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The birth of the European Liver transplant registry

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This personal account, written on the occasion of the fortieth anniversary of the European Liver Transplant Registry (ELTR), traces the origins of the Registry from the earliest days of liver transplantation in Europe to its present scale. Beginning with a handful of pioneering centres in the 1970s and the scepticism that surrounded the procedure, the narrative follows the events of 1983 that transformed the field, the creation of an informal registry at Paul Brousse, and its extension to a European network following a founding meeting in Hannover in October 1985. It describes the early design choices that shaped the Registry, the methodological debates that defined its core definitions, and the scientific contributions that followed, including landmark findings on patient survival and on hepatitis B recurrence after transplantation, as well as the 1993 Paris Consensus Conference on indications for liver transplantation. The account closes with the Registry's transition to new stewardship and its present scope, spanning more than 200,000 transplants recorded across 32 countries. The history illustrates how informal, trust-based collaboration among a small number of European surgeons gave rise to one of the longest-running transplant registries in the world.

KEYWORDS
consensus conference, European liver transplant registry, hepatitis B, history of medicine, liver transplantation

Introduction

This manuscript, which I am honoured to present on the occasion of the European Liver Transplant Registry's (ELTR) fortieth anniversary, tells the story of how it began, and of the European transplant community that made it possible.

Origins and early context

There is, as with any birth, a precise date - 16 October 1986 - and a precise place: Hannover. And before this "birth" came its "pregnancy": a year earlier in Paris, when the small group of French surgeons beginning liver transplantation met to share their first experiences.

I recall those years vividly. When we performed our first liver transplant at Paul Brousse in 1974, a single case (that, at the time, represented twenty-five per cent of all European experience!), I could not have imagined where that first operation would lead. Liver transplantation in Europe was confined to a very small number of centres. Cambridge, under Roy Calne, and Hannover, under Rudolph Pichlmayr, were the dominant units. A handful of others, Vienna, Paul Brousse, Innsbruck, and Groningen, had performed only modest numbers of procedures, and some experience was frankly anecdotal (Table 1).

TABLE 1 European Canters' activity before 1984 (17 centers).

Center	Head	Date of 1st LT	No LT before 1984
Cambridge	R. Calne	02/05/1968	147
Wien	F. Pisa	10/07/1972	17
Hannover	R. Pichlmayr	25/11/1972	109
Paris P. Brousse	H. Bismuth	14/01/1974	17
Bordeaux	J. Saric	06/09/1974	2
Innsbruck	R. Margreiter	03/02/1977	11
Strasbourg	J. Cinqualbre	02/02/1978	6
Rennes	B. Launois	21/04/1978	6
Groningen	MJH. Sloof	12/03/1979	34
Birmingham	P. McMaster	23/01/1982	9
Paris Cochin	Y. Chapuis	29/03/1982	1
Roma	R. Cortesini	20/05/1982	2
Helsinki	C. Hockerstedt	12/12/1982	1
Berlin	R. Häring	12/04/1983	2
Brussels	JB. Otte	21/12/1983	1
Milan	D. Galmarini	09/06/1983	1
Bern	P. Gertsch	19/12/1983	2

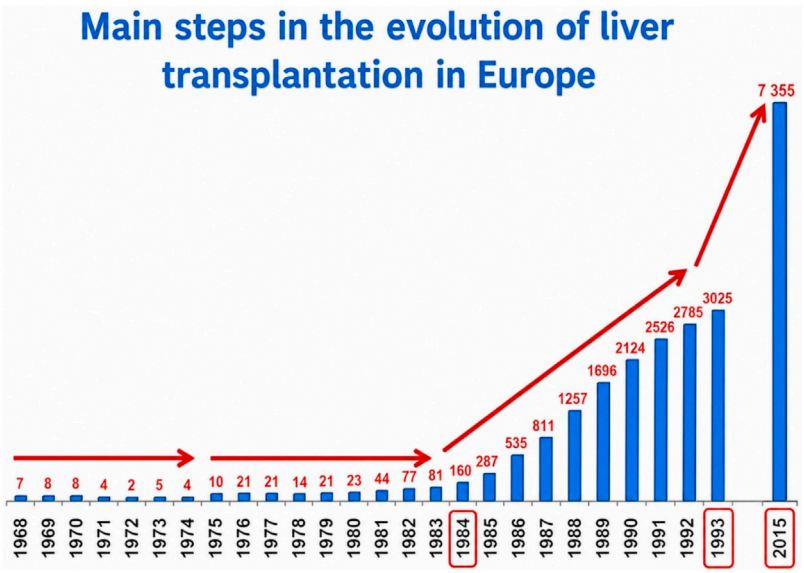
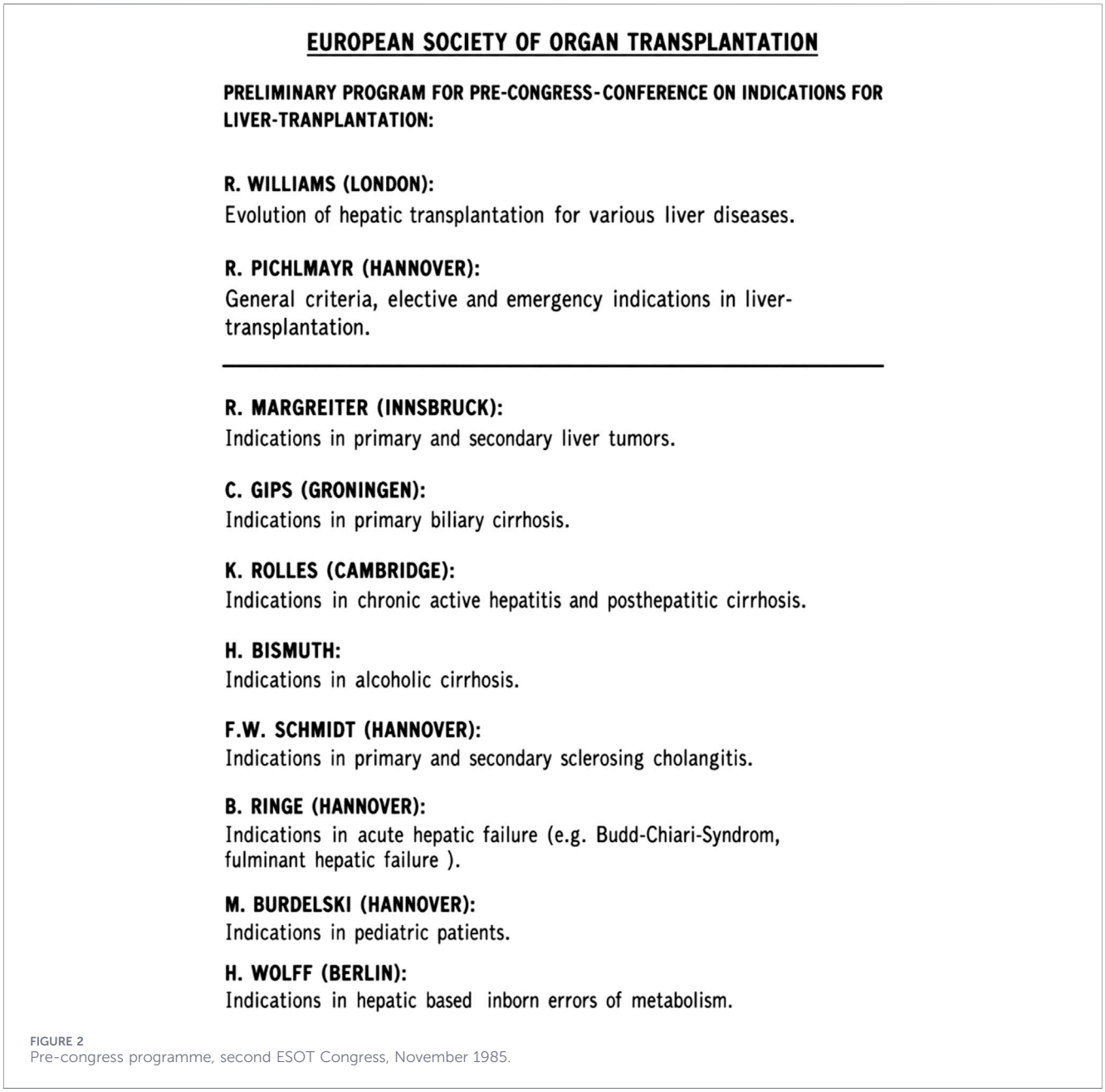


FIGURE 1
Annual liver transplant volume in Europe, 1968–2015.

The clinical atmosphere was far from encouraging. Patients were referred for transplantation only as a last resort, and mortality was substantial. Dame Sheila Sherlock of the Royal Free Hospital had written that a liver transplant recipient could be regarded as fortunate if he survived 6 months post-operatively, and that the procedure was not justified when the natural course of disease would allow the patient to live longer. In July 1980, Thomas Starzl published data documenting a decline in survival after liver transplantation, reinforcing the prevailing scepticism [1].



EUROPEAN SOCIETY OF ORGAN TRANSPLANTATION

PRELIMINARY PROGRAM FOR PRE-CONGRESS-CONFERENCE ON INDICATIONS FOR LIVER-TRANPLANTATION:

R. WILLIAMS (LONDON):
Evolution of hepatic transplantation for various liver diseases.

R. PICHLMAYR (HANNOVER):
General criteria, elective and emergency indications in liver-transplantation.

R. MARGREITER (INNSBRUCK):
Indications in primary and secondary liver tumors.

C. GIPS (GRONINGEN):
Indications in primary biliary cirrhosis.

K. ROLLES (CAMBRIDGE):
Indications in chronic active hepatitis and posthepatitic cirrhosis.

H. BISMUTH:
Indications in alcoholic cirrhosis.

F.W. SCHMIDT (HANNOVER):
Indications in primary and secondary sclerosing cholangitis.

B. RINGE (HANNOVER):
Indications in acute hepatic failure (e.g. Budd-Chiari-Syndrom, fulminant hepatic failure).

M. BURDELSKI (HANNOVER):
Indications in pediatric patients.

H. WOLFF (BERLIN):
Indications in hepatic based inborn errors of metabolism.

FIGURE 2
Pre-congress programme, second ESOT Congress, November 1985.

The 1983 turning point

Two events in 1983 changed the landscape decisively. First, the Washington Consensus Development Conference addressed the question of whether liver transplantation constituted a genuine treatment for end-stage liver disease. At that time, the US insurance companies routinely declined to reimburse the procedure because it remained experimental. Following deliberations led principally by Thomas Starzl, the Conference concluded that liver transplantation was a promising alternative to current therapy in the management of the late phase of several forms of serious liver disease, and that it had the potential to transition from an experimental procedure to a clinical service [2]. This endorsement was pivotal.

Second, the clinical introduction of cyclosporine, through the pioneering work of Roy Calne, transformed immunosuppressive management and dramatically improved outcomes. Together, these developments produced a striking inflection in activity: annual liver transplant volumes rose from single figures to two-digit numbers within a very short period (Figure 1).

The French prototype registry

In 1984, the Paul Brousse experience was still very limited: only 19 cases over 10 years. Other French centres soon joined us - Strasbourg, Rennes, Bordeaux, Cochin, and Saint-Antoine. We were working in relative isolation within our hospitals; most hepatologists showed little interest, and the literature was scarce

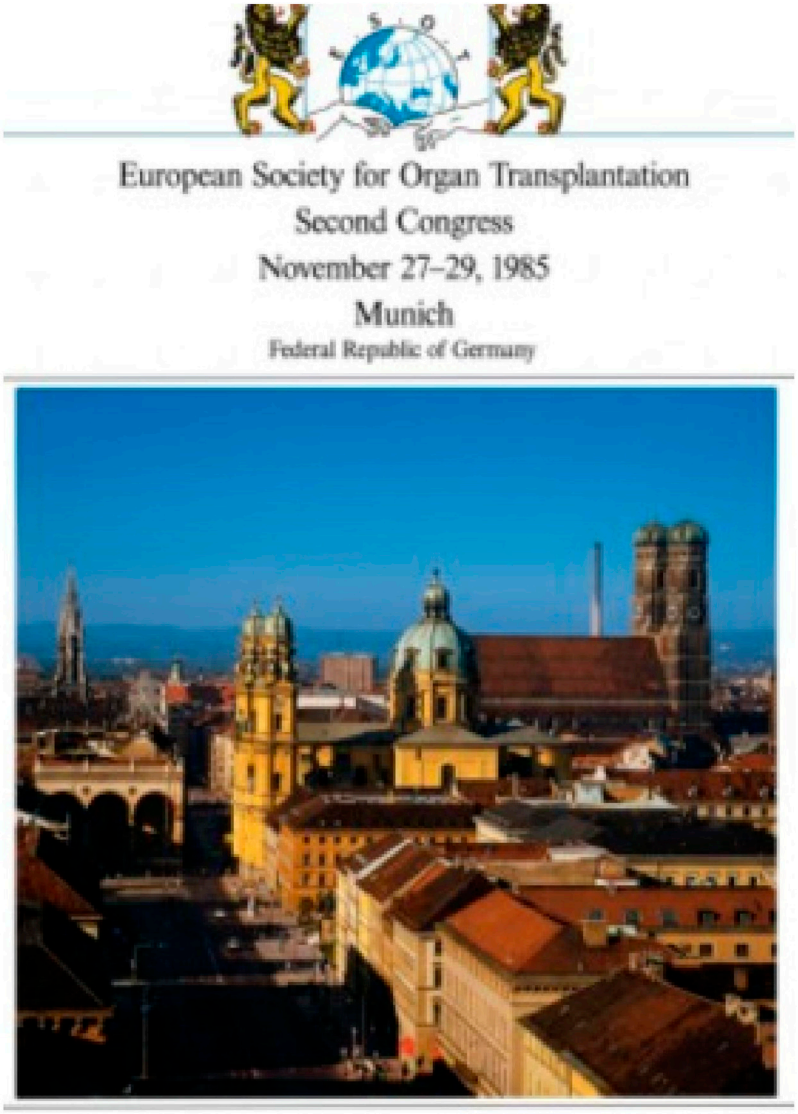


FIGURE 3
Second ESOT Congress, Munich, November 27–29, 1985.

and largely experimental. We therefore decided to hold regular meetings to discuss our patients. To prepare for these meetings and structure our discussions, I proposed to compile our cases in advance in a sort of registry, which was circulated to the group before each meeting. It was a simple list of cases, recording disease aetiology, type of transplant, and key complications. This informal French registry, born at Paul Brousse, served as the direct model for what would follow at the European level.

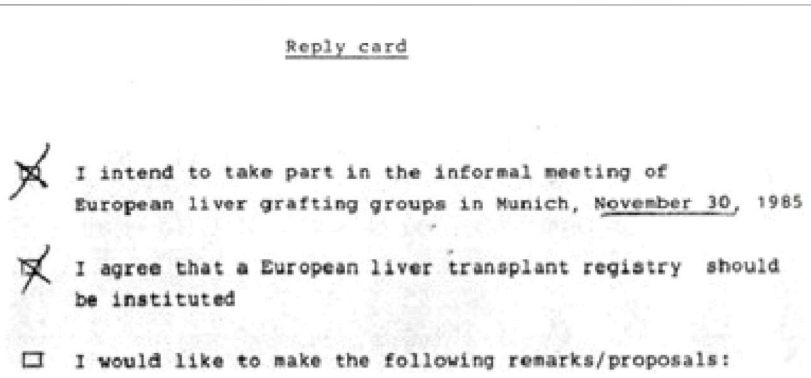
When the European Society for Organ Transplantation (ESOT) held its inaugural congress in 1983 in Zurich, there were only two presentations on liver transplantation. But for the first time, the small group of European liver transplant surgeons met. At the subsequent International Transplantation Society congress, in 1984, our group decided to convene a dedicated liver transplantation session at the second ESOT congress, scheduled for late November 1985 in Munich, with the session organised by Rudolf Pichlmayr (Figure 2).

The founding meeting, hannover, 16 October 1985

One month before the Munich congress, Pichlmayr convened a preparatory meeting in Hannover on 16 October 1985. Those present included Roy Calne, Carl Groth, Maarten Sloof, and myself, five participants in all. It was at that meeting that I proposed extending the French registry to the European level. The proposal was immediately accepted, and I confess that the swiftness of that acceptance surprised even me.

At the subsequent Munich ESOT on 27 November 1985 (Figure 3), at the end of the Liver session, I proposed the concept of this Registry.

A short circular was distributed, the first document to bear the name “European Liver Transplant Registry” (Figure 4), inviting centers to participate in what we described as the first collaborative

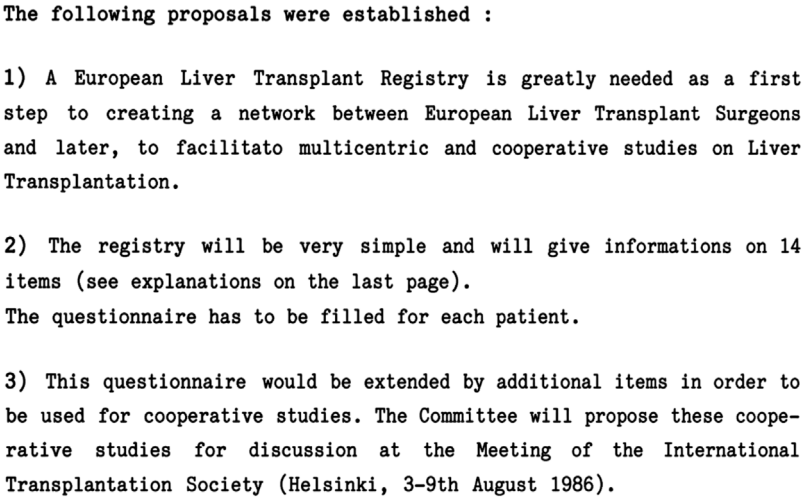

Reply card

☒ I intend to take part in the informal meeting of European liver grafting groups in Munich, November 30, 1985

☒ I agree that a European liver transplant registry should be instituted

☐ I would like to make the following remarks/proposals:

FIGURE 4
Reply card circulated to potential ELTR participants, November 1985.


The following proposals were established :

1) A European Liver Transplant Registry is greatly needed as a first step to creating a network between European Liver Transplant Surgeons and later, to facilitato multicentric and cooperative studies on Liver Transplantation.

2) The registry will be very simple and will give informations on 14 items (see explanations on the last page).
The questionnaire has to be filled for each patient.

3) This questionnaire would be extended by additional items in order to be used for cooperative studies. The Committee will propose these cooperative studies for discussion at the Meeting of the International Transplantation Society (Helsinki, 3-9th August 1986).

FIGURE 5
Founding objectives of the ELTR (1986).

exchange of the European liver grafting groups. The response was positive.

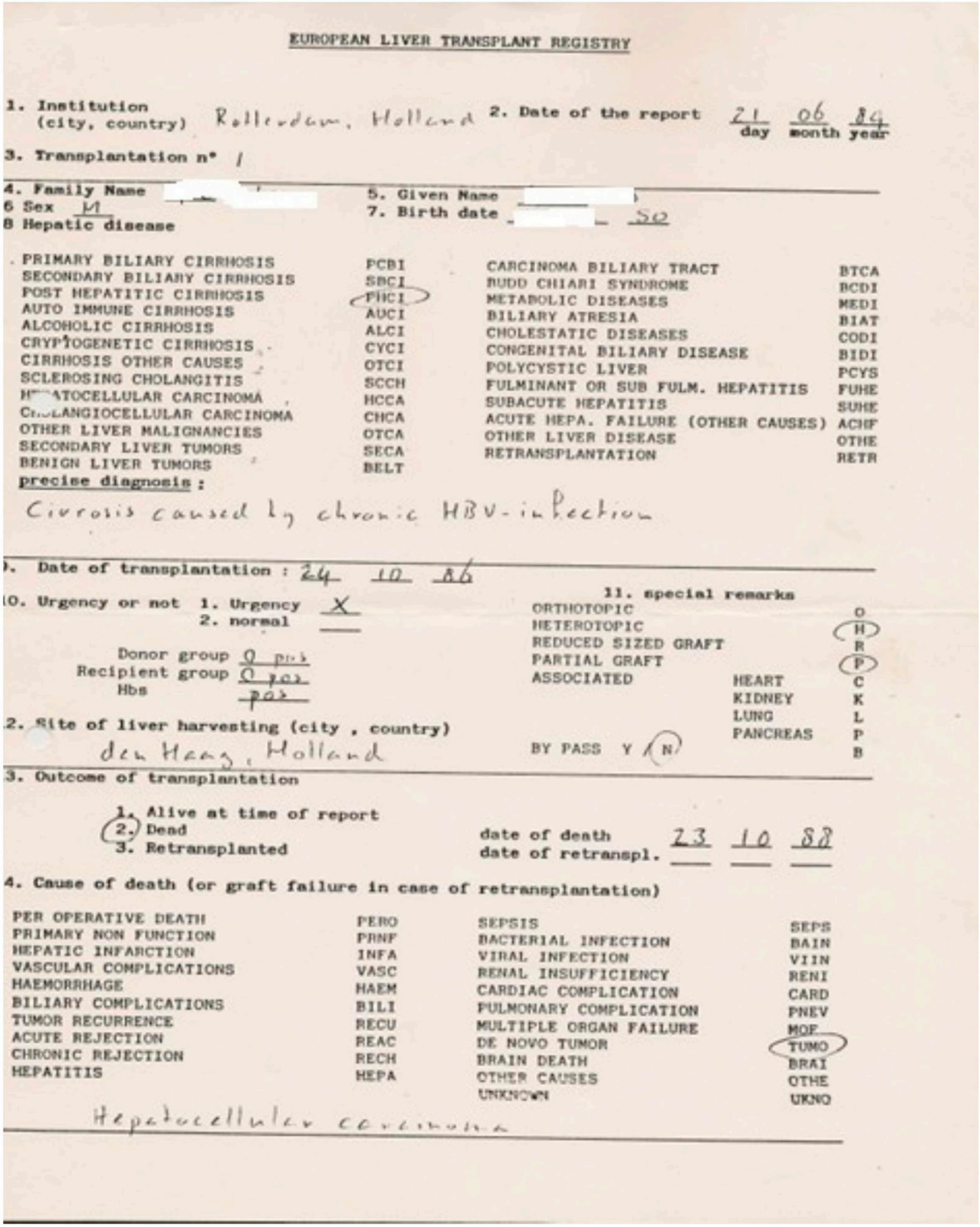
A coordinating committee was constituted, comprising Bo-Göran Ericzon, Jean-Bernard Otte, Burckhardt Ringe, Keith Rolles, and Maarten Sloof. The first formal ELTR meeting was held in Paris on 7 January 1986, at which the registry's objectives were defined (Figure 5).

Design principles and early operation

From the outset, I insisted that the ELTR questionnaire be kept deliberately simple (Figure 6). Simplicity was, in my view, essential for ensuring compliance from contributing centres. Coverage was intended to be comprehensive: all liver transplants performed in Europe were to be included, so as to produce a representative and statistically robust dataset. With Cambridge and Hannover, the two largest units, having agreed to participate, we assumed that others would follow, and they did.

Updates were planned on a quarterly basis, an ambitious schedule that proved workable in practice. Because neither personal computers nor the internet existed in any practical form at the time, data submission relied entirely on paper questionnaires. Hundreds of completed forms were received at Paul Brousse. I must pay particular tribute to my co-worker Denis Castaing, whose management of data entry and statistical analysis was indispensable to the early operation of the registry. Without his rigour, the ELTR could not have functioned.

It was only on 15 September 1995 that Vincent Karam joined the ELTR team, initiating the shift towards a fully professionalised secretariat, with biostatistician Valérie Cailliez and secretary Eva Cochet, whose work would underpin and advance the Registry in the years that followed.



EUROPEAN LIVER TRANSPLANT REGISTRY

1. Institution (city, country) Rotterdam, Holland 2. Date of the report 21 day 06 month 84 year

3. Transplantation n° 1

4. Family Name [redacted] 5. Given Name [redacted]
6 Sex M 7. Birth date [redacted] 50
8 Hepatic disease

PRIMARY BILIARY CIRRHOSIS	PCBI	CARCINOMA BILIARY TRACT	BTCA
SECONDARY BILIARY CIRRHOSIS	SBCI	BUDD CHIARI SYNDROME	BCDI
POST HEPATITIC CIRRHOSIS	PHCI	METABOLIC DISEASES	MEDI
AUTO IMMUNE CIRRHOSIS	AUCI	BILIARY ATRESIA	BIAT
ALCOHOLIC CIRRHOSIS	ALCI	CHOLESTATIC DISEASES	CODI
CRYPTOGENETIC CIRRHOSIS	CYCI	CONGENITAL BILIARY DISEASE	BIDI
CIRRHOSIS OTHER CAUSES	OTCI	POLYCYSTIC LIVER	PCYS
SCLEROSING CHOLANGITIS	SCCH	FULMINANT OR SUB FULM. HEPATITIS	FUHE
HEPATOCELLULAR CARCINOMA	HCCA	SUBACUTE HEPATITIS	SUHE
CHOLANGIOCELLULAR CARCINOMA	CHCA	ACUTE HEPA. FAILURE (OTHER CAUSES)	ACHF
OTHER LIVER MALIGNANCIES	OTCA	OTHER LIVER DISEASE	OTHE
SECONDARY LIVER TUMORS	SECA	RETRANSPLANTATION	RETR
BENIGN LIVER TUMORS	BELT		

precise diagnosis : Cirrosis caused by chronic HBV-infection

9. Date of transplantation : 24 10 86

10. Urgency or not 1. Urgency X 2. normal ___

Donor group O pos
Recipient group O pos
Hbs pos

11. special remarks

ORTHOTOPIC		O
HETEROTOPIC		H
REDUCED SIZED GRAFT		R
PARTIAL GRAFT		P
ASSOCIATED	HEART	C
	KIDNEY	K
	LUNG	L
	PANCREAS	P
BY PASS Y / N		B

12. Site of liver harvesting (city , country) den Haag, Holland

13. Outcome of transplantation

1. Alive at time of report
2. Dead
3. Retransplanted

date of death 23 10 86
date of retranspl. ___ ___ ___

14. Cause of death (or graft failure in case of retransplantation)

PER OPERATIVE DEATH	PERO	SEPSIS	SEPS
PRIMARY NON FUNCTION	PRNF	BACTERIAL INFECTION	BAIN
HEPATIC INFARCTION	INFA	VIRAL INFECTION	VIIN
VASCULAR COMPLICATIONS	VASC	RENAL INSUFFICIENCY	RENI
HAEMORRHAGE	HAEM	CARDIAC COMPLICATION	CARD
BILIARY COMPLICATIONS	BILI	PULMONARY COMPLICATION	PNEV
TUMOR RECURRENCE	RECU	MULTIPLE ORGAN FAILURE	MOF
ACUTE REJECTION	REAC	DE NOVO TUMOR	TUMO
CHRONIC REJECTION	RECH	BRAIN DEATH	BRAI
HEPATITIS	HEPA	OTHER CAUSES	OTHE
		UNKNOWN	UKNO

Hepatocellular carcinoma

FIGURE 6
First ELTR questionnaire (1986 - 21 items).

Methodological challenges

Early operation revealed important definitional ambiguities. When Paul Brousse submitted a case of intraoperative death due to haemorrhage, it appeared to be the first case reported, and it became apparent that other centres had excluded such events because transplantation had not been completed. This discrepancy prompted a formal debate on when transplantation should be

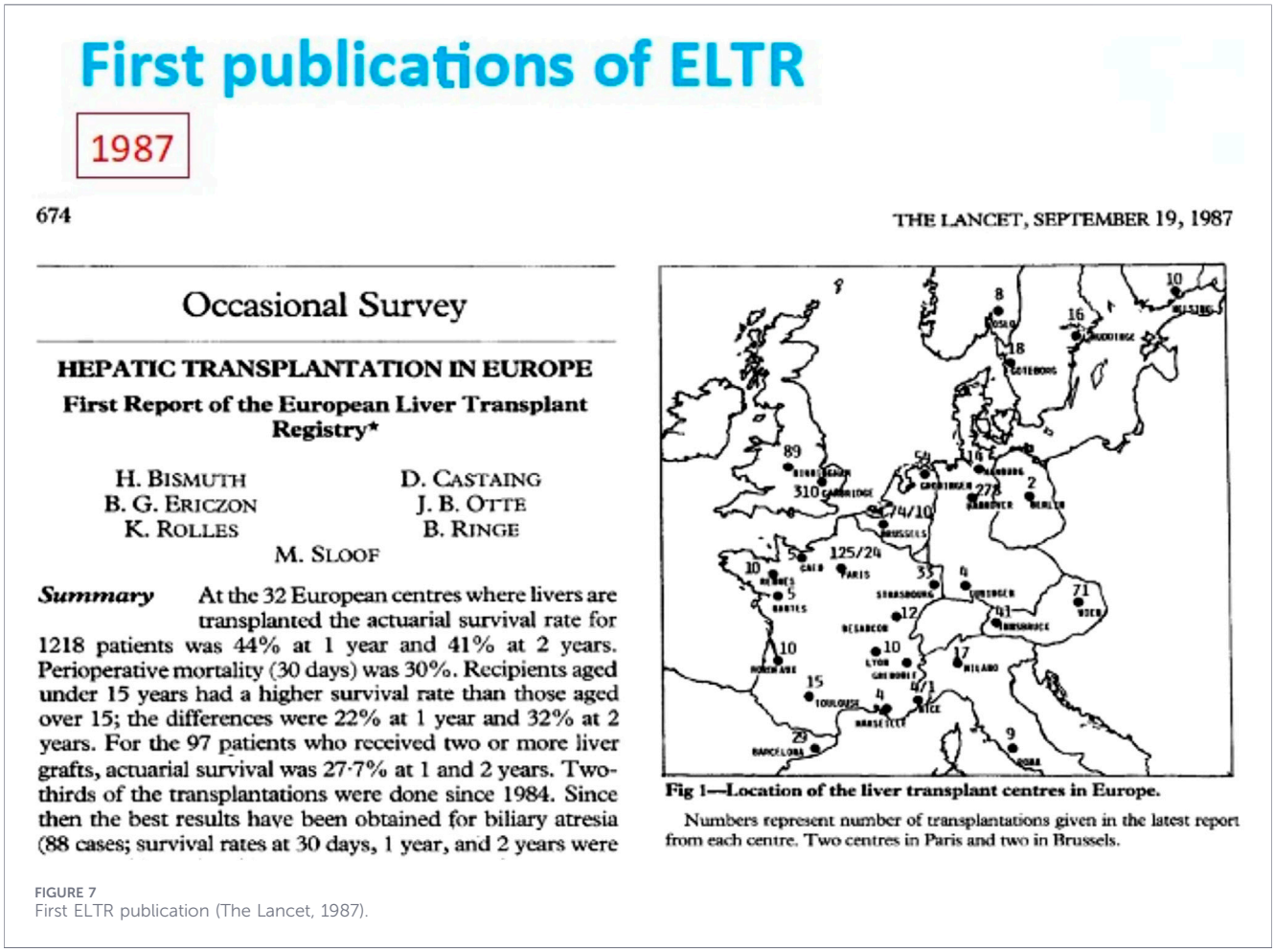


FIGURE 7
First ELTR publication (The Lancet, 1987).

considered to have occurred and should be registered: at anaesthetic induction, at laparotomy, at hepatectomy, at graft implantation, or at vascular declamping?

We reached consensus that transplantation is complete, and the patient is therefore registrable, at the moment of vascular declamping, when the graft first becomes functional. That definition has remained in use ever since, though I have always acknowledged its imperfections: in hepatic resection, deaths at any point during the procedure are attributed to the operation, a standard that our transplant definition does not fully replicate.

Scientific contributions

Data collection began in 1986, and the first ELTR report was published the following year in The Lancet, in September 1987, based on 1,218 patients [3]. It was, at the time, the largest liver transplant series in the world, assembling data from centres across Europe. One-year and two-year patient survival rates of 44% and 41%, respectively, constituted a definitive rebuttal of the earlier pessimism that had surrounded the field, and confirmed liver transplantation as a valid therapeutic option for end-stage liver disease (Figure 7).

The Registry had been criticised since the beginning for the paucity of the data collected, not enabling it to be used for valuable scientific studies. The registry's second major scientific contribution arose from work on hepatitis B virus (HBV) recurrence after transplantation. My colleague Didier Samuel was investigating prophylactic immunoglobulin therapy to prevent HBV recurrence on the graft, but individual centres had insufficient patient numbers for a convincing study. However, the Registry allowed us to identify the centres with the largest number of HBV-transplanted patients through the ELTR network. By distributing to these centers an extended questionnaire, we assembled a collaborative dataset that formed the basis for a landmark publication in the New England Journal of Medicine in 1993 [4]. That paper established prophylactic immunoglobulin as the standard of care for HBV-infected transplant recipients, and I regard it as one of the registry's most consequential contributions.

A further landmark came in June 1993 with the second Consensus Development Conference, held in Paris exactly 10 years after the Washington conference. That Conference aimed to answer the question: Is Liver Transplantation a therapeutic procedure? Now the question was: To which patient? Drawing on the ELTR database, an international panel that included Thomas Starzl, Ronald Busuttil, Nancy Ascher, and European liver transplant surgeons and hepatologists (Roy Calne, Roger Williams, Rudolf Pichlmaier, Carl Groth, Bo-Göran Ericzon, Jean-Pierre Benhamou, Marteen Sloof, Jean Bernard Otte, Paul McMaster) produced a consensus statement defining the actual indications

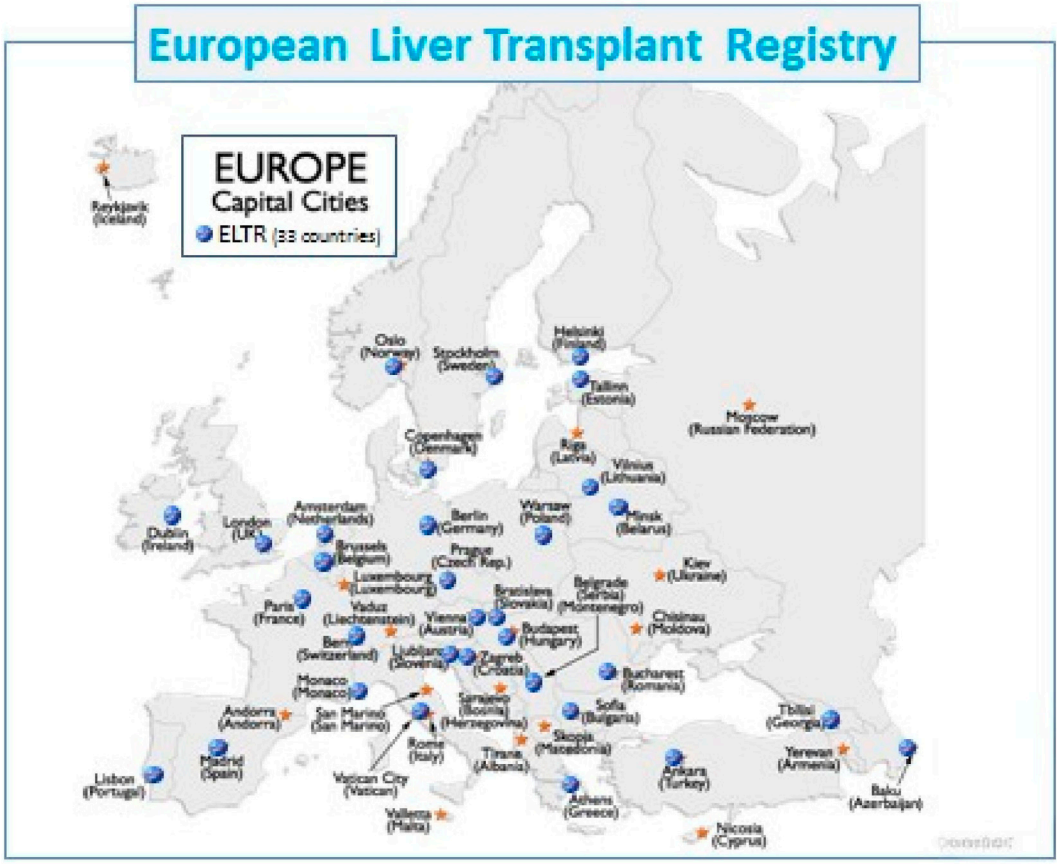


FIGURE 8
European Liver Transplant Registry - 32 participating countries.

for liver transplantation. The Paris Consensus, published in a special issue of Hepatology, shaped clinical practice globally for years thereafter [5].

Transition and maturity

In 1997, twelve years after the registry's foundation, I transferred stewardship of the ELTR to René Adam, who guided the Registry through its consolidation and expansion.

Quality assurance became an explicit priority, with audit visits to contributing centres initiated in 1998 and led by Vincent Karam, who assembled and coordinated a multinational team to verify the accuracy and completeness of the data.

A formal quality-control programme, reported in 2003, confirmed the registry's reliability and credibility as a representative source of data on European liver transplant practice [6].

The ELTR predated the European Liver and Intestine Transplant Association (ELITA) and may have contributed to the conditions that enabled its formation. Equally, the registry's pan-European scope gave it a significance beyond the purely scientific: at its inception, European scientific cooperation was still in its infancy, and the ELTR offered a model for collaborative data-sharing that transcended national boundaries.

The ELTR today

Today, the ELTR has accumulated data on more than 200,000 liver transplants performed in 174 centres across 32 countries. More than 114 peer-reviewed publications have drawn on its dataset, and registry data have underpinned the development of risk models for predicting liver transplant outcomes. The ELTR owes its enduring success not only to its founders, successive custodians, and ELITA board members, but also to the sustained commitment of all contributing European liver transplant centres and organ-sharing organisations (Figure 8).

Looking back, what strikes me most is not the scale the registry has reached, but the simplicity of what began it: a handful of surgeons, in Hannover on an October afternoon, agreeing that we would do better together than apart. The ELTR was built on trust, and it is trust that has sustained it.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

Ethical approval was not required for the study involving humans in accordance with the local legislation and institutional requirements. Written informed consent to participate in this study was not required from the participants or the participants' legal guardians/next of kin in accordance with the national legislation and the institutional requirements.

Author contributions

HB developed this point of view with the support of Vincent Karam, acknowledged at the end of the manuscript.

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Conflict of interest

The author(s) declared that this work was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Generative AI statement

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