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Pain and agitation treatment in severe dementia patients: The need for Italian Mobilization–Observation–Behavior–Intensity–Dementia (I-MOBID2) pain scale translation, adaptation and validation with psychometric testing

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ABSTRACT

The 97% of dementia patients develops fluctuant neuropsychiatric symptoms often related to under-diagnosed and unrelieved pain. Up to 80% severe demented nursing home residents experiences chronic pain due to age-related comorbidities. Patients lacking self-report skills risk not to be appropriately treated for pain. Mobilization–Observation–Behavior–Intensity–Dementia (MOBID2) is the sole pain scale to consider the frequent co-occurrence of musculoskeletal and visceral pain and to unravel concealed pain through active guided movements. Accordingly, the Italian real-world setting can benefit from its translation and validation. This clinical study provides a translated, adapted and validated version of the MOBID2, the Italian I-MOBID2. The translation, adaptation and validation of the scale for non-verbal, severe demented patients was conducted according to current guidelines in a cohort of 11 patients over 65 with mini-mental state examination ≤ 12. The I-MOBID2 proves: good face and scale content validity index (0.89); reliable internal consistency (Cronbach's $\alpha = 0.751$); good to excellent inter-rater (Intraclass correlation coefficient, and test-retest (ICC = 0.902) reliability. The construct validity is high (Rho = 0.748 $p < 0.05$ for 11 patients, Spearman rank order correlation of the overall pain intensity score with the maximum item score of I-MOBID2 Part 1; rho=0.895 $p < 0.01$ for 11 patients, for the overall pain intensity score with the maximum item score of I-MOBID2 Part 2) and a good rate of inter-rater and test-retest agreement was demonstrated by Cohen's K = 0.744. The average execution time is of 5.8 min, thus making I-MOBID2 a useful tool suitable also for future development in community setting with administration by caregivers.

Abbreviations: AD, Alzheimer's disease; COSMIN, COnsensus-based Standards for the selection of health Measurement Instruments; COVID-19, Coronavirus disease-19; ICC, Intraclass correlation coefficient; MMSE, Mini-mental state examination; MOBID2, Mobilization–Observation–Behavior–Intensity–Dementia; NPS, neuropsychiatric symptoms; PD, Parkinson's disease.

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1. Introduction

Over 55 million people suffer from dementia worldwide, estimated to increase up to 78 million by 2030, and this is the condition associated to the highest proportional increase in serious-related suffering by 2060 [1]. This issue is even more serious if we consider that some 75% of patients affected by dementia (reaching 90% in low- and middle-income countries) is not diagnosed and 90% clinicians points at further delays in diagnosis due to the current Coronavirus disease (COVID)−19 pandemic [2,3], in which the latter pay the highest price, also because of the cardiocerebrovascular burden of inappropriate treatments [4]. In fact, dementia sufferers in the 97% of cases develop fluctuant neuropsychiatric symptoms (NPS) [5], treated with atypical antipsychotics, often off-label in the community context [6], endowed with some doubled mortality risk [7]. Incidentally, patients with dementia belong to the over 65 fragile population very often affected by clinical conditions that induce chronic, inflammatory and neuropathic pain, underdiagnosed due to the loss of communication and, consequently, self-report capabilities [8]. Therefore, agitation, representing one of the worst NPS, is developed as help-seeking behavior for unrelieved pain and it can be effectively managed through analgesia [9]. NPS pattern was even preclinically associated with aging pain perception and treatment modifications [10]. Unfortunately, access to pain treatment, particularly chronic and neuropathic, is limited for patients suffering from dementia [6,11,12] also due to the lack of studies of the treatment of specific pain conditions in these patients [13,14]. The intensity of pain is correlated with the presence of NPS and the use of antipsychotics [15]. The priority of analgesia in the handling of NPS was demonstrated by a Delphi consensus [16]. An appropriate and integrated pain management [17] can reduce the use of antipsychotics [18,19]. Thus, one of the most challenging barriers to NPS and pain adequate treatment is represented by pain assessment in severely uncommunicative demented patients. In fact, patients who have lost the skill to communicate cannot convey the pain that they perceive to the care provider; therefore, behavioral observational pain assessment scales are needed for the caregiver to rate inferred pain intensity. The recently proposed biopsychosocial framework of pain and dementia points at the fundamental need for appropriate pain assessment tools [20]. Moreover, the level of certainty of nurses/operators and their decision making process after pain assessment is crucial for its management [21]. Although some observational scales are translated in Italian, the national real-world setting cannot make use of a pain assessment device, i.e. the Mobilization–Observation–Behavior–Intensity–Dementia (MOBID2) Pain Scale that is peculiar for its organization since it is the sole to consider the frequent co-occurrence of musculoskeletal and visceral pain [22]. In fact, it is the extension of the MOBID Pain Scale (first part, also studied [23] in settings different from that of the developers) consisting of two parts [24]: the first is used for the assessment of musculoskeletal pain, through behavioral indicators, that are pain noises, facial expression of pain and defensive behaviors, during the execution of five guided movements of different body parts; the second part is used for the assessment of pain from internal organs, head and skin, through pain behaviors and localization of pain on pain drawings. It was tested in severe dementia proving to be endowed with good face and construct (Part1 rho=0.82; Part2 rho=0.61) validity, very good inter-rater (ICC (1, 1) 0.80–0.94) and test–retest (ICC (1, 1) 0.60–0.94) reliability for pain intensity. This observational pain scale cannot be used in the Italian context since an Italian version does not exist. Thus, the present study aims at providing Italian clinicians with a translated, adapted and validated version of the MOBID2, the Italian I-MOBID2. The validation of the I-MOBID2 is essential to evaluate the accuracy and effectiveness of the analgesic treatments administered [25], for nociceptive and neuropathic pain conditions, in patients suffering from severe dementia. Indeed, the tool needs to be responsive, that means detecting change over time in the construct to be measured based on the COnsensus-based Standards for the selection of health Measurement Instruments (COSMIN) initiative [26]. The present validation of the I-MOBID2 pain scale is the first, essential and unavoidable step of the process to improve pain and NPS treatment in the fragile population of the patients with severe dementia in the Italian context.

2. Methods

The pain assessment tool used in this study is reproduced with permission for the use of developing scales in nonprofit academic research from the original article by Husebo et al. [24]. The translation, adaptation and validation with ascertainment of clear understanding of the translated version of the scale by nurses/health caregivers to assess pain in non-verbal severely demented patients is conducted on the basis of current guidelines [27–29] according to the European Group for Health Measurement and Quality of Life Assessment through a cross cultural adaptation of the Nottingham Health Profile (NHP) and in agreement with previous Italian translations and psychometric testing of scales for Alzheimer's (AD) and Parkinson's disease (PD) [30–33]. In particular, the study consists of a four-stage process of translation: 1) forward translation, 2) back-translation, 3) expert reviews with modifications and set up of the final instrument and 4) validation study (Fig. 1). This trial was approved by the Calabria Region Ethics Committee with protocol n. 156 of May 21st, 2020. According to the D.lgs 196/2003, the Helsinki agreements and subsequent amendments, the Good Clinical Practice and current legislation, the Guidelines for the treatment of personal data in clinical trials of 24 July 2008 and in accordance with European data protection legislation, each participant or his/her legal representative was required to sign a consent form as acceptance of all aspects of the study contained in the patient information sheet and as a consequent expression of his willingness to participate in the study. The information sheet was duly illustrated to the subjects or legal representatives by the study staff and the same staff ensured that the consent form was properly signed and dated by all the parties involved before any procedure foreseen by the protocol was carried out.

2.1. Translation and adaptation

The first step of the study is the preliminary translation of the scale into the second language, i.e. Italian. Two independent literal translations by two bilingual Italian mother tongue translators, one with medical background and a naive translator without medical or clinic background, are carried out. Content, meaning, clarity of expression and comparability to the original item are verified. Back translation to the original language, i.e. English, is produced by two native-English speaking translators blind to the original questionnaire and without medical background according to guidelines. Any discrepancies in the two English language documents produced are resolved by the primary researcher and the back translation is compared to the original document. Questions with discrepancies can be redrafted and the procedure can be repeated several times. At this point, establishment of the cross-language equivalence between the original and the translated questionnaires is performed to guarantee that the final translation captures the closest meaning of the original item and the questionnaire is tested for cross-language equivalence. Finally, a multidisciplinary expert committee including researchers skilled with pain study and assessment (methodologists), clinicians expert in the treatment of non-communicative demented patients, bilingual professionals, psychologists and representatives of the clinical nurse/health caregivers that administer the pain assessment tool, produces an appraisal of the translated and adapted observational pain assessment scale. The committee evaluates the semantic, idiomatic, experiential and conceptual equivalence (cross-language equivalence) and provides a full written documentation assessing the I-MOBID2 face and content validity, acceptability and feasibility of use through a 4-point scale (1 = not relevant, 2 = somewhat relevant, 3 = quite relevant, 4 = highly

relevant), refining the questionnaire to obtain the final translation that needs to be understandable by a 10/12-year old child (roughly a Grade 6 level of reading, as recommended for questionnaires) up to the final I-MOBID2 for field testing [34–36]. The item and scale content validity indexes are computed to indicate the percentage of agreement among the experts of the panel [37,38].

2.2. Validation

Since validity is assessed by an expert committee, in the validation stage the establishment of the reliability of the I-MOBID2 is performed to ensure psychometric properties at item and scale level. In fact, the validation consists in evaluating the inter-rater and test-retest reliability of the I-MOBID2 in 11 patients from the target setting, thus affected by severe dementia. The construct validity is evaluated as the association of the overall pain intensity score with the maximum item score of I-MOBID2 Part 1 and 2 rated by healthcare assessors and it is calculated by Spearman's rank order correlation (rho) [24]. The inter-rater and test–retest agreement of observed pain behavior indicators and localization of pain sites on the pain drawing is analyzed by kappa (k) statistics, demonstrating concordance within and between the raters with the following meaning: $k \leq 0.20$ (poor), $k = 0.21–0.40$ (fair), $k = 0.41–0.60$ (moderate), $k = 0.61–0.80$ (good), $k \geq 0.81$ (very good agreement) [24]. The inter-rater reliability of the nurses' inferred pain intensity score is calculated pairwise for each item and for overall pain intensity. The test–retest reliability is calculated between the ratings at day 1 and 2 [24]. In particular, relative reliability is examined by Intraclass Correlation Coefficient (ICC) one-way random model [24]. Internal consistency, demonstrating that the items of the scale are measuring the same underlying construct, is examined using Cronbach's α formula with values that should be > 0.7 and < 0.9 [24].

2.3. Statistical analysis

Patients are considered in pain when the I-MOBID2 items or the overall pain intensity are scored ≥ 3 [24]. All the statistical analyses were performed with Microsoft Office Excel 10 (Microsoft, Milan, Italy) and SPSS-22 for Windows (IBM SPSS, Chicago, IL, USA).

3. Results

3.1. Forward and back translation

As described in the Methods, two independent written reports of forward translation, also summarizing the rationale for the translators' choices, were merged to create the final Italian draft by the primary researcher. The synthesis of the translations, in the presence of a recording observer, is carefully documented in a written report. Among the several modifications, the second singular person was adopted in all the instructions for consistency and to make the execution of the scale more direct. To establish the correspondence between the preliminary Italian translation and the original scale, two independent back translations were conducted and the latter correspondence resulted verified. This process produced the final I-MOBID2 (Table 1, Fig. 2a)-b)).

3.2. Face and content validity

Face validity was assessed by an expert panel in following meetings evaluating behavior indicators, instructions for both the musculoskeletal and the visceral part, pain drawing and inferred pain intensity scores. Content validity is defined as "the extent to which an instrument adequately samples the research domain of interest when attempting to measure phenomena" [39,40] and the quantitative measure is chosen in this study, instead of the only qualitative measure among content experts, for the definition of the scale and item CVI (i.e. S- and I-CVI) [40]. To this aim, an experts committee evaluated the consistency of each item with the construct assessed by the scale, computing the percentage of items relevant for each expert and calculating the average congruency percentage among experts [40]. In this context, the panel is asked to rate the relevance of each item to the scale construct. The parameters calculated include: the I-CVI that represents the Content Validity of individual Items, i.e. the proportion of experts rating the item a relevance score of 3 or 4; the S-CVI/Ave that is the average of the I-CVIs for all the items of the scale; the S-CVI/UA consisting in the proportion of items that achieves a relevance rating of 3 or 4 by all the experts [37,38]. The results show very good I-CVI values for all the items, except the item 1: I-CVI= 1 for the items 2–3–4–5–7, I-CVI= 0.86 for the items 6–8–9–10 and I-CVI= 0.43 for the item 1. The S-CVI/Ave= 0.89 for the overall scale proves a good degree of experts' agreement. The collected data are reported in Table 2.

3.3. Cohort characteristics

The patients enrolled to the validation study present an age range of 73–94 years with MMSE from 0 to 10.3, proving their lack of communication capabilities. Chronic inflammatory (gonarthrosis, rheumatic polymialgia, osteoarthrosis) and neuropathic pain is common in this sample of population, consistently with age. The main features of the participants recruited are reported in Table 3.

3.4. Training of the caregivers

The nurses received a 2-hour training and observed for a week the patients to assess pain using the I-MOBID2. The instructions they were provided with include explaining clearly to the patient what is going to happen, asking him "Mrs., can you please open and close your left hand? I will help you!" [24]. For the first part the items 1–5 consist in the execution of standardized active, guided movements, that, are performed by the nurse in case the patient is not able to execute them on his own. For each item the healthcare operator asks the patients "How intense do you regard the pain to be?" [24] and rates inferred pain intensity on the 0–10 point line of a numeric rating scale (NRS). In the second part the nurses pay attention to observed pain behavior today or during the last days (the week of observation) likely from internal organs, head and skin and to cross/shade/circle the pain sites on the included pain drawing, according to the pain behavioral indicator observed (pain noises, facial expression and defense). Noteworthly, pain drawings can unravel dermatomal, sclerotomal or myotomal distributions or, frequently in chronic pain, a combination of the latter with unusual distribution often mistaken [41]. Nevertheless, the pain drawing does not serve only for pain location, but also to indicate body surface in pain, i.e. extent of pain, in fact, it is scored for percentage of total body surface in pain and location of pain [42]. The crosses performed on the pain drawing are quantified for the presence/absence of pain in each of the 45 body areas presented [43]. In fact, the pain drawing is divided into 45 anatomical areas with boundaries

Fig. 1. The process of translation, adaptation and validation consists of 4 stages: 1) forward translation, 2) back-translation, 3) expert reviews with modifications and set up of the final instrument and 4) validation study.

Table 1
The process of forward and back translation originated the Italian Mobilization–Observation–Behavior–Intensity–Dementia I-MOBID2. Forward translation and final Italian translation for validation are reported.

Forward translation

Translator1

Appendice

Scala del dolore MOBID-2

MOBILIZZAZIONE - **O**SSERVAZIONE - **C**OMPORTAMENTO - **I**NTENSITÀ – **D**EMENZA

Nome del paziente: Data: Orario: Unità:

Parte 1

Prestare attenzione al comportamento del paziente rispetto al dolore durante le cure mattutine. Osservare il paziente prima di iniziare la mobilizzazione. Spiegare chiaramente cosa sta per accadere. Guidare accuratamente il paziente nelle attività 1–5. Invertire immediatamente il movimento se si percepisce un comportamento doloroso. Valutare la propria osservazione dopo ogni attività:

Comportamento del dolore	**Rumori del dolore**	**Intensità del dolore**
Spuntare la casella per Rumori del dolore, Espressione facciale e Difesa ogniqualvolta osservi tale comportamento	Ahia Gemere Ansimare, Urlare **Espressione facciale** Smorfie Accigliato Stringere la bocca Chiudere gli occhi **Difesa** Irrigidimento Protezione Spinta Accovacciarsi	Sulla base del comportamento doloroso, valuta l'intensità del dolore apponendo una croce sulle linee (o-10)
1. Guidare ad aprire entrambe le mani, una mano la volta 2. Guidare ad allungare le braccia verso la testa, un braccio la volta 3. Guidare ad allungare e piegare entrambe le ginocchia e le anche, una gamba per volta 4. Guidare a girarsi nel letto su entrambi i lati 5. Guidare a sedersi sul letto	Puoi mettere una spunta su diverse caselle per ogni attività	Come reputi essere intenso il dolore? 0 è non dolore e 10 è il dolore massimo possibile

Parte 2

Hai osservato, oggi o negli ultimi giorni (una settimana), che il paziente esprimeva dolore relativo al capo, agli organi interni e/o alla cute, che può essere causato da una malattia, ferita, infezione e/o trauma?

Comportamento Doloroso		**Intensità del dolore**
Apponi una o più croci sul disegno del dolore (davanti e dietro), sulla base del comportamento doloroso osservato (Rumori del dolore, Espressione facciale e Difesa)	6. Capo, bocca, collo 7. Cuore, polmoni, cassa toracica 8. Addome 9. Pelvi, organi genitali 10. Cute	**Sulla base del comportamento doloroso, valuta l'intensità del dolore apponendo una croce sulle linee (o-10)** Come reputi essere intenso il dolore? 0 è non dolore e 10 è il dolore massimo possibile

Sulla base di tutte le osservazioni, valuta l'intensità complessiva del dolore del paziente

Translator2

Appendice

Scala del dolore MOBID-2

MOBILIZZAZIONE - OSSERVAZIONE - COMPORTAMENTO - INTENSITÀ – DEMENZA

Nome del Paziente Data Orario Reparto /Unità

Parte 1

Prestare attenzione al comportamento del paziente rispetto al dolore durante le cure mattutine. Osservare il paziente prima di iniziare la mobilizzazione. Spiegare al paziente chiaramente cosa sta per accadere. Con attenzione guidare il paziente attraverso le attività 1–5. Invertire immediatamente il movimento se si percepisce un comportamento doloroso. Valutare la propria osservazione dopo ogni attività:

Comportamento del dolore	Rumori del dolore	Intensità del dolore
Spuntare le caselle per i rumori del dolore, espressione del viso e difesa, ogniqualvolta hai osservato tale comportamento	Ahia! Gemere Ansimare Urlare Espressione facciale Smorfie Accigliato Stringere la bocca Chiudere gli occhi Difesa Bloccarsi Proteggersi Spingere Accovacciarsi	In riferimento al comportamento del dolore, valuta l'intensità del dolore con una croce sulle linee (0–10)
1. Guidare ad aprire entrambe le mani, una mano alla volta 2. Guidare ad allungare entrambe le braccia verso la testa, un braccio alla volta 3. Guidare ad allungare e piegare entrambi ginocchia e anche, una gamba alla volta 4. Guidare a girarsi nel letto su entrambi i lati 5. Guidare a sedersi al capezzale del letto	È POSSIBILE SELEZIONARE PIÙ CASELLE PER OGNI ATTIVITÀ	QUANTO INTENSO CONSIDERI CHE SIA IL DOLORE? 0 non è dolore e 10 è il massimo del dolore

Parte 2

E' stato possibile osservare, oggi o negli ultimi giorni (non più di una settimana), se il paziente avesse espresso comportamenti dolorosi legati alla testa, agli organi interni e/o pelle, che possono essere stati causati da una malattia, ferita, infezione e/o lesione?

Comportamento del Dolore		Intensità del dolore
Segnare con una o più croci sul disegno (fronte e retro), in riferimento al comportamento del dolore osservato (Rumori del dolore, espressione facciale e difesa)	6. Testa, bocca, collo 7. Cuore, Polmone, Cavità toracica 8. Addome 9. Bacino e organi genitali 10. Pelle	In riferimento al comportamento del dolore, valutare l'intensità del dolore con una croce sulle linee (0–10) QUANTO INTENSO CONSIDERI CHE SIA IL DOLORE? 0 non è dolore e 10 è il massimo del dolore

Sulla base di tutte le osservazioni, valutare l'intensità complessiva del dolore del paziente

corresponding mainly to joints [43] (Fig. 3, reproduced with permission from [43]). To achieve the total percentage of body surface in pain, according to Margolis et al., 1986 [43], for each of the 45 areas, a score of 1 is rated if the crosses indicate presence of pain and a score of 0 in absence of pain marks [43]. Weights are assigned to body areas equal to the percentage of body surface that they cover (Table 4, reproduced with permission from [43]), obtaining a final weighted score reflecting the total percentage of body surface in pain [43] (Table 4). A single cross involving all the area of head and of sacroiliac joint was computed as two marks covering both sides of the whole-body location. Each item from 6 to 10 of I-MOBID2 is rated according to the answer to the question whether the patient might be affected by pain from the internal organs, head and skin, inferring pain intensity on the provided NRS. After completion scoring the 10 separate items of I-MOBID2, an independent overall pain intensity score is rated using the NRS. For the purpose of the study to assess reliability, the same group of patients was rated concurrently and independently by two groups of nurses (N1 and N2) for the evaluation of inter-rater reliability, while for test–retest reliability, N1 and N2 performed the second rating on the following day [24]. The time necessary to complete the assessment with the I-MOBID2 was reported to evaluate its ease of use in clinical practice. In particular, an average execution time of 5.38 min was obtained, confirming the

a)

Scala del Dolore I-MOBID2

MOBILIZZAZIONE - OSSERVAZIONE - COMPORTAMENTO – INTENSITA' - DEMENZA

Nome del paziente: Data: Ora: Unità:

Presta attenzione al comportamento di dolore del paziente durante la cura mattutina. Osserva il paziente prima di iniziare la mobilizzazione. Spiega chiaramente cosa sta per succedere. Guida con attenzione il paziente attraverso le attività da 1 a 5. Inverti immediatamente il movimento se si percepisce un comportamento di dolore. Valuta la tua osservazione dopo ogni attività:

Comportamento di dolore

Spunta le caselle per i Rumori di dolore, l' Espressione facciale e la Difesa, ogni volta che hai osservato un simile comportamento di dolore

Rumori di dolore	Espressione Facciale	Difesa
Ahia!	Smorfie	Bloccarsi
Gemere	Accigliamento	Stare in guardia
Ansimare	Bocca serrata	Spingere
Urlare	Strizzare gli occhi	Rannicchiarsi

Intensità del dolore

In base al comportamento del dolore, valuta l'intensità con una croce sulle linee (0-10)

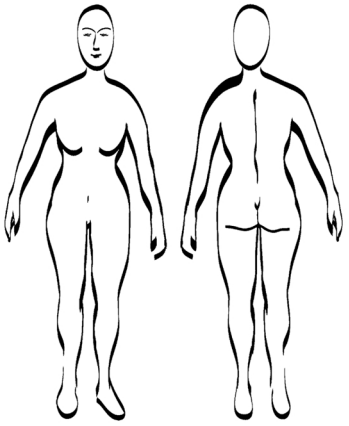
	PUOI SPUNTARE PIÙ CASELLE PER OGNI ATTIVITÀ	QUANTO INTENSO CONSIDERI IL DOLORE? 0 è assenza di dolore e 10 è il peggior dolore possibile
1.Guida ad aprire entrambe le mani, una mano alla volta	☐ ☐ ☐	0 1 2 3 4 5 6 7 8 9 10
2.Guida ad allungare entrambe le braccia verso la testa, un braccio alla volta	☐ ☐ ☐	0 1 2 3 4 5 6 7 8 9 10
3.Guida ad allungare e piegare sia ginocchia sia fianchi, una gamba alla volta	☐ ☐ ☐	0 1 2 3 4 5 6 7 8 9 10
4.Guida a girarsi nel letto da entrambi i lati	☐ ☐ ☐	0 1 2 3 4 5 6 7 8 9 10
5.Guida a sedersi al capezzale	☐ ☐ ☐	0 1 2 3 4 5 6 7 8 9 10

b)

Hai osservato, oggi o negli ultimi giorni (una settimana), che il paziente ha manifestato comportamenti di dolore legati alla testa, agli organi interni e/o alla pelle, che possono essere causati da una malattia, ferita, infezione e/o lesione?

Comportamento di dolore

Traccia una o più croce/i sul disegno del dolore (davanti e dietro), in base al comportamento di dolore osservato (Rumori del dolore, Espressione facciale e Difesa



Intensità del dolore

In base al comportamento del dolore, valuta l'intensità con una croce sulle linee (0-10)

QUANTO INTENSO CONSIDERI IL DOLORE?

0 è assenza di dolore e 10 è il peggior dolore possibile

6.Testa, bocca, collo	0 1 2 3 4 5 6 7 8 9 10
7.Cuore, polmone, parete toracica	0 1 2 3 4 5 6 7 8 9 10
8.Addome	0 1 2 3 4 5 6 7 8 9 10
9.Pelvi, organi genitali	0 1 2 3 4 5 6 7 8 9 10
10.Pelle	0 1 2 3 4 5 6 7 8 9 10

Sulla base di tutte le osservazioni, valuta l'intensità complessiva del dolore del paziente 0 1 2 3 4 5 6 7 8 9 10

Fig. 2. The Italian version of the Mobilization–Observation–Behavior–Intensity–Dementia, the I-MOBID-2, a) part 1 and b) part 2.

Table 2
Expert agreement on the relevance of each item to the content of the Italian version of the MOBID2, the I-MOBID2, and on the entire scale in terms of item (I-) and scale (S-) content validity index (CVI). I-CVI represents the Content Validity of individual Items, i.e. the proportion of experts rating the item a relevance score of 3 or 4. S-CVI/Ave is the average of the I-CVIs for all the items of the scale. S-CVI/UA consists in the proportion of items that achieves a relevance rating of 3 or 4 by all the experts (n = 7).

Item	Expert 1	Expert 2	Expert 3	Expert 4	Expert 5	Expert 6	Expert 7	Number Agreement	I-CVI
1	2	2	2	2	3	4	4	3	0.43
2	3	4	3	3	4	4	4	7	1
3	4	4	3	3	4	4	4	7	1
4	3	4	4	4	3	4	4	7	1
5	3	3	4	4	3	4	4	7	1
6	3	3	3	2	3	3	4	6	0.86
7	4	3	3	4	4	4	3	7	1
8	2	4	4	4	4	4	3	6	0.86
9	3	2	3	3	4	4	4	6	0.86
10	2	3	3	3	4	3	4	6	0.86
								S-CVI/Ave	0.89
								TOTAL AGREEMENT	5
								S-CVI/UA	0.5

Table 3
The participants' (N = 11) characteristics show the presence of pain according to the physician's assessment in 7 out of 11 patients, aged 73–94 years and with absent communication capabilities.

Patient identification code	Age	Mini-mental state examination (MMSE)	Diseases associated to pain
1	85	10.3	– Bilateral gonarthrosis; – Discal protrusion L5-S1 with discal arthrosic alterations and L1 vertebral collapse.
2	94	10	– No
3	90	5	–Bilateral coxarthrosis
4	73	2	–No
5	92	1	–Rheumatic polymyalgia, shoulder chronic tenosynovitis, generalized osteoarthrosis, left knee prothesis, lumbar scoliosis
6	93	5	–No
7	90	2	–Cicatricial pemphigoid
8	84	6.7	–Previous pertrochanteric femoral fracture, arthrosis
9	75	0	–No
10	84	2.4	–Varus knees, 4th and 5th foot fingers amputation
11	85	6.2	–Gonarthrosis

feasibility of use of the instrument.

3.5. Percentage of body surface in pain

Pain prevalence was measured based on the percentage of body surface in pain. Neck, nape, head, shoulder, forearm, hands, hips, knees and legs were recorder most often, demonstrating the highest prevalence for musculoskeletal and low back pain. Pain prevalence ranges from 11% to 17% (4 patients) to 21.5–45% (7 patients), highlighting a high percentage of body surface in pain for the 63.6% of the participants to the trial. The pain prevalence is illustrated in Table 5.

3.6. Internal consistency

The internal consistency represents the level at which the items (i) making up the scale actually measure the same construct, i.e. pain. The results obtained demonstrate the best inter-item correlation for the following items: i1-i2 = 0.665; i1-i3 = 0.641; i3-i4 = 0.710; i3-i10 = 0.510; i4-i5 = 0.517; i4-i6 = 0.450; i4-i9 = 0.475; i5-i3 = 0.529; i5-i9 = 0.512; i6-i9 = 0.482; i8-i10 = 0.494. Based on the statistical analysis, the item 7 (i7) was removed from the Chronbach's α score calculation having a variance= 0. The inter-item correlation matrix is reported in Table 6.

The total Cronbach's α = 0.751 demonstrates good internal consistency of the scale, since the Cronbach's α coefficient of a scale should be > 0.7 and < 0.9. Interestingly, under the present experimental conditions, the deletion of the items 2 and 8 could improve the overall internal consistency of the scale. The item-total and reliability statistics based on the I-MOBID2 are reported in Table 7.

3.7. Construct validity

The construct validity is calculated as the correlation between the overall pain intensity score and the maximum item score of I-MOBID2 Part 1 and 2 rated by healthcare assessors and it is expressed as rho. The construct validity is demonstrated by statistically significant Spearman rank order correlation of the overall pain intensity score with the maximum item score of I-MOBID2 Part 1 and 2. Rho= 0.748 for the overall pain intensity score with the maximum item score of I-MOBID2 Part 1 corresponds to $p < 0.05$ for 11 patients and rho is very high (0.895) and statistically significant ($p < 0.01$) for the overall pain intensity score with the maximum item score of I-MOBID2 Part 2. The construct validity measures are reported in Table 8.

3.8. Reliability

Inter-rater and test-retest reliability for pain behavior indicators and for pain drawing are retained in comparison with the original version of the scale. Since the inter-rater and test-retest agreement about the presence of pain for pain behavior indicators in the Part 1 of I-MOBID2 is total, the inter-rater and test-retest K statistics is calculated for pain drawings in the Part 2 of I-MOBID2. The scoring of K is: ≤ 0.20 (poor), 0.21–0.40 (fair), 0.41–0.60 (moderate), 0.61–0.80 (good), ≥ 0.81 (very good agreement). In particular, the Cohen's K = 0.744 demonstrates good inter-rater and test-retest agreement for pain drawings in the Part 2 of I-MOBID2 (Table 9).

The inter-rater reliability for pain intensity scores and test–retest reliability at day 1 and 2 for I-MOBID2 were assessed by Intraclass Correlation Coefficient (ICC), using one-way random model since the patients assessed do not represent a variable. The scoring of intraclass correlation coefficient ICC ≥ 0.7 is reliable and ICC ≥ 0.80 represents good to excellent reliability. Therefore, the inter-rater reliability of the I-MOBID2 is good as demonstrated by average measure of relative reliability across the rater ICC = 0.778, that is reasonably higher than the absolute reliability by ratings of a single rater (ICC = 0.637) (Table 10). The test-retest reliability is good to excellent as highlighted by average measure of relative reliability across the rater ICC = 0.949 and absolute reliability of a single test ICC = 0.902 (Table 11).

Therefore, the inter-rater (ICC = 0.778) and test-retest

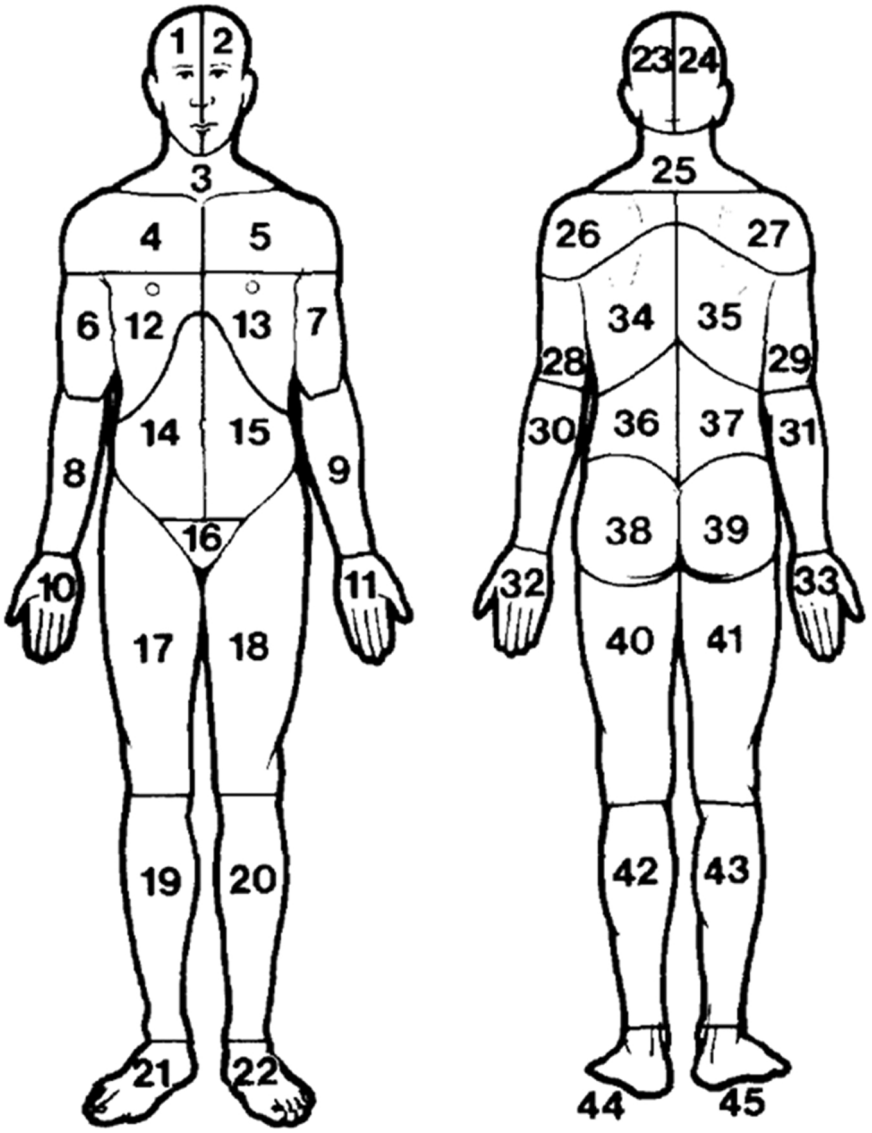


Fig. 3. The pain locations are divided into 45 anatomical areas for scoring of pain distribution and extent.
Reproduced with permission from [43].

Table 4
Conversion of the body areas scores to percentage of body surface in pain.

Area numbers	Percent each
25, 26, 27	0.50
4, 5, 16	1.00
3, 8, 9 10, 11, 30, 31, 32, 33	1.50
1, 2, 21,22, 23, 24, 44, 45	1.75
6, 7, 12, 13, 28, 29, 36, 37	2.00
38, 39	2.50
14,15	3.00
19, 20, 42, 43	3.50
34, 35	4.00
17,18, 40, 41	4.75

Source:Reproduced with permission from [43].

(ICC = 0.902) reliability is good to excellent.

4. Discussion

The results of the process of I-MOBID2 translation, adaptation and validation provide the clinicians with a very easy to apply pain assessment tool for non-communicative patients suffering from severe dementia, one of a kind since capable to assess both musculoskeletal and visceral, even concealed, pain conditions. The I-MOBID2, obtained from a rigorous stepwise process of forward and back translation, proves to retain most of the psychometric features of the originally developed MOBID2 and to be easy for clinical use, since only ~5–6 min are required for its completion. Face validity and content validity are very good with remarkable I-CVI values for all the items, except the item 1, ranging from 0.86 to 1. The S-CVI/Ave= 0.89 confirms a very good degree of experts' agreement and, consequently, of content validity for the overall scale. According to the Cronbach's α score statistics, the internal consistency of the Italian version of the MOBID2, i.e. the I-MOBID2 pain assessment scale, is good with an overall Cronbach's α coefficient= 0.751. Furtherly, inter-item correlation is good for the following items: i1-i2 = 0.665; i1-i3 = 0.641; i3-i4 = 0.710; i3-i10 = 0.510; i4-i5 = 0.517; i4-i6 = 0.450; i4-i9 = 0.475; i5-i3 = 0.529; i5-i9 = 0.512; i6-i9 = 0.482; i8-i10 = 0.494. In the present experimental setting, if the items 2 and 8 are deleted, Cronbach's α of I-MOBID2 increases up to 0.768 and 0.752, respectively. The construct validity of the Italian version of the scale is high as confirmed by

Table 5
Pain prevalence in the cohort recruited. The most frequent pain conditions are musculoskeletal and low back. Pain prevalence ranges from 11% to 17% (4 patients) to 21.5–45% (7 patients). Therefore, the 63.6% of the patients enrolled to the trial experiences pain in a percentage of body surface equal to 21.5–45%.

Patient identification code	Age	Diseases associated to pain	Pain localizations on pain drawing	Percentage of body surface in pain
1	85	– Bilateral gonarthrosis; – Discal protrusion L5-S1 with discal arthrosic alterations and L1 vertebral collapse.	Knees and legs, shoulder blade humeral joint, cervical location and head	4.75 + 4.75 + 0.50 + 1.00 + 0.50 + 1.75 + 1.75 = 15%
2	94	–No	Forearm, shoulder blade humeral joint, hand, knees and head	1.50 + 1.50 + 1.00 + 4.75 + 4.75 + 1.75 + 1.75 = 17%
3	90	–Bilateral coxarthrosis	Head, shoulder blade humeral joint, knees, coxofemoral joints, pelvis, low back pain	1.75 + 1.75 + 1.00 + 4.75 + 4.75 + 4.75 + 4.75 + 1.00 + 2.00 + 2.00 + 2.50 + 2.50 = 33.5%
4	73	–No	Neck, nape, arm, hands, knees, legs, low back pain	1.50 + 0.50 + 2.00 + 1.50 + 1.50 + 4.75 + 4.75 + 3.50 + 3.50 + 2.50 + 2.50 = 28.5%
5	92	–Rheumatic polymyalgia, shoulder chronic tenosynovitis, generalized osteoarthrosis, left knee prothesis, lumbar scoliosis	Head, shoulder, forearm, hand, hips, knees	1.75 + 1.75 + 1.00 + 1.50 + 1.50 + 4.75 + 4.75 + 4.75 + 4.75 = 26.5%
6	93	–No	Nape, shoulder, forearm, hands, hip, knees, legs, low back pain, hand	0.50 + 1.00 + 1.50 + 1.50 + 1.50 + 4.75 + 4.75 + 4.75 + 3.50 + 3.50 + 3.50 + 2.50 + 2.50 + 1.50 = 37.25%
7	90	–No	Nape, shoulder, hands, knees, low back pain, hips, thighs, legs	0.50 + 1.00 + 1.50 + 1.50 + 4.75 + 4.75 + 4.75 + 4.75 + 2.50 + 2.50 + 4.75 + 4.75 + 3.50 + 3.50 = 45%
8	84	–Previous pertrochanteric femoral fracture, arthrosis	Nape, hip, knee, shoulder	0.50 + 1.00 + 4.75 + 4.75 = 11%
9	75	–No	Nape, shoulder, hip, knee	0.50 + 1.00 + 4.75 + 4.75 = 11%
10	84	–Varus knees, 4th and 5th foot fingers amputation	Nape, shoulders, lumbar region, abdomen, knees, hip, pelvis, hand	0.50 + 1.00 + 1.00 + 2.00 + 2.00 + 3.00 + 3.00 + 4.75 + 4.75 + 4.75 + 1.00 + 1.50 = 29.25%
11	85	–Gonarthrosis	Nape, shoulder, hips, pelvis, knees	0.50 + 1.00 + 4.75 + 4.75 + 1.00 + 4.75 + 4.75 = 21.5%

statistically significant rho of the overall pain intensity score with the maximum item score of I-MOBID2 Part 1. In particular, rho = 0.748 for Spearman rank order correlation of the overall pain intensity score with the maximum item score of I-MOBID2 Part 1 corresponds to $p < 0.05$ for 11 patients and rho= 0.895 corresponds to $p < 0.01$ for 11 patients for the overall pain intensity score with the maximum item score of I-MOBID2 Part 2. Neck, nape, head, shoulder, forearm, hands, hips, knees and legs were recorded most often, demonstrating the highest prevalence for musculoskeletal and low back pain in accordance with the diseases associated to pain reported during the clinical physical examination with pain diagnosis and the anamnesis collection. The presence of pain originating from head, skin and internal organs was reported less frequently than from musculoskeletal system in agreement with the original tool validation study [9]. However, chronic and, mainly, neuropathic pain is still remarkably undertreated in our setting and even more during the COVID-19 pandemic [4]. A noteworthy percentage of body surface in pain was demonstrated for the 63.6% of the participants to the trial, in agreement with the international literature highlighting

Table 6
Inter-item correlation matrix of the I-MOBID2. The best values of inter-item correlation based on Chronbach's α score calculation are the following: i1-i2 = 0.665; i1-i3 = 0.641; i3-i4 = 0.710; i3-i10 = 0.510; i4-i5 = 0.517; i4-i6 = 0.450; i4-i9 = 0.475; i5-i3 = 0.529; i5-i9 = 0.512; i6-i9 = 0.482; i8-i10 = 0.494.

	i1	i2	i3	i4	i5	i6	i8	i9	i10
i1	1.000	0.665	0.641	0.394	0.109	0.050	0.135	-0.297	0.231
i2	0.665	1.000	0.168	0.313	0.027	0.171	-0.113	-0.192	-0.318
i3	0.641	0.168	1.000	0.710	0.529	0.189	0.215	0.235	0.510
i4	0.394	0.313	0.710	1.000	0.517	0.450	0.083	0.475	0.191
i5	0.109	0.027	0.529	0.517	1.000	0.343	0.036	0.512	0.542
i6	0.050	0.171	0.189	0.450	0.343	1.000	0.092	0.482	0.083
i8	.135	-0.113	0.215	0.083	0.036	0.092	1.000	0.184	0.494
i9	-0.297	-0.192	0.235	0.475	0.512	0.482	0.184	1.000	0.170
i10	0.231	-0.318	0.510	0.191	0.542	0.083	0.494	0.170	1.000

Table 7
Item-total and reliability statistics of the I-MOBID2. The total Cronbach's α = 0.751 demonstrates good internal consistency of the scale. If the items 2 and 8 are deleted, Cronbach's α increases to 0.768 and 0.752, respectively.

	Scale mean if item deleted	Scale variance if item deleted	Corrected item-total correlation	Squared multiple correlation	Cronbach's α if item deleted
i1	28.6364	153.855	0.362	0.902	0.738
i2	25.4545	169.673	0.139	0.845	0.768
i3	24.7273	145.818	0.728	0.857	0.694
i4	26.1818	130.564	0.702	0.719	0.678
i5	29.1818	128.164	0.602	0.749	0.694
i6	26.4545	146.673	0.407	0.354	0.732
i8	30.0000	169.600	0.236	0.458	0.752
i9	29.3636	152.655	0.361	0.658	0.739
i10	29.4545	146.073	0.387	0.805	0.737
Cronbach's α total					0.751

over 60% demented patients in nursing homes to experience pain [25], most often under-diagnosed [44.45]. Particularly, the pain prevalence described in our setting doubles the 32% described for Italian facilities [46]. A high rate of inter-rater and test-retest agreement demonstrated by Cohen's K = 0.744, with relatively short training. The inter-rater (ICC = 0778) and test-retest (ICC = 0.902) reliability are good to excellent, thus making I-MOBID2 a useful tool suitable also for future development in community setting with administration by caregivers. A multicentric clinical trial is ongoing to assess responsiveness to change, according to the COSMIN initiative, that means it detects change over time in the construct to be measured, recruiting a wider population of participants meeting the inclusion criteria. In the frame of this study both the responsiveness to change in the context of analgesic treatment and with agitation [47] will be evaluated because the most important aim of the I-MOBID2 validation consists in providing a safe and effective pain treatment to the fragile population of severe dementia patients. In particular, the effectiveness of the analgesics administered to patients affected by severe dementia and the reduction of agitation due to analgesic treatment will be assessed. The I-MOBID2 is the pain assessment tool selected for the evaluation of pain in a randomized, double-blind, placebo-controlled trial (NCT04321889) [48] to evaluate the efficacy of NanoBEO [49], the engineered essential oil of bergamot endowed with strong preclinically proven analgesic [44,50] and anxiolytic [51] properties, in the control of agitation and pain in patients suffering from severe dementia.

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CRediT authorship contribution statement

D. Scuteri: Conceptualization, Data curation, Formal analysis, Methodology. **M. Contrada:** Data curation, Formal analysis, Methodology. **T. Loria:** Data curation, Formal analysis, Methodology. **D. Sturino:** Data curation, Formal analysis, Methodology. **A. Cerasa:** Data curation, Formal analysis, Methodology. **P. Tonin:** Conceptualization.

Table 9
Inter-rater and test-retest agreement of pain behavior indicators of I-MOBID2 part1 and of pain drawing of I-MOBID2 part2 evaluated as Kappa statistics (K). Cohen's K = 0.744 with 0.01 significance, demonstrating good inter-rater agreement.

		Value	Asymp. std. error[a]	Approx. T[b]	Approx. Sign.
Measure of agreement	Kappa	0.744	0.236	2.553	0.011
N. of valid cases		11			

[a] Not assuming the null hypothesis.
[b] Using the asymptotic standard error assuming the null hypothesis.

Table 8
Construct validity of I-MOBID2 measured as Spearman's rank order correlation (rho) statistics. Rho = 0.748 for Spearman rank order correlation of the overall pain intensity score with the maximum item score of I-MOBID2 Part 1 corresponds to $p < 0.05$ for 11 patients. Rho = 0.895 for the overall pain intensity score with the maximum item score of I-MOBID2 Part 2 corresponds to $p < 0.01$ for 11 patients.

			Overall intensity	MAximum item score Part 1	Maximum item score Part 2
Spearman's rho	Overall intensity	Correlation coefficient	1.000	0.748*	0.895**
		Two-tailed significance	.	0.013	0.000
		N	10	10	10
	Maximum item score Part 1	Correlation coefficient	0.748*	1.000	0.530
		Two-tailed significance	0.013	.	0.094
		N	10	11	11
	Maximum item score Part 2	Correlation coefficient	0.895**	0.530	1.000
		Two-tailed significance	0.000	0.094	.
		N	10	11	11

* Significant correlation $p < 0.05$.
** Significant correlation $p < 0.01$.

Table 10
Inter-rater reliability expressed as inter-rater intraclass correlation coefficient (ICC). The inter-rater reliability is good as demonstrated by average measure of relative reliability across the raters ICC = 0.778. The model used for ICC statistics is the one-way random.

	Intraclass correlation	95% Confidence Interval		F Test with true value 0			
		Lower limit	Upper limit	Value	Degrees of freedom 1	Degrees of freedom 2	Sign.
Single measures	0.637	0.088	0.894	4.508	9	10	0.014
Average measures	0.778	0.162	0.944	4.508	9	10	0.014
Chronbach's α	0.754						

One-way random model (since patients are not a variable). Single measures: absolute reliability by ratings of a single rater; Average measures: relative reliability across the raters.

Table 11
Test-retest reliability expressed as inter-rater intraclass correlation coefficient (ICC). The test-retest reliability is good to excellent as demonstrated by average measure of relative reliability across the tests ICC = 0.942. The model used for ICC statistics is the one-way random.

	Intraclass correlation	95% Confidence Interval		F Test with true value 0			
		Lower limit	Upper limit	Value	Degrees of freedom 1	Degrees of freedom 2	Sign.
Single measures	0.902	0.693	0.972	19.420	10	11	0.000
Average measures	0.949	0.818	0.986	19.420	10	11	0.000
Chronbach's α							0.943

One-way random model (since patients are not a variable). Single measures: absolute reliability by ratings of a single test; Average measures: relative reliability across the two tests.

G. Sandrini: Conceptualization. **S. Tamburin:** Conceptualization. **A.C. Bruni:** Conceptualization. **P. Nicotera:** Conceptualization. **M.T. Corasaniti:** Conceptualization. **G. Bagett:** Conceptualization. All authors have read and approved the final manuscript.

Conflict of interest statement

The authors declare no conflict of interest.

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