

REVIEW

Italian Intersociety Recommendations on pain management in the emergency setting (SIAARTI, SIMEU, SIS 118, AISD, SIARED, SICUT, IRC)

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ABSTRACT

Background. Pain is the primary reason for admission to the Emergency Department (ED). However, the management of pain in this setting is often inadequate because of opioidphagia, fear of excessive sedation, and fear of compromising an adequate clinical assessment.

Methods. An intersociety consensus conference was held in 2010 on the assessment and treatment of pain in the emergency setting. This report is the Italian Intersociety recommendations on pain management in the emergency department setting.

Results. The list of level A recommendations includes: 1) use of IV acetaminophen for opioid sparing properties and reduction of opioid related adverse events; 2) ketamine-midazolam combination preferred over fentanyl-midazolam

fentanyl-propofol in pediatric patients; 3) boluses of ketamine IV (particularly in the population under the age of 2 years and over the age of 13) can lead to impairment of the upper airways, including the onset of laryngospasm, requiring specific expertise and skills for administration; 4) the use of ketamine increases the potential risk of psychomotor agitation, which can happen in up to 30% of adult patients (this peculiar side effect can be significantly reduced by concomitant systemic use of benzodiazepines); 5) for shoulder dislocations and fractures of the upper limbs, the performance of brachial plexus block reduces the time spent in ED compared to sedation; 6) pain relief and the use of opioids in patients with acute abdominal pain do not increase the risk of error in the diagnostic and therapeutic pathway in adults; 7) in newborns, the administration of sucrose reduces behavioural responses to blood sampling from a heel puncture; 8) in newborns, breastfeeding or formula feeding during the procedure reduces the measures of distress; 9) in pediatric patients, non-pharmacological techniques such as distraction, hypnosis and cognitive-behavioural interventions reduce procedural pain caused by the use of needles; 10) in pediatric patients, preventive application of eutectic mixtures of prilocaine and lidocaine allows arterial and venous samples to be taken in optimum conditions; 11) in pediatric patients, the combination of hypnotics (midazolam) and N₂O is effective for procedural pain, but may be accompanied by loss of consciousness.

Conclusion. The diagnostic-therapeutic pathway of pain management in emergency should be implemented, through further interdisciplinary trials, in order to improve the EBM level of specific guidelines.

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Key words: Analgesia - Pain - Emergency treatment - Wounds and injuries - Child.

Pain is the primary reason for admission to the Departments of Emergency and Urgent Care (DEA-*Dipartimento di Emergenza e Accettazione*)¹ and adequate analgesia is one of the cornerstones of effective emergency management. However, numerous studies have documented inadequate pain control in the prehospital setting and in the Emergency Department (ED).²⁻⁴

The aim of these recommendations is to provide all emergency operators with an interdisciplinary review on diagnosis and treatment of pain in the different emergency contexts. Scientific literature highlighted the trend towards systematic oligoanalgesia and opiophobia in the context of an emergency department practice.⁵⁻⁹

In light of the recent introduction of the Italian Law 38/2010,¹⁰ containing the implementation of the project "Ospedale-territorio senza dolore" (Pain-Free Hospital and Territory) (Art. 6) and the obligation to report the assessment of pain in the medical record (Art. 7), the interdisciplinary working group asserts the need for a document that could be a useful tool for healthcare professionals in diagnosing and treating pain in the emergency setting.

Materials and methods

The project emerged from the collaboration between two SIAARTI Study Groups: "Emergency" and "Acute and Chronic Pain". It was then extended to other interdisciplinary and inter-professional societies: Società Italiana di Medicina di Emergenza Urgenza (SIMEU), Italian Resuscitation Council (IRC), Società Italiana di Anestesia Rianimazione Emergenza e Dolore (SIARED), Società Italiana Sistema 118 (SIS 118), Associazione Italiana per lo Studio del Dolore (AISD), Società Italiana di Chirurgia d'Urgenza e del Trauma (SICUT).

During the annual Area Culturale Dolore SIAARTI convention in 2010, an intersociety consensus conference was held (SIAARTI, SIMEU, IRC, SIARED, SIS 118, AISD, SICUT) on the assessment and treatment of pain in the emergency setting. Following identification of clinical needs, a careful review of the literature was carried out according to evidence-based medicine (EBM) methodology.

Bibliographical research was conducted using PubMed (www.pubmed.gov) and including human studies from January 1991 to June 2013.

An advanced draft, drawn up in 2012, was brought to the attention of the respective Executive Councils of all the scientific societies in-

TABLE I.—FLACC scale (face, legs, activity, cry, consolability).

Category	Score		
	0	1	2
Face	Neutral expression or smile	Occasional grimace or frown, withdrawn, disinterested expression	Frequent to constant frown, clenched jaw, quivering chin
Legs	Normal or relaxed position	Uneasy, restless, tense	Kicks or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense	Arched, rigid or jerking
Cry	No cry (awake or asleep)	Moans or whimpers, occasional complaint	Crying steadily, screams or sobs, frequent complaints
Consolability	Content, relaxed	Reassured by occasional touching, hugging or being talked to; distractable	Difficult to console or comfort

The FLACC scale is indicated for newborns and children under the age of 7. Each of the categories can be assigned a score from 0 to 2, for a total of between 0 and 10. Modified from Merkel SI *et al.*²²

involved, which produced their comments by October 30, 2012. The final version was released in June 2013 and the Scientific Societies involved expressed their approval.

The literature review has been validated according to the levels of evidence proposed by the SIGN guidelines.¹¹

A series of questions were identified regarding issues for which it is not possible to give validated EBM recommendations, due to the lack of adequate scientific literature available. This document includes the answers that obtained the agreement of >75% of participants, in accordance with the Delphi method.¹²

By applying GRADE methodology to level A findings, a list of evidence, which can be labelled as “strong recommendations”, is abstracted at the end of the conclusions.^{11, 13}

The authors have disclosed that they have no significant relationships with or financial interests in any commercial companies related to these recommendations. They also declared that neither public nor private sponsorship/funding supported this study. Finally, the authors committed to revise these recommendations by 2018.

Pain assessment in the emergency setting

An accurate assessment of the patient and the pain symptoms is essential for the choice both of the analgesic and of its route of administration.

It is equally important to reassess the patient after each analgesic intervention (Level B).¹⁴

The diagnosis of acute pain and its treatment should be performed consistently for all patients treated in emergency, both in a prehospital context and in the ED. Upon their arrival in the ED, all patients should be assessed for any allergies and intolerances, their level of pain should be measured and its intensity should be reported in the clinical chart (medical records, triage card and 118-national emergency system-card).^{15, 16}

The introduction of pain assessment among the parameters to be recorded during triage leads to a major clinical improvement, as it reduces the time required for patients to receive appropriate analgesic treatment.¹⁷ As a first choice, it is appropriate to use the NRS (Numeric Rating Scale) from 0, no pain, to 10, maximum pain imaginable.¹⁸ A reasonable alternative is the semantic assessment of pain using the VRS (Verbal Rating Scale).^{19, 20} In pediatric patients it is possible to use the FACES pain rating scale for children who are able to speak²¹ and the FLACC (Face, Legs, Activity, Cry, Consolability) scale for those who are unable to speak^{22, 23} (Table I).

In adults with mild-moderate cognitive impairment, it is possible to use descriptive scales enabling verbal assessment,^{24, 25} while in adults who are unable to speak it is necessary to adopt the so-called Pain Assessment IN Advanced Dementia (PAINAD)²⁶ scale (Table II).

TABLE II.—PAINAD (*Pain Assessment IN Advanced Dementia*) scale.

Category	Score		
	0	1	2
Breathing	Normal	Occasional laboured breathing, short period of hyperventilation	Laboured breathing, hyperventilation, Cheyne-Stokes respiration
Vocalisation	None	Occasional moans, occasional negative expressions	Repeated calls, moans, crying
Facial expression	Smiling or inexpressive	Sad, frightened, frown	Grimaces
Body language	Relaxed	Tense, nervous movements, restlessness	Rigid, fidgety, knees bent, striking out
Consolability	No need for consolation	Distracted or reassured by voice or touch	Inconsolable, cannot be distracted nor reassured

The PAINAD scale is indicated for adult patients who are unable to speak. Each of the categories can be assigned a score from 0 to 2, for a total of between 0 and 10. Modified from Costardi D *et al.*²⁶

Identification of red flags

When first approaching a patient with pain symptoms, it is strongly recommended to obtain a quick medical history and an initial physical examination, in order to exclude diagnostic red flags²⁷ (Appendix 1) and to identify patients who require further in-depth investigation²⁸ (Level B).

Prehospital and Emergency Department care

In the prehospital assistance and on arrival at the ED, the interdisciplinary group proposed the following recommendations (Level D):

1. perform systematic assessment and documentation of pain in appropriate forms. Proceed to reassessment after each analgesic intervention;
2. define clinical protocols of outpatient pain treatment in accordance with the local 118 operative center and the hospital EDs;
3. provide emergency vehicles with an adequate supply of analgesics and specific protocols for their use;
4. provide special training sessions for health-care professionals involved in territorial health emergency activities.

Prehospital analgesia

Moderate to severe pain is common in both adult and pediatric patients in a prehospital environment²⁹ (Level D); it is, therefore, required to carefully plan the analgesic regimen (drug,

dose and route of administration) for optimal efficacy.

The ideal prehospital analgesic should be easy to use, safe, effective, and have a predictable dose-response relationship with rapid onset and a short duration of action.

The first-line medications for prehospital analgesia, in the case of severe pain (NRS 7-10), are opiates; intravenous (IV) morphine, fentanyl and tramadol are equally effective in a prehospital environment³⁰⁻³² (Level B).

There is no proven difference between fentanyl and IV morphine in ensuring effective analgesia for up to 30 minutes during prehospital care³³⁻³⁵ (Level B).

The recommended adult dosages are reported in Appendix 2.

Preventive use of IV paracetamol provides good analgesia and reduces morphine consumption and the relative adverse events, as shown in postoperative pain trials³⁶ (Level A).

In a prehospital environment it is possible to ensure effective analgesia by using ketamine³⁷⁻⁴⁰ (Level D).

The use of opioids in patients with traumatic brain injury should be based on an individual assessment of the risk-benefit ratio on the basis of potential side effects, such as the possibility of interfering with the neurological assessment and the possibility of causing respiratory depression with hypercapnia and increased intracranial pressure.^{41, 42}

Analgesia in the Emergency Department

In the ED systemic analgesia and regional techniques should be considered.^{43, 44}

SYSTEMIC ANALGESICS

Paracetamol (Acetaminophen).—For mild pain (NRS 1-3), paracetamol is the first choice, in its oral formulation at the dosage of 1 g, repeatable every 8 hours.⁴⁵ It can also be used in its orodispersible formulation, in a protocol based on pain assessment by nurses, enabling satisfactory analgesia to be achieved in ED.⁴⁶

For moderate pain (NRS>3), paracetamol can be used at the dosage of 1 g IV for up to 4 daily doses, to reduce opioids consumption (Appendix 2). Paracetamol 1 g IV has proven effective compared with a dose of 0.1 mg/kg of morphine, in the reduction of pain associated with renal colic⁴⁷ and in the treatment of moderate/severe isolated injury to the limbs.⁴⁸

A cross-sensitivity between NSAIDs and paracetamol allergy has been described. If the patient is combative and uncooperative, pain and drug/alcohol overdose should be considered, when prescribing paracetamol.

Non-steroidal anti-inflammatory drugs (NSAIDs).—NSAIDs are indicated for the treatment of mild-moderate musculoskeletal pain, trauma, renal or biliary colic and for certain forms of acute headache.⁴⁹⁻⁵¹ Prior to administration of NSAIDs, it is recommended to take a quick medical history for the purposes of exclusion of any allergies or side effects (gastropathies, coagulopathies, renal failure).

Tramadol.—Tramadol can be used for moderate-severe pain as a single IV treatment or orally in the available combinations with paracetamol.⁵² In the management of pain due to trauma IV tramadol is an acceptable alternative to morphine⁵³ (Level B).

Opioids.—In ED, opioids are frequently prescribed for severe pain and they should preferably be administered intravenously. Doses should be adjusted according to age and titrated until the desired effect is reached (halving the initial level

of pain or otherwise NRS<4), using the lowest effective dose. Patients treated with *i.v.* opioids require close observation in a protected environment, where continuous monitoring with pulse oximetry/capnometry, oxygen therapy and naloxone are available, due to the possible side effects (sedation, hypotension and respiratory depression)^{54, 55} (Level D).

The best method of ensuring rapid and effective analgesia is to titrate the opioids to clinical effect, by stratifying patients according to pathology, age, comorbidities, concomitant use of psychotropic medications.

Most patients report effective analgesia 10 minutes after IV morphine 0.1 mg/kg followed by 0.05 mg/kg every 5 minutes³⁴ (Level B). In hemodynamically unstable or potentially critical patients, individual titration with IV morphine is carried out with relatively low doses, equivalent to 1-2 mg, repeated every 5-10 minutes until the desired effects are reached; or alternatively, particularly in unstable patients, fentanyl can be used at the dose of 0.5-1 µg/kg IV, or intranasally (IN).

The combination of benzodiazepines and opioids may increase the risk of respiratory depression and desaturation, necessitating careful monitoring of the neurological state of the patient and the arterial saturation.⁵⁶

In children, 1.5 µg/kg IN fentanyl ensures effective analgesia in ED and procedural pain⁵⁷⁻⁶⁰ and it is the first choice for the treatment for severe pain (Level B).

In the case of “intractable” pain, which is non-responsive to a proper approach with titration of major opiates, it is necessary to activate a referral to the Pain Unit, if present in the hospital, or to the anaesthetist of the Acute Pain Service (APS) or the Medical Emergency Team (MET) (Level D).⁶¹

Although supported by recent scientific literature, immediate release (IR) opioids or rapid onset opioids (ROO), approved only for the treatment of breakthrough pain in the setting of chronic pain, can be used off-label for the treatment of acute pain only if included in the guidelines of the 118 centres and the ED, after approval of the local Ethics Committees. In order to manage any complications related to the use of opioids by

such routes, rapid venous or intraosseous access must be provided in an emergency.

Analgesics by inhalation.—The use of analgesics by inhalation is not common in Italy. In English literature, however, a mixture of nitrous oxide (N₂O) and 50% oxygen has been proposed for minor procedures in adults and children⁶² (Level B).

Ketamine.—The ketamine-midazolam combination is more effective and has fewer side effects than fentanyl-midazolam or fentanyl-propofol in reducing pediatric fractures in ED⁶³ (Level A). Boluses of IV ketamine result in significant morphine-sparing effect, ensuring adequate levels of analgesia if used in the treatment of severe pain due to trauma in the ED⁷ (Level B).

However, particularly under the age of 2 years and over 13, IV ketamine can lead to impairment of the upper airways and laryngospasm,⁶⁴ requiring specific expertise and skills for administration⁶⁵ (Level A).

Ketamine increases the potential risk of psychomotor agitation in up to 30% of adult patients, but side effects can be significantly reduced by concomitant use of benzodiazepines⁶⁶ (Level A)

Regional techniques

Topical local anesthetics (including liposomal formulations) (Level A), with (Level B) or without epinephrine, ensure effective analgesia in the treatment of wounds in the ED.⁶⁷

Regional anesthesia provides high-quality site-specific analgesia, avoids the potential risks of respiratory depression, sedation or bleeding, which are typical of opioids and NSAIDs,⁶⁸ and it is particularly indicated for the management of post-traumatic pain in the ED.

For fractures of the femoral neck, the three-in-one femoral block, in combination with IV morphine, ensures analgesia that is superior to IV morphine alone, reducing the use of rescue doses⁶⁹ (Level B). For rib fractures, continuous intercostal blocks improve lung function and pain control, and reduce the length of hospital stays⁷⁰ (Level B). For shoulder dislocations and fractures of the upper limbs, brachial plexus block reduced the time spent in the ED compared to sedation^{71,72} (Level A).

Peripheral nerve blocks, however, requires specific training, currently pertaining to anaesthetists and resuscitators. Therefore, emergency operators should improve their knowledge and systematic use of “elementary” regional techniques (subcutaneous, subfascial, truncular, plexus infiltrations with local anaesthetics), in order to reduce and/or eliminate post-traumatic and procedural pain.⁷³ Blockade of the iliac fascia, which is considered a safe technique because it is carried out far from vascular structures, ensures better analgesia than IV opioids alone in the treatment of femoral neck fracture⁷⁴ (Level B). However, even “elementary” regional techniques require specific experience and expertise.

Ultrasound-guided techniques can facilitate and improve the safety of regional techniques.⁷⁵ Therefore, educational courses aimed at improving knowledge of ultrasound-guided techniques should be implemented^{43,44} (Level B).

Non-pharmacological approaches

While analgesics are essential for pain control in the ED, the importance of non-pharmacological treatments should not be overlooked: application of ice, immobilisation of fractures, management of the psychological aspects of the patient, and patient information on the causes and the prognosis of his pain in order to reduce anxiety.⁷⁶

Analgo-sedation for procedural pain

The management of procedural pain in the ED normally requires a process of close multidisciplinary collaboration.

Current analgo-sedation usually includes midazolam, propofol, ketamine and opiates, resulting in a continuum of effects on consciousness, from anxiolysis to light sedation (or conscious sedation, *i.e.* without loss of verbal contact with the patient) and even to deep sedation (with loss of verbal contact) and actual general anesthesia.^{77,78}

As a rule, non-anaesthetists should limit their practice to conscious sedation techniques.

The mixtures of N₂O and 50% oxygen, self-administered by patients with one-way valves, are only partially effective and should be administered in environments with high laminar flows.⁷⁹

During analgosedation for procedural pain in the ED, the same levels of safety currently required in the operating theatre must be ensured, even for minor procedures.⁸⁰⁻⁸² The exact type of monitoring of the vital functions and extent of such monitoring remains controversial. The measurement of blood pressure, peripheral saturation and continuous ECG are considered unavoidable controls.⁸⁰ The use of continuous capnography remains controversial, for the limited availability of instruments, their cost and the risk of false positives. However, capnography may have a decisive role in detecting respiratory depression caused and/or masked by supplementary oxygen administration.⁸³⁻⁸⁶

Regional analgesia techniques and non-pharmacological methods should also be promoted.

No studies have determined that a fasting period is necessary before undergoing an analgosedation procedure in emergency.⁸⁷ Literature data are lacking to pronounce an absolute recommendation (Level D). In emergency conditions, for patients who cannot wait, recent intake of food is not an absolute contraindication for analgosedation; however, physicians must consider the risk of aspiration, balancing it with the potential benefit of pain control.⁸⁸

For patients who can wait, a fasting period of at least 2 hours should be observed for clear liquids, at least 4 hours for breast milk, and at least 6 hours for solids and non-breast milk.⁸⁹

Special conditions

Trauma

General recommendations for the treatment of pain in trauma patients (Level B) are:

1. to insert pain assessment on the triage charts of the trauma center;⁹⁰
2. to include elements of differential diagnostics of pain in the secondary assessment;
3. to develop methods of treatment such as:
 - appropriate use of paracetamol
 - use of opiate titration⁹¹
 - use of regional anesthesia for the transport and invasive procedures;
4. after the stabilisation phase, to identify the

patients who may develop chronic neuropathic pain due to inadequate analgesic treatment⁹² and make a “pro-active” plan for the prevention of chronic pain, including:

- continuous regional blocks⁹³
- treatment of neuropathic pain
- use of opioids even for prolonged periods in Intensive Care Units, use of guidelines for analgo-sedation, for the management of pain and the prevention of delirium^{94, 95}
- physio-kinesio-therapy and early rehabilitation
- early psycho-behavioral approach aimed at preventing and treating post-traumatic stress syndrome.⁹⁶

Abdominal pain

A common belief is that analgesia masks the signs and symptoms of acute abdominal pathologies.⁹⁷ Pain relief and the use of opioids in patients with acute abdominal pain do not actually increase the risk of error in the diagnostic and therapeutic pathway, neither in adults (Level A)⁹⁸ nor in children⁹⁹ (Level B). In the case of severe pain, the administration of opioids may be necessary. Although in the past the use of pethidine (meperidine) as a substitute for morphine was recommended, particularly for renal¹⁰⁰ and biliary colic because of the theoretical risk of spasm of smooth muscle, there is no current evidence supporting this position.

Headache

After excluding causes of headache that pose an immediate risk to the life and health of the patient (Appendix 1), a rapid and effective control of pain symptoms is recommended.¹⁰¹

For emergency treatment of migraine, prochlorperazine is superior to all the other classes of medications; triptans and dihydroergotamine are as effective as dopamine antagonists, but must be avoided in patients at vascular risk; NSAIDs and opioids can be used, but not as a first choice; magnesium may be a useful adjuvant, especially in pregnant patients (Level B).¹⁰²⁻¹⁰⁴

Elderly patients

In emergency departments and prehospital settings, elderly patients who complain about pain are less likely to receive analgesics compared with younger patients.^{105, 106}

For mild-moderate pain, the first choice is paracetamol 1000 mg orally, 3 times daily or IV paracetamol 500-1000 mg every 6 hours. Valid alternatives include combinations of paracetamol with weak opioids (codeine or tramadol)⁵⁴ or with low-dose oxycodone by oral route.¹⁰⁷

NSAIDs should not be considered first-line agents and should be used with extreme caution in elderly patients, because they are associated with renal failure and an increased risk of bleeding of the upper gastrointestinal tract.¹⁰⁸ Among NSAIDs, ibuprofen is the most reasonable choice (there is evidence suggesting to avoid indomethacin). It is recommended to use the lowest effective dose for a short period of time (e.g., 200-400 mg orally 3-4 times a day).^{109, 110} For elderly patients, NSAIDs and COX-2 inhibitors should always be prescribed in combination with a proton pump inhibitor.¹¹¹

Elderly patients tend to need lower doses of opioids compared with younger patients.

Terminally ill patients

In order to reduce the persistently high number of inappropriate admissions to the ED areas and the Intensive Care Departments for terminally ill patients, protocols should be adopted and shared between the 118 operating centers and the continuity of care network for terminally ill patients.¹¹² Protocols should contain the rules to be adopted in emergencies that occur in the course of palliative care, identifying in advance those that require hospital admission or temporary placement in the Short-Term Intensive Observation Unit (Level D).

Children

The main focus of pediatric scientific studies on pain control in emergency is the management of procedural pain.

In newborns, the administration of sucrose reduces behavioral responses to blood sampling

from a heel puncture¹¹³ (Level A); likewise, breastfeeding or formula feeding during the procedure reduces the measures of distress¹¹⁴ (Level A).

In pediatric patients, non-pharmacological techniques such as distraction, hypnosis and cognitive-behavioral interventions reduce procedural pain caused by the use of needles^{115, 116} (Level A); preventive application of eutectic mixtures of prilocaine and lidocaine allows arterial and venous samples to be taken in optimum conditions.¹¹⁷ "Needle-free" lidocaine/tetracaine patch can be used for needle injections and for surgical procedures in children from the age of 3 years and older.¹¹⁸ Minor surgical procedures (cutaneous sutures, reduction of fractures) can easily be carried out, by combining topical anesthesia and 50% inhalation of N₂O without the onset of major side effects.^{119, 120} The combination of midazolam and N₂O is effective but may be accompanied by loss of consciousness^{79, 121} (Level A). Administration of N₂O must be carried out in environments with an adequate number of air changes per hour. In experienced hands, a combination of hypnotics and analgesics is effective in reducing procedural pain of moderate intensity¹²² (Level B). Adverse events in pediatric patients are frequent in the absence of adequate monitoring, advanced training in cardiopulmonary resuscitation (Paediatric Advanced Life Support, PALS) and in the case of multiple medication use.

Recent reports reassess the use of ketamine in combination or not with propofol^{123, 124} and propose the use of dexmedetomidine, particularly for advanced medication in burn patients.¹²⁵

There are numerous reports of intranasal administration of opiates (fentanyl 1-2 µg/kg) as an alternative to IV morphine in a prehospital setting or in the ED,^{126, 127} also in the treatment of severe pain due to sickle-cell disease.¹²⁸

A partial response to the use of off-label analgesedation medications, which is the norm for paediatric patients, was recently given in the Determination of 27 July 2012 by the Italian Medicines Agency (AIFA), which authorised the commercial use of analgesic and sedative-hypnotic medications also for pediatric patients.¹²⁹

Pregnant patients

Pregnant women are at risk of not receiving adequate treatment of pain or not receiving any,

TABLE III.—FDA medication categories in pregnancy.

Category	Interpretation
A	Controlled studies in pregnant women fail to demonstrate an increased risk of fetal abnormalities to the fetus in the first trimester (and there is no evidence of a risk in later trimesters), and the possibility of fetal harm appears remote.
B	Either animal-reproduction studies have not demonstrated a fetal risk but there are no controlled studies in pregnant women, or animal-reproduction studies have shown an adverse effect (other than a decrease in fertility) that was not confirmed in controlled studies in women in the first trimester (and there is no evidence of a risk in later trimesters).
C	Either studies in animals have revealed adverse effects on the fetus (teratogenic or embryocidal or other) and there are no controlled studies in women, or studies in women and animals are not available. Drugs should be given only if the potential benefit justifies the potential risk to the fetus.
D	There is positive evidence of human fetal risk, but the benefits from use in pregnant women may be acceptable despite the risk (e.g., if the drug is needed in a life-threatening situation or for a serious disease for which safer drugs cannot be used or are ineffective).
X	Studies in animals or human beings have demonstrated fetal abnormalities, or there is evidence of fetal risk based on human experience or both, and the risk of the use of the drug in pregnant women clearly outweighs any possible benefit. The drug is contraindicated in women who are or may become pregnant.

because of widespread fear associated with the use of medications during pregnancy. The analgesics most commonly used in pregnancy are paracetamol, NSAIDs and opioids.¹³⁰

In accordance with the Food and Drug Administration (FDA) (Table III), paracetamol in therapeutic doses is safe in all stages of pregnancy and is classified in Risk Category B.¹³¹ Most NSAIDs are also classified in Risk Category B; however, several trials have shown that prenatal exposure to NSAIDs may increase the risk of structural abnormalities (ventricular septal defect, diaphragmatic hernia, intrauterine growth retardation).^{132, 133} Few data are available on COX-2 inhibitors; therefore they are classified in Risk Category C. Opioids have mainly been studied in the third trimester (labour analgesia) and, therefore, little information is available on their possible teratogenicity. Tramadol and codeine are in Risk Category C; fentanyl, morphine and oxycodone (Risk Category B) are all equally effective, but must be used with caution, especially if the pregnancy is at term, due to the risk of neonatal respiratory depression and/or neonatal abstinence syndrome.¹³⁴ In the last stage of pregnancy, opioids are in Risk Category D. There are no analgesics in Risk Category A.

Differences in gender and race

In the treatment of pain in emergency departments, inequalities may occur with respect to gender and race.

Women who come to the ED with abdominal pain are less likely to receive analgesics compared with men.¹³⁵ Similarly, patients of a low socio-economic level¹³⁶ and the population of non-Caucasian race (blacks and Hispanics) who come to the ED with abdominal pain or lower back pain receive fewer analgesics and experience longer waiting times compared with whites.¹³⁷

The use of standardised protocols for analgesia in emergency may help to reduce these disparities. Gender differences in pain perception must also be taken into consideration. Although the majority of studies have demonstrated no difference between the two genders with respect to pain intensity, cognitive and social factors, rather than hormonal or psychological factors, seem to explain the gender differences (allodynia and secondary hyperalgesia may be more pronounced in females).^{138, 139}

In-hospital emergencies

Calls from surgical, medical and oncology departments

In line with the objectives of the Pain-Free Hospital and Territory project, a shared organisational model should be created for the assessment of postoperative pain and its proper treatment, with particular attention to the complications and adverse events linked to it and their solutions.^{140, 141}

Identification of hospital emergency codes

TABLE IV.—*Basic pain support – Core curriculum.*

BPS: basic pain support
Epidemiology of pain in an emergency
Pathophysiology of pain
Pain rating and measuring scales
Monitoring, and reassessment after an intervention
Pain therapy: analgesic medications and titration of opiates
Regional techniques
Prevention of chronic pain
In-hospital analgesic emergencies
Integration with pain therapy and palliative care networks (Italian Law 38/2010)
Credentialing, and regular monitoring of competency in non-anesthetists/pain physicians/ED physicians

used to alert the Medical Emergency Team/ Acute Pain Service (MET/APS) may reduce preventable adverse events¹⁴² (Level C).

Medical and oncology departments should be closely integrated with the Pain Medicine Operative Unit, for proper identification of requests for pain therapy consultations in an emergency.¹⁴²

The complete clinical documentation must always be available. Standardised protocol should be adopted for reassessment of pain symptoms and for review of the therapeutic plan (Level C).

End of life choices and palliative care pathways

For terminally ill patients and the management of end of life care, specific SIAARTI guidelines are available on the subject.¹¹²

Palliative care must be guaranteed not only to cancer patients, but also in the advanced stages of other chronic pathologies, such as chronic obstructive pulmonary disease (COPD).^{143, 144}

Conclusions

For educational purposes, the working group has chosen to adopt an algorithm on the diagnosis and treatment of acute pain created by the Institute for Clinical Systems Improvement (ICSI) in 2008,^{145, 146} modified and adapted to the Italian context (Appendix 3).

According to the guidelines approved by the Section and Board of Anesthesiology of the European Union of Medical Specialists (EUMS),^{147, 148} the working group proposes a basic course on pain in emergency, called BASIC PAIN SUPPORT (Table IV).

TABLE V.—*Strong recommendations (Level A).*

Statement	Reference
Preventive use of IV paracetamol provides good analgesia and helps to reduce morphine consumption and the relative adverse events, as shown in the clinical trials on postoperative pain.	36
For procedural pain, the ketamine-midazolam combination is more effective and has fewer side effects than fentanyl-midazolam or fentanyl-propofol in reducing pediatric fractures in ED.	63
Boluses of IV ketamine (particularly in the population under the age of 2 years and over the age of 13) can lead to impairment of the upper airways, including the onset of laryngospasm, requiring specific expertise and skills for administration.	64, 65
The use of ketamine increases the potential risk of psychomotor agitation, which can happen in up to 30% of adult patients. This peculiar side effect can be significantly reduced by concomitant systemic use of benzodiazepines.	66
For shoulder dislocations and fractures of the upper limbs, the performance of brachial plexus block reduces the times spent in ED compared to sedation.	71, 72
Pain relief and the use of opioids in patients with acute abdominal pain do not increase the risk of error in the diagnostic and therapeutic pathway in adults.	99
In newborns, the administration of sucrose reduces behavioral responses to blood sampling from a heel puncture.	113
In newborns, breastfeeding or formula feeding during the procedure reduce the measures of distress.	114
In pediatric patients, non-pharmacological techniques such as distraction, hypnosis and cognitive-behavioral interventions reduce procedural pain caused by the use of needles.	115, 116
In pediatric patients, preventive application of eutectic mixtures of prilocaine and lidocaine allows arterial and venous samples to be taken in optimum conditions.	117
In pediatric patients, the combination of hypnotics (midazolam) and N ₂ O is effective for procedural pain, but may be accompanied by loss of consciousness.	79, 121

Key messages

— Diagnostic-therapeutic pathways on pain in emergency require an interdisciplinary approach.

— These recommendations highlight the need for an improved knowledge and promote the use of opioids titration and regional techniques.

— Level A evidence is limited to pediatric procedural pain control (Table V).

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APPENDIX I

Red flags in the assessment of pain in the emergency setting**RED FLAGS in the case of HEADACHE**

neurological deficits (severe or persistent reduction of vision, strength or speech)
 personality alterations or onset of epileptic seizures
 fever, confusion, stiff or sore neck
 very severe headache attacks or worsening of a previous pattern of headaches
 headache attacks after 35 years
 severe and known disease (cancer, hypertension, diabetes or trauma)
 headache that comes on after an injury to the head, especially if there has been a loss of consciousness

RED FLAGS in the case of LOW BACK PAIN

patients aged <20 years or >55 who have pain for the first time
 pain after a violent trauma
 recurrent, continuous pain, which worsens despite treatment
 pain radiating to the upper part of the back
 history of cancer
 treatment with steroids
 medication abuse
 HIV infection
 fever
 significant weight loss
 sensory alterations, impotence, sphincter incontinence, etc.
 emergence of structural deformities
 debilitating pain that persists after 4-6 weeks of treatment

RED FLAGS in the case of CAUDA EQUINA or QUICKLY PROGRESSIVE NEUROLOGICAL DEFICITSMEDICAL HISTORY

saddle anaesthesia
 recent onset of bladder dysfunction (e.g. urinary retention, increased urination, incontinence)
 recent onset of faecal incontinence

PHYSICAL EXAMINATION

severe or progressive neurological deficit in the lower extremities
 unexpected laxity of the anal sphincter
 loss of perianal/perineal sensation
 greater motor weakness: knee extension, ankle plantar eversion, dorsiflexion of the foot

In the case of one or more flags, send immediately for emergency investigations and definitive treatment

RED FLAGS in the case of MUSCULOSKELETAL PAIN**Factors that require the immediate attention of the doctor**

bloody sputum
 alterations in the state of consciousness
 neurological deficits that are not related to monoradiculopathy
 paraesthesia in the perineal region
 bladder and bowel pathologies
 symptoms that do not depend on mechanical pain
 progressive neurological deficit
 pulsating abdominal mass

Factors that require further study, careful examination and medical treatment

age >50 years
 clonus
 fever
 High ESR (erythrocyte sedimentation rate)
 GALT deficiency
 history of infections or haemorrhages
 disorders of bone metabolism
 history of cancer
 disability due to a recent injury
 long-term use of cortisones
 request for abstinence from work activities/early retirement/disability
 unhealed wounds
 recent weight loss
 pain during the transition from lying/sitting to a standing position

Factors that require further diagnostic confirmation

altered reflexes
 unilateral or bilateral radiculopathy or paresthesia
 reported pain is inexplicable
 weakness in the lower or upper limbs

RED FLAGS for SUICIDAL ATTEMPT

depression
 previous suicide attempts
 open declaration of the will to commit suicide
 development of a suicide plan
 self-harm (cuts, burns, etc...)
 risk behaviour (reckless driving, alcohol and drug abuse or unprotected sex)
 sudden mood swings for no apparent reason

YELLOW FLAGS for ADDICTION (Psychological Dependency)

aggressive demand for higher doses of medication
 accumulation of the medication during periods when the symptoms are reduced
 demand for specific medication
 acquisition of similar medications from other doctors
 dose escalation without a prescription or other behaviour showing poor compliance with the treatment
 reference to psychic effects not seen by the doctor
 attitude of resistance to changes in therapy associated with tolerable side effects due to anxiety about the return of severe symptoms

RED FLAGS for ADDICTION (Psychological Dependency)

prescription forgery
 stealing medications from others
 selling prescription medications
 obtaining the prescription for medications from non-medical personnel
 injection of oral formulations
 concomitant abuse of alcohol or illegal substances
 multiple-dose escalation or other attitudes showing poor compliance with therapy
 multiple episodes of "loss" of a prescription
 repeated request for prescriptions from other doctors without informing the doctor in charge of the treatment plan
 evident deterioration of their capabilities in the workplace, in the family or in society
 repeated resistance to changes in therapy despite evidence of physical or psychosocial side effects of the medication

APPENDIX 2

Analgesia in the emergency setting

Level of pain	Analgesic treatment
NRS 1-3	<p>Adult patient</p> <p>Oral/orodispersible paracetamol 1 g (max 3 g per day)</p> <p>NSAIDs ¹</p>
	<p>Pediatric patient (1-10 yrs)</p> <p>Paracetamol</p> <ul style="list-style-type: none"> - syrup (30 mg per 1 mL) 10-15 mg/kg (repeatable every 6 hours) - suppositories 10-15 mg/kg (repeatable every 6 hours) <p>Ibuprofen 4-10 mg/kg (repeatable every 6-8 hours)</p>
NRS 4-6	<p>Adult patient</p> <p>Paracetamol IV 1 g (max 4 g per day)</p> <p>Paracetamol in combination with weak opioids orally</p> <ul style="list-style-type: none"> - paracetamol/codeine 500/30 mg (repeatable every 6 hours) - paracetamol/tramadol 325/37.5 mg (repeatable every 6 hours) <p>NSAIDs ¹</p>
	<p>Pediatric patient (1-10 yrs)</p> <p>Paracetamol IV 15 mg/kg (repeatable every 6 hours). The maximum daily dose must not exceed 60 mg/kg (not to exceed 2 g per day).</p> <p>Paracetamol/codeine:</p> <ul style="list-style-type: none"> - syrup (25/1.5 mg per 1 mL) 1 mL per 4 kg of body weight (repeatable every 6 hours) - suppositories 200/5 mg (repeatable every 8-12 hours) ² <p>Tramadol (choose the lowest effective analgesic dose)</p> <ul style="list-style-type: none"> - drops (2.5 mg per drop) 1-2 mg/kg. The maximum daily dose must not exceed 8 mg/kg (not to exceed 400 mg per day) - 1-2 mg/kg IV

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NRS 7-10	<p>Adult patient</p> <p>Opioids³</p> <ul style="list-style-type: none"> - morphine (initial dose 4-6 mg IV)⁴ - fentanyl (initial dose 50-100 µg IV)
	<p>Pediatric patient (1-10 yrs)</p> <p>Opioids</p> <ul style="list-style-type: none"> - morphine IV 0.05-0.1 mg/kg (perform titration to the lowest effective dose) - fentanyl IV 1-2 µg/kg

¹Prior to administration of NSAIDs, a quick anamnesis to exclude any allergies or side effects (gastropathies, coagulopathies, renal failure) is highly recommended. Consider possible cross-sensitivity between NSAIDs and paracetamol.

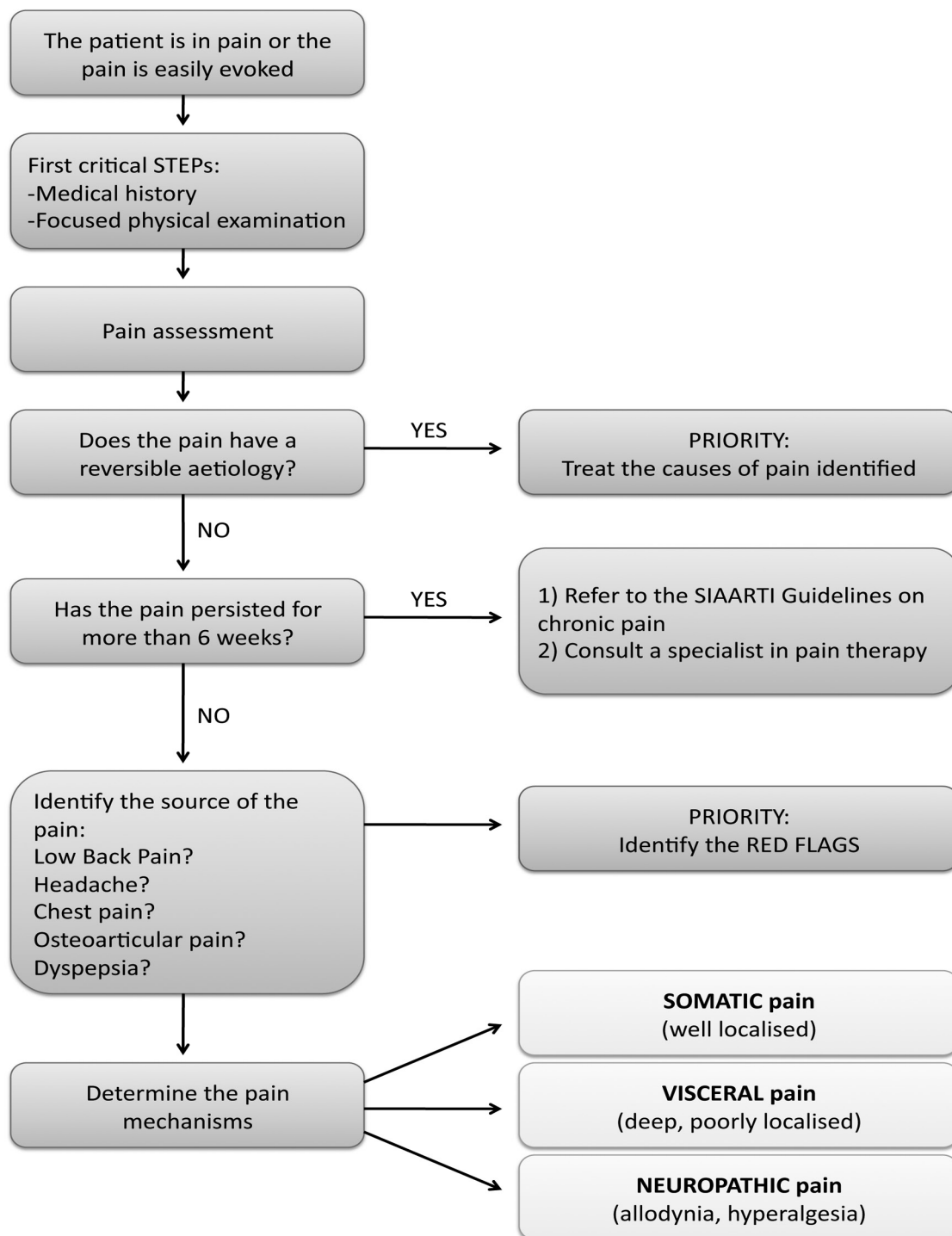
²In a recent warning (July 29, 2013), AIFA denied the use of codeine in patients under 12 years, for the risk of opioid toxicity. This risk seems to be increased among rapid metabolizers children and in those where codeine is used for postoperative analgesia after tonsillectomy and adenoidectomy.

³Perform titration until the lowest effective dose is reached (halving the initial NRS).

⁴Only in stable patients aged <65 yrs. For patients aged >65 years and/or unstable patients, halve the initial dose.

APPENDIX 3

Algorithm for diagnosis and treatment of pain in the emergency setting



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