



UNIVERSIDADE  
ESTADUAL de LONDRINA

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ALEXANDRE SANCHES LARANGEIRA

**EFEITO DA MUDANÇA DE MODELO DE TRIAGEM PARA  
ADMISSÃO NA UNIDADE DE TERAPIA INTENSIVA NO  
DESFECHO DE PACIENTES GRAVES**

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Londrina  
2022

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Tese de Doutorado apresentada ao Programa de Pós-Graduação em Ciências da Saúde, Centro de Ciências da Saúde, Universidade Estadual de Londrina, como requisito parcial para a obtenção do título de Doutor.

Orientador: Profa. Dra. Cintia Magalhães Carvalho Grion.

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**BANCA EXAMINADORA - TITULARES**

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Londrina, 03 de maio de 2022.

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Londrina, 03 de maio de 2022.

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LARANGEIRA, A.S. **Efeito da mudança de modelo de triagem para admissão na unidade de terapia intensiva no desfecho de pacientes graves.** 2022. Tese (Doutorado em Ciências da Saúde) – Universidade Estadual de Londrina, Londrina. 2022.

## RESUMO

**Introdução:** Considerando o desequilíbrio entre a demanda e a disponibilidade de leitos de unidade de terapia intensiva (UTI) e profissionais com formação especializada, é necessário escolher quem será admitido. Estabelecer critérios para triar pacientes é uma forma de gerenciar os recursos e racionalizar a decisão do profissional responsável pela triagem. A base da triagem do paciente grave é o prognóstico, que pode ser avaliado por meio de escores de gravidade, de disfunções orgânicas e de quantidade de trabalho da equipe. **Objetivo:** Analisar o efeito da implementação de novo modelo de priorização e triagem para admissão em unidade de terapia intensiva no desfecho de pacientes graves. **Métodos:** Foi realizado um estudo longitudinal retrospectivo, envolvendo pacientes adultos admitidos em UTI de hospital universitário no período de janeiro de 2013 a dezembro de 2017. Foram excluídos os pacientes com tempo de permanência menor que 24 horas e as readmissões na UTI durante a mesma internação hospitalar. O desfecho primário foi considerado estado vital na saída do hospital. Os escores avaliados no estudo foram o *Acute Physiology and Chronic Health Evaluation (APACHE II)*, *Sequential Organ Failure Assessment (SOFA)* e *Therapeutic Intervention Scoring System (TISS 28)*. Os pacientes foram divididos em dois grupos de acordo com o período do estudo. Foram considerados período pré mudança do modelo de triagem os anos de 2013 a 2014 (período 1). Até o final do ano 2014 o protocolo institucional para triagem e admissão em UTI era fundamentado no critério cronológico (primeiro a chegar, primeiro a receber tratamento). Os anos de 2015 a 2017 foram considerados período pós mudança do modelo de triagem (período 2). A partir do início do ano 2015 foi implantado um modelo de priorização baseado na diretriz da *Society of Critical Care Medicine*, que leva em consideração a gravidade e a possibilidade de recuperação do paciente. O nível de significância utilizado foi de 5% e as análises foram realizadas utilizando-se o programa *SPSS Statistics for Windows* versão 19. **Resultados:** Foram analisados 3.283 pacientes, sendo que 1.227 foram admitidos no período 1 e 2.056 no período 2. Os pacientes admitidos no período 2 do estudo eram mais velhos, com menor proporção de doenças crônicas, tinham valor médio do escore APACHE II e do escore TISS 28 maiores comparados aos pacientes do período 1. O diagnóstico de sepse foi maior no segundo período do estudo. Foi observado aumento do número de admissões ao longo do período de estudo. No período 2 os pacientes apresentaram uma tendência a permanecer menor tempo internados na UTI e no hospital e tiveram menor mortalidade na saída da UTI e do hospital. **Conclusões:** A mudança do modelo de triagem, de um modelo cronológico para um modelo de priorização resultou em melhora do desempenho de uma unidade de terapia intensiva, com aumento do número de admissões, redução da taxa de mortalidade hospitalar, além de uma tendência de redução do tempo de permanência hospitalar.

**Palavras-chave:** cuidados críticos; triagem; admissão do paciente; unidades de terapia intensiva; ocupação de leitos.

LARANGEIRA, A.S. **Effects of changing the triage model for admission to the intensive care unit on the outcome of critically ill patients.** 2022. Tese (Doutorado em Ciências da Saúde) – Universidade Estadual de Londrina, Londrina. 2022.

## ABSTRACT

**Introduction:** Considering the imbalance between the demand and availability of intensive care unit (ICU) beds and professionals with specialized training, it is necessary to choose who will be admitted. Establishing criteria for screening patients is a way to manage resources and rationalize the decision of the professional responsible for the triage. The basis for triage of critically ill patients is the prognosis, which can be assessed through prognosis scores, organ dysfunction, and burden of health care work. **Objective:** To analyze the effect of implementing a new prioritization and triage model for admission to the intensive care unit on the outcome of critically ill patients. **Methods:** A retrospective longitudinal study was carried out, involving adult patients admitted to the ICU of a university hospital from January 2013 to December 2017. Patients with a length of stay less than 24 hours and readmissions to the ICU during the same hospitalization were excluded. The primary outcome was considered vital status on discharge from the hospital. The scores evaluated in the study were the Acute Physiology and Chronic Health Evaluation (APACHE II), Sequential Organ Failure Assessment (SOFA) and Therapeutic Intervention Scoring System (TISS 28). Patients were divided into two groups according to the study period. The years from 2013 to 2014 (period 1) were considered before the change of the triage model. Until the end of 2014, the institutional protocol for triage and admission to the ICU was based on chronological criteria (first come, first served). The years 2015 to 2017 were considered the period after the change in the triage model (period 2). From the beginning of 2015, a prioritization model based on the Society of Critical Care Medicine guideline was implemented, which considers the severity and probability of the patient's recovery. The significance level used was 5% and the analyzes were performed using the *SPSS Statistics for Windows* versão 19. **Results:** A total of 3,283 patients were analyzed, 1,227 of which were admitted in period 1 and 2,056 in period 2. Patients admitted in period 2 of the study were older, with a lower proportion of chronic diseases, had mean APACHE II score and score TISS 28 higher compared to patients from period 1. The diagnosis of sepsis was higher in the second period of the study. An increase in the number of admissions was observed over the study period. In period 2, patients had a tendency to remain in the ICU and hospital for a shorter time and had lower mortality at ICU and hospital discharge. **Conclusions:** Changing the screening model from a chronological model to a prioritization model resulted in an improvement in the performance of an intensive care unit, with an increase in the number of admissions, a reduction in the hospital mortality rate and a tendency of reduction in the hospital length of stay.

**Key words:** critical care; triage; patient admission; intensive care units; bed occupancy.

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## LISTA DE SIGLAS

<b>APACHE</b>	<i>Acute Physiology and Chronic Health Evaluation</i>
<b>ATS</b>	<i>American Thoracic Society</i>
<b>CAAE</b>	Certificado de Apresentação de Apreciação Ética
<b>CEP-UEL</b>	Comitê de Ética em Pesquisa Envolvendo Seres Humanos da Universidade Estadual de Londrina
<b>CFM</b>	Conselho Federal de Medicina
<b>CVC</b>	Cateter venoso central
<b>DP</b>	Desvio padrão
<b>DVA</b>	Droga vasoativa
<b>HR</b>	Razão de risco proporcional; <i>hazard ratio</i>
<b>HU</b>	Hospital Universitário de Londrina
<b>IC 95%</b>	Intervalo de confiança 95%
<b>IRA</b>	injúria renal aguda
<b>ITQ</b>	Intervalo interquartilico; <i>interquartile range</i>
<b>MS</b>	Ministério da Saúde
<b>N</b>	Número
<b>NP</b>	Nutrição parenteral
<b>PIC</b>	Pressão intracraniana
<b>PO</b>	Pós-operatório
<b>SCCM</b>	<i>Society of Critical Care Medicine</i>
<b>SOFA</b>	<i>Sequential Organ Failure Assessment</i>
<b>SPSS</b>	<i>Statistical Package for the Social Sciences</i>
<b>SUS</b>	Sistema Único de Saúde
<b>TISS</b>	<i>Therapeutic Intervention Scoring System</i>
<b>UCI</b>	Unidade de Cuidados Intermediários
<b>UEL</b>	Universidade Estadual de Londrina
<b>UTI</b>	Unidade de terapia intensiva
<b>VM</b>	Ventilação mecânica

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## 1 1 INTRODUÇÃO

2

3 O cuidado ao paciente grave em leito de terapia intensiva requer recursos  
4 humanos e financeiros. A demanda crescente por leito especializado exige que o  
5 sistema de saúde se organize para contemplar o atendimento ao paciente com  
6 qualidade e de forma racional. Existem fatores epidemiológicos que determinam a  
7 demanda pelos leitos de unidade de terapia intensiva (UTI), como o envelhecimento  
8 populacional, gravidade de pacientes hospitalizados e avanço de tratamentos que  
9 exigem monitorização pelo especialista. O conhecimento sobre o uso dos leitos  
10 permite melhor planejamento ao gestor e consequente otimização de recursos.(1,2)

11 O envelhecimento é um dos maiores responsáveis pela demanda de leito  
12 especializado, considerando o aumento da expectativa de vida da população. No  
13 mundo, atualmente existem 727 milhões de pessoas com 65 anos ou mais. A  
14 expectativa é que este número ultrapasse 1,5 bilhão em 2050.(3) Existem fatores que  
15 determinam o prognóstico desta população na UTI, como critérios anteriores à  
16 admissão: fragilidade, funcionalidade e comorbidades. Este grupo de pacientes, pelas  
17 particularidades da fisiologia, responde de forma diversa aos insultos agudos,  
18 diferentemente de jovens. Na ocasião da alta do leito especializado, este grupo exige  
19 cuidados de reabilitação e reinserção em seu meio social.(4-6) Idosos admitidos na  
20 terapia intensiva têm maior benefício do que os não admitidos.(7-8) No Brasil, o  
21 envelhecimento populacional também se reflete na idade média dos pacientes  
22 admitidos em UTI, que é de 62 anos.(9)

23 Em situações em que a demanda por leitos é superior à disponibilidade deles,  
24 como em catástrofes e pandemias, a organização para triagem de admissões é  
25 mandatória. Estabelecer critérios para triar pacientes é uma forma de, além de  
26 gerenciar os recursos, racionalizar a decisão do profissional responsável por  
27 encaminhar esses pacientes à UTI. A alocação de recursos envolve o conhecimento  
28 sobre doença aguda, fatores de risco para mortalidade, sobrevida a longo prazo,  
29 probabilidade de recuperação e princípios éticos. A sistematização da triagem do  
30 paciente deve ser abordada com a equipe assistente em sua totalidade, paciente e  
31 família. Os protocolos de priorização e triagem devem ser estabelecidos para garantir  
32 o uso dos recursos de forma ética e com o melhor aproveitamento em termos de  
33 recuperação e sobrevida aos pacientes.(10-14)

34 A base da triagem do paciente grave é o prognóstico, que pode ser avaliado por  
35 meio de escores de gravidade, de disfunções orgânicas e de quantidade de trabalho  
36 da equipe. Escores prognósticos são desenvolvidos em populações de pacientes  
37 graves a partir de variáveis clínicas prévias à admissão e da situação da doença

1 aguda. Esses escores discriminam pacientes, entre outros desfechos, especialmente  
2 em grupos de sobreviventes e não sobreviventes.(15) O escore *Acute Physiology and*  
3 *Chronic Health Evaluation* (APACHE II) foi desenhado considerando variáveis clínicas  
4 e laboratoriais das primeiras 24 horas de admissão do paciente em leito especializado,  
5 além de quadro mórbido prévio.(16) O *Sequential Organ Failure Assessment* (SOFA) é  
6 um escore de disfunção orgânica que leva em consideração exames laboratoriais e  
7 parâmetros clínicos para avaliar sistemas.(17) O *Therapeutic Intervention Scoring*  
8 *System* (TISS 28) avalia a gravidade do paciente a partir da quantidade de  
9 intervenções e cuidados pela equipe de enfermagem.(18)

10 Mesmo com a padronização da gravidade do paciente através de escores,  
11 estabelecer quais pacientes se beneficiam da admissão em leito especializado é um  
12 desafio ao intensivista. Os estudos nesse sentido objetivam verificar quais pacientes  
13 apresentam impacto estatístico na sobrevida após o insulto agudo. Tal análise indica o  
14 perfil do indivíduo com maior benefício de uso dos recursos. A instrumentalização dos  
15 critérios é superior à observação clínica, uma vez que minimiza fatores de confusão  
16 que podem existir durante a seleção de pacientes para o leito de UTI.(19-21) O  
17 prognóstico do paciente também é modificado quanto maior for o tempo de espera  
18 para admissão em leito especializado, uma vez que cada hora de espera por um leito  
19 de UTI aumenta em 1,5% a mortalidade. (22)

20 Nos Estados Unidos da América, houve o aumento de 92% dos custos com  
21 Medicina Intensiva de 2000 a 2010, o que representou o total de 108 bilhões de  
22 dólares. A diária em UTI representa 4300 dólares. Mais de 5 milhões de pacientes  
23 naquele país são admitidos anualmente em leitos especializados. Estima-se que o  
24 número de leitos de UTI aumentou de 88.235 para 103.900 leitos de 2000 a 2010.(23)

25 No Brasil, estima-se que 24% dos estabelecimentos de saúde apresentem UTI,  
26 totalizando cerca de 8% dos leitos hospitalares. Enquanto o estado de São Paulo  
27 representa aproximadamente 24% dos estabelecimentos com UTI do país, o estado de  
28 Roraima contempla aproximadamente 0,2%. A maior parte (44%) dos  
29 estabelecimentos com UTI está em serviço privado, enquanto 77% dos atendimentos  
30 configuram pacientes do Sistema Único de Saúde (SUS). Para cada 10.000 habitantes  
31 no país, existem 2 leitos de UTI. Existem cerca de 11.500 médicos intensivistas, 2500  
32 enfermeiros intensivistas e 4500 técnicos de enfermagem especialistas em terapia  
33 intensiva no território nacional.(24)

34 Em 1997, a *American Thoracic Society* (ATS) publicou diretrizes para o uso de  
35 leitos de UTI, considerando discussões sobre vontade do paciente, alocação de  
36 recursos financeiros e humanos e disponibilidade de leitos quando a demanda supera  
37 a oferta de leitos. Na ocasião, a orientação consistia em admitir pacientes no leito

1 especializado por ordem cronológica, considerando o princípio de *first-come, first-*  
2 *served*, assim como não dar alta para os pacientes até que houvesse condições  
3 clínicas para tanto.(25)

4 Conforme surgiram evidências sobre prognóstico de doentes graves, foram  
5 escritas orientações para padronizar critérios para admitir pacientes. Para orientar o  
6 clínico a discriminar melhor quais seriam os pacientes “*too well to benefit*” e “*too sick to*  
7 *benefit*”, em 1999 a *Society of Critical Care Medicine* (SCCM) publicou um *guideline*  
8 para agrupar pacientes em grupos de prioridades, que são:

9 1) Prioridade 1: pacientes em estado crítico, instáveis, que precisam de  
10 tratamento intensivo e monitoramento que não podem ser fornecidos fora da  
11 UTI. Normalmente esses tratamentos incluem suporte ventilatório, como a  
12 infusão contínua de drogas vasoativas. Os pacientes de prioridade 1  
13 geralmente não têm limites para a extensão da terapia que devem receber;

14 2) Prioridade 2: pacientes que requerem monitoramento intensivo e podem  
15 potencialmente precisar de intervenção imediata. Em geral, nenhum limite  
16 terapêutico é estipulado para esses pacientes. Os exemplos incluem  
17 pacientes com condições crônicas que desenvolvem doença clínica ou  
18 cirúrgica aguda grave;

19 3) Prioridade 3: pacientes instáveis que estão gravemente enfermos, mas têm  
20 uma probabilidade reduzida de recuperação devido à doença subjacente ou à  
21 natureza de sua doença aguda. Os pacientes de Prioridade 3 podem receber  
22 tratamento intensivo para aliviar a doença aguda; no entanto, podem ser  
23 estabelecidos limites aos esforços terapêuticos, como ausência de intubação  
24 ou ressuscitação cardiopulmonar e

25 4) Prioridade 4: são pacientes que geralmente não são adequados para  
26 admissão na UTI (“*too well to benefit*” ou “*too sick to benefit*”). A admissão  
27 desses pacientes deve ser individual, em circunstâncias incomuns e a critério  
28 do diretor da UTI.(26)

29  
30 Em 2016, a SCCM atualizou o documento com base em 15 anos de  
31 publicações sobre o tema, incluindo uma quinta prioridade e organizando os grupos  
32 em níveis de atenção em:

33 1) UTI

34 a) Prioridade 1: Pacientes gravemente enfermos que requerem suporte de  
35 vida para falência de órgãos, monitoramento intensivo, e terapias oferecidas  
36 apenas em ambiente de UTI. O suporte de vida inclui ventilação invasiva,  
37 terapias de substituição renal contínuas, monitoramento hemodinâmico

1 invasivo para direcionar intervenções hemodinâmicas agressivas, oxigenação  
2 por membrana extracorpórea, bombas de balão intra-aórtico e outras  
3 situações que requerem cuidados intensivos (por exemplo, pacientes com  
4 hipoxemia grave ou em choque);

5 b) Prioridade 2: Pacientes, conforme descrito acima, com probabilidade  
6 significativamente menor de recuperação e que gostariam de receber terapias  
7 de terapia intensiva, mas não reanimação cardiopulmonar em caso de parada  
8 cardíaca (por exemplo, pacientes com câncer metastático e insuficiência  
9 respiratória secundária a pneumonia ou em choque séptico requerendo  
10 vasopressores);

## 11

### 12 2) Unidade de Cuidados Intermediários (UCI)

13 a) Prioridade 3: Pacientes com disfunção orgânica que requerem  
14 monitoramento intensivo e / ou terapias (por exemplo, ventilação não  
15 invasiva), ou que, na opinião clínica do médico responsável pela triagem,  
16 poderiam ser gerenciados em um nível de cuidado inferior ao da UTI (por  
17 exemplo, pacientes pós-operatórios que requerem monitoramento rigoroso  
18 para risco de deterioração ou requerem cuidados pós-operatórios intensos,  
19 pacientes com insuficiência respiratória tolerando ventilação não invasiva  
20 intermitente). Esses pacientes podem precisar ser internados na UTI se o  
21 manejo precoce falhar em prevenir a deterioração ou se não houver  
22 capacidade de UCI no hospital;

23 b) Prioridade 4: Pacientes, conforme descrito acima, mas com menor  
24 probabilidade de recuperação / sobrevivência (por exemplo, pacientes com  
25 doença metastática subjacente) que não desejam ser intubados ou  
26 ressuscitados. Como acima, se o hospital não tiver capacidade de UCI, esses  
27 pacientes podem ser considerados para UTI em circunstâncias especiais e  
28

### 29 3) Cuidados Paliativos

30 a) Prioridade 5: Pacientes terminais ou moribundos sem possibilidade de  
31 recuperação; tais pacientes geralmente não são adequados para admissão na  
32 UTI (a menos que sejam potenciais doadores de órgãos). Nos casos em que  
33 os indivíduos recusaram inequivocamente as terapias de terapia intensiva ou  
34 têm processos irreversíveis, como câncer metastático, sem opções adicionais  
35 de quimioterapia ou radioterapia, cuidados paliativos devem ser inicialmente  
36 oferecidos.(27)

1 O Conselho Federal de Medicina (CFM), em 2016, publicou os critérios  
2 nacionais para admissão de pacientes em UTI, estabelecendo também 5 prioridades,  
3 distribuídas em internações sugeridas em UTI, UCI (prioridades 2 e 4) e unidade de  
4 cuidados paliativos (prioridade 5):

5 1) Prioridade 1: Pacientes que necessitam de intervenções de suporte à  
6 vida, com alta probabilidade de recuperação e sem nenhuma limitação de  
7 suporte terapêutico.

8 2) Prioridade 2: Pacientes que necessitam de monitorização intensiva, pelo  
9 alto risco de precisarem de intervenção imediata, e sem nenhuma  
10 limitação de suporte terapêutico.

11 3) Prioridade 3: Pacientes que necessitam de intervenções de suporte à  
12 vida, com baixa probabilidade de recuperação ou com limitação de  
13 intervenção terapêutica.

14 4) Prioridade 4: Pacientes que necessitam de monitorização intensiva, pelo  
15 alto risco de precisarem de intervenção imediata, mas com limitação de  
16 intervenção terapêutica.

17 5) Prioridade 5: Pacientes com doença em fase de terminalidade, ou  
18 moribundos, sem possibilidade de recuperação. Em geral, esses pacientes  
19 não são apropriados para admissão na UTI (exceto se forem potenciais  
20 doadores de órgãos). No entanto, seu ingresso pode ser justificado em  
21 caráter excepcional, considerando as peculiaridades do caso e condicionado  
22 ao critério do médico intensivista.(28)

23  
24 O aspecto ético que envolve a admissão ou não de um paciente no leito  
25 especializado envolve todos os participantes envolvidos no cuidado – o próprio  
26 paciente, o médico assistente responsável pela internação do paciente, o médico  
27 intensivista, o médico substituto no caso da não admissão na UTI, o médico gerente de  
28 fluxo, o gestor, o governo, a família do paciente e também os outros pacientes que  
29 precisam de leito de UTI. Os valores envolvidos nessa decisão abrangem todos os  
30 princípios bioéticos no cuidado do paciente admitido e também do paciente não  
31 admitido: não maleficência (não causar mal aos pacientes); beneficência (fazer o bem);  
32 respeito à autonomia (desejos de ambos os pacientes) e justiça (distribuição igual ou  
33 desigual para beneficiar o menos favorecido). O desafio de equilibrar os princípios na  
34 seleção de qual paciente será ou não recebido na UTI ainda é um grande dilema na  
35 atualidade, apesar de todos os avanços no conhecimento sobre prognóstico de  
36 doenças e uso de recursos de suporte de vida. Assim como a primeira admissão, a

1 readmissão em UTI é outro aspecto que merece discussão ética sobre os recursos  
2 disponíveis e o prognóstico do paciente. (29-31)

3 Considerando que a demanda por leitos de UTI e profissionais com formação  
4 especializada é maior que a disponibilidade dos mesmos, é necessário selecionar  
5 quem será admitido. Os dilemas éticos e técnicos envolvidos na seleção do paciente  
6 que acessará a UTI abrangem questões como quem deve realizar essa triagem, o que  
7 pode limitar o acesso do paciente ao leito e quem é o paciente que se beneficia do  
8 cuidado do especialista. Há necessidade de estudos que tornem mais objetiva a  
9 triagem desses pacientes, permitindo que a seleção seja adequada e benéfica a todas  
10 as partes envolvidas nessa decisão, especialmente em situações de catástrofes e de  
11 contingência de recursos. (32-35)

12

### 13 **1.1 Justificativa**

14 A preocupação com o correto uso dos recursos humanos e materiais nos  
15 hospitais e UTIs é crescente, principalmente em relação às decisões sobre priorização  
16 e triagem de pacientes a serem admitidos em ambientes de terapia intensiva,  
17 entretanto, as informações sobre os impactos de protocolos para esse fim são  
18 escassas.

19 A avaliação da implementação de um protocolo de priorização e triagem para  
20 admissão de pacientes críticos em UTI e as respectivas repercussões na mortalidade,  
21 tempo de permanência e gravidade destes pacientes antes e depois de tal protocolo,  
22 pode colaborar para o desenvolvimento de novas técnicas que possibilitem a  
23 otimização do uso de recursos humanos e financeiros no cuidado ao paciente crítico.

24

1 **2 OBJETIVOS**

2

3 **2.1 OBJETIVO GERAL**

4

5 Analisar o efeito da implementação de novo modelo de triagem por prioridades  
6 para admissão em unidade de terapia intensiva no desfecho de pacientes graves.

7

8 **2.2 OBJETIVOS ESPECÍFICOS**

9

- 10 1. Caracterizar os pacientes adultos admitidos em unidades de terapia intensiva  
11 de acordo com aspectos clínicos e demográficos.
- 12 2. Comparar as características clínicas e critérios de gravidade nos períodos do  
13 estudo.
- 14 3. Comparar o tempo de permanência em terapia intensiva e no hospital nos  
15 períodos do estudo.
- 16 4. Comparar a taxa de mortalidade hospitalar nos períodos do estudo.
- 17 5.

## 1 **3 MÉTODOS**

2

### 3 **3.1 Delineamento**

4

5 Estudo longitudinal retrospectivo.

6

### 7 **3.2 População de estudo**

8

9 Pacientes adultos internados na Unidade de Terapia Intensiva do Hospital  
10 Universitário de Londrina.

11

### 12 **3.3 Amostragem e local de estudo**

13

14 Amostragem de conveniência dos pacientes adultos admitidos na Unidade de  
15 Terapia Intensiva (UTI) do Hospital Universitário de Londrina (HU), no período de  
16 janeiro de 2013 a dezembro de 2017. O HU é um órgão suplementar da Universidade  
17 Estadual de Londrina (UEL), atualmente com cerca de 291 leitos e constitui o maior  
18 hospital geral público que atende o município de Londrina - Paraná e região. O número  
19 de leitos da UTI adulto deste hospital variou de 17 a 20 leitos no período do estudo e  
20 nela são internados pacientes clínicos e cirúrgicos.

21

### 22 **3.4 Critérios de seleção**

23

- 24 • Inclusão: todos os pacientes adultos admitidos na unidade de terapia intensiva  
25 no período de estudo.
- 26 • Exclusão: pacientes menores de 18 anos, pacientes com tempo de  
27 permanência na UTI menor que 24 horas, readmissões na UTI durante a  
28 mesma internação hospitalar.

29

### 30 **3.5 Aspectos éticos**

31

32 O presente estudo foi submetido e aprovado pelo Comitê de Ética em Pesquisa  
33 Envolvendo Seres Humanos da Universidade Estadual de Londrina (CEP-UEL)  
34 conforme parecer substanciado do CEP-UEL no. 3.377.114; CAAE  
35 13959319.4.0000.5231, data da relatoria 07/06/2019. Devido ao delineamento e  
36 objetivo do estudo foi solicitada a dispensa do Termo de Consentimento Livre e

1 Esclarecido. O autor se comprometeu a desenvolver a pesquisa de acordo com a  
2 Resolução do Conselho Nacional de Saúde/MS nº 466 de 12 de dezembro de 2012.

### 3 4 **3.6 Acompanhamento**

5  
6 Dados completos foram coletados de todos os pacientes inseridos no estudo  
7 até o desfecho hospitalar. O desfecho primário foi considerado estado vital na saída do  
8 hospital.

### 9 10 **3.7 Coleta de dados**

11  
12 Os dados gerais coletados para todas as admissões na UTI foram idade,  
13 gênero, data de internação no hospital e na UTI, tipo de admissão, diagnóstico de  
14 admissão na UTI, setor de origem, data da alta da UTI e do hospital, desfecho à saída  
15 da UTI e do hospital.

16 Os dados coletados durante a internação na UTI foram: presença de doença  
17 crônica, necessidade de ventilação mecânica, uso de drogas vasoativas e os escores  
18 *Acute Physiology and Chronic Health Evaluation* (APACHE II), *Sequential Organ*  
19 *Failure Assessment* (SOFA) e *Therapeutic Intervention Scoring System* (TISS 28).

20 As fontes utilizadas para a coleta de dados foram os prontuários dos pacientes.  
21 Todos os dados para cálculo dos escores foram coletados como dados brutos,  
22 utilizando-se os extremos de anormalidade durante as primeiras 24 horas de  
23 internação na UTI. O cálculo dos escores foi efetuado segundo as definições dos  
24 respectivos sistemas. Os pacientes foram acompanhados diariamente até o desfecho  
25 final, considerado estado vital na saída do hospital.

### 26 27 **3.8 Períodos do estudo**

28  
29 Os pacientes internados na UTI no período do estudo foram divididos em  
30 período pré e pós alteração do modelo de triagem para admissão na UTI.

31 Até o ano 2015 o protocolo institucional para triagem e admissão em UTI era  
32 cronológico conforme data e horário de solicitação da vaga (primeiro a chegar,  
33 primeiro a receber tratamento) com base nos guidelines da *American Thoracic Society*.  
34 No contexto de alta demanda de cuidados intensivos, este hospital implantou naquele  
35 ano um modelo de priorização para admissão em UTI com base na diretriz da *Society*  
36 *of Critical Care Medicine* (26). Este modelo se baseia na classificação dos pacientes  
37 com demanda de cuidados intensivos em quatro grupos assim denominados:

- 1 • Prioridade 1: pacientes críticos que necessitam de intervenção e monitorização  
2 que não pode ser obtida fora do ambiente de terapia intensiva;
- 3 • Prioridade 2: pacientes que necessitam de monitorização intensiva e que  
4 eventualmente poderão necessitar intervenções imediatas;
- 5 • Prioridade 3: pacientes críticos e instáveis, mas que possuem uma baixa  
6 probabilidade de recuperação por ocasião do seu quadro atual ou devido às  
7 comorbidades subjacentes;
- 8 • Prioridade 4: são pacientes que geralmente não são apropriados para  
9 admissão em UTI e podem ser subdivididos nas categorias A que seriam os  
10 pacientes que pouco se beneficiariam dos cuidados intensivos e na categoria B  
11 composta pelos pacientes com doenças terminais e irreversíveis na iminência  
12 de morte.

13 Em 2016 esse modelo de priorização foi atualizado (27) de modo a acrescentar  
14 um novo grupo (prioridade 5) que seria constituído por pacientes sem possibilidades  
15 de recuperação e a quem deveriam ser oferecidos os cuidados paliativos. Nesta  
16 atualização além de mudanças na definição de cada grupo de prioridade, o documento  
17 também sugere que os pacientes classificados como prioridade 3 e 4 poderiam ser  
18 admitidos em unidades de cuidados intermediários, quando existentes:

- 19 • Prioridade 1: pacientes críticos que necessitam de intervenção e/ou  
20 monitorização intensiva que não pode ser obtida fora do ambiente de terapia  
21 intensiva;
- 22 • Prioridade 2: pacientes críticos que necessitam de intervenção e/ou  
23 monitorização intensiva com probabilidade baixa de recuperação que desejam  
24 receber cuidados intensivos exceto ressuscitação cardiopulmonar na hipótese  
25 de parada cardiorrespiratória;
- 26 • Prioridade 3: pacientes com disfunções orgânicas que necessitam de  
27 monitorização intensiva e terapias pouco ou não invasivas e que poderiam ser  
28 manejados em ambientes de cuidados intermediários;
- 29 • Prioridade 4: pacientes com disfunções orgânicas que necessitam de  
30 monitorização intensiva e terapias pouco ou não invasivas, mas que também  
31 apresentam baixa probabilidade de recuperação/sobrevida e que não desejam  
32 ser entubados ou ressuscitados, podendo ser alocados na UTI em  
33 circunstâncias especiais;
- 34 • Prioridade 5: Pacientes terminais ou sem possibilidade de recuperação (exceto  
35 se for potencial doador de órgãos) que geralmente não são apropriados para o

1 ambiente de terapia intensiva e a quem deveriam ser iniciados os cuidados  
2 paliativos.

3 Em janeiro de 2017, esta atualização foi adaptada e praticada na triagem dos  
4 pacientes que necessitam de cuidados intensivos no HU-UEL. Foram considerados  
5 período pré mudança do modelo de triagem os anos de 2013 e 2014. Os anos de 2015  
6 a 2017 foram considerados período pós mudança do modelo de triagem.

7

### 8 **3.9 Análise Estatística**

9

10 Variáveis contínuas foram expressas como média e desvio padrão (DP) ou  
11 mediana e intervalo interquartil (ITQ) de acordo com a distribuição dos dados. As  
12 variáveis categóricas foram expressas como proporção. Estatística descritiva foi  
13 utilizada para a apresentação de todas as variáveis relevantes. Os dados estão  
14 apresentados em gráficos e tabelas. O teste não paramétrico de Mann-Whitney foi  
15 usado para a comparação das variáveis contínuas. As variáveis categóricas foram  
16 comparadas usando o teste de Qui-quadrado de Pearson ou exato de Fisher e o teste  
17 de qui-quadrado de tendência linear. Foi realizada análise bivariada para analisar a  
18 associação da triagem com as variáveis do estudo. A análise de regressão de Cox foi  
19 aplicada para avaliar fatores que contribuem de forma independente para explicar o  
20 desfecho hospitalar, o efeito de cada fator foi expresso em razão de risco proporcional  
21 (HR) e intervalo de 95% de confiança (IC 95%). O risco acumulado da mortalidade  
22 hospitalar foi descrito pela análise da curva de sobrevivência de Kaplan - Meier. O  
23 nível de significância utilizado foi de 5% e as análises foram realizadas utilizando-se o  
24 programa *SPSS Statistics for Windows* versão 19.

1 **4 ARTIGO CIENTÍFICO A SER SUBMETIDO À REVISTA *INTENSIVE CARE***  
2 ***MEDICINE* (instruções aos autores: ANEXO 4)**

3

4 **TÍTULO: Melhora da performance de uma unidade de terapia intensiva após**  
5 **mudança de modelo de triagem para admissão**

6

7 **4.1 Resumo**

8

9 **Objetivo:** Analisar o efeito da implementação de um modelo de priorização e triagem  
10 para admissão em unidade de terapia intensiva no desfecho de pacientes graves.

11 **Métodos:** Estudo longitudinal retrospectivo realizado por amostragem de conveniência  
12 dos pacientes adultos admitidos na Unidade de Terapia Intensiva (UTI) do Hospital  
13 Universitário de Londrina (HU), no período de janeiro de 2013 a dezembro de 2017. O  
14 desfecho primário foi considerado estado vital na saída do hospital. Foram coletados  
15 dados clínicos e os escores *Acute Physiology and Chronic Health Evaluation II*  
16 (APACHE II), *Sequential Organ Failure Assessment* (SOFA) e *Therapeutic Intervention*  
17 *Scoring System 28* (TISS 28) na admissão da UTI. Os pacientes foram divididos em  
18 período pre e pós alteração do modelo de triagem. O período 1 (triagem cronológica)  
19 foram os anos de 2013 a 2014. O período 2 (triagem por priorização) foram os anos de  
20 2015 a 2017. O nível de significância utilizado foi de 5% e as análises foram realizadas  
21 utilizando-se o programa SPSS Statistics for Windows, Versão 19.0.

22 **Resultados:** Foram analisados 3.283 pacientes, sendo que 1.227 foram admitidos no  
23 período 1 e 2.056 no período 2. Os pacientes admitidos no período 2 do estudo eram  
24 mais velhos (59,8 anos  $\pm$ 18,3), com menor proporção de doenças crônicas (13,6%),  
25 tinham valor médio do escore APACHE II (21,0 ITQ 14-29) e do escore TISS 28 (28,0  
26 ITQ 21-36) maiores comparados aos pacientes do período 1. O diagnóstico de sepse  
27 foi mais frequente (50,5%) no segundo período do estudo. Foi observado aumento do  
28 número de admissões ao longo do período de estudo. No período 2 os pacientes  
29 apresentaram uma tendencia a permanecerem menor tempo internados na UTI (8,5  
30 dias  $\pm$  11,8) e no hospital (22,8 dias  $\pm$  27,2) e tiveram menor mortalidade na saída da  
31 UTI (32,8%) e do hospital (44,2%).

32 **Conclusões:** A mudança do modelo de triagem, de um modelo cronológico para um  
33 modelo de priorização resultou em melhora do desempenho de uma unidade de  
34 terapia intensiva, com aumento do número de admissões, redução da taxa de  
35 mortalidade hospitalar e uma tendência à redução do tempo de permanência

36 **Descritores:** Cuidados Críticos; Triagem; Admissão do Paciente; Unidades de Terapia  
37 Intensiva; Ocupação de Leitos.

## 1 **4.2 Introdução**

2 É consenso que existe limitação dos recursos de saúde. No que diz respeito ao  
3 acesso a leitos especializados em terapia intensiva, frequentemente não há  
4 disponibilidade para todas as pessoas que necessitam. Para otimizar os recursos  
5 disponíveis é parte das atribuições de um intensivista tomar decisões sobre  
6 prioridades de acesso a unidades de terapia intensiva (UTI) (1).

7 Quando os recursos disponíveis são suplantados pela demanda de um  
8 determinado serviço, forma-se uma fila de atendimento, ou seja, uma demanda  
9 reprimida. Para entender os motivos da formação dessa fila pode-se remeter à teoria  
10 da fila. A teoria das filas é uma área das ciências exatas que estuda a probabilidade da  
11 formação de filas. O processo de fila é composto por três elementos: regime de  
12 chegada, regime de serviço e disciplina da fila. Na formação da fila devem ser  
13 considerados se a população é ou não infinita, o intervalo de tempo entre as  
14 chegadas, a disponibilidade do serviço, capacidade do sistema, duração do tempo do  
15 serviço para abrir nova vaga, além da disciplina da fila. A disciplina da fila se refere às  
16 normas que definem a ordenação dada aos pacientes que serão atendidos. Para isso,  
17 existem diversas possibilidades, como o atendimento pela ordem de chegada,  
18 atendimento aleatório ou a prioridade para certas categorias de clientes (2).

19 O modelo intuitivo mais lógico e mais aplicado no dia a dia é o cronológico, ou  
20 seja, os primeiros a chegarem são os primeiros a serem atendidos. No entanto, no  
21 sistema de saúde e em situações de grande demanda reprimida por leitos de UTI,  
22 esse modelo pode ter consequências graves especialmente para pacientes com  
23 maiores chances de recuperação. A espera por um leito de UTI pode implicar em  
24 redução dessas chances de sobrevivência pois existem tratamentos que podem estar  
25 disponíveis exclusivamente dentro do ambiente da UTI (3).

26 Para decidir sobre a admissão em uma UTI existem diversos modelos a serem  
27 considerados (4-7). Nos modelos por diagnósticos é utilizada uma lista de condições  
28 que indicam tratamento em UTI. Nos modelos por parâmetros objetivos são  
29 estabelecidos limites de variáveis fisiológicas e laboratoriais que levam à decisão  
30 sobre admissão em UTI. O modelo por parâmetros objetivos pode ser utilizado em  
31 combinação com o modelo diagnóstico para melhorar o processo de decisão. Há  
32 também o modelo de priorização de admissão na UTI, em que a disciplina da fila de  
33 espera obedece a um sistema de triagem estruturado.

34 Um sistema de triagem deve ser tão preciso quanto possível. A triagem  
35 levemente permissiva é preferível, mas em um sistema muito sobrecarregado pode  
36 não ser viável, especialmente em situações de grande aumento por demanda de  
37 leitos. Se a triagem for excessivamente permissível, pode tornar o sistema

1 sobrecarregado. Se a triagem for excessivamente restritiva, pode se associar a  
2 aumento da mortalidade. Uma força tarefa da sociedade norte americana de medicina  
3 intensiva propôs um sistema de triagem com cinco níveis de prioridade, onde o nível 1  
4 é o de maior prioridade para admissão na UTI e o nível 5 o de menor prioridade (5).

5 Existe limitação significativa de evidências científicas sobre o tema de triagem  
6 para admissão na UTI. É assunto complexo que envolve aspectos médicos, éticos e  
7 legais e que afeta diretamente a prática médica rotineira. O uso adequado de recursos  
8 de saúde limitados é uma grande responsabilidade, assim como a decisão sobre a  
9 admissão de um paciente em leito de UTI.

10 O objetivo deste estudo é analisar o efeito da implementação de um modelo de  
11 priorização e triagem para admissão em unidade de terapia intensiva no desfecho de  
12 pacientes graves.

### 14 **4.3 Métodos**

15 Estudo longitudinal retrospectivo realizado por amostragem de conveniência  
16 dos pacientes adultos admitidos na Unidade de Terapia Intensiva (UTI) do Hospital  
17 Universitário de Londrina (HU), no período de janeiro de 2013 a dezembro de 2017. O  
18 HU é um órgão suplementar da Universidade Estadual de Londrina (UEL), atualmente  
19 com cerca de 291 leitos e constitui o maior hospital geral público que atende o  
20 município de Londrina - Paraná e região. O número de leitos da UTI adulto deste  
21 hospital variou de 17 a 20 leitos no período do estudo e nela são internados pacientes  
22 clínicos e cirúrgicos. Foram excluídos da análise os pacientes menores de 18 anos,  
23 pacientes com tempo de permanência na UTI menor que 24 horas, readmissões na  
24 UTI durante a mesma internação hospitalar.

25 Dados completos foram coletados de todos os pacientes inseridos no estudo  
26 até o desfecho hospitalar. O desfecho primário foi considerado estado vital na saída do  
27 hospital.

28 Os dados gerais coletados para todas as admissões na UTI foram idade, sexo,  
29 data de internação no hospital e na UTI, diagnóstico principal de admissão na UTI,  
30 setor de origem, data da alta da UTI e do hospital, desfecho à saída da UTI e do  
31 hospital.

32 Também foram coletadas informações sobre presença de doença crônica,  
33 necessidade de ventilação mecânica, necessidade de diálise, uso de drogas  
34 vasoativas e os escores *Acute Physiology and Chronic Health Evaluation II* (APACHE  
35 II) (8), *Sequential Organ Failure Assessment* (SOFA) (9) do primeiro dia de internação  
36 na UTI e *Therapeutic Intervention Scoring System 28* (TISS 28) (10). Outras variáveis

1 importantes coletadas foram o tempo de permanência hospitalar e tempo de  
2 permanência na UTI.

3 As fontes utilizadas para a coleta de dados foram os prontuários dos pacientes.  
4 Todos os dados para os cálculos dos escores foram coletados como dados brutos,  
5 utilizando-se os extremos de anormalidade durante as primeiras 24 horas de  
6 internação na UTI. Os cálculos dos escores foram efetuados segundo as definições  
7 dos respectivos sistemas.

8 Os pacientes internados na UTI no período do estudo foram divididos em  
9 período pré e pós alteração do modelo de triagem para admissão na UTI. Foram  
10 considerados período pré mudança do modelo de triagem os anos de 2013 a 2014,  
11 denominado período 1. Os anos de 2015 a 2017 foram considerados período pós  
12 mudança do modelo de triagem, denominado período 2.

13 Até o ano 2015 o protocolo institucional para triagem e admissão em UTI era  
14 fundamentado na publicação da *American Thoracic Society* (7) e era basicamente  
15 cronológico (primeiro a chegar, primeiro a receber tratamento). No contexto de alta  
16 demanda de cuidados intensivos, este hospital alterou a forma de triagem para um  
17 modelo de priorização para admissão em UTI baseado na diretriz da *Society of Critical*  
18 *Care Medicine* (11). Este modelo se baseia na classificação dos pacientes com  
19 demanda de cuidados intensivos em quatro grupos assim denominados:

- 20 • Prioridade 1: pacientes críticos que necessitam de intervenção e monitorização  
21 que não pode ser obtida fora do ambiente de terapia intensiva;
- 22 • Prioridade 2: pacientes que necessitam de monitorização intensiva e que  
23 eventualmente poderão necessitar intervenções imediatas;
- 24 • Prioridade 3: pacientes críticos e instáveis, mas que possuem uma baixa  
25 probabilidade de recuperação por ocasião do seu quadro atual ou devido às  
26 comorbidades subjacentes;
- 27 • Prioridade 4: são pacientes que geralmente não são apropriados para  
28 admissão em UTI e podem ser subdivididos nas categorias A que seriam os  
29 pacientes que pouco se beneficiariam dos cuidados intensivos e na categoria B  
30 composta pelos pacientes com doenças terminais e irreversíveis na iminência  
31 de morte.

32 Em 2016 esse modelo de priorização foi atualizado de modo a acrescentar um  
33 novo grupo (prioridade 5) que seria constituído por pacientes com nenhuma  
34 possibilidade de recuperação e a quem deveria ser oferecidos os cuidados paliativos  
35 (5). Nesta atualização foram confirmadas as definições de cada grupo de prioridade,  
36 também ficou sugerido que os pacientes classificados como prioridade 3 e 4 poderiam

1 ser admitidos em unidades de cuidados intermediários, quando existentes. Em janeiro  
2 de 2017 esta atualização foi adaptada e praticada na priorização e triagem dos  
3 pacientes que necessitam de cuidados intensivos no HU-UJEL.

#### 4 Análise Estatística

6 Variáveis contínuas foram expressas como média e desvio padrão (DP) ou  
7 mediana e intervalo interquartil (ITQ) de acordo com a distribuição dos dados. As  
8 variáveis categóricas foram expressas como proporção. Estatística descritiva foi  
9 utilizada para a apresentação de todas as variáveis relevantes. Os dados estão  
10 apresentados em gráficos e tabelas. O teste não paramétrico de Mann-Whitney foi  
11 usado para a comparação das variáveis contínuas. As variáveis categóricas foram  
12 comparadas usando o teste de Qui-quadrado de Pearson ou exato de Fisher e o teste  
13 de qui-quadrado de tendência linear. Foi realizada análise bivariada para analisar a  
14 associação da triagem com as variáveis do estudo. A análise de regressão de Cox foi  
15 aplicada para avaliar fatores que contribuem de forma independente para explicar o  
16 desfecho hospitalar, o efeito de cada fator foi expresso em razão de risco proporcional  
17 (HR) e intervalo de 95% de confiança (IC 95%). O risco acumulado da mortalidade  
18 hospitalar foi descrito pela análise da curva de sobrevivência de Kaplan - Meier.

19 O nível de significância utilizado foi de 5% e as análises foram realizadas  
20 utilizando-se o programa *SPSS Statistics for Windows*, Versão 19.0 (Armonk, NY: IBM  
21 Corp.).

#### 23 **4.4 Resultados**

24 Durante o período de estudo, foram admitidos 3.644 pacientes nos leitos de  
25 terapia intensiva da instituição da pesquisa. Foram excluídos 69 pacientes com idade  
26 menor de 18 anos, 164 pacientes readmitidos na UTI na mesma internação hospitalar  
27 e 128 por tempo de permanência na UTI menor que 24 horas. Foram analisados 3.283  
28 pacientes, sendo que 1.227 foram admitidos no período 1 e 2.056 no período 2.

29 A tabela 1 apresenta a comparação das características clínicas na admissão da  
30 UTI e dos desfechos de acordo com os períodos do estudo. Os pacientes admitidos no  
31 período 2 do estudo eram mais velhos (59,8 anos  $\pm$ 18,3), com menor proporção de  
32 doenças crônicas (13,6%), tinham valor médio do escore APACHE II (21,0 ITQ 14-29)  
33 e do escore TISS 28 (28,0 ITQ 21-36) maiores comparados aos pacientes do período  
34 1. O diagnóstico de sepse foi maior no segundo período do estudo. No período 2 os  
35 pacientes apresentaram tendência a permanecerem menor tempo internados na UTI e  
36 no hospital e tiveram menor mortalidade na saída da UTI e do hospital.

1 A tabela 2 apresenta as intervenções terapêuticas utilizadas pelos pacientes no  
2 primeiro dia de permanência na UTI durante os períodos do estudo. A necessidade de  
3 ventilação mecânica invasiva e de diálise foi semelhante nos períodos do estudo. O  
4 uso de droga vasoativa única na admissão da UTI foi mais frequente no segundo  
5 período do estudo, enquanto o uso de drogas vasoativas múltiplas foi mais frequente  
6 no primeiro período do estudo. Houve aumento da realização de traqueostomias no  
7 período 2 do estudo.

8 Na tabela 3 é observado aumento do número de admissões ao longo do  
9 período de estudo e um aumento da proporção de admissões clínicas e de pós-  
10 operatório de cirurgias eletivas.

11 A tabela 4 apresenta a regressão de Cox com as variáveis independentes para  
12 o desfecho morte na saída do hospital. Os fatores de risco para morte foram idade e  
13 os escores APACHE II, SOFA e TISS 28. O período 2 do estudo, modelo de triagem  
14 por priorização, foi fator protetor para morte hospitalar, assim como o sexo masculino.  
15 A curva de sobrevivência de Kaplan-Meier para o desfecho morte na saída do hospital  
16 mostra redução da mortalidade dos pacientes no período 2 do estudo (Figura 1).

#### 17 **4.5 Discussão**

18 O presente estudo analisa o desempenho de uma unidade de terapia intensiva  
19 comparando dois períodos de estudo separados pela mudança do modelo de triagem  
20 para admissão de pacientes. A mudança de um modelo cronológico para um modelo  
21 de priorização resultou em mudança das características clínicas dos pacientes,  
22 aumento do escore de gravidade e do escore de intervenções terapêuticas, redução  
23 da taxa de mortalidade hospitalar dos pacientes e ao mesmo tempo uma tendência de  
24 redução do tempo de permanência

25 A decisão sobre a triagem de pacientes para admissão em unidades de terapia  
26 intensiva continua sendo um tema desafiador. Em geral, a aplicação de triagem para  
27 atendimento de pacientes tem o objetivo de salvar o maior número de pessoas em  
28 momentos de restrição da oferta do atendimento. As decisões para a realização da  
29 triagem podem ser feitas com base no benefício terapêutico, escolhendo os melhores  
30 candidatos aos leitos disponíveis, ou pode ser feita pelo critério cronológico, com a  
31 premissa de que os primeiros a chegarem serão os primeiros a serem atendidos (12-  
32 16).

33 Em situações ideais de disponibilidade de leitos especializados em terapia  
34 intensiva, aplicar o critério cronológico para admissão de pacientes parece ser uma  
35 opção viável. Com o aumento da demanda por leitos sem a respectiva oferta  
36 proporcional, as decisões de triagem devem dar prioridade para os pacientes que irão  
37

1 se beneficiar desse cuidado especializado (5,17). Para auxiliar no processo de decisão  
2 sobre triagem de pacientes para atendimento em situações de restrição de recursos,  
3 vários protocolos e ferramentas de triagem foram desenvolvidos (18-23); no entanto,  
4 algumas experiências de vida real falharam em documentar priorização adequada com  
5 as ferramentas desenvolvidas (20, 22).

6 As decisões sobre triagem de pacientes podem gerar ansiedade nos  
7 profissionais responsáveis. Dúvidas sobre os riscos pessoais e familiares, limitações  
8 do sistema e do paciente, falta de experiência e sobrecarga no trabalho são  
9 sentimentos que permeiam essas decisões. Dessa forma é recomendável que o  
10 profissional responsável pelas decisões de triagem não seja da mesma equipe que  
11 será responsável pelas decisões de alta dos pacientes (24). Essas equipes devem ter  
12 capacitação específica para essas funções e devem ter o apoio institucional com  
13 manutenção adequada dos serviços além de apoio jurídico durante esse processo.

14 Ao longo dos anos de observação houve aumento importante da demanda de  
15 vagas por leitos de terapia intensiva na instituição onde foi realizada a presente  
16 pesquisa e esse fato motivou a mudança de modelo de triagem. Com essa mudança  
17 de triagem, foi possível observar que não houve impacto clínico significativo da média  
18 de idade dos pacientes admitidos na UTI, com aumento médio de dois anos de idade  
19 no segundo período. Dessa forma, o modelo de priorização não resultou em restrição  
20 de acesso do idoso ao leito de terapia intensiva. A admissão do idoso na UTI é motivo  
21 de discussão nos modelos de triagem, pois de um lado existe o envelhecimento da  
22 população que aumenta a demanda de leitos pelos idosos, e por outro lado existe a  
23 preocupação na triagem de admitir os pacientes idosos que irão se beneficiar do  
24 tratamento. De um modo geral, os muito idosos tendem a receber a mesma  
25 intensidade de tratamento e ter prognóstico semelhante aos idosos (26).

26 Após a mudança do modelo de triagem no presente estudo também foi  
27 observada maior gravidade de doença na admissão na UTI, com grau de disfunções  
28 orgânicas semelhantes, maior intensidade de intervenção terapêutica e ao mesmo  
29 tempo menor tempo de permanência na UTI e redução da mortalidade. Esses achados  
30 levam a supor melhora do desempenho da unidade de terapia intensiva, que passou a  
31 admitir pacientes mais graves, porém resultando em melhores desfechos. Por esses  
32 achados é possível supor que o novo modelo de priorização resultou em melhora da  
33 triagem por pacientes com maiores chances de recuperação. Dentro do cenário de  
34 grande demanda por leitos, esse modelo de priorização provavelmente resultou em  
35 menor tempo de espera para admissão na UTI e uma recuperação mais acelerada dos  
36 pacientes admitidos. O modelo de priorização resultou em fator de proteção com  
37 redução de 13% na chance de morte na saída do hospital no presente estudo.

1           A redução de um dia no tempo de permanência na UTI significa um aumento  
2 da disponibilidade de leitos (27) e isso se refletiu em aumento importante do número  
3 de admissões ao longo dos anos do estudo. Mesmo levando-se em consideração que  
4 houve um aumento de três leitos de UTI na instituição da pesquisa no ano de 2014, só  
5 foi possível observar aumento do número de admissões a partir do ano de 2016, após  
6 a mudança do modelo de triagem.

7           Apesar deste estudo não ser um estudo clínico randomizado, este desenho não  
8 seria aplicável na amplitude no contexto a que se refere, sendo então uma boa  
9 maneira de avaliar as diferentes abordagens de problemas de logística e estratégia no  
10 que se refere à demanda por leitos de alta complexidade. Uma grande limitação deste  
11 estudo é ter sido realizado em um centro único, porém o fato de demonstrar que é  
12 possível melhorar o desempenho de unidades complexas como as de terapia intensiva  
13 com readequações das metodologias de triagem e organização de fluxos internos  
14 justifica o investimento em novos estudos sobre o tema.

15

#### 16 **4.6 Conclusão**

17           A mudança da triagem de pacientes graves, de um modelo cronológico para  
18 um modelo de priorização, resultou em melhora do desempenho de uma unidade de  
19 terapia intensiva. Foi observado aumento do número de admissões, redução do tempo  
20 de permanência na UTI e no hospital, além de redução da taxa de mortalidade  
21 hospitalar.

22

## 4.7 Referências

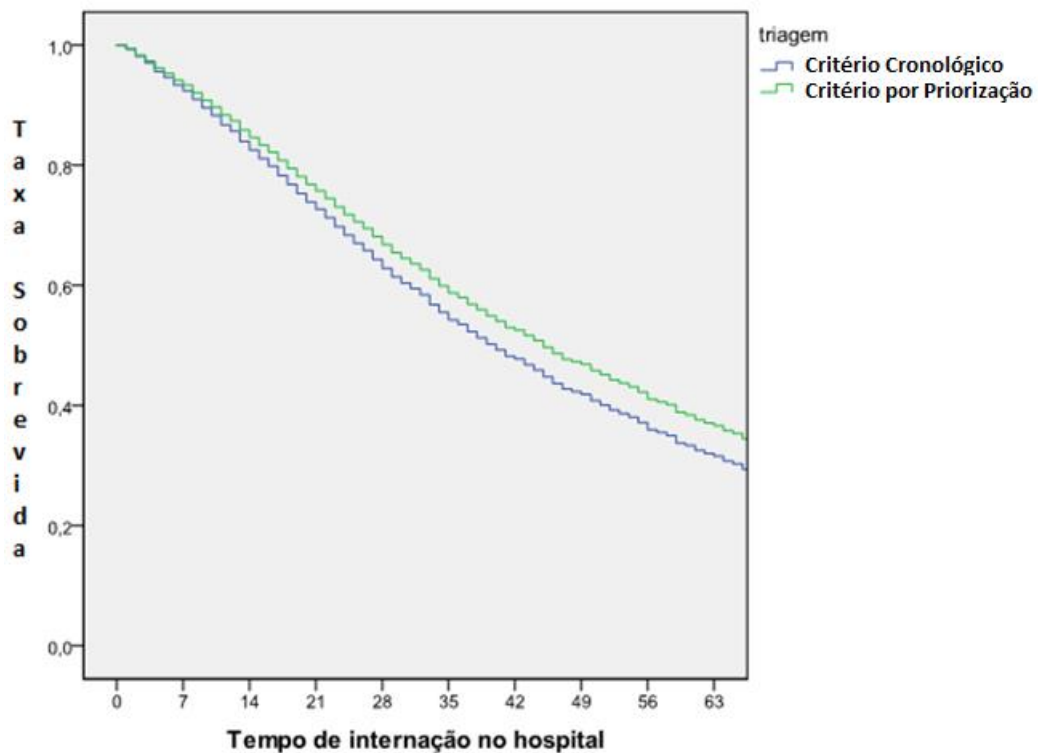
1. Bassford, C. Decisions regarding admission to the ICU and international initiatives to improve the decision-making process. *Crit Care* 21, 174 (2017).  
<https://doi.org/10.1186/s13054-017-1749-3>.
2. Goldwasser RS, Lobo MSC, Arruda EF, Angelo SA, Ribeiro ECO, Silva JRLE. Planning and understanding the intensive care network in the State of Rio de Janeiro (RJ), Brazil: a complex societal problem. *Rev Bras Ter Intensiva*. 2018 Jul-Sept;30(3):347-357. doi: 10.5935/0103-507X.20180053.
3. Cardoso LT, Grion CM, Matsuo T, Anami EH, Kauss IA, Seko L, Bonametti AM. Impact of delayed admission to intensive care units on mortality of critically ill patients: a cohort study. *Crit Care*. 2011;15(1):R28. doi: 10.1186/cc9975.
4. White ST, Cardenas YR, Nates JL. What every intensivist should know about intensive care unit admission criteria. *Rev Bras Ter Intensiva*. 2017 Oct-Dec;29(4):414-417. doi: 10.5935/0103-507X.20170073. PMID: 29340534; PMCID: PMC5764552.
5. Nates JL, Nunnally M, Kleinpell R, Blosser S, Goldner J, Birriel B, Fowler CS, Byrum D, Miles WS, Bailey H, Sprung CL. ICU Admission, Discharge, and Triage Guidelines: A Framework to Enhance Clinical Operations, Development of Institutional Policies, and Further Research. *Crit Care Med*. 2016 Aug;44(8):1553-602. doi: 10.1097/CCM.0000000000001856. PMID: 27428118.
6. Blanch L, Abillama FF, Amin P, Christian M, Joynt GM, Myburgh J, Nates JL, Pelosi P, Sprung C, Topeli A, Vincent JL, Yeager S, Zimmerman J; Council of the World Federation of Societies of Intensive and Critical Care Medicine. Triage decisions for ICU admission: Report from the Task Force of the World Federation of Societies of Intensive and Critical Care Medicine. *J Crit Care*. 2016 Dec;36:301-305. doi: 10.1016/j.jcrc.2016.06.014. Epub 2016 Jun 22. PMID: 27387663.
7. Fair allocation of intensive care unit resources. American Thoracic Society. *Am J Respir Crit Care Med*. 1997 Oct;156(4 Pt 1):1282-301. doi: 10.1164/ajrccm.156.4.ats7-97. Erratum in: *Am J Respir Crit Care Med* 1998 Feb;157(2):671. PMID: 9351636.
8. Knaus W, Draper E, Wagner D, Zimmerman J. APACHE II: A severity of disease classification system. *Crit Care Med*. 1985;13(10):818-29.
9. Vincent JL, de Mendonça A, Cantraine F, Moreno R, Takala J, Suter PM, Sprung CL, Colardyn F, Blecher S. Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: results of a multicenter, prospective study. Working group on "sepsis-related problems" of the European

- 1 Society of Intensive Care Medicine. *Crit Care Med.* 1998 Nov;26(11):1793-800.  
2 doi: 10.1097/00003246-199811000-00016. PMID: 9824069.
- 3 10. Miranda DR, Rijk A, Schaufeli W. Simplified therapeutic intervention scoring  
4 system: the TISS- 28 items--results from a multicenter study. *Crit Care Med.*  
5 1996;24(1):64-73
- 6 11. Guidelines for intensive care unit admission, discharge, and triage. Task Force of  
7 the American College of Critical Care Medicine, Society of Critical Care Medicine.  
8 *Crit Care Med.* 1999 Mar;27(3):633-8. PMID: 10199547.
- 9 12. Sprung CL, Zimmerman JL, Christian MD, Joynt GM, Hick JL, Taylor B, Richards  
10 GA, Sandrock C, Cohen R, Adini B; European Society of Intensive Care Medicine  
11 Task Force for Intensive Care Unit Triage during an Influenza Epidemic or Mass  
12 Disaster. Recommendations for intensive care unit and hospital preparations for an  
13 influenza epidemic or mass disaster: summary report of the European Society of  
14 Intensive Care Medicine's Task Force for intensive care unit triage during an  
15 influenza epidemic or mass disaster. *Intensive Care Med.* 2010 Mar;36(3):428-43.  
16 doi: 10.1007/s00134-010-1759-y. Epub 2010 Feb 5. PMID: 20135090; PMCID:  
17 PMC7079971.
- 18 13. Christian MD, Joynt GM, Hick JL, Colvin J, Danis M, Sprung CL; European Society  
19 of Intensive Care Medicine's Task Force for intensive care unit triage during an  
20 influenza epidemic or mass disaster. Chapter 7. *Critical care triage.*  
21 Recommendations and standard operating procedures for intensive care unit and  
22 hospital preparations for an influenza epidemic or mass disaster. *Intensive Care*  
23 *Med.* 2010 Apr;36 Suppl 1(Suppl 1):S55-64. doi: 10.1007/s00134-010-1765-0.  
24 PMID: 20213422; PMCID: PMC4849534.
- 25 14. Christian MD, Sprung CL, King MA, Dichter JR, Kissoon N, Devereaux AV,  
26 Gomersall CD; Task Force for Mass Critical Care; Task Force for Mass Critical  
27 Care. Triage: care of the critically ill and injured during pandemics and disasters:  
28 CHEST consensus statement. *Chest.* 2014 Oct;146(4 Suppl):e61S-74S. doi:  
29 10.1378/chest.14-0736. PMID: 25144591; PMCID: PMC7127536.
- 30 15. Sprung CL, Joynt GM, Christian MD, Truog RD, Rello J, Nates JL. Adult ICU  
31 Triage During the Coronavirus Disease 2019 Pandemic: Who Will Live and Who  
32 Will Die? Recommendations to Improve Survival. *Crit Care Med.* 2020  
33 Aug;48(8):1196-1202.
- 34 16. White DB, Lo B. A Framework for Rationing Ventilators and Critical Care Beds  
35 During the COVID-19 Pandemic. *JAMA.* 2020 May 12;323(18):1773-1774. doi:  
36 10.1001/jama.2020.5046. PMID: 32219367.

- 1 17. Christian MD. Triage. *Crit Care Clin.* 2019 Oct;35(4):575-589. doi:  
2 10.1016/j.ccc.2019.06.009. Epub 2019 Jul 27. PMID: 31445606; PMCID:  
3 PMC7127292.
- 4 18. Talmor D, Jones AE, Rubinson L, Howell MD, Shapiro NI. Simple triage scoring  
5 system predicting death and the need for critical care resources for use during  
6 epidemics. *Crit Care Med.* 2007 May;35(5):1251-6. doi:  
7 10.1097/01.CCM.0000262385.95721.CC. PMID: 17417099.
- 8 19. Christian MD, Hamielec C, Lazar NM, Wax RS, Griffith L, Herridge MS, Lee D,  
9 Cook DJ. A retrospective cohort pilot study to evaluate a triage tool for use in a  
10 pandemic. *Crit Care.* 2009;13(5):R170. doi: 10.1186/cc8146. Epub 2009 Oct 29.  
11 PMID: 19874595; PMCID: PMC2784402.
- 12 20. Guest T, Tantam G, Donlin N, Tantam K, McMillan H, Tillyard A. An observational  
13 cohort study of triage for critical care provision during pandemic influenza:  
14 'clipboard physicians' or 'evidenced based medicine'? *Anaesthesia.* 2009  
15 Nov;64(11):1199-206. doi: 10.1111/j.1365-2044.2009.06084.x. PMID: 19825055.
- 16 21. Adeniji KA, Cusack R: The Simple Triage Scoring System (STSS) successfully  
17 predicts mortality and critical care resource utilization in H1N1 pandemic flu: A  
18 retrospective analysis. *Crit Care* 2011;15:R39
- 19 22. Shahpori R, Stelfox HT, Doig CJ, Boiteau PJ, Zygun DA. Sequential Organ Failure  
20 Assessment in H1N1 pandemic planning. *Crit Care Med.* 2011 Apr;39(4):827-32.  
21 doi: 10.1097/CCM.0b013e318206d548. PMID: 21263327.
- 22 23. Myles PR, Nguyen-Van-Tam JS, Lim WS, Nicholson KG, Brett SJ, Enstone JE,  
23 McMenamin J, Openshaw PJ, Read RC, Taylor BL, Bannister B, Semple MG.  
24 Comparison of CATs, CURB-65 and PMEWS as triage tools in pandemic influenza  
25 admissions to UK hospitals: case control analysis using retrospective data. *PLoS*  
26 *One.* 2012;7(4):e34428. doi: 10.1371/journal.pone.0034428. Epub 2012 Apr 3.  
27 PMID: 22509303; PMCID: PMC3317953.
- 28 24. Emanuel EJ, Persad G, Upshur R, Thome B, Parker M, Glickman A, Zhang C,  
29 Boyle C, Smith M, Phillips JP. Fair Allocation of Scarce Medical Resources in the  
30 Time of Covid-19. *N Engl J Med.* 2020 May 21;382(21):2049-2055. doi:  
31 10.1056/NEJMs2005114. Epub 2020 Mar 23. PMID: 32202722.
- 32 25. Taylor BL, Montgomery HE, Rhodes A, Sprung CL; European Society of Intensive  
33 Care Medicine's Task Force for intensive care unit triage during an influenza  
34 epidemic or mass disaster. Chapter 6. Protection of patients and staff during a  
35 pandemic. Recommendations and standard operating procedures for intensive  
36 care unit and hospital preparations for an influenza epidemic or mass disaster.

- 1 Intensive Care Med. 2010 Apr;36 Suppl 1(Suppl 1):S45-54. doi: 10.1007/s00134-  
2 010-1764-1. PMID: 20213421; PMCID: PMC7080106.
- 3 26. Garrouste-Orgeas M, Ruckly S, Grégoire C, Dumesnil AS, Pommier C, Jamali S,  
4 Golgran-Toledano D, Schwebel C, Clec'h C, Soufir L, Fartoukh M, Marcotte G,  
5 Argaud L, Verdière B, Darmon M, Azoulay E, Timsit JF. Treatment intensity and  
6 outcome of nonagenarians selected for admission in ICUs: a multicenter study of  
7 the Outcomerea Research Group. Ann Intensive Care. 2016 Dec;6(1):31. doi:  
8 10.1186/s13613-016-0133-9. Epub 2016 Apr 14. PMID: 27076186; PMCID:  
9 PMC4830777.
- 10 27. Lagoe, R. Abbott, J. and Littau, S. (2021) Reducing Hospital Lengths of Stay: A  
11 Five-Year Study. Case Reports in Clinical Medicine, 10, 160-167. doi:  
12 10.4236/crcm.2021.106020.

**FIGURA 1 – Curva de sobrevida de Kaplan-Meier para o desfecho hospitalar de acordo com o período de triagem por critério cronológico e por critério de priorização, durante os primeiros 60 dias do estudo**



1  
2

1 **TABELA 1: Características clínicas e desfechos de acordo com período do**  
 2 **estudo**

Variável	Período 1 (n=1.227)	Período 2 (n=2.056)	Total (n=3.283)	Valor de p
<b>Idade</b>				< 0,001*
Média ± DP	57,3 ± 19,0	59,8 ± 18,3	58,9 ± 18,6	
Mediana (ITQ)	59,0 (44-73)	63,0 (48-74)	61,0 (47-74)	
<b>Sexo masculino</b>	733 (59,7%)	1.177 (57,2%)	1.910 (58,2%)	0,161**
<b>Procedência</b>				0,001***
Centro cirúrgico	809 (65,9%)	1.312 (63,8%)	2.121	
Emergência	289 (23,6%)	588 (28,6%)	(64,6%)	
Enfermaria	128 (10,4%)	152 (7,4%)	877 (26,7%)	
Outro hospital	1 (0,1%)	4 (0,2%)	280 (8,5%) 5 (0,2%)	
<b>Doença crônica</b>	235 (19,2%)	280 (13,6%)	2.768 (15,7%)	0,001**
<b>Tipo de admissão</b>				
Clínico	385 (31,4%)	721 (35,1%)	1.106	0,030**
PO urgência	399 (32,5%)	543 (26,4%)	(33,7%)	<0,001**
PO eletivo	426 (34,7%)	784 (38,1%)	942 (28,7%)	0,500**
			1.210 (36,9%)	
<b>IRA admissão</b>	329 (26,8%)	750 (36,5%)	1.079 (32,9%)	<0,001**
<b>VM admissão</b>	656 (53,5%)	1.166 (56,7%)	1.822 (55,5%)	0,070**
<b>Sepse na internação</b>	567 (46,2%)	1.039 (50,5%)	1.606 (48,9%)	0,016**
<b>DVA</b>	525 (42,8%)	850 (41,3%)	1.375 (41,9%)	0,417**
<b>APACHE II</b>				<0,001*
Média ± DP	19,5 ± 9,9	22,1 ± 10,3	21,2 ± 10,2	
Mediana (ITQ)	18,0 (12-26)	21,0 (14-29)	20,0 (13-28)	
<b>SOFA</b>				0,325*
Média ± DP	7,0 ± 4,7	7,2 ± 4,6	7,1 ± 4,7	
Mediana (ITQ)	6,0 (3-11)	7,0 (3-11)	7,0 (3-11)	
<b>TISS 28</b>				<0,001*
Média ± DP	26,9 ± 7,4	29,5 ± 10,4	28,5 ± 9,5	
Mediana (ITQ)	27,0 (21-32)	28,0 (21-36)	28,0 (21-34)	
<b>Tempo de UTI</b>				0,060*
Média ± DP	9,6 ± 16,0	8,5 ± 11,8	8,9 ± 13,5	
Mediana (ITQ)	4,00 (1-12)	4,0 (1-11)	4,0 (1-11)	
<b>Tempo de hospital</b>				0,117*
Média ± DP	24,2 ± 28,0	22,8 ± 27,2	23,3 ± 27,5	
Mediana (ITQ)	17,0 (8-31)	16,0 (8-28)	16,0 (8-29)	
<b>Óbito UTI</b>	453 (36,9%)	674 (32,8%)	1.127	0,016**

			(34,3%)	
<b>Óbito hospital</b>	587 (47,8%)	908 (44,2%)	1.495	0,041**
			(45,5%)	

---

1

2 Legenda: DP - Desvio padrão; ITQ - Intervalo interquartilico; PO - Pós-operatório; IRA - injúria  
3 renal aguda; VM - Ventilação mecânica; DVA - Droga vasoativa; APACHE - *Acute Physiology*  
4 *and Chronic Health Evaluation*; SOFA - *Sequential Organ Failure Assessment*; TISS -  
5 *Therapeutic Intervention Scoring System*; UTI - Unidade de terapia intensiva  
6 \* Teste de Mann-Whitney; \*\* Teste de qui-quadrado; \*\*\*Teste exato de Fisher

7

1 **TABELA 2: Intervenções terapêuticas de acordo com período do estudo**

2

Variável	Período 1	Período 2	Total	Valor de p
<b>VM na internação</b>	755 (61,5%)	1.251 (60,8%)	2.006 (61,1%)	0,697**
<b>Dias de VM</b>				0,189*
Média ± DP	12,3 ± 15,5	11,1 ± 11,8	11,5 ± 13,4	
Mediana (ITQ)	6,0 (3-17)	7,0 (3-14)	7,0 (3-15)	
<b>Diálise</b>	252 (20,5%)	462 (22,5%)	714 (21,7%)	0,194**
<b>Dias de diálise</b>				0,267*
Média ± DP	10,3 ± 21,4	8,8 ± 13,0	9,4 ± 16,5	
Mediana (ITQ)	6,0 (1-13)	4,0 (1-11)	4,0 (1-12)	
<b>PIC</b>	51 (4,2%)	86 (4,2%)	137 (4,2%)	0,971**
<b>CVC</b>	960 (78,2)	1.581 (76,9%)	2.541 (77,4%)	0,374**
<b>Enteral</b>	648 (52,8%)	1.154 (56,1%)	1.802 (54,9%)	0,065**
<b>Dias enteral</b>				0,346*
Média ± DP	12,8 ± 19,1	11,6 ± 13,3	12,0 ± 15,6	
Mediana (ITQ)	8,0 (3-16)	8,0 (3-16)	8,0 (3-16)	
<b>NP</b>	80 (6,5%)	63 (3,1%)	143 (4,4%)	<0,001**
<b>Dias NP</b>				0,328*
Média ± DP	11,7 ± 10,8	10,3 ± 10,8	11,1 ± 10,8	
Mediana (ITQ)	9,0 (3-16,5)	7,0 (3-14)	8,0 (3-15)	
<b>DVA única na</b>	293 (23,9%)	903 (43,9%)	1.196 (36,4%)	<0,001**
<b>admissão</b>				
<b>DVA múltipla na</b>	464 (37,8%)	643 (31,3%)	1.107 (33,7%)	<0,001**
<b>admissão</b>				
<b>Arteriotomia</b>	518 (42,2%)	796 (38,7%)	1.314 (40,0%)	0,048**
<b>Cateter Swan Ganz</b>	15 (1,2%)	8 (0,4%)	23 (0,7%)	0,006**
<b>Traqueotomia</b>	205 (16,7%)	407 (19,8%)	612 (18,6%)	0,028**

3 Legenda: VM - Ventilação mecânica; DP - Desvio padrão; ITQ - Intervalo interquartilico; PIC -  
4 Pressão intracraniana; CVC - Cateter venoso central; NP - nutrição parenteral; DVA - Droga  
5 vasoativa

6 \* Teste de Mann-Whitney; \*\* Teste de qui-quadrado

7

1 **TABELA 3 - Número e tipo de admissão por ano de estudo**

2

	<b>2013</b>	<b>2014</b>	<b>2015</b>	<b>2016</b>	<b>2017</b>	<b>Valor de p*</b>
<b>N. admissões</b>	628 (19,1%)	566 (17,2%)	548 (16,7%)	717 (21,8%)	824 (25,1%)	
<b>Clínico</b>	189 (30,1%)	180 (31,8%)	204 (37,2%)	249 (34,7%)	284 (34,5%)	0,054
<b>PO urgência</b>	198 (31,5%)	191 (33,7%)	158 (28,8%)	181 (25,2%)	214 (26,0%)	< 0,001
<b>PO eletivo</b>	228 (36,3%)	191 (33,7%)	181 (33,0%)	287 (40,0%)	323 (39,2%)	0,033

3

Legenda: N - número; PO - Pós-operatório; \* Qui-quadrado de tendência linear

4

1 **TABELA 4 – Regressão de COX para desfecho hospitalar**

2

<b>Variável</b>	<b>Hazard ratio</b>	<b>IC 95%</b>	<b>Valor de p</b>
<b>Idade</b>	1,015	1,011 - 1,018	<0,001
<b>Sexo masculino</b>	0,881	0,794 - 0,979	0,018
<b>Doença crônica</b>	1,084	0,952 - 1,234	0,225
<b>Período 2 do estudo</b>	0,870	0,780 - 0,971	0,013
<b>APACHE II</b>	1,034	1,026 - 1,042	<0,001
<b>SOFA</b>	1,085	1,066 - 1,105	<0,001
<b>TISS 28</b>	1,008	1,002 - 1,015	0,011

3 Legenda: APACHE - *Acute Physiology and Chronic Health Evaluation*; SOFA - *Sequential*  
4 *Organ Failure Assessment*; TISS - *Therapeutic Intervention Scoring System*; IC 95% - Intervalo  
5 de confiança 95%.

6

## 1 **5 CONSIDERAÇÕES FINAIS**

2 Apesar da decisão sobre a seleção de qual paciente será admitido na unidade  
3 de terapia intensiva ser uma rotina para o médico intensivista, esses profissionais  
4 frequentemente estão incertos do real significado da aplicação de critérios de triagem.  
5 Além de escolher e priorizar os pacientes a serem atendidos, triagem também significa  
6 utilizar os recursos escassos para fazer o maior bem ao maior número de pessoas.

7 Nesse contexto, devemos ter em mente o significado real dos termos  
8 subtriagem e supertriagem. Nos casos de subtriagem, um paciente grave pode não ser  
9 reconhecido, resultando em demora no seu atendimento e provavelmente reduzindo  
10 suas chances de recuperação. Nos casos de supertriagem, um paciente não grave  
11 pode ser priorizado para o atendimento em detrimento de outros que poderiam estar  
12 em maior necessidade. Em ambas as situações pode haver demora no atendimento  
13 de pessoas na fila de atendimento, uso inadequado de recursos e pior desempenho no  
14 atendimento.

15 Ao tomar decisões sobre triagem, é preciso lembrar que quando o acesso a  
16 uma unidade de terapia intensiva é priorizado, não significa que o paciente não irá  
17 receber tratamento e que certamente irá morrer. Essa não é uma decisão binária, mas  
18 sim uma decisão sobre probabilidade de sobrevida ao longo de toda a permanência do  
19 seu tratamento. Além disso, é importante considerar que a sobrevida não é o único  
20 desfecho importante nessa situação, mas igualmente importante é considerar a  
21 qualidade de vida dos sobreviventes.

22 Recentemente o mundo viveu situação de restrição de oferta de recursos da  
23 saúde por aumento incontrolável da sua necessidade durante uma pandemia. Esses  
24 efeitos são sentidos até a data de hoje. É objetivo pessoal deste autor que essa tese  
25 de doutorado venha a contribuir para otimizar os processos de triagem dos pacientes  
26 graves na instituição onde essa pesquisa foi desenvolvida e que isso sirva de exemplo  
27 e inspiração para outras instituições.

**6 REFERÊNCIAS CITADAS NOS ITENS 1 e 3**

- 1 xGarland, A., Olafson, K., Ramsey, C.D. *et al.* Epidemiology of critically ill patients in  
2 intensive care units: a population-based observational study. *Crit Care* **17**, R212  
3 (2013). <https://doi.org/10.1186/cc13026>  
4
- 5 2. Wild C, Narath M. Evaluating and planning ICUs: methods and approaches to  
6 differentiate between need and demand. *Health Policy*. 2005 Mar;**71**(3):289-301.  
7 doi: 10.1016/j.healthpol.2003.12.020. PMID: 15694497.
- 8 3. United Nations. Population Division Department of Economic and Social Affairs:  
9 World Population Ageing 2020 Highlights. New York, 2020. Available at:  
10 [https://www.un.org/development/desa/pd/sites/www.un.org.development.desa.pdf/](https://www.un.org/development/desa/pd/sites/www.un.org.development.desa.pdf/files/undesa_pd-2020_world_population_ageing_highlights.pdf)  
11 [files/undesa\\_pd-2020\\_world\\_population\\_ageing\\_highlights.pdf](https://www.un.org/development/desa/pd/sites/www.un.org.development.desa.pdf/files/undesa_pd-2020_world_population_ageing_highlights.pdf). Accessed July 19,  
12 2021.
- 13 4. Flaatten H, de Lange DW, Artigas A *et al.* The status of intensive care medicine  
14 research and a future agenda for very old patients in the ICU. *Intensive Care Med.*  
15 2017 Sep;**43**(9):1319-1328. doi: 10.1007/s00134-017-4718-z. Epub 2017 Feb 25.  
16 PMID: 28238055.
- 17 5. Vallet H, Riou B, Boddaert J. Réanimation du sujet âgé : revue de la littérature et  
18 point de vue du gériatre [Elderly patients and intensive care: Systematic review  
19 and geriatrician's point of view]. *Rev Med Interne*. 2017 Nov;**38**(11):760-765.  
20 French. doi: 10.1016/j.revmed.2017.01.014. Epub 2017 Feb 16. PMID: 28215925.
- 21 6. Riou B, Boddaert J. The Elderly Patient and the ICU: Where Are We Going,  
22 Where Should We Go? *Crit Care Med*. 2016 Jan;**44**(1):231-2. doi:  
23 10.1097/CCM.0000000000001446. PMID: 26672927.
- 24 7. Sprung CL, Baras M, Iapichino G *et al.* The Eldicus prospective, observational  
25 study of triage decision making in European intensive care units: part I--European  
26 Intensive Care Admission Triage Scores. *Crit Care Med*. 2012 Jan;**40**(1):125-31.  
27 doi: 10.1097/CCM.0b013e31822e5692. PMID: 21926598.
- 28 8. Sprung CL, Artigas A, Kesecioglu J *et al.* The Eldicus prospective, observational  
29 study of triage decision making in European intensive care units. Part II: intensive  
30 care benefit for the elderly. *Crit Care Med*. 2012 Jan;**40**(1):132-8. doi:  
31 10.1097/CCM.0b013e318232d6b0. PMID: 22001580.
- 32 9. Zampieri FG, Soares M, Borges LP, Salluh JIF, Ranzani OT. The Epimed Monitor  
33 ICU Database®: a cloud-based national registry for adult intensive care unit  
34 patients in Brazil. *Rev Bras Ter Intensiva*. 2017 Oct-Dec;**29**(4):418-426. doi:  
35 10.5935/0103-507X.20170062. Epub 2017 Nov 30. PMID: 29211187; PMCID:  
36 PMC5764553.

- 1 10. Associação de Medicina Intensiva Brasileira. Protocolo AMIB de alocação de  
2 recursos em esgotamento durante a pandemia por COVID-19. São Paulo, 2020.  
3 Available at:  
4 [https://www.amib.org.br/fileadmin/user\\_upload/amib/2020/abril/24/Protocolo\\_AMI](https://www.amib.org.br/fileadmin/user_upload/amib/2020/abril/24/Protocolo_AMI)  
5 [B\\_de\\_alocacao\\_de\\_recursos\\_em\\_esgotamento\\_durante\\_a\\_pandemia\\_por\\_COVI](https://www.amib.org.br/fileadmin/user_upload/amib/2020/abril/24/Protocolo_AMI)  
6 [D-19.pdf](https://www.amib.org.br/fileadmin/user_upload/amib/2020/abril/24/Protocolo_AMI). Accessed July 19, 2021.
- 7 11. Maglio I, Valdez P, Cámara L et al. Guías éticas para la atención durante la  
8 pandemia COVID-19. Recomendaciones multisocietarias para asignación de  
9 recursos [Ethical guides, criteria for admission in intensive care, palliative care.  
10 Multi-society recommendations for allocation of resources during the COVID-19  
11 pandemic]. *Medicina (B Aires)*. 2020;80 Suppl 3:45-64. Spanish. PMID:  
12 32658848.
- 13 12. Sprung CL, Zimmerman JL, Christian MD et al. European Society of Intensive  
14 Care Medicine Task Force for Intensive Care Unit Triage during an Influenza  
15 Epidemic or Mass Disaster. Recommendations for intensive care unit and hospital  
16 preparations for an influenza epidemic or mass disaster: summary report of the  
17 European Society of Intensive Care Medicine's Task Force for intensive care unit  
18 triage during an influenza epidemic or mass disaster. *Intensive Care Med*. 2010  
19 Mar;36(3):428-43. doi: 10.1007/s00134-010-1759-y. Epub 2010 Feb 5. PMID:  
20 20135090; PMCID: PMC7079971.
- 21 13. White DB, Lo B. A Framework for Rationing Ventilators and Critical Care Beds  
22 During the COVID-19 Pandemic. *JAMA*. 2020 May 12;323(18):1773-1774. doi:  
23 10.1001/jama.2020.5046. PMID: 32219367.
- 24 14. Christian MD, Sprung CL, King MA, Dichter JR, Kissoon N, Devereaux AV,  
25 Gomersall CD; Task Force for Mass Critical Care; Task Force for Mass Critical  
26 Care. Triage: care of the critically ill and injured during pandemics and disasters:  
27 CHEST consensus statement. *Chest*. 2014 Oct;146(4 Suppl):e61S-74S. doi:  
28 10.1378/chest.14-0736. PMID: 25144591; PMCID: PMC7127536.
- 29 15. Keegan MT, Soares M. What every intensivist should know about prognostic  
30 scoring systems and risk-adjusted mortality. *Rev Bras Ter Intensiva*. 2016  
31 Sep;28(3):264-269. doi: 10.5935/0103-507X.20160052. PMID: 27737416;  
32 PMCID: PMC5051184.
- 33 16. Knaus W, Draper E, Wagner D, Zimmerman J. APACHE II: A severity of disease  
34 classification system. *Crit Care Med*. 1985;13(10):818-29.
- 35 17. Vincent JL, Mendonça A De, Cantraine F, Moreno R, Takala J, Suter P, et al. Use  
36 of the SOFA score to assess the incidence of organ dysfunction/failure in intensive

- 1 care units: Results of a multicenter, prospective study. *Crit Care Med.*  
2 1998;26(November 1998):1793–800.
- 3 18. Miranda DR, Rijk A, Schaufeli W. Simplified therapeutic intervention scoring  
4 system: the TISS- 28 items--results from a multicenter study. *Crit Care Med.*  
5 1996;24(1):64-73.
- 6 19. Khan I, Ridley S. Intensive Care: Who Benefits? *Journal of the Intensive Care*  
7 *Society.* 2014;15(4):297-303. doi:10.1177/175114371401500406
- 8 20. Hill AD, Fowler RA, Pinto R et al. Long-term outcomes and healthcare utilization  
9 following critical illness--a population-based study. *Crit Care.* 2016 Mar 31;20:76.  
10 doi: 10.1186/s13054-016-1248-y. PMID: 27037030; PMCID: PMC4818427.
- 11 21. Pirracchio R, Sprung C, Payen D et al. Benefits of ICU admission in critically ill  
12 patients: whether instrumental variable methods or propensity scores should be  
13 used. *BMC Med Res Methodol.* 2011 Sep 21;11:132. doi: 10.1186/1471-2288-11-  
14 132. PMID: 21936926; PMCID: PMC3185268.
- 15 22. Cardoso LT, Grion CM, Matsuo T et al. Impact of delayed admission to intensive  
16 care units on mortality of critically ill patients: a cohort study. *Crit Care.*  
17 2011;15(1):R28. doi: 10.1186/cc9975. Epub 2011 Jan 18. PMID: 21244671;  
18 PMCID: PMC3222064.
- 19 23. Society of Critical Care Medicine. Critical Care Statistics. United States of  
20 America, 2021. Available at: [https://www.sccm.org/Communications/Critical-Care-](https://www.sccm.org/Communications/Critical-Care-Statistics)  
21 [Statistics.](https://www.sccm.org/Communications/Critical-Care-Statistics) Accessed July 19, 2021.
- 22 24. Associação de Medicina Intensiva Brasileira. CENSO AMIB 2016. São Paulo,  
23 2016. Available at:  
24 [https://www.amib.org.br/fileadmin/user\\_upload/amib/2018/marco/19/Analise\\_de\\_](https://www.amib.org.br/fileadmin/user_upload/amib/2018/marco/19/Analise_de_Dados_UTI_Final.pdf)  
25 [Dados\\_UTI\\_Final.pdf.](https://www.amib.org.br/fileadmin/user_upload/amib/2018/marco/19/Analise_de_Dados_UTI_Final.pdf) Accessed July 19, 2021.
- 26 25. Fair allocation of intensive care unit resources. American Thoracic Society. *Am J*  
27 *Respir Crit Care Med.* 1997 Oct;156(4 Pt 1):1282-301. doi:  
28 10.1164/ajrccm.156.4.ats7-97. Erratum in: *Am J Respir Crit Care Med* 1998  
29 Feb;157(2):671. PMID: 9351636.
- 30 26. Guidelines for intensive care unit admission, discharge, and triage. Task Force of  
31 the American College of Critical Care Medicine, Society of Critical Care Medicine.  
32 *Crit Care Med.* 1999 Mar;27(3):633-8. PMID: 10199547.
- 33 27. Nates JL, Nunnally M, Kleinpell R et al. ICU Admission, Discharge, and Triage  
34 Guidelines: A Framework to Enhance Clinical Operations, Development of

- 1 Institutional Policies, and Further Research. *Crit Care Med.* 2016 Aug;44(8):1553-  
2 602. doi: 10.1097/CCM.0000000000001856. PMID: 27428118.
- 3 28. Conselho Federal de Medicina. Resolução nº 2156/2016, de 17 de novembro de  
4 2016. Estabelece os critérios de admissão e alta em unidade de terapia  
5 intensiva. Brasília, 2016. Disponível em:  
6 <https://sistemas.cfm.org.br/normas/visualizar/resolucoes/BR/2016/2156>. Acesso  
7 em: 19 jul. 2021.
- 8 29. Rigaud JP, Giabicani M, Beuzelin M et al. Ethical aspects of admission or non-  
9 admission to the intensive care unit. *Ann Transl Med.* 2017 Dec;5(Suppl 4):S38.  
10 doi: 10.21037/atm.2017.06.53. PMID: 29302594; PMCID: PMC5750248.
- 11 30. Page K. The four principles: can they be measured and do they predict ethical  
12 decision making? *BMC Med Ethics.* 2012 May 20;13:10. doi: 10.1186/1472-6939-  
13 13-10. PMID: 22606995; PMCID: PMC3528420.
- 14 31. Beauchamp TL, Childress JF. *Principles of biomedical ethics.* 5th. New York:  
15 Oxford University Press; 2001.
- 16 32. Blanch L, Abillama FF, Amin P et al; Council of the World Federation of Societies  
17 of Intensive and Critical Care Medicine. Triage decisions for ICU admission:  
18 Report from the Task Force of the World Federation of Societies of Intensive and  
19 Critical Care Medicine. *J Crit Care.* 2016 Dec;36:301-305. doi:  
20 10.1016/j.jcrc.2016.06.014. Epub 2016 Jun 22. PMID: 27387663.
- 21 33. Guidet B, Hejblum G, Joynt G. Triage: what can we do to improve our practice?  
22 *Intensive Care Med.* 2013 Nov;39(11):2044-6. doi: 10.1007/s00134-013-3063-0.  
23 Epub 2013 Aug 28. PMID: 23982726.
- 24 34. Sprung CL, Danis M, Iapichino G et al. Triage of intensive care patients:  
25 identifying agreement and controversy. *Intensive Care Med.* 2013  
26 Nov;39(11):1916-24. doi: 10.1007/s00134-013-3033-6. Epub 2013 Aug 8. PMID:  
27 23925544; PMCID: PMC5549951.
- 28 35. Tyrrell CSB, Mytton OT, Gentry SV et al. Managing intensive care admissions  
29 when there are not enough beds during the COVID-19 pandemic: a systematic  
30 review. *Thorax.* 2021 Mar;76(3):302-312. doi: 10.1136/thoraxjnl-2020-215518.  
31 Epub 2020 Dec 17. PMID: 33334908; PMCID: PMC7892390.
- 32

ANEXOS

ANEXO 1 – Acute Physiology and Chronic Health Evaluation II (APACHE II)

THE APACHE II SEVERITY OF DISEASE CLASSIFICATION SYSTEM

PHYSIOLOGIC VARIABLE	HIGH ABNORMAL RANGE					LOW ABNORMAL RANGE			
	+4	+3	+2	+1	0	+1	+2	+3	+4
TEMPERATURE — rectal (°C)	≥ 41.1	39.4-40.9*		38.5-38.9*	36.5-38.4*	34.5-35.9*	32.5-33.9*	30.5-31.9*	< 29.9*
MEAN ARTERIAL PRESSURE — mm Hg	≥ 180	130-159	110-129		70-109		50-69		< 49
HEART RATE (ventricular response)	≥ 180	140-179	110-139		70-109		55-69	40-54	< 39
RESPIRATORY RATE — (non-ventilated or ventilated)	≥ 50	35-49		25-34	12-24	10-11	6-9		< 5
OXYGENATION: A-aDO <sub>2</sub> or PaO <sub>2</sub> (mm Hg)									
a. FIO <sub>2</sub> ≥ 0.5 record A-aDO <sub>2</sub>	≥ 500	350-499	200-349		< 200				
b. FIO <sub>2</sub> < 0.5 record only PaO <sub>2</sub>					PO <sub>2</sub> > 70	PO <sub>2</sub> 61-70		PO <sub>2</sub> 55-60	PO <sub>2</sub> < 55
ARTERIAL pH	≥ 7.7	7.6-7.69		7.5-7.59	7.33-7.49		7.25-7.32	7.15-7.24	< 7.15
SERUM SODIUM (mMol/L)	≥ 180	160-179	155-159	150-154	130-149		120-129	111-119	< 110
SERUM POTASSIUM (mMol/L)	≥ 7	6.6-9		5.5-5.9	3.5-5.4	3.3-4	2.5-2.9		< 2.5
SERUM CREATININE (mg/100 ml) (Double point score for acute renal failure)	≥ 3.5	2.3-4	1.5-1.9		0.6-1.4		< 0.6		
HEMATOCRIT (%)	≥ 80		50-59	46-49	30-45		20-29		< 20
WHITE BLOOD COUNT (total/mm <sup>3</sup> ) (in 1,000s)	≥ 40		20-39	15-19	3-14		1-2		< 1
GLASGOW COMA SCORE (GCS): Score = 15 minus actual GCS									
<b>A</b> Total ACUTE PHYSIOLOGY SCORE (APS): Sum of the 12 individual variable points									
Serum HCO <sub>3</sub> (venous-mMol/L) [Not preferred, use if no ABGs]	≥ 52	41-51.9		32-40.9	22-31.9		18-21.9	15-17.9	< 15

**B** AGE POINTS: Assign points to age as follows

AGE(yrs)	Points
< 44	0
45-54	2
55-64	3
65-74	5
≥ 75	6

**C** CHRONIC HEALTH POINTS

If the patient has a history of severe organ system insufficiency or is immuno-compromised assign points as follows

- a. for nonoperative or emergency postoperative patients — 5 points
- or
- b. for elective postoperative patients — 2 points

**DEFINITIONS**

**ORGAN INSUFFICIENCY** or immuno-compromised state must have been evident prior to this hospital admission and conform to the following criteria

**LIVER:** Biopsy proven cirrhosis and documented portal hypertension; episodes of past upper GI bleeding attributed to portal hypertension; or prior episodes of hepatic failure/encephalopathy/coma

**CARDIOVASCULAR:** New York Heart Association Class IV.

**RESPIRATORY:** Chronic restrictive, obstructive, or vascular disease resulting in severe exercise restriction, i.e., unable to climb stairs or perform household duties; or documented chronic hypoxia, hypercapnia, secondary polycythemia, severe pulmonary hypertension (>40mmHg), or respirator dependency

**RENAL:** Receiving chronic dialysis

**IMMUNO-COMPROMISED:** The patient has received therapy that suppresses resistance to infection, e.g., immuno-suppression, chemotherapy, radiation, long term or recent high dose steroids, or has a disease that is sufficiently advanced to suppress resistance to infection, e.g., leukemia, lymphoma, AIDS

**APACHE II SCORE**

Sum of **A** + **B** + **C**

**A** APS points

**B** Age points

**C** Chronic Health points

Total APACHE II

- 5
- 6
- 7
- 8
- 9
- 10
- 11
- 12
- 13
- 14
- 15
- 16
- 17
- 18
- 19
- 20
- 21
- 22
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- 25
- 26

Fonte: Knaus WA, Draper EA, Wagner DP, Zimmerman JE. Apache II: A severity of disease classification system. Crit Care Med. 1985; 13(10): 818-29. Available from: file:///C:/Users/Usuario/Downloads/APACHE\_II\_a\_severity\_of\_disease\_classification\_sys.pdf

## 1 ANEXO 2 – Sequential Organ Failure Assessment (SOFA)

	SOFA Score				
	0	1	2	3	4
Respiration					
Pao <sub>2</sub> /Fio <sub>2</sub> (torr)	>400	≤400	≤300	≤200 With respiratory support	≤100 With respiratory support
Coagulation					
Platelets (×10 <sup>9</sup> /mm <sup>3</sup> )	>150	≤150	≤100	≤50	≤20
Liver					
Bilirubin (mg/dL)	<1.2	1.2-1.9	2.0-5.9	6.0-11.9	>12.0
(μmol/L)	<20	20-32	33-101	102-204	>204
Cardiovascular					
Hypotension	No hypotension	MAP <70 mm Hg	Dopamine ≤5 or dobutamine (any dose)*	Dopamine >5 or epi ≤0.1 or norepi ≤0.1*	Dopamine >15 or epi >0.1 or norepi >0.1*
Central Nervous System					
Glasgow Coma Score	15	13-14	10-12	6-9	<6
Renal					
Creatinine (mg/dL)	<1.2	1.2-1.9	2.0-3.4	3.5-4.9	>5.0
(μmol/L)	<110	110-170	171-299	300-440	>440
or urine output				or <500 mL/day	or <200 mL/day

epi, epinephrine; norepi, norepinephrine.

\*Adrenergic agents administered for at least 1 hr (doses given are in μg/kg/min).

To convert torr to kPa, multiply the value by 0.1333.

Fonte: Vincent J-L, de Mendonça A, Cantraine F, Moreno R, Takala J, Suter PM, et al.

Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: Results of a multicenter, prospective study. Crit Care Med.

1998;26(11):1793–800.

## ANEXO 3 – Therapeutic Intervention Scoring System-28 (TISS-28)

**Table 1.** Therapeutic Intervention Scoring System-28

	Points
<b>Basic Activities</b>	
Standard monitoring Hourly vital signs, regular registration and calculation of fluid balance	5
Laboratory. Biochemical and microbiological investigations	1
Single medication. Intravenously, intramuscularly, subcutaneously, and/or orally (e.g., gastric tube)	2
Multiple intravenous medication More than one drug, single shots, or continuously	3
Routine dressing changes. Care and prevention of decubitus and daily dressing change	1
Frequent dressing changes. Frequent dressing change (at least one time per each nursing shift) and/or extensive wound care	1
Care of drains All (except gastric tube)	3
<b>Ventilatory Support</b>	
Mechanical ventilation. Any form of mechanical ventilation/assisted ventilation with or without positive end-expiratory pressure, with or without muscle relaxants, spontaneous breathing with positive end-expiratory pressure	5
Supplementary ventilatory support Breathing spontaneously through endotracheal tube without positive end-expiratory pressure: supplementary oxygen by any method, except if mechanical ventilation parameters apply	2
Care of artificial airways. Endotracheal tube or tracheostoma	1
Treatment for improving lung function. Thorax physiotherapy, incentive spirometry, inhalation therapy, intratracheal suctioning	1
<b>Cardiovascular Support</b>	
Single vasoactive medication. Any vasoactive drug	3
Multiple vasoactive medication. More than one vasoactive drug, disregard type and doses	4
Intravenous replacement of large fluid losses. Fluid administration >3 L/m <sup>2</sup> /day, disregard type of fluid administered	4
Peripheral arterial catheter	5
Left atrium monitoring Pulmonary artery flotation catheter with or without cardiac output measurement	8
Central venous line	2
Cardiopulmonary resuscitation after arrest; in the past 24 hrs (single precordial percussion not included)	3
<b>Renal Support</b>	
Hemofiltration techniques. Dialytic techniques	3
Quantitative urine output measurement (e.g., by urinary catheter à demeure)	2
Active diuresis (e.g., furosemide >0.5 mg/kg/day for overload)	3
<b>Neurologic Support</b>	
Measurement of intracranial pressure	4
<b>Metabolic Support</b>	
Treatment of complicated metabolic acidosis/alkalosis	4
Intravenous hyperalimentation	3
Enteral feeding. Through gastric tube or other gastrointestinal route (e.g., jejunostomy)	2
<b>Specific Interventions</b>	
Single specific intervention in the intensive care unit. Naso- or orotracheal intubation, introduction of pacemaker, cardioversion, endoscopies, emergency surgery in the past 24 hrs, gastric lavage. Routine interventions without direct consequences to the clinical condition of the patient, such as radiographs, echography, electrocardiogram, dressings, or introduction of venous or arterial catheters, are not included	3
Multiple specific interventions in the intensive care unit. More than one, as described above	5
Specific interventions outside the intensive care unit Surgery or diagnostic procedures	5

Criteria of exclusion are applied in four conditions: "Multiple intravenous medication" excludes "single medication", "mechanical ventilation" excludes "supplementary ventilatory support", "multiple vasoactive medication" excludes "single vasoactive medication", "multiple specific interventions in the intensive care unit" excludes "single specific interventions in the intensive care unit"

- 1 Fonte: Miranda DR, de Rijk A, Schaufeli W. Simplified Therapeutic Intervention
- 2 Scoring System: The TISS-28 items - results from a multicenter study. *Cri Care Med.*
- 3 1996; 24 (1):64-73.

## ANEXO 4 – Instruções aos autores da *INTENSIVE CARE MEDICINE*

Disponível em: <https://www.springer.com/journal/134/submission-guidelines> (01/06/2020)

## Instructions for Authors

### General

All papers providing pre-clinical data (experimental, animal, in-vitro, bench studies or studies without patients) should be submitted to ICM Experimental *ICM Experimental*. It is necessary for you to upload the appropriate EQUATOR checklist for your study. Please find the appropriate checklist at [EQUATOR Network](#).

All manuscripts undergo review. An initial check is conducted soon after submission to ensure that all manuscripts comply with the guidelines outlined in the Instructions for Authors. A pre-evaluation is then performed by the Editor-in-Chief and one or more Editors to determine which papers are sent for external peer review. Papers not sent out for review will be immediately rejected.

Research articles must meet the following criteria:

- The manuscript presents the results of primary scientific research.
- The results have not been published in full elsewhere.
- Analyses are performed to a high technical standard and are described in full in the manuscript.
- Conclusions are presented in a clear and concise manner and are supported by the data.
- Manuscripts must be written English using standard scientific terms.
- The research meets all applicable ethical standards.
- The article adheres to appropriate reporting guidelines and community standards for full data disclosure.
- All conflicts of interest should be clearly stated in the manuscript.
- According to the Uniform Requirements for Manuscripts Submitted to Biomedical Journals, designation as an author must satisfy three conditions. The author must have:
  - Contributed substantially to the conception and design of the study, the acquisition of data, or the analysis and interpretation of the data.
  - Drafted or provided critical revision of the article.
  - Provided final approval of the version submitted for publication.
- Authors of original papers and reviews are requested to provide the following information:
  - A "Take-home message" (two-sentences) which summarizes how the manuscript adds to current knowledge. This will appear in the final published version of the paper.
  - A 140-character Tweet that may appear online via the Intensive Care Medicine website or social media platforms. This Tweet will not form part of the print version of the manuscript.
- The role of authors and contributors has recently been clarified by the ICMJE

### **Types of Papers**

ICM is not accepting papers providing pre-clinical data (experimental, animal, in-vitro, bench studies or studies without patients). These manuscripts should be submitted to ICM Experimental

#### *Original Papers*

**Research articles must meet the following criteria:**

- The manuscript presents the results of primary scientific research
- The results have not been published in full elsewhere
- Analyses are performed to a high technical standard and are described in full in the manuscript
- Conclusions are presented in a clear and concise manner and are supported by the data
- Manuscripts must be written in English using standard scientific terms
- The research meets all applicable ethical standards
- The article adheres to appropriate reporting guidelines and community standards for full data disclosure. In general papers of studies that have been pre-registered or have a pre-published or approved protocol and analysis plan are prioritized
- All conflicts of interest should be clearly stated in the manuscript
- It is mandatory to upload the appropriate EQUATOR checklist for your study. Please find the appropriate checklist at [EQUATOR Network](#)
- According to the Uniform Requirements for Manuscripts Submitted to Biomedical Journals, designation as an author must satisfy three conditions. Each author must have:
  - Contributed substantially to the conception and design of the study, the acquisition of data, or the analysis and interpretation of the data

- Drafted or provided critical revision of the article
- Provided final approval of the version submitted for publication
- A statement detailing the role of each author in the study should be reported in an appropriate Authorship statement section of the manuscript in compliance with the ICMJE recommendations.
- At the Editor's discretion, authors may be asked to reduce the number of authors in the byline, whenever appropriate. The authors may add a study group name as an author in the byline and list the study group members in an appropriate footnote in the first page of the manuscript in order to have their names entered in PubMed as Collaborators.
- In addition to the abovementioned statements an Authorship and Conflict of Interest form should be completed, signed by each author and uploaded with the manuscript. The form can be downloaded [here](#).
- A 250-word abstract and 3-5 keywords are required
- Original papers must not exceed 3,000 words and should include no more than 5 illustrations and tables.
- Up to 50 references are permitted. If a higher number of references is needed, explain the reasons during the submission processes.
- When reporting the results of a randomized controlled trial, author(s) should use the CONSORT statement as a guide in preparing the manuscript.
- If the authors consider that their manuscript needs to be longer than 3,000 words or contain more figures or tables, the reasons for this should be justified in the cover letter to the Editor-in-Chief.
- Supplementary information can be published in electronic supplements without limitation.
- The journal considers only pre-registered trials. A statement should be reported in the manuscript.
- The journal does not consider single centre retrospective studies
- IRB/ethical committee approval and patient informed consent statements should be reported in the manuscript in the Materials and Methods section or in a separate section at the end of the manuscript
- Authors of original papers and reviews are requested to provide the following information:
  - A "Take-home message" (two sentences) which summarizes how the manuscript adds to current knowledge. This will appear in the final published version of the paper.
  - A 140-character Tweet that may appear online via the Intensive Care Medicine website or social media platforms. This Tweet will not form part of the print version of the manuscript

#### CONSORT-statement

##### *7-Day Profile Publications*

- Only high-quality manuscripts providing new findings from large prospective observational or interventional studies can be submitted as a 7-day profile publication, allowing important data to be rapidly available in the public domain
- 7-day profile publications are initially assessed by the Editor-in-Chief and Deputy Editors, and those deemed suitable for this format sent to external reviewers. A decision will be notified to the authors within 7 working days
- .
- Manuscripts will either be provisionally accepted, rejected or transferred to the standard peer review process. In the case of provisional acceptance, authors will have one day to address the reviewers' comments and resubmit a revised manuscript.
- From a manuscript preparation point of view, please comply with the instructions for Original Articles

##### *Review Articles, Systematic Reviews, Meta-Analyses*

- Review articles should only be submitted after prior consultation with the editors and are subject to the peer review process. The journal is primarily interested in receiving systematic reviews and meta-analyses that use high-quality methodology (pre-registered,

published protocol, systematic search, selection and reporting paper) and address relevant clinical questions not already or completely addressed in the literature.

- Review articles must not exceed 4,000 words and 75 references. Supplementary information can be published in electronic supplements without limitation.
- Proposals for review articles should be submitted as a two-page outline so that content can be discussed at an early stage. Review articles must include original tables, figures, graphs, and other didactic materials. They must provide unique information not available elsewhere.
- Authorship should comply with the ICMJE recommendation for authorship and the role of each author should be specified in the first page of the manuscript below the byline.
- At the Editor's decision, authors may be asked to reduce the number of authors in the byline whenever appropriate. The authors may add a study group name as an author in the byline and list the study group members in an appropriate footnote in the first page of the manuscript in order to have their names entered in PubMed as Collaborators.
- In addition to the abovementioned statements an Authorship and Conflict of Interest form should be completed, signed by each author and uploaded with the manuscript. The form can be downloaded [here](#).
- Authors of original papers and reviews are requested to provide the following information:
  - A "Take-home message" (two sentences) which summarizes how the manuscript adds to current knowledge. This will appear in the final published version of the paper.
  - A 140-character Tweet that may appear online via the Intensive Care Medicine website or social media platforms. This Tweet will not form part of the print version of the manuscript

Two types of reviews are considered: Systematic Reviews and Meta-Analyses (or a combination of both). It is strongly recommended that systematic reviews and meta-analyses comply with the PRISMA Statement, which is available

#### *Narrative/Scoping Reviews*

Narrative/Scoping Reviews should only be submitted after prior consultation with the Editors and are subject to the peer-review process. They represent the state-of-the-art in a specific field of research and are prepared by senior authors with a broad knowledge of the field.

- Narrative reviews should not exceed 4,000 words and 80 references and should contain figures and tables
- Authorship should not exceed 3 authors, preferably from different centres/countries, although some exceptions can be made by the Editors on a case by case basis depending on the topic
- A statement detailing each Author's role in the study and conflict of interest is mandatory for all papers
- In addition to the abovementioned statements an Authorship and Conflict of Interest form should be completed, signed by each author and uploaded with the manuscript. The form can be downloaded [here](#).
- IRB/ethical committee approval and informed consent statements are not required
- A structured abstract is not required

#### *Editorials*

- Editorials are always commissioned by the Editors and comment on one or more articles in the same issue of the Journal. Editorials must not exceed 1,000 words and up to 15 references, and include a mandatory table or figure.
- Editorials have a maximum of 3 authors
- No abstract
- Conflict of interest disclosure is mandatory for all papers
- Conflict of interest disclosure is mandatory for all papers and should be accompanied by a form to be signed by each author. The form can be downloaded [here](#).

#### *What's New in Intensive Care?*

- What's New articles can only be submitted after invitation by an Editor
- Expert clinicians and scientists are invited to outline the most striking advances in their field of expertise. The manuscript should focus on the most recent knowledge and address ICM's global readership.
- What's New articles are in the format of editorials and typically entitled "What's New in ...". They must not exceed 1,000 words and up to 15 references, and include a mandatory table or figure. A maximum of three authors is permitted.
- Expert clinicians and scientists are invited to outline the most striking advances in their field of expertise. The manuscript should focus on the most recent knowledge and address ICM's global readership.
- No abstract

#### *Understanding the Disease*

"Understanding the disease" articles can only be submitted after invitation by an Editor. Authors should outline a clinical challenge in intensive care medicine and can include a specific disease state, a syndrome, and a clinical abnormality or an intervention. The manuscript should communicate best practice in this field in a focused and structured way that is accessible to a broad group of clinical colleagues, while outlining the most recent advances.

- They are prepared in the format of editorials and must not exceed 1,000 words and up to 15 references.
- A single image is mandatory
- A maximum of three authors is permitted
- No abstract is required

#### *Less is more in Intensive Care*

"Less is more in Intensive Care" articles can only be submitted upon invitation by an Editor.

They should not exceed 1,000 words and 20 references.

- A maximum of three authors is permitted, preferably from different centres/countries
- No abstract is required

#### *Images*

- Submission under the Image section must be of high scientific quality and value as well as providing didactic and self-explanatory lessons. They must be unique and adhere to ethical standards with patient/relative approval when appropriate, protection of patient identity and privacy, and local ethics approval as appropriate.
- The accompanying text must not exceed 200 words. A maximum of four authors is permitted.
- No abstract or references
- The section is not supposed for the publication of case-reports. The focus is on the images

#### *Correspondence*

Correspondence articles provide an opportunity to debate published articles on ICM. The Correspondence is aimed at commenting on an ICM article.

- The Correspondence article must not exceed 500 words, 5 references (including the ICM article which is referred) and 1 figure or table
- The total number of authors should not exceed 5
- At the Editor's discretion the authors of the commented original article may be invited to write a reply, which also should not exceed 500 words, 5 references (including the original ICM article and the related correspondence) and 1 figure or table

#### *Letters to the Editor*

- Letters to the editor provide an opportunity to present results of high scientific value where a short format is most appropriate. Typically, letters are dedicated to small pilot/feasibility studies and/or preliminary data. They must not exceed 500 words, 5 references and 1 figure or table.

- The journal does not consider case reports or brief reports for publication.
- Authorship of letters to the editor should be limited to 5 authors or less. In case of letters which stem from an original study with a higher number of authors, a choice must be made by the authors on the names that should appear in the byline and those that may appear in a footnote or in a study group
- Study group collaborating authors should be included in the front page but separate from the byline
- To the Editor's discretion the authors may be asked to specify the role of each author in the article preparation

#### *From the Inside*

- From the inside includes poetry, trivia, personal stories, thoughts and memories, sounding boards, obituaries or other qualitative materials that authors wish to share with colleagues.

### **Manuscript Submission**

#### *Manuscript Submission*

Submission of a manuscript implies: that the work described has not been published before; that it is not under consideration for publication anywhere else; that its publication has been approved by all co-authors, if any, as well as by the responsible authorities – tacitly or explicitly – at the institute where the work has been carried out. The publisher will not be held legally responsible should there be any claims for compensation.

#### *Permissions*

Authors wishing to include figures, tables, or text passages that have already been published elsewhere are required to obtain permission from the copyright owner(s) for both the print and online format and to include evidence that such permission has been granted when submitting their papers. Any material received without such evidence will be assumed to originate from the authors.

#### *Online Submission*

Please follow the hyperlink "Submit online" on the right and upload all of your manuscript files following the instructions given on the screen.

Please ensure you provide all relevant editable source files. Failing to submit these source files might cause unnecessary delays in the review and production process.

### **Title page**

#### *Title Page*

Please use this **template title page** for providing the following information.

The title page should include:

- The name(s) of the author(s)
- A concise and informative title
- The affiliation(s) of the author(s), i.e. institution, (department), city, (state), country
- A clear indication and an active e-mail address of the corresponding author
- If available, the 16-digit ORCID of the author(s)

If address information is provided with the affiliation(s) it will also be published.

For authors that are (temporarily) unaffiliated we will only capture their city and country of residence, not their e-mail address unless specifically requested.

#### *Abstract*

Please provide a structured abstract of 150 to 250 words which should be divided into the following sections:

- Purpose (stating the main purposes and research question)
- Methods
- Results
- Conclusion

#### *For life science journals only (when applicable)*

Trial registration number and date of registration

Trial registration number, date of registration followed by "retrospectively registered"

#### *Keywords*

Please provide 4 to 6 keywords which can be used for indexing purposes.

### *Declarations*

All manuscripts must contain the following sections under the heading 'Declarations'. If any of the sections are not relevant to your manuscript, please include the heading and write 'Not applicable' for that section.

*To be used for non-life science journals*

**Funding** (information that explains whether and by whom the research was supported)

**Conflicts of interest/Competing interests** (include appropriate disclosures)

**Availability of data and material** (data transparency)

**Code availability** (software application or custom code)

**Authors' contributions** (optional: please review the submission guidelines from the journal whether statements are mandatory)

*To be used for life science journals + articles with biological applications*

**Funding** (information that explains whether and by whom the research was supported)

**Conflicts of interest/Competing interests** (include appropriate disclosures)

**Ethics approval** (include appropriate approvals or waivers)

**Consent to participate** (include appropriate statements)

**Consent for publication** (include appropriate statements)

**Availability of data and material** (data transparency)

**Code availability** (software application or custom code)

**Authors' contributions** (optional: please review the submission guidelines from the journal whether statements are mandatory)

Please see the relevant sections in the submission guidelines for further information as well as various examples of wording. Please revise/customize the sample statements according to your own needs.

*Please note:*

- An abstract is not required for Editorials, Short articles such as 'Focus on, Less is More in Intensive Care, Understanding the Disease, etc.'
- For details, or to submit an outline of your manuscript, please contact the Intensive Care Medicine Managing Editor at [intensivemedicine@unimib.it](mailto:intensivemedicine@unimib.it)

### **Text**

#### *Text Formatting*

Manuscripts should be submitted in Word.

- Use a normal, plain font (e.g., 10-point Times Roman) for text.
- Use italics for emphasis.
- Use the automatic page numbering function to number the pages.
- Do not use field functions.
- Use tab stops or other commands for indents, not the space bar.
- Use the table function, not spreadsheets, to make tables.
- Use the equation editor or MathType for equations.
- Save your file in docx format (Word 2007 or higher) or doc format (older Word versions).

Manuscripts with mathematical content can also be submitted in LaTeX.

#### *Headings*

Please use no more than three levels of displayed headings.

#### *Abbreviations*

Abbreviations should be defined at first mention and used consistently thereafter.

#### *Footnotes*

Footnotes can be used to give additional information, which may include the citation of a reference included in the reference list. They should not consist solely of a reference citation, and they should never include the bibliographic details of a reference. They should also not contain any figures or tables.

Footnotes to the text are numbered consecutively; those to tables should be indicated by superscript lower-case letters (or asterisks for significance values and other statistical data). Footnotes to the title or the authors of the article are not given reference symbols.

Always use footnotes instead of endnotes.

#### *Acknowledgments*

Acknowledgments of people, grants, funds, etc. should be placed in a separate section on the title page. The names of funding organizations should be written in full.

#### *Zotero*

If you use Zotero, the ICM styling template can be found here.

#### **Scientific style**

Generic names of drugs and pesticides are preferred; if trade names are used, the generic name should be given at first mention.

#### **References**

##### *Citation*

Reference citations in the text should be identified by numbers in square brackets. Some examples:

1. Negotiation research spans many disciplines [3].
2. This result was later contradicted by Becker and Seligman [5].
3. This effect has been widely studied [1-3, 7].

##### *Reference list*

The list of references should only include works that are cited in the text and that have been published or accepted for publication. Personal communications and unpublished works should only be mentioned in the text. Do not use footnotes or endnotes as a substitute for a reference list.

The entries in the list should be numbered consecutively.

- Journal article  
Gamelin FX, Baquet G, Berthoin S, Thevenet D, Nourry C, Nottin S, Bosquet L (2009) Effect of high intensity intermittent training on heart rate variability in prepubescent children. *Eur J Appl Physiol* 105:731-738.  
<https://doi.org/10.1007/s00421-008-0955-8>  
Ideally, the names of all authors should be provided, but the usage of “et al” in long author lists will also be accepted:  
Smith J, Jones M Jr, Houghton L et al (1999) Future of health insurance. *N Engl J Med* 341:325–329
- Article by DOI  
Slifka MK, Whitton JL (2000) Clinical implications of dysregulated cytokine production. *J Mol Med.* <https://doi.org/10.1007/s001090000086>
- Book  
South J, Blass B (2001) *The future of modern genomics*. Blackwell, London
- Book chapter  
Brown B, Aaron M (2001) The politics of nature. In: Smith J (ed) *The rise of modern genomics*, 3rd edn. Wiley, New York, pp 230-257
- Online document  
Cartwright J (2007) Big stars have weather too. IOP Publishing PhysicsWeb. <http://physicsweb.org/articles/news/11/6/16/1>. Accessed 26 June 2007
- Dissertation  
Trent JW (1975) *Experimental acute renal failure*. Dissertation, University of California

Always use the standard abbreviation of a journal's name according to the ISSN List of Title Word Abbreviations, see

If you are unsure, please use the full journal title.

For authors using EndNote, Springer provides an output style that supports the formatting of in-text citations and reference list.

#### *Please note:*

References are not necessary for the following sections: Correspondences, Imaging, and From the inside.

#### **Tables**

- All tables are to be numbered using Arabic numerals.

- Tables should always be cited in text in consecutive numerical order.
- For each table, please supply a table caption (title) explaining the components of the table.
- Identify any previously published material by giving the original source in the form of a reference at the end of the table caption.
- Footnotes to tables should be indicated by superscript lower-case letters (or asterisks for significance values and other statistical data) and included beneath the table body.

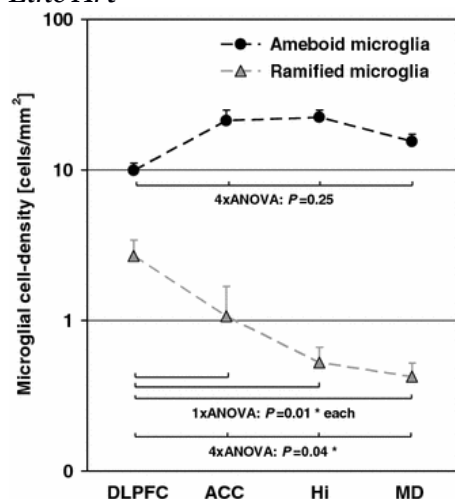
Tables for ICM publication should be prepared taking into account the current style of the journal. Tables that do not exceed the A4 width of a page (portrait format) are preferred. Decimals should be limited to two digits, unless data require to specify up to the third or fourth decimal digit (e.g. 0.0004). Unnecessary decimals should be avoided (e.g. 4.00 should be 4).

### Artwork and Illustrations Guidelines

#### Electronic Figure Submission

- Supply all figures electronically.
- Indicate what graphics program was used to create the artwork.
- For vector graphics, the preferred format is EPS; for halftones, please use TIFF format. MSOffice files are also acceptable.
- Vector graphics containing fonts must have the fonts embedded in the files.
- Name your figure files with "Fig" and the figure number, e.g., Fig1.eps.

#### Line Art



- Definition: Black and white graphic with no shading.
- Do not use faint lines and/or lettering and check that all lines and lettering within the figures are legible at final size.
- All lines should be at least 0.1 mm (0.3 pt) wide.
- Scanned line drawings and line drawings in bitmap format should have a minimum resolution of 1200 dpi.
- Vector graphics containing fonts must have the fonts embedded in the files.

#### Halftone Art

- Definition: Photographs, drawings, or paintings with fine shading, etc.
- If any magnification is used in the photographs, indicate this by using scale bars within the figures themselves.
- Halftones should have a minimum resolution of 300 dpi.

#### Combination Art

- Definition: a combination of halftone and line art, e.g., halftones containing line drawing, extensive lettering, color diagrams, etc.
- Combination artwork should have a minimum resolution of 600 dpi.

#### Color Art

- Color art is free of charge for online publication.

- If black and white will be shown in the print version, make sure that the main information will still be visible. Many colors are not distinguishable from one another when converted to black and white. A simple way to check this is to make a xerographic copy to see if the necessary distinctions between the different colors are still apparent.
- If the figures will be printed in black and white, do not refer to color in the captions.
- Color illustrations should be submitted as RGB (8 bits per channel).

#### *Figure Lettering*

- To add lettering, it is best to use Helvetica or Arial (sans serif fonts).
- Keep lettering consistently sized throughout your final-sized artwork, usually about 2–3 mm (8–12 pt).
- Variance of type size within an illustration should be minimal, e.g., do not use 8-pt type on an axis and 20-pt type for the axis label.
- Avoid effects such as shading, outline letters, etc.
- Do not include titles or captions within your illustrations.

#### *Figure Numbering*

- All figures are to be numbered using Arabic numerals.
- Figures should always be cited in text in consecutive numerical order.
- Figure parts should be denoted by lowercase letters (a, b, c, etc.).
- If an appendix appears in your article and it contains one or more figures, continue the consecutive numbering of the main text. Do not number the appendix figures, "A1, A2, A3, etc." Figures in online appendices (Electronic Supplementary Material) should, however, be numbered separately.

#### *Figure Captions*

- Each figure should have a concise caption describing accurately what the figure depicts. Include the captions in the text file of the manuscript, not in the figure file.
- Figure captions begin with the term Fig. in bold type, followed by the figure number, also in bold type.
- No punctuation is to be included after the number, nor is any punctuation to be placed at the end of the caption.
- Identify all elements found in the figure in the figure caption; and use boxes, circles, etc., as coordinate points in graphs.
- Identify previously published material by giving the original source in the form of a reference citation at the end of the figure caption.

#### *Figure Placement and Size*

- Figures should be submitted separately from the text, if possible.
- When preparing your figures, size figures to fit in the column width.
- For large-sized journals the figures should be 84 mm (for double-column text areas), or 174 mm (for single-column text areas) wide and not higher than 234 mm.
- For small-sized journals, the figures should be 119 mm wide and not higher than 195 mm.

#### *Permissions*

If you include figures that have already been published elsewhere, you must obtain permission from the copyright owner(s) for both the print and online format. Please be aware that some publishers do not grant electronic rights for free and that Springer will not be able to refund any costs that may have occurred to receive these permissions. In such cases, material from other sources should be used.

#### *Accessibility*

In order to give people of all abilities and disabilities access to the content of your figures, please make sure that

- All figures have descriptive captions (blind users could then use a text-to-speech software or a text-to-Braille hardware)
- Patterns are used instead of or in addition to colors for conveying information (colorblind users would then be able to distinguish the visual elements)

- Any figure lettering has a contrast ratio of at least 4.5:1

*Please note: General Guidelines*

Some general guidelines to prepare figures in the style of the journal:

- Font: Helvetica
- Colours: navy blue #0c385c; light blue #1770b8; light mauve blue #d0d9f0; dark mauve blue #6b8ac5
- Tables should be preferably vertical within an A4 page. They may be horizontal if the table size is half an A4 page.

At the Editor's discretion some figures may be re-drawn. The authors may be asked to coordinate with the Managing Editor for figures to be re-drawn by the journal illustrator at no cost for the authors.

**Color Art**

Color illustrations: Publication of color illustrations is free of charge.

**Electronic Supplementary Material**

Springer accepts electronic multimedia files (animations, movies, audio, etc.) and other supplementary files to be published online along with an article or a book chapter. This feature can add dimension to the author's article, as certain information cannot be printed or is more convenient in electronic form.

Before submitting research datasets as electronic supplementary material, authors should read the journal's Research data policy. We encourage research data to be archived in data repositories wherever possible.

*Submission*

- Supply all supplementary material in standard file formats.
- Please include in each file the following information: article title, journal name, author names; affiliation and e-mail address of the corresponding author.
- To accommodate user downloads, please keep in mind that larger-sized files may require very long download times and that some users may experience other problems during downloading.

*Audio, Video, and Animations*

- Aspect ratio: 16:9 or 4:3
- Maximum file size: 25 GB
- Minimum video duration: 1 sec
- Supported file formats: avi, wmv, mp4, mov, m2p, mp2, mpg, mpeg, flv, mxf, mts, m4v, 3gp

*Text and Presentations*

- Submit your material in PDF format; .doc or .ppt files are not suitable for long-term viability.
- A collection of figures may also be combined in a PDF file.

*Spreadsheets*

- Spreadsheets should be submitted as .csv or .xlsx files (MS Excel).

*Specialized Formats*

- Specialized format such as .pdb (chemical), .wrl (VRML), .nb (Mathematica notebook), and .tex can also be supplied.

*Collecting Multiple Files*

- It is possible to collect multiple files in a .zip or .gz file.

*Numbering*

- If supplying any supplementary material, the text must make specific mention of the material as a citation, similar to that of figures and tables.
- Refer to the supplementary files as "Online Resource", e.g., "... as shown in the animation (Online Resource 3)", "... additional data are given in Online Resource 4".
- Name the files consecutively, e.g. "ESM\_3.mpg", "ESM\_4.pdf".

*Captions*

- For each supplementary material, please supply a concise caption describing the content of the file.

*Processing of supplementary files*

- Electronic supplementary material will be published as received from the author without any conversion, editing, or reformatting.

*Accessibility*

In order to give people of all abilities and disabilities access to the content of your supplementary files, please make sure that

- The manuscript contains a descriptive caption for each supplementary material
- Video files do not contain anything that flashes more than three times per second (so that users prone to seizures caused by such effects are not put at risk)

**Ethical Responsibilities of Authors**

This journal is committed to upholding the integrity of the scientific record. As a member of the Committee on Publication Ethics (COPE) the journal will follow the COPE guidelines on how to deal with potential acts of misconduct.

Authors should refrain from misrepresenting research results which could damage the trust in the journal, the professionalism of scientific authorship, and ultimately the entire scientific endeavour. Maintaining integrity of the research and its presentation is helped by following the rules of good scientific practice, which include\*:

- The manuscript should not be submitted to more than one journal for simultaneous consideration.
- The submitted work should be original and should not have been published elsewhere in any form or language (partially or in full), unless the new work concerns an expansion of previous work. (Please provide transparency on the re-use of material to avoid the concerns about text-recycling ('self-plagiarism').
- A single study should not be split up into several parts to increase the quantity of submissions and submitted to various journals or to one journal over time (i.e. 'salami-slicing/publishing').
- Concurrent or secondary publication is sometimes justifiable, provided certain conditions are met. Examples include: translations or a manuscript that is intended for a different group of readers.
- Results should be presented clearly, honestly, and without fabrication, falsification or inappropriate data manipulation (including image based manipulation). Authors should adhere to discipline-specific rules for acquiring, selecting and processing data.
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- Research articles and non-research articles (e.g. Opinion, Review, and Commentary articles) must cite appropriate and relevant literature in support of the claims made. Excessive and inappropriate self-citation or coordinated efforts among several authors to collectively self-cite is strongly discouraged.
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- Research that may be misapplied to pose a threat to public health or national security should be clearly identified in the manuscript (e.g. dual use of research). Examples include creation of harmful consequences of biological agents or toxins, disruption of immunity of vaccines, unusual hazards in the use of chemicals, weaponization of research/technology (amongst others).
- Authors are strongly advised to ensure the author group, the Corresponding

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\*All of the above are guidelines and authors need to make sure to respect third parties rights such as copyright and/or moral rights.

Upon request authors should be prepared to send relevant documentation or data in order to verify the validity of the results presented. This could be in the form of raw data, samples, records, etc. Sensitive information in the form of confidential or proprietary data is excluded.

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- The author's institution may be informed
- A notice of suspected transgression of ethical standards in the peer review system may be included as part of the author's and article's bibliographic record.

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Authors have an obligation to correct mistakes once they discover a significant error or inaccuracy in their published article. The author(s) is/are requested to contact the journal and explain in what sense the error is impacting the article. A decision on how to correct the literature will depend on the nature of the error. This may be a correction or retraction. The retraction note should provide transparency which parts of the article are impacted by the error.

#### *Suggesting / excluding reviewers*

Authors are welcome to suggest suitable reviewers and/or request the exclusion of certain individuals when they submit their manuscripts. When suggesting reviewers, authors should make sure they are totally independent and not connected to the work in any way. It is strongly recommended to suggest a mix of reviewers from different countries and different institutions. When suggesting reviewers, the Corresponding Author must provide an institutional email address for each suggested reviewer, or, if this is not possible to include other means of verifying the identity such as a link to a personal homepage, a link to the publication record or a researcher or author ID in the submission letter. Please note that the Journal may not use the suggestions, but suggestions are appreciated and may help facilitate the peer review process.

#### **Authorship principles**

These guidelines describe authorship principles and good authorship practices to which prospective authors should adhere to.

#### *Authorship clarified*

The Journal and Publisher assume all authors agreed with the content and that all gave explicit consent to submit and that they obtained consent from the responsible authorities

at the institute/organization where the work has been carried out, **before** the work is submitted.

The Publisher does not prescribe the kinds of contributions that warrant authorship. It is recommended that authors adhere to the guidelines for authorship that are applicable in their specific research field. In absence of specific guidelines it is recommended to adhere to the following guidelines\*:

All authors whose names appear on the submission

- 1) made substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data; or the creation of new software used in the work;
- 2) drafted the work or revised it critically for important intellectual content;
- 3) approved the version to be published; and
- 4) agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

\* Based on/adapted from:

ICMJE, Defining the Role of Authors and Contributors.

Transparency in authors' contributions and responsibilities to promote integrity in scientific publication, McNutt et al., PNAS February 27, 2018

#### *Disclosures and declarations*

All authors are requested to include information regarding sources of funding, financial or non-financial interests, study-specific approval by the appropriate ethics committee for research involving humans and/or animals, informed consent if the research involved human participants, and a statement on welfare of animals if the research involved animals (as appropriate).

The decision whether such information should be included is not only dependent on the scope of the journal, but also the scope of the article. Work submitted for publication may have implications for public health or general welfare and in those cases it is the responsibility of all authors to include the appropriate disclosures and declarations.

#### *Data transparency*

All authors are requested to make sure that all data and materials as well as software application or custom code support their published claims and comply with field standards. Please note that journals may have individual policies on (sharing) research data in concordance with disciplinary norms and expectations. Please check the Instructions for Authors of the Journal that you are submitting to for specific instructions.

#### *Role of the Corresponding Author*

**One author** is assigned as Corresponding Author and acts on behalf of all co-authors and ensures that questions related to the accuracy or integrity of any part of the work are appropriately addressed.

The Corresponding Author is responsible for the following requirements:

- ensuring that all listed authors have approved the manuscript before submission, including the names and order of authors;
- managing all communication between the Journal and all co-authors, before and after publication;\*
- providing transparency on re-use of material and mention any unpublished material (for example manuscripts in press) included in the manuscript in a cover letter to the Editor;
- making sure disclosures, declarations and transparency on data statements from all authors are included in the manuscript as appropriate (see above).

\* The requirement of managing all communication between the journal and all co-authors during submission and proofing may be delegated to a Contact or Submitting Author. In this case please make sure the Corresponding Author is clearly indicated in the manuscript.

#### *Author contributions*

In absence of specific instructions and in research fields where it is possible to describe

discrete efforts, the Publisher recommends authors to include contribution statements in the work that specifies the contribution of every author in order to promote transparency. These contributions should be listed at the separate title page.

**Examples of such statement(s) are shown below:**

• Free text:

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by [full name], [full name] and [full name]. The first draft of the manuscript was written by [full name] and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

• Conceptualization: [full name], ...; Methodology: [full name], ...; Formal analysis and investigation: [full name], ...; Writing - original draft preparation: [full name, ...]; Writing - review and editing: [full name], ...; Funding acquisition: [full name], ...; Resources: [full name], ...; Supervision: [full name],....

For **review articles** where discrete statements are less applicable a statement should be included who had the idea for the article, who performed the literature search and data analysis, and who drafted and/or critically revised the work.

For articles that are based primarily on the **student's dissertation or thesis**, it is recommended that the student is usually listed as principal author:

*Affiliation*

The primary affiliation for each author should be the institution where the majority of their work was done. If an author has subsequently moved, the current address may additionally be stated. Addresses will not be updated or changed after publication of the article.

*Changes to authorship*

Authors are strongly advised to ensure the correct author group, the Corresponding Author, and the order of authors at submission. Changes of authorship by adding or deleting authors, and/or changes in Corresponding Author, and/or changes in the sequence of authors are **not accepted after acceptance** of a manuscript.

- **Please note that author names will be published exactly as they appear on the accepted submission!**

Please make sure that the names of all authors are present and correctly spelled, and that addresses and affiliations are current.

Adding and/or deleting authors at revision stage are generally not permitted, but in some cases it may be warranted. Reasons for these changes in authorship should be explained. Approval of the change during revision is at the discretion of the Editor-in-Chief. Please note that journals may have individual policies on adding and/or deleting authors during revision stage.

*Author identification*

Authors are recommended to use their ORCID ID when submitting an article for consideration or acquire an ORCID ID via the submission process.

*Deceased or incapacitated authors*

For cases in which a co-author dies or is incapacitated during the writing, submission, or peer-review process, and the co-authors feel it is appropriate to include the author, co-authors should obtain approval from a (legal) representative which could be a direct relative.

*Authorship issues or disputes*

In the case of an authorship dispute during peer review or after acceptance and publication, the Journal will not be in a position to investigate or adjudicate. Authors will be asked to resolve the dispute themselves. If they are unable the Journal reserves the right to withdraw a manuscript from the editorial process or in case of a published paper raise the issue with the authors' institution(s) and abide by its guidelines.

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Authors should treat all communication with the Journal as confidential which includes correspondence with direct representatives from the Journal such as Editors-in-Chief

and/or Handling Editors and reviewers' reports unless explicit consent has been received to share information.

### **Compliance with Ethical Standards**

To ensure objectivity and transparency in research and to ensure that accepted principles of ethical and professional conduct have been followed, authors should include information regarding sources of funding, potential conflicts of interest (financial or non-financial), informed consent if the research involved human participants, and a statement on welfare of animals if the research involved animals.

Authors should include the following statements (if applicable) in a separate section entitled "Compliance with Ethical Standards" when submitting a paper:

- Disclosure of potential conflicts of interest
- Research involving Human Participants and/or Animals
- Informed consent

Please note that standards could vary slightly per journal dependent on their peer review policies (i.e. single or double blind peer review) as well as per journal subject discipline. Before submitting your article check the instructions following this section carefully.

The corresponding author should be prepared to collect documentation of compliance with ethical standards and send if requested during peer review or after publication.

The Editors reserve the right to reject manuscripts that do not comply with the above-mentioned guidelines. The author will be held responsible for false statements or failure to fulfill the above-mentioned guidelines.

*Please note:*

Before submitting your article check also the specific instructions of ethical standard adherence for each type of article carefully. You may find such specific instructions in the chapter Types of Paper.

### **Disclosure of Potential Conflicts of Interest**

Conflicts of interest of all authors must be disclosed in an appropriate section of the manuscript. In addition to the statement the corresponding author is required to collect all co-authors signatures and submit the pdf file upon manuscript submission. A template of the form is available [here](#).

### **Research involving human participants, their data or biological material**

#### *Ethics approval*

When reporting a study that involved human participants, their data or biological material, authors should include a statement that confirms that the study was approved (or granted exemption) by the appropriate institutional and/or national research ethics committee (including the name of the ethics committee) and certify that the study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. If doubt exists whether the research was conducted in accordance with the 1964 Helsinki Declaration or comparable standards, the authors must explain the reasons for their approach, and demonstrate that an independent ethics committee or institutional review board explicitly approved the doubtful aspects of the study. If a study was granted exemption from requiring ethics approval, this should also be detailed in the manuscript (including the reasons for the exemption).

#### *Retrospective ethics approval*

If a study has not been granted ethics committee approval prior to commencing, retrospective ethics approval usually cannot be obtained and it may not be possible to consider the manuscript for peer review. The decision on whether to proceed to peer review in such cases is at the Editor's discretion.

#### *Ethics approval for retrospective studies*

Although retrospective studies are conducted on already available data or biological material (for which formal consent may not be needed or is difficult to obtain) ethics approval may be required dependent on the law and the national ethical guidelines of a country. Authors should check with their institution to make sure they are complying with the specific requirements of their country.

### *Ethics approval for case studies*

Case reports require ethics approval. Most institutions will have specific policies on this subject. Authors should check with their institution to make sure they are complying with the specific requirements of their institution and seek ethics approval where needed. Authors should be aware to secure informed consent from the individual (or parent or guardian if the participant is a minor or incapable) See also section on Informed Consent.

### *Cell lines*

If human cells are used, authors must declare in the manuscript: what cell lines were used by describing the source of the cell line, including when and from where it was obtained, whether the cell line has recently been authenticated and by what method. If cells were bought from a life science company the following need to be given in the manuscript: name of company (that provided the cells), cell type, number of cell line, and batch of cells.

It is recommended that authors check the [NCBI database](#) for misidentification and contamination of human cell lines. This step will alert authors to possible problems with the cell line and may save considerable time and effort.

Further information is available from the [International Cell Line Authentication Committee](#) (ICLAC).

Authors should include a statement that confirms that an institutional or independent ethics committee (including the name of the ethics committee) approved the study and that informed consent was obtained from the donor or next of kin.

### *Research Resource Identifiers (RRID)*

Research Resource Identifiers (RRID) are persistent unique identifiers (effectively similar to a DOI) for research resources. This journal encourages authors to adopt RRIDs when reporting key biological resources (antibodies, cell lines, model organisms and tools) in their manuscripts.

### *Clinical Trial Registration*

The World Health Organization (WHO) definition of a clinical trial is "any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes". The WHO defines health interventions as "A health intervention is an act performed for, with or on behalf of a person or population whose purpose is to assess, improve, maintain, promote or modify health, functioning or health conditions" and a health-related outcome is generally defined as a change in the health of a person or population as a result of an intervention.

To ensure the integrity of the reporting of patient-centered trials, authors must register prospective clinical trials (phase II to IV trials) in suitable publicly available repositories. For example [www.clinicaltrials.gov](http://www.clinicaltrials.gov) or any of the primary registries that participate in the [WHO International Clinical Trials Registry Platform](#).

The trial registration number (TRN) and date of registration should be included as the last line of the manuscript abstract.

For clinical trials that have not been registered prospectively, authors are encouraged to register retrospectively to ensure the complete publication of all results. The trial registration number (TRN), date of registration and the words 'retrospectively registered' should be included as the last line of the manuscript abstract.

Purely observational trials will not require registration.

### *Standards of reporting*

Springer Nature advocates complete and transparent reporting of biomedical and biological research and research with biological applications. Authors are recommended to adhere to the minimum reporting guidelines hosted by the [EQUATOR Network](#) when preparing their manuscript.

Exact requirements may vary depending on the journal; please refer to the journal's Instructions for Authors.

Checklists are available for a number of study designs, including:

Randomised trials ([CONSORT](#)) and Study protocols ([SPIRIT](#))

Observational studies (STROBE)

Systematic reviews and meta-analyses (PRISMA) and protocols (Prisma-P)

Diagnostic/prognostic studies (STARD) and (TRIPOD)

Case reports (CARE)

Clinical practice guidelines (AGREE) and (RIGHT)

Qualitative research (SRQR) and (COREQ)

Animal pre-clinical studies (ARRIVE)

Quality improvement studies (SQUIRE)

Economic evaluations (CHEERS)

*Summary of requirements*

The above should be summarized in a statement and placed in a “**Declarations**” section before the reference list under a heading of ‘**Ethics approval**’.

Please see the various examples of wording below and revise/customize the sample statements according to your own needs.

Examples of statements to be used when ethics approval has been obtained:

- All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Bioethics Committee of the Medical University of A (No. ...).
- This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of University B (Date.../No. ...).
- Approval was obtained from the ethics committee of University C. The procedures used in this study adhere to the tenets of the Declaration of Helsinki.
- The questionnaire and methodology for this study was approved by the Human Research Ethics committee of the University of D (Ethics approval number: ...).

Examples of statements to be used for a retrospective study:

- Ethical approval was waived by the local Ethics Committee of University A in view of the retrospective nature of the study and all the procedures being performed were part of the routine care.
- This research study was conducted retrospectively from data obtained for clinical purposes. We consulted extensively with the IRB of XYZ who determined that our study did not need ethical approval. An IRB official waiver of ethical approval was granted from the IRB of XYZ.
- This retrospective chart review study involving human participants was in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The Human Investigation Committee (IRB) of University B approved this study.

Examples of statements to be used when no ethical approval is required/exemption granted:

- This is an observational study. The XYZ Research Ethics Committee has confirmed that no ethical approval is required.
- The data reproduced from Article X utilized human tissue that was procured via our Biobank AB, which provides de-identified samples. This study was reviewed and deemed exempt by our XYZ Institutional Review Board. The BioBank protocols are in accordance with the ethical standards of our institution and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Authors are responsible for correctness of the statements provided in the manuscript.

See also Authorship Principles. The Editor-in-Chief reserves the right to reject submissions that do not meet the guidelines described in this section.

### **Informed consent**

All individuals have individual rights that are not to be infringed. Individual participants in studies have, for example, the right to decide what happens to the (identifiable) personal data gathered, to what they have said during a study or an interview, as well as to any photograph that was taken. This is especially true concerning images of vulnerable

people (e.g. minors, patients, refugees, etc) or the use of images in sensitive contexts. In many instances authors will need to secure written consent before including images. Identifying details (names, dates of birth, identity numbers, biometrical characteristics (such as facial features, fingerprint, writing style, voice pattern, DNA or other distinguishing characteristic) and other information) of the participants that were studied should not be published in written descriptions, photographs, and genetic profiles unless the information is essential for scholarly purposes and the participant (or parent or guardian if the participant is incapable) gave written informed consent for publication. Complete anonymity is difficult to achieve in some cases. Detailed descriptions of individual participants, whether of their whole bodies or of body sections, may lead to disclosure of their identity. Under certain circumstances consent is not required as long as information is anonymized and the submission does not include images that may identify the person.

Informed consent for publication should be obtained if there is any doubt. For example, masking the eye region in photographs of participants is inadequate protection of anonymity. If identifying characteristics are altered to protect anonymity, such as in genetic profiles, authors should provide assurance that alterations do not distort scientific meaning.

Exceptions where it is not necessary to obtain consent:

- Images such as x rays, laparoscopic images, ultrasound images, brain scans, pathology slides unless there is a concern about identifying information in which case, authors should ensure that consent is obtained.
- Reuse of images: If images are being reused from prior publications, the Publisher will assume that the prior publication obtained the relevant information regarding consent. Authors should provide the appropriate attribution for republished images.

#### **Consent and already available data and/or biologic material**

Regardless of whether material is collected from living or dead patients, they (family or guardian if the deceased has not made a pre-mortem decision) must have given prior written consent. The aspect of confidentiality as well as any wishes from the deceased should be respected.

#### **Data protection, confidentiality and privacy**

When biological material is donated for or data is generated as part of a research project authors should ensure, as part of the informed consent procedure, that the participants are made what kind of (personal) data will be processed, how it will be used and for what purpose. In case of data acquired via a biobank/biorepository, it is possible they apply a broad consent which allows research participants to consent to a broad range of uses of their data and samples which is regarded by research ethics committees as specific enough to be considered "informed". However, authors should always check the specific biobank/biorepository policies or any other type of data provider policies (in case of non-bio research) to be sure that this is the case.

#### *Consent to Participate*

For all research involving human subjects, freely-given, informed consent to participate in the study must be obtained from participants (or their parent or legal guardian in the case of children under 16) and a statement to this effect should appear in the manuscript. In the case of articles describing human transplantation studies, authors must include a statement declaring that no organs/tissues were obtained from prisoners and must also name the institution(s)/clinic(s)/department(s) via which organs/tissues were obtained. For manuscripts reporting studies involving vulnerable groups where there is the potential for coercion or where consent may not have been fully informed, extra care will be taken by the editor and may be referred to the Springer Nature Research Integrity Group.

#### *Consent to Publish*

Individuals may consent to participate in a study, but object to having their data published in a journal article. Authors should make sure to also seek consent from individuals to publish their data prior to submitting their paper to a journal. This is in particular applicable to case studies. A consent to publish form can be found

### *Summary of requirements*

The above should be summarized in a statement and placed in a “**Declarations**” section before the reference list under a heading of ‘**Consent to participate**’ and/or ‘**Consent to publish**’.

Please see the various examples of wording below and revise/customize the sample statements according to your own needs.

Provide “**Consent to participate**” as a heading

Sample statements for consent to participate:

Informed consent was obtained from all individual participants included in the study.

Informed consent was obtained from legal guardians.

Written informed consent was obtained from the parents.

Verbal informed consent was obtained prior to the interview.

Sample statements for “**Consent to publish**”:

The authors affirm that human research participants provided informed consent for publication of the images in Figure(s) 1a, 1b and 1c.

The participant has consented to the submission of the case report to the journal.

Patients signed informed consent regarding publishing their data and photographs.

Sample statements if identifying information about participants is available in the article:

Additional informed consent was obtained from all individual participants for whom identifying information is included in this article.

Additional informed consent was obtained from all individual participants for whom identifying information is included in this article.

Authors are responsible for correctness of the statements provided in the manuscript.

See also Authorship Principles. The Editor-in-Chief reserves the right to reject submissions that do not meet the guidelines described in this section.

Images will be removed from publication if authors have not obtained informed consent or the paper may be removed and replaced with a notice explaining the reason for removal.

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- Visiting the English language tutorial which covers the common mistakes when writing in English.
- Using a professional language editing service where editors will improve the English to ensure that your meaning is clear and identify problems that require your review. Two such services are provided by our affiliates Nature Research Editing Service and American Journal Experts. Springer authors are entitled to a 10% discount on their first submission to either of these services, simply follow the links below.

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If your manuscript is accepted it will be checked by our copyeditors for spelling and formal style before publication.

## ANEXO 4 – Instruções aos autores da *INTENSIVE CARE MEDICINE*

Disponível em: <https://www.springer.com/journal/134/submission-guidelines> (01/06/2020)

### Instructions for Authors

#### General

All papers providing pre-clinical data (experimental, animal, in-vitro, bench studies or studies without patients) should be submitted to ICM Experimental ICM Experimental. It is necessary for you to upload the appropriate EQUATOR checklist for your study. Please find the appropriate checklist at EQUATOR Network.

All manuscripts undergo review. An initial check is conducted soon after submission to ensure that all manuscripts comply with the guidelines outlined in the Instructions for Authors. A pre-evaluation is then performed by the Editor-in-Chief and one or more Editors to determine which papers are sent for external peer review. Papers not sent out for review will be immediately rejected.

Research articles must meet the following criteria:

- The manuscript presents the results of primary scientific research.
- The results have not been published in full elsewhere.
- Analyses are performed to a high technical standard and are described in full in the manuscript.
- Conclusions are presented in a clear and concise manner and are supported by the data.
- Manuscripts must be written English using standard scientific terms.
- The research meets all applicable ethical standards.
- The article adheres to appropriate reporting guidelines and community standards for full data disclosure.
- All conflicts of interest should be clearly stated in the manuscript.
- According to the Uniform Requirements for Manuscripts Submitted to Biomedical Journals, designation as an author must satisfy three conditions. The author must have:
  - Contributed substantially to the conception and design of the study, the acquisition of data, or the analysis and interpretation of the data.
  - Drafted or provided critical revision of the article.
  - Provided final approval of the version submitted for publication.
- Authors of original papers and reviews are requested to provide the following information:
  - A "Take-home message" (two-sentences) which summarizes how the manuscript adds to current knowledge. This will appear in the final published version of the paper.
  - A 140-character Tweet that may appear online via the Intensive Care Medicine website or social media platforms. This Tweet will not form part of the print version of the manuscript.
- The role of authors and contributors has recently been clarified by the ICMJE

#### Types of Papers

ICM is not accepting papers providing pre-clinical data (experimental, animal, in-vitro, bench studies or studies without patients). These manuscripts should be submitted to ICM Experimental

#### *Original Papers*

**Research articles must meet the following criteria:**

- The manuscript presents the results of primary scientific research
- The results have not been published in full elsewhere
- Analyses are performed to a high technical standard and are described in full in the manuscript
- Conclusions are presented in a clear and concise manner and are supported by the data

- Manuscripts must be written in English using standard scientific terms
  - The research meets all applicable ethical standards
  - The article adheres to appropriate reporting guidelines and community standards for full data disclosure. In general papers of studies that have been pre-registered or have a pre-published or approved protocol and analysis plan are prioritized
  - All conflicts of interest should be clearly stated in the manuscript
  - It is mandatory to upload the appropriate EQUATOR checklist for your study. Please find the appropriate checklist at [EQUATOR Network](#)
  - According to the Uniform Requirements for Manuscripts Submitted to Biomedical Journals, designation as an author must satisfy three conditions. Each author must have:
    - Contributed substantially to the conception and design of the study, the acquisition of data, or the analysis and interpretation of the data
    - Drafted or provided critical revision of the article
    - Provided final approval of the version submitted for publication
  - A statement detailing the role of each author in the study should be reported in an appropriate Authorship statement section of the manuscript in compliance with the ICMJE recommendations.
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  - In addition to the abovementioned statements an Authorship and Conflict of Interest form should be completed, signed by each author and uploaded with the manuscript. The form can be downloaded [here](#).
  - A 250-word abstract and 3-5 keywords are required
  - Original papers must not exceed 3,000 words and should include no more than 5 illustrations and tables.
  - Up to 50 references are permitted. If a higher number of references is needed, explain the reasons during the submission processes.
  - When reporting the results of a randomized controlled trial, author(s) should use the CONSORT statement as a guide in preparing the manuscript.
  - If the authors consider that their manuscript needs to be longer than 3,000 words or contain more figures or tables, the reasons for this should be justified in the cover letter to the Editor-in-Chief.
  - Supplementary information can be published in electronic supplements without limitation.
  - The journal considers only pre-registered trials. A statement should be reported in the manuscript.
  - The journal does not consider single centre retrospective studies
  - IRB/ethical committee approval and patient informed consent statements should be reported in the manuscript in the Materials and Methods section or in a separate section at the end of the manuscript
  - Authors of original papers and reviews are requested to provide the following information:
    - A "Take-home message" (two sentences) which summarizes how the manuscript adds to current knowledge. This will appear in the final published version of the paper.
    - A 140-character Tweet that may appear online via the Intensive Care Medicine website or social media platforms. This Tweet will not form part of the print version of the manuscript
- CONSORT-statement  
*7-Day Profile Publications*
- Only high-quality manuscripts providing new findings from large prospective observational or interventional studies can be submitted as a 7-day profile publication, allowing important data to be rapidly available in the public domain
  - 7-day profile publications are initially assessed by the Editor-in-Chief and Deputy

Editors, and those deemed suitable for this format sent to external reviewers. A decision will be notified to the authors within 7 working days

- Manuscripts will either be provisionally accepted, rejected or transferred to the standard peer review process. In the case of provisional acceptance, authors will have one day to address the reviewers' comments and resubmit a revised manuscript.

- From a manuscript preparation point of view, please comply with the instructions for Original Articles

*Review Articles, Systematic Reviews, Meta-Analyses*

- Review articles should only be submitted after prior consultation with the editors and are subject to the peer review process. The journal is primarily interested in receiving systematic reviews and meta-analyses that use high-quality methodology (pre-registered, published protocol, systematic search, selection and reporting paper) and address relevant clinical questions not already or completely addressed in the literature.

- Review articles must not exceed 4,000 words and 75 references. Supplementary information can be published in electronic supplements without limitation.

- Proposals for review articles should be submitted as a two-page outline so that content can be discussed at an early stage. Review articles must include original tables, figures, graphs, and other didactic materials. They must provide unique information not available elsewhere.

- Authorship should comply with the ICMJE recommendation for authorship and the role of each author should be specified in the first page of the manuscript below the byline.

- At the Editor's decision, authors may be asked to reduce the number of authors in the byline whenever appropriate. The authors may add a study group name as an author in the byline and list the study group members in an appropriate footnote in the first page of the manuscript in order to have their names entered in PubMed as Collaborators.

- In addition to the abovementioned statements an Authorship and Conflict of Interest form should be completed, signed by each author and uploaded with the manuscript. The form can be downloaded [here](#).

- Authors of original papers and reviews are requested to provide the following information:

- A "Take-home message" (two sentences) which summarizes how the manuscript adds to current knowledge. This will appear in the final published version of the paper.

- A 140-character Tweet that may appear online via the Intensive Care Medicine website or social media platforms. This Tweet will not form part of the print version of the manuscript

Two types of reviews are considered: Systematic Reviews and Meta-Analyses (or a combination of both). It is strongly recommended that systematic reviews and meta-analyses comply with the PRISMA Statement, which is available

*Narrative/Scoping Reviews*

Narrative/Scoping Reviews should only be submitted after prior consultation with the Editors and are subject to the peer-review process. They represent the state-of-the-art in a specific field of research and are prepared by senior authors with a broad knowledge of the field.

- Narrative reviews should not exceed 4,000 words and 80 references and should contain figures and tables

- Authorship should not exceed 3 authors, preferably from different centres/countries, although some exceptions can be made by the Editors on a case by case basis depending on the topic

- A statement detailing each Author's role in the study and conflict of interest is mandatory for all papers

- In addition to the abovementioned statements an Authorship and Conflict of Interest form should be completed, signed by each author and uploaded with the manuscript. The form can be downloaded [here](#).

- IRB/ethical committee approval and informed consent statements are not required

- A structured abstract is not required

#### *Editorials*

- Editorials are always commissioned by the Editors and comment on one or more articles in the same issue of the Journal. Editorials must not exceed 1,000 words and up to 15 references, and include a mandatory table or figure.
- Editorials have a maximum of 3 authors
- No abstract
- Conflict of interest disclosure is mandatory for all papers
- Conflict of interest disclosure is mandatory for all papers and should be accompanied by a form to be signed by each author. The form can be downloaded [here](#).

#### *What's New in Intensive Care?*

- What's New articles can only be submitted after invitation by an Editor
- Expert clinicians and scientists are invited to outline the most striking advances in their field of expertise. The manuscript should focus on the most recent knowledge and address ICM's global readership.
- What's New articles are in the format of editorials and typically entitled "What's New in ...". They must not exceed 1,000 words and up to 15 references, and include a mandatory table or figure. A maximum of three authors is permitted.
- Expert clinicians and scientists are invited to outline the most striking advances in their field of expertise. The manuscript should focus on the most recent knowledge and address ICM's global readership.
- No abstract

#### *Understanding the Disease*

"Understanding the disease" articles can only be submitted after invitation by an Editor. Authors should outline a clinical challenge in intensive care medicine and can include a specific disease state, a syndrome, and a clinical abnormality or an intervention. The manuscript should communicate best practice in this field in a focused and structured way that is accessible to a broad group of clinical colleagues, while outlining the most recent advances.

- They are prepared in the format of editorials and must not exceed 1,000 words and up to 15 references.
- A single image is mandatory
- A maximum of three authors is permitted
- No abstract is required

#### *Less is more in Intensive Care*

"Less is more in Intensive Care" articles can only be submitted upon invitation by an Editor.

They should not exceed 1,000 words and 20 references.

- A maximum of three authors is permitted, preferably from different centres/countries
- No abstract is required

#### *Images*

- Submission under the Image section must be of high scientific quality and value as well as providing didactic and self-explanatory lessons. They must be unique and adhere to ethical standards with patient/relative approval when appropriate, protection of patient identity and privacy, and local ethics approval as appropriate.
- The accompanying text must not exceed 200 words. A maximum of four authors is permitted.
- No abstract or references
- The section is not supposed for the publication of case-reports. The focus is on the images

#### *Correspondence*

Correspondence articles provide an opportunity to debate published articles on ICM. The Correspondence is aimed at commenting on an ICM article.

- The Correspondence article must not exceed 500 words, 5 references (including the ICM article which is referred) and 1 figure or table
- The total number of authors should not exceed 5
- At the Editor's discretion the authors of the commented original article may be invited to write a reply, which also should not exceed 500 words, 5 references (including the original ICM article and the related correspondence) and 1 figure or table

#### *Letters to the Editor*

- Letters to the editor provide an opportunity to present results of high scientific value where a short format is most appropriate. Typically, letters are dedicated to small pilot/feasibility studies and/or preliminary data. They must not exceed 500 words, 5 references and 1 figure or table.
- The journal does not consider case reports or brief reports for publication.
- Authorship of letters to the editor should be limited to 5 authors or less. In case of letters which stem from an original study with a higher number of authors, a choice must be made by the authors on the names that should appear in the byline and those that may appear in a footnote or in a study group
- Study group collaborating authors should be included in the front page but separate from the byline
- To the Editor's discretion the authors may be asked to specify the role of each author in the article preparation

#### *From the Inside*

- From the inside includes poetry, trivia, personal stories, thoughts and memories, sounding boards, obituaries or other qualitative materials that authors wish to share with colleagues.

### **Manuscript Submission**

#### *Manuscript Submission*

Submission of a manuscript implies: that the work described has not been published before; that it is not under consideration for publication anywhere else; that its publication has been approved by all co-authors, if any, as well as by the responsible authorities – tacitly or explicitly – at the institute where the work has been carried out. The publisher will not be held legally responsible should there be any claims for compensation.

#### *Permissions*

Authors wishing to include figures, tables, or text passages that have already been published elsewhere are required to obtain permission from the copyright owner(s) for both the print and online format and to include evidence that such permission has been granted when submitting their papers. Any material received without such evidence will be assumed to originate from the authors.

#### *Online Submission*

Please follow the hyperlink "Submit online" on the right and upload all of your manuscript files following the instructions given on the screen.

Please ensure you provide all relevant editable source files. Failing to submit these source files might cause unnecessary delays in the review and production process.

### **Title page**

#### *Title Page*

Please use this **template title page** for providing the following information.

The title page should include:

- The name(s) of the author(s)
- A concise and informative title
- The affiliation(s) of the author(s), i.e. institution, (department), city, (state), country
- A clear indication and an active e-mail address of the corresponding author
- If available, the 16-digit ORCID of the author(s)

If address information is provided with the affiliation(s) it will also be published.

For authors that are (temporarily) unaffiliated we will only capture their city and country of residence, not their e-mail address unless specifically requested.

### *Abstract*

Please provide a structured abstract of 150 to 250 words which should be divided into the following sections:

- Purpose (stating the main purposes and research question)
- Methods
- Results
- Conclusion

*For life science journals only (when applicable)*

Trial registration number and date of registration

Trial registration number, date of registration followed by “retrospectively registered”

### *Keywords*

Please provide 4 to 6 keywords which can be used for indexing purposes.

### *Declarations*

All manuscripts must contain the following sections under the heading 'Declarations'.

If any of the sections are not relevant to your manuscript, please include the heading and write 'Not applicable' for that section.

*To be used for non-life science journals*

**Funding** (information that explains whether and by whom the research was supported)

**Conflicts of interest/Competing interests** (include appropriate disclosures)

**Availability of data and material** (data transparency)

**Code availability** (software application or custom code)

**Authors' contributions** (optional: please review the submission guidelines from the journal whether statements are mandatory)

*To be used for life science journals + articles with biological applications*

**Funding** (information that explains whether and by whom the research was supported)

**Conflicts of interest/Competing interests** (include appropriate disclosures)

**Ethics approval** (include appropriate approvals or waivers)

**Consent to participate** (include appropriate statements)

**Consent for publication** (include appropriate statements)

**Availability of data and material** (data transparency)

**Code availability** (software application or custom code)

**Authors' contributions** (optional: please review the submission guidelines from the journal whether statements are mandatory)

Please see the relevant sections in the submission guidelines for further information as well as various examples of wording. Please revise/customize the sample statements according to your own needs.

*Please note:*

- An abstract is not required for Editorials, Short articles such as 'Focus on, Less is More in Intensive Care, Understanding the Disease, etc.'
- For details, or to submit an outline of your manuscript, please contact the Intensive Care Medicine Managing Editor at [intensivecaremedicine@unimib.it](mailto:intensivecaremedicine@unimib.it)

## **Text**

### *Text Formatting*

Manuscripts should be submitted in Word.

- Use a normal, plain font (e.g., 10-point Times Roman) for text.
- Use italics for emphasis.
- Use the automatic page numbering function to number the pages.
- Do not use field functions.
- Use tab stops or other commands for indents, not the space bar.
- Use the table function, not spreadsheets, to make tables.
- Use the equation editor or MathType for equations.
- Save your file in docx format (Word 2007 or higher) or doc format (older Word versions).

Manuscripts with mathematical content can also be submitted in LaTeX.

#### *Headings*

Please use no more than three levels of displayed headings.

#### *Abbreviations*

Abbreviations should be defined at first mention and used consistently thereafter.

#### *Footnotes*

Footnotes can be used to give additional information, which may include the citation of a reference included in the reference list. They should not consist solely of a reference citation, and they should never include the bibliographic details of a reference. They should also not contain any figures or tables.

Footnotes to the text are numbered consecutively; those to tables should be indicated by superscript lower-case letters (or asterisks for significance values and other statistical data). Footnotes to the title or the authors of the article are not given reference symbols. Always use footnotes instead of endnotes.

#### *Acknowledgments*

Acknowledgments of people, grants, funds, etc. should be placed in a separate section on the title page. The names of funding organizations should be written in full.

#### *Zotero*

If you use Zotero, the ICM styling template can be found here.

#### **Scientific style**

Generic names of drugs and pesticides are preferred; if trade names are used, the generic name should be given at first mention.

#### **References**

##### *Citation*

Reference citations in the text should be identified by numbers in square brackets. Some examples:

1. Negotiation research spans many disciplines [3].
2. This result was later contradicted by Becker and Seligman [5].
3. This effect has been widely studied [1-3, 7].

##### *Reference list*

The list of references should only include works that are cited in the text and that have been published or accepted for publication. Personal communications and unpublished works should only be mentioned in the text. Do not use footnotes or endnotes as a substitute for a reference list.

The entries in the list should be numbered consecutively.

- Journal article  
Gamelin FX, Baquet G, Berthoin S, Thevenet D, Nourry C, Nottin S, Bosquet L (2009) Effect of high intensity intermittent training on heart rate variability in prepubescent children. *Eur J Appl Physiol* 105:731-738.  
<https://doi.org/10.1007/s00421-008-0955-8>  
Ideally, the names of all authors should be provided, but the usage of “et al” in long author lists will also be accepted:  
Smith J, Jones M Jr, Houghton L et al (1999) Future of health insurance. *N Engl J Med* 341:325–329
- Article by DOI  
Slifka MK, Whitton JL (2000) Clinical implications of dysregulated cytokine production. *J Mol Med*. <https://doi.org/10.1007/s001090000086>
- Book  
South J, Blass B (2001) *The future of modern genomics*. Blackwell, London
- Book chapter  
Brown B, Aaron M (2001) The politics of nature. In: Smith J (ed) *The rise of modern genomics*, 3rd edn. Wiley, New York, pp 230-257
- Online document  
Cartwright J (2007) Big stars have weather too. IOP Publishing PhysicsWeb. <http://physicsweb.org/articles/news/11/6/16/1>. Accessed 26 June 2007

- Dissertation  
Trent JW (1975) Experimental acute renal failure. Dissertation, University of California

Always use the standard abbreviation of a journal's name according to the ISSN List of Title Word Abbreviations, see

If you are unsure, please use the full journal title.

For authors using EndNote, Springer provides an output style that supports the formatting of in-text citations and reference list.

*Please note:*

References are not necessary for the following sections: Correspondences, Imaging, and From the inside.

### Tables

- All tables are to be numbered using Arabic numerals.
- Tables should always be cited in text in consecutive numerical order.
- For each table, please supply a table caption (title) explaining the components of the table.
- Identify any previously published material by giving the original source in the form of a reference at the end of the table caption.
- Footnotes to tables should be indicated by superscript lower-case letters (or asterisks for significance values and other statistical data) and included beneath the table body.

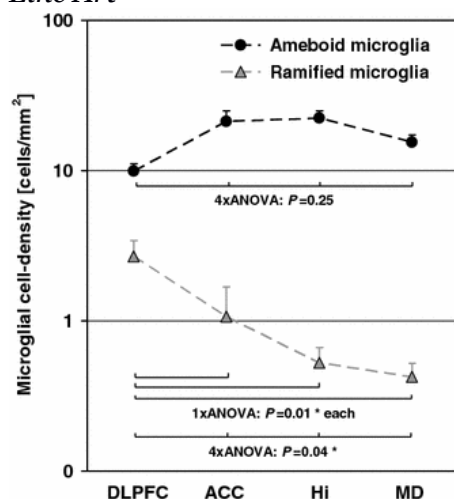
Tables for ICM publication should be prepared taking into account the current style of the journal. Tables that do not exceed the A4 width of a page (portrait format) are preferred. Decimals should be limited to two digits, unless data require to specify up to the third or fourth decimal digit (e.g. 0.0004). Unnecessary decimals should be avoided (e.g. 4.00 should be 4).

### Artwork and Illustrations Guidelines

#### Electronic Figure Submission

- Supply all figures electronically.
- Indicate what graphics program was used to create the artwork.
- For vector graphics, the preferred format is EPS; for halftones, please use TIFF format. MSOffice files are also acceptable.
- Vector graphics containing fonts must have the fonts embedded in the files.
- Name your figure files with "Fig" and the figure number, e.g., Fig1.eps.

#### Line Art



- Definition: Black and white graphic with no shading.
- Do not use faint lines and/or lettering and check that all lines and lettering within the figures are legible at final size.
- All lines should be at least 0.1 mm (0.3 pt) wide.
- Scanned line drawings and line drawings in bitmap format should have a

minimum resolution of 1200 dpi.

- Vector graphics containing fonts must have the fonts embedded in the files.

#### *Halftone Art*

- Definition: Photographs, drawings, or paintings with fine shading, etc.
- If any magnification is used in the photographs, indicate this by using scale bars within the figures themselves.
- Halftones should have a minimum resolution of 300 dpi.

#### *Combination Art*

- Definition: a combination of halftone and line art, e.g., halftones containing line drawing, extensive lettering, color diagrams, etc.
- Combination artwork should have a minimum resolution of 600 dpi.

#### *Color Art*

- Color art is free of charge for online publication.
- If black and white will be shown in the print version, make sure that the main information will still be visible. Many colors are not distinguishable from one another when converted to black and white. A simple way to check this is to make a xerographic copy to see if the necessary distinctions between the different colors are still apparent.
- If the figures will be printed in black and white, do not refer to color in the captions.
- Color illustrations should be submitted as RGB (8 bits per channel).

#### *Figure Lettering*

- To add lettering, it is best to use Helvetica or Arial (sans serif fonts).
- Keep lettering consistently sized throughout your final-sized artwork, usually about 2–3 mm (8–12 pt).
- Variance of type size within an illustration should be minimal, e.g., do not use 8-pt type on an axis and 20-pt type for the axis label.
- Avoid effects such as shading, outline letters, etc.
- Do not include titles or captions within your illustrations.

#### *Figure Numbering*

- All figures are to be numbered using Arabic numerals.
- Figures should always be cited in text in consecutive numerical order.
- Figure parts should be denoted by lowercase letters (a, b, c, etc.).
- If an appendix appears in your article and it contains one or more figures, continue the consecutive numbering of the main text. Do not number the appendix figures, "A1, A2, A3, etc." Figures in online appendices (Electronic Supplementary Material) should, however, be numbered separately.

#### *Figure Captions*

- Each figure should have a concise caption describing accurately what the figure depicts. Include the captions in the text file of the manuscript, not in the figure file.
- Figure captions begin with the term Fig. in bold type, followed by the figure number, also in bold type.
- No punctuation is to be included after the number, nor is any punctuation to be placed at the end of the caption.
- Identify all elements found in the figure in the figure caption; and use boxes, circles, etc., as coordinate points in graphs.
- Identify previously published material by giving the original source in the form of a reference citation at the end of the figure caption.

#### *Figure Placement and Size*

- Figures should be submitted separately from the text, if possible.
- When preparing your figures, size figures to fit in the column width.
- For large-sized journals the figures should be 84 mm (for double-column text areas), or 174 mm (for single-column text areas) wide and not higher than 234 mm.
- For small-sized journals, the figures should be 119 mm wide and not higher than

195 mm.

#### *Permissions*

If you include figures that have already been published elsewhere, you must obtain permission from the copyright owner(s) for both the print and online format. Please be aware that some publishers do not grant electronic rights for free and that Springer will not be able to refund any costs that may have occurred to receive these permissions. In such cases, material from other sources should be used.

#### *Accessibility*

In order to give people of all abilities and disabilities access to the content of your figures, please make sure that

- All figures have descriptive captions (blind users could then use a text-to-speech software or a text-to-Braille hardware)
- Patterns are used instead of or in addition to colors for conveying information (colorblind users would then be able to distinguish the visual elements)
- Any figure lettering has a contrast ratio of at least 4.5:1

#### *Please note: General Guidelines*

Some general guidelines to prepare figures in the style of the journal:

- Font: Helvetica
- Colours: navy blue #0c385c; light blue #1770b8; light mauve blue #d0d9f0; dark mauve blue #6b8ac5
- Tables should be preferably vertical within an A4 page. They may be horizontal if the table size is half an A4 page.

At the Editor's discretion some figures may be re-drawn. The authors may be asked to coordinate with the Managing Editor for figures to be re-drawn by the journal illustrator at no cost for the authors.

#### **Color Art**

Color illustrations: Publication of color illustrations is free of charge.

#### **Electronic Supplementary Material**

Springer accepts electronic multimedia files (animations, movies, audio, etc.) and other supplementary files to be published online along with an article or a book chapter. This feature can add dimension to the author's article, as certain information cannot be printed or is more convenient in electronic form.

Before submitting research datasets as electronic supplementary material, authors should read the journal's Research data policy. We encourage research data to be archived in data repositories wherever possible.

#### *Submission*

- Supply all supplementary material in standard file formats.
- Please include in each file the following information: article title, journal name, author names; affiliation and e-mail address of the corresponding author.
- To accommodate user downloads, please keep in mind that larger-sized files may require very long download times and that some users may experience other problems during downloading.

#### *Audio, Video, and Animations*

- Aspect ratio: 16:9 or 4:3
- Maximum file size: 25 GB
- Minimum video duration: 1 sec
- Supported file formats: avi, wmv, mp4, mov, m2p, mp2, mpg, mpeg, flv, mxf, mts, m4v, 3gp

#### *Text and Presentations*

- Submit your material in PDF format; .doc or .ppt files are not suitable for long-term viability.
- A collection of figures may also be combined in a PDF file.

#### *Spreadsheets*

- Spreadsheets should be submitted as .csv or .xlsx files (MS Excel).

#### *Specialized Formats*

- Specialized format such as .pdb (chemical), .wrl (VRML), .nb (Mathematica notebook), and .tex can also be supplied.

#### *Collecting Multiple Files*

- It is possible to collect multiple files in a .zip or .gz file.

#### *Numbering*

- If supplying any supplementary material, the text must make specific mention of the material as a citation, similar to that of figures and tables.
- Refer to the supplementary files as “Online Resource”, e.g., “... as shown in the animation (Online Resource 3)”, “... additional data are given in Online Resource 4”.
- Name the files consecutively, e.g. “ESM\_3.mpg”, “ESM\_4.pdf”.

#### *Captions*

- For each supplementary material, please supply a concise caption describing the content of the file.

#### *Processing of supplementary files*

- Electronic supplementary material will be published as received from the author without any conversion, editing, or reformatting.

#### *Accessibility*

In order to give people of all abilities and disabilities access to the content of your supplementary files, please make sure that

- The manuscript contains a descriptive caption for each supplementary material
- Video files do not contain anything that flashes more than three times per second (so that users prone to seizures caused by such effects are not put at risk)

### **Ethical Responsibilities of Authors**

This journal is committed to upholding the integrity of the scientific record. As a member of the Committee on Publication Ethics (COPE) the journal will follow the COPE guidelines on how to deal with potential acts of misconduct.

Authors should refrain from misrepresenting research results which could damage the trust in the journal, the professionalism of scientific authorship, and ultimately the entire scientific endeavour. Maintaining integrity of the research and its presentation is helped by following the rules of good scientific practice, which include\*:

- The manuscript should not be submitted to more than one journal for simultaneous consideration.
- The submitted work should be original and should not have been published elsewhere in any form or language (partially or in full), unless the new work concerns an expansion of previous work. (Please provide transparency on the re-use of material to avoid the concerns about text-recycling ('self-plagiarism').
- A single study should not be split up into several parts to increase the quantity of submissions and submitted to various journals or to one journal over time (i.e. 'salami-slicing/publishing').
- Concurrent or secondary publication is sometimes justifiable, provided certain conditions are met. Examples include: translations or a manuscript that is intended for a different group of readers.
- Results should be presented clearly, honestly, and without fabrication, falsification or inappropriate data manipulation (including image based manipulation). Authors should adhere to discipline-specific rules for acquiring, selecting and processing data.
- No data, text, or theories by others are presented as if they were the author's own ('plagiarism'). Proper acknowledgements to other works must be given (this includes material that is closely copied (near verbatim), summarized and/or paraphrased), quotation marks (to indicate words taken from another source) are used for verbatim copying of material, and permissions secured for material that is copyrighted.

#### **Important note: the journal may use software to screen for plagiarism.**

- Authors should make sure they have permissions for the use of software,

- questionnaires/(web) surveys and scales in their studies (if appropriate).
- Research articles and non-research articles (e.g. Opinion, Review, and Commentary articles) must cite appropriate and relevant literature in support of the claims made. Excessive and inappropriate self-citation or coordinated efforts among several authors to collectively self-cite is strongly discouraged.
  - Authors should avoid untrue statements about an entity (who can be an individual person or a company) or descriptions of their behavior or actions that could potentially be seen as personal attacks or allegations about that person.
  - Research that may be misapplied to pose a threat to public health or national security should be clearly identified in the manuscript (e.g. dual use of research). Examples include creation of harmful consequences of biological agents or toxins, disruption of immunity of vaccines, unusual hazards in the use of chemicals, weaponization of research/technology (amongst others).
  - Authors are strongly advised to ensure the author group, the Corresponding Author, and the order of authors are all correct at submission. Adding and/or deleting authors during the revision stages is generally not permitted, but in some cases may be warranted. Reasons for changes in authorship should be explained in detail. Please note that changes to authorship cannot be made after acceptance of a manuscript.

\*All of the above are guidelines and authors need to make sure to respect third parties rights such as copyright and/or moral rights.

Upon request authors should be prepared to send relevant documentation or data in order to verify the validity of the results presented. This could be in the form of raw data, samples, records, etc. Sensitive information in the form of confidential or proprietary data is excluded.

If there is suspicion of misbehavior or alleged fraud the Journal and/or Publisher will carry out an investigation following COPE guidelines. If, after investigation, there are valid concerns, the author(s) concerned will be contacted under their given e-mail address and given an opportunity to address the issue. Depending on the situation, this may result in the Journal's and/or Publisher's implementation of the following measures, including, but not limited to:

- If the manuscript is still under consideration, it may be rejected and returned to the author.
- If the article has already been published online, depending on the nature and severity of the infraction:
  - an erratum/correction may be placed with the article
  - an expression of concern may be placed with the article
  - or in severe cases retraction of the article may occur.

The reason will be given in the published erratum/correction, expression of concern or retraction note. Please note that retraction means that the article is **maintained on the platform**, watermarked "retracted" and the explanation for the retraction is provided in a note linked to the watermarked article.

- The author's institution may be informed
- A notice of suspected transgression of ethical standards in the peer review system may be included as part of the author's and article's bibliographic record.

#### *Fundamental errors*

Authors have an obligation to correct mistakes once they discover a significant error or inaccuracy in their published article. The author(s) is/are requested to contact the journal and explain in what sense the error is impacting the article. A decision on how to correct the literature will depend on the nature of the error. This may be a correction or retraction. The retraction note should provide transparency which parts of the article are impacted by the error.

#### *Suggesting / excluding reviewers*

Authors are welcome to suggest suitable reviewers and/or request the exclusion of certain individuals when they submit their manuscripts. When suggesting reviewers,

authors should make sure they are totally independent and not connected to the work in any way. It is strongly recommended to suggest a mix of reviewers from different countries and different institutions. When suggesting reviewers, the Corresponding Author must provide an institutional email address for each suggested reviewer, or, if this is not possible to include other means of verifying the identity such as a link to a personal homepage, a link to the publication record or a researcher or author ID in the submission letter. Please note that the Journal may not use the suggestions, but suggestions are appreciated and may help facilitate the peer review process.

### **Authorship principles**

These guidelines describe authorship principles and good authorship practices to which prospective authors should adhere to.

#### *Authorship clarified*

The Journal and Publisher assume all authors agreed with the content and that all gave explicit consent to submit and that they obtained consent from the responsible authorities at the institute/organization where the work has been carried out, **before** the work is submitted.

The Publisher does not prescribe the kinds of contributions that warrant authorship. It is recommended that authors adhere to the guidelines for authorship that are applicable in their specific research field. In absence of specific guidelines it is recommended to adhere to the following guidelines\*:

All authors whose names appear on the submission

- 1) made substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data; or the creation of new software used in the work;
- 2) drafted the work or revised it critically for important intellectual content;
- 3) approved the version to be published; and
- 4) agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

\* Based on/adapted from:

[ICMJE, Defining the Role of Authors and Contributors.](#)

[Transparency in authors' contributions and responsibilities to promote integrity in scientific publication, McNutt at all, PNAS February 27, 2018](#)

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All authors are requested to include information regarding sources of funding, financial or non-financial interests, study-specific approval by the appropriate ethics committee for research involving humans and/or animals, informed consent if the research involved human participants, and a statement on welfare of animals if the research involved animals (as appropriate).

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- ensuring that all listed authors have approved the manuscript before submission,

- including the names and order of authors;
- managing all communication between the Journal and all co-authors, before and after publication;\*
- providing transparency on re-use of material and mention any unpublished material (for example manuscripts in press) included in the manuscript in a cover letter to the Editor;
- making sure disclosures, declarations and transparency on data statements from all authors are included in the manuscript as appropriate (see above).

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In absence of specific instructions and in research fields where it is possible to describe discrete efforts, the Publisher recommends authors to include contribution statements in the work that specifies the contribution of every author in order to promote transparency. These contributions should be listed at the separate title page.

#### **Examples of such statement(s) are shown below:**

- Free text:

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by [full name], [full name] and [full name]. The first draft of the manuscript was written by [full name] and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

- Conceptualization: [full name], ...; Methodology: [full name], ...; Formal analysis and investigation: [full name], ...; Writing - original draft preparation: [full name, ...]; Writing - review and editing: [full name], ...; Funding acquisition: [full name], ...; Resources: [full name], ...; Supervision: [full name],....

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- Informed consent

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When reporting a study that involved human participants, their data or biological material, authors should include a statement that confirms that the study was approved (or granted exemption) by the appropriate institutional and/or national research ethics committee (including the name of the ethics committee) and certify that the study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. If doubt exists whether the research was conducted in accordance with the 1964 Helsinki Declaration or comparable standards, the authors must explain the reasons for their approach, and demonstrate that an independent ethics committee or institutional review board explicitly approved the

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If a study has not been granted ethics committee approval prior to commencing, retrospective ethics approval usually cannot be obtained and it may not be possible to consider the manuscript for peer review. The decision on whether to proceed to peer review in such cases is at the Editor's discretion.

#### *Ethics approval for retrospective studies*

Although retrospective studies are conducted on already available data or biological material (for which formal consent may not be needed or is difficult to obtain) ethics approval may be required dependent on the law and the national ethical guidelines of a country. Authors should check with their institution to make sure they are complying with the specific requirements of their country.

#### *Ethics approval for case studies*

Case reports require ethics approval. Most institutions will have specific policies on this subject. Authors should check with their institution to make sure they are complying with the specific requirements of their institution and seek ethics approval where needed. Authors should be aware to secure informed consent from the individual (or parent or guardian if the participant is a minor or incapable) See also section on Informed Consent.

#### *Cell lines*

If human cells are used, authors must declare in the manuscript: what cell lines were used by describing the source of the cell line, including when and from where it was obtained, whether the cell line has recently been authenticated and by what method. If cells were bought from a life science company the following need to be given in the manuscript: name of company (that provided the cells), cell type, number of cell line, and batch of cells.

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Further information is available from the [International Cell Line Authentication Committee](#) (ICLAC).

Authors should include a statement that confirms that an institutional or independent ethics committee (including the name of the ethics committee) approved the study and that informed consent was obtained from the donor or next of kin.

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To ensure the integrity of the reporting of patient-centered trials, authors must register prospective clinical trials (phase II to IV trials) in suitable publicly available repositories. For example [www.clinicaltrials.gov](http://www.clinicaltrials.gov) or any of the primary registries that participate in the [WHO International Clinical Trials Registry Platform](#).

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#### *Summary of requirements*

The above should be summarized in a statement and placed in a “**Declarations**” section before the reference list under a heading of ‘**Ethics approval**’.

Please see the various examples of wording below and revise/customize the sample statements according to your own needs.

Examples of statements to be used when ethics approval has been obtained:

- All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Bioethics Committee of the Medical University of A (No. ...).
- This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of University B (Date.../No. ...).
- Approval was obtained from the ethics committee of University C. The procedures used in this study adhere to the tenets of the Declaration of Helsinki.
- The questionnaire and methodology for this study was approved by the Human Research Ethics committee of the University of D (Ethics approval number: ...).

Examples of statements to be used for a retrospective study:

- Ethical approval was waived by the local Ethics Committee of University A in view of the retrospective nature of the study and all the procedures being performed were part of the routine care.
- This research study was conducted retrospectively from data obtained for clinical purposes. We consulted extensively with the IRB of XYZ who determined that our study did not need ethical approval. An IRB official waiver of ethical approval was granted from the IRB of XYZ.
- This retrospective chart review study involving human participants was in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The Human Investigation Committee (IRB) of University B approved this study.

Examples of statements to be used when no ethical approval is required/exemption granted:

- This is an observational study. The XYZ Research Ethics Committee has confirmed that

no ethical approval is required.

- The data reproduced from Article X utilized human tissue that was procured via our Biobank AB, which provides de-identified samples. This study was reviewed and deemed exempt by our XYZ Institutional Review Board. The BioBank protocols are in accordance with the ethical standards of our institution and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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### **Informed consent**

All individuals have individual rights that are not to be infringed. Individual participants in studies have, for example, the right to decide what happens to the (identifiable) personal data gathered, to what they have said during a study or an interview, as well as to any photograph that was taken. This is especially true concerning images of vulnerable people (e.g. minors, patients, refugees, etc) or the use of images in sensitive contexts. In many instances authors will need to secure written consent before including images. Identifying details (names, dates of birth, identity numbers, biometrical characteristics (such as facial features, fingerprint, writing style, voice pattern, DNA or other distinguishing characteristic) and other information) of the participants that were studied should not be published in written descriptions, photographs, and genetic profiles unless the information is essential for scholarly purposes and the participant (or parent or guardian if the participant is incapable) gave written informed consent for publication. Complete anonymity is difficult to achieve in some cases. Detailed descriptions of individual participants, whether of their whole bodies or of body sections, may lead to disclosure of their identity. Under certain circumstances consent is not required as long as information is anonymized and the submission does not include images that may identify the person.

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- Reuse of images: If images are being reused from prior publications, the Publisher will assume that the prior publication obtained the relevant information regarding consent. Authors should provide the appropriate attribution for republished images.

### **Consent and already available data and/or biologic material**

Regardless of whether material is collected from living or dead patients, they (family or guardian if the deceased has not made a pre-mortem decision) must have given prior written consent. The aspect of confidentiality as well as any wishes from the deceased should be respected.

### **Data protection, confidentiality and privacy**

When biological material is donated for or data is generated as part of a research project authors should ensure, as part of the informed consent procedure, that the participants are made what kind of (personal) data will be processed, how it will be used and for what purpose. In case of data acquired via a biobank/biorepository, it is possible they apply a broad consent which allows research participants to consent to a broad range of uses of their data and samples which is regarded by research ethics committees as specific enough to be considered "informed". However, authors should always check the specific biobank/biorepository policies or any other type of data provider policies (in case of non-bio research) to be sure that this is the case.

*Consent to Participate*

For all research involving human subjects, freely-given, informed consent to participate in the study must be obtained from participants (or their parent or legal guardian in the case of children under 16) and a statement to this effect should appear in the manuscript. In the case of articles describing human transplantation studies, authors must include a statement declaring that no organs/tissues were obtained from prisoners and must also name the institution(s)/clinic(s)/department(s) via which organs/tissues were obtained. For manuscripts reporting studies involving vulnerable groups where there is the potential for coercion or where consent may not have been fully informed, extra care will be taken by the editor and may be referred to the Springer Nature Research Integrity Group.

#### *Consent to Publish*

Individuals may consent to participate in a study, but object to having their data published in a journal article. Authors should make sure to also seek consent from individuals to publish their data prior to submitting their paper to a journal. This is in particular applicable to case studies. A consent to publish form can be found

#### *Summary of requirements*

The above should be summarized in a statement and placed in a “**Declarations**” section before the reference list under a heading of ‘**Consent to participate**’ and/or ‘**Consent to publish**’.

Please see the various examples of wording below and revise/customize the sample statements according to your own needs.

Provide “**Consent to participate**” as a heading

Sample statements for consent to participate:

Informed consent was obtained from all individual participants included in the study.

Informed consent was obtained from legal guardians.

Written informed consent was obtained from the parents.

Verbal informed consent was obtained prior to the interview.

Sample statements for “**Consent to publish**”:

The authors affirm that human research participants provided informed consent for publication of the images in Figure(s) 1a, 1b and 1c.

The participant has consented to the submission of the case report to the journal.

Patients signed informed consent regarding publishing their data and photographs.

Sample statements if identifying information about participants is available in the article:

Additional informed consent was obtained from all individual participants for whom identifying information is included in this article.

Additional informed consent was obtained from all individual participants for whom identifying information is included in this article.

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