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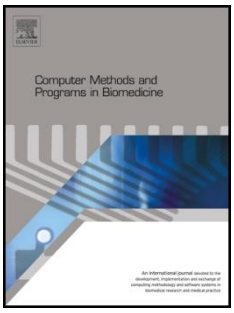

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Decision support in addiction: the development of an e-health tool to assess and prevent risk of fatal overdose. The ORION Project

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Summary Points:

- The overdose risk information (ORION) tool has been designed with the aim of being easy-to use and informative to both patients and clinicians in various clinical settings.
- The ORION tool went through risk estimation processes using Delphi methods
- The ORION tool utilised state of the art design systems to help engage the user
- A pilot implementation of the ORION tool was conducted in the four countries to assess the feasibility of implementing the tool across various clinical settings.

Abstract

Background and Objective: The application of e-health technology to the field of substance use disorders is at a relatively early stage, and methodological quality is still variable. Few

have explored the extent of utilization of communication technology in exploring risk perception by patients enrolled in substance abuse services.

The Overdose RIsk InfOrmatioN (ORION) project is a European Commission funded programme, aimed to develop and pilot an e-health psycho-educational tool to provide information to drug using individuals about the risks of suffering a drug overdose.

Methods: In this article we report on phase 1 (risk estimation), phase 2 (design), and phase 3 (feasibility) of the ORION project.

Results: The development of ORION e-health tool underlined the importance of an evidence-based intervention aimed in obtaining reliable evaluation of risk. The ORION tool supported a decision making process aimed at influencing the substance users' self-efficacy and the degree to which the substance users' understand risk factors. Therefore its innovative power consisted in translating risks combination into a clear estimation for the user who will then appear more likely to be interested in his/her risk perception.

Conclusion: Exploratory field testing and validation confirmed the next stage of evaluation, namely, collection of routine patient samples in study clinics. The associations between risk perception of overdose, engagement with the ORION tool and willingness to alter overdose risk factors, in a clinical setting across various EU member states will further confirm the ORION tool's generalisability and effectiveness.

Keywords: Risk, Opioids, Decision making

Introduction

Illicit drug overdose is a leading cause of premature death and morbidity among opioid users [1]. Several systematic reviews have identified conditions that increase the risk of drug-related deaths [2-8]. The severity of dependence, polysubstance use, polypharmacy, history of suicide attempt, length of drug using career, number of network members who inject drugs and homelessness, all have been reported as important risk factors for fatal overdoses [9-14].

The perception of risk is a cognitive and learning process through which variably individuals assign positive or negative properties to a determined object or event, potentially exposing them to high risk behaviour [15]. However 'risk perception is not a unified phenomenon but one that is conditional on social status, social rules and rewards within particular contexts' [16]**.** Usually it is conceptualized in terms of personal vulnerability to the health effects of their risky behaviour, optimistic bias (inaccurate estimation of lower personal risk in comparison to other counterparts) and precaution effectiveness (believing that engaging in precautionary behaviour will be beneficial to their health) [17].

Since health behaviour models are mostly based on decision theories, risk behaviours are assumed to represent conscious actions. However, the relationship between risk perception and risky behaviour is inconclusive. Meta-analysis by Harrison *et al* [18] showed that the average correlation between risk perception measures and health behaviours never exceeded 0.22 [19, 20]. Knowledge itself of being engaged in risky activities may lead to a heightened sense of personal risk but at the same time, a reduced sense of vulnerability, contributing to greater risk taking [21]. Risk perception may increase with maturation due to

(1) a decrease in sensation seeking and decline in danger invulnerability [22] (2) a greater exposure to health problems, lower optimism about avoiding harm and misfortune [23] and (c) a higher sense of health responsibility related to the change from the present-hedonistic perspective toward a more future orientation [24].

The adoption of a broader public health approach concerned with risk, rather than a clinical focus restricted to consumption or the treatment of dependence, has been extremely influential among adult drug using population [25]. Secondary prevention objectives among substance users may either be *specific* to risk behaviours (e.g. reduction in current drug consumption, prevention of injecting, take home naloxone), or *generic* (addressing the totality of a young person's relationship to drugs). A systematic review on the effectiveness of take-home naloxone [26] identified only one interrupted time-series study**,** showing 'that overall educational and training interventions complemented by take-home naloxone would decrease overdose-related mortality' [27]. However literature exploring these same educational and training interventions shows poor evidence in sustaining a reduction in mortality rates in the long term [28]. At most, they can have a short-term effect in raising awareness and changing the way these phenomena are understood but not necessarily changing behaviours [29]. Indeed, assessment of short-term intervention effect on risk perception may be the logical first step in the evaluation of intervention efficacy [30].

The application of e-health technology to the field of substance use is at a relatively early stage, and methodological quality is still variable [31, 32]. A number of researchers have explored the role that information and communication technologies may play in the delivery of evidence-based behavioural interventions in improving the effectiveness, cost-

effectiveness, and reach of efforts to assess, treat, and support the recovery management of substance use disorders and other risk behaviours [32-36]. Few have explored the extent of utilization of communication technology by patients enrolled in substance abuse services [37]. Overall most decision aids did not explore risk perception and in some there are concerns about the completeness, balance and accuracy of information included [38].

Helpful evidence come from the chronic disease conditions field, with many attempts to develop tools to estimate risks of complex behaviours [39-41]. For example, a Cochrane review on decision making tools in the field of oncology has established that there is strong evidence that personalised risk estimates incorporated within communication interventions for screening programmes enhance informed choices [42].

The Overdose RIsk InfOrmatioN (ORION) project, a European Commission funded programme, aimed to develop and pilot an e-health psycho-educational tool to provide information to drug using individuals about the risks of suffering a drug overdose [43]**.** This overdose risk information (ORION) tool has therefore been designed with the aim of being easy-to use and informative to both patients and clinicians in various clinical settings. In this article we report on phase 1 (risk estimation), phase 2 (design), and phase 3 (feasibility) of the ORION tool

Methods

Setting: Recruitment occurred with the same three month period in treatment centres across four European countries: UK, Germany, Italy and Denmark, in both in- and out-patient healthcare settings (NHS Fife Addiction Services in Scotland, Essen LVR-Hospital in

Germany; Monza Regional Addiction Service in Italy and Aarhus University Hospital in Denmark).

Participants: A pragmatic opportunistic approach was taken to recruit a number of consented patients from the participating centres balancing the tight timeframe workpackages provided by our EU funders and the need to apply through different research and ethical governance approval processes. We initially recruited 10 patients from one centre in the UK (NHS Fife Addiction Service) and their key workers to 'test' the feasibility of ORION template tool before introducing the finalised tool to patients aged between 18 and 55 years old who were seeking treatment for their opioid dependence attending the four identified centres. Individuals with a current history of psychosis, confirmed learning disabilities, acute intoxication and patients who were unable to give informed consent for other reasons were excluded from this study **(Table 1**). All staff involved in the feasibility stage of this study were addiction nurses trained in both mental health and addictions and working as key workers to individuals suffering from dependency issues.

INSERT TABLE 1 here

Study Design: The design of the ORION project utilised a Delphi consensus process known as the International Patient Decision Aids Standards (IPDAS) Collaboration [44] ,which recommends that one needs to develop two critical activities to produce workable on-line decision tools; (1) prototype field-testing and (2) exploratory field-testing [45, 46].

Statistical analyses

Phase 1: Risk estimation modelling. Overdose risk factors initially identified through a systematic review as 'individual', 'situational' and /or 'organisational' risk factors were sub-categorised into: drug use, circumstances of overdose, experience of treatment, psychiatric and physical health problems, social contexts, consequences of intervening, treatment and use of emergency service. The model shows a point estimate of relative risk expressed as a percentage.

The relative risk percentage was obtained using the follow steps. In order to develop the mortality risk (**Table 2**):

1. For eight age-gender combinations the annual mortality rates in England and Wales general population were obtained from the Office of National Statistics [47]. A table with 4,096 rows was constructed. This corresponds to 9 (risk/protective) factors each with 2 levels (yes/no) x gender (male/female) x 4 age bands.
2. For each row, the estimated relative risk ratio (i.e. 1 equals no difference compared to general population) of overdose was inputted.
3. If a participant had no risk factors, the baseline mortality rate was multiplied by a factor of 1.1, to allow for the fact that even with no risk factors drug users are likely to have a higher mortality rate.
4. The percentage relative risk was calculated by dividing each risk profile's risk by the baseline population risk.

5. As the range of the relative risk percentage was 10 to 2980, it was standardized to a scale ranging from 0-100.

Thus for a female aged 15-24 with one risk factor (mixing drugs), the annual mortality risk is 1.63 per 1,000 population (the baseline risk is 0.295 per 1,000 population). Dividing the annual mortality risk by the baseline risk and converting it to a percentage, yields a figure of 450%. Converting this to a risk scale of 0-100 (based on the spectrum of relative risk ranging from 10-2980%) gives a figure of 15.1%.

In summary, the risk score shown is a relative measure ranging from non-users to individuals with all nine risk factors for potential overdose present.

INSERT TABLE 2 here

Phase 2: Interface and system design: The visual design and computer programming of the software was undertaken by experts from Keele University, and was designed to reside on a PC laptop for flexible utilisation in various clinical settings. The initial prototype was approved by experts at St Andrews University and ensured quality control to the actual coding, programming and platform compatibility of the interface.

Phase 3: Feasibility of the ORION eHealth tool:

Service users and staff from NHS Fife Addiction Services, Scotland tested the validation of the prototype to ensure the delivered product was functioning and user friendly (prototype field testing). This group were also asked to give feedback aimed at verifying users' comprehensibility of this eHealth tool. The tool was subsequently tested on a wider patient population attending the four health care addiction centres (exploratory field testing).

Mechanical issues (e.g. ability of patients in another country to open the computer, switching it on, logging in, opening the software and follow instructions) and interpretative issues (e.g. understanding what is asked of them, language issues, ability to follow the screen shots and participating in risk perception and changes as per instructions) were considered as the ORION study's criteria of validation.

Research governance: Formal ethics and management approvals were secured in all four clinical centres for the ORION protocol.

Results: Development of the Overdose Risk Information (ORION) software programme

Phase 1 – Risk estimation

A fundamental step for development of a e-health intervention tool is building consensus among experts with the aim of identifying, through a literature review, factors influencing overdose risk (predictors), referring to individual, situational and organizational categories.

The first consideration for the ORION project was the specification of benefit and risk in relation to overdose prevention. Benefit and risk were defined as reduction or increase

consecutively in behaviour that will result or not in a subsequent fatal or non fatal overdose. Our model shows final point estimates of risk in percentages.

Seven aggregate risk factors were identified for inclusion, either on the basis of being within the control of the individual or particularly relevant to the specific clinical settings. The aggregate risk factors were: mixing drugs, no intervention, mental health difficulties, not receiving treatment, injecting behaviour, previous overdoses and recent (2 weeks) release from prison (**Table 3**).

INSERT TABLE 3 here

Phase 2: Interface and system design

A master document was compiled in the English language, which was then translated and back translated into German, Italian, and Danish. The final software included visually engaging and user friendly screens. The screen shots, once ORION tool was opened, involved:

1. Welcome Screen – describing the programme and legal disclaimer regarding overdose risk estimation.

2. Demographic Information – prompting the users to enter their participant number, as well as gender and age band.

3. Initial Risk Assessment Questions – nine risk assessment questions with drop down menus allowing the users to indicate whether or not this particular risk factor applies to them **(Figure 1).**

4. First Overdose Risk Feedback – displayed by a black marker placed along a horizontal bar ranging from low to high overdose risk, which was placed against the overdose risk of a non drug user for comparison. The risk is shown on a scale of 0-100 where 0 = lowest risk and 100 = highest risk of suffering a drugs overdose (**Figure 2).**

5. Option to Change Answers and Review of Modified Risk – participants were given the option to review their answers and visually inspect how different answers to the overdose risk questions are reflected in changes in the overdose risk feedback graphic (**Figure 3).**

6. Debriefing Screen – thanking the participants and explaining that the risk feedback can be recorded and reviewed at a later time.

INSERT FIGURES 1-3 here

Phase 3: Feasibility of the ORION e-Health tool

There were no mechanical and/or interpretative issues arising from the field testing stages.. Satisfactory reports were received on the quality of translation, ease of use of instructions and ability to follow the risk estimation procedure. The exploratory field-testing was instructive in that it showed the value of the staff member being present to provide prompts to navigate the tool and act as an adjunct to the on-screen instructions.

We report on the general domains identified as necessary components to a successful tool that might help in risk reduction to dysfunctional potentially lethal behaviour.

1. User involvement. The inclusion of users at the early stage of tool design is crucial to attain acceptance and match literacy levels. A balance between 'house tradition' and matching drug-users preference for ease of use and attractive features needs to be considered carefully and with wide consultation.

2. Computer literacy: Drug users comprise individuals from all lifestyles including their experiences with computers. Therefore, a further level of difficulty needs to be overcome with those who are unfamiliar with information presented on screen. Drug users in treatment were found to have poorer computer literacy than other matched controls when comparing their skills on seeking employment, strengthening the need to design clear and straightforward approaches for engaging drug-users in computer assisted health care approaches [48]. The alternative would be to enable the drug-user to work alongside a member of staff to assist with the process of working with the aid of a computer application. This was the approach that was actively introduced with the ORION programme.

3. Staff training: A neglected area is the attention paid to the training of staff that were requested to assist with the delivery of materials such as the ORION software. Not only will patients be varied in their interest and competence to make use of computer assisted tools but also staff will vary in this respect. Whereas patients may feel justified in stating their difficulties it may not be quite so easy for staff to voice concerns over the use of such tools for fear of criticism and lack of motivation for a

new potentially valuable aid to clinical care. Some evidence suggests that staff were aware (50%) that service users do check information about their condition and status on the internet but failed to check (24% only) whether the patient consulted online information [49].

4. Ethics: Close attention is needed to explore the security of information that has the potential to be collected routinely on computer assisted tools. The current system devised for ORION was engineered so that all internet capability was removed. This somewhat surprising feature was chosen to allow quick and easy access to clinical populations for research data collection and gain ethical committee approval in the various European Member States where the data were being collected. Question responses and additional behavioural data (time spent on screen, key stroke actions etc.) were collected through encrypted memory sticks by the research team [50]. The support needed for individuals who become aware of the risk of overdose and are not part of a treatment environment should also be looked at sensitively. One should consider providing the opportunity for individuals to get psychological support to potential distress caused by such new information obtained through the use of the ORION tool.

5. Ecological validity: Essentially the tool has to perform an important function within the assessment, advisory and support role of the drug treatment service.

Discussion

The development of ORION e-health tool underlines the importance of an evidence-based intervention aimed in obtaining reliable evaluation of risk. The ORION tool supports a decision making process aimed at influencing the substance users' self-efficacy and the degree to which the substance users' understand risk factors. Therefore its innovative power consists in translating risks combination into a clear estimation for the user who will appear more likely interested in his/her risk perception.

We acknowledge several limitations in setting up this e-health tool. The risk estimation model used for opioid fatal overdose was derived from published literature. This reduces specificity (e.g. local sociodemographic predictors and service user's drug taking behaviours), but increases generalisability based on the rigor of the selected studies. Our model shows final point estimates of risk in percentages. This is useful in decision making analysis, but these numbers, without confidence intervals, may create a false sense of certainty. Finally logistic regression models have their limitations when used to predict aberrant behaviour such as fatal overdose events as there is an assumption of implicit interactions based upon the initial estimates of risk. These are mathematical devices for inclusion in the algorithm, but clinical data may reveal subsequently more complex relationships

We were not able to collect data that would have given us more information on (1) digital/computer literacy, (2) educational status and (3) neuropsychological domains on decision making that would have influenced the outcomes of their understanding and usability of the ORION tool. This needs further investigation. The ORION tool had the option to be used by patient accompanied by their key worker. This approach was used more

frequently as the ORION project team did not feel it was important at this stage of the study to restrict different methods of conducting this ehealth tool. This collaborative approach was seen as an attractive option as it introduced an opportunity to discuss risk perception and reduction initiatives possible [51]. Satisfactory reports were received on the quality of translation, ease of use of instructions and ability to follow the risk estimation procedure. This was assisted by the presence of the staff member to answer questions, or direct patients around the screen, especially with those patients who were less competent readers. Consequently a version which removes the staff member from the ORION e health administration would require additional development in the design to assist with navigation prompts as the patient works through the tool's screens.

The patients recruited were heterogenous in age and gender with some centres recruiting more females and/or older participants. The ORION project did not *a priori* attempt to match populations as it tried to recruit as much as possible a 'real life ' population within which the tool could be utilised. However collecting drug use history, severity of opioid dependency and recent risky lifestyle behaviours would have provided a better understanding of the population studied. This would have contextualised better the utilisation to the e-health tool to the risks experienced by the participants.

Finally the ORION Tool utilised qualitative methodologies. It does not make use of objective markers that might shed light to (a) the opioid pharmacokinetics and/or pharmacodynamics, which are known to affect addiction potential [52] and (b) opioid pharmacogenetic variabilities, which can be involved in increasing the individual probability of fatal outcomes with opioid use occurring [53]. In France, a major effort is underway to extend clinical pharmacokinetics integrated with pharmacogenetics for quantitative prediction of the effect

induced by cytochrome P450 gene polymorphisms in general, and opioid drug dose regimen designs [54]. This quantitative approach to opioid dosing has the potential of mitigating both addiction potential and fatal outcomes. The approach is underpinned by DDI-Predictor (http://www.ddi-predictor.org/) a web-based Bayesian computational database engine constructed by the Genophar II Working Group [55].

Conclusion

The overdose risk information (ORION) tool has been designed for ease of use to both patients and clinical services. The pilot implementation of the ORION tool was conducted in the four countries to assess the feasibility of tool implementation. Exploratory field testing and validation confirmed the next stage of evaluation, namely, collection of routine patient samples in study clinics. The associations between risk perception of overdose, engagement with the ORION tool and willingness to alter overdose risk factors, in a clinical setting across various EU member states will further confirm the ORION tool's generalisability and effectiveness. A practical overdose risk assessment tool for effective implementation in the substance misuse field is indicated. The ORION eHealth tool is available for free download at http://orion-euproject.com/download-software/.

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Conflicts of Interests

None

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FIGURES

Figure 1: Overdose Risk Questions

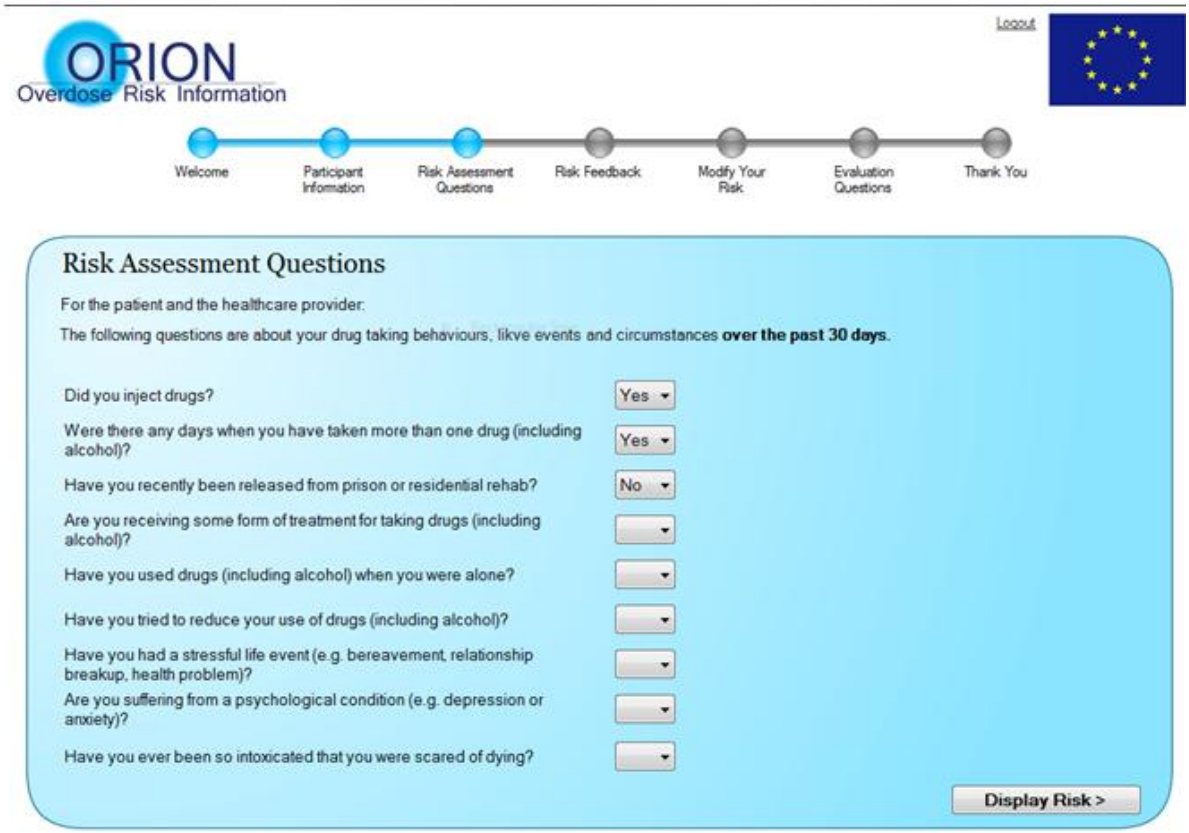

Figure 2: Overdose Risk Feedback

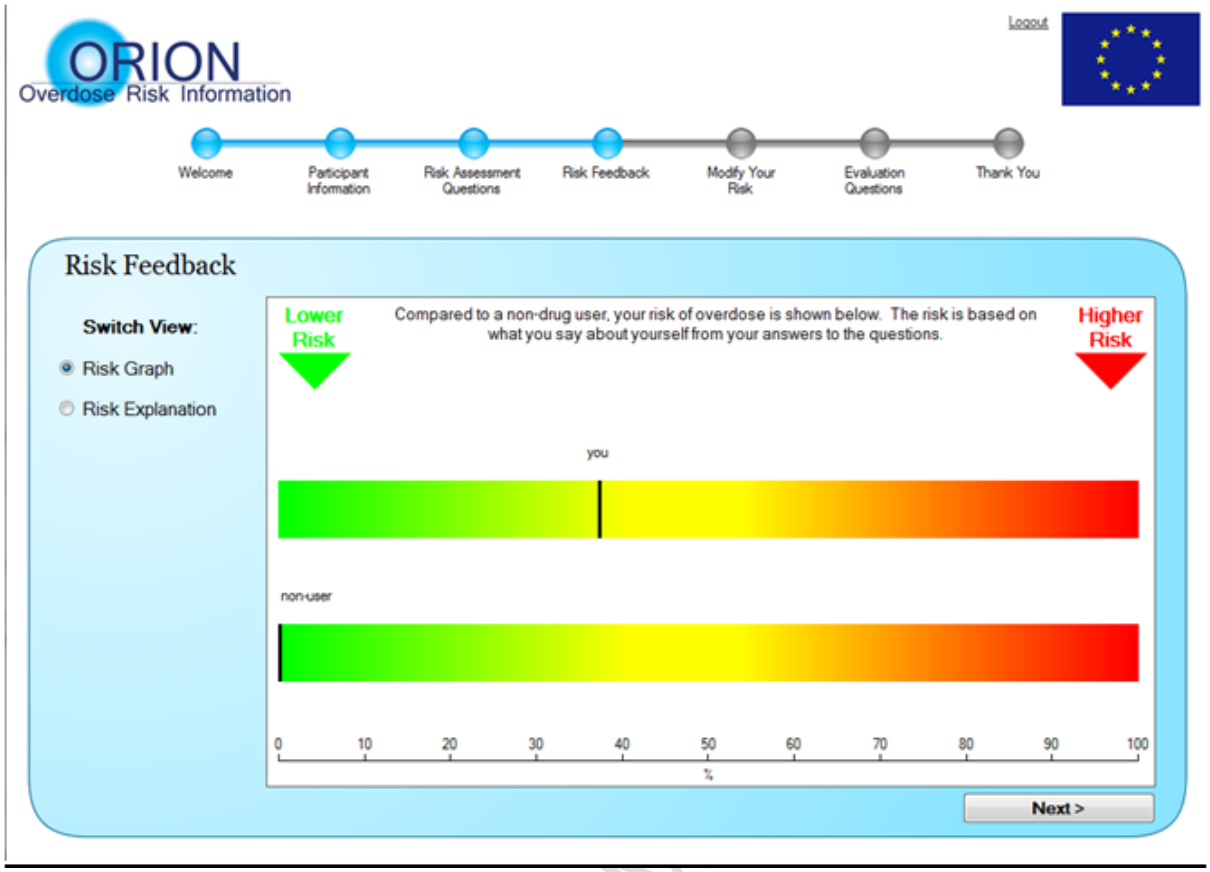

Figure 3: Modification of Risk Factors and Estimated Risk of Overdose Relative to Non-Drug User

Table 1: Age and Gender of the Patient Participants by Country

	UK	Germany	Italy	Denmark	Total
Gender					
Male	29	77	39	7	152
Female	2	21	1	1	25
M:F Ratio	14.5	36.7	39	7	6.08
Age Mean (s.d.)	30.03 (5.39)	40.03 (7.81)	41.90 (8.12)	35.38 (3.78)	38.76 (7.95)

s.d.= standard deviation

Table 2: Estimating Risk of Overdose Relative to Non-Drug User

Row	relriskpercent	relrisk100
1	10	0.34
2	120	4.03
3	230	7.72
4	340	11.41
5	450	15.10
6	560	18.79
7	670	22.48
8	780	26.17
9	890	29.87
10	1000	33.56
11	1110	37.25
12	1220	40.94
13	1330	44.63
14	1440	48.32
15	1550	52.01
16	1660	55.70
17	1770	59.40
18	1880	63.09
19	1990	66.78
20	2100	70.47
21	2210	74.16
22	2320	77.85
23	2430	81.54
24	2540	85.23
25	2650	88.93
26	2760	92.62
27	2870	96.31
28	**2980**	100.00

Relriskpercent= relative risk percent

Table 3: Factors and Odds Ratio Contributing to Fatal Overdose Risk Estimation Model in Opioid Users: Characteristics of Included Studies

Aggregate Risk factor	Source	Country	Size	Odds Ratio
Mixing drugs	Coffin *et al*, 2003	USA	7451	5
	Bernstein *et al*, 2007	USA	8774	
	Rome *et al*, 2008	Scotland	328	
No intervention	Tobin *et al*, 2005	USA	397	2
	Rome *et al*, 2008	Scotland	328	
	Dietze *et al*, 2002	Australia	6173	
Mental health difficulties	Bohnert *et al*, 2011	USA	15491	3
	Oliver *et al*, 2007	England	30	
	Gossop *et al*, 2002	England	1075	
Not receiving treatment	Clausen *et al*, 2009	Norway	208	7
	Brugal *et al*, 2005	Spain	5049	
	Fugelstad *et al*, 1995	Sweden	472	
	Davoli *et al*, 1993	Italy	405	2
Injecting behaviour	Arendt *et al*, 2011	Denmark	7996	
	Quan *et al*, 2010	Northern Thailand	314	
	Colon *et al*, 2006	USA	637	
Previous overdoses	Cook *et al*, 1998	Switzerland	190	2
	Stoove *et al*, 2009	Australia	4884	
	Darke *et al*, 2003	Australia	1033	
Recent (2 weeks) release from prison	Ødegård *et al*, 2010	Norway	338	9
	Krinsky *et al*, 2009	USA	96	
	Farrell and Marsden, 2008	England and Wales	48771	
	Kariminia *et al*, 2007	Australia	85203	
	Christensen *et al*, 2006	Denmark	15885	
	Bird and Hutchinson, 2003	Scotland	19486	
	Seaman *et al*, 1998	Scotland	316	