Efficacy and safety of analgesic treatment for depression in people with advanced dementia: randomised, multicentre, double-blind, placebo-controlled trial (DEP.PAIN.DEM)

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ELECTRONIC SUPPLEMENTARY MATERIAL

Drugs & Aging

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MOBID–2 Pain Scale

MOBILIZATION – **O**BSERVATION – **B**EHAVIOUR – **I**NTENSITY – **D**EMENTIA

Patient´s name: **Date:**   **Time:**   **Unit:**

Pay attention to the patient´s pain behaviour during morning care. Observe the patient before you start mobilization. Explain clearly what is going to happen. Guide the patient carefully through the activities 1–5. Reverse the movement immediately if pain behaviour is perceived. Rate your observation after each activity:

Pain Behaviour

Tick the boxes for Pain noises, Facial expression and Defence, whenever you observed such pain behaviour

Pain noises	Facial expression	Defence
Ouch!	Grimacing	Freezing
Groaning	Frowning	Guarding
Gasping	Tightening mouth	Pushing
Screaming	Closing eyes	Crouching

YOU MAY TICK SEVERAL BOXES FOR EACH ACTIVITY

Pain Intensity

Based on pain behaviour, rate the pain intensity with a cross on the lines (0–10)

HOW INTENSE DO YOU REGARD THE PAIN TO BE?
0 is no pain and 10 is as bad as it possibly could be

1. Guide to open both hands, one hand at a time
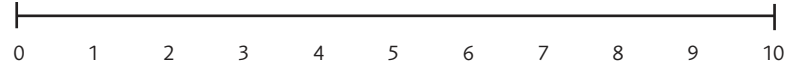
☐ ☐ ☐

0 1 2 3 4 5 6 7 8 9 10
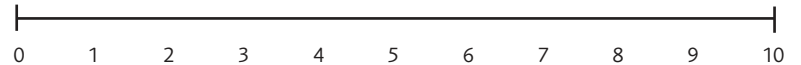
2. Guide to stretch both arms towards head, one arm at a time

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0 1 2 3 4 5 6 7 8 9 10
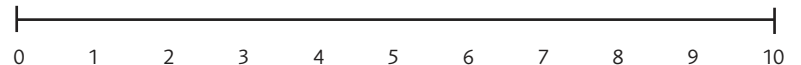
3. Guide to stretch and bend both knees and hips, one leg at a time

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0 1 2 3 4 5 6 7 8 9 10

4. Guide to turn in bed to both sides

☐ ☐ ☐

0 1 2 3 4 5 6 7 8 9 10
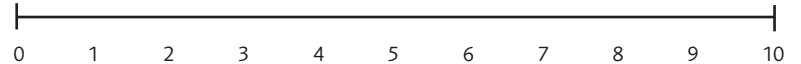
5. Guide to sit at the bedside

0 1 2 3 4 5 6 7 8 9 10
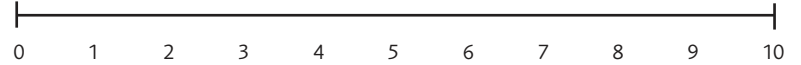
Did you observe, today or in the last days (one week), that the patient expressed pain behaviour related to head, internal organs and/or skin, which may be caused by a disease, wound, infection and/or injury?

Pain Behaviour

Make one or more cross/es on the pain drawing (front and back), according to observed pain behaviour (Pain noises, Facial expression and Defence)
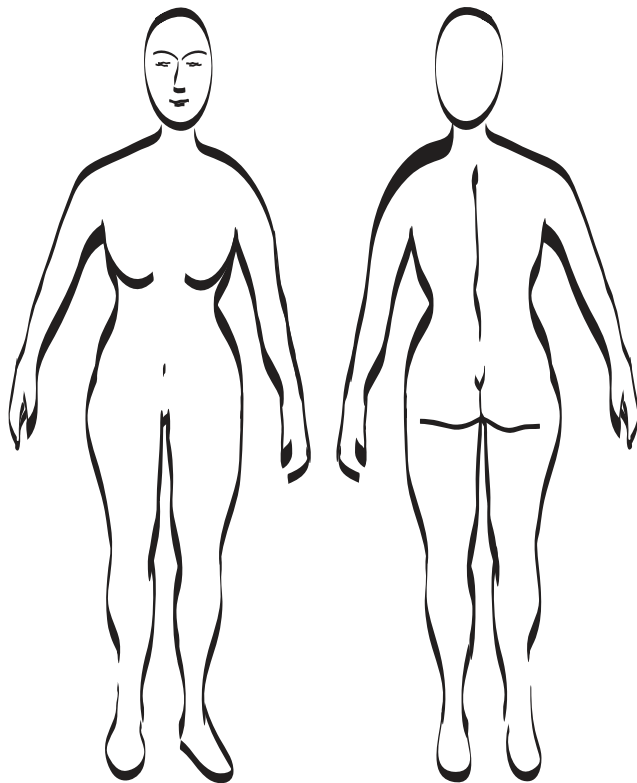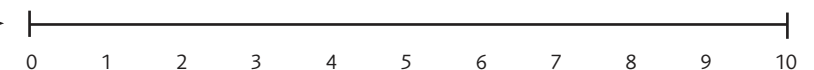
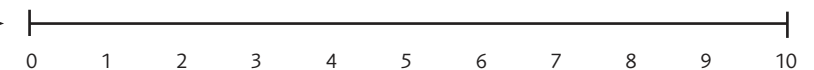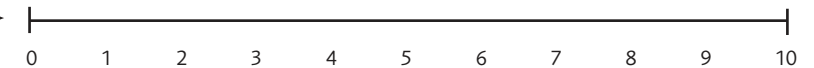## Pain Intensity

Based on pain behaviour, rate the pain intensity with a cross on the lines (0–10)

HOW INTENSE DO YOU REGARD THE PAIN TO BE?
0 is no pain and 10 is as bad as it possibly could be

6. Head, mouth, neck

| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |

7. Heart, lung, chest wall

| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |

8. Abdomen

| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |

9. Pelvis, genital organs

| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |

10. Skin

| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
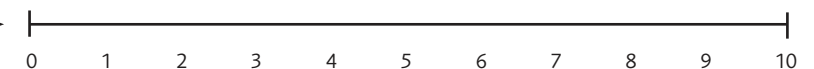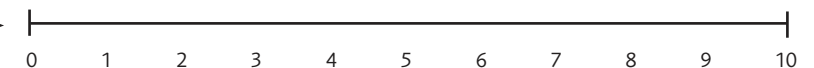
Based on all observations, rate the patient's overall pain intensity

| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
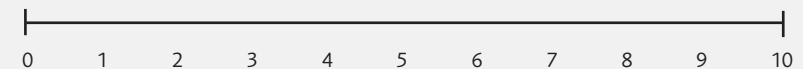
Online Resource 2. Estimated effect of active analgesic treatment on CSDD depressive symptoms compared to placebo; all coefficients from mixed model analysis.

	Change from baseline to 13 weeks			Change from baseline to 6 weeks			Change from 6 weeks to 13 weeks			P-int	ICC NH	ICC pat
	Placebo (95% CI)	Active (95% CI)	Treatment effect (95% CI)	Placebo (95% CI)	Active (95% CI)	Treatment effect (95% CI)	Placebo (95% CI)	Active (95% CI)	Treatment effect (95% CI)			
All patients	**-3.30** **(-4.68, -1.92)**	-0.66 (-2.27, 0.94)	**2.64** **(0.55, 4.72)**	**-1.67** **(-2.86, -0.47)**	-0.92 (-2.24, 0.40)	0.74 (-1.03, 2.52)	**-1.64** **(-3.06, -0.21)**	0.26 (-1.41, 1.93)	1.89 (-0.29, 4.08)	0.05	0.14	0.25
MMSE 11-20	-2.37 (-4.75, 0.00)	-0.13 (-2.68, 2.42)	2.24 (-1.24, 5.72)	-0.34 (-2.32, 1.64)	-0.01 (-2.03, 2.02)	0.33 (-2.50, 3.16)	-2.03 (-4.75, 0.68)	-0.12 (-3.00, 2.75)	1.91 (-2.05, 5.86)	0.44	0.20	0.21
MMSE 0-10	**-3.55** **(-5.21, -1.88)**	**-2.45** **(-4.47, -0.42)**	1.10 (-1.49, 3.69)	**-2.21** **(-3.76, -0.66)**	-1.65 (-3.36, 0.07)	0.56 (-1.75, 2.86)	-1.34 (-3.13, 0.45)	-0.80 (-2.98, 1.38)	0.54 (-2.27, 3.35)	0.69	0.27	0.28
Paracetamol	**-3.04** **(-4.93, -1.15)**	-1.06 (-3.09, 0.97)	1.98 (-0.79, 4.74)	**-2.13** **(-4.07, -0.18)**	-1.73 (-3.73, 0.27)	0.40 (-2.39, 3.18)	-0.91 (-3.02, 1.19)	0.67 (-1.57, 2.90)	1.58 (-1.49, 4.64)	0.35	0.27	0.27
Buprenorphine	**-3.44** **(-5.39, -1.50)**	-0.41 (-2.88, 2.07)	3.04 (-0.11, 6.19)	-1.24 (-2.80, 0.31)	-0.28 (-2.12, 1.56)	0.96 (-1.45, 3.37)	**-2.20** **(-4.12, -0.29)**	-0.13 (-2.65, 2.39)	2.07 (-1.06, 5.20)	0.85	<0.01	0.21
MOBID2 <3	**-2.64** **(-4.83, -0.44)**	0.02 (-2.24, 2.27)	2.65 (-0.49, 5.80)	**-2.83** **(-4.54, -1.12)**	-1.41 (-3.12, 0.30)	1.42 (-1.00, 3.83)	0.19 (-1.61, 2.00)	1.43 (-0.49, 3.35)	1.24 (-1.40, 3.87)	0.09	0.18	0.26
MOBID-2 ≥3	**-3.63** **(-5.37, -1.89)**	-1.38 (-3.57, 0.82)	2.25 (-0.55, 5.04)	-1.03 (-2.62, 0.56)	-0.56 (-2.42, 1.30)	0.47 (-1.98, 2.91)	**-2.60** **(-4.53, -0.66)**	-0.82 (-3.23, 1.60)	1.78 (-1.31, 4.88)	0.29	0.07	0.24
MOBID-2 ≥3, paracetamol	-2.94 (-5.93, 0.04)	-1.32 (-4.43, 1.80)	1.63 (-2.68, 5.94)	-1.29 (-4.21, 1.64)	-1.66 (-4.59, 1.26)	-0.38 (-4.51, 3.76)	-1.66 (-4.81, 1.49)	0.35 (-2.90, 3.59)	2.01 (-2.52, 6.53)	0.64	0.02	0.18
MOBID-2 ≥3, buprenorphine	**-3.91** **(-5.94, -1.89)**	-1.73 (-4.63, 1.18)	2.19 (-1.35, 5.73)	-0.89 (-2.84, 1.06)	0.42 (-2.10, 2.95)	1.32 (-1.87, 4.51)	**-3.02** **(-5.11, -0.93)**	-2.15 (-5.22, 0.92)	0.87 (-2.84, 4.58)	0.44	<0.01	0.31

CSDD, Cornell Scale for Depression in Dementia; ICC NH, intracluster correlation on nursing home unit level; ICC pat, intracluster correlation on patient level; MMSE, Mini-Mental State Examination; MOBID-2, Mobilisation-Observation-Behaviour-Intensity-Dementia-2 Pain Scale; P-int, P for interaction, obtained by likelihood ratio test.

Online Resource 3. Estimated effect of active analgesic treatment on MOBID-2 pain intensity compared to placebo; all coefficients from mixed model analysis.

	Change from baseline to 13 weeks			Change from baseline to 6 weeks			Change from 6 weeks to 13 weeks			P-int	ICC NH	ICC pat
	Placebo (95% CI)	Active (95% CI)	Treatment effect (95% CI)	Placebo (95% CI)	Active (95% CI)	Treatment effect (95% CI)	Placebo (95% CI)	Active (95% CI)	Treatment effect (95% CI)			
All patients	-0.09 (-0.63, 0.46)	-0.28 (-0.90, 0.35)	-0.19 (-1.02, 0.64)	-0.51 (-1.03, 0.00)	-0.32 (-0.92, 0.27)	0.19 (-0.59, 0.97)	0.43 (-0.13, 0.98)	0.05 (-0.62, 0.72)	-0.38 (-1.25, 0.49)	0.69	0.31	0.55
MMSE 11-20	0.39 (-0.56, 1.34)	-0.63 (-1.69, 0.44)	-1.01 (-2.44, 0.41)	-0.42 (-1.34, 0.50)	-0.02 (-0.99, 0.95)	0.39 (-0.94, 1.73)	0.81 (-0.16, 1.77)	-0.60 (-1.65, 0.44)	-1.41 (-2.83, 0.01)	0.13	0.46	0.55
MMSE 0-10	-0.23 (-0.97, 0.50)	-0.11 (-0.99, 0.76)	0.12 (-1.02, 1.26)	-0.39 (-1.08, 0.30)	-0.37 (-1.20, 0.47)	0.03 (-1.05, 1.11)	0.16 (-0.59, 0.91)	0.25 (-0.72, 1.23)	0.09 (-1.13, 1.32)	0.98	0.17	0.56
Paracetamol	0.31 (-0.36, 0.99)	-0.66 (-1.43, 0.11)	-0.98 (-2.00, 0.05)	-0.23 (-0.88, 0.42)	-0.09 (-0.80, 0.62)	0.14 (-0.83, 1.10)	0.54 (-0.14, 1.23)	-0.57 (-1.37, 0.22)	**-1.11 (-2.16, -0.06)**	0.08	<0.01	0.70
Buprenorphine	-0.40 (-1.20, 0.40)	0.07 (-0.88, 1.01)	0.47 (-0.77, 1.71)	-0.69 (-1.45, 0.06)	-0.49 (-1.40, 0.43)	0.21 (-0.98, 1.39)	0.29 (-0.54, 1.12)	0.55 (-0.49, 1.59)	0.26 (-1.06, 1.59)	0.75	0.29	0.45
MOBID-2 ≥3	-0.71 (-1.44, 0.01)	**-1.29 (-2.24, -0.33)**	-0.57 (-1.77, 0.62)	**-1.13 (-1.83, -0.42)**	**-1.28 (-2.11, -0.45)**	-0.16 (-1.24, 0.93)	0.41 (-0.33, 1.15)	-0.01 (-0.97, 0.96)	-0.42 (-1.63, 0.79)	0.63	0.31	0.35
MOBID-2 ≥3, Paracetamol	-0.61 (-1.82, 0.61)	**-1.97 (-3.45, -0.48)**	-1.36 (-3.27, 0.55)	-1.04 (-2.28, 0.20)	-0.96 (-2.20, 0.28)	0.07 (-1.67, 1.82)	0.43 (-0.77, 1.62)	-1.00 (-2.38, 0.38)	-1.43 (-3.25, 0.39)	0.24	0.13	0.38
MOBID-2 ≥3, buprenorphine	-0.87 (-1.79, 0.04)	-0.65 (-1.90, 0.61)	0.23 (-1.32, 1.77)	**-1.19 (-2.04, -0.34)**	**-1.57 (-2.72, -0.42)**	-0.38 (-1.81, 1.05)	0.32 (-0.63, 1.26)	0.92 (-0.43, 2.27)	0.60 (-1.04, 2.25)	0.77	0.30	0.36

ICC NH, intracluster correlation on nursing home unit level; ICC pat, intracluster correlation on patient level; MMSE, Mini-Mental State Examination; MOBID-2, Mobilisation-Observation-Behaviour-Intensity-Dementia-2 Pain Scale; P-int, P for interaction, obtained by likelihood ratio test.