

# **Adequacy of telephone triage using the Netherlands Triage Standard in out-of-hospital primary care patients with sepsis: a retrospective study.**

Marlie Kuenen<sup>1</sup>, 4260066.

Supervisors: F.J. Loots, M.S. Smits, R.P. Venekamp<sup>2</sup>.

Julius Center for Health Sciences and Primary care.

Period: 22-11-2021 – 25-02-2022.

<sup>1</sup> Medical student, University Medical Centre Utrecht, Heidelberglaan 100, 3584 CX, Utrecht, The Netherlands.

<sup>2</sup> Associate professor of general practice, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, University Utrecht, Heidelberglaan 100, 3584 CX, Utrecht, The Netherlands.

Word count (exclusive: abstract, tables, figures and references): 3,402.

## **Abbreviations**

NTS: Netherlands Triage Standard.

OOH: Out-of-hours.

GP: General practitioner.

ICU: Intensive care unit.

MTS: Manchester Triage System.

ED: Emergency department.

CBS: Central Bureau for Statistics.

ASRO: Adverse sepsis-related outcome.

OR: Odds ratio.

CI: Confidence interval.

## Abstract

**Background:** The key factor to improve outcomes of patients with sepsis is early initiation of adequate treatment. The Netherlands Triage Standard (NTS) is a decision support tool for telephone triage used at the Dutch out-of-hours general practitioner (OOH GP) cooperatives, which has never been validated against the clinical outcome sepsis.

**Aim:** To determine the adequacy of the NTS urgency allocation for patients with sepsis.

**Method:** A retrospective study using routine registration data from 2017-2019. Data were retrieved from the electronic medical records of the OOH GP cooperatives and were linked to the medical records of the patients' own GP, hospital records and deaths registration. The primary outcome was adverse sepsis related outcome (ASRO), defined as (1) intensive care-unit admission <7 days, or (2) death due to infection <30 days. For each entrance complaint, the odds ratio for the outcome ASRO was calculated. The allocated urgency was dichotomised into high-urgent (U1-U2) and low-urgent (U3-U5) and the proportion of high-urgent cases was calculated for each entrance complaint.

**Results:** 287.385 contacts were included of which 1721 had the outcome ASRO. Of all contacts with outcome ASRO, 58% were triaged as high-urgent. Complaints of arm or leg (26%), urinary problems (30%), diarrhoea (33%), cough (38%) and strange or suicidal behaviour (44%), general malaise (52%) had a significantly lower proportion triaged as high urgent. Of those, strange or suicidal behaviour and general malaise had the highest odds ratio for the outcome ASRO: 1.4 (95% CI: 1.1-1.7) and 4.3 (95% CI: 3.8-5.0), respectively.

**Conclusion:** Our study showed that the urgency allocation with telephone triage according to the NTS for patients with sepsis is suboptimal. The correctness of the urgency allocation varied between the entrance complaints.

## Introduction

Sepsis is a life-threatening condition caused by a dysregulated host response to an infection. [1] The clinical presentation of a sepsis patient is highly variable, and the manifestations of both infection and organ dysfunction may be subtle. Clinical presentation depends on the primary site of infection, the patient's underlying health status, and how fast treatment is started. [2] The most common initial sites of infection are the respiratory tract, followed by intraabdominal and urinary tract infections. [3-6] Multiple risk factors are associated with sepsis, such as old age, chronic disease, and the use of immunosuppressive agents. [4,7] The in-hospital mortality of patients with sepsis is circa 25%. [4,8]

Early initiation of adequate treatment of sepsis is the key factor to benefit patient outcomes. Patients with sepsis should be treated with the same level of urgency as patients with other time-sensitive diseases, such as stroke. Lower mortality was found among patients who had received antibiotic treatment within the first hour. [9-15] To achieve early initiation of adequate treatment, prehospital delay should be minimised. This calls for early recognition of sepsis in primary care. A large proportion of patients with sepsis had contacted the GP cooperative for out-of-hours primary care. [16] This can be explained by the typical acute presentation of a sepsis patient, which cannot wait until the next day.

In the Netherlands, out-of-hours (OOH) primary care is provided by about 120 GP cooperatives. [17] The process of OOH primary care starts with telephone triage. Since 2007, the Netherlands Triage Standard (NTS) has been used. Currently, the NTS is used in all Dutch OOH GP cooperatives, in half of the ambulance dispatching centres, and 20% of hospital emergency departments (ED). [18,19] The goal of the NTS is to guarantee safe and efficient care. [20]

Ideally, each sepsis patient who needs intensive care unit (ICU) treatment should be immediately transported by ambulance to the ED. However, unnecessary referrals should be prevented. Therefore, there is a need for adequate telephone triage combined with adequate assessment of patients with sepsis by a GP to refer the right patients.

Still, in practice, GPs' clinical detection of sepsis in primary care is complicated. Half of the patients admitted to an ICU

due to community-acquired sepsis had prior contact with a GP cooperative, and one-third of these patients were not referred to the hospital after the first contact. [16]

The NTS has never been validated against the clinical outcome of sepsis. Therefore, the aim of this paper is to determine the adequacy of the NTS urgency allocation for patients with sepsis.

### NTS urgency allocation

Telephone triage begins with a mandatory 'ABCDE' check. [22] This check determines life-threatening problems for which an ambulance must be sent directly. In case of no direct life-threatening situation, the triagist has to choose one of 56 entry complaints to continue the urgency evaluation. Each entry complaint contains hierarchically ordered triage questions. [23] Based on the triage nurses' responses, the NTS automatically generates an urgency level ranging from U0 to U5. This urgency level tells the triagist the response time within which a patient should receive a medical assessment (see table 1). [24] The triagist can overrule the automatically generated urgency allocation.

The following research questions will be answered:

- (1) What are the most common entry complaints in patients with sepsis who contacted the OOH GP cooperative?
- (2) How many patients with sepsis who contacted the OOH GP cooperative are recognised as highly urgent (U1-U2)?
- (3) Is there a difference in recognising patients with sepsis as a high-urgency demand for care between the different entrance complaints?

## **Methods**

### *Design and setting*

We performed a retrospective study of electronic medical records of adult patients who contacted an out-of-hours (OOH) GP cooperative. We retrieved data from 5 OOH GP cooperatives in the Netherlands between 1 January 2017 and 31 December 2019. These OOH GP cooperatives provide OOH primary care for approximately 1 million people living in diverse urban, suburban and rural areas.

We linked the OOH GP cooperatives data to the data from the patients' (regular) GP practices. Contacts were only included if there was data from both the OOH GP cooperative and the regular GP (10% of all cases).

### *Inclusion and exclusion criteria*

We included all medical records of adult patients who contacted the OOH GP cooperatives between 2017 and 2019. We excluded entrance complaints that would unlikely lead to sepsis, such as trauma, intoxication, and birth-related problems.. Individual patients could be included more than once when they had contacted the OOH GP cooperatives more than one time between 2017 and 2019. We excluded those cases when the time interval between two physical contacts (clinic consultation or home visit) was less than seven days.

Additionally, we excluded terminal patients because they often have mutual agreements about referral with their GP. The exclusion of terminal patients was based on the following information of the regular GP: diagnosis of malignancy, prescribed benzodiazepine medication such as midazolam, or conversation about euthanasia.

An overview of all exclusion criteria is given in Table 2.

### *Data collection*

We collected the following data from the OOH GP cooperatives: gender, date and time of contact, type of contact (telephone consultation, clinic consultation, home visit), urgency (U1-U5), entrance complaint, diagnosis of GP (ICPC code), and prescribed antibiotics. In addition, we collected the following data from the GP practices and linked this to the data from the OOH GP cooperatives: date of contact with GP, co-morbidities, use of immunosuppressive or benzodiazepine medication, conversations about euthanasia, and prescribed antibiotics.

Additionally, we obtained information of all hospital admissions; date and time of hospital admission, admission to ICU and discharge diagnosis. We established the hospital admission due to an infection based on discharge diagnosis of the hospital admission and suspected diagnosis of the GP of the OOH GP cooperatives. Furthermore, we retrieved the following information from the Central Bureau for Statistics (CBS): date and cause of death. All data collected was stored and analysed in a secure environment facilitated by the CBS.

Besides the data collection of the OOH GP cooperatives, the regular GP practices, and the hospital admissions, we collected information from the NTS for qualitative evaluation. We retrieved all triage questions of all entrance complaints of the NTS.

#### *Evaluation of triage questions*

The hierarchically ordered triage questions within the entrance complaint of the NTS were evaluated for completeness depending on the knowledge in the literature.

#### *Outcome measures*

The primary outcome measure is adverse sepsis-related outcome (ASRO). ASRO is defined as (1) ICU admission <7 days after the OOH GP cooperative contact, or (2) death due to infection <30 days after the OOH GP cooperative contact.

The secondary outcome is ASRO with shorter time intervals between contact with the OOH GP cooperative and hospital admission or death. It is defined as (1) ICU admission <48 hours after contact with OOH GP cooperative or (2) death due to infection <7 days after contact with OOH GP cooperative.

#### *Determination of cut-off values urgency*

Based on the given information of the lower mortality when treatment occurs within the first hour, we assumed that the determination of the urgency level has an immediate effect on mortality. Therefore, allocations of patients with outcome ASRO to urgency categories U1 and U2 were considered correct in this study. The urgency categories U3, U4, and U5, were judged to be inadequate prioritisations.

#### *Data analysis*

Initially, we described baseline characteristics of the study population using the median and interquartile range (IQR) for variables with a skewed distribution and the mean and standard deviation for continuous variables with a normal distribution. Secondly, we calculated odds ratios (OR) with a 95% confidence interval (CI) for the association between each entrance complaint and outcome ASRO.

Subsequently, urgency categories were dichotomised into high (U1 and U2) and low (U3, U4, U5) urgency levels. Descriptive statistics were used for the frequencies of the allocated urgency for the ASRO-group. The  $\chi^2$  test was used for comparing the allocated urgency between the different entrance complaints. Finally, to evaluate the results using the primary outcome ASRO, the analyses were repeated using the secondary outcome. All data analyses were performed using SPSS statistical software programme Version 25.0. Results were considered significant at  $p < 0.05$ .

## Results

### *Characteristics of study population*

In total, 287,385 patients were included for analysis. The median age was 51 years (IQR 32-70), and 40% was male. Table 3 shows an overview of the characteristics of patients with and without the outcome ASRO. There were differences between both populations. Firstly, the population with outcome ASRO was older; the median age was 81 years (IQR 72-91). Additionally, a larger proportion of the ASRO-group had at least one co-morbidity (80%) and used immunosuppressive medication (19%) in comparison to the patients without ASRO; 36% and 6%, respectively.

The time of day of the contact with the OOH GP cooperative was similar for both populations. However, there were differences in type of contact; patients with ASRO were more often assessed during a home visit (71%) compared to the patients without ASRO (13%). Furthermore, the ASRO-group had contacted the regular GP before contact with the GP cooperatives twice as often as the patients without ASRO. Finally, antibiotics were prescribed more often before the contact with the GP cooperative in the ASRO-group (14%) in comparison to the patients without ASRO (5%).

### *Entrance complaints and urgency*

During the ABCDE-check 83 cases with ASRO (5%) were assessed as (potentially) unstable. The majority, 1638 cases with ASRO (95%), was triaged using the other entrance complaints. Figure 1 shows the odds ratios of all entrance complaints in which ASROs occurred. The following entrance complaints showed an increased risk of ASRO: ABCDE, dyspnoea, general malaise, fever, strange or suicidal behaviour, neurological deficit, vomiting and diabetes. The fifteen entrance complaints with the highest odds ratios are further explored in tables 4 and 5.

After dichotomisation into high (U0-U2) and low urgent (U3-U5) categories, 998 cases (58%) of the total population with outcome ASRO were triaged as high-urgent and 723 (42%) as low-urgent. A significant higher proportion of patients with ASRO with the following entrance complaints were triaged as high-urgent: ABCDE (97%), dyspnoea (75%), and neurological deficit (84%). A significant lower proportion of patients with ASRO with strange / suicidal behaviour (44%) and general malaise (52%) were triaged as high-urgent (table 4).

Table 5 shows an overview of the proportion triaged as high-urgent of fifteen entrance complaints in the group with the outcome ASRO. The only entrance complaint with a lower proportion triaged as high-urgent in the ASRO-group compared to the patients without ASRO was strange / suicidal behaviour. All other entrance complaints had a higher proportion triaged as high-urgent in the ASRO group in comparison to the patients without ASRO.

### *Sensitivity analyses*

The analyses using the secondary outcome (ASRO with a shorter time-interval for hospital admission or death) resulted in similar findings as the analyses using the primary outcome ASRO. The secondary outcome resulted in the same fifteen entrance complaints with the highest odds ratios. Also, the same entrance complaints had triaged the same proportions as

high or low-urgent within the patients with the secondary outcome as the patients with ASRO.

### *Questions NTS*

The hierarchically ordered answers to the questions of the NTS are displayed in Figure 2. Figure 2a and 2b provide an overview of the NTS within the entrance complaint strange or suicidal behaviour and general malaise. These entrance complaints had both a significant higher odds ratio than one for the outcome ASRO and a significant lower proportion of contacts triaged as high-urgent. Figure 2a shows that within the entrance complaint strange or suicidal behaviour no-sepsis related symptoms lead to U1 or U2 urgency allocation. The symptom fever would lead to a U3 urgency allocation within this entrance complaint. Figure 2b shows that within the entrance complaint general malaise the symptom chills lead to U2 urgency allocation and the symptoms petechiae and meningeal stimulation to U1. This is the same for the entrance complaint fever, which had a high odds ratio for ASRO. Figure 2c showed that high-risk patients within the entrance complaint fever lead to U3 urgency allocation.

Fig. 2d-h showed the entrance complaints urinary problems, cough, diarrhoea and complaint of arm or leg. All these entrance complaints had a significantly lower proportion triaged as high-urgent, but did not have the highest odds ratios. Within these entrance complaints, the combination of high-risk patient and fever led to U3 urgency allocation. Fig. 2h showed that within the entrance complaint, complaints of arm or leg, there were no systemic symptoms of sepsis (for example, altered mental status) within the questions.

## **Discussion**

### *Summary*

In this retrospective study, 287,385 contacts were included, of which 1721 had the outcome ASRO. A small proportion (5%) of the patients with ASRO was assessed as (potentially) unstable according to the questions within the ABCDE-check. The majority of the patients with ASRO were triaged using the regular entrance complaints (95%). This underlines the importance of the adequacy of the NTS within the regular entrance complaints.

The following entrance complaints showed an increased risk of ASRO: ABCDE, dyspnoea, general malaise, fever, strange or suicidal behaviour, neurological deficit, vomiting and diabetes. Of all patients with the outcome ASRO, 58% were triaged as high-urgent. The entrance complaints dyspnoea, and neurological deficit, and the ABCDE-check had a significantly higher proportion triaged as high-urgent (75%, 84% and 97%, respectively), whereas strange or suicidal behaviour (44%) and general malaise (52%) had a significantly lower proportion triaged as high urgent.

We evaluated the questions of the NTS. Within the entrance complaint strange or suicidal behaviour we found no sepsis-related questions which lead to high urgency allocation. Also, within the entrance complaints fever and general malaise high-risk patients did not lead to high-urgency allocation except for the combination of fever and chills.

### *Comparison with existing literature*

To the best of our knowledge, there are no studies performed in the OOH GP cooperative setting in which urgency allocation using telephone triage was compared with the presence or absence of the clinical outcome sepsis. A previous observational study by Gräff et al. examined the Validity of the Manchester Triage System (MTS) in patients with sepsis at the emergency department. [25] The MTS is a five-stage triage system similar to the NTS. The proportion of patients with sepsis which were triaged as high urgent was 70%. This proportion is higher than in our study. This higher proportion triaged as high-urgent could be explained by the option that also vital parameters can be included in the MTS. However, also these authors conclude there are shortcomings of this triage system for sepsis. Another finding of the study by Gräff et al. was that among patients with sepsis who were correctly classified, the most commonly used presentational flow chart was 'shortness of breath' in adults. This finding is similar to our findings: dyspnoea had one of the three highest odds ratios and a proportion of 75% triaged as high-urgent. Another study by Chamberlain et al. examined patients with severe sepsis with the Australasian Triage Scale (ATS). [26] The ATS is a comparable triage system to the MTS. In this study, the proportion to triage sepsis as high-urgent was 71%. Also a comparable proportion (71%) was found in the study of Geier et al., which evaluated the Emergency Severity Index (ESI) in a prospective study in patients with severe sepsis and septic shock. [27]

Also, we critically compared the NTS questions with literature. First of all, within the entrance complaints, general malaise and fever, symptoms neck stiffness and petechiae lead to U1 urgency allocation. Petechiae and neck stiffness could be symptoms of meningococcal disease, possibly accompanied with meningococcal sepsis. In 2002, the monovalent meningococcal C conjugate vaccine was introduced in the Netherlands. Afterwards the incidence of meningococcal disease decreased enormously. The overall incidence rate significantly reduced from 17.3/100,000 population during the epidemic in 2001 to 0.06/100,000 population in 2012. It is still important to triage this disease as high-urgent, but due to the decreased incidence of meningococcal sepsis, these questions (petechiae and neck stiffness) triaged a small part of all sepsis patients as high-urgent. [28,29]

On the other hand, chills are in the NTS often used to identify patients how need urgent care. Chills led to U2 urgency allocation within the entrance complaints fever, general malaise, and urinary problems. The study of Loots et al. showed that chills were not associated with sepsis. [30] Therefore, reconsideration of the usefulness that the symptom chills leads to U2 is needed.

Additionally, there are multiple risk factors associated with sepsis, for example, old age, chronic disease, or the use of immunosuppressive agents. [7,8] Within the following entrance complaints led risk patient to U3 urgency allocation: fever, urinary problems, and diarrhoea. Within the entrance complaint cough, strongly reduced resistance led to U3 urgency allocation. Patients with sepsis often present with a combination of fever, altered mental status and risk factors. [2] Currently, the combination of these factors, according to the question of the NTS, did not lead to high-urgency allocation.

Lastly, there are no sepsis-related questions within the entrance complaint strange or suicidal behaviour that lead to U1 or U2 urgency allocation. Fever led to U3 urgency

allocation within this entrance complaint. Altered mental status is association with severe sepsis. [2] Patients with an altered mental status may present themselves with strange behaviour. Our study confirmed this, because the entrance complaint strange or suicidal behaviour had one of the four highest odds ratio of all entrance complaints. Currently, if these patients were triaged within the entrance complaint strange or suicidal behaviour and patients also had a fever, this led to a U3 urgency allocation.

### *Strength and limitations*

The major strength of our study is that we were able to include a large sample of patients who had contact with the OOH GP cooperative and who were diversely located in urban, suburban and rural areas. Therefore, we are confident that our results are generalisable to Dutch OOH primary care settings.

However, several limitations have to be mentioned. Firstly, we did not collect detailed information about the answers to the triage questions of the NTS. Secondly, we defined by approximation patients with sepsis with the primary outcome ASRO. Because of the chosen definition with a 72 hours time-interval to ICU-admission or 30-day mortality, it is possible that patients were selected who did not benefit from high-urgent allocation. Therefore, we used a secondary outcome with a shorter time interval, namely ICU-admission within 48 hours or 7-day mortality. The secondary outcome was chosen to select patients who were more likely to benefit from high-urgent allocation. When repeating our analyses using the secondary outcome, our findings were confirmed. This suggests that our findings are clinically relevant. Finally, with our observational study design, we could not compare the NTS to another telephone triage system. Therefore, we do not know to what extent telephone triage could be improved.

### *Implications for future research*

In telephone triage, a balance between safety and efficiency must be found. More safety (a higher proportion of patients with sepsis triaged as high-urgent) may lead to less efficiency (more unneeded referrals or assessed patients). Our study suggests that revision of the NTS is needed for the entrance complaint strange or suicidal behaviour. There is need for sepsis-related symptoms within this entrance complaint, because these entrance complaint had one of the four highest odds ratios. To specify the revision of the NTS for other entrance complaints, future research has to focus on the triage nurses' answers. After revising the NTS, effects on allocated urgency and patient outcomes should be evaluated.

Combining sepsis related symptoms (altered mental status) with risk factors (old age, use of immunosuppressive medication) might also be useful to identify patients needing high-urgent assessment. Instead of the combination fever and chills what is currently leading to high-urgency allocation within the following entrance complaints general malaise, fever and urinary problems. For this suggestion, future research could focus on these combination, therefore prediction models are needed based on multivariable analyses to provide evidence-based basis for which risk factors are helpful for triaging and not.

## **Conclusion**

Our study showed that the urgency allocation with NTS telephone triage for patients with sepsis was suboptimal. The adequacy of the urgency allocation varied between the different entrance complaints. Especially for the combination of altered mental status and risk factors within the entrance complaints general malaise, urinary problems, diarrhoea and fever, more research into the required modifications is advised to recognise more patients with sepsis as high-urgent during triage while preventing unneeded referrals.

## References

1. Singer, Mervyn, et al. "The third international consensus definitions for sepsis and septic shock (Sepsis-3)." *Jama* 315.8 (2016): 801-810.
2. Angus, Derek C., and Tom Van der Poll. "Severe sepsis and septic shock." *N Engl J Med* 369 (2013): 840-851.
3. Lagu, Tara, et al. "Hospitalizations, costs, and outcomes of severe sepsis in the United States 2003 to 2007." *Critical care medicine* 40.3 (2012): 754-761.
4. Angus, Derek C., et al. "Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated costs of care." *Critical care medicine* 29.7 (2001): 1303-1310.
5. Ranieri, V. Marco, et al. "Drotrecogin alfa (activated) in adults with septic shock." *New England Journal of Medicine* 366.22 (2012): 2055-2064.
6. Vincent, Jean-Louis, et al. "International study of the prevalence and outcomes of infection in intensive care units." *Jama* 302.21 (2009): 2323-2329.
7. Henriksen, Daniel Pilsgaard, et al. "Risk factors for hospitalization due to community-acquired sepsis—a population-based case-control study." *PLoS One* 10.4 (2015): e0124838.
8. Friedman, Gilberto, Eliezer Silva, and Jean-Louis Vincent. "Has the mortality of septic shock changed with time?." *Critical care medicine* 26.12 (1998): 2078-2086.
9. Chaudhary, T., C. Hohenstein, and O. Bayer. "Die goldene Stunde der Sepsis." *Medizinische Klinik-Intensivmedizin und Notfallmedizin* 109.2 (2014): 104-108.
10. Machado, Flavia R., et al. "Late recognition and illness severity are determinants of early death in severe septic patients." *Clinics* 68 (2013): 586-591.
11. Gaieski, David F., et al. "Impact of time to antibiotics on survival in patients with severe sepsis or septic shock in whom early goal-directed therapy was initiated in the emergency department." *Critical care medicine* 38.4 (2010): 1045-1053.
12. Jalili, Mohammad, et al. "Effect of door-to-antibiotic time on mortality of patients with sepsis in emergency department: a prospective cohort study." *Acta Medica Iranica* (2013): 454-460.
13. Rhodes, Andrew, et al. "Surviving sepsis campaign: international guidelines for management of sepsis and septic shock: 2016." *Intensive care medicine* 43.3 (2017): 304-377.
14. Sherwin, Robert, et al. "Does early and appropriate antibiotic administration improve mortality in emergency department patients with severe sepsis or septic shock?." *The Journal of emergency medicine* 53.4 (2017): 588-595.
15. Seymour, Christopher W., et al. "Time to treatment and mortality during mandated emergency care for sepsis." *New England Journal of Medicine* 376.23 (2017): 2235-2244.
16. Loots, Feike J., et al. "Management of sepsis in out-of-hours primary care: a retrospective study of patients admitted to the intensive care unit." *BMJ open* 8.9 (2018): e022832.
17. Smits, Marleen, et al. "The development and performance of after-hours primary care in the Netherlands: a narrative review." *Annals of internal medicine* 166.10 (2017): 737-742.
18. Keizer, Ellen, et al. "Reducing the use of out-of-hours primary care services: a survey among Dutch general practitioners." *European Journal of General Practice* 22.3 (2016): 189-195.
19. Smits, Marleen, et al. "Reliability and validity of the Netherlands Triage Standard in emergency care settings: a case scenario study." *Emergency Medicine Journal* (2022).
20. Huibers, Linda, et al. "Safety of telephone triage in out-of-hours care: a systematic review." *Scandinavian journal of primary health care* 29.4 (2011): 198-209.
21. van Ierland, Yvette, et al. "Validity of telephone and physical triage in emergency care: the Netherlands Triage System." *Family practice* 28.3 (2011): 334-341.
22. Thim, Troels, et al. "Initial assessment and treatment with the Airway, Breathing, Circulation, Disability, Exposure (ABCDE) approach." *International journal of general medicine* 5 (2012): 117.

23. van Ierland, Yvette, et al. "Validity of telephone and physical triage in emergency care: the Netherlands Triage System." *Family practice* 28.3 (2011): 334-341.
24. Netherlands Triage Standard [Nederlandse Triage Standaard], 2019. Accessed at [www.de-nts.nl](http://www.de-nts.nl) on 29 January 2022.
25. Gräff, Ingo, et al. "Validity of the Manchester Triage System in patients with sepsis presenting at the ED: a first assessment." *Emergency Medicine Journal* 34.4 (2017): 212-218.
26. Chamberlain, Diane J., et al. "Identification of the severe sepsis patient at triage: a prospective analysis of the Australasian Triage Scale." *Emergency Medicine Journal* 32.9 (2015): 690-697.
27. Geier, Felicitas, et al. "Severity illness scoring systems for early identification and prediction of in-hospital mortality in patients with suspected sepsis presenting to the emergency department." *Wiener klinische Wochenschrift* 125.17 (2013): 508-515.
28. Bijlsma, Merijn W., et al. "Epidemiology of invasive meningococcal disease in the Netherlands, 1960–2012: an analysis of national surveillance data." *The Lancet infectious diseases* 14.9 (2014): 805-812.
29. Tin Tin Htar, Myint, et al. "Systematic literature review of the impact and effectiveness of monovalent meningococcal C conjugated vaccines when used in routine immunization programs." *BMC public health* 20.1 (2020): 1-15.
30. Loots, Feike J., et al. "Development and external validation of a new clinical prediction model for early recognition of sepsis in adult patients in primary care: a diagnostic study." *British Journal of General Practice* (2022).

## Appendix

**Table 1. Description of urgency levels of the Netherlands Triage Standard**

Urgency Level	Title	Description	Response time
U0	Resuscitation	Failure of vital functions	Immediate
U1	Life-threatening	Vital functions are unstable	As soon as possible
U2	Emergent	Vital functions are threatened	Within 1 hour
U3	Urgent	Risk for damage	Within a few hours
U4	Non-urgent	Negligible risk for damage	Within 24 hours
U5	Advice	No risk for damage	Next working day

**Table 2. Inclusion- and exclusion criteria.**

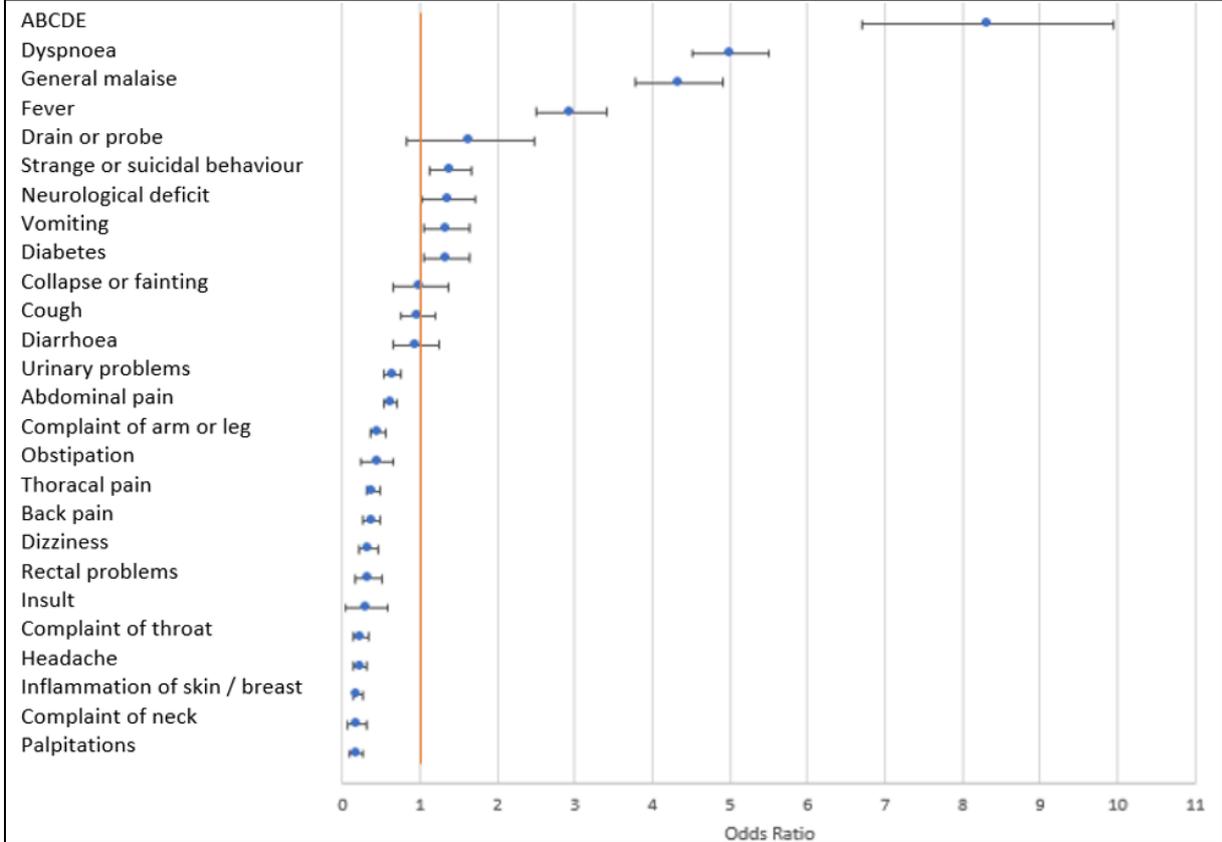
	Included	Excluded
Entrance complaints	ABCDE, general malaise, vomiting, abdominal pain, diabetes, diarrhoea, cough, fever, dyspnoea, neurological deficit, urinary problems, strange or suicidal behaviour, collapse or fainting, complaints of arm or leg, complaints of neck, palpitations, obstipation, insult, complaint of throat, pain back, drain or probe, pain thorax, rectal complaints, headache, inflammation of skin or mamma.	Allergic reaction, nose bleeding, burn, foreign body, complaints of teeth, intoxication, complaints of eye or ear, child-birth problems, trauma face, trauma extremity, trauma abdomen, trauma neck, trauma back, trauma head, trauma thorax, vaginal bleeding, drowning, pregnancy, wound, implantable cardioverter-defibrillator, death.
Age	≥18 years	<18 years
Other		Terminal patients Two contacts <7 days.

**Table 3. Patient characteristics, by adverse sepsis related outcome.**

	<b>ASRO (n=1721)</b>	<b>No ASRO (n= 285664)</b>
<b>Demographics</b>		
Age, median (IQR), y	81 (72-91)	51 (32-70)
Sex, No. (%)		
Men	884 (51)	112642 (39)
<b>Comorbidities, No. (%)</b>		
Diabetes	542 (32)	42288 (15)
Cardiovascular	927 (54)	57749 (20)
COPD	424 (25)	23236 (8)
Neurological disorder	148 (9)	11742 (4)
Kidney disorder	432 (25)	22472 (8)
Malignancy	165 (10)	11684 (4)
Number of comorbidities		
0	340 (20)	182404 (64)
1	559 (33)	57219 (20)
≥2	822 (48)	46041 (16)
Immunosuppressive use	329 (19)	17680 (6)
<b>Information about contact, No. (%)</b>		
Time of day		
Mo-Fr 8.00-23.59h	439 (26)	81334 (29)
Sat-Sun / holiday 8.00-23.59h	881 (51)	146152 (51)
Night 0.00-7.59h	403 (23)	58178 (20)
Type of contact		
Telephone	250 (15)	117269 (41)
Consult	249 (15)	130329 (46)
Visit	1222 (71)	38066 (13)
Number of entrance complaints		
0	8 (0.5)	692 (0.2)
1	1438 (83.6)	244452 (85.6)
2	232 (13.5)	36359 (12.7)
3	18 (1.0)	3242 (1.1)
5	25 (1.5)	613 (0.2)
Triage urgency category		
U1	130 (7.6)	13848 (4.8)
U2	873 (50.7)	70577 (24.7)
U3	623 (36.2)	101576 (35.6)
U4	44 (2.6)	41284 (14.5)
U5	51(3.0)	58367 (20.4)
<b>Care prior to or during contact No. (%)</b>		
AB prescribed by regular GP 3 days prior to contact OOH GPC	153 (14.1)	7375 (5.2)
Contact with regular GP 3 days prior to contact OOH GPC	604 (35.1)	51741 (18.1)
AB prescribed during contact OOH GPC	281 (16.3)	37014 (13.0)
<b>Care during follow-up</b>		
Hospital admission within 7 days, No. (%)	1089 (63.3)	8608 (3.0)
Length of stay, mean (SD), days	11 (13)	6 (6)
30-day mortality, No. (%)	1222 (71)	4153 (1.5)

Abbreviations: ASRO: adverse sepsis related outcome, IQR: interquartile range, COPD: chronic obstructive pulmonary disease, GP: general practitioner, OOH GPC: out-of-hours general practitioner cooperative, SD: standard deviation. AB: antibiotics

**Figure 1. Odds ratios (95% CI) per entrance complaint**



Abbreviations: CI: confidence interval.

**Table 4. High- and low urgent per entry complaints - cases with adverse sepsis related outcome.**

Entrance complaints	High-urgent	Low-urgent	P-value
	U1-U2, No. (%)	U3-U5, No. (%)	
ABCDE	87 (97)	3 (3)	<b>&lt;0.001</b>
Abdominal pain	105 (61)	67 (39)	0.438
Collapse or fainting	17 (85)	3 (15)	<b>0.015</b>
Complaints of arm or leg	20 (26)	58 (74)	<b>&lt;0.001</b>
Cough	24 (38)	40 (63)	<b>0.001</b>
Diabetes	32 (52)	30 (48)	0.278
Diarrhoea	10 (33)	20 (67)	<b>0.005</b>
Dyspnoea	390 (75)	129 (25)	<b>&lt;0.001</b>
Fever	78 (53)	68 (47)	0.214
General malaise	124 (52)	115 (48)	<b>0.031</b>
Neurological deficit	41 (84)	8 (16)	<b>&lt;0.001</b>
Obstipation	4 (40)	6 (60)	0.240
Strange / suicidal behaviour	37 (44)	47 (56)	<b>0.007</b>
Urinary problems	35 (30)	83 (70)	<b>&lt;0.001</b>
Vomiting	34 (49)	35 (51)	0.122
Total <sup>1</sup>	998 (58)	723 (42)	

NB The fifteen entrance complaints with the highest odds ratios for the outcome ASRO are analysed.

<sup>1</sup>. Total is not the total of these fifteen entrance complaints, but total of all entrance complaints with adverse sepsis related outcome.

**Table 5. High-urgent per entrance complaint by outcome ASRO.**

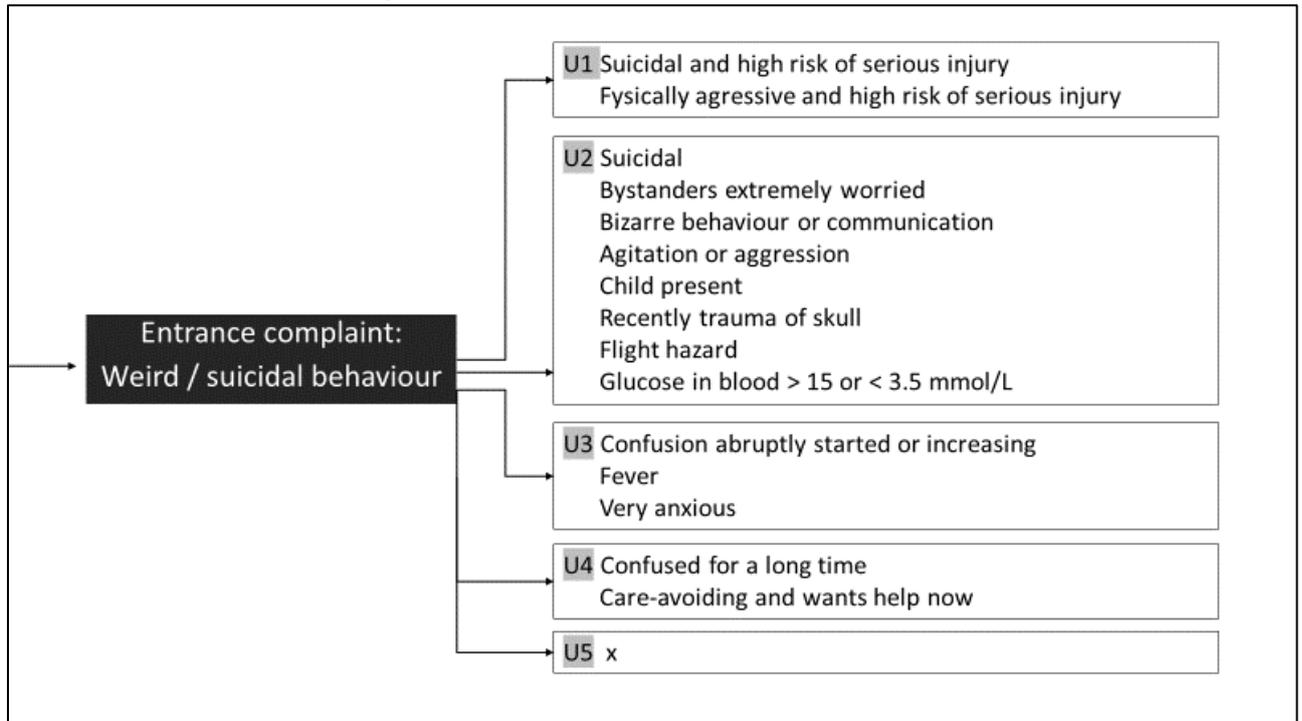
Entrance complaints	High-urgent, ASRO	High-urgent, No ASRO
	No. (%)	No. (%)
ABCDE	87 (97)	1765 (93)
Abdominal pain	105 (61)	18033 (43)
Collapse or fainting	17 (85)	1754 (53)
Complaints of arm or leg	20 (26)	2660 (10)
Cough	24 (38)	1217 (11)
Diabetes	32 (52)	1195 (15)
Diarrhoea	10 (33)	582 (11)
Dyspnoea	390 (75)	12608 (56)
Fever	78 (53)	2572 (30)
General malaise	124 (52)	2523 (25)
Neurological deficit	41 (84)	4309 (72)
Obstipation	4 (40)	488 (13)
Strange / suicidal behaviour	37 ( <b>44</b> )	5426 ( <b>53</b> )
Urinary problems	35 (30)	2473 (9)
Vomiting	34 (49)	2555 (30)
Total <sup>1</sup>	998 (58)	84425 (30)

NB The fifteen entrance complaints with the highest odds ratios for the outcome ASRO are analysed.  
High-urgent included U1 and U2.

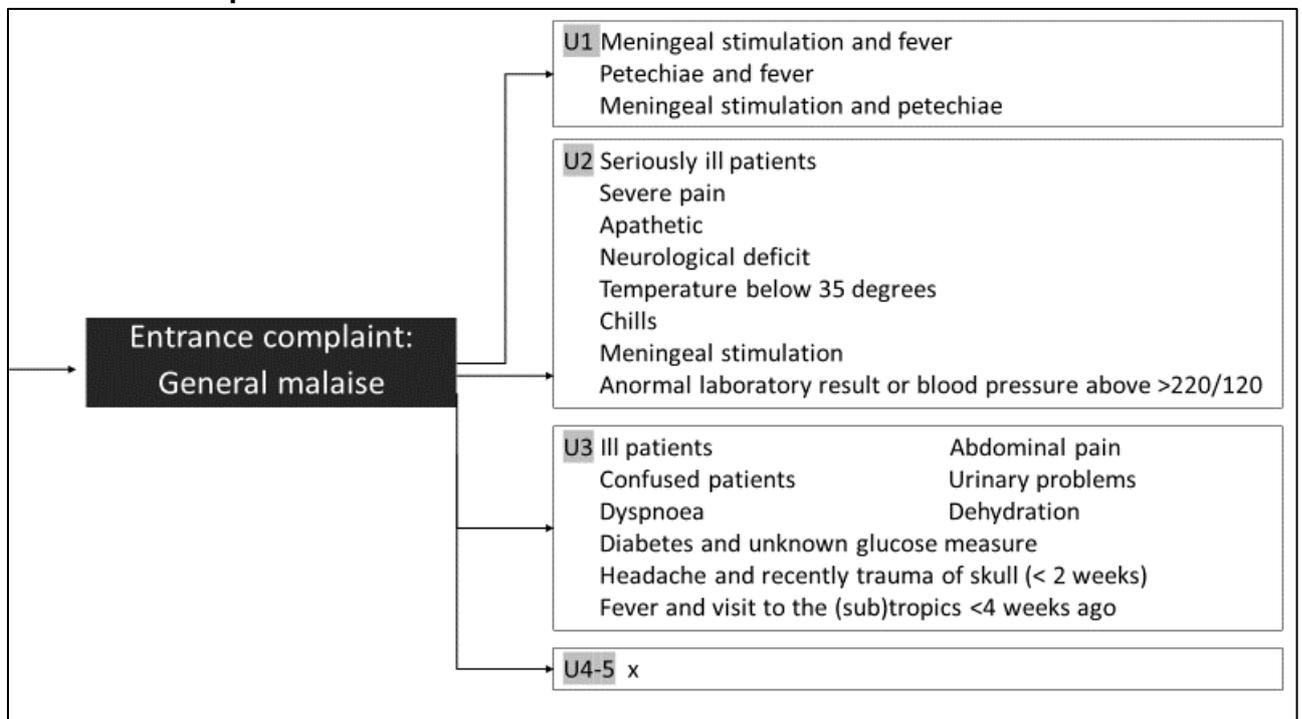
<sup>1</sup>. Total of all patients including patients with other entrance complaints than listed in this table.

**Figure 2. Flowcharts: hierarchically ordered answers to the questions of the Netherlands Triage Standard.**

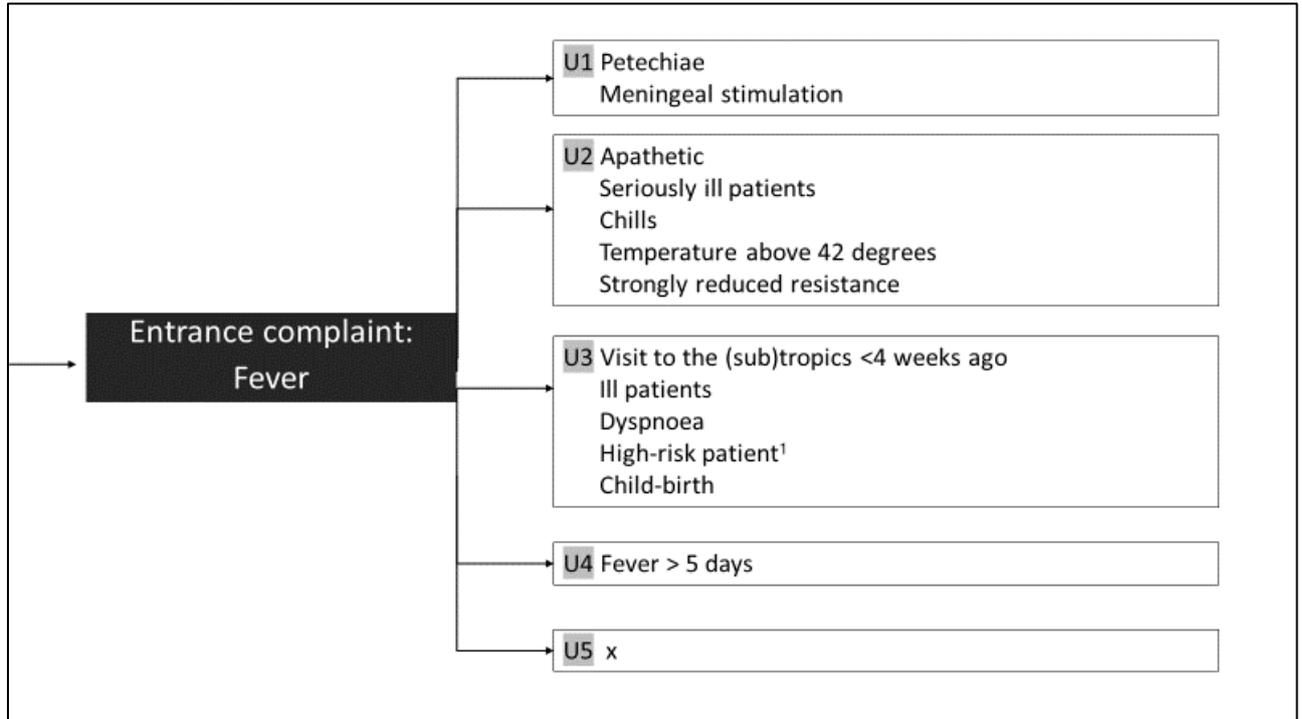
**2.a. Entrance complaint: Strange / suicidal behaviour.**



**2.b. Entrance complaint: General malaise.**

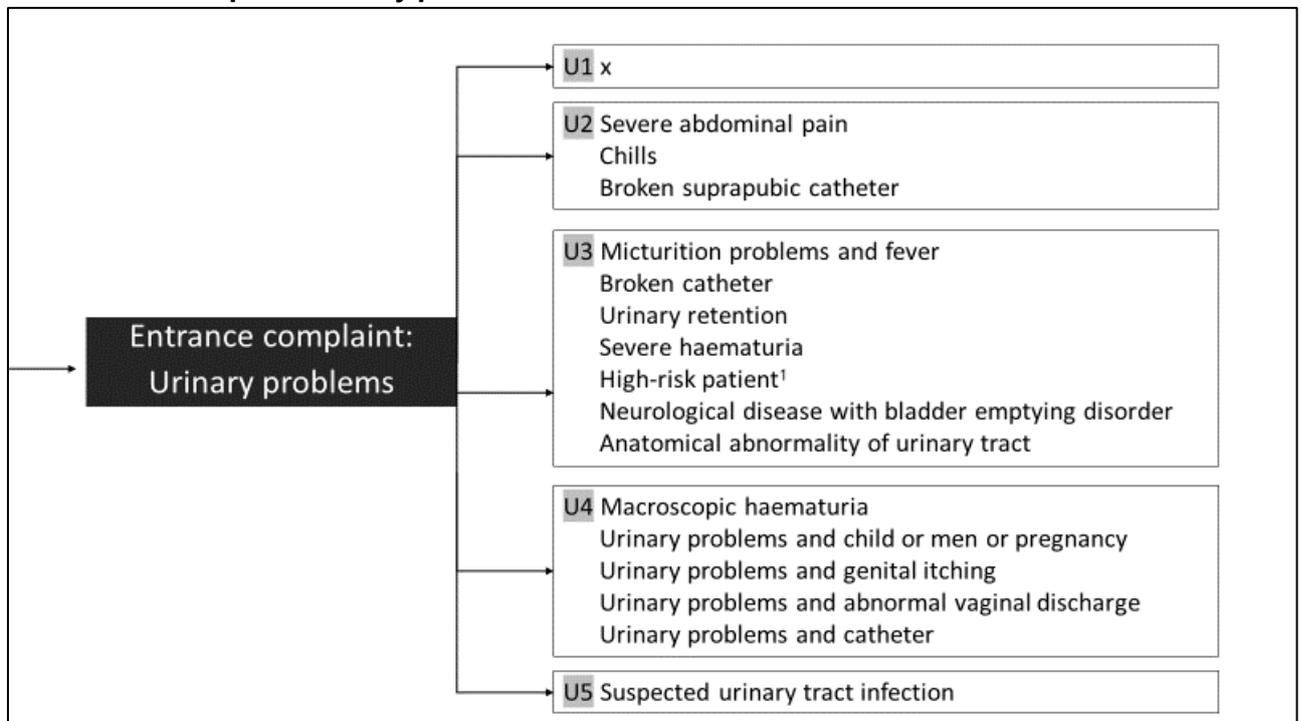


## 2.c. Entrance complaint: Fever.



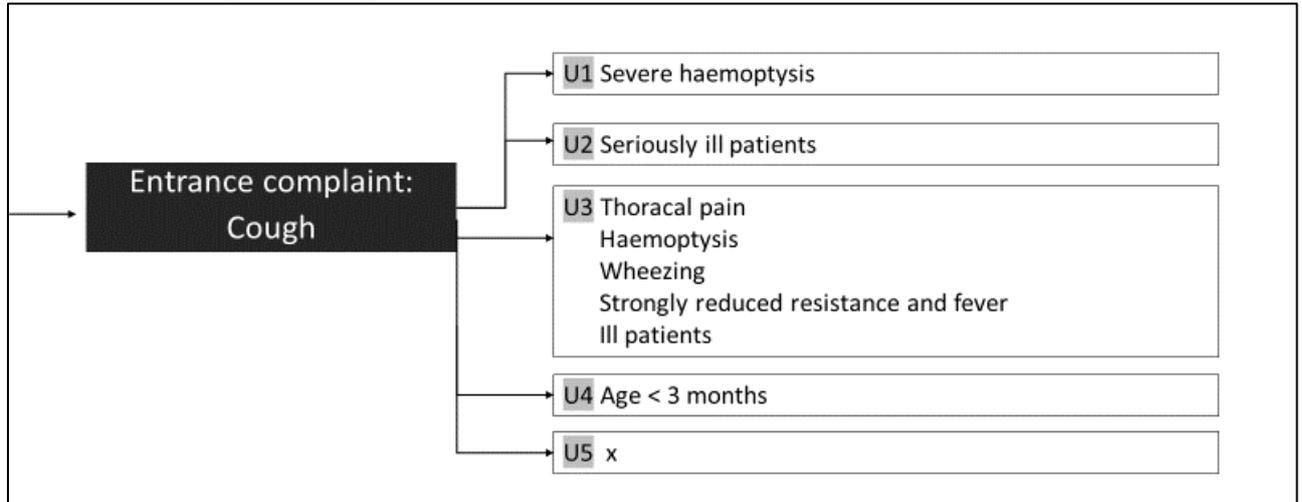
<sup>1</sup>High-risk patient: old age, chronic disease, reduced resistance (caused by chemotherapy, transplantation, immunosuppressiv medication), recent surgery or admission in hospital, inconsistent or wrong story.

## 2.d. Entrance complaint: Urinary problems.

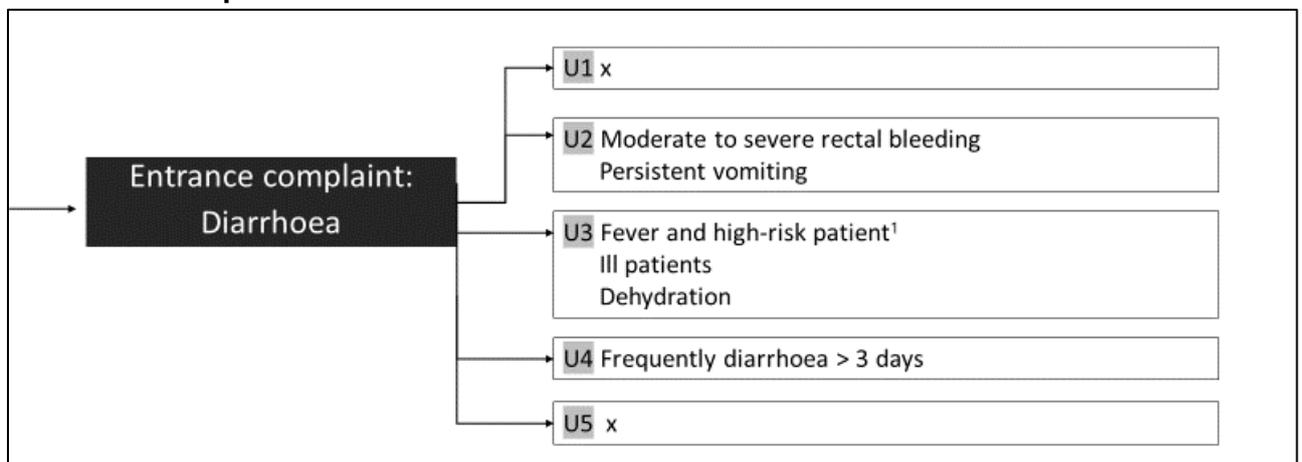


<sup>1</sup>High-risk patient: old age, chronic disease, reduced resistance (caused by chemotherapy, transplantation, immunosuppressiv medication), recent surgery or admission in hospital, inconsistent or wrong story.

### 2.e. Entrance complaint: Cough.



### 2.f. Entrance complaint: Diarrhoea



## 2.h. Entrance complaint: Complaints of arm or leg

