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Impact of advance directives on factors involved in the decision-making in ICU

Margot Smirdec

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UNIVERSITÉ CLERMONT-AUVERGNE

UFR DE MÉDECINE

THÈSE

Pour le

DOCTORAT EN MÉDECINE

(Diplôme d'état)

PAR

SMIRDEC, Margot, Jeanne, Léa

Présentée et soutenue publiquement le Vendredi 13 avril 2018

**IMPACT DES DIRECTIVES ANTICIPÉES SUR LES FACTEURS
INFLUENÇANT LA PRISE DE DÉCISION EN RÉANIMATION**

Impact of Advance Directives on factors involved in the decision-making in ICU.

Titre abrégé : Facing Decision – ICU

Preliminary results

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*Pour toi Matthieu,
Pour tous ceux qui souffrent en silence,
Pour plus de bienveillance et d'humanité,*

**« Rude est la confrontation avec soi-même,
Lourd est le poids de l'ego.
Fragile est la confiance âprement gagnée,
Sombres sont les pensées du souci,
Du doute et de la mauvaise foi.
Arides sont les terres de l'indifférence,
Traître est le chemin de l'oubli.
Seule une lueur persiste indéfiniment.
Au bout on peut l'apercevoir
Si l'on scrute attentivement l'horizon.

Alors nait l'espérance. »**

Matthieu Narring

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ABBREVIATIONS

AD: Advance Directives

HAS: Haute Autorité de Santé (*French Health Authority*)

ICU: Intensive Care Unit

1. INTRODUCTION

We live in a autonomous model chosen by the population (1). A lot of people near the end of life are unable to make decisions for themselves about whether to accept life-sustaining treatments or not (2,3). When the patients' preferences are unknown at this time, the physicians' decisions are influenced by their own preferences (religion, philosophy, culture)(4,5). But physicians' decisions can vary. There would be an important inter-individual variability between the physicians themselves in the level of management of patients in intensive care concerning withholding or withdrawing therapies (6). This variability would persist within the same specialty and structure (7). Moreover, the patients would like their preferences (possibly given by the family) to be followed rather than the physician's preferences. They have two ways to communicate their wishes when they cannot express themselves: through their family or relatives and through their advance directives (AD). Wills reported by the family do not necessarily reflect the patients' wishes (8). They could be influenced by the family's own preferences and sometimes the family may have psychotic symptoms (anxiety/depression, PTSD)(9) that may prevent them from reporting clear wishes. Family can have misperceptions about prognosis of the patient (10) that biases what they say. The patients can also write their wishes in the form of AD. AD require clear, faithful and complete information before being written by the patients. They could improve physicians' adherence to the patients' wishes (3,11,12). However, two problems remain with AD. First we do not know how to clearly and fully inform the patient. In a French randomized study (13), published in 2013, Philippart and others suggested to make interviews with the patients and showed them videos about hospitalization in intensive care units (ICU) and life-sustaining treatments to guide them in writing their AD. But even after a clear information, AD can change over time (14). Then, physicians do

not really know how to interpret these AD (15). Sometimes AD have more weight than physicians' preferences on therapeutic choices but sometimes physicians do not follow AD (16).

The main objective of this study was to evaluate the impact of AD according to the knowledge of the way they have been written (with complete information provided by a physician) on the therapeutic choices. The second objectives were to evaluate the factors involved in the variability of each physician (intra-individual variability) and between physicians themselves (inter-individual variability) for decisions of admission, withholding or withdrawing therapies.

2. METHODS

The trial was approved by the French ethical committee (Comité de Protection des Personnes Sud-Est VI de Clermont-Ferrand, n°: 2016 / CE87). A consent form was collected for all the patients. Before this, they were informed orally and received a written information form. The physicians received all the information by email. Study was registered on the website ClinicalTrials.gov at number: NCT03013530 for the 6th January 2017.

Study procedures

We conducted a multicentre, prospective, observational study in 28 ICUs in 14 university hospitals and in 9 general hospitals, in France from the 13th January 2017 to the 20th March 2018. The study was carried out in five steps (figure 1).

For the first step, real patients were recruited. Seven referring physicians recruited patients and the characteristics of the patients were collected. . These physicians proposed the drafting of the AD to all their patients with chronic disabling pathology, who had a reduced life expectancy and at the same time were clinically stable. They should not have cognitive impairment. They received information about AD during this first consult. Then physician offered the patients to participate to this study and provided the information form of the study, the AD HAS template (HAS Haute autorité de Santé: French Health Authority), the AD HAS information form and the HAS information form for surrogates.

For the second step, these patients wrote AD after clear and full information. An interview was carried out with an ICU physician in the place chosen by the patient (home or hospital). During the interviews, they had to watch a video of 10 minutes explaining the AD and the use of life-

sustaining treatments. The patients could ask all the questions they wanted on this subject. Then, the patients drafted their AD during this interview or in the days after according to the current HAS AD template. HAS model AD consists in a free text with oriented questions. The patients were also invited to discuss about AD with their relatives and to think about appointing a surrogate. The following data were collected about patients: age, sex, housing, occupation, religion, social status, detailed medical history, level of dependence and life quality (with validated scales (17–21)).

For the third step, two simulation scenarios were developed. A multidisciplinary team created 2 simulations (4 physicians of the ethical board of Clermont-Ferrand and a physician specialized in pain and palliative care). The first simulation was about the management of a severe bacterial acute pneumonia, followed by 6 closed questions and one open-ended question. The second simulation regarded a septic shock 5 days after a surgery of occlusive syndrome, followed by 4 closed questions (see Appendix 1). The simulations were oriented towards the patient admission decision, the setting up of life sustaining treatments and withholding and withdrawing therapies.

For the fourth step, ICU physicians were recruited to answer to simulation scenarios. The physicians working in these 28 recruited intensive care units received an e-mail to inform them about the study and the request registration. All the participants were informed that the authorization to use patient and physician data could be withdrawn at any time. The factors which could influence the physicians' decisions were collected: age, sex, professional status, type of degree, place of practice, type of hospital (university, general), characteristics of ICU (medical, surgical, mixed; number of beds and number of physicians in the ICU; existence of a protocol for withholding and withdrawing therapies; number of withholding and withdrawing therapies), length

of professional practice, religion, interest in ethics, evaluation of burnout and traumatic experience of an end-of-life situation.

For the fifth step, three rounds of simulations were submitted to the physicians. The 2 simulations scenarios described in step 3 were submitted to the physicians recruited in step 4 with the characteristics of the real patients selected in step 1 and the AD written in step 2, in 3 different rounds. Round 1 (R1): the physicians answered to the 2 simulations for the real patients with their characteristics and without the AD. Round 2 (R2): the physicians answered to the 2 simulations with patients' characteristics and with the AD. Round 3 (R3): the physicians answered to the 2 simulations with the same characteristics, the same AD and with the knowledge of how these AD were carried out (the interview with an ICU physician, the video and the dependence and life quality scales). The answers were anonymous. The simulations were submitted to the physicians using the Redcap software by successive questionnaires. A minimum delay of 2 weeks separated each round. Each round was divided in 2 different mailing of questionnaires to improve the physicians' adhesion (about 15-20 minutes for one round for 4 patients).

Statistical analysis:

The primary outcome was the impact of AD on the physicians' decisions in simulations. Secondary outcomes determined inter-individual variability, intra-individual variability, impact of the knowledge of how these AD were carried out and factors involved in variability.

All statistical analysis were performed using Stata software (version 13, StataCorp, College Station USA, TX). Quantitative data were expressed as mean \pm standard deviation or median [interquartile range] according to statistical distribution. The assumption of normality was studied

using the Shapiro-Wilk test and the categorical parameters were studied by numbers and associated percentages.

The concordance study considered the estimation of the rate of concordant cases and the Kappa coefficient of concordance for repeated data (multiple data for the same ICU physician and multiple data for the same patient). It was interpreted through the light of the recommendations usually reported in the literature: <0.2 (negligible agreement), $0.20-0.39$ (weak agreement), from 0.40 to 0.59 (moderate agreement), $0.60-0.79$ (good agreement) and ≥ 0.8 (excellent agreement)(22,23).

All analyses considered mixed models to study the effect of ICU physicians' characteristics (including age, sex, type of degree, type of activity, hospital structure, length of practice, religion, level of burnout) on the responses provided for each question while taking into account the different sources of variability (ICU physician and patient).

Indeed, the use of more usual inferential statistical tests would have resulted in biased estimates due to the non-independence of the data. Thus, for binary (yes/no) or ordinal (3-class) dependent variables, generalized mixed linear models (logistic or polynomial respectively) were implemented. The session effect associated with the 3 measurement times was studied in a similar way. The results are expressed in terms of regression coefficients and 95% confidence intervals.

All analyses were performed bilaterally for a type I error of 5%. Thus, a difference was considered statistically significant when the degree of significance was less than 0.05.

3. RESULTS

Of the 23 patients contacted for the study by the 7 referring physicians, 1 died before the interview, 1 was transferred to a palliative care unit, 1 was unavailable, 10 refused to participate. 10 agreed to participate. 2 refused to do the AD after the interview. 8 patients wrote their AD after the interview. The interviews lasted approximately 90 minutes (average 85.6 minutes [60-120]). Of the 245 invited ICU physicians, 177 agreed to participate and started the questionnaires and 82 completed the three rounds. Table 1 report the characteristics of the 177 ICU physicians. The results of the questionnaires presented for the three rounds are preliminary results with the first 82 physicians who have completed all the questionnaires.

Variability between physicians themselves (inter-individual variability)

The variability between physicians about admission decisions and withholding or withdrawing therapies decisions was high (Figure 2 and Table 2). Among the 80 questions (10 questions per patient, $n=8$) of the round 1, there were 40, 23 and 17 questions with an agreement $> 80\%$, $80-60\%$ and $<60\%$ respectively. The AD significantly decreased the number of questions with an agreement $> 80\%$ or $80-60\%$ and increased the number of questions with an agreement $<60\%$ ($n=18$, $n=11$, $n=31$ for round 2, $p<0.001$; $n=23$, $n=9$, $n=28$ for round 3, $p<0.05$, respectively). There was no difference between the round 2 and the round 3 ($p=0.6$).

Variability of each physician (intra-individual variability)

The intra-individual variability between the round 1 and the round 2 was very high (Table 3). Among the 80 questions, there were 20, 46 and 14 questions with a kappa coefficient <0.2 , $0.2-0.39$, ≥ 0.4 between the round 1 and the round 2 respectively. The highest kappa coefficient between

the round 1 and the round 2 was 0.59. The number of questions with a kappa coefficient ≥ 0.4 between the round 2 and round 3 significantly increased compared to the kappa coefficients between the round 1 and the round 2 ($n=36$, $p<0.001$).

Factors involved in inter-individual and intra-individual variability

Few physicians' characteristics were associated with the inter-individual variability (Table 4 and 5) for some questions. But no characteristic was associated with the inter-individual variability for all the questions.

The AD were significantly associated with the intra-individual variability between the round 1 and the rounds 2 or 3 for all the questions after adjustment on characteristics of the physicians and of the patients (Table 6). The AD lead the physicians to decrease the ICU admissions and make more decisions of withholding or withdrawing therapies (Table 6). The knowledge of how the AD were carried out did not affect the physicians' decisions, except for the questions S2Q2 and S2Q3 (Table 6), for which the impact of the decision between these two questions was opposite.

4. DISCUSSION

This study highlights the impact of the AD for the ICU physicians' decisions. The variability of decisions about ICU admissions and withholding or withdrawing therapies between the physicians is high. No physician characteristic is strongly associated with the inter-individual variability. The AD affect the decisions of the ICU physicians by decreasing the ICU admissions and by increasing the decisions to forgo life-sustaining therapies. Moreover, the AD significantly increase the inter-individual variability. It is relevant to notice that the knowledge of how the AD were carried out has a very low impact on the physicians' decisions.

Nowadays, more and more patients are ending their lives in an ICU and about half of time after a decision to withholding or withdrawing of life-sustaining treatments (24). The futility of maintaining these life-sustaining treatments is the subject of many questions and debates and the decisions of withholding or withdrawing therapies have a great impact on the mortality of patients (25). In our study, we found a huge inter-individual variability between the physicians in the level of management of patients in ICU about the decisions to admit or withhold and withdraw therapies, which is consistent with the last literature review (6). We found a really low impact of the structural variables, not exactly in accordance with the study of Azoulay and others (26). In the same way, we did not find a great impact of psychological feature and of the experience of the physicians. Maybe because we had only asked the memory or not of a traumatic experience of end-of-life situation, and we could have explored more precisely the psychological state of each physician.

We were expecting find some help in the AD of patients to diminish this variability among physicians and respect the patients' autonomy. Several studies found an influence of the AD on the physicians' decisions (3,12), even if the physicians do not always follow the patients' wills (27). In

our study, the AD had a great impact on the physicians' decisions for all the questions and all the patients. But the variability between the physicians themselves was increased. We assume that this variability reflects a difference in the interpretation of these AD among physicians themselves. Indeed, in the French model, the AD are in the form of a free text in the context of open-ended questions. The AD with closed-ended questions might result in fewer differences in the interpretation of the AD when deciding whether to admit or not a patient or to withhold/withdraw or not a life-sustaining treatment.

We did not find a difference between the round 2 and the round 3, except for two questions. This suggests that the physicians do not have a critical look according to the way of how the AD have been written. The patients were real patients, the AD were real AD made after clear information and in accordance with the recommended form and with the HAS form. The AD corresponded with the AD found in real life, i.e. few formal refusals of life-sustaining treatments but witnesses of patients' lives and aspirations. We can conclude that the physicians take into account the AD no matter how they were made. Maybe it is a danger of the autonomous model. When the patient is competent, we usually take his opinion into account once he has received clear, faithful, complete and appropriate information described as the relational autonomy by Walter and others (28). It is the physician's obligation to provide this information and the prerequisite for the patient's decision-making power even we know that the information provided can differ between the physicians themselves (29). In the AD, there are only the patient's decisions and no information about the understanding of the patient and the information received by the patient. When the patients are unable to make decisions for themselves, the physicians of our study applied the AD without the knowledge of how these AD had been written. We can assume that the physicians presumed that information had been given in the good way (clear, faithful, full and appropriate

information). We believe that it is essential to know how the AD have been written before deciding to take these AD into account. It could be much more important for AD in the style of closed-ended questions, less prone to interpretation. There may still be room for the concept of protective paternalism before we reach an ideal of care where all patients would be properly informed.

Our study had important limitations. First, we studied only 8 patients, 7 male and only 1 female, 3 dialysis patients and more than half of the patients (5/8) were over 75 years of age. Intensive care hospitalisation is not always beneficial for elderly patients (30) and is therefore more controversial. Second, simulation cases were used so they were different from the reality lived by the physicians even if the patients were real patients and even we tried to get as close to the real life as possible by creating the scenarios in a multidisciplinary team. Third, there was no information on family, surrogates, team discussions or staff opinion, but we were not able to assess all the factors together and to identify the impact of the AD and physicians on the decisions, so the opinions of surrogates or of the team were not noticed. Finally, the experiences lived between the three rounds may influence the responses. But only few weeks separated the different rounds.

5. CONCLUSION

The variability of each physician (intra-individual variability) and the variability between physicians themselves (inter-individual variability) are important for the ICU admissions or for the decisions of withholding or withdrawing therapies. A major finding of our study is that AD written in accordance with the French model have a significant impact in ICU physician decision-making for this kind of decision, and interestingly increase the inter-individual variability. The knowledge of how these AD have been written has a very low impact. We should be careful with this autonomous model and be aware of its weaknesses. We probably need to invent a new decision-making model, a more consensual one between physicians themselves and in accordance with the patients' wishes.



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7. TABLES

Table 1: Physician characteristics.

Physician characteristics	(N=177)
Age, median, [25-75 th]	38[33-46]
Sex, No, (%)	
Male	113(63,8)
Female	64(36,2)
Type of degree, No, (%)	
Anaesthetics and intensive care	104(59,1)
Medical discipline and intensive care	72(40,9)
Hospital, No, (%)	
Academic hospital	134(75,7)
General hospital	37(20,9)
Cancer centre	6(3,4)
Department's activity	
Surgical	20(11,5)
Medical	76(43,7)
Mixed	78(44,8)
Number of beds in ICU, median, [25-75 th]	15(10-18)
Number of physicians in ICU, median, [25-75 th]	7(5-10)
Length of practice, No, (%)	
<5 years	64(36,2)
5-15 years	75(42,4)
>15 years	38(21,5)
Religion	
Catholic	70(41,4)
Atheist	87(51,5)
Other	12(7,1)
Protocol for withholding or withdrawing therapies, No, (%)	
Yes	118(68,6)
No	54(31,4)
Number of withholding or withdrawing therapies decisions, No, (%)	
<12/years	18(11)
1/month-1/week	61(37,2)
>1/week	85(51,8)
Interest in ethics	
Lack of interest	2(1,1)
Moderate interest	43(24,3)
Great interest	132(74,6)
Evaluation of burnout, median, [25-75 th]	30 [11-58]
Traumatic experience memory of an end-of-life situation, No, (%)	
Yes	82(46,3)
No	95(53,7)

Table 2: Percentage of answers (A) in each Round: Round 1 (R1), Round 2 (R2) and Round 3 (R3) for each Patient (P) and each Question (Q).

P	Q	A	R1	R2	R3	P	Q	A	R1	R2	R3	P	Q	A	R1	R2	R3	P	Q	A	R1	R2	R3
P1	S1Q1	a	15,9%	30,5%	26,8%	P3	S1Q1	a	1,2%	13,4%	8,5%	P5	S1Q1	a	7,3%	6,1%	12,2%	P7	S1Q1	a	0,0%	6,1%	4,9%
P1	S1Q1	b	22,0%	35,4%	42,7%	P3	S1Q1	b	31,7%	31,7%	37,8%	P5	S1Q1	b	30,5%	43,9%	36,6%	P7	S1Q1	b	11,0%	9,8%	8,5%
P1	S1Q1	c	62,2%	34,1%	30,5%	P3	S1Q1	c	67,1%	54,9%	53,7%	P5	S1Q1	c	62,2%	50,0%	51,2%	P7	S1Q1	c	89,0%	84,1%	86,6%
P1	S1Q2	a	25,6%	35,4%	40,2%	P3	S1Q2	a	14,6%	20,7%	12,2%	P5	S1Q2	a	15,9%	12,2%	19,5%	P7	S1Q2	a	2,4%	9,8%	4,9%
P1	S1Q2	b	26,8%	32,9%	35,4%	P3	S1Q2	b	28,0%	26,8%	36,6%	P5	S1Q2	b	29,3%	41,5%	34,1%	P7	S1Q2	b	13,4%	9,8%	9,8%
P1	S1Q2	c	47,6%	31,7%	24,4%	P3	S1Q2	c	57,3%	52,4%	51,2%	P5	S1Q2	c	54,9%	46,3%	46,3%	P7	S1Q2	c	84,1%	80,5%	85,4%
P1	S1Q3	a	35,4%	49,5%	49,6%	P3	S1Q3	a	34,1%	45,1%	42,7%	P5	S1Q3	a	35,4%	54,9%	59,8%	P7	S1Q3	a	3,7%	13,4%	15,9%
P1	S1Q3	b	64,6%	50,5%	50,4%	P3	S1Q3	b	65,9%	54,9%	57,3%	P5	S1Q3	b	64,6%	45,1%	40,2%	P7	S1Q3	b	96,3%	86,6%	84,1%
P1	S1Q4	a	17,1%	43,9%	51,2%	P3	S1Q4	a	12,2%	29,3%	20,7%	P5	S1Q4	a	17,1%	24,4%	32,9%	P7	S1Q4	a	2,4%	13,4%	9,8%
P1	S1Q4	b	37,8%	28,0%	30,5%	P3	S1Q4	b	30,5%	26,8%	31,7%	P5	S1Q4	b	26,8%	34,1%	26,8%	P7	S1Q4	b	17,1%	15,9%	20,7%
P1	S1Q4	c	45,1%	28,0%	18,3%	P3	S1Q4	c	57,3%	43,9%	47,6%	P5	S1Q4	c	56,1%	41,5%	40,2%	P7	S1Q4	c	80,5%	70,7%	69,5%
P1	S1Q5	a	80,5%	92,7%	97,6%	P3	S1Q5	a	74,4%	90,2%	82,9%	P5	S1Q5	a	70,7%	85,4%	89,0%	P7	S1Q5	a	24,4%	51,2%	50,0%
P1	S1Q5	b	19,5%	7,3%	2,4%	P3	S1Q5	b	25,6%	9,8%	17,1%	P5	S1Q5	b	29,3%	14,6%	11,0%	P7	S1Q5	b	75,6%	48,8%	50,0%
P1	S1Q6	a	96,3%	93,9%	98,8%	P3	S1Q6	a	91,5%	92,7%	93,9%	P5	S1Q6	a	91,5%	92,7%	97,6%	P7	S1Q6	a	61,0%	87,8%	81,7%
P1	S1Q6	b	3,7%	6,1%	1,2%	P3	S1Q6	b	8,5%	7,3%	6,1%	P5	S1Q6	b	8,5%	7,3%	2,4%	P7	S1Q6	b	39,0%	12,2%	18,3%
P1	S2Q1	a	9,8%	23,2%	17,1%	P3	S2Q1	a	3,7%	11,0%	11,0%	P5	S2Q1	a	4,9%	6,1%	9,8%	P7	S2Q1	a	0,0%	6,1%	6,1%
P1	S2Q1	b	22,0%	35,4%	39,0%	P3	S2Q1	b	20,7%	36,6%	30,5%	P5	S2Q1	b	30,5%	32,9%	34,1%	P7	S2Q1	b	11,0%	9,8%	12,2%
P1	S2Q1	c	68,3%	41,5%	43,9%	P3	S2Q1	c	75,6%	52,4%	58,5%	P5	S2Q1	c	64,6%	61,0%	56,1%	P7	S2Q1	c	89,0%	84,1%	81,7%
P1	S2Q2	a	45,1%	70,7%	74,4%	P3	S2Q2	a	25,6%	53,7%	41,5%	P5	S2Q2	a	32,9%	47,6%	50,0%	P7	S2Q2	a	9,8%	15,9%	15,9%
P1	S2Q2	b	54,9%	29,3%	25,6%	P3	S2Q2	b	74,4%	46,3%	58,5%	P5	S2Q2	b	67,1%	52,4%	50,0%	P7	S2Q2	b	90,2%	84,1%	84,1%
P1	S2Q3	a	89,0%	97,6%	98,8%	P3	S2Q3	a	85,4%	95,1%	97,6%	P5	S2Q3	a	80,5%	96,3%	97,6%	P7	S2Q3	a	59,8%	80,5%	85,4%
P1	S2Q3	b	11,0%	2,4%	1,2%	P3	S2Q3	b	14,6%	4,9%	2,4%	P5	S2Q3	b	19,5%	3,7%	2,4%	P7	S2Q3	b	40,2%	19,5%	14,6%
P1	S2Q4	a	85,4%	92,7%	93,9%	P3	S2Q4	a	86,6%	91,5%	95,1%	P5	S2Q4	a	81,7%	96,3%	93,9%	P7	S2Q4	a	78,0%	89,0%	87,8%
P1	S2Q4	b	14,6%	7,3%	6,1%	P3	S2Q4	b	13,4%	8,5%	4,9%	P5	S2Q4	b	18,3%	3,7%	6,1%	P7	S2Q4	b	22,0%	11,0%	12,2%
P2	S1Q1	a	3,7%	26,8%	17,1%	P4	S1Q1	a	1,2%	2,4%	3,7%	P6	S1Q1	a	58,5%	54,9%	42,7%	P8	S1Q1	a	19,5%	40,2%	34,1%
P2	S1Q1	b	14,6%	24,4%	26,8%	P4	S1Q1	b	8,5%	13,4%	13,4%	P6	S1Q1	b	30,5%	28,0%	35,4%	P8	S1Q1	b	41,5%	29,3%	34,1%
P2	S1Q1	c	81,7%	48,8%	56,1%	P4	S1Q1	c	90,2%	84,1%	82,9%	P6	S1Q1	c	11,0%	17,1%	22,0%	P8	S1Q1	c	39,0%	30,5%	31,7%
P2	S1Q2	a	11,0%	29,3%	23,2%	P4	S1Q2	a	6,1%	6,1%	7,3%	P6	S1Q2	a	68,3%	59,8%	52,4%	P8	S1Q2	a	34,1%	50,0%	41,5%
P2	S1Q2	b	15,9%	24,4%	25,6%	P4	S1Q2	b	8,5%	13,4%	12,2%	P6	S1Q2	b	25,6%	24,4%	26,8%	P8	S1Q2	b	34,1%	24,4%	32,9%
P2	S1Q2	c	73,2%	46,3%	51,2%	P4	S1Q2	c	85,4%	80,5%	80,5%	P6	S1Q2	c	6,1%	15,9%	20,7%	P8	S1Q2	c	31,7%	25,6%	25,6%
P2	S1Q3	a	17,1%	48,8%	45,1%	P4	S1Q3	a	3,7%	17,1%	12,2%	P6	S1Q3	a	91,5%	84,1%	82,9%	P8	S1Q3	a	62,2%	73,2%	69,5%
P2	S1Q3	b	82,9%	51,2%	54,9%	P4	S1Q3	b	96,3%	82,9%	87,8%	P6	S1Q3	b	8,5%	15,9%	17,1%	P8	S1Q3	b	37,8%	26,8%	30,5%
P2	S1Q4	a	8,5%	36,6%	28,0%	P4	S1Q4	a	1,2%	11,0%	7,3%	P6	S1Q4	a	72,0%	72,0%	61,0%	P8	S1Q4	a	39,0%	56,1%	51,2%
P2	S1Q4	b	32,9%	34,1%	31,7%	P4	S1Q4	b	12,2%	23,2%	22,0%	P6	S1Q4	b	20,7%	14,6%	23,2%	P8	S1Q4	b	35,4%	26,8%	30,5%
P2	S1Q4	c	58,5%	29,3%	40,2%	P4	S1Q4	c	86,6%	65,9%	70,7%	P6	S1Q4	c	7,3%	13,4%	15,9%	P8	S1Q4	c	25,6%	17,1%	18,3%
P2	S1Q5	a	64,6%	92,7%	89,0%	P4	S1Q5	a	29,3%	52,4%	58,5%	P6	S1Q5	a	98,8%	95,1%	96,3%	P8	S1Q5	a	95,1%	90,2%	93,9%
P2	S1Q5	b	35,4%	7,3%	11,0%	P4	S1Q5	b	70,7%	47,6%	41,5%	P6	S1Q5	b	1,2%	4,9%	3,7%	P8	S1Q5	b	4,9%	9,8%	6,1%
P2	S1Q6	a	95,1%	96,3%	96,3%	P4	S1Q6	a	59,8%	78,0%	81,7%	P6	S1Q6	a	95,1%	96,3%	96,3%	P8	S1Q6	a	95,1%	97,6%	96,3%
P2	S1Q6	b	4,9%	3,7%	3,7%	P4	S1Q6	b	40,2%	22,0%	18,3%	P6	S1Q6	b	4,9%	3,7%	3,7%	P8	S1Q6	b	4,9%	2,4%	3,7%
P2	S2Q1	a	4,9%	18,3%	14,6%	P4	S2Q1	a	1,2%	1,2%	2,4%	P6	S2Q1	a	45,1%	48,8%	36,6%	P8	S2Q1	a	14,6%	31,7%	26,8%
P2	S2Q1	b	12,2%	28,0%	30,5%	P4	S2Q1	b	11,0%	17,1%	18,3%	P6	S2Q1	b	31,7%	25,6%	36,6%	P8	S2Q1	b	37,8%	31,7%	39,0%
P2	S2Q1	c	82,9%	53,7%	54,9%	P4	S2Q1	c	87,8%	81,7%	79,3%	P6	S2Q1	c	23,2%	25,6%	26,8%	P8	S2Q1	c	47,6%	36,6%	34,1%
P2	S2Q2	a	18,3%	57,3%	43,9%	P4	S2Q2	a	9,8%	22,0%	14,6%	P6	S2Q2	a	84,1%	79,3%	70,7%	P8	S2Q2	a	58,5%	68,3%	68,3%
P2	S2Q2	b	81,7%	42,7%	56,1%	P4	S2Q2	b	90,2%	78,0%	85,4%	P6	S2Q2	b	15,9%	20,7%	29,3%	P8	S2Q2	b	41,5%	31,7%	31,7%
P2	S2Q3	a	89,0%	97,6%	98,8%	P4	S2Q3	a	63,0%	79,3%	85,4%	P6	S2Q3	a	95,1%	93,9%	97,6%	P8	S2Q3	a	92,7%	97,6%	98,8%
P2	S2Q3	b	11,0%	2,4%	1,2%	P4	S2Q3	b	37,0%	20,7%	14,6%	P6	S2Q3	b	4,9%	6,1%	2,4%	P8	S2Q3	b	7,3%	2,4%	1,2%
P2	S2Q4	a	84,1%	91,5%	92,7%	P4	S2Q4	a	80,5%	85,4%	86,6%	P6	S2Q4	a	87,8%	92,7%	92,7%	P8	S2Q4	a	90,2%	97,6%	92,7%
P2	S2Q4	b	15,9%	8,5%	7,3%	P4	S2Q4	b	19,5%	14,6%	13,4%	P6	S2Q4	b	12,2%	7,3%	7,3%	P8	S2Q4	b	9,8%	2,4%	7,3%

Table 3: Intra-individual variability between each Round: between R1 and R2 (R1-R2) ; between R2 and R3 (R2-R3) and between R1 and R3 (R1-R3).

P: Patient; Q: Question; %A: percentage of agreement; K: Kappa coefficient

Note: A low kappa coefficient with a high percentage of agreement means that the physicians responded overwhelmingly the same response and that the physicians who responded differently significantly changed their response between the 2 rounds.

		R1-R2		R2-R3		R1-R3				R1-R2		R2-R3		R1-R3	
P	Q	%A	K	%A	K	%A	K	P	Q	%A	K	%A	K	%A	K
P1	S1Q1	63,4	0,45	61,0	0,41	53,7	0,31	P5	S1Q1	67,1	0,40	63,4	0,36	62,2	0,33
P1	S1Q2	64,6	0,47	62,2	0,43	58,5	0,40	P5	S1Q2	61,0	0,36	59,8	0,35	63,4	0,40
P1	S1Q3	63,4	0,33	76,8	0,46	57,3	0,24	P5	S1Q3	65,9	0,34	73,2	0,45	63,4	0,31
P1	S1Q4	51,2	0,30	63,4	0,43	48,8	0,28	P5	S1Q4	52,4	0,25	53,7	0,30	50,0	0,23
P1	S1Q5	83,0	0,29	92,7	0,22	78,1	-0,05	P5	S1Q5	73,2	0,24	84,2	0,29	74,4	0,24
P1	S1Q6	92,7	0,21	92,7	-0,02	95,1	-0,02	P5	S1Q6	86,6	0,08	90,2	-0,04	89,0	-0,04
P1	S2Q1	56,1	0,29	61,0	0,39	64,6	0,41	P5	S2Q1	65,9	0,32	68,3	0,41	64,6	0,33
P1	S2Q2	62,2	0,27	74,4	0,36	68,3	0,39	P5	S2Q2	68,3	0,36	75,6	0,51	58,5	0,17
P1	S2Q3	89,0	0,15	96,3	-0,02	87,8	-0,02	P5	S2Q3	81,7	0,16	96,3	0,38	80,5	0,07
P1	S2Q4	85,4	0,26	89,0	0,12	84,2	0,16	P5	S2Q4	80,5	0,05	95,1	0,48	80,5	0,12
P2	S1Q1	53,7	0,17	62,2	0,39	63,4	0,26	P6	S1Q1	72,0	0,51	72,0	0,55	61,0	0,37
P2	S1Q2	57,3	0,28	63,4	0,42	57,3	0,24	P6	S1Q2	70,7	0,44	73,2	0,54	58,5	0,26
P2	S1Q3	61,0	0,21	69,5	0,39	62,2	0,19	P6	S1Q3	87,8	0,44	84,2	0,42	86,6	0,41
P2	S1Q4	47,6	0,23	65,9	0,49	59,8	0,37	P6	S1Q4	80,5	0,56	64,6	0,30	65,9	0,32
P2	S1Q5	69,5	0,19	91,5	0,49	68,3	0,18	P6	S1Q5	93,9	-0,02	96,3	0,55	95,1	-0,02
P2	S1Q6	91,5	-0,04	92,7	-0,04	91,5	-0,04	P6	S1Q6	93,9	0,25	92,7	-0,04	93,9	0,25
P2	S2Q1	59,8	0,21	56,1	0,26	62,2	0,24	P6	S2Q1	65,9	0,47	68,3	0,52	62,2	0,42
P2	S2Q2	53,7	0,15	64,6	0,31	59,8	0,13	P6	S2Q2	87,8	0,59	86,6	0,65	79,3	0,42
P2	S2Q3	89,0	0,15	96,3	-0,02	87,8	-0,02	P6	S2Q3	91,5	0,18	96,3	0,56	92,7	-0,03
P2	S2Q4	78,1	-0,01	86,6	0,08	84,2	0,24	P6	S2Q4	85,4	0,17	90,2	0,28	85,4	0,17
P3	S1Q1	64,6	0,33	61,0	0,32	65,9	0,34	P7	S1Q1	82,9	0,29	76,8	0,11	82,9	0,22
P3	S1Q2	61,0	0,34	62,2	0,38	65,9	0,42	P7	S1Q2	80,5	0,37	75,6	0,18	78,1	0,18
P3	S1Q3	76,8	0,52	78,1	0,55	72,0	0,41	P7	S1Q3	85,4	0,09	80,5	0,22	80,5	-0,06
P3	S1Q4	63,4	0,42	69,5	0,53	65,9	0,44	P7	S1Q4	73,2	0,33	73,2	0,42	70,7	0,27
P3	S1Q5	81,7	0,40	90,2	0,58	79,3	0,39	P7	S1Q5	63,4	0,28	64,6	0,29	69,5	0,39
P3	S1Q6	89,0	0,25	93,9	0,51	90,2	0,28	P7	S1Q6	65,9	0,18	86,6	0,48	69,5	0,29
P3	S2Q1	64,3	0,32	69,5	0,46	67,1	0,33	P7	S2Q1	84,2	0,34	79,3	0,30	79,3	0,20
P3	S2Q2	67,1	0,36	70,7	0,42	67,1	0,28	P7	S2Q2	84,2	0,30	78,1	0,18	79,3	0,08
P3	S2Q3	90,2	0,46	95,1	0,31	85,4	0,11	P7	S2Q3	72,0	0,36	82,9	0,40	64,6	0,18
P3	S2Q4	82,9	0,13	91,5	0,32	86,6	0,21	P7	S2Q4	79,3	0,26	86,6	0,35	78,1	0,24
P4	S1Q1	81,7	0,20	79,3	0,27	80,5	0,19	P8	S1Q1	53,7	0,32	62,2	0,43	57,3	0,36
P4	S1Q2	79,3	0,30	78,1	0,34	75,6	0,18	P8	S1Q2	51,2	0,27	62,2	0,42	54,9	0,32
P4	S1Q3	79,3	-0,06	78,1	0,13	86,6	0,10	P8	S1Q3	72,0	0,37	76,8	0,43	68,3	0,30
P4	S1Q4	64,6	0,12	73,2	0,44	70,7	0,19	P8	S1Q4	54,9	0,30	69,5	0,49	53,7	0,28
P4	S1Q5	62,2	0,26	72,0	0,43	58,5	0,23	P8	S1Q5	90,2	0,29	89,0	0,25	91,5	0,18
P4	S1Q6	67,1	0,26	81,7	0,43	70,7	0,33	P8	S1Q6	92,7	-0,03	93,9	-0,03	91,5	-0,04
P4	S2Q1	81,7	0,31	75,6	0,24	76,8	0,18	P8	S2Q1	53,7	0,30	63,4	0,45	57,3	0,34
P4	S2Q2	80,5	0,29	75,6	0,19	85,4	0,32	P8	S2Q2	73,2	0,43	78,1	0,49	78,1	0,53
P4	S2Q3	72,0	0,26	81,7	0,38	78,1	0,38	P8	S2Q3	92,7	0,22	96,3	-0,02	91,5	-0,02
P4	S2Q4	78,1	0,23	76,8	0,04	76,8	0,16	P8	S2Q4	90,2	0,17	92,7	0,22	85,4	0,06

Table 6: Impact of AD on the intra-individual variability for each question while taking into account the different sources of variability (ICU physician and patient).

Positives values mean change the answers from a to b, b to c or a to c. Negatives values mean change of the answers from b to a, c to b or c to a. [cf Appendix; Simulations]

	Impact of AD on R2			Impact of AD on R3			R2-R3
	RC	95% CI	P value	RC	95% CI	P value	P value
S1Q1	0,94	0,73_1,15	<0,001	0,72	0,49_0,95	<0,001	0,059
S1Q2	0,69	0,48_0,89	<0,001	0,48	0,26_0,71	<0,001	0,078
S1Q3	-1,33	-1,6-1,06	<0,001	-1,23	-1,52-0,94	<0,001	0,47
S1Q4	1,16	0,95-1,36	<0,001	0,99	0,77_1,21	<0,001	0,14
S1Q5	-1,34	-1,63-1,05	<0,001	-1,47	-1,79-1,14	<0,001	0,45
S1Q6	0,93	0,59-1,28	<0,001	0,93	0,55-1,32	<0,001	0,999
S2Q1	0,98	0,77-1,20	<0,001	0,82	0,58-1,05	<0,001	0,15
S2Q2	-1,28	-1,53-1,02	<0,001	-0,92	-1,19-0,64	<0,001	0,0091
S2Q3	-1,37	-1,73-1,01	<0,001	-2,00	-2,47-1,54	<0,001	0,0079
S2Q4	0,79	0,49-1,09	<0,001	0,79	0,44-1,12	<0,001	0,98

8. FIGURES

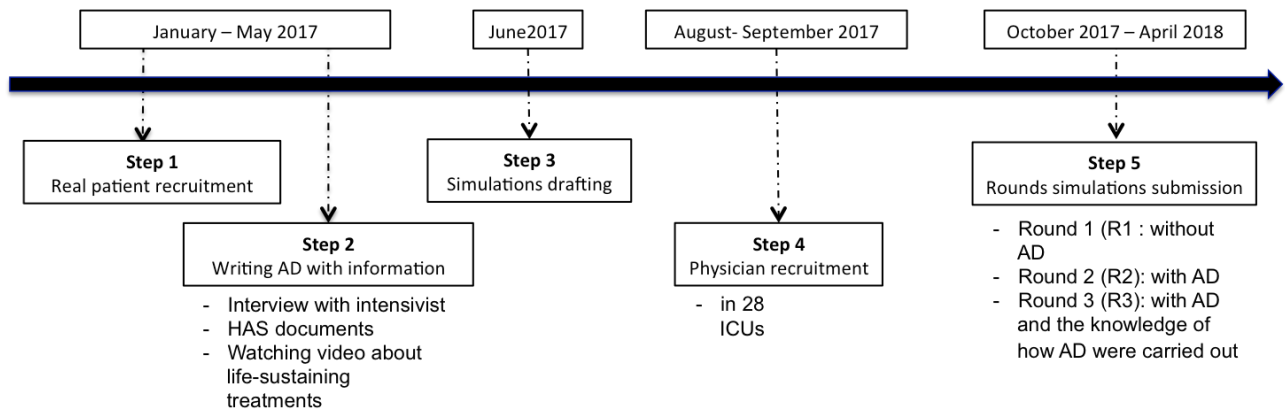
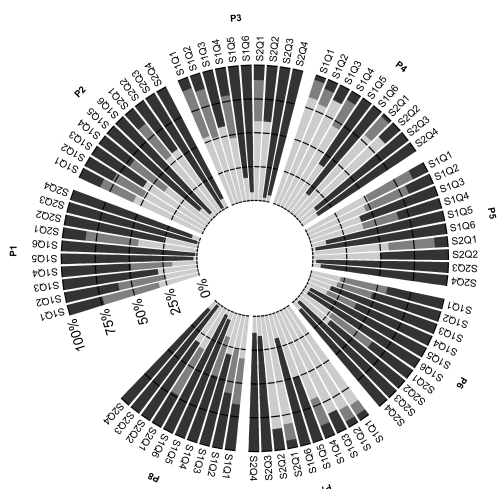
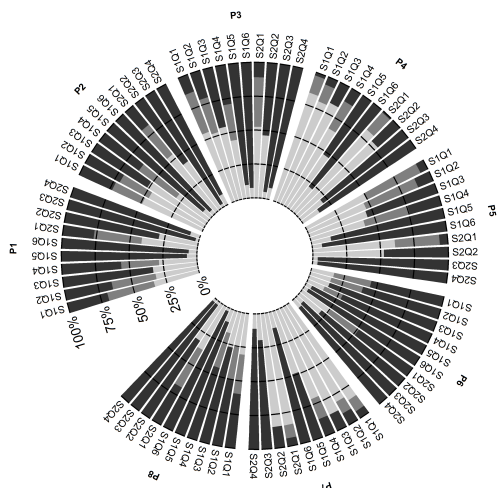


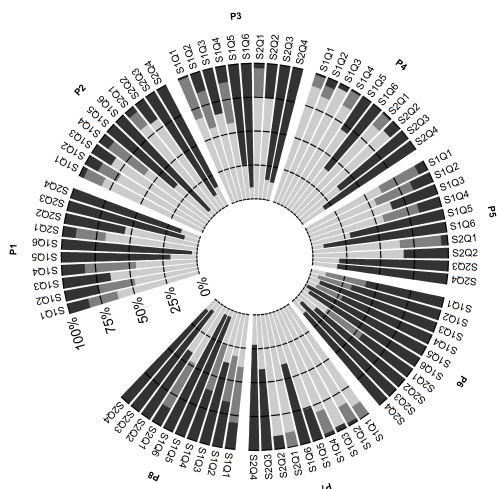
Figure 1: Study procedures



Round 1 : without AD



Round 2: with AD



Round 3: with AD*

Figure 2: Physician responses by percentage for Round 1, Round 2 and Round 3 for the 8 patients (P1 to P8) for the 2 simulations (S1 & S2) for all questions (Q1 to Q4 or Q6 depending on the simulation).

*: and the knowledge of how AD they have been written.

S1Q1; S1Q2; S2Q1: The black colour corresponds to no admission in ICU; the dark grey colour corresponds to admission in ICU for intensive care; the light grey colour corresponds to admission in ICU for resuscitation.
 Other questions: The black colour corresponds to withholding or withdrawing therapy; the dark grey colour corresponds to life-sustaining treatment with limits; the light grey colour corresponds to life-sustaining treatment without limit.

9. LIST OF APPENDICES

Appendix 1: Simulations

Appendix 2: Serments d'Hippocrate

APPENDIX 1: Simulations

SIMULATION 1

The Emergency Mobile Medical Team brings the patient to the emergency room. He or she suffers from an acute infectious respiratory failure probably bacterial. The first respiratory symptoms appeared 48 hours earlier. On admission to the emergency room: T°C 38.8°C; HR 120/min; MAP 60mmHg; RR 40/min; spO₂ at 75%; signs of breathing difficulty; the patient is confused. Chest X-ray reveals a pulmonary consolidation on the right base. Extra oxygen delivery in a non-rebreather mask is not very successful.

- 1) The emergency physician calls you to ask you to admit this patient in an ICU. Would you admit this patient to the ICU?
 - a. Yes in the ICU stage 1 (all available life-sustaining therapies)
 - b. Yes in the ICU stage 2 (available life-sustaining therapy: non-invasive mechanical ventilation)
 - c. No
- 2) If there were only one bed remaining in the ICU, would you have admitted this patient?
 - a. Yes in the ICU stage 1
 - b. Yes in the ICU stage 2
 - c. No
- 3) The patient is admitted to your department. If you would manage his or her after non-invasive ventilation failure, would you intubate this patient?
 - a. No
 - b. Yes
- 4) At H6, hemodynamic instability caused by a septic shock appears. Would you start vasopressor agent?
 - a. Yes
 - b. Yes with a maximum threshold that you set (example 0.5; 1; 1.2 microg/kg/min)
 - c. No

5) Breathing condition has gradually improved. He or she could have been extubated after 8 days of mechanical ventilation. At D10 in the ward, the respiratory status deteriorates again; he -she- presents a new pneumonia with a severe acute respiratory distress syndrome (ARDS). Would you intubate the patient again?

a. No

b. Yes

6) The Patient was intubated again, then neuromuscular-blocking drug was started; he or she had 3 sessions of PR (Prone Position) during 16 hours. At D12 in the department, the pulmonary function does not improve despite these therapies. Would you consider withholding or withdrawing life-sustaining treatment now?

a. No

b. Yes

i. If yes, what measures would you consider (precise for each technique of life support if you withhold or withdraw the therapy)?

SIMULATION 2

The patient is admitted to the emergency room with an intestinal obstruction associated with peritonitis. A broad-spectrum antibiotic and fluid resuscitation are initiated early. The abdominal CT scan reveals an intestinal obstruction because of an intra-abdominal adhesion. A surgery is performed within the 6 first hours after the admission. After being monitored in the Post Anesthesia Care Unit (PACU), he or she is transferred to the surgical department.

At Day 5, he or she has hypotension despite well-conducted fluid resuscitation, associated with impaired consciousness.

1) Would you admit this patient to the ICU?

- a. Yes in the ICU stage 1
- b. Yes in the ICU stage 2
- c. No

2) After 48 hours of optimal care in ICU, the hemodynamic status is stable with norepinephrine 0.3microg/kg/min but the respiratory status deteriorates because of heart failure. Would you intubate this patient?

- a. No
- b. Yes

3) The respiratory condition and the cardiac function of the patient gradually improve by means of mechanical ventilation, positive inotropic agent and renal replacement therapy (RRT). Positive inotropic agent can be weaned at D7. At D18 in the department, after 2 extubation failures on pulmonary oedema and malnutrition, the patient is still ventilator dependant. Would you consider a tracheostomy?

- a. No
- b. Yes

4) A percutaneous tracheotomy was performed. At D30 in the ICU, the patient is still ventilator dependant (assisted mode) on the tracheostomy cannula and RRT dependant. Would you consider withdrawing therapy for one or both of these life-sustaining treatments?

- a. No
- b. Yes

SERMENT D'HIPPOCRATE

En présence des Maîtres de cette FACULTE et de mes chers CONDISCIPLES, je promets et je jure d'être fidèle aux lois de l'Honneur et de la Probité dans l'exercice de la Médecine.

Je donnerai mes soins gratuits à l'indigent et je n'exigerai jamais un salaire au-dessus de mon travail. Admise dans l'intérieur des maisons, mes yeux ne verront pas ce qui s'y passe, ma langue taira les secrets qui me seront confiés et mon état ne servira pas à corrompre les mœurs ni à favoriser le crime.

Respectueuse et reconnaissante envers mes MAÎTRES, je rendrai à leurs enfants l'instruction que j'ai reçue de leurs pères.

Que les HOMMES m'accordent leur estime si je suis fidèle à mes promesses. Que je sois couverte d'OPPROBRE et méprisée de mes confrères si j'y manque.

(Conseil national de l'ordre des médecins)

SERMENT D'HIPPOCRATE

Au moment d'être admise à exercer la médecine, je promets et je jure d'être fidèle aux lois de l'honneur et de la probité.

Mon premier souci sera de rétablir, de préserver ou de promouvoir la santé dans tous ses éléments, physiques et mentaux, individuels et sociaux.

Je respecterai toutes les personnes, leur autonomie et leur volonté, sans aucune discrimination selon leur état ou leurs convictions. J'interviendrai pour les protéger si elles sont affaiblies, vulnérables ou menacées dans leur intégrité ou leur dignité. Même sous la contrainte, je ne ferai pas usage de mes connaissances contre les lois de l'humanité.

J'informerai les patients des décisions envisagées, de leurs raisons et de leurs conséquences.

Je ne tromperai jamais leur confiance et n'exploiterai pas le pouvoir hérité des circonstances pour forcer les consciences.

Je donnerai mes soins à l'indigent et à quiconque me les demandera. Je ne me laisserai pas influencer par la soif du gain ou la recherche de la gloire.

Admise dans l'intimité des personnes, je tairai les secrets qui me seront confiés. Reçue à l'intérieur des maisons, je respecterai les secrets des foyers et ma conduite ne servira pas à corrompre les mœurs.

Je ferai tout pour soulager les souffrances. Je ne prolongerai pas abusivement les agonies. Je ne provoquerai jamais la mort délibérément.

Je préserverai l'indépendance nécessaire à l'accomplissement de ma mission. Je n'entreprendrai rien qui dépasse mes compétences. Je les entretiendrai et les perfectionnerai pour assurer au mieux les services qui me seront demandés.

J'apporterai mon aide à mes confrères ainsi qu'à leurs familles dans l'adversité.

Que les hommes et mes confrères m'accordent leur estime si je suis fidèle à mes promesses ; que je sois déshonorée et méprisée si j'y manque.

SMIRDEC Margot, Jeanne, Léa :

**Impact des directives anticipées sur les facteurs influençant la prise de décision en réanimation ;
Impact of Advance Directives on factors involved in the decision-making in ICU ; Facing Decision –
ICU; preliminary results.**

Th Medecine, Faculté de Clermont-Ferrand, Année 2018

ABSTRACT:

Introduction: Physicians do not know how to follow the patients' wishes when they are unable to express themselves. We assessed the impact of Advances Directives (AD) and how they have been written on the physician's decisions.

Methods: A multicentre, prospective, interventional, simulation study was carried out. Height patients were recruited and wrote AD after receiving clear and complete information by video and interview with one ICU physician. Two simulation scenarios including 10 questions about ICU admission and situations of withholding/withdrawing therapies using the patients' characteristics were submitted to ICU physicians from 28 French ICU, in three rounds (R): simulation without knowledge of the patient's AD (R1), with these AD (R2) and with these AD and the knowledge of how they were carried out (R3).

Results: The preliminary results were performed on data of 82 physicians. The variability between physicians themselves was high. Among the 80 questions of R1, there were 40, 23 and 17 questions with an agreement > 80%, 80-60% and <60% respectively. The AD significantly decreased the number of questions with an agreement > 80%, and increased the number of questions with an agreement <60% (p<0.001). There was no difference between the rounds 2 and 3 (p=0.6). Few physicians' characteristics were associated with the inter-individual variability. The intra-individual variability between R1 and R2 was very high and the AD were significantly associated with this variability after adjustment on characteristics of the physicians and the patients. It is relevant to notice that the knowledge of how AD were carried out has a very low impact on the physicians' decisions.

Conclusion: The AD have a major impact on the physicians' decisions for admission, withholding and withdrawing therapies decisions and increase the inter-individual variability but not the knowledge of how these AD have been written. It might be a limit of the autonomous model.

MOTS-CLÉS: Intensive care unit; Triage and Therapy; Advance Directives (AD); Simulation model of real situations; physicians' decision.

JURY :

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Membres :	Monsieur Jean-Michel CONSTANTIN	Professeur
	Monsieur Emmanuel FUTIER	Professeur
	<u>Monsieur Alexandre LAUTRETTE</u>	Professeur
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	Madame Anne-Marie REGNOUX	Avocate

DATE DE LA SOUTENANCE : Vendredi 13 avril 2018

ADRESSE DE L'AUTEUR: