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Cohort Profile: The Management of Post-transplant Infections in Collaborating Hospitals (MATCH) Program - A prospective cohort of all transplant recipients at Copenhagen University Hospital – Rigshospitalet, Denmark

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Cohort Profile: The Management of Post-transplant Infections in Collaborating Hospitals (MATCH) Program

- A prospective cohort of all transplant recipients at Copenhagen University Hospital – Rigshospitalet, Denmark

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Abstract

Purpose The MATCH program, initiated in 2011 and still ongoing, was created to: 1) optimize the implementation of existing preventive strategies against viral infections in solid organ transplant (SOT) recipients and allogeneic hematopoietic stem-cell transplant (HSCT) recipients, and 2) advance research in the field of transplantation by collecting data from a multitude of sources.

Participants All SOT and HSCT recipients at Copenhagen University Hospital, Rigshospitalet, are followed in MATCH. By February 2021, a total of 1192 HSCT recipients and 2039 SOT recipients have been included. Participants are followed life-long. An automated electronic data capture system retrieves prospective data from nationwide registries. Data from the years prior to transplantation are also collected.

Findings to Date Data entries before and after transplantation include: Biochemistry: 13,995,222 and 26,127,817; Microbiology, cultures: 242,023 and 410,558; Other microbiological analyses: 265,007 and 566,402; and Pathology: 170,884 and 200,394. There are genomic data on 2,431 transplant recipients, whole blood biobank samples from 1,003 transplant recipients and faeces biobank samples from 207 HSCT recipients. Clinical data collected in MATCH has contributed to 50 scientific papers published in peer-reviewed journals and has demonstrated success in reducing CMV-disease in SOT recipients. The program has established international collaborations with the Swiss Transplant Cohort Study and the lung transplant cohort at Toronto General Hospital.

Future Plans Enrolment into MATCH is ongoing with no planned end date for enrolment or follow-up. MATCH will continue to provide high quality data on transplant recipients and expand and strengthen international collaborations.

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Strengths and limitations of this study

1. MATCH is an unselected prospective cohort with complete enrolment, encompassing all transplant recipients at Rigshospitalet, Copenhagen University Hospital, Denmark.
2. All patients followed in MATCH have a civil registration number, and linkage to the Danish civil registration system ensures almost complete life-long follow-up despite patients being transferred to other centres in Denmark.
3. The Danish civil registration system allows for linkage to multiple nationwide registries containing data on e.g. biochemistry, pathology, microbiology, imaging, prescriptions and hospital contacts, including ICD-codes for diagnoses and procedures, both from the period before and after transplantation.
4. MATCH patients, who have given consent to sampling, have provided whole blood samples, plasma samples, bronchoalveolar lavage and faeces samples to an extensive biobank.
5. MATCH enrolls patients from a single centre, reducing the generalizability of findings.

Introduction

The first transplantation worldwide was performed in 1954 and the first in Denmark in 1964.^{1,2} The field has developed significantly since then with better surgical technique, better understanding of transplant immunology, the development of immunotherapy, and several other advances in the field of medicine. In spite of these advances, transplantations are still associated with reduced life expectancy, with cancer, allograft rejection, and infectious complications being the most important causes.³

Transplant procedures remain relatively rare, underscoring the importance of systematical gathering of knowledge from expansive groups or cohorts. Many aspects in the field of transplantation, including prevention of infectious disease, lack consensus on best practices due to a paucity of strong evidence.⁴⁻⁶ Therefore, the Management of Post-transplant Infections in Collaborating Hospitals (MATCH) program was developed at the Copenhagen University Hospital – Rigshospitalet, Denmark.

The prospective MATCH program was initiated in 2011. It was created for two main reasons: firstly, to optimize the implementation of existing preventive strategies against viral infections in solid organ transplant (SOT) recipients and hematopoietic stem-cell transplant (HSCT) recipients,

and secondly, to advance research in the field of transplantation by creating an overarching database collecting data from a multitude of data sources. The clinical part of MATCH seeks to improve outcomes of SOT patients, and has succeeded in reducing cytomegalovirus (CMV) disease by among other things implementing an electronic clinical support tool ensuring critical follow-up on both screening samples taken and not taken.³ The MATCH cohort has been the basis of more than 50 publications published in peer-review journals so far.

This article aims to describe the profile of the MATCH cohort and provide transparency on its organization and the data available and thereby nurture further research and enhance collaborations.

Cohort Description

MATCH Organization

MATCH is anchored in the Centre of Excellence in Health, Immunity, and Infection (CHIP), at Copenhagen University Hospital – Rigshospitalet, Denmark. MATCH is led by a steering committee with two chairmen, a representative from each transplant department, a representative for the paediatric transplant recipients, and two representatives from the Centre of Excellence in Health, Immunity, and Infection (CHIP). The steering committee acts as a governing body, overseeing scientific and clinical operations in MATCH.

All transplant recipients from Rigshospitalet are systematically enrolled in MATCH when donor and recipients are matched. This includes all patients receiving a lung and/or liver transplantation in Denmark and all recipients of HSCT, kidney and heart transplantation from Eastern Denmark. Patients have been enrolled prospectively from 2011. Additionally, all transplant recipients from January 2004 until 2010 at the MATCH-departments have been added retrospectively to the MATCH program.

Data Infrastructure

The MATCH database is operated by CHIP and embedded into the data structure of PERSIMUNE (Centre of Excellence for Personalised Medicine of Infectious Complications in Immune Deficiency). CHIP is responsible for overall operation, data processing, stability, and access control of the MATCH database.

The PERSIMUNE Datawarehouse (DWH) receives data on patients in the MATCH cohort from a multitude of sources (Figure 1). This is enabled by the Danish civil registration system (CRS).⁷

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Every Danish resident is registered in the CRS with a unique ten-digit Civil Personal Register (CPR) number. The CPR-number is used in all Danish registers and thereby allows linkage of data across multiple sources. Denmark has multiple national health registers, linked by the CPR-number. Provided that the relevant approvals have been obtained from the research legal department data specific for individual research projects can be imported into the DWH and thereafter linked with other data already available in the DWH in a pseudonymized combined data extract. An example is the import of data on consecutive pulmonary lung function tests on lung transplant recipients for a specific lung transplant project.

Data sources

DWH receive data from many of the national health registers, including The National Patient Register, The National Organ Donor Database, The Danish Hospital Medication Register, The Danish Microbiology Database (MiBa), The Danish Pathology Register, and The Cause of Death Register. More specifically, DWH receive data on investigations performed as part of clinical practice from: LABKA I (2005-2009) and LABKA II (2009-) provides data on biochemistry, MEDCOM (2004-) provides data on microbiology, pathology, and additional biochemistry. Data on medication and all outpatient prescriptions is provided by EPM1 (2005-2020), EPM3 (2012-2016) and Sundheds-databanken provides data on hospital contacts and -procedures and diagnosis codes. Data on demographics, deaths and emigration are obtained from the CRS and The Cause of Death Register (2010-). MADS (2005-), a local database, provides additional microbiology data. RIS/PACS (2005-) is a local data source that provide data on imaging. The DWH obtain clinical data from electronic medical files and genetic data from other internal sources.

Quality assurance

Before being incorporated into the data stream, data from each data source is checked by a five-step procedure, involving source identification, obtaining documentation, clarification of which data columns/types to collect, establishment of data harvest, and finally an assessment of the data harvest. An ongoing data cleaning and quality assurance (QA) process is performed. This process includes, but is not limited to, generating QA-tables, generating histograms for analysis, triangulation/cross validation of data, defining rules for clean-up, testing and validating clean-up rules, defining rules for monitoring data, and implementing monitoring rules and surveillance. Furthermore, clinical biochemistry and microbiology data are grouped according to sample material and type of analysis.

Data Enrichment

After import and cleaning of data in the DWH, PERSIMUNE performs additional data enrichment, combining data variables from data sources to create calculated variables based on standardized definitions. An example is the calculation of a Charlson comorbidity index (CCI).⁸ Another example is a CMV infection algorithm used to define if a transplant recipient has a CMV infection. The algorithm checks if a recipient has two consecutive plasma CMV PCR taken within 14 days of each other with a viral load ≥ 273 IU/mL or one sample with a viral load ≥ 2730 IU/mL.

Clinical data

In overall numbers until February 28th 2021, the following data are available from the MATCH cohort: 464,783 medical diagnosis codes, 314,961 data entries on medication before recipient transplantation and 367,839 after transplantation. Biochemistry data is available with 13,995,222 entries before transplantation and 26,127,817 after. Microbiology data is available with 242,023 culture results before transplantation and 410,558 after, and data on other microbiology analysis performed is available with 265,007 results before transplantation and 566,402 after. Data on pathological examinations is available on 170,884 samples before and 200,394 after transplantation.

Some research projects result in additional data being incorporated into the DWH and is available for other research projects upon approval. One such example is the Classification of death causes after transplantation (CLASS) project.⁹ CLASS is a methodology used to systematically and reliably determine and classify an accurate cause of death in all transplant recipients, than otherwise obtainable from Danish causes of death register.

Genetic Data

In 2017, after ethical approval samples from all patients in the MATCH cohort, with available material for analysis at that time point, were genotyped using the Infinium[®] Global Screening Array-24 v1.0 from DeCode. In 2019, all patients in the MATCH cohort with available material for analysis were genotyped at 770558 SNP loci using a custom array from Affymetrix, designed to enrich for genes relating to immune dysfunction. In total, 2431 (75.2 %) transplant recipients have been genotyped.

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Biobank

In 2015, a biobank for future research was established by PERSIMUNE, in collaboration with Rigshospitalet and the Department of clinical immunology, with samples being continuously collected from patients in the MATCH cohort (amongst others) that gave their consent. A total of 1731 patients have provided samples into the biobank. Blood samples are collected before transplantation and 1 year after transplantation, with 1207 (69.7 %) recipients having contributed at least one whole blood sample. In 2016, faeces samples were added to the collection scheme for two transplant recipient groups: HSCT and kidney transplant recipients with living donors. For HSCT recipients who have consented to this, faeces samples are collected pre-transplantation and at days 7, 14, 21, 28, and 180 after transplantation. For kidney transplant recipient, faeces samples are collected pre-transplantation, within 3 months and 3 months after transplantation. Since 2021, bronchoalveolar lavage fluid is collected and stored upon every bronchoscopy performed in lung transplant recipients who have consented to this.

Cohort participants

From 2011 until February 28th 2021, 3231 transplant recipients have been enrolled prospectively in the MATCH program with the majority being HSCT or kidney transplant recipients (Figure 2a). The number of patients enrolled has been stable over time, with a slight upwards trend (Figure 2b). Among the 3231 transplant recipients, 4.3% had a re-transplantation. Overall, 59.6 % of transplant recipients were male. Age at transplantation was similar across the transplant groups with a mean age of 50 (IQR 35, 60). The proportion of transplant recipients under the age of 18 years, was 19.8 %, 12.5 %, 10.6 %, 4.3% and 0.6% for HSCT, liver-, heart-, kidney and lung recipients, respectively. The donor/recipient CMV and EBV serostatus in the cohort at baseline is summarized in Table 1. There was a CCI score available for 2961 (91.6 %) of the transplant recipients with a median score of 1 (IQR of 1-3) at time of transplantation.

Until February 28th 2021, a total of 796/3231 (24.6 %) have died during follow-up. The total follow-up time for HSCT and SOT recipients is 5192 and 8840 years, median 2.9 (IQR 0.9 – 6.2) and 4.3 (IQR 1.8 – 7.2), respectively. Follow-up of those who are alive is ongoing.

Findings to Date

With the right regulatory approvals, researchers can get access to the clinical data collected in the MATCH program. Since 2011 until 2023, clinical data from the MATCH program have been the basis of more than 50 scientific publications. A full publication list is available in the supplementary material.

CMV

The implementation of MATCH succeeded in reducing CMV disease among non-lung SOT recipients as demonstrated by Ekenberg et al, with an adjusted hazard ratio of 0.27 [0.11-0.63], $P = 0.003$, early after implementation, and an adjusted hazard ratio of 0.17 [0.06-0.52], $P = 0.002$, late after implementation, both compared with prior to MATCH.¹⁰

Other elements of the CMV management in MATCH have also been studied, including the development of antiviral resistance.^{10–20}

Other infections

The epidemiology of a range of other infectious diseases in transplant recipients has also been studied based on the MATCH cohort with findings amongst other: a high incidence of invasive aspergillosis the first three months after CMV infection, and a high incidence of herpes vira (CMV, EBV, Herpes simplex type 1 and 2, and Varicella Zoster) infections.^{21–29}

CLASS

The CLASS study aimed to develop a method to improve our understanding of the cause of death in transplant recipients, thereby helping identify emerging trends and health challenges in transplant recipients. The method uses trained investigators to complete a case report form (CRF) on fatal cases, which is then assessed by two external reviewers, that if not in agreement are further evaluated by an expert panel.⁹ This method was used in another study, finding a trend towards lower incidence of death from cardiovascular disease, graft failure and cancer over time, while non-organ specific causes did not decrease.³ The method also identified a sub-group of transplant recipients with an increased risk of death to cancer or cardiovascular disease, namely patients with either pre- or post- diabetes mellitus.³⁰

Vitamins

Some studies also examined the role of vitamins A, E, and D in the acute graft- versus-host response in HSCT patients.^{31–33}

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Microbiome

The role of the gut microbiome in transplant recipients have also been investigated.^{34–37} One landmark study showed that the composition of the pre-transplant gut microbiome is associated with risk of acute graft-versus host disease in HSCT patients.³⁸

Cancer and PTLT

Cancer in transplant recipients has been a focus area with one study finding an increased risk of de novo or secondary cancers after solid organ or allogenic haematopoietic stem cell transplantation compared to the general population.³⁹ One study examined the predictive value of EBV DNA in detection of posttransplant lymphoproliferative disorders (PTLD) in transplant recipients and investigated how addition of other variables in the model could improve prediction of PTLD.⁴⁰ Another study examined early- and late-onset PTLD among adult kidney and liver transplant recipients⁴¹, and in the same year a risk score for PTLD in SOT-recipients was developed and validated.⁴²

Other research areas

Other studies based on the clinical data from the MATCH program investigated the clinical utility of different medical devices and scoring systems, different biomarkers such as ST2 and CRP, treatment options, and the role of immune reconstitution and function in transplant recipients.^{42–52}

Partnerships and collaborations

MATCH has several international research collaborations. MATCH is collaborating with a transplant cohort based at the Toronto General Hospital regarding infectious complications in lung transplant recipients. MATCH is also collaborating with the Swiss Transplant Cohort study (STCS) aiming to merge more than 10,000 SOT recipients from both cohorts to evaluate and compare outcomes of different strategies against CMV infection.⁵⁴ Representatives from MATCH have also worked with the CMV Resistance Working group, a subgroup of the CMV Drug Development Forum, on definitions of resistant and refractory CMV in transplant recipients.¹⁸

Collaboration

MATCH encourages both local and international collaborations. Research projects seeking to use data from MATCH must be approved by the MATCH Steering Committee. Additionally, a research project must apply for all required approvals by the Danish regulatory boards according to the type

of project. For more details on how to get involved, see figure 3 and the website:
(<https://www.persimune.dk/How-to-get-involved>).

Future Perspectives

The MATCH program has existed for 13 years, contributing a great amount of data in high granularity and of high quality that can be utilized for research purposes. This data has been used in a series of scientific publications. Future endeavors involve expanding and strengthening international collaborations to improve the quality, generalizability, and utility of evidence in the transplantation field. Large collaborations are essential to overcome limitations posed by the rarity of transplantations.

Further Details

Data Sharing Statement

Data are available on reasonable request. MATCH data are open for researchers and data access is regulated by the MATCH Steering Committee. Additionally, the research project must have all required approvals by the Danish regulatory boards according to the type of project.

Contributorship

Guarantor: MH; Conceptualisation, writing: FVLE, CGC, MH; Formal analysis: FVLE, SZ, NN; Review, edit, revision: KSM, NN, DDM, CM, FG, HS, MP, NAS, SSS, JM, VBC and JL. All authors have read and agreed to the published version of the manuscript.

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Patient and Public Involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Competing Interests

None declared.

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Figure 1, overview of MATCH data sources and flow. Data is collected from various local and national sources and incorporated into the PERSIMUNE Datawarehouse from where data on MATCH patients can be requested.

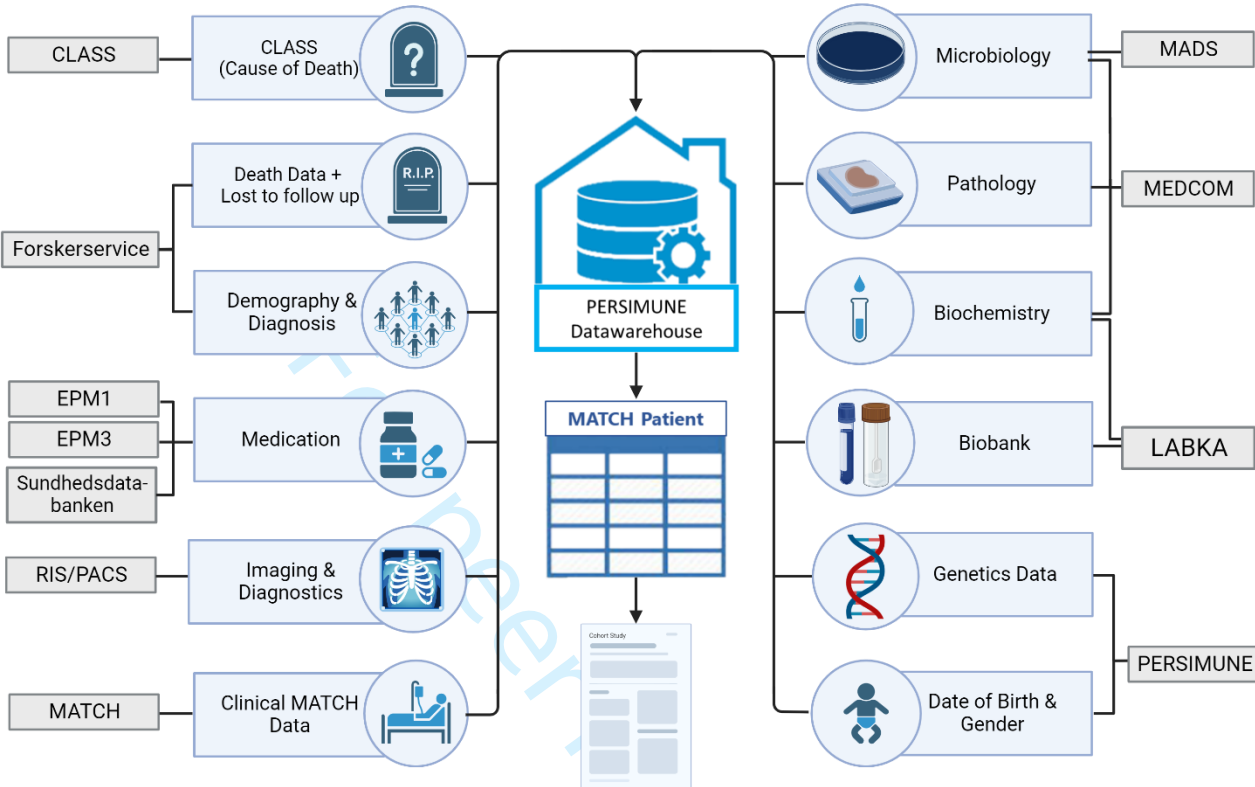
Table 1 Baseline characteristics of transplant recipients enrolled in MATCH between 2010 and February 2021						
	Total	HSCT	Kidney	Liver	Lung	Heart
Transplant type, N (%)	3231	1192 (36.9)	1007 (31.2)	551 (17.1%)	330 (10.2)	151 (4.7%)
Retransplantation, N (%)	140 (4.3)	45 (3,8)	43 (4.3)	42 (7.6)	10 (3.0)	0
Age (years) at Trans-plantation, median (IQR)	50 (35,60)	50 (25,63)	50 (38, 60)	48 (34,56)	53 (44,59)	50 (33, 59)
Age < 18 years, N (%)	356 (11.0)	236 (19.8)	36 (3.6)	69 (12.5)	2 (0.6)	16 (10.6)
Sex, N (%)						
Female	1306 (40.4)	477 (40.0)	373 (37.0)	244 (44.3)	160 (48.5)	52 (34.4)
Male	1925 (59.6)	715 (60.0)	634 (63.0)	307 (55.7)	170 (51.5)	99 (65.6)
Donor/recipient CMV IgG Serostatus at transplantation, N (%)						
D+/R-	475 (14.7)	110 (9.2)	179 (17.8)	91 (16.5)	60 (18.2)	35 (23.2)
D+/R+	1334 (41.3)	427 (35.8)	468 (46.5)	268 (48.6)	129 (39.1)	42 (27.8)
D-/R+	852 (26.4)	373 (31.3)	228 (22.6)	119 (21.6)	85 (25.8)	47 (31.1)
D-/R-	492 (15.2)	252 (21.1)	117 (11.6)	62 (11.3)	46 (13.9)	15(9.9)
Unknown	78 (2.4)	30 (2.5)	15 (1.49)	11 (2.0)	10 (3.0)	12 (7.9)
Donor/recipient EBV IgG Serostatus at transplantation, N (%)						
D+R-	156 (4.8)	61 (5.1)	51 (5.1)	27 (4.9)	11 (3.3)	6 (4.0)
D+R+	2207 (68.3)	800 (67.1)	730 (72.5)	366 (66.4)	214 (64.8)	97 (64.2)
D-/R+	315 (9.7)	124 (10.4)	87 (8.6)	61 (11.1)	24 (7.3)	19 (12.6)
D-/R-	39 (1.2)	16 (1.3)	11 (1.1)	8 (1.5)	2 (0.6)	2 (1.3)
Unknown	514 (15.9)	191 (16.0)	128 (12.7)	89 (16.2)	79 (23.9)	27 (17.9)
Charlson Comorbidity Index, median (IQR)						
CCI	1 (1,3)	2 (2,2)	1 (1,2)	4 (4,5)	1 (1,2)	2 (2,3)
N (%)	2961	970	1005	546	290	150
Recipients who died, with a CLASS cause of death available						
N (%)	621 (78.0)	316 (78.8)	101 (66.8)	77 (79.4)	106 (84.1)	21 (91.3)

Figure 2. A: number of transplant recipients each year per type of transplantation. HSCT, Hematopoietic stem-cell transplantation recipients. B: overview of the distribution of recipients by organ type, included in MATCH from 2010 to February 2021

Figure 3, How to Obtain Data for Research in MATCH. An optional feasibility request can be made to evaluate if data of interest is available. When the researcher has confirmed that the data of interest is available, the next step is to submit a project proposal. Once the project has been approved, a data request must be made defining the patient group, all data elements required, as well as all relevant regulatory approvals. Data will be delivered in a pseudonymized form. Finally, all collaborators are asked to contribute to the ongoing data cleaning, standardization and enrichment of data used in their research project.

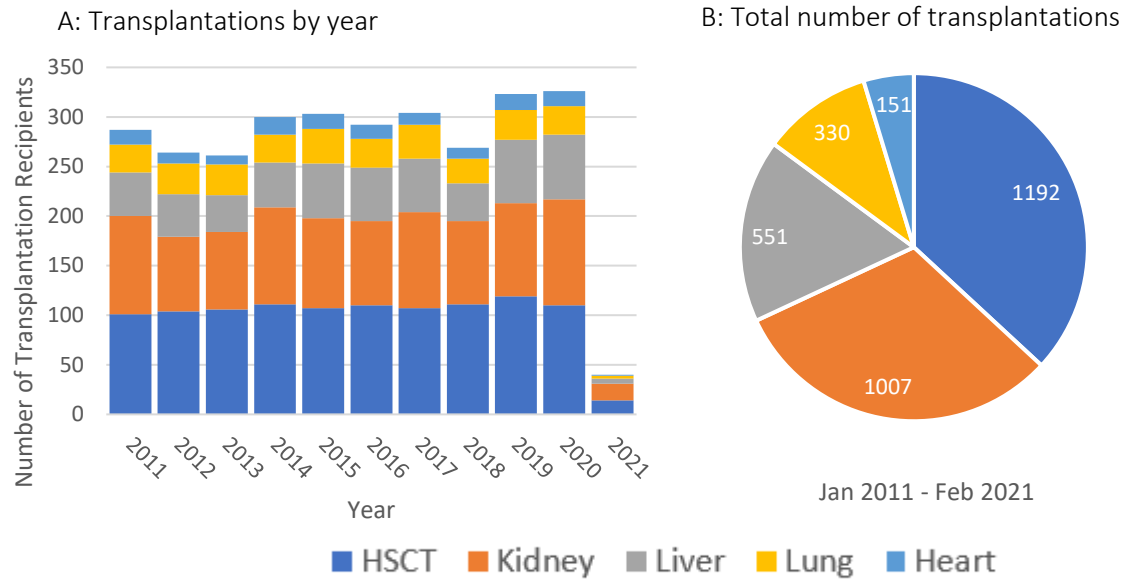
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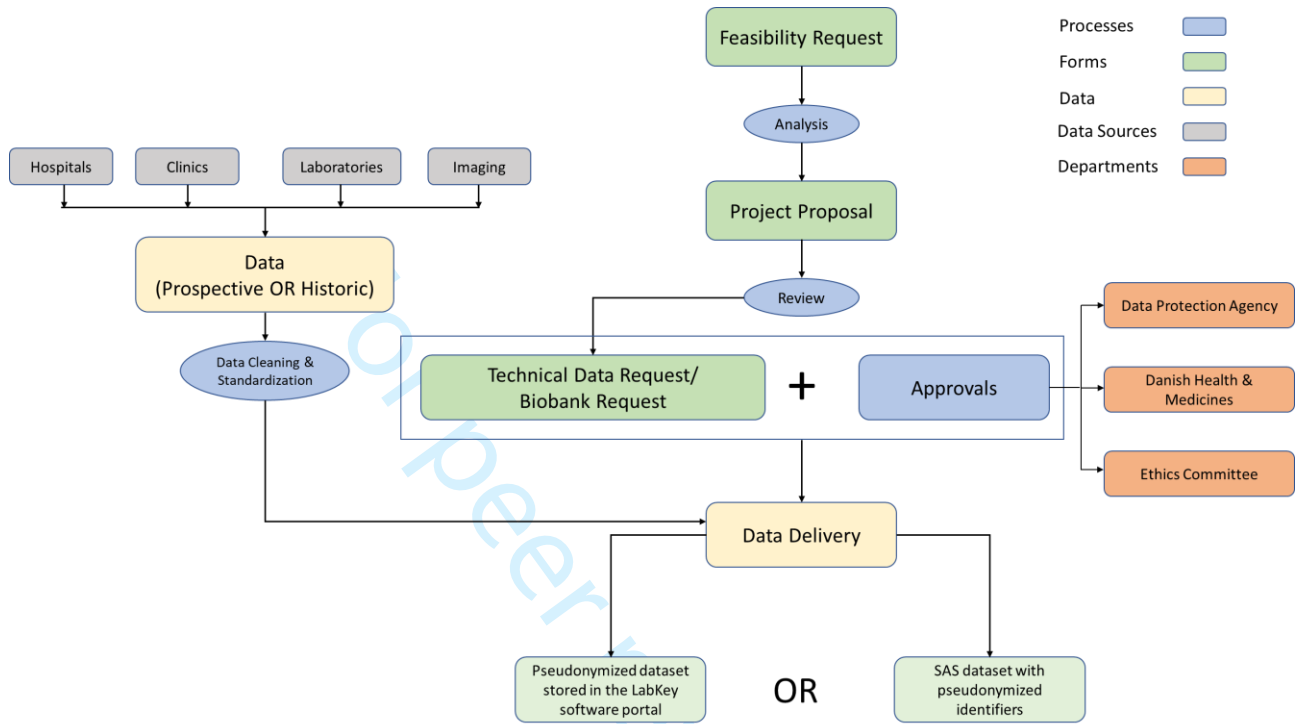
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Project: 50**Cancer: 4**

Early- and late-onset posttransplant lymphoproliferative disorders among adult kidney and liver transplant recipients

Development and Validation of a Risk Score for Post-Transplant Lymphoproliferative Disorders among Solid Organ Transplant Recipients

Neval E Wareham 1, Qiuju Li 2, Henrik Sengeløv 3, Caspar Da Cunha-Bang 4, Finn Gustafsson 4, Carsten Heilman

The clinical utility of PDG PET/CT among solid organ transplant recipients suspected of malignancy or infection

CMV: 11

Development and Dynamics of Cytomegalovirus UL97 Ganciclovir Resistance Mutations in Transplant Recipients Detected by Next-Generation Sequencing

Evaluation of an electronic, patient-focused management system aimed at preventing cytomegalovirus disease following solid organ transplantation

Absolute Lymphocyte Count as a Predictor of Cytomegalovirus (CMV) Infection and Recurrence in Hematopoietic Stem Cell Transplant (HSCT) Recipients

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Definitions of Resistant and Refractory Cytomegalovirus Infection and Disease in Transplant Recipients for Use in Clinical Trials

Risk Factors for Failure of Primary (Val)ganciclovir Prophylaxis Against Cytomegalovirus Infection and Disease in Solid Organ Transplant Recipients

Impact of CMV PCR Blips in Recipients of Solid Organ and Hematopoietic Stem Cell Transplantation

Cytomegalovirus (CMV) Disease Despite Weekly Preemptive CMV Strategy for Recipients of Solid Organ and Hematopoietic Stem Cell Transplantation

Cytomegalovirus Viral Load in Bronchoalveolar Lavage to Diagnose Lung Transplant Associated CMV Pneumonia.

Clinical Application of Variation in Replication Kinetics during Episodes of Post-Transplant Cytomegalovirus Infections.

The time course of development and impact from viral resistance against ganciclovir in cytomegalovirus infection.

Factors associated with the development of cytomegalovirus infection following solid organ transplantation

Microbiome:5

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Impact of Antibiotic Treatment on the Gut Microbiome and its Resistome in Hematopoietic Stem Cell Transplant Recipients

Metabolic Potential of the Gut Microbiome Is Significantly Impacted by Conditioning Regimen in Allogeneic Hematopoietic Stem Cell Transplantation Recipients

Pre-Transplant Prediction of Acute Graft-versus-Host Disease Using the Gut Microbiome

Associations of the gut microbiome and clinical factors with acute GVHD in allogeneic HSCT recipients

Gut microbiome comparability of fresh-frozen versus stabilized-frozen samples from hospitalized patients using 16S rRNA gene and shotgun

Other Infections: 15

Associations between invasive aspergillosis and cytomegalovirus in lung transplant recipients: a nationwide cohort study

Prediction of herpes virus infections after solid organ transplantation: a prospective study of immune function

Achromobacter spp. in a Cohort of Non-Selected Pre- and Post-Lung Transplant Recipients

Adverse Events Associated with Universal versus Targeted Antifungal Prophylaxis among Lung Transplant Recipients-A Nationwide Cohort Study 2010-2019

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Incidence and Impact of Parvovirus B19 Infection in Seronegative Solid Organ Transplant Recipients
Bacterial and fungal bloodstream infections in solid organ transplant recipients: results from a Danish cohort with nationwide follow-up
An Observational Prospective Cohort Study of Incidence and Outcome of <i>Streptococcus pneumoniae</i> and <i>Hemophilus influenzae</i> Infections in Adult Solid Organ Transplant Recipients
<i>Pneumocystis jirovecii</i> pneumonia in liver transplant recipients in an era of routine prophylaxis
Bacterial and fungal bloodstream infections in pediatric liver and kidney transplant recipients
Measles, Mumps, Rubella, and Varicella Zoster Virus Serology and Infections in Solid Organ Transplant Recipients During the First Year Posttransplantation
Tuberculosis among Patients Undergoing Solid Organ Transplantation or Dialysis in a Low-Endemic Country, 2004-2017

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Incidence Rates and Risk Factors of *Clostridioides difficile* Infection in Solid Organ and Hematopoietic Stem Cell Transplant Recipients

The value of EBV DNA in early detection of post-transplant lymphoproliferative disorders among solid organ and hematopoietic stem cell transplant recipients.

Renal Dysfunction in a Cohort of Renal Transplant Recipients: Impact of BK Polyomavirus

Risk of infectious diseases among first-degree relatives of transplant recipients who develop CMV infection: is the infectious phenotype inheritable?

Other: 8

Pretransplantation Plasma ST2 Level as a Prognostic Biomarker of 1-Year Nonrelapse Mortality in Allogeneic Hematopoietic Cell Transplantation

Post-Transplantation Anemia and Risk of Death Following Lung Transplantation

Functional immune reconstitution early after allogeneic haematopoietic cell transplantation: A comparison of pre- and post-transplantation cytokine responses in stimulated whole blood

Immune function as predictor of infectious complications and clinical outcome in patients undergoing solid organ transplantation (the ImmuneMo:SOT study): a prospective non-interventional observational trial

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Improved Overall Survival, Relapse-Free-Survival, and Less Graft-vs.-Host-Disease in Patients With High Immune Reconstitution of TCR Gamma Delta Cells 2 Months After Allogeneic Stem Cell Transplantation
Extracorporeal photopheresis is a valuable treatment option in steroid-refractory or steroid-dependent acute graft versus host disease-experience with three different approaches
C-Reactive Protein Levels at Diagnosis of Acute Graft-versus-Host Disease Predict Steroid-Refractory Disease, Treatment-Related Mortality, and Overall Survival after Allogeneic Hematopoietic Stem Cell Transplantation.
MELD score measured day 10 after orthotopic liver transplantation predicts death and re-transplantation within the first year
CLASS: 3
Trends in underlying causes of death in solid organ transplant recipients between 2010 and 2020: Using the CLASS method for determining specific causes of death
Posttransplantation Diabetes Mellitus Among Solid Organ Recipients in a Danish Cohort
Classification of death causes after transplantation (CLASS): Evaluation of methodology and initial results
Vitamins: 4

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Hyaluronic Acid Is a Biomarker for Allograft Dysfunction and Predicts 1-Year Graft Loss After Liver Transplantation

Vitamin E and acute graft-versus-host disease after myeloablative allogeneic hematopoietic cell transplantation

Pretransplantation vitamin A plasma levels and risk of acute graft-versus-host disease following allogeneic hematopoietic stem cell transplantation

Pre-transplantation plasma vitamin D levels and acute graft-versus-host disease after myeloablative hematopoietic cell transplantation in adults

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Publish year
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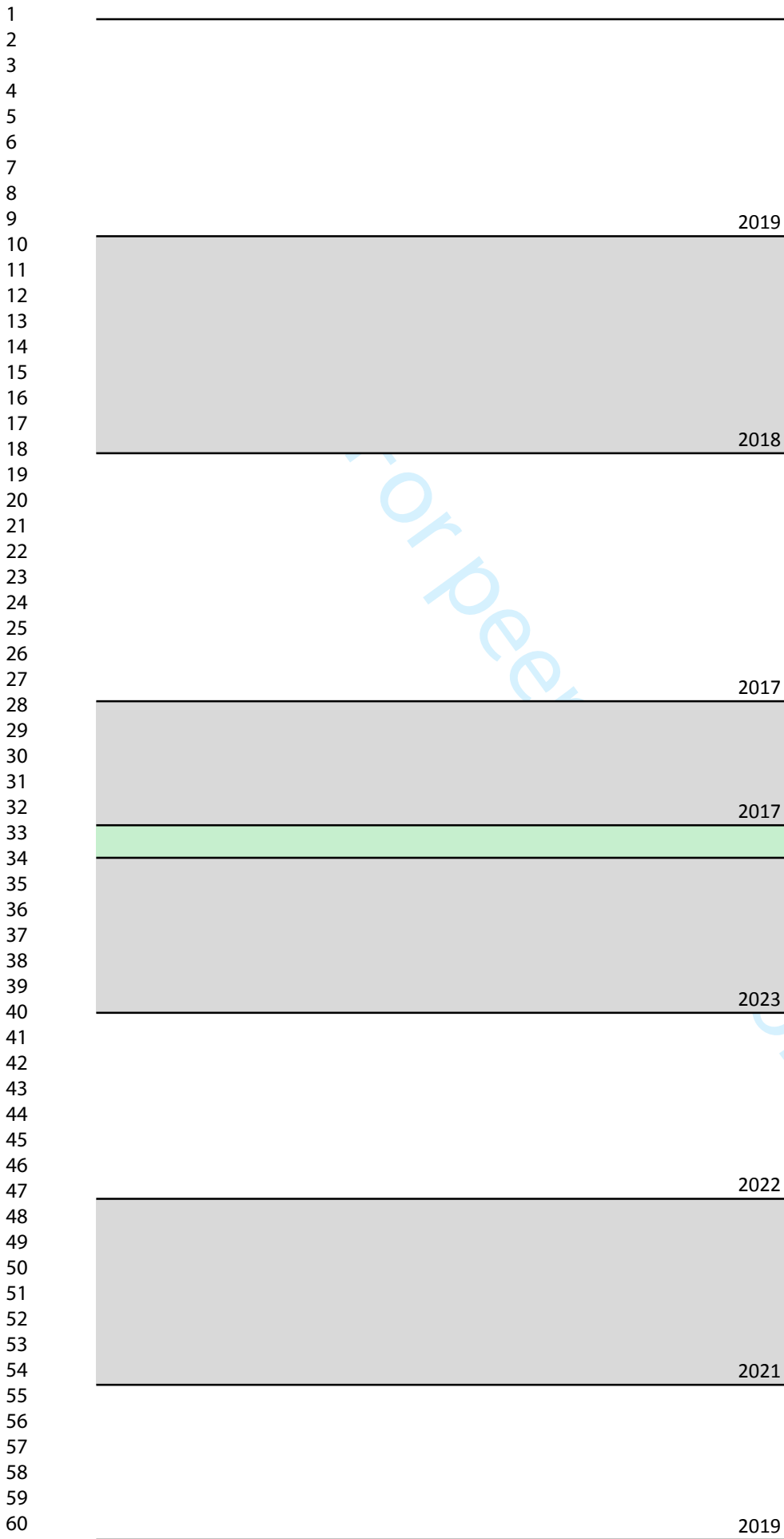
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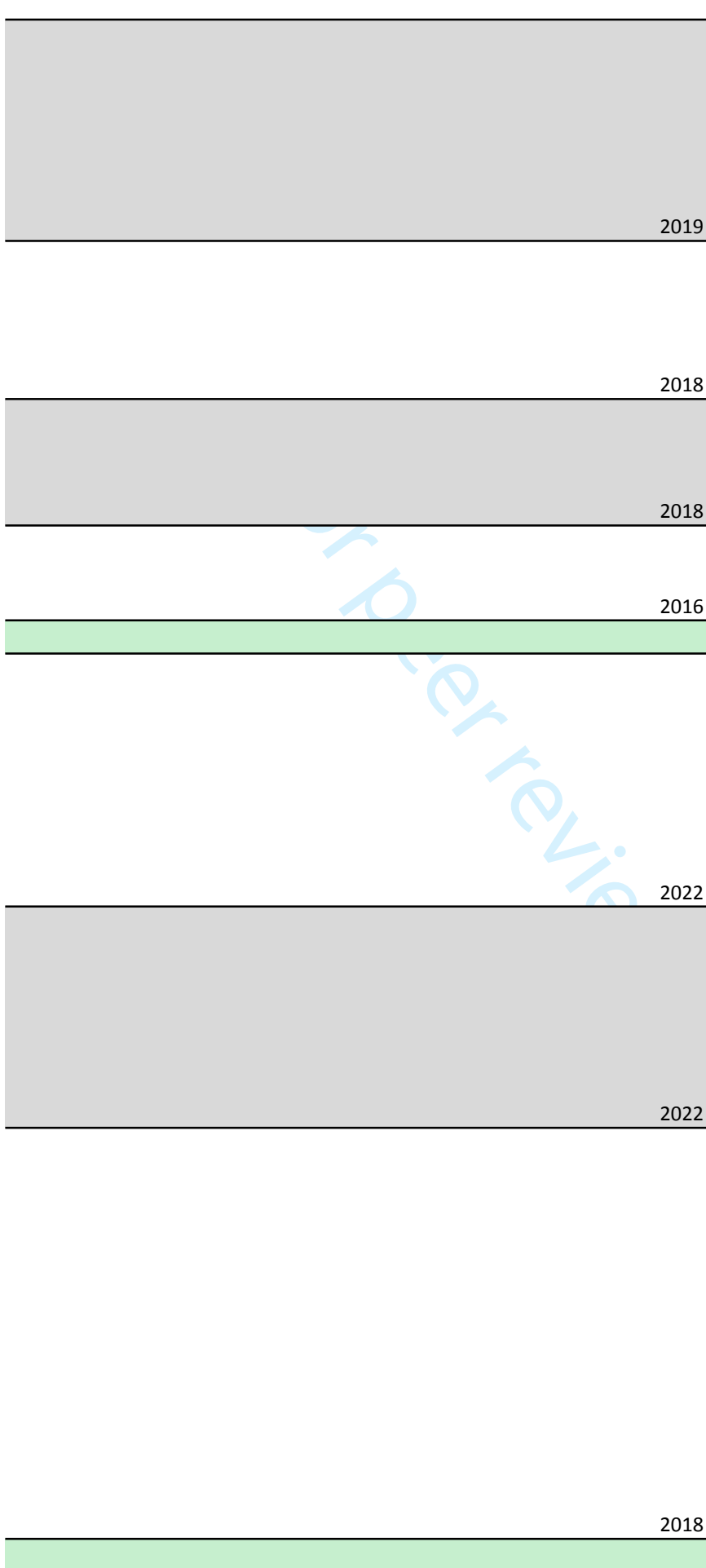
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Cohort Profile: The Management of Post-transplant Infections in Collaborating Hospitals (MATCH) Program - A prospective cohort of all transplant recipients at Copenhagen University Hospital – Rigshospitalet, Denmark

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Cohort Profile: The Management of Post-transplant Infections in Collaborating Hospitals (MATCH) Program

- A prospective cohort of all transplant recipients at Copenhagen University Hospital – Rigshospitalet, Denmark

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Abstract

Purpose The MATCH program, initiated in 2011 and still ongoing, was created to: 1) optimize the implementation of existing preventive strategies against viral infections in solid organ transplant (SOT) recipients and allogeneic hematopoietic stem-cell transplant (HSCT) recipients, and 2) advance research in the field of transplantation by collecting data from a multitude of sources.

Participants All SOT and HSCT recipients at Copenhagen University Hospital, Rigshospitalet, are followed in MATCH. By February 2021, a total of 1192 HSCT recipients and 2039 SOT recipients have been included. Participants are followed life-long. An automated electronic data capture system retrieves prospective data from nationwide registries. Data from the years prior to transplantation are also collected.

Findings to Date Data entries before and after transplantation include: Biochemistry: 13,995,222 and 26,127,817; Microbiology, cultures: 242,023 and 410,558; Other microbiological analyses: 265,007 and 566,402; and Pathology: 170,884 and 200,394. There are genomic data on 2,431 transplant recipients, whole blood biobank samples from 1,003 transplant recipients and faeces biobank samples from 207 HSCT recipients. Clinical data collected in MATCH has contributed to 50 scientific papers published in peer-reviewed journals and has demonstrated success in reducing CMV-disease in SOT recipients. The program has established international collaborations with the Swiss Transplant Cohort Study and the lung transplant cohort at Toronto General Hospital.

Future Plans Enrolment into MATCH is ongoing with no planned end date for enrolment or follow-up. MATCH will continue to provide high quality data on transplant recipients and expand and strengthen international collaborations.

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Introduction

The first transplantation worldwide was performed in 1954 and the first in Denmark in 1964.^{1,2} The field has developed significantly since then with better surgical technique, better understanding of transplant immunology, the development of immunotherapy, and several other advances in the field of medicine. In spite of these advances, transplantations are still associated with reduced life expectancy, with cancer, allograft rejection, and infectious complications being the most important causes.³

Transplant procedures remain relatively rare, underscoring the importance of systematical gathering of knowledge from expansive groups or cohorts. Many aspects in the field of transplantation, including prevention of infectious disease, lack consensus on best practices due to a paucity of strong evidence.⁴⁻⁶ Therefore, the Management of Post-transplant Infections in Collaborating Hospitals (MATCH) program was developed at the Copenhagen University Hospital – Rigshospitalet, Denmark.

The prospective MATCH program was initiated in 2011. It was created for two main reasons: firstly, to optimize the implementation of existing preventive strategies against viral infections in solid organ transplant (SOT) recipients and hematopoietic stem-cell transplant (HSCT) recipients, and secondly, to advance research in the field of transplantation by creating an overarching database collecting data from a multitude of data sources. The clinical part of MATCH seeks to improve outcomes of SOT patients, and has succeeded in reducing cytomegalovirus (CMV) disease by among other things implementing an electronic clinical support tool ensuring critical follow-up on both screening samples taken and not taken.³ The MATCH cohort has been the basis of more than 50 publications published in peer-review journals so far.

This article aims to describe the profile of the MATCH cohort and provide transparency on its organization and the data available and thereby nurture further research and enhance collaborations.

Cohort Description

MATCH Organization

MATCH is anchored in the Centre of Excellence in Health, Immunity, and Infection (CHIP), at Copenhagen University Hospital – Rigshospitalet, Denmark. MATCH is led by a steering committee with two chairmen, a representative from each transplant department, a representative

for the paediatric transplant recipients, and two representatives from the Centre of Excellence in Health, Immunity, and Infection (CHIP). The steering committee acts as a governing body, overseeing scientific and clinical operations in MATCH.

All transplant recipients from Rigshospitalet are systematically enrolled in MATCH when donor and recipients are matched. This includes all patients receiving a lung and/or liver transplantation in Denmark and all recipients of HSCT, kidney and heart transplantation from Eastern Denmark. Patients have been enrolled prospectively from 2011. Additionally, all transplant recipients from January 2004 until 2010 at the MATCH-departments have been added retrospectively to the MATCH program.

Data Infrastructure

The MATCH database is operated by CHIP and embedded into the data structure of PERSIMUNE (Centre of Excellence for Personalised Medicine of Infectious Complications in Immune Deficiency). CHIP is responsible for overall operation, data processing, stability, and access control of the MATCH database.

The PERSIMUNE Datawarehouse (DWH) receives data on patients in the MATCH cohort from a multitude of sources (Figure 1). This is enabled by the Danish civil registration system (CRS).⁷ Every Danish resident is registered in the CRS with a unique ten-digit Civil Personal Register (CPR) number. The CPR-number is used in all Danish registers and thereby allows linkage of data across multiple sources. Denmark has multiple national health registers, linked by the CPR-number. Provided that the relevant approvals have been obtained from the research legal department data specific for individual research projects can be imported into the DWH and thereafter linked with other data already available in the DWH in a pseudonymized combined data extract. An example is the import of data on consecutive pulmonary lung function tests on lung transplant recipients for a specific lung transplant project.

Data sources

DWH receive data from many of the national health registers, including The National Patient Register, The National Organ Donor Database, The Danish Hospital Medication Register, The Danish Microbiology Database (MiBa), The Danish Pathology Register, and The Cause of Death Register. More specifically, DWH receive data on investigations performed as part of clinical practice from: LABKA I (2005-2009) and LABKA II (2009-) provides data on biochemistry,

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MEDCOM (2004-) provides data on microbiology, pathology, and additional biochemistry. Data on medication and all outpatient prescriptions is provided by EPM1 (2005-2020), EPM3 (2012-2016) and Sundheds-databanken provides data on hospital contacts and -procedures and diagnosis codes. Data on demographics, deaths and emigration are obtained from the CRS and The Cause of Death Register (2010-). MADS (2005-), a local database, provides additional microbiology data. RIS/PACS (2005-) is a local data source that provide data on imaging. The DWH obtain clinical data from electronic medical files and genetic data from other internal sources.

Quality assurance

Before being incorporated into the data stream, data from each data source is checked by a five-step procedure, involving source identification, obtaining documentation, clarification of which data columns/types to collect, establishment of data harvest, and finally an assessment of the data harvest. An ongoing data cleaning and quality assurance (QA) process is performed. This process includes, but is not limited to, generating QA-tables, generating histograms for analysis, triangulation/cross validation of data, defining rules for clean-up, testing and validating clean-up rules, defining rules for monitoring data, and implementing monitoring rules and surveillance. Furthermore, clinical biochemistry and microbiology data are grouped according to sample material and type of analysis. An example of how a biochemistry variable undergoes quality assurance is available in the supplemental material Example of Data Cleaning.

Data Enrichment

After import and cleaning of data in the DWH, PERSIMUNE performs additional data enrichment, combining data variables from data sources to create calculated variables based on standardized definitions. An example is the calculation of a Charlson comorbidity index (CCI).⁸ Another example is a CMV infection algorithm used to define if a transplant recipient has a CMV infection. The algorithm checks if a recipient has two consecutive plasma CMV PCR taken within 14 days of each other with a viral load ≥ 273 IU/mL or one sample with a viral load ≥ 2730 IU/mL.

Clinical data

In overall numbers until February 28th 2021, the following data are available from the MATCH cohort: 464,783 medical diagnosis codes, 314,961 data entries on medication before recipient transplantation and 367,839 after transplantation. Biochemistry data is available with 13,995,222 entries before transplantation and 26,127,817 after. Microbiology data is available with 242,023

culture results before transplantation and 410,558 after, and data on other microbiology analysis performed is available with 265,007 results before transplantation and 566,402 after. Data on pathological examinations is available on 170,884 samples before and 200,394 after transplantation.

Some research projects result in additional data being incorporated into the DWH and is available for other research projects upon approval. One such example is the Classification of death causes after transplantation (CLASS) project.⁹ CLASS is a methodology used to systematically and reliably determine and classify an accurate cause of death in all transplant recipients, than otherwise obtainable from Danish causes of death register.

Genetic Data

In 2017, after ethical approval samples from all patients in the MATCH cohort, with available material for analysis at that time point, were genotyped using the Infinium® Global Screening Array-24 v1.0 from DeCode. In 2019, all patients in the MATCH cohort with available material for analysis were genotyped at 770558 SNP loci using a custom array from Affymetrix, designed to enrich for genes relating to immune dysfunction. In total, 2431 (75.2 %) transplant recipients have been genotyped.

Biobank

In 2015, a biobank for future research was established by PERSIMUNE, in collaboration with Rigshospitalet and the Department of clinical immunology, with samples being continuously collected from patients in the MATCH cohort (amongst others) that gave their consent. A total of 1731 patients have provided samples into the biobank. Blood samples are collected before transplantation and 1 year after transplantation, with 1207 (69.7 %) recipients having contributed at least one whole blood sample. In 2016, faeces samples were added to the collection scheme for two transplant recipient groups: HSCT and kidney transplant recipients with living donors. For HSCT recipients who have consented to this, faeces samples are collected pre-transplantation and at days 7, 14, 21, 28, and 180 after transplantation. For kidney transplant recipient, faeces samples are collected pre-transplantation, within 3 months and 3 months after transplantation. Since 2021, bronchoalveolar lavage fluid is collected and stored upon every bronchoscopy performed in lung transplant recipients who have consented to this.

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Cohort participants

From 2011 until February 28th 2021, 3231 transplant recipients have been enrolled prospectively in the MATCH program with the majority being HSCT or kidney transplant recipients (Figure 2a). The number of patients enrolled has been stable over time, with a slight upwards trend (Figure 2b) Among the 3231 transplant recipients, 4.3% had a re-transplantation. Overall, 59.6 % of transplant recipients were male. Age at transplantation was similar across the transplant groups with a mean age of 50 (IQR 35, 60). The proportion of transplant recipients under the age of 18 years, was 19.8 %, 12.5 %, 10.6 %, 4.3% and 0.6% for HSCT, liver-, heart-, kidney and lung recipients, respectively. The donor/recipient CMV and EBV serostatus in the cohort at baseline is summarized in Table 1. There was a CCI score available for 2961 (91.6 %) of the transplant recipients with a median score of 1 (IQR of 1-3) at time of transplantation.

Until February 28th 2021, a total of 796/3231 (24.6 %) have died during follow-up. In the MATCH cohort, the causes of death in the SOT recipients were cancer (19.1 %), graft rejection (18.4 %), infections (17.4 %), other organ specific or non-specific causes (15.4 %), Graft failure (11.7 %), and cardiovascular disease (10.0%). For 8% of SOT recipients, the cause of death was unknown.³ For HSCT recipients, death from relapse was the most frequent cause of death (46.0%), followed by graft vs host disease (22.1%), other causes (13.5%), and infections (12.1%). The cause of death was unknown for 6.2% of HSCT recipients.¹⁰

The total follow-up time for HSCT and SOT recipients is 5192 and 8840 years, median 2.9 (IQR 0.9 – 6.2) and 4.3 (IQR 1.8 – 7.2), respectively. Follow-up of those who are alive is ongoing and independent of graft-loss.

Findings to Date

With the right regulatory approvals, researchers can get access to the clinical data collected in the MATCH program. Since 2011 until 2023, clinical data from the MATCH program have been the basis of more than 50 scientific publications. A full publication list is available in the supplemental material Full Publication List.

CMV

The implementation of MATCH succeeded in reducing CMV disease among non-lung SOT recipients as demonstrated by Ekenberg et al, with an adjusted hazard ratio of 0.27 [0.11-0.63], P =

0.003, early after implementation, and an adjusted hazard ratio of 0.17 [0.06-0.52], $P=0.002$, late after implementation, both compared with prior to MATCH.¹¹

Other elements of the CMV management in MATCH have also been studied, including the development of antiviral resistance.¹¹⁻²¹

Other infections

The epidemiology of a range of other infectious diseases in transplant recipients has also been studied based on the MATCH cohort with findings amongst other: a high incidence of invasive aspergillosis the first three months after CMV infection, and a high incidence of herpes vira (CMV, EBV, Herpes simplex type 1 and 2, and Varicella Zoster) infections.²²⁻³⁰

CLASS

The CLASS study aimed to develop a method to improve our understanding of the cause of death in transplant recipients, thereby helping identify emerging trends and health challenges in transplant recipients. The method uses trained investigators to complete a case report form (CRF) on fatal cases, which is then assessed by two external reviewers, that if not in agreement are further evaluated by an expert panel.⁹ This method was used in another study, finding a trend towards lower incidence of death from cardiovascular disease, graft failure and cancer over time, while non-organ specific causes did not decrease.³ The method also identified a sub-group of transplant recipients with an increased risk of death to cancer or cardiovascular disease, namely patients with either pre- or post- diabetes mellitus.³¹

Vitamins

Some studies also examined the role of vitamins A, E, and D in the acute graft- versus-host response in HSCT patients.³²⁻³⁴

Microbiome

The role of the gut microbiome in transplant recipients have also been investigated.³⁵⁻³⁸ One landmark study showed that the composition of the pre-transplant gut microbiome is associated with risk of acute graft-versus host disease in HSCT patients.³⁹

Cancer and PTLT

Cancer in transplant recipients has been a focus area with one study finding an increased risk of de novo or secondary cancers after solid organ or allogeneic haematopoietic stem cell transplantation compared to the general population.⁴⁰ One study examined the predictive value of EBV DNA in

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detection of posttransplant lymphoproliferative disorders (PTLD) in transplant recipients and investigated how addition of other variables in the model could improve prediction of PTLD.⁴¹ Another study examined early- and late-onset PTLD among adult kidney and liver transplant recipients⁴², and in the same year a risk score for PTLD in SOT-recipients was developed and validated.⁴³

Other research areas

Other studies based on the clinical data from the MATCH program investigated the clinical utility of different medical devices and scoring systems, different biomarkers such as ST2 and CRP, treatment options, and the role of immune reconstitution and function in transplant recipients.^{43–53}

Partnerships and collaborations

MATCH has several international research collaborations. MATCH is collaborating with a transplant cohort based at the Toronto General Hospital regarding infectious complications in lung transplant recipients. MATCH is also collaborating with the Swiss Transplant Cohort study (STCS) aiming to merge more than 10,000 SOT recipients from both cohorts to evaluate and compare outcomes of different strategies against CMV infection.⁵⁵ Representatives from MATCH have also worked with the CMV Resistance Working group, a subgroup of the CMV Drug Development Forum, on definitions of resistant and refractory CMV in transplant recipients.¹⁹

Collaboration

MATCH encourages both local and international collaborations. Research projects seeking to use data from MATCH must be approved by the MATCH Steering Committee. For more details, please see data sharing statement.

Future Perspectives

The MATCH program has existed for 13 years, contributing a great amount of data in high granularity and of high quality that can be utilized for research purposes. This data has been used in a series of scientific publications. Future endeavors involve expanding and strengthening international collaborations to improve the quality, generalizability, and utility of evidence in the transplantation field. Large collaborations are essential to overcome limitations posed by the rarity of transplantations.

Further Details

Strengths and limitations of this study

1. MATCH is an unselected prospective cohort with complete enrolment, encompassing all transplant recipients at Rigshospitalet, Copenhagen University Hospital, Denmark.
2. All patients followed in MATCH have a civil registration number, and linkage to the Danish civil registration system ensures almost complete life-long follow-up despite patients being transferred to other centres in Denmark.
3. The Danish civil registration system allows for linkage to multiple nationwide registries containing data on e.g. biochemistry, pathology, microbiology, imaging, prescriptions and hospital contacts, including ICD-codes for diagnoses and procedures, both from the period before and after transplantation.
4. MATCH patients, who have given consent to sampling, have provided whole blood samples, plasma samples, bronchoalveolar lavage and faeces samples to an extensive biobank.
5. MATCH enrolls patients from a single centre, reducing the generalizability of findings.

Ethical Approval

This project was approved by the Centre for Regional Development (Journal-nr.: R-21018786), which approves projects seeking to retrospectively access treatment systems or electronic health records for research purposes on behalf of the Danish Data Protection Agency.

Data Sharing Statement

Data are available on reasonable request. MATCH data are open for researchers and data access is regulated by the MATCH Steering Committee. Additionally, the research project must have all required approvals by the Danish regulatory boards according to the type of project. For more details on how to get involved, see figure 3 and the website: (<https://www.persimune.dk/How-to-get-involved>).

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Contributorship

Guarantor: MH; Conceptualisation, writing: FVLE, CGC, MH; Formal analysis: FVLE, SZ, NN; Review, edit, revision: KSM, NN, DDM, CM, FG, HS, MP, NAS, SSS, JM, VBC and JL. All authors have read and agreed to the published version of the manuscript.

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Patient and Public Involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Competing Interests

None declared.

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Figure 1, overview of MATCH data sources and flow. Data is collected from various local and national sources and incorporated into the PERSIMUNE Datawarehouse from where data on MATCH patients can be requested.

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Table 1

Baseline characteristics of transplant recipients enrolled in MATCH between 2010 and February 2021

	Total	HSCT	Kidney	Liver	Lung	Heart
Transplant type, N (%)	3231	1192 (36.9)	1007 (31.2)	551 (17.1)	330 (10.2)	151 (4.7)
Myeloablative		643				
Non - myeloablative		499				
Umbilical cord blood		50				
Living donor			370	3		
Deceased donor			637	548		
Retransplantation, N (%)	140 (4.3)	45 (3.8)	43 (4.3)	42 (7.6)	10 (3.0)	0
Age (years) at transplantation, median (IQR)	50 (35,60)	50 (25,63)	50 (38, 60)	48 (34,56)	53 (44,59)	50 (33,59)
Age < 18 years, N (%)	356 (11.0)	236 (19.8)	36 (3.6)	69 (12.5)	2 (0.6)	16 (10.6)
Sex, N (%)						
Female	1306 (40.4)	477 (40.0)	373 (37.0)	244 (44.3)	160 (48.5)	52 (34.4)
Male	1925 (59.6)	715 (60.0)	634 (63.0)	307 (55.7)	170 (51.5)	99 (65.6)
Donor/recipient CMV IgG serostatus at transplantation, N (%)						
D+/R-	475 (14.7)	110 (9.2)	179 (17.8)	91 (16.5)	60 (18.2)	35 (23.2)
D+/R+	1334 (41.3)	427 (35.8)	468 (46.5)	268 (48.6)	129 (39.1)	42 (27.8)
D-/R+	852 (26.4)	373 (31.3)	228 (22.6)	119 (21.6)	85 (25.8)	47 (31.1)
D-/R-	492 (15.2)	252 (21.1)	117 (11.6)	62 (11.3)	46 (13.9)	15 (9.9)
Missing	78 (2.4)	30 (2.5)	15 (1.49)	11 (2.0)	10 (3.0)	12 (7.9)
Donor/recipient EBV IgG serostatus at transplantation, N (%)						
D+R-	156 (4.8)	61 (5.1)	51 (5.1)	27 (4.9)	11 (3.3)	6 (4.0)
D+R+	2207 (68.3)	800 (67.1)	730 (72.5)	366 (66.4)	214 (64.8)	97 (64.2)
D-/R+	315 (9.7)	124 (10.4)	87 (8.6)	61 (11.1)	24 (7.3)	19 (12.6)
D-/R-	39 (1.2)	16 (1.3)	11 (1.1)	8 (1.5)	2 (0.6)	2 (1.3)
Missing	514 (15.9)	191 (16.0)	128 (12.7)	89 (16.2)	79 (23.9)	27 (17.9)
Charlson Comorbidity Index at transplantation,						
CCI, median (IQR)	1 (1,3)	2 (2,2)	1 (1,2)	4 (4,5)	1 (1,2)	2 (2,3)
N (%)	2961 (91.6)	970 (81.4)	1005 (99.8)	546 (99.1)	290 (87.9)	150 (99.3)
Recipients who died, with a CLASS cause of death available						
N (%)	621 (78.0)	316 (78.8)	101 (66.8)	77 (79.4)	106 (84.1)	21 (91.3)

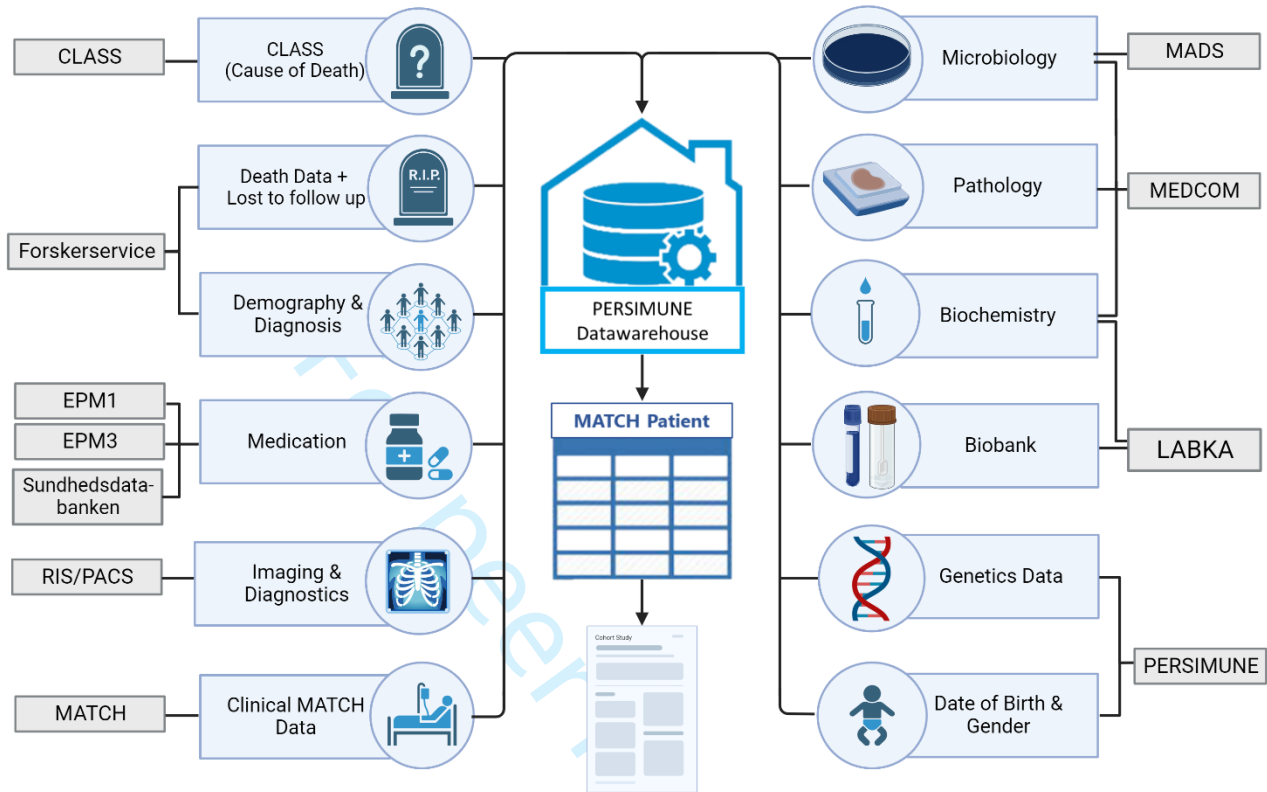
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Figure 2. A: number of transplant recipients each year per type of transplantation. HSCT, Hematopoietic stem-cell transplantation recipients. B: overview of the distribution of recipients by organ type, included in MATCH from 2010 to February 2021

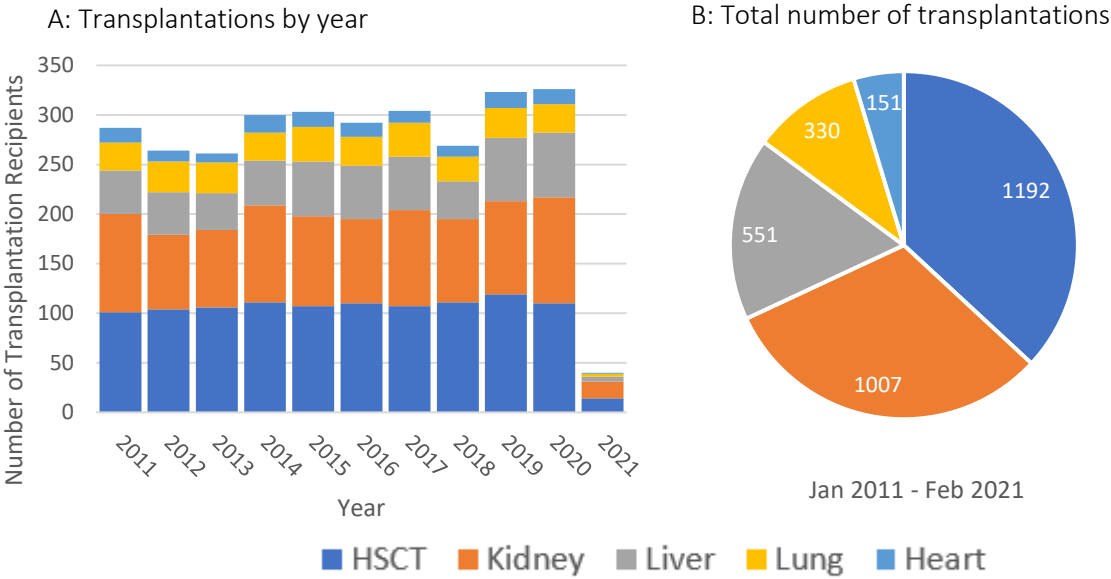
Figure 3, How to Obtain Data for Research in MATCH. An optional feasibility request can be made to evaluate if data of interest is available. When the researcher has confirmed that the data of interest is available, the next step is to submit a project proposal. Once the project has been approved, a data request must be made defining the patient group, all data elements required, as well as all relevant regulatory approvals. Data will be delivered in a pseudonymized form. Finally, all collaborators are asked to contribute to the ongoing data cleaning, standardization and enrichment of data used in their research project.

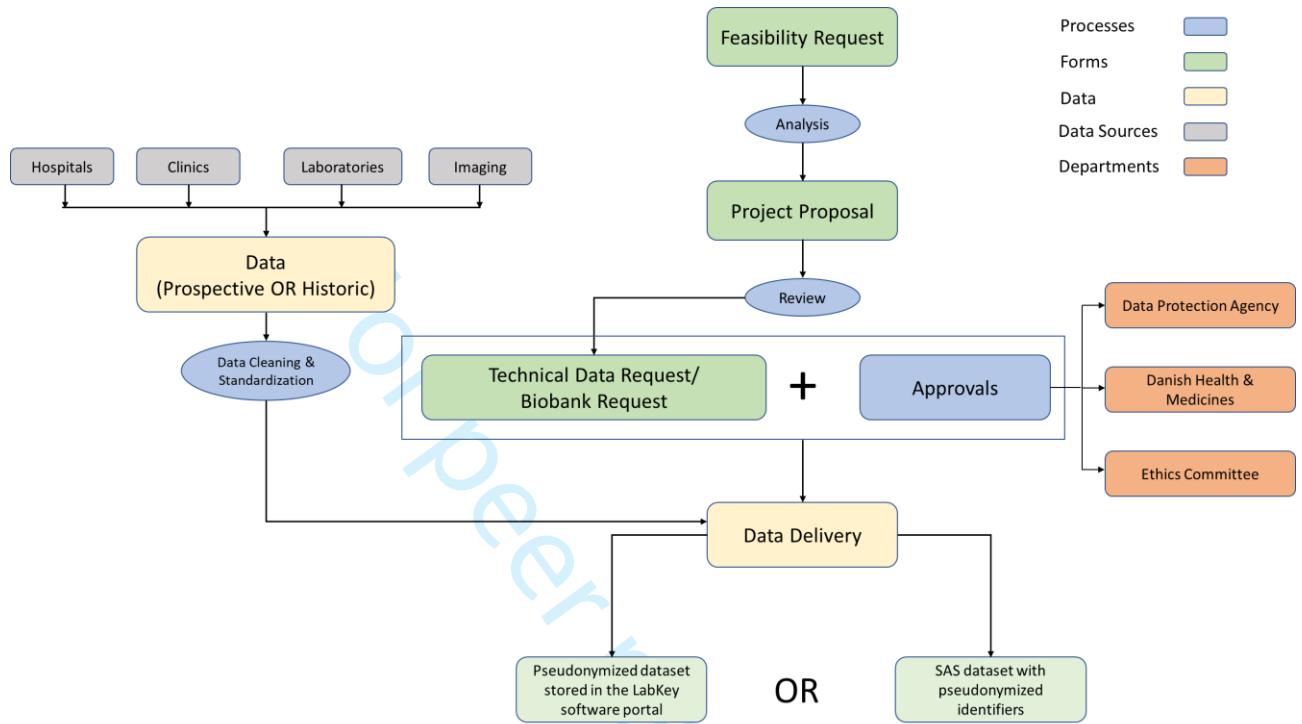
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Supplemental Material MATCH Cohort Article – Example data cleaning

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How to find your analysis (data existence)

Analysis of how to find your codes

- Go through the entire list of NPU codes, find all relevant codes pertaining to the analysis in question
 - Deliver an excel to us with the following entries

Analysiscode	LAB_ID	Full name of analysis
--------------	--------	-----------------------

- LAB_ID is the name for the analyses by HICDEP standard, or if it is not in HICDEP yet, we have to create a name that is logical and cannot be confused with others
- For local codes, make sure they do not have a twin code referring to another analysis
- Go through descriptives for clinical assessment:
 - Unit type
 - Reference interval type and values
 - Complete name of analysis
- Check whether "Operator" is always NULL for your test or if it needs to be included in data analyses (operator is for instance "<")
- Check whether any of analyses codes are ABL or POC tests for future reference (usually described in short or complete name)

Are data existence analyses complete?

Checklist for data existence

- I have found all possible NPU codes relevant for my analysis
- I have checked if there is a lab_id relevant for my analysis at HICDEP
- I have checked that none of the NPU codes I have found also refers to another analysis than the one I have investigated
- I have found no problems pertaining unit type, reference interval type and values
- I have checked the complete name of all my NPU codes and have found no possible errors
- I have checked for Operator dependent result values
- I have checked for ABL/POC tests

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How to examine data quality

Analysis of data quality

- Go through a clinical system to see if dates, values and number of tests found in PERSIMUNE matches for instance OPUS/LABKA on a single patient
- Check the range, median and IQR of the analysis result values, does it match what is expected? (across labs, across NPU codes, over time)
- Find the non-numeric test result values and check if an algorithm is needed to extract data
- Check if duplicates are introduced systematically
- Check for missing values
- For every identified problem, please formulate a solution rule for the database managers to implement

How to examine data frequencies and medians etc.

Analysis of data

- Frequencies
 - Frequency over time
 - Frequency per lab over time
 - Frequency per NPU code over time
 - Frequency per patient the first year after inclusion in PERSIMUNE
- Means/Medians
 - Mean/median over time
 - Mean/median per lab over time
 - Mean/median per NPU code over time

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Project: 50**Cancer: 4**

Early- and late-onset posttransplant lymphoproliferative disorders among adult kidney and liver transplant recipients

Development and Validation of a Risk Score for Post-Transplant Lymphoproliferative Disorders among Solid Organ Transplant Recipients

Neval E Wareham 1, Qiuju Li 2, Henrik Sengeløv 3, Caspar Da Cunha-Bang 4, Finn Gustafsson 4, Carsten Heilman

The clinical utility of PDG PET/CT among solid organ transplant recipients suspected of malignancy or infection

CMV: 11

Development and Dynamics of Cytomegalovirus UL97 Ganciclovir Resistance Mutations in Transplant Recipients Detected by Next-Generation Sequencing

Evaluation of an electronic, patient-focused management system aimed at preventing cytomegalovirus disease following solid organ transplantation

Absolute Lymphocyte Count as a Predictor of Cytomegalovirus (CMV) Infection and Recurrence in Hematopoietic Stem Cell Transplant (HSCT) Recipients

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Definitions of Resistant and Refractory Cytomegalovirus Infection and Disease in Transplant Recipients for Use in Clinical Trials

Risk Factors for Failure of Primary (Val)ganciclovir Prophylaxis Against Cytomegalovirus Infection and Disease in Solid Organ Transplant Recipients

Impact of CMV PCR Blips in Recipients of Solid Organ and Hematopoietic Stem Cell Transplantation

Cytomegalovirus (CMV) Disease Despite Weekly Preemptive CMV Strategy for Recipients of Solid Organ and Hematopoietic Stem Cell Transplantation

Cytomegalovirus Viral Load in Bronchoalveolar Lavage to Diagnose Lung Transplant Associated CMV Pneumonia.

Clinical Application of Variation in Replication Kinetics during Episodes of Post-Transplant Cytomegalovirus Infections.

The time course of development and impact from viral resistance against ganciclovir in cytomegalovirus infection.

Factors associated with the development of cytomegalovirus infection following solid organ transplantation

Microbiome:5

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Impact of Antibiotic Treatment on the Gut Microbiome and its Resistome in Hematopoietic Stem Cell Transplant Recipients

Metabolic Potential of the Gut Microbiome Is Significantly Impacted by Conditioning Regimen in Allogeneic Hematopoietic Stem Cell Transplantation Recipients

Pre-Transplant Prediction of Acute Graft-versus-Host Disease Using the Gut Microbiome

Associations of the gut microbiome and clinical factors with acute GVHD in allogeneic HSCT recipients

Gut microbiome comparability of fresh-frozen versus stabilized-frozen samples from hospitalized patients using 16S rRNA gene and shotgun

Other Infections: 15

Associations between invasive aspergillosis and cytomegalovirus in lung transplant recipients: a nationwide cohort study

Prediction of herpes virus infections after solid organ transplantation: a prospective study of immune function

Achromobacter spp. in a Cohort of Non-Selected Pre- and Post-Lung Transplant Recipients

Adverse Events Associated with Universal versus Targeted Antifungal Prophylaxis among Lung Transplant Recipients-A Nationwide Cohort Study 2010-2019

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Incidence and Impact of Parvovirus B19 Infection in Seronegative Solid Organ Transplant Recipients
Bacterial and fungal bloodstream infections in solid organ transplant recipients: results from a Danish cohort with nationwide follow-up
An Observational Prospective Cohort Study of Incidence and Outcome of <i>Streptococcus pneumoniae</i> and <i>Hemophilus influenzae</i> Infections in Adult Solid Organ Transplant Recipients
<i>Pneumocystis jirovecii</i> pneumonia in liver transplant recipients in an era of routine prophylaxis
Bacterial and fungal bloodstream infections in pediatric liver and kidney transplant recipients
Measles, Mumps, Rubella, and Varicella Zoster Virus Serology and Infections in Solid Organ Transplant Recipients During the First Year Posttransplantation
Tuberculosis among Patients Undergoing Solid Organ Transplantation or Dialysis in a Low-Endemic Country, 2004-2017

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Incidence Rates and Risk Factors of *Clostridioides difficile* Infection in Solid Organ and Hematopoietic Stem Cell Transplant Recipients

The value of EBV DNA in early detection of post-transplant lymphoproliferative disorders among solid organ and hematopoietic stem cell transplant recipients.

Renal Dysfunction in a Cohort of Renal Transplant Recipients: Impact of BK Polyomavirus

Risk of infectious diseases among first-degree relatives of transplant recipients who develop CMV infection: is the infectious phenotype inheritable?

Other: 8

Pretransplantation Plasma ST2 Level as a Prognostic Biomarker of 1-Year Nonrelapse Mortality in Allogeneic Hematopoietic Cell Transplantation

Post-Transplantation Anemia and Risk of Death Following Lung Transplantation

Functional immune reconstitution early after allogeneic haematopoietic cell transplantation: A comparison of pre- and post-transplantation cytokine responses in stimulated whole blood

Immune function as predictor of infectious complications and clinical outcome in patients undergoing solid organ transplantation (the ImmuneMo:SOT study): a prospective non-interventional observational trial

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Improved Overall Survival, Relapse-Free-Survival, and Less Graft-vs.-Host-Disease in Patients With High Immune Reconstitution of TCR Gamma Delta Cells 2 Months After Allogeneic Stem Cell Transplantation
Extracorporeal photopheresis is a valuable treatment option in steroid-refractory or steroid-dependent acute graft versus host disease-experience with three different approaches
C-Reactive Protein Levels at Diagnosis of Acute Graft-versus-Host Disease Predict Steroid-Refractory Disease, Treatment-Related Mortality, and Overall Survival after Allogeneic Hematopoietic Stem Cell Transplantation.
MELD score measured day 10 after orthotopic liver transplantation predicts death and re-transplantation within the first year
CLASS: 3
Trends in underlying causes of death in solid organ transplant recipients between 2010 and 2020: Using the CLASS method for determining specific causes of death
Posttransplantation Diabetes Mellitus Among Solid Organ Recipients in a Danish Cohort
Classification of death causes after transplantation (CLASS): Evaluation of methodology and initial results
Vitamins: 4

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Hyaluronic Acid Is a Biomarker for Allograft Dysfunction and Predicts 1-Year Graft Loss After Liver Transplantation

Vitamin E and acute graft-versus-host disease after myeloablative allogeneic hematopoietic cell transplantation

Pretransplantation vitamin A plasma levels and risk of acute graft-versus-host disease following allogeneic hematopoietic stem cell transplantation

Pre-transplantation plasma vitamin D levels and acute graft-versus-host disease after myeloablative hematopoietic cell transplantation in adults

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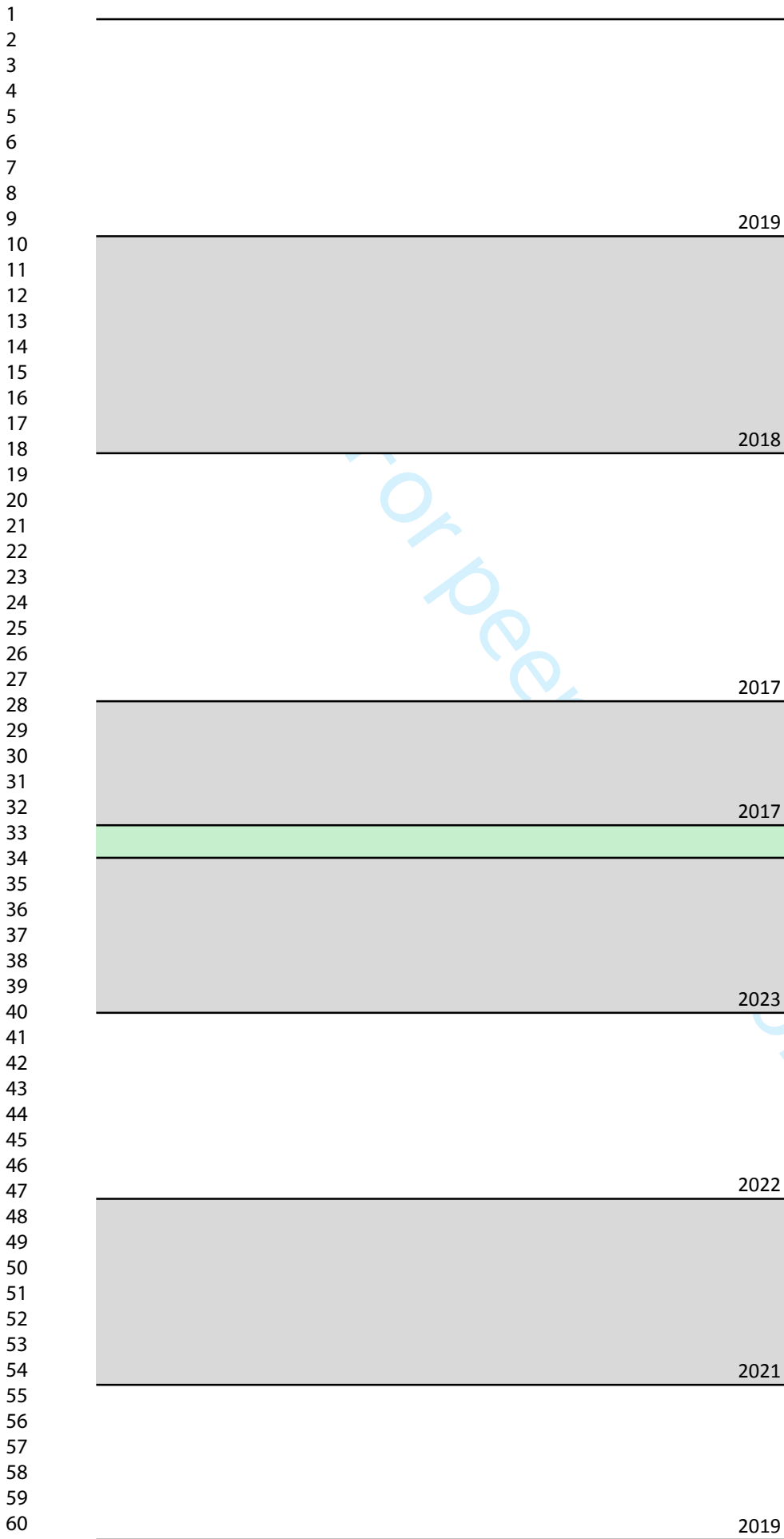
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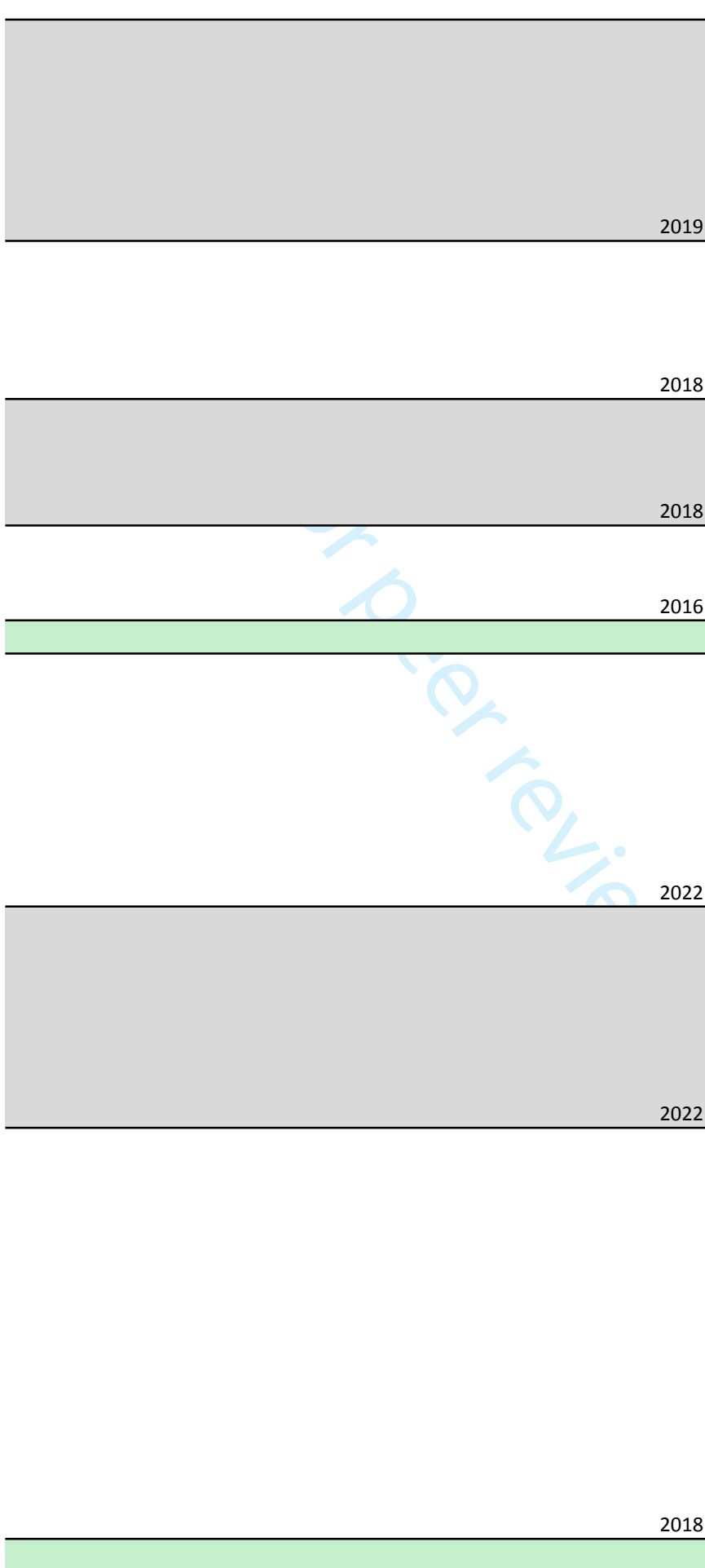
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