# Organ donation for transplantation

## Evidence Update January 2014

A summary of selected new evidence relevant to NICE clinical guideline 135 'Organ donation for transplantation: improving donor identification and consent rates for deceased organ donation' (2011)

**Evidence Update 51**

Evidence Updates provide a summary of selected new evidence published since the literature search was last conducted for the accredited guidance they relate to. They reduce the need for individuals, managers and commissioners to search for new evidence. Evidence Updates highlight key points from the new evidence and provide a commentary describing its strengths and weaknesses. They also indicate whether the new evidence may have a potential impact on current guidance. For contextual information, this Evidence Update should be read in conjunction with 'Organ donation for transplantation: improving donor identification and consent rates for deceased organ donation' (NICE clinical guideline 135).

**Evidence Updates do not replace current accredited guidance and do not provide formal practice recommendations.**

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**National Institute for Health and Care Excellence**

Level 1A
City Tower
Piccadilly Plaza
Manchester M1 4BT
www.nice.org.uk

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# Introduction

This Evidence Update identifies new evidence that is relevant to, and may have a potential impact on, the following reference guidance:

[1]

**Organ donation for transplantation. NICE clinical guideline 135 (2011)**

A search was conducted for new evidence from 1 June 2010 to 14 August 2013. A total of 1722 pieces of evidence were initially identified. Following removal of duplicates and a series of automated and manual sifts, 11 items were selected for the Evidence Update (see Appendix A for details of the evidence search and selection process). An Evidence Update Advisory Group, comprising topic experts, reviewed the prioritised evidence and provided a commentary.

Although the process of updating NICE guidance is distinct from the process of an Evidence Update, the relevant NICE guidance development centres have been made aware of the new evidence, which will be considered when guidance is reviewed.

## NICE Pathways

- Organ donation for transplantation. NICE Pathway

## Feedback

If you have any comments you would like to make on this Evidence Update, please email contactus@evidence.nhs.uk

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[1] NICE-accredited guidance is denoted by the Accreditation Mark

# Key points

The following table summarises what the Evidence Update Advisory Group (EUAG) decided were the key points for this Evidence Update. It also indicates the EUAG's opinion on whether the new evidence may have a potential impact on the current guidance listed in the introduction. For further details of the evidence behind these key points, please see the full commentaries.

The section headings used in the table below are taken from the guidance.

**Evidence Updates do not replace current accredited guidance and do not provide formal practice recommendations.**

| Key point | Potential impact on guidance | |
|---|:---:|:---:|
| | Yes | No |
| **Identifying patients who are potential donors** | | |
| • Assessment tools, particularly the Full Outline of UnResponsiveness (FOUR) score, may be of some use in identifying patients likely to become eligible for donation after brainstem death (DBD). | | ✓ |
| • Uncontrolled donation after circulatory death (DCD) in the emergency department and the techniques necessary for organ preservation appear to be acceptable to patients and relatives. | | ✓ |
| • Neonatal DCD might provide a means of increasing the pool of potential organ donors. | | ✓ |
| **Assessing best interests** | | |
| • Personal religious and cultural beliefs, family relationships, knowledge of the organ donation process and attitudes towards the healthcare system can affect people's views on DBD and DCD. | | ✓ |
| **Discussions in all cases** | | |
| • The consent discussion should be timed sensitively, and those close to the patient should receive understandable information on organ donation to support their decision. | | ✓ |
| • Age, ethnicity, culture and religion of patients and those close to them, may influence the likelihood of consent. | | ✓ |
| • The effect on consent to organ donation of offering relatives the opportunity to be present during determination of neurological death in a family member is unclear. | | ✓ |
| • Providing those close to the patient with support during consent, in particular providing information on neurological death and the consent process and time to consider the information, can improve the likelihood of consent. | | ✓ |
| **Organisation of the identification, referral and consent processes** | | |
| • Education of healthcare professionals and the general public on organ donation procedures could positively influence attitudes towards donation and consent rates. | | ✓ |

# 1 Commentary on new evidence

These commentaries analyse the key references identified specifically for the Evidence Update. The commentaries focus on the 'key references' (those identified through the search process and prioritised by the EUAG for inclusion in the Evidence Update), which are identified in bold text. Section headings are taken from the guidance.

## 1.1 Identifying patients who are potential donors

NICE clinical guideline 135 (NICE CG135) recommends that all patients who are potentially suitable organ donors should be identified as early as possible, through a systematic approach. While recognising that clinical situations vary, identification should be based on either of the following criteria:

- defined clinical trigger factors in patients who have had a catastrophic brain injury, namely:
  - the absence of one or more cranial nerve reflexes and
  - a Glasgow Coma Scale (GCS) score of 4 or less that is not explained by sedation

unless there is a clear reason why the above clinical triggers are not met (for example because of sedation) and/or a decision has been made to perform brainstem death tests, whichever is the earlier

- the intention to withdraw life-sustaining treatment in patients with a life-threatening or life-limiting condition which will, or is expected to, result in circulatory death.

**Identifying potential DBD donors using clinical triggers**

A retrospective study by **de Groot et al. (2011)** tested 3 tools for identifying patients who may imminently become brainstem dead and who would, therefore, have been potential heart-beating organ donors (also known as donation after brainstem death [DBD] donors). A total of 564 patients diagnosed with subarachnoid haemorrhage, traumatic brain injury or intracerebral haemorrhage were identified over a 3 year period at a single intensive care unit (ICU) in the Netherlands. Data on patient demographics, brain activity (GCS and last known brainstem reflexes), clinical outcome and whether or not organs were procured were extracted from medical records. The 3 tools used to identify patients with imminent brain or neurological death (and therefore identify potential donors) were:

- Full Outline of UnResponsiveness (FOUR) score:
  Imminent brainstem death=FOUR score of $E_0 M_0 B_0 R_0$: eyelids remaining closed with pain; no response to pain or generalised myoclonus status; absent pupillary, corneal and cough reflex; and absence of spontaneous ventilation or apnoea.
- GCS:
  Imminent brainstem death=GCS score of 3 (no eye opening to pain, no verbal response and no motor response to pain) and absence of at least 3 out of 6 brainstem reflexes.
- Organ Procurement Transplantation Network (OPTN) definition:
  Imminent neurological death defined as 'a patient … with severe neurological injury and requiring ventilator support, who upon clinical evaluation … has an absence of at least 3 brainstem reflexes'.

Of the 179 patients in the cohort who died, 36 (20%) became organ donors (23 DBD donors and 13 donation after circulatory death [DCD] donors). For each of the tools, the number of potential DBD donors identified and the number of those who went on to become actual DBD donors were:

- FOUR score: 63 potential donors, 23 actual donors (37% donor conversion rate).
- GCS: 85 potential donors, 23 actual donors (27% donor conversion rate).
- OPTN definition: 88 potential donors, 23 actual donors (26% donor conversion rate).

The 3 tools did not identify 7 potential DBD donors, and most of the patients identified as potential donors did not go on to fulfil official neurological death criteria.

Limitations of the evidence included that:

- The study reported prediction of actual donation rather than progression to brainstem death. Some patients whose relatives did not consent to organ donation before testing for brainstem death may have progressed to brainstem death and thus been potential donors.
- The study was conducted at a single centre.
- The study was retrospective and observational, so some potential donors may have been missed.
- GCS and absence of brainstem reflexes were recorded at different stages of treatment across patients.
- The FOUR score is not in common use in England and Wales.

Limited evidence suggests that assessment tools, particularly the FOUR score, may be of some use in identifying patients likely to become eligible for DBD. These findings add to the body of evidence supporting the clinical trigger factors to identify potentially suitable donors among patients with catastrophic brain injury outlined in NICE CG135. A more specific trigger may increase clinician uptake and use. Although indicating potential future refinements to triggers, limitations of the evidence mean that these data are currently unlikely to have an impact on guidance. Prospective studies are needed to determine whether these tools improve identification and referral rates.

**Key reference**
de Groot YJ, Wijdicks EF, van der Jagt M et al. (2011) Donor conversion rates depend on the assessment tools used in the evaluation of potential organ donors. Intensive Care Medicine 37: 665–70

**Identifying potential DCD donors in the emergency department**

NICE CG135 recommends identifying all patients who are potentially suitable donors as early as possible, through a systematic approach. One of the criteria on which identification should be based is 'the intention to withdraw life-sustaining treatment in patients with a life-threatening or life-limiting condition which will, or is expected to, result in circulatory death.' The guideline makes no recommendations specific to 'uncontrolled DCD' after death in the emergency department – for example, after a cardiac arrest where organ donation has not been planned for – although evidence focusing on emergency departments was considered during development of the recommendations.

A cross-sectional survey by **Bruce et al. (2013)** sought people's opinions on uncontrolled DCD. Patients and relatives aged over 15 years attending the emergency department of a large teaching hospital in Scotland over a 3-day period were asked to complete a 17-item questionnaire. The questions covered whether respondents would in theory be willing to discuss and consent to organ donation soon after the circulatory death of a relative in the emergency department. Respondents were also asked their thoughts on the acceptability of 3 organ preservation procedures: insertion of a small tube into the groin to deliver cold fluid, continuation of mechanical chest compressions, and continuation of mechanical ventilation.

During the study period, 200 questionnaires were completed (88% of respondents were white British, mean age=40.4 years).

Willingness of people to discuss organ donation after confirmation of circulatory death in the emergency department (72%) was no different than after confirmation of brainstem death in an ICU (72%). Just over half (56%) of respondents said they would be willing to discuss organ donation soon after the cardiac arrest of a relative in the emergency department (with 21% not willing to discuss organ donation at this point, and 23% having no strong views). A similar proportion (59%) would consider donating their relative's tissues (such as corneas and heart valves) in this situation, whereas 16% would not consider donation and 25% were undecided. People were mostly happy for the 3 organ preservation procedures to be used after circulatory death of a relative (48–69% thought the procedures were acceptable compared with 9–28% who thought they were not). Respondents were significantly more likely to accept the use of the 3 procedures after they had discussed organ donation than before the discussion (p<0.001 for each of the 3 procedures), but only around one-fifth (21–28%) stated that they thought use of such procedures before discussion was 'not acceptable'.

Limitations of the evidence included that:

- The study used a convenience sample.
- Participants were asked about a theoretical scenario.
- Response rate was not recorded, which precluded any comparison of the characteristics of responders with non-responders.

Limited evidence suggests that uncontrolled DCD in the emergency department and the techniques necessary for organ preservation appear to be acceptable to patients and relatives. Uncontrolled DCD could act as a new source of potential donors in the UK in the future. This evidence is consistent with the recommendation in NICE CG135 that patients who will, or are expected to, reach circulatory death should be considered as potential organ donors. Further research, along with continuing observation of the limited numbers of centres performing this technique in the UK, is needed.

**Key reference**
Bruce CM, Reed MJ, MacDougall M (2013) Are the public ready for organ donation after out of hospital cardiac arrest? Emergency Medicine Journal 30: 226–31

**Identifying potential DCD donors in neonatal ICUs**

Although NICE CG135 discusses arrangements for organ donation in paediatric ICUs, neonatal ICUs are not specifically referred to. However, the recommendations in NICE CG135 apply to any critical care setting. Two studies recently assessed the potential for organ donation following circulatory death in neonates.

A retrospective study in the USA by **Labrecque et al. (2011)** examined the proportion of deaths in neonatal ICUs that would theoretically have been eligible for DCD. Medical records over a 3-year period at 3 level III neonatal ICUs were reviewed to identify infants born at 23 weeks' gestation or later who subsequently died. Exclusion criteria were: postmenstrual age less than 37 weeks and weight less than 3 kg at death; lack of mechanical ventilation at time of withdrawal of life support; active infection (including HIV) or sepsis; active malignancy; encephalopathy of unknown aetiology; and neurological death.

During the study period, the 3 neonatal ICUs admitted 7955 infants, with 192 deaths among those born at a gestational age of 23 weeks or more. After exclusions, 16 (8%) infants had a warm ischaemic time (defined as the interval from withdrawal of life support to circulatory death) of less than 1 hour and were therefore potential liver and kidney DCD candidates. After exclusions because of organ failure, the 16 infants would have yielded 14 livers and 18 kidneys. Of these 16 infants, 12 infants had a warm ischaemic time less than 30 minutes

and were therefore also suitable candidates for cardiac DCD. After exclusions for vasoactive medications and major congenital heart disease, the 12 infants would have yielded 10 hearts.

A similar retrospective study in the USA by **Mathur et al. (2011)** estimated the proportion of neonates who might be potential candidates for cardiac DCD. Medical records of all infants discharged over a 5-year period from 1 neonatal ICU were screened to identify those who weighed more than 2.5 kg at the time of death and who died after planned withdrawal of life support. Exclusion criteria were active sepsis, HIV infection, significant cardiac dysfunction, congenital heart disease, death after cardiopulmonary resuscitation or neurological death, and a 'do not resuscitate' order in place.

Over the 5-year study period, 266 deaths were recorded in the neonatal ICU, of which 117 (44%) were infants weighing more than 2.5 kg. After exclusions, 16 infants would have been potential candidates for DCD. Only 5 of these infants (2% of all deaths, 4% of deaths in infants weighing more than 2.5 kg) had a warm ischaemic time of 30 minutes or less and therefore would have been suitable for cardiac DCD.

Limitations common to both studies included that:

- The analyses were retrospective.
- A minimum weight criterion of 2.5–3 kg would result in small organs that may have a limited recipient pool.
- A number of ethical issues exist with respect to organ donation and transplantation in infants, in particular with cardiac DCD.

In addition, Labrecque et al. (2011) may have overestimated the time between withdrawal of life support and certification of death (medical equipment is commonly removed from infants near death for the benefit of family members, and the need to ascertain time of death must be balanced with privacy and dignity of the family). The number of potential DCD candidates may therefore have been underestimated.

Taken together, these 2 studies suggest that neonatal DCD might provide a means of increasing the pool of potential organ donors. The evidence is unlikely to have an impact on NICE CG135 because cardiac DCD is largely experimental and the evidence in neonates remains at a preliminary stage.

**Key references**
Labrecque M, Parad R, Gupta M et al. (2011) Donation after cardiac death: the potential contribution of an infant organ donor population. Journal of Pediatrics 158: 31–6

Mathur M, Castleberry D, Job L (2011) Identifying potential heart donors among newborns undergoing circulatory determination of death. Journal of Heart and Lung Transplantation 30: 389–94

## 1.2    Patients who have capacity

No new key evidence was found for this section.

## 1.3    Assessing best interests

In assessing a patient's best interests, NICE CG135 recommends that healthcare professionals should consider:

- the patient's known wishes and feelings, in particular any advance statement or registration on the NHS organ donor register but also any views expressed by the patient to those close to the patient
- the beliefs or values that would be likely to influence the patient's decision if they had the capacity to make it
- any other factors they would be likely to consider if they were able to do so

- the views of the patient's family, friends and anyone involved in their care as appropriate as to what would be in the patient's best interests; and
- anyone named by the patient to be consulted about such decisions.

**Views on organ donation**

A systematic review by **Irving et al. (2012)** analysed factors influencing the general public's attitudes towards organ donation. Qualitative studies were included that used focus groups, interviews or both to explore community attitudes to living and deceased heart, lung, liver and kidney donation. A total of 18 studies were identified (n=1019) from the UK (6 studies), Canada (4 studies), USA (5 studies), South Africa, Malta and Australia (1 study each). Text from the results and conclusions was extracted and concepts were recorded that focused on:

- attitudes towards organ donation
- the reasons for particular beliefs
- the interpretations given of perspectives on organ donation.

The concepts were then examined and emerging themes identified.

The analysis established 8 themes: relational ties; religious beliefs; cultural beliefs; family influence; body integrity; knowledge and information about donation; previous interaction with the healthcare system; and major reservations about donation (even among those supporting donation). Relational ties positively affected people's views of organ donation, with many participants willing to donate a kidney to a family member or friend. The influence of religion on attitudes to organ donation was mixed: some people felt that their religion supported donation whereas others did not. Cultural beliefs (in particular, those linked to death and dying), family views, and views about body integrity (maintaining the 'wholeness' of the body in death) influenced, often negatively, whether people supported organ donation.

Lack of knowledge and information on organ donation was often reported as a barrier to whether people would consent. Some participants had negative views of the healthcare system and the organ donation process that affected their attitudes towards donation, with people from minority populations expressing a sense of marginalisation from the healthcare system that underpinned a refusal to donate. Reservations about donation often manifested as competing beliefs: people with serious misgivings about donation were also able to recognise its huge potential to help people. Positive and negative influences within each of the identified themes had the potential to tip the balance of the decision whether or not to donate in either direction.

A limitation of this study was that the majority of the studies analysed set out to explore barriers to organ donation, which may have skewed the results towards factors that negatively influence views on donation.

The evidence suggests that personal religious and cultural beliefs, family relationships, knowledge of the organ donation process and attitudes towards the healthcare system can affect people's views on DBD and DCD. This evidence strengthens the recommendation in NICE CG135 that healthcare professionals should take account of the patient's beliefs or values and any other factors the patient would be likely to consider when assessing whether to take steps to facilitate organ donation. Further research is needed on how well those close to the patient understand the concepts of DCD and DBD when they make a decision on consent.

**Key reference**
Irving MJ, Tong A, Jan S et al. (2012) Factors that influence the decision to be an organ donor: a systematic review of the qualitative literature. Nephrology Dialysis Transplantation 27: 2526–33

## 1.4    Seeking consent to organ donation

No new key evidence was found for this section.

## 1.5    Approach to those close to the patient

No new key evidence was found for this section.

## 1.6    Discussions in all cases

**Factors influencing decision-making by those close to the patient**

*Practical and personal factors*
NICE CG135 recommends that before approaching those close to the patient to request consent for organ donation, a check should be made of the NHS organ donor register and for any advance statements or Lasting Power of Attorney for health and welfare. In addition, any cultural and religious issues that may have an impact on consent should be identified.

Those close to the patient should be approached in a setting suitable for private and compassionate discussion and in a professional, compassionate and caring manner. Those close to the patient should also be given sufficient time to consider the information. Assurance should be provided that the primary focus is on the care and dignity of the patient (whether the donation occurs or not) and sufficient time should be allowed for those close to the patient to understand the inevitability of the death or anticipated death and to spend time with the patient. Withdrawal of life-sustaining treatment or neurological death should be discussed before, and at a different time from, discussing organ donation, unless those close to the patient initiate these discussions in the same conversation

A review by **de Groot et al. (2012)** explored decision-making by relatives of neurologically dead potential donors. The study employed an 'integrative review' process that allowed for the inclusion and combination of diverse methodologies, such as experimental and non-experimental research. The authors identified 70 empirical, theoretical and practical articles that assessed donation requests and decision-making in the relatives of neurologically dead adults. Results and conclusions were extracted from these articles and grouped under 3 themes: decision-making; evaluation of the decision; and need for support.

Several factors affected families' decision whether to consent, some of which were modifiable (timing, privacy, quality of care, and sympathetic requesting) and others less so (demographics, religious and cultural values, duration of the patient's stay in hospital, and circumstances or cause of death). Relatives' values (such as protecting and respecting the body), and respect for the deceased's wishes, were also deemed important. When asked to evaluate their decision, the likelihood of regretting the decision was lower among families who consented to donation (ranging from 6–14%) than among non-donor families (of whom at least one-third, and up to 42%, said they would respond differently if asked again). Refusal and regret often appeared to be associated with not knowing the deceased's wishes.

Some studies reported that families wanted more information about the organ donation process but felt unable to ask pertinent questions or understand the responses, which affected their ability to make a stable decision. Several studies highlighted the importance of 'decoupling' the conversation with families about neurological death from the discussion of consent. Many of the studies that assessed support during the consent process focused on maximising consent rates rather than assisting families in their decision-making. Support in making an informed decision and counselling appeared to help families to make a sound decision about organ donation.

Limitations of the evidence included that studies were not assessed for quality. In addition, many of the studies struggled to recruit families who did not agree to organ donation, so fewer data were available on relatives of non-donors than of donors.

The evidence suggests that the consent discussion should be timed sensitively, and those close to the patient should receive understandable information on organ donation to support their decision. The evidence is consistent with the recommendation in NICE CG135 that discussions about organ donation with those close to the patient should only take place after they understand that death is inevitable or has occurred. The guidance also recommends that families should be provided with a clear explanation of and information on the process of organ donation and retrieval and should be offered support. More research is needed on whether providing family members with support in exploring their values and the wishes of the patient can lead to more stable consent decisions.

**Key reference**
de Groot J, Vernooij-Dassen M, Hoedemaekers C et al. (2012) Decision making by relatives about brain death organ donation: an integrative review. Transplantation 93: 1196–211

### *Cultural and religious factors*
NICE CG135 recommends that before approaching those close to the patient, any cultural and religious issues that may have an impact on consent should be identified. An assessment should be made of whether family support is required – for example faith representative, family liaison officer, bereavement service, trained interpreter, advocate. The multidisciplinary team responsible for planning the approach and discussing organ donation with those close to the patient should include local faith representative(s) where relevant.

Two studies looked at how age, ethnicity, religion and culture influence the decision of those close to the patient on whether to consent to donation in neurologically dead relatives.

A retrospective study by **Goldberg et al. (2013)** analysed national data from the USA to identify variation in consent rates between different age and ethnic groups. Consent, age and ethnicity data were extracted from the Organ Procurement and Transplantation Network database for deaths in 2008–2011 among patients aged up to 70 years declared neurologically dead and with no medical conditions precluding donation. The study analysed 31,408 deaths at 59 organisations where consent had not been provided before death through a registry or legal documentation.

Consent for donation, the primary outcome, had been obtained from family or other decision makers in 21,601 (69%) deaths. Compared with consent rates for white patients (77.0%), likelihood of consent was lower for Asian patients (48.1%; odds ratio [OR]=0.31, 95% confidence interval [CI] 0.25 to 0.37), patients of 'other' ethnicity, such as Native American and multiracial patients (59.0%; OR=0.33, 95% CI 0.20 to 0.55), black patients (54.9%; OR=0.35, 95% CI 0.31 to 0.39), and Hispanic patients (67.5%; OR=0.54, 95% CI 0.44 to 0.65; p<0.001 for all). Consent rates were higher when the request process satisfied the organisation's criteria for being an 'effective request', for example, using skilled staff and ensuring that relatives understand neurological death (OR=3.80, 95% CI 3.08 to 4.68, p<0.001). Compared with relatives of white patients, relatives of patients from other ethnic groups were no more or less likely to receive an effective request. The exception was relatives of Asian patients, where an effective request was significantly less likely (OR=0.76, 95% CI 0.65 to 0.88, p<0.001).

Analysis of age data showed that compared with patients aged 18–39 years, consent to donation was lower for patients aged 40–54 years (OR=0.84, 95% CI 0.78 to 0.90), aged 55–64 years (OR=0.72, 95% CI 0.67 to 0.77) and aged 65 years or older (OR=0.58, 95% CI 0.52 to 0.64; p<0.001 for all). Relatives of patients aged 40 years and older were less likely to experience an effective request than relatives of those aged 18–39 years (p<0.001).

Limitations of the evidence included that the analysis covered only patients who were neurologically dead at the time of reporting, which would have excluded any patients with severe neurologic injury that may have subsequently met the criteria for neurological death. The study also relied on data reported by organ procurement organisations, which might have under-reported the number of eligible deaths.

A second retrospective analysis by **Ashkenazi and Klein (2012)** sought to identify factors that might predict whether family members would donate a relative's organs. Standardised demographic information was collected from 20 Israeli hospitals on people who had been declared neurologically dead and 2 first-degree relatives (father, mother, brother, sister, son, daughter or spouse) who had played a prominent role in the consent decision. Data from 995 relatives were analysed, most of whom were Jewish (76%); 16% were Muslim and 7% were Christian.

Among all family members, just over half (56%) agreed to donate their relative's organs during the 5-year period analysed. Religion was the biggest predictor of whether relatives agreed to organ donation: two thirds (68%) of Christians consented, compared with half (56%) of Jews and just under a quarter (22%) of Muslims. Female relatives were more likely to consent than male relatives (64% versus 49%, $p<0.001$), and willingness to donate decreased with increasing education level achieved (75% for primary school level, 55% for high school level, and 26% for higher level. $p<0.001$).

Among Jews, level of education was the biggest predictor of consent (ranging from 24% in family members with primary school education to 75% in those with higher education), but the association between education level and likelihood of consent appeared inverse to that seen among the whole study population. The authors speculated that this finding might be attributable to degree of religiousness. In Israeli Jews, level of education correlates with religiousness in that deeply religious and ultraorthodox Jews may be more likely to attend religious institutions as opposed to university.

Family relationship was the biggest predictor of donation in Christians and Muslims. Among Christians, brothers, daughters, fathers and mothers were more likely to donate than were spouses, sisters and sons (76% versus 60%). In Muslims, sisters, daughters, fathers and mothers were more likely to donate than were spouses, sons, brothers, and uncles (38% versus 16%).The authors noted that in traditional Muslim families, men largely make decisions; for example, a patient's brother would be more likely to make a decision on organ donation that would his wife or sister.

Limitations of the evidence included that if any 1 family member opposed donation, the record showed that the family refused to donate. As such, the consent rate for individual family members could differ from the overall consent rate in Israel. In addition, the case mix of the study population might limit the generalisability of the findings to the UK.

The evidence indicates that age, ethnicity, culture and religion of patients and those close to them, may influence the likelihood of consent. Following best practice for securing consent, and better understanding and accommodation of issues related to patient and family demographics and beliefs (particularly for minority ethnic groups), could potentially improve rates of consent to donation.

The evidence is consistent with the recommendation in NICE CG135 that cultural and religious issues that may affect consent, and the use of local faith representatives, should be considered when approaching those close to the patient. The findings also strengthen the recommendation that consultant staff should have specific communication skills and knowledge necessary to improve consent ratios for organ donation. Further research is needed to identify the reasons behind family refusal and whether any of the reasons are changeable and could be targeted by interventions.

**Key references**

Ashkenazi T, Klein M (2012) Predicting willingness to donate organs according to the demographic characteristics of the deceased's family. Progress in Transplantation 22: 304–10

Goldberg DS, Halpern SD, Reese PP (2013) Deceased organ donation consent rates among racial and ethnic minorities and older potential donors. Critical Care Medicine 41: 496–505

## *Understanding of neurological death*

NICE CG135 recommends that those close to the patient should be provided with a clear explanation of how death is diagnosed using neurological criteria and how this is confirmed and what happens next. The guidance does not make any specific recommendations about the possibility of those close to a patient being present during determination of neurological death, although evidence on this approach was considered during development of the recommendations.

A prospective trial in the Netherlands by **Kompanje et al. (2012)** investigated the effect on consent rate of relatives' presence during determination of neurological death. Patients with severe and irreversible brain injury admitted to the ICU at any of 5 participating hospitals during the 15-month study period were screened. Patients were eligible if neurological death was suspected, they were suitable organ donors, and family members were present. Of 27 eligible relatives, 8 agreed to be present during determination of neurological death (GCS scoring, testing of brainstem reflexes, and the apnoea test). They were then asked to consider organ donation. The primary end point was consent to organ donation, but the recruitment target of 50 family members was not reached, so analysis of this outcome was not possible. Of the 8 relatives present during determination of neurological death, 7 (88%) consented to organ donation.

The secondary end point was relatives' understanding of neurological death as death of the patient (assessed via telephone 3 to 6 months after confirmation of neurological death). Relatives' views on being present during the process were also obtained. At telephone follow-up, family members showed mixed understanding of the concept of neurological death and had varying views on the value of being present during the determination process. The authors also noted that medical and technical staff were uneasy about having relatives present during neurological testing.

The study was considerably limited by the recruitment target not being reached, so no conclusions could be drawn on the primary end point of consent to organ donation. The low number of participants also meant that no statistically significant conclusions could be drawn. The authors stated that a reason for the recruitment issues may have been that common practice in the Netherlands is to gain consent before formal neurological testing, and staff may have been unwilling to break this practice to comply with the study protocol. Finally, there was a risk of reporting bias in the follow-up interviews with family members.

Limited evidence indicates that the effect on consent to organ donation of offering relatives the opportunity to be present during determination of neurological death in a family member is unclear. The possibility of being present during neurological testing is not covered explicitly by NICE CG135, but limitations of the evidence mean that this evidence is unlikely to have an impact on the guidance. More research is needed on whether having families present during neurological death testing improves consent for organ donation and is of psychological benefit to family members.

**Key reference**

Kompanje EJ, de Groot YJ, Bakker J et al. (2012) A national multicenter trial on family presence during brain death determination: the FABRA study. Neurocritical Care 17: 301–8

**Support for those close to the patient**

NICE CG135 recommends that before approaching those close to the patient, an assessment should be made of whether family support is required – for example faith representative, family liaison officer, bereavement service, trained interpreter, advocate. The multidisciplinary team involved in the initial approach to those close to the patient should have the necessary skills and knowledge to provide appropriate support and accurate information about organ donation. The multidisciplinary team should also include local faith representative(s) where relevant.

In all cases those close to the patient should be approached in a professional, compassionate and caring manner and given sufficient time to consider the information. For discussions where neurological death is anticipated, provide a clear explanation on how death is diagnosed using neurological criteria, how this is confirmed and what happens next.

A retrospective cross-sectional survey by **Jacoby and Jaccard (2010)** evaluated the support family members received when considering whether to donate the organs of a neurologically dead relative. The authors identified a study population of 326 families whose relative had died at 1 of 6 organ procurement organisations in the USA over a 6 year period. Potential participants were contacted 8 to 10 months after the death, and 199 family members agreed to participate (61% of those contacted). Participants were interviewed by telephone for 45 minutes during which they completed a 65-item questionnaire on the emotional, practical and informational support they had received during the consent process.

Overall, 154 (77%) of the 199 participants had agreed to donation. Family members who consented to donation were more likely than those who did not consent to:

- have had a member of staff or volunteer present who:
  - showed understanding (89% versus 76%, p=0.04)
  - was there in case of need (88% versus 71%, p=0.002)
  - listened (84% versus 62%, p=0.003)
  - gave them hope to go on (62% versus 33%, p=0.001).
- have been provided with physical necessities, such as blankets or toiletries (61% versus 40%, p=0.01).
- have received 'understandable' information about neurological death (79% versus 58%, p=0.002) and organ donation (90% versus 42%, p=0.001)
- have been given enough time to understand brainstem death before making a decision (73% versus 49%, p=0.001).

In a logistic regression analysis, provision of informational support correlated most strongly with consent to donation (r=0.55 for information about organ donation and r=0.35 for information about neurological death), followed by provision of emotional support (r=0.29) and practical support (r=0.19; p<0.01 for all). Family members who agreed to donation were more likely to feel that they and their relative had been treated with dignity and respect (p=0.002).

Limitations of the evidence included the retrospective nature of the study, with data comprising self-reports of past events that could be subject to recall bias. In addition, no data was available on the characteristics of family members who did not take part in the survey.

The evidence suggests that providing those close to the patient with support during consent, in particular providing information on neurological death and the consent process and time to consider the information, can improve the likelihood of consent. Training on these modifiable factors affecting consent could potentially be incorporated into professional education programmes. The evidence is consistent with NICE CG135, which recommends that those close to the patient should be given a clear explanation of how neurological death is confirmed using neurological criteria and the process of organ donation and retrieval, as well

as sufficient time to understand the inevitability of the death or anticipated death and to spend time with the patient.

More research is needed on whether family members who have a more positive experience of the consent process are more likely to consent and to identify components of the process that are key to improving the experience.

**Key reference**
Jacoby L, Jaccard J (2010) Perceived support among families deciding about organ donation for their loved ones: donor vs nondonor next of kin. American Journal of Critical Care 19: e52–61

## 1.7 Organisation of the identification, referral and consent processes

NICE CG135 recommends that all healthcare professionals involved in identification, referral to specialist nurse for organ donation, and consent processes should:

- have knowledge of the basic principles and the relative benefits of, DCD versus DBD
- understand the principles of the diagnosis of death using neurological or cardiorespiratory criteria and how this relates to the organ donation process
- be able to explain neurological death clearly to families
- understand the use of clinical triggers to identify patients who may be potential organ donors
- understand the processes, policies and protocols relating to donor management
- adhere to relevant professional standards of practice regarding organ donation and
- end-of-life care.

Consultant staff should have specific knowledge and skills in:

- the law surrounding organ donation
- medical ethics as applied to organ donation
- the diagnosis and confirmation of death using neurological or cardiorespiratory criteria
- the greater potential for transplantation of organs retrieved from DBD donors compared with organs from DCD donors
- legally and ethically appropriate clinical techniques to secure physiological optimisation in patients who are potential organ donors
- communication skills and knowledge necessary to improve consent ratios for organ donation.

A systematic review by **Bastami et al. (2013)** looked at the attitudes of the general public and of healthcare professionals to DCD. Peer-reviewed qualitative, quantitative and case studies about attitudes, opinions, views or perceptions of DCD were eligible. A total of 20 studies were included. A thematic analysis was then performed of the qualitative data. The themes identified among the included studies were: levels of support for DBD versus DCD; attitudes to post-mortem measures without previous consent; lack of knowledge about DCD; concerns about the 'dead donor rule' (which states that organs should be taken only from people who are dead); the potential for conflict of interest; making donation happen; and the call for standardised DCD protocols.

Several studies showed support for organ donation among the general public and healthcare professionals, although the evidence varied as to whether people supported DBD over DCD or vice versa. With DCD, people preferred that consent was obtained before organ preservation techniques were started. Several studies reported poor knowledge of DCD procedures among healthcare professionals, and one found that increased knowledge of the process among healthcare professionals correlated with support for DCD. Determining death and application of the dead donor rule was an area of concern among healthcare

professionals, with many preferring brainstem death rather than circulatory death as a means of declaring death. A recurring theme was the potential conflict of interest between caring for the donor and optimising the likelihood of successful DCD, which caused some mistrust of healthcare professionals among the public. People were keen that patients and relatives who wanted to donate organs after circulatory death were supported to do so, and many wanted standardised DCD protocols to facilitate this.

Limitations of the evidence included that most (14 out of 20) of the studies analysed were from the USA and all were in English, which may limit the generalisability of the findings. In addition, only 1 reviewer assessed study quality, which could cause reviewer bias.

The evidence suggests that education of healthcare professionals and the general public on organ donation procedures could positively influence attitudes towards donation and consent rates. This evidence strengthens the recommendation in NICE CG135 that healthcare professionals should understand the basic principles DCD and DBD, and of diagnosis of death using neurological or cardiorespiratory criteria, and be able to explain these concepts clearly to families.

**Key reference**
Bastami S, Matthes O, Krones T et al. (2013) Systematic review of attitudes toward donation after cardiac death among healthcare providers and the general public. Critical Care Medicine 41: 897–905

# 2    New evidence uncertainties

During the development of the Evidence Update, the following evidence uncertainties were identified for the UK Database of Uncertainties about the Effects of Treatments (UK DUETs).

**Discussions in all cases**

- Does family presence during brain stem death (BSD) diagnosis increase consent to organ donation?

Further evidence uncertainties for organ donation can be found in the UK DUETs database and in the NICE research recommendations database.

UK DUETs was established to publish uncertainties about the effects of treatments that cannot currently be answered by referring to reliable up-to-date systematic reviews of existing research evidence.

# Appendix A: Methodology

## Scope

The scope of this Evidence Update is taken from the scope of the reference guidance:

- Organ donation for transplantation. NICE clinical guideline 135 (2011)

## Searches

The literature was searched to identify studies and reviews relevant to the scope. Searches were conducted of the following databases, covering the dates 1 June 2010 (the end of the search period of NICE clinical guideline 135) to 14 August 2013:

- CDSR (Cochrane Database of Systematic Reviews)
- CENTRAL (Cochrane Central Register of Controlled Trials)
- CINAHL (Cumulative Index to Nursing and Allied Health Literature)
- DARE (Database of Abstracts of Reviews of Effects)
- HTA (Health Technology Assessment) database
- MEDLINE (Medical Literature Analysis and Retrieval System Online)
- MEDLINE In-Process
- NHS EED (Economic Evaluation Database)

The Evidence Update search strategies replicate the strategy used by the original guidance as far as possible. The search strategy used for this Evidence Update was based on the strategies used by the original guidance for key words, index terms and concepts, combining these into a single search.

Table 1 provides details of the MEDLINE search strategy used (based on the search strategy for the reference guidance), which was adapted to search the other databases listed above.
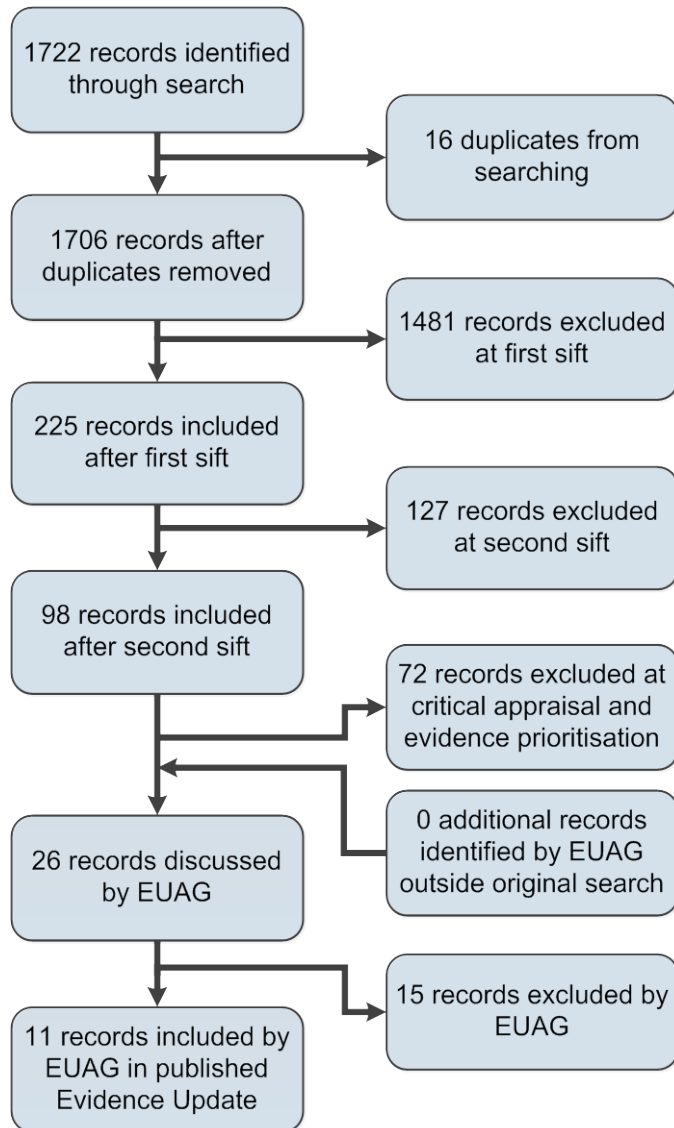
Figure 1 provides details of the evidence selection process. The long list of evidence excluded after review by the Chair of the EUAG, and the full search strategies, are available on request from contactus@evidence.nhs.uk

There is more information about how NICE Evidence Updates are developed on the NICE Evidence Services website.

**Table 1 MEDLINE search strategy (adapted for individual databases)**

| | |
|---|---|
| 1 | exp Death, Sudden/ |
| 2 | Brain death/ |
| 3 | (("brain stem" or brainstem or brain-stem or brain or neuro* or medulla*) adj3 (death* or dead or injur* or sever* or irreversib* or damage* or traum* or fail* or arrest*)).ti,ab. |
| 4 | ((cardiac or heart or cardio*) adj3 (death* or injur* or sever* or irreversib* or damage* or traum* or fail* or arrest*)).ti,ab. |
| 5 | (post mortem* or cadaver* or dead or death* or deceased).ti,ab. |
| 6 | or/1-5 |
| 7 | exp "Tissue and organ procurement"/ or Tissue donors/ |
| 8 | ((don* or procur*) adj3 (tissue* or organ*)).ti,ab. |
| 9 | or/7-8 |
| 10 | Decision Making/ |
| 11 | (identif* or select* or confirm* or establish* or ascertain* or verif* or distinguish* or classif* or recogniz* or recognis* or determin* or deci* or qualif* or refer* or recruit* or initiat* or criteri* or accept* or potential* or attitud* or characteris* or find* or discover* or verif* or diagnos*).ti,ab. |
| 12 | exp Informed Consent/ or exp Third-Party Consent/ or exp Consent Forms/ or exp Presumed Consent/ or exp Parental Consent/ |
| 13 | (consent* or agree* or accept* or allow* or permi* or sanction* or approv* or cooperat* or co-operat* or compl* or obtain* or assent* or |

| | |
|---|---|
| | authoris* or authoriz* or concur* or accede* or endors*).ti,ab. |
| 14 | Time/ or Time Factors/ or Time Management/ |
| 15 | (time* or timing*).ti,ab. |
| 16 | 14 or 15 |
| 17 | 12 or 13 |
| 18 | 16 and 17 |
| 19 | Critical pathways/ |
| 20 | "Delivery of Health Care, Integrated"/ |
| 21 | Patient care planning/ |
| 22 | ((care or clinical or integrated or multidisciplinary or critical) adj3 (pathway* or path* or plan* or protocol* or procedure* or program* or programme* or manag* or process* or outline* or algorithm* or map* or schedul*)).ti,ab. |
| 23 | 10 or 11 or 12 or 13 or 18 or 19 or 20 or 21 or 22 |
| 24 | 6 and 9 and 23 |
| 25 | trigger*.ti,ab. |
| 26 | "Referral and Consultation"/ |
| 27 | Models, Organizational/ |
| 28 | ("task force" or "taskforce" or "task-force").ti,ab. |
| 29 | or/25-28 |
| 30 | 9 and 29 |
| 31 | 24 or 30 |
| 32 | animals/ not humans/ |
| 33 | 31 not 32 |

**Figure 1 Flow chart of the evidence selection process**

```
┌─────────────────────────┐
│ 1722 records identified │
│    through search       │
└─────────────────────────┘
            │              ┌─────────────────────────┐
            ├─────────────▶│  16 duplicates from     │
            │              │      searching          │
            ▼              └─────────────────────────┘
┌─────────────────────────┐
│  1706 records after     │
│  duplicates removed     │
└─────────────────────────┘
            │              ┌─────────────────────────┐
            ├─────────────▶│  1481 records excluded  │
            │              │     at first sift       │
            ▼              └─────────────────────────┘
┌─────────────────────────┐
│  225 records included   │
│     after first sift    │
└─────────────────────────┘
            │              ┌─────────────────────────┐
            ├─────────────▶│  127 records excluded   │
            │              │     at second sift      │
            ▼              └─────────────────────────┘
┌─────────────────────────┐
│  98 records included    │
│    after second sift    │
└─────────────────────────┘
            │              ┌───────────────────────────┐
            ├─────────────▶│  72 records excluded at   │
            │              │  critical appraisal and   │
            │              │  evidence prioritisation  │
            │              └───────────────────────────┘
            │              ┌───────────────────────────┐
            │◀─────────────│  0 additional records     │
            │              │  identified by EUAG       │
            ▼              │  outside original search  │
┌─────────────────────────┐└───────────────────────────┘
│  26 records discussed   │
│      by EUAG            │
└─────────────────────────┘
            │              ┌─────────────────────────┐
            ├─────────────▶│  15 records excluded by │
            │              │        EUAG             │
            ▼              └─────────────────────────┘
┌─────────────────────────┐
│  11 records included by │
│  EUAG in published      │
│  Evidence Update        │
└─────────────────────────┘
```

EUAG – Evidence Update Advisory Group

# Appendix B: The Evidence Update Advisory Group and Evidence Update project team

## Evidence Update Advisory Group

The Evidence Update Advisory Group is a group of topic experts who review the prioritised evidence obtained from the literature search and provide the commentary for the Evidence Update.

**Dr Angus Vincent – Chair**

Consultant in Intensive Care Medicine and Anaesthesia, Newcastle upon Tyne Hospitals NHS Foundation Trust

**Simon Bramhall**

Consultant HPB & Liver Transplant Surgeon, University Hospital Birmingham NHS Foundation Trust

**Dr James Fraser**

Consultant in Paediatric Intensive Care, Bristol Royal Hospital for Children

**Karen Morgan**

Regional Manager, Organ Donation and Transplantation, NHS Blood and Transplant, Bristol

**Professor Ronan O'Carroll**

Professor of Psychology, University of Stirling

**Dr Huw Twamley**

Consultant in Critical Care and Anaesthesia, Lancashire Teaching Hospitals NHS Foundation Trust, Preston

**Professor Gurch Randhawa**

Professor of Diversity in Public Health and Director, University of Bedfordshire

## Evidence Update project team

**Marion Spring**
Associate Director

**Dr Chris Alcock**
Clinical Lead – NICE Evidence Services

**Chris Weiner**
Consultant Clinical and Public Health Adviser

**Cath White**
Programme Manager

**Swapna Mistry**
Project Manager

**Fran Wilkie**

Critical Appraiser

**Michael Raynor**

Information Specialist

**Helen Jaques**

Medical Writer