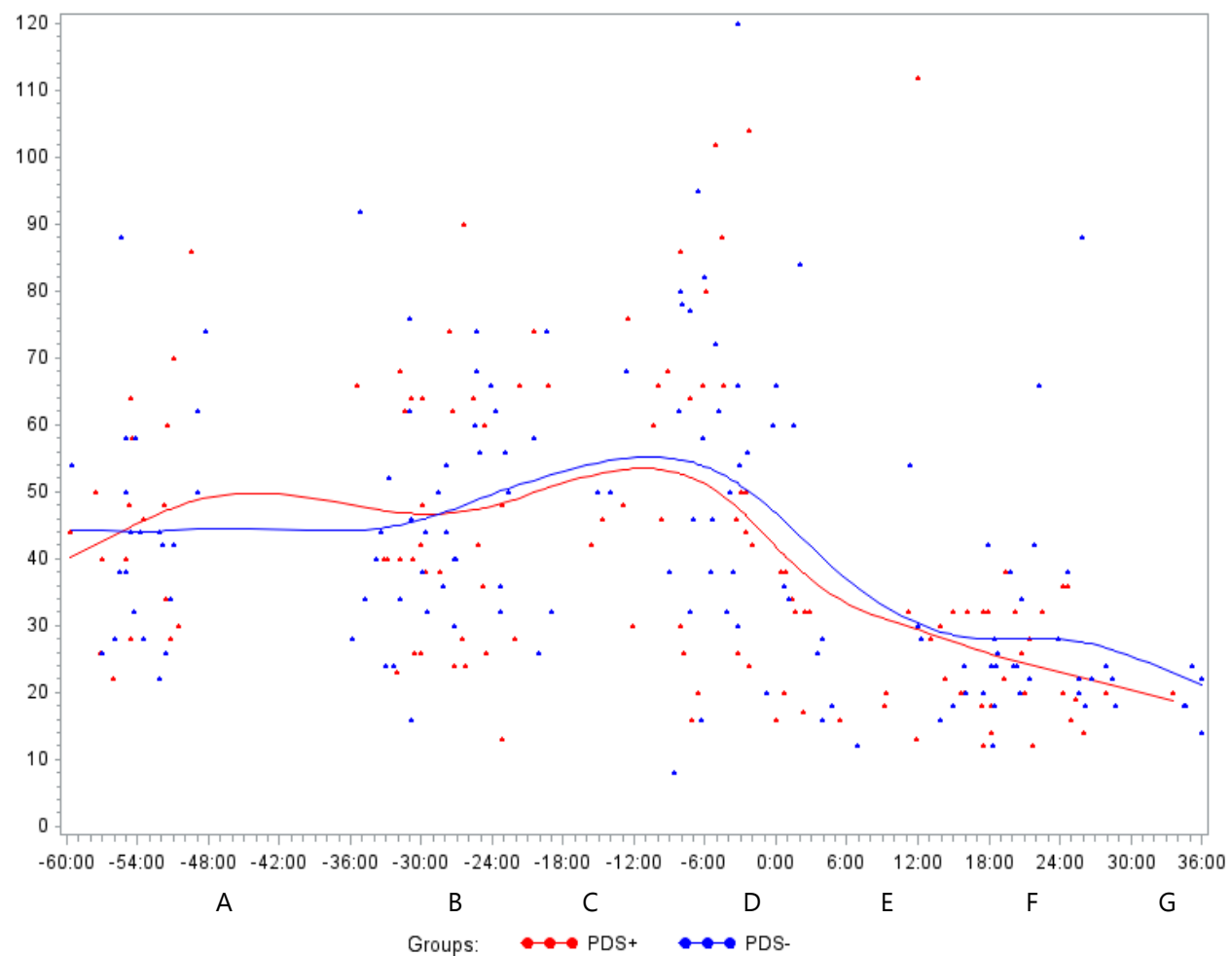
Resultater – Feber

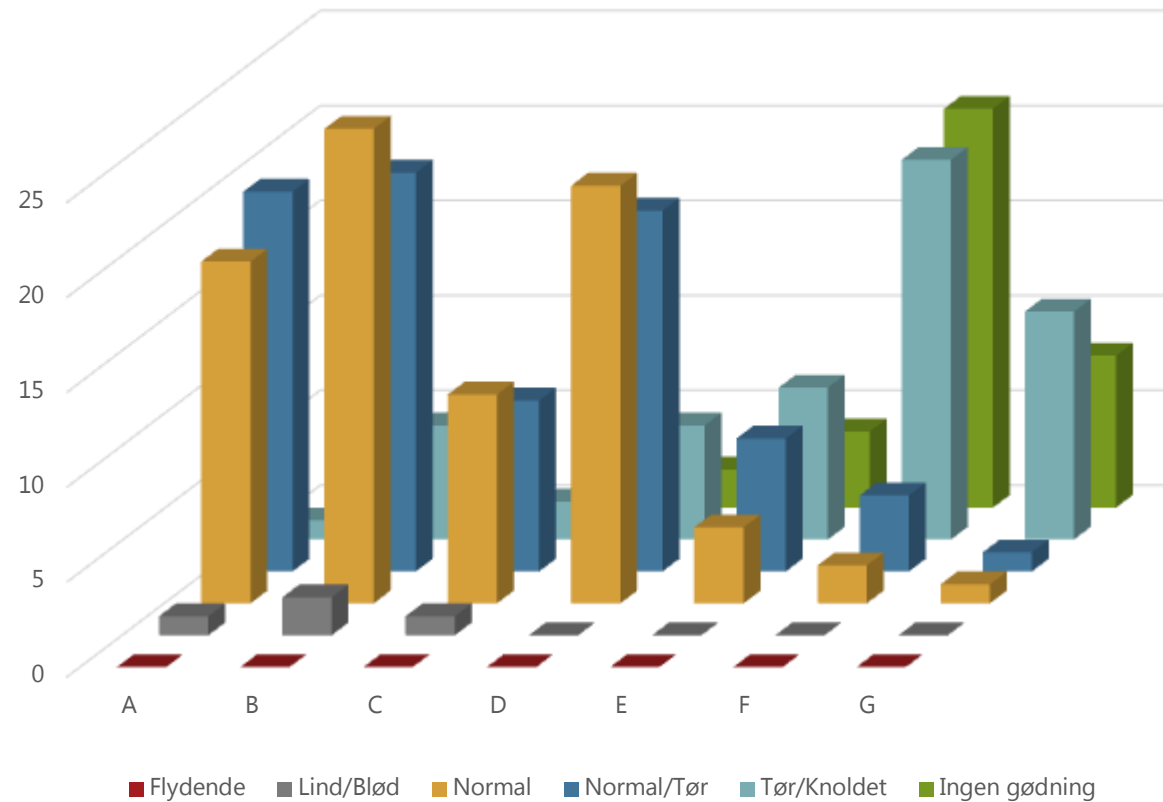
Temperatur		A. (-60 til -36 h)	B. (-36 til -24 h)	C. (-24 til -12 h)	D. (-12 til 0 h)	E. (0 til 12 h)	F. (12 til 24 h)	G. (24 til 36 h)
PDS+	Mean	38,1	38,2	38,2	38,3	38,9	39,5	39,6
	Min	37,4	37,4	37,9	37	38	38,1	39
	Max	38,7	38,9	38,4	39,5	40,1	40,5	40,5
PDS-	Mean	38,2	38,3	38,2	38,2	38,6	39	38,8
	Min	37,6	37,6	37,8	37,2	37,3	38,1	38,1
	Max	38,8	38,8	38,4	39,1	39,3	39,3	39,3

Hjertefrekvens over tid



Respirationsfrekvens over tid





Gødningskonsistens i tidsinterval A – B

Gødningskonsistensen ændrede sig over tid ($P < 0.0001$)

Der var ingen forskel i gødningskonsistens mellem PDS+ og PDS- søer ($P=0.4739$) (data ikke vist)

Huld

- Ingen forskel mellem PDS+ og PDS-



Klinisk undersøgelse af yver

Ødem

- Hyppigst hos PDS+ søer ($P < 0,05$)

Rødme, varme og hårdhed

- Stiger signifikant med tiden ($P < 0.001$)
- Ikke forskel mellem PDS+ og PDS-

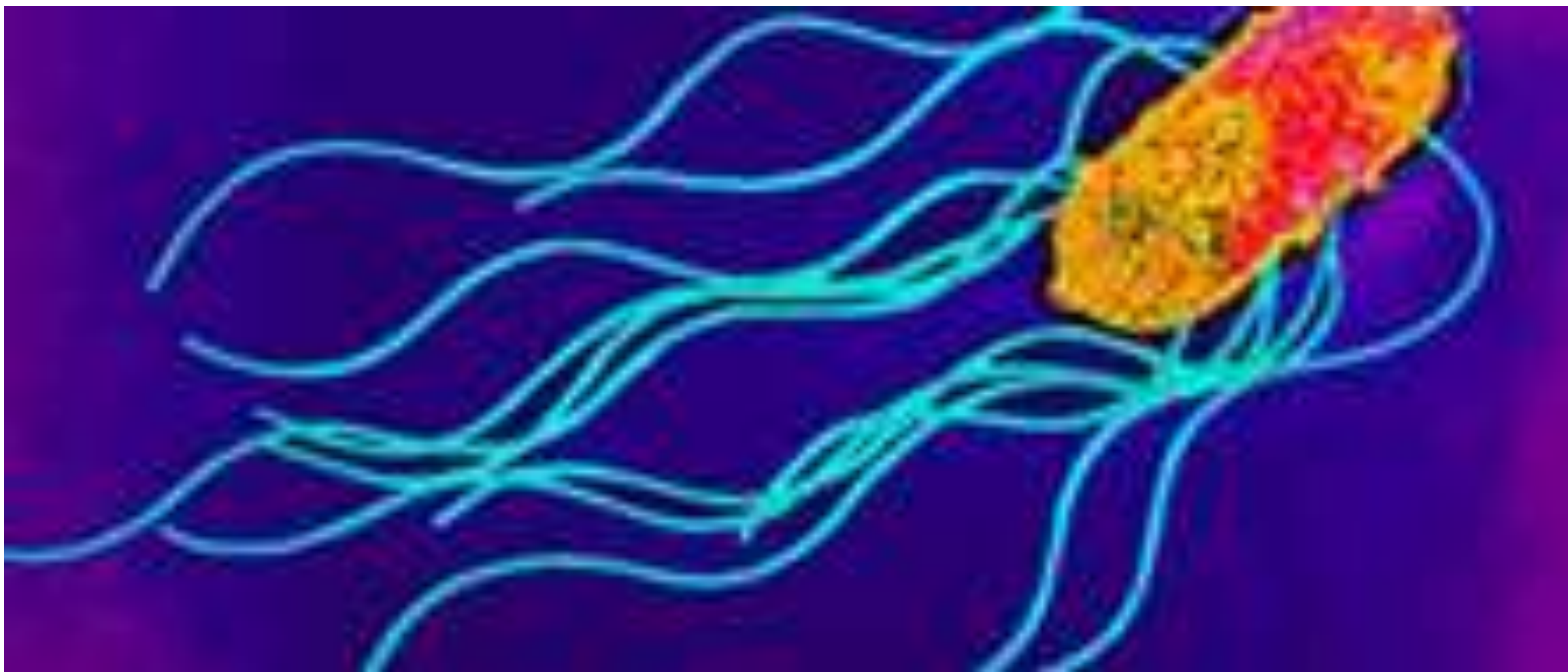
...MEN, det er min vurdering, at yverødem alligevel er *uegnet* til diagnosticering af PDS



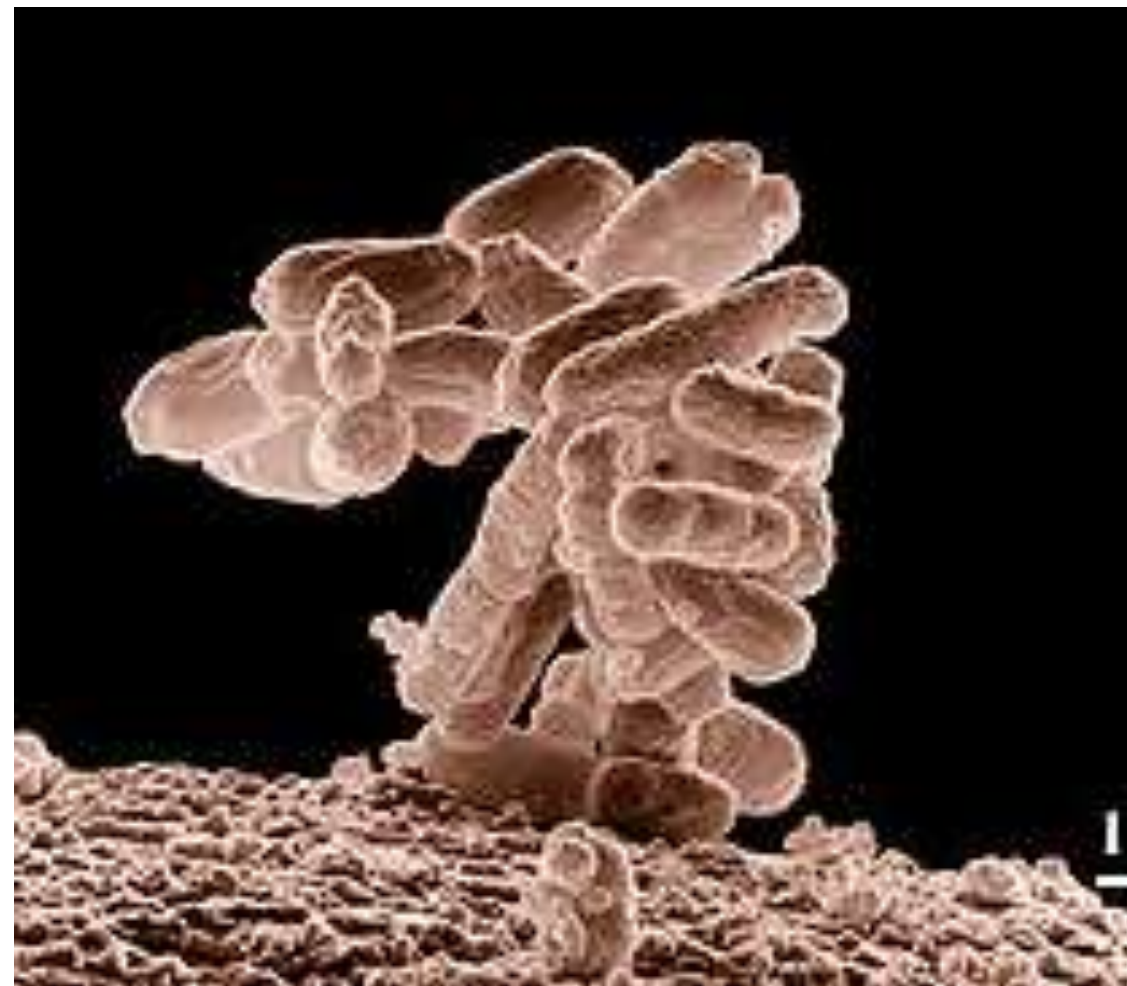
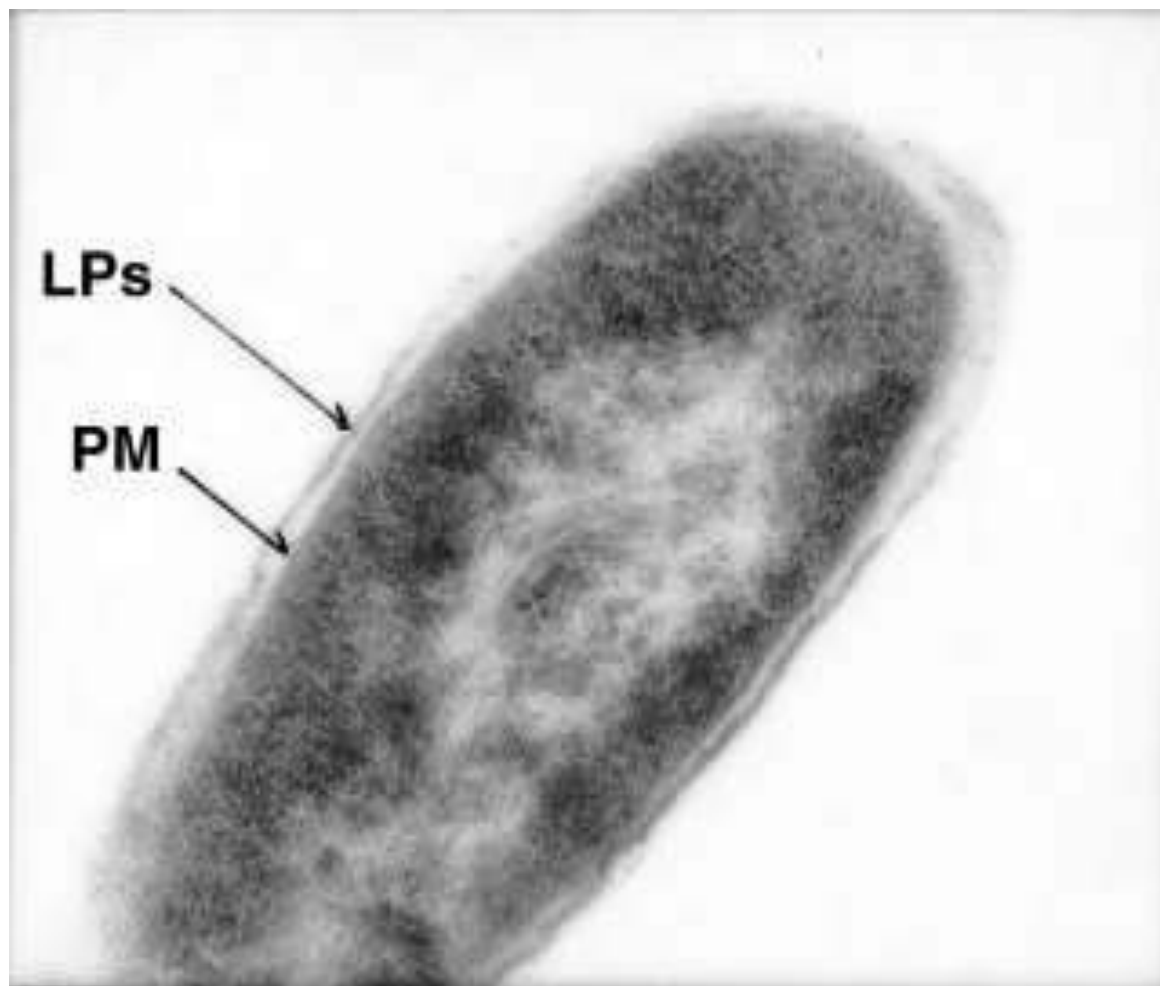
Resultater – Inflammation i kroppen



E. coli

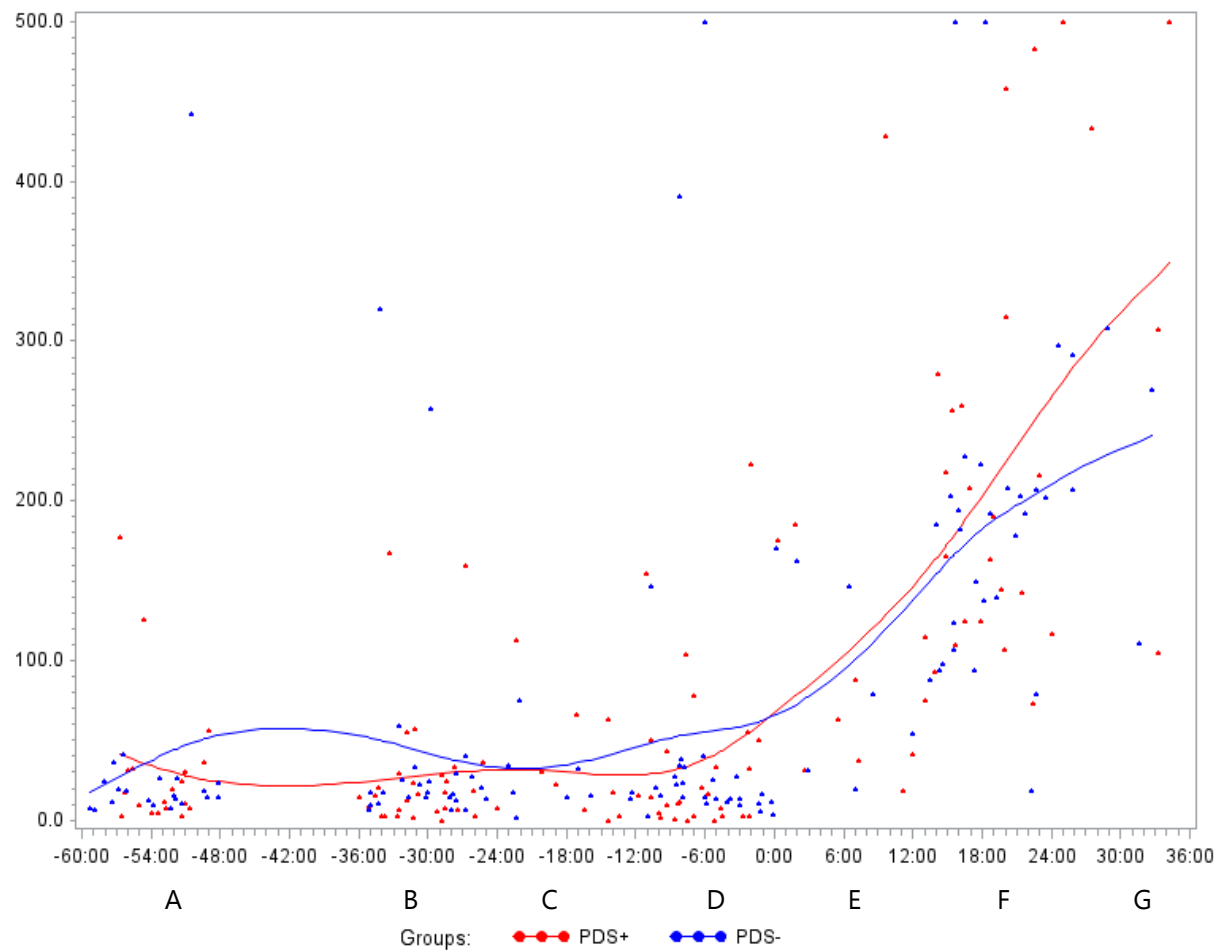


LPS



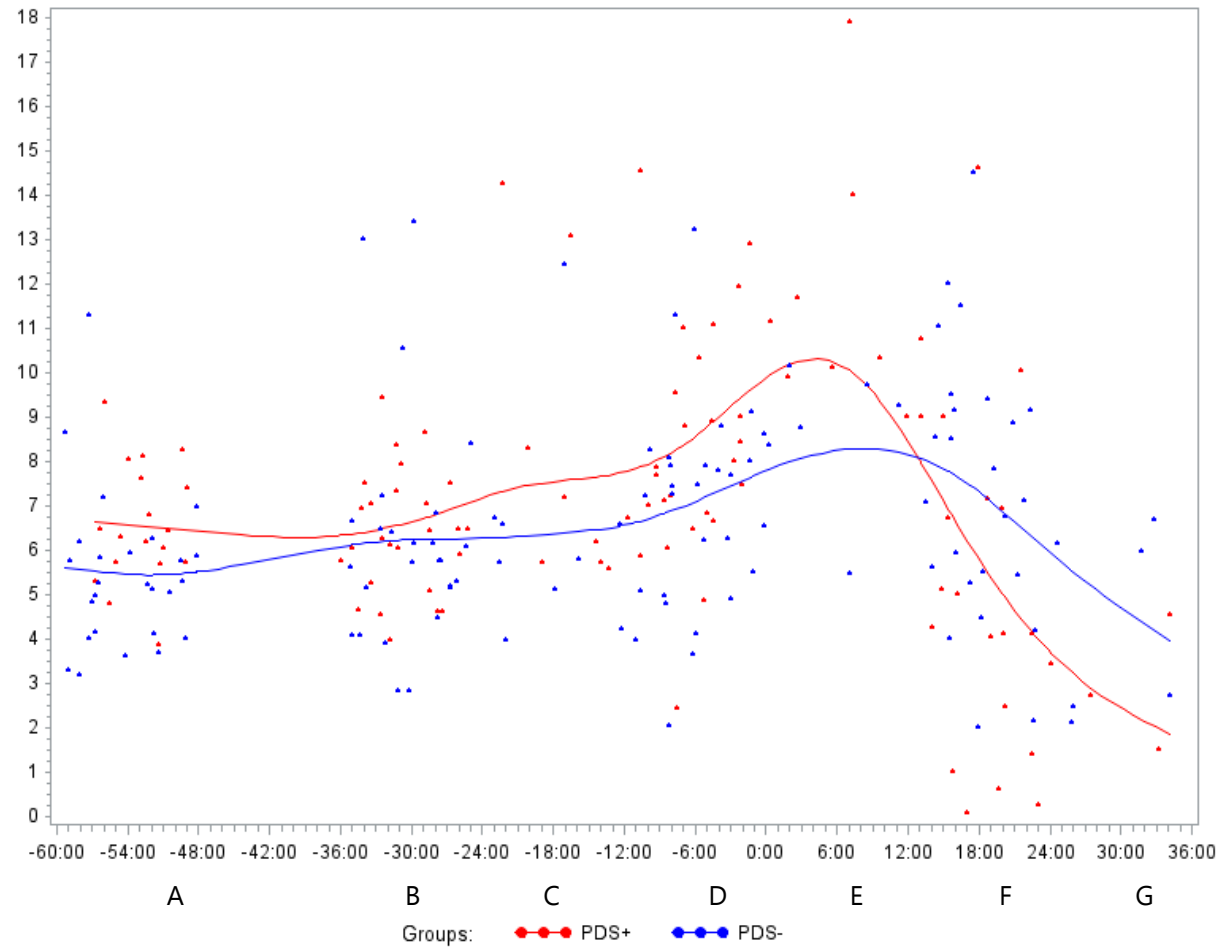
Måling af inflammation - Eksempel

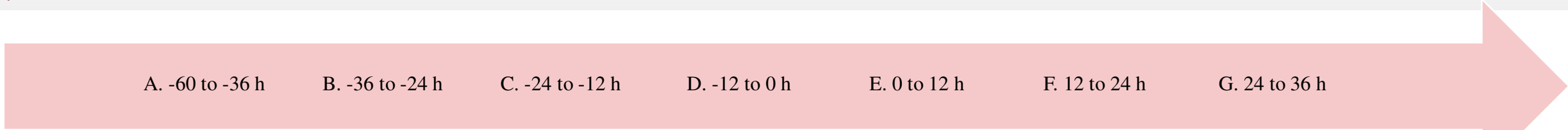
Serum Amyloid A 10^{-3} g/L



Måling af inflammation - Eksempel

Neutrofile granulocytter 10^{-9} g/L





A. -60 to -36 h B. -36 to -24 h C. -24 to -12 h D. -12 to 0 h E. 0 to 12 h F. 12 to 24 h G. 24 to 36 h

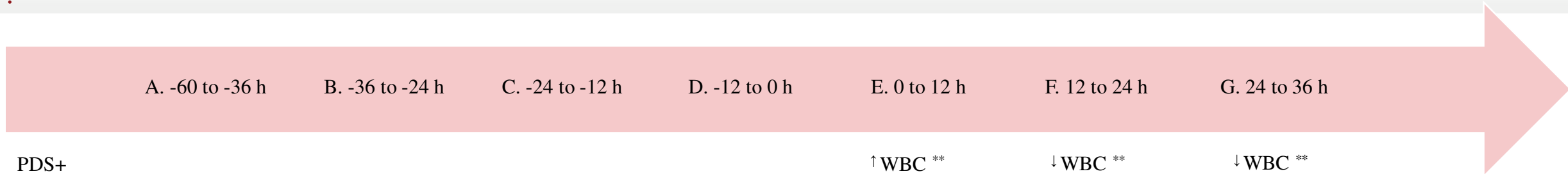
PDS+

			XXX		XXX		XXX
			XXX		XXX		XXX
					XXX		XXX
					XXX		XXX
					XXX		XXX
					XXX		XXX
			XXX		XXX		XXX
					XXX		XXX
			XXX		XXX		XXX
					XXX		XXX

PDS-

					XXX		
					XXX		
			XXX				XXX
			XXX				XXX
					XXX		XXX
					XXX		XXX
			XXX		XXX		XXX
					XXX		XXX
			XXX		XXX		XXX
					XXX		XXX

Asterisk symbols indicate differences between time interval A and each of the time intervals B, C, D, E, F or G: **** $p < 0.0001$, *** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$

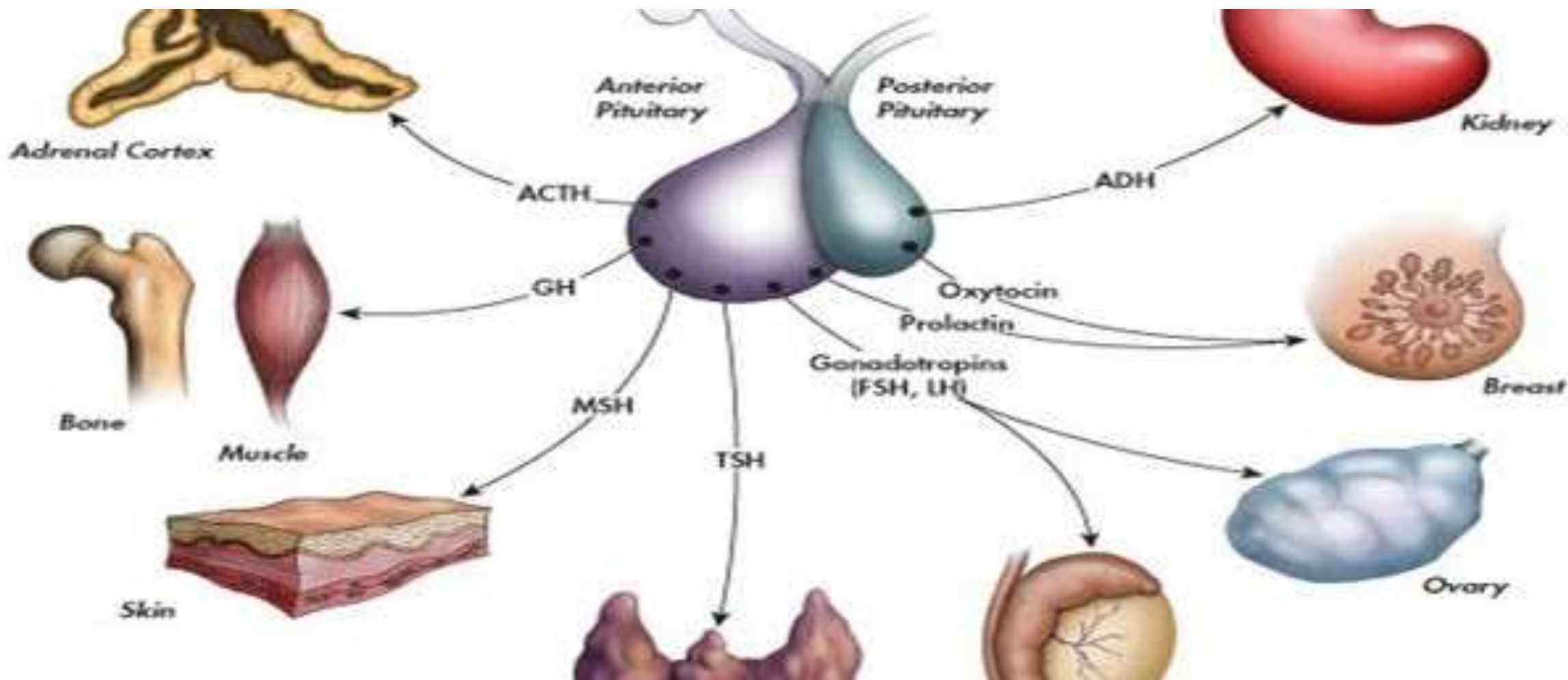


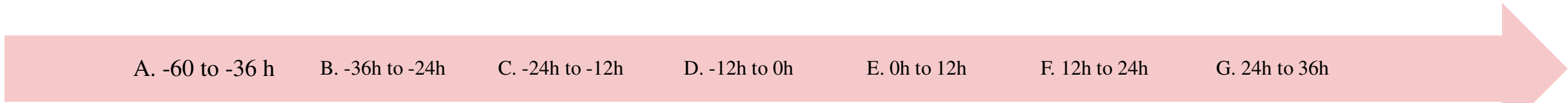
	A. -60 to -36 h	B. -36 to -24 h	C. -24 to -12 h	D. -12 to 0 h	E. 0 to 12 h	F. 12 to 24 h	G. 24 to 36 h
PDS+				↑ Neutrophil ** ↓ Lymphocyte **** ↑ CRP * ↓ Fe **	↑ WBC ** ↑ Neutrophil **** ↓ Lymphocyte **** ↑ SAA ** ↑ CRP *** ↓ Fe **	↓ WBC ** ↓ Lymphocyte **** ↑ TNF-α **** ↑ IL-6 **** ↑ SAA **** ↑ CRP **** ↑ Hp **** ↑ ALB **	↓ WBC ** ↓ Neutrophil * ↓ Lymphocyte **** ↑ TNF-α **** ↑ IL-6 * ↑ SAA **** ↑ CRP **** ↑ Hp **** ↓ Fe *
PDS-				↑ Neutrophil * ↓ Lymphocyte ** ↑ CRP ** ↑ ALB *	↑ WBC * ↑ Neutrophil ** ↑ SAA ** ↑ CRP ****	↑ Neutrophil ** ↓ Lymphocyte * ↑ TNF-α *** ↑ SAA **** ↑ CRP **** ↑ Hp **** ↑ ALB *	↓ Lymphocyte ** ↑ TNF-α * ↑ SAA **** ↑ CRP **** ↑ Hp **** ↑ ALB **

Asterisk symbols indicate differences between time interval A and each of the time intervals B, C, D, E, F or G: **** $p < 0.0001$, *** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$

			A. (-60 to -36 h)		B. (-36 to -24 h)		C. (-24 to -12 h)		D. (-12 to 0 h)		E. (0 to 12 h)		F. (12 to 24 h)		G. (24 to 36 h)	
Parameter	Group	n	LSMEANS	±SD	LSMEANS	±SD	LSMEANS	±SD	LSMEANS	±SD	LSMEANS	±SD	LSMEANS	±SD	LSMEANS	±SD
White blood cells	PDS+	110	11.46	0.69	11.29	0.58	12.62	1.04	12.14	0.58	15.45	1.04	8.74****	0.66	6.15	1.45
	PDS-	126	10.77	0.58	11.22	0.57	11.68	0.97	11.09	0.55	13.94	1.16	12.20****	0.60	9.24	1.18
Neutrophils	PDS+	110	6.35	0.59	6.36	0.49	7.93	0.90	8.34	0.49	11.53	0.89	5.22**	0.56	3.35	1.25
	PDS-	126	5.57	0.49	6.39	0.49	6.43	0.83	7.09	0.48	8.9	1.00	7.46**	0.51	4.35	1.01
Lymphocytes	PDS+	110	3.96	1.07	3.81	1.05	3.69	1.10	2.74*	1.05	2.43	1.10	2.22****	1.06	1.90*	1.14
	PDS-	126	3.95	1.05	3.75	1.05	3.83	1.01	3.20*	1.05	3.23	1.12	3.30****	1.06	2.69*	1.12
Tumor necrosis factor-α	PDS+	121	30.04	1.15	31.81	1.13	32.27	1.21	31.02	1.13	34.35	1.21	130.43****	1.14	130.36*	1.26
	PDS-	119	31.53	1.15	32.80	1.13	29.87	1.20	31.71	1.13	34.23	1.22	55.21****	1.14	58.99*	1.25
Interleukin 6	PDS+	121	19.10	1.13	22.28	1.11	19.94	1.20	24.61	3.03	24.76	1.20	39.20***	1.13	39.54	1.25
	PDS-	119	20.50	1.13	22.23	1.12	21.15	1.20	22.81	1.11	20.70	1.22	22.06***	1.12	21.47	1.24
Serum amyloid A	PDS+	120	15.01	1.27	12.81	1.22	13.33	1.42	14.84	1.23	54.20	1.42	187.41	1.26	234.58	1.53
	PDS-	122	18.45	1.26	20.63	1.24	19.81	1.41	21.36	1.23	69.06	1.46	145.13	1.24	292.72	1.52
C-reactive protein	PDS+	122	10.03	1.18	8.71	1.13	13.72	1.26	14.86	1.16	24.60	1.26	56.30	1.17	71.52	1.32
	PDS-	122	9.23	1.18	11.80	1.16	11.05	1.25	14.65	1.16	29.14	1.27	48.52	1.17	53.02	1.31
Haptoglobin	PDS+	122	2.24	0.08	2.26	0.08	2.35	0.10	2.30	0.08	2.31	0.10	2.73*	0.08	2.92*	0.12
	PDS-	122	2.11	0.08	2.15	0.08	2.16	0.10	2.15	0.08	2.23	0.10	2.46*	0.08	2.56*	0.11
Iron	PDS+	122	24.36	1.51	23.40	1.23	22.16	2.23	18.30	1.27	16.75	2.22	20.86	1.38	17.97*	2.73
	PDS-	125	23.30	1.44	21.22	1.30	23.42	2.20	21.12	1.25	21.28	2.32	24.08	1.30	26.40*	2.68
Albumin	PDS+	122	37.31	1.09	37.38	0.90	37.82	1.60	37.74	0.93	38.38	1.59	41.99	1.00	40.15	1.95
	PDS-	125	36.67	1.04	38.52	0.94	37.17	1.57	39.73	0.91	37.79	1.66	39.88	0.95	42.83	1.91
Total protein	PDS+	122	72.29	1.03	71.20	1.02	72.76	1.04	70.74	1.02	70.73	1.04	76.14	1.03	76.50	1.05
	PDS-	125	69.30	1.03	72.54	1.02	68.87	1.04	73.29	1.02	68.92	1.04	72.93	1.02	77.71	1.05
Hemoglobin	PDS+	110	6.51	0.12	6.32	0.10	6.31	0.17	6.31	0.10	6.02	0.17	6.41	0.11	6.50	0.23
	PDS-	126	6.44	0.10	6.34	0.10	6.38	0.16	6.29	0.10	6.46	0.18	6.22	0.10	6.39	0.19
Hematocrit	PDS+	110	0.35	0.01	0.34	0.01	0.34	0.01	0.34	0.01	0.32	0.01	0.34	0.01	0.34	0.01
	PDS-	126	0.34	0.01	0.34	0.01	0.35	0.01	0.33	0.01	0.35	0.01	0.33	0.01	0.34	0.01

Resultater – Hormoner og stofskifte





A. -60 to -36 h

B. -36h to -24h

C. -24h to -12h

D. -12h to 0h

E. 0h to 12h

F. 12h to 24h

G. 24h to 36h

PDS+

XXX
XXX

xxx
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PDS-

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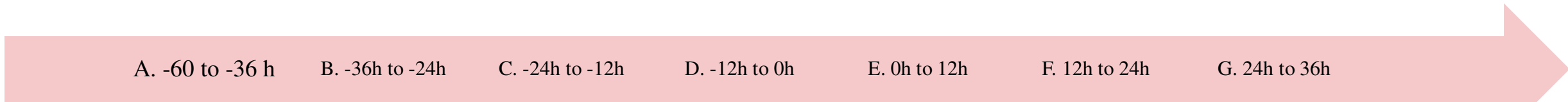
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PDS+

			↑ Serum cortisol *** ↑ Saliva cortisol ***	↑ Serum cortisol **** ↑ Saliva cortisol **	↑ Serum cortisol **** ↑ Saliva cortisol **** ↑ Fasting glucose * ↑ Serum glucose *	↑ Serum cortisol ** ↑ Saliva cortisol *
			↑ Serum glucose **	↓ C-peptid **	↓ C-peptid *	

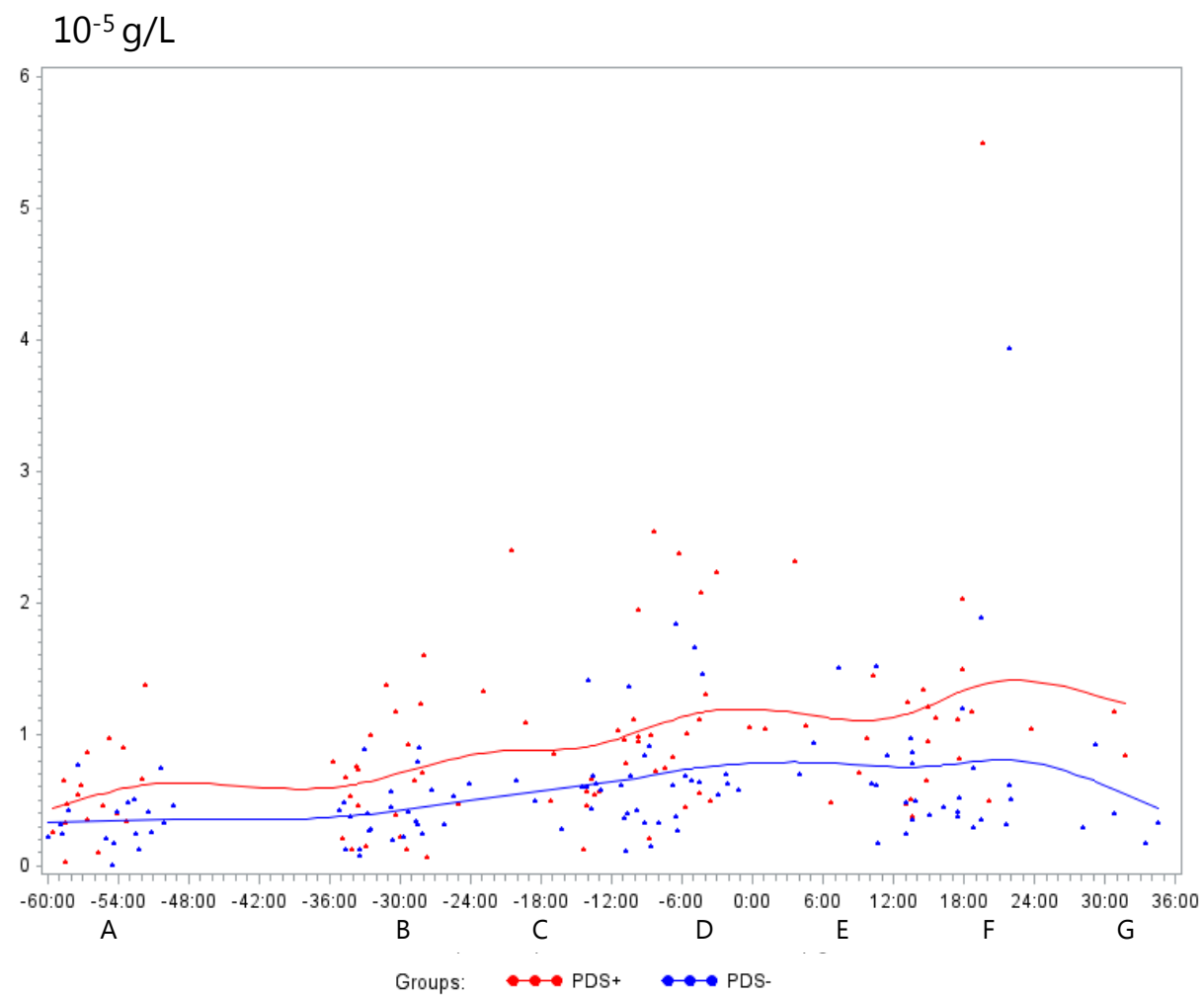
PDS-

		↑ Saliva cortisol *	↑ Serum cortisol ** ↑ Saliva cortisol **	↑ Saliva cortisol **** ↑ Fasting glucose *	↑ Saliva cortisol **** ↑ Fasting glucose * ↑ Serum glucose **	↓ Serum cortisol * ↑ Saliva cortisol *** ↑ Fasting glucose ****
↑ Serum glucose *	↑ Serum glucose **		↑ Serum glucose **			↓ Prolactin *
			↓ 8-epi-PGF2α *		↓ 8-epi-PGF2α *	

**** $p < 0.0001$, *** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$

Parameter	Group	n	A. (-60 to -36 h)		B. (-36 to -24 h)		C. (-24 to -12 h)		D. (-12 to 0 h)		E. (0 to 12 h)		F. (12 to 24 h)		G. (24 to 36 h)	
			LSMEANS	±SD	LSMEANS	±SD	LSMEANS	±SD	LSMEANS	±SD	LSMEANS	±SD	LSMEANS	±SD	LSMEANS	±SD
Serum cortisol	PDS+	38	3.14	1.10	3.07*	1.08	3.34	1.15	4.84	1.08	6.36***	1.15	5.55****	1.09	5.43***	1.19
	PDS-	38	3.18	1.10	3.89*	1.09	3.63	1.15	4.58	1.08	2.79***	1.17	3.14****	1.09	2.12***	1.19
Saliva cortisol	PDS+	38	0.35	1.12	0.37	1.10	0.50	1.16	0.61*	1.10	0.71	1.21	1.09	1.13	0.82	1.39
	PDS-	38	0.28	1.11	0.32	1.10	0.44	1.16	0.44*	1.10	0.84	1.19	0.95	1.11	0.66	1.23
Chromogranin A***	PDS+	38	0.39	1.19	0.46	1.16	0.68	1.25	0.98	1.16	0.97	1.31	1.07	1.19	1.18	1.62
	PDS-	38	0.26	1.18	0.35	1.16	0.58	1.25	0.56	1.15	0.70	1.28	0.61	1.17	0.34	1.37
Fasting glucose	PDS+	38	3.76	0.37	3.91	0.36	4.07	0.50	4.10	0.36	4.53	0.49	4.89	0.40	4.64****	0.69
	PDS-	38	3.85	0.37	3.74	0.35	4.76	0.60	4.09	0.35	5.35	0.57	4.98	0.36	9.55****	0.63
Serum glucose	PDS+	38	4.38	0.25	4.77	0.21	5.04	0.37	5.25	0.21	5.03	0.37	5.14	0.23	5.30	0.46
	PDS-	38	4.38	0.24	5.15	0.22	5.68	0.37	5.38	0.21	4.95	0.39	5.26	0.22	5.32	0.45
C-peptid	PDS+	38	301.9	1.21	326.42	1.17	222.29	1.33	240.95	1.18	109.22	1.35	161.14**	1.20	220.37	1.42
	PDS-	38	267.25	1.20	285.60	1.18	303.87	1.33	182.97	1.18	238.13	1.35	349.32**	1.18	412.03	1.41
Prolactin	PDS+	38	11553.00	1.13	12358.51	1.11	12891.20	1.18	12356.04	1.11	9075.19	1.18	11896.50	1.12	7873.04	1.22
	PDS-	38	12610.69	1.12	13355.72	1.11	12187.91	1.18	12410.52	1.11	11292.57	1.18	11443.76	1.12	8304.06	1.21
8-epi prostaglandin F2 α	PDS+	38	41.71	4.91	40.78	4.08	44.02	7.18	42.60*	4.19	31.87	7.15	38.41	4.62	25.37	8.75
	PDS-	38	44.39	4.70	38.10	4.12	44.07	7.06	30.07*	4.09	34.39	7.42	30.23	4.28	29.36	8.53
Natrium	PDS+	38	148.58	1.02	148.68	1.01	150.63	1.02	147.00	1.01	149.64	1.02	153.62	1.02	152.23	1.03
	PDS-	38	147.41	1.02	151.64	1.01	144.68	1.03	151.40	1.01	148.96	1.03	151.28	1.01	155.18	1.03
Potassium	PDS+	38	4.47	1.03	4.55	1.03	4.35	1.05	4.34	1.03	4.69	1.05	4.50	1.03	4.27	1.06
	PDS-	38	4.37	1.03	4.53	1.03	4.24	1.04	4.45	1.03	4.47	1.05	4.44	1.03	4.89	1.05

Cromogranin A

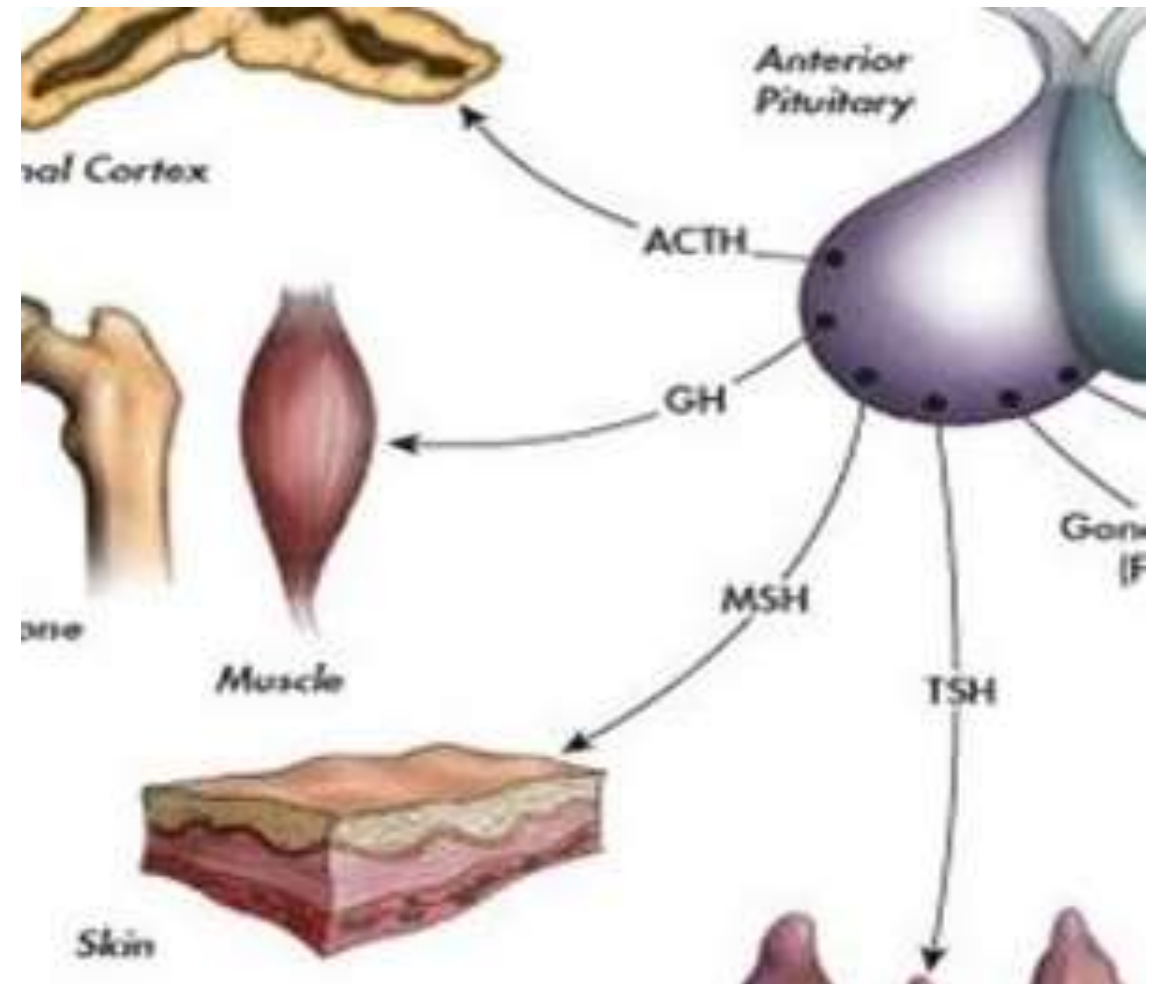


Cromogranin A

Lokaliseret i det entriske nervesystem

Udskilles i tilknytning til
tarmsystemet

Spyt



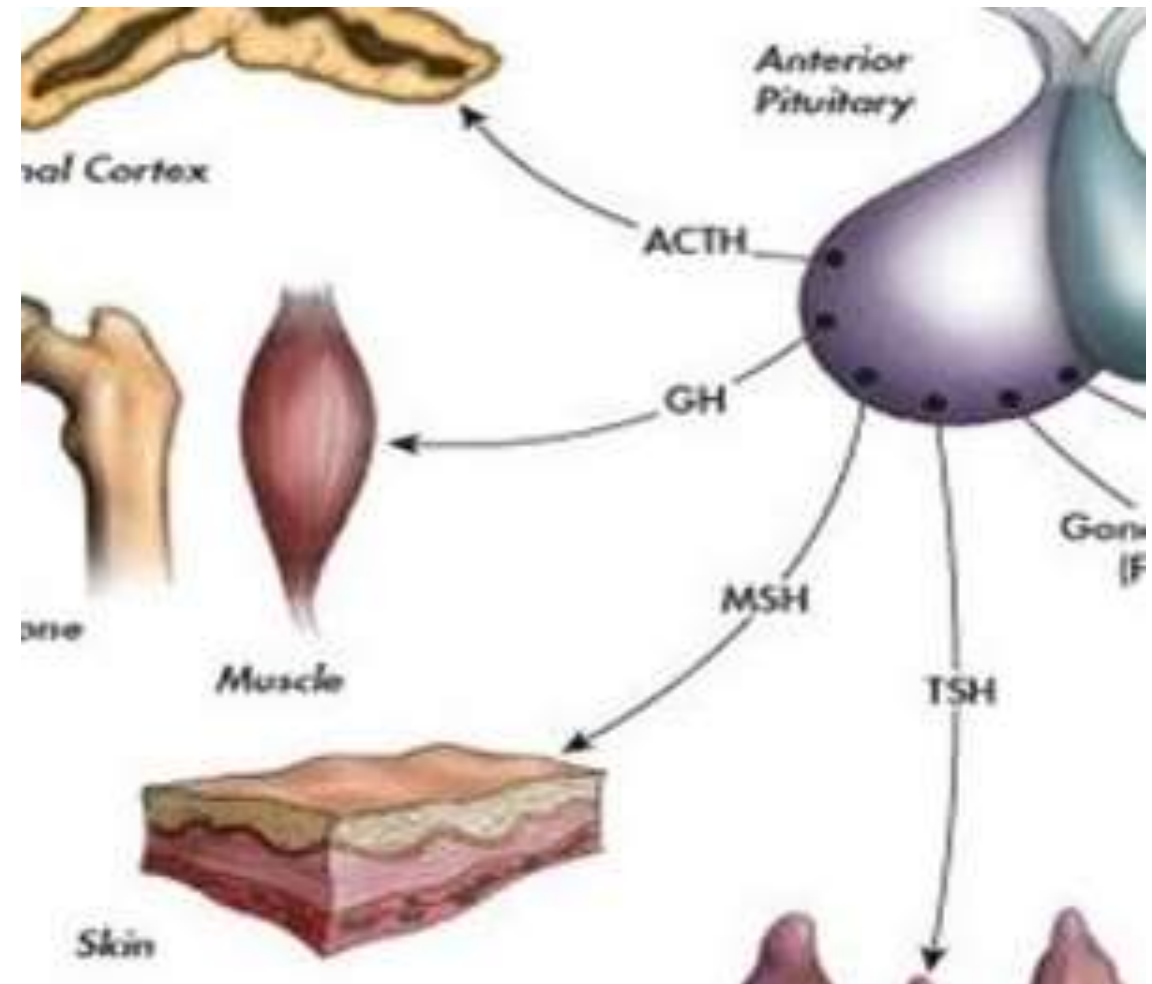
Nogle relevante egenskaber af Cromogranin A

Stress markør - frigives ved sekretion af katekolaminer (Sympatisk nervesystem)

Regulering af vaskulære homeostasis og hjertet

Regulering af mave-tarm kanalens motilitet

Har potent anti-mikrobiel aktivitet mod bakterier, svampe og gær



Foreløbig overordnet konklusion

- ✓ Forstyrrelse i kroppens homeostasis
 - Immunsystemet supprimeres
- ✓ Kredsløbet er kompromitteret
- ✓ Inflammation i begge grupper ...men signifikant kraftigere i PDS+søer

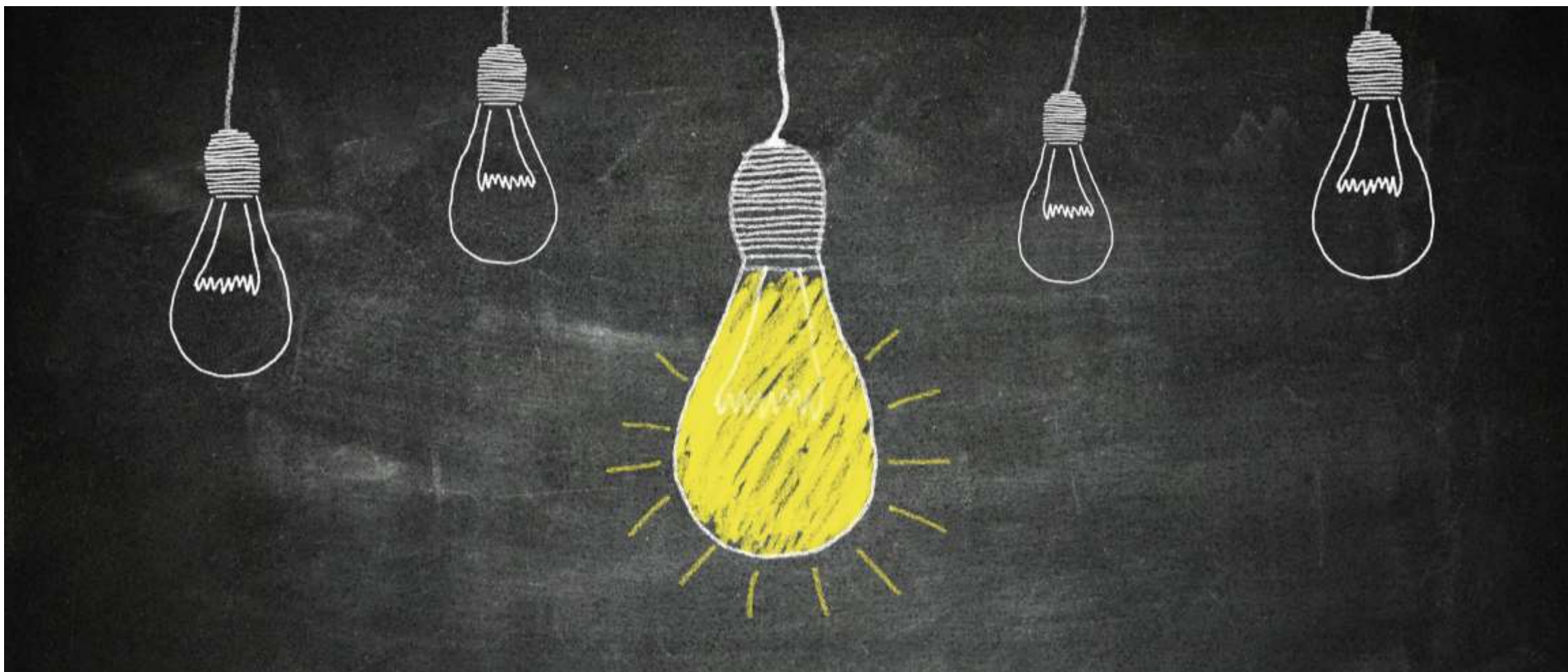


Foreløbig og meget overordnet konklusion

- ✓ PDS+ og PDS- søer er mindre følsom overfor insulin
 - ...Men, efterspørgslen efter energi er højere hos PDS- søer
- ✓ Lidt yverbetændelse
 - Forekommer, men antagelig et mindre problem (resultater ikke vist)

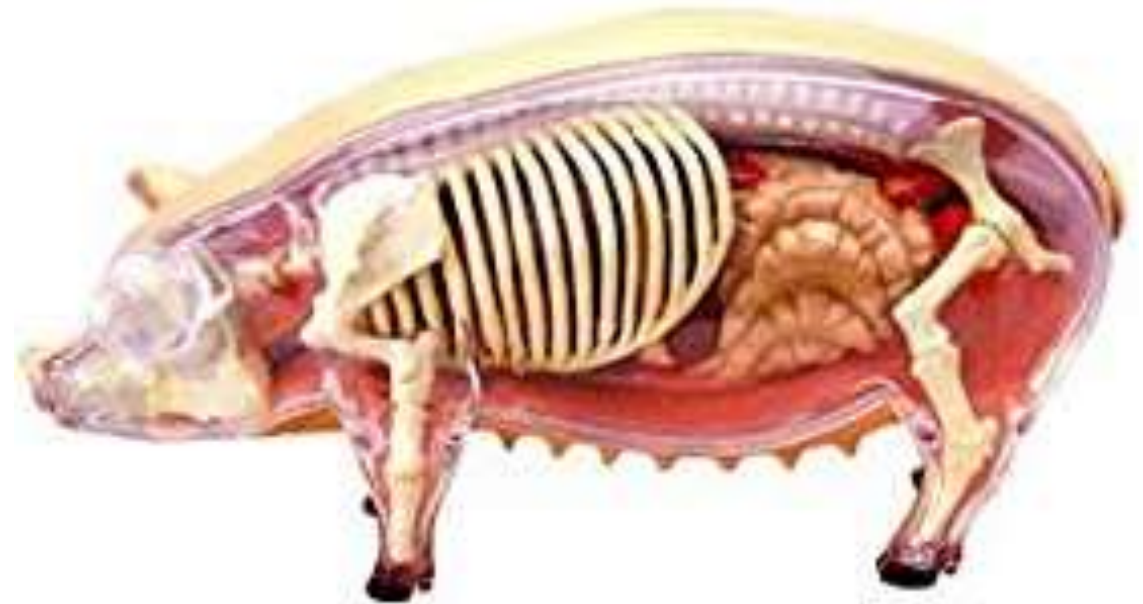


Perspektiv



Mere et tarmproblem end et yverproblem?

- Viste og ikke viste resultater indikere, at der kan være tale om et tarmproblem



Nye hypoteser

- Aktivering af det entriske nervesystem?
- Tarmens mikrobiologi?
- Stress?
- Øget mængde frie radikaler og oxidativ stress?
- ...
- ...



Diagnose – Mulige biomarkører?

Forskel mellem PDS+ og PDS- søer

Total antal hvide blodlegemer, neutrofile granulocytter, lymfocytter, TNF- α , IL-6, Hp, Fe, CgA, kortisol, C-peptid og 8-epi-PGF2 α

Før faring

Total antal hvide blodlegemer, CgA, kortisol, C-peptid og 8-epi-PGF2 α



Praktisk håndtering for nuværende...

TAG TEMPERATUR!

- $\geq 39,5^{\circ} \text{C}$
- To gange dagligt





Tak for opmærksomheden

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